

## 2-Methoxyphenyl isocyanate: A chemoselective multitasking reagent for amine protection/deprotection sequence

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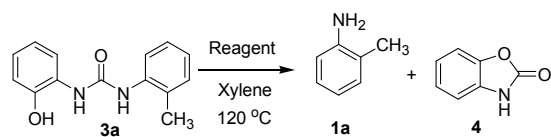
### Supporting Information I

**Table 1:** Details of the reaction condition, time and yield for all the amine molecules.

Entry	Amine	Time	2a-u Isolated yield (%)	Time	3a-u Isolated yield (%)	Time	Amine 1a-u GC yield (%)	4 GC yield (%)
1a	<i>o</i> -Toluidine	10 min	100	3 h	97	3 h	100	
1b	<i>p</i> -Fluoroaniline	45 min	89	3 h	96	3 h	75.8	
1c	<i>o</i> -Chloroaniline	30 min	93	3 h	92	3 h	95.3	
1d	<i>m</i> -Bromoaniline	30 min	90	3 h	95	3 h	72.3	
1e	<i>m</i> -Trifluorotoluidine	1 h	87	3 h	94	3 h	60.7	
1f	<i>p</i> -Cyanoaniline	2 h	98	3 h	90	3 h	96.7	
1g	<i>p</i> -nitroaniline	1 h	94	3 h	93	3 h	100	
1h	(R)-Phenylethylamine	1 h	95	2 h	93	3 h	93.8	
1i	(S)-Phenylethylamine	1 h	90	2 h	90	3 h	95.6	
1j	Morpholine	10 min	96	3 h	96	3 h	100	
1k	Piperidine	10 min	89	3 h	95	3 h	100	
1l	1-Adamantylamine	30 min	93	4 h	-	-	100	
1m	Cyclohexylamine	10 min	97	2 h	97	3 h	100*	100
1n	Geranylamine	10 min	96	2 h	-	-	100	
1o	<i>p</i> -Fluorobenzylamine	10 min	92	2 h	95	3 h	100	
1p	L-Phenylalanine(OMe)	20 min	93	3 h	-	-	100	
1q	L-Valine(OMe)	20 min	95	3 h	-	-	100*	100
1r	<i>o</i> -Fluoroaniline	45 min	92	3 h	96	3 h	87.1	
1s	<i>m</i> -Fluoroaniline	30 min	92	3 h	95	3 h	91.5	
1t	<i>m</i> -Chloroaniline	30 min	93	3 h	90	3 h	95.5	
1u	<i>o</i> -Trifluorotoluidine	1.5 h	74	3 h	97	3 h	100*	100

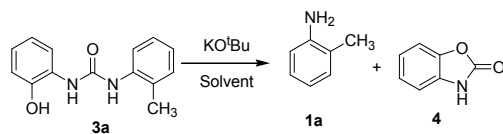
\*Free amine merged with solvent

**Table 2: Screening of different reagents for deprotection.**



Reagent	Time	% of conversion by GC
p-TSA	3 h	93.8
ZnCl <sub>2</sub>	3 h	87.3
Zn (OAc) <sub>2</sub>	3 h	100
Water	3 h	96.3
Neat	2 h	72.2
KO <sup>t</sup> Bu	3 h	100
NaH	3 h	86.3
DBU	3 h	100
CaH <sub>2</sub>	3 h	87.1
Oxone	3 h	71.7
CAN	3 h	81.2

**Table 3: Screening of different solvents for the final deprotection step.**



Solvent	Temperature (°C)	Time	D (%) Isolated
DMF	130	3 h	55.3
DMAC	130	3 h	92.7
MeOH	65	3 h	63.7
Xylene	120	3 h	97.5
Toluene	110	3 h	87.6
DMSO	130	3 h	61.2
Py	115	3 h	48.3
Dioxane	100	3 h	72.2
NMP	130	3 h	85.7

## **Experimental:**

### ***Reagents and instrumentation:***

All the chemicals were purchased from SigmaAldrich, Alfa Aesar and Merck Chemicals. Column chromatographic separations were performed using silica gel (100-200 mesh). Solvents were dried and distilled following standard procedures. TLC was carried out on pre-coated plates (Merck silica gel 60, f254), and the spots were visualized with UV light or by charring the plates dipped in 10% PMA solution in methanol or 5% H<sub>2</sub>SO<sub>4</sub>/vanillin/EtOH. <sup>1</sup>H NMR (300, 400 MHz) and <sup>13</sup>C NMR (75, 100 MHz) spectra were recorded on a Bruker NMR spectrometer (d scale). UV-vis measurements were made using a Perkin Elmer UV-vis spectrophotometer (Model Lambda 25). Mass spectra (HRMS) had been recorded using Waters Mass Spectrometer (model XevoG2QTof). Mass analysis (LRMS) of compounds was determined by the applied Biosystems 4800 PLUS MALDI TOF/TOF analyser using TiO<sub>2</sub> as a matrix. To check reaction profiles Dionex ICS 3000 HPLC system was used with a semi-preparative BEH130 C18 (10 × 250 mm) column. Following gradient elution method was used: 50% A to 100 % B in 33min; A = 0.1% TFA in CH<sub>3</sub>CN/H<sub>2</sub>O (5:95); B = 0.1 % TFA in CH<sub>3</sub>CN / H<sub>2</sub>O (1:1) with a flow rate of 2 mL/min. Whereas, for chiral molecules we used HyperClone 5µm BDS C18 130Å column (250 x 4.6 mm) and Lux 5µm i-Amylose-1 column (250 x 4.6 mm). Yield were determined by GC with area normalization; GC conditions: RTX-5 Column, 60 m × 0.32 mm, initial column temperature was increased from 130 to 250 °C at the rate of 7 °C/min; FID detector, 280 °C; Injector, 260 °C; Carrier Gas: N<sub>2</sub>; Rate: 2.00 mL/min.

### ***1-(2-methoxyphenyl)-3-(o-tolyl)urea (2a):***

To a well stirred solution of *o*-toulidine (0.400 g, 3.73 mmol) in DCM (10 ml), 2-methoxyphenyl isocyanate (0.556 g, 3.73 mmol) was added and kept for stirring at room temperature for 10 min (checked by TLC). The solid thus obtained was filtered through a sintered funnel and partitioned between 5% NaHCO<sub>3</sub> and EtOAc for the removal of residual carbamaic acid. The organic portion was then dried over Na<sub>2</sub>SO<sub>4</sub> and concentrated under reduced pressure. We obtained **2a** as a white solid (0.957 g, 100%; m. p. 184±2 °C). For NMR quality sample we purified 0.070 g of it by column chromatography (30% EtOAc in hexane). <sup>1</sup>H-NMR in CDCl<sub>3</sub> + d<sub>6</sub>-DMSO (300 MHz): δ 2.29 (s, 3H), 3.85 (s, 3H), 6.86-6.84 (m, 1ArH), 6.96-6.92 (m, 2ArH), 7.04-6.98 (m, 1ArH), 7.20-7.15 (m, 2ArH), 7.76-7.73 (m, 2ArH), 8.03 (bs, 1NH), 8.27-8.21 (m, 1NH). <sup>13</sup>C-NMR in CDCl<sub>3</sub> + d<sub>6</sub>-DMSO (75 MHz): δ 17.5, 54.9, 109.5, 118.4, 120.1, 120.9, 121.7, 122.4, 125.4, 127.9, 128.3, 129.4, 136.5, 147.2, 152.7. MALDI-TOF: m/z calcd for C<sub>15</sub>H<sub>16</sub>KN<sub>2</sub>O<sub>2</sub> [M+K]<sup>+</sup>: 295.09; found: 294.02.

### ***1-(2-Hydroxyphenyl)-3-o-tolyl)urea (3a):***

To **2a** (0.400 g, 1.56 mmol) in DCM (5 ml), BBr<sub>3</sub> (0.430 g, 1.72 mmol) was added and kept for stirring room temperature for 3 hours (checked by TLC). The DCM was removed under reduced pressure and the solid thus obtained was partitioned between EtOAc and 5% aqueous NaHCO<sub>3</sub>. The organic layer was then washed with dried over Na<sub>2</sub>SO<sub>4</sub> to obtain **3a** as white solid (0.367 g, 97%; m. p. 160±2 °C). For NMR quality sample we purified 0.070 g of it by column chromatography (35% EtOAc in hexane). <sup>1</sup>H-NMR in CDCl<sub>3</sub> (300 MHz): δ 2.35 (s, 3H), 6.43 (bs, 1ArH), 6.59 (bs, 2ArH), 6.81-6.77 (m, 2ArH), 7.11-7.01 (m, 2ArH), 7.33-7.28 (m, 2ArH), 7.45-7.43 (m, 1NH). <sup>13</sup>C-NMR in d<sub>6</sub>-DMSO (75 MHz): δ 18.6, 114.9, 119.4, 119.6, 122.0, 122.1, 123.1, 126.5, 128.3, 128.5, 130.6, 138.0, 146.2, 153.4. MALDI-TOF: m/z calcd for C<sub>14</sub>H<sub>14</sub>KN<sub>2</sub>O<sub>2</sub> [M+K]<sup>+</sup>: 281.07; found: 281.04.

### ***1-(4-fluorophenyl)-3-(2-methoxyphenyl)urea (2b):***

To a well stirred solution of *p*-fluoroaniline (0.400 g, 3.59 mmol) in DCM (10 ml), 2-methoxyphenyl isocyanate (0.535 g, 3.59 mmol) was added and kept for stirring at room temperature for 45 min (checked by TLC). The solid thus obtained was filtered through a sintered funnel and partitioned between 5% NaHCO<sub>3</sub> and EtOAc for the removal of residual carbamaic acid. The organic portion was then dried over Na<sub>2</sub>SO<sub>4</sub> and concentrated under reduced pressure. We obtained **2b** as a white solid (0.892 g, 89%; m. p. 160±2 °C). For NMR quality sample we purified 0.070 g of it by column chromatography (30% EtOAc in hexane). <sup>1</sup>H NMR (300 MHz) in CDCl<sub>3</sub> + d<sub>6</sub>-DMSO: δ 3.89 (s, 3H), 6.89-6.85 (m, 1ArH), 7.00-6.90 (m, 4ArH), 7.47-7.31 (m, 2ArH), 7.90 (bs, 1NH), 8.25-8.20 (m, 1ArH), 8.67 (bs, 1NH). <sup>13</sup>C-NMR (75 MHz) CDCl<sub>3</sub> + d<sub>6</sub>-DMSO: δ 55.7, 110.2, 115.3 (d, J = 22.50 Hz), 119.4, 120.6 (d, J = 7.50 Hz), 121.1, 122.1, 128.8, 135.6 (d, J = 2.25 Hz), 148.0, 153.4, 158.3 (d, J = 238.5 Hz). MALDI-TOF: m/z calcd for C<sub>14</sub>H<sub>13</sub>FN<sub>2</sub>O<sub>2</sub> [M+K]<sup>+</sup>: 299.06; found: 298.98.

### ***1-(4-fluorophenyl)-3-(2-Hydroxyphenyl)urea (3b):***

To **2b** (0.400 g, 1.54 mmol) in DCM (5 ml), BBr<sub>3</sub> (0.423 g, 1.69 mmol) was added and kept for stirring room temperature for 3 hours (checked by TLC). The DCM was removed under reduced pressure and the solid thus obtained was partitioned between EtOAc and 5% aqueous NaHCO<sub>3</sub>. The organic layer was then washed with dried over Na<sub>2</sub>SO<sub>4</sub> to obtain **3b** as white solid (0.363 g, 96%; m. p. 168±2 °C). For NMR quality sample we purified 0.070 g of it by column chromatography (35% EtOAc in hexane). <sup>1</sup>H-NMR (300 MHz) in CDCl<sub>3</sub> + d<sub>6</sub>-DMSO: δ 7.02-6.71 (m, 5ArH), 7.47-7.40 (m, 2ArH), 7.57-7.51 (m, 1-OH), 7.76-7.72 (m, 1ArH), 8.15 (bs, 1NH), 8.88 (bs, 1NH). <sup>13</sup>C-NMR (75 MHz) CDCl<sub>3</sub> + d<sub>6</sub>-DMSO: δ 114.4 (d, J = 22.50 Hz), 115.1, 118.9, 119.1, 119.4 (d, J = 7.50 Hz), 122.0, 126.9, 135.0 (d, J = 3.00 Hz), 145.6, 153.1,

157.2 (d,  $J = 238.5$  Hz). MALDI-TOF:  $m/z$  calcd for  $C_{13}H_{11}FKN_2O_2$   $[M+K]^+$ : 285.04; found: 284.97.

***1-(2-Chlorophenyl)-3-(2-methoxyphenyl)urea (2c):***

To a well stirred *o*-chloroaniline (0.400 g, 3.13 mmol) in DCM (10ml), 2-methoxyphenyl isocyanate (0.467 g, 3.13 mmol) was added and kept for stirring at room temperature for 30 min (checked by TLC). The solid thus obtained was filtered through a sintered funnel and partitioned between 5%  $NaHCO_3$  and EtOAc for the removal of residual carbamaic acid. The organic portion was then dried over  $Na_2SO_4$  and concentrated under reduced pressure. We obtained **2c** as a white solid (0.807 g, 93%; m. p.  $170 \pm 2$  °C). For NMR quality sample we purified 0.070 g of it by column chromatography (30% EtOAc in hexane).  $^1H$ -NMR in  $CDCl_3$  (300MHz):  $\delta$  3.89 (s, 3H), 6.91 (dd,  $J = 1.2, 7.8$  Hz, 1ArH), 7.10-6.96 (m, 5ArH), 7.30-7.24 (m, 1ArH), 7.35 (dd,  $J = 1.5, 8.1$  Hz, 1ArH), 8.04 (dd,  $J = 1.5, 7.8$  Hz, 1NH), 8.20 (dd,  $J = 1.5, 8.4$  Hz, 1NH).  $^{13}C$ -NMR (75 MHz) in  $d_6$ -DMSO:  $\delta$  56.2, 111.3, 119.7, 120.9, 122.8, 122.8, 123.0, 123.9, 127.9, 128.9, 129.7, 136.6, 148.7, 152.9. MALDI-TOF:  $m/z$  calcd for  $C_{14}H_{13}ClKN_2O_2$   $[M+K]^+$ : 315.03; found: 315.08.

***1-(2-Chlorophenyl)-3-(2-hydroxyphenyl)urea (3c):***

To **2c** (0.400 g, 1.52 mmol) in DCM (5 ml),  $BBr_3$  (0.418 g, 1.67 mmol) was added and kept for stirring at room temperature for 3 hours (checked by TLC). The DCM was removed under reduced pressure and the solid thus obtained was partitioned between EtOAc and 5% aqueous  $NaHCO_3$ . The organic layer was then washed with dried over  $Na_2SO_4$  to obtain **3c** as white solid (0.349 g, 92%; m. p.  $154 \pm 2$  °C). For NMR quality sample we purified 0.070 g of it by column chromatography (30% EtOAc in hexane).  $^1H$ -NMR (300MHz) in  $CDCl_3$ :  $\delta$  6.76 (bs, 1ArH), 6.90 (t,  $J = 6.9$  Hz, 1ArH), 7.16-7.03 (m, 4ArH), 7.33-7.31 (m, 1ArH), 7.39 (d,  $J = 8.1$  Hz, 1ArH), 8.01 (bs, 1NH), 8.07 (d,  $J = 8.1$  Hz, 1NH).  $^{13}C$ -NMR (75 MHz) in  $CDCl_3 + d_6$ -DMSO:  $\delta$  116.2, 119.2, 120.3, 121.5, 122.4, 122.6, 123.1, 126.6, 128.5, 135.4, 146.7, 153.4. MALDI-TOF:  $m/z$  calcd for  $C_{13}H_{11}ClKN_2O_2$   $[M+K]^+$ : 301.02; found: 300.94.

***1-(3-bromophenyl)-3-(2-methoxyphenyl)urea (2d):***

To a well stirred solution of *m*-bromoaniline (0.400 g, 2.24 mmol) in DCM (10 ml), 2-methoxyphenyl isocyanate (0.333 g, 2.23 mmol) was added and kept for stirring at room temperature for 30 min (checked by TLC). The solid thus obtained was filtered through a sintered funnel and partitioned between 5%  $NaHCO_3$  and EtOAc for the removal of residual carbamaic acid. The organic portion was then dried over  $Na_2SO_4$  and concentrated under reduced pressure. We obtained **2d** as a pale yellow solid (0.672 g, 90%; m. p.  $112 \pm 2$  °C). For NMR quality sample we purified 0.070 g of it by column chromatography (30% EtOAc in hexane).  $^1H$  NMR (300 MHz) in  $CDCl_3$ :  $\delta$  3.78 (s, 3H), 6.85 (dd,  $J = 1.2, 8.1$  Hz, 1ArH), 6.93 (dt,  $J = 1.5, 7.8$

Hz, 1ArH), 7.03 (dd,  $J = 1.5, 7.8$  Hz, 1ArH), 7.17-7.07 (m, 2ArH), 7.29-7.25 (m, 1ArH), 7.39 (bs, 1NH), 7.45 (bs, 1NH), 7.55 (t,  $J = 1.8$  Hz, 1ArH), 8.03 (dd,  $J = 1.8, 7.8$  Hz, 1ArH).  $^{13}\text{C}$ -NMR (75 MHz)  $\text{CDCl}_3 + d_6\text{-DMSO}$ :  $\delta$  55.7, 110.2, 116.8, 119.1, 120.9, 121.1, 122.0, 122.4, 124.6, 128.6, 130.0, 141.3, 147.9, 152.8. MALDI-TOF:  $m/z$  calcd for  $\text{C}_{14}\text{H}_{13}\text{BrKN}_2\text{O}_2$   $[\text{M}+\text{K}]^+$ : 358.98; found: 359.04.

#### ***1-(3-bromophenyl)-3-(2-Hydroxyphenyl)urea (3d):***

To **2d** (0.400 g, 1.25 mmol) in DCM (5 ml),  $\text{BBr}_3$  (0.343 g, 1.37 mmol) was added and kept for stirring room temperature for 3 hours (checked by TLC). The DCM was removed under reduced pressure and the solid thus obtained was partitioned between EtOAc and 5% aqueous  $\text{NaHCO}_3$ . The organic layer was then washed with dried over  $\text{Na}_2\text{SO}_4$  to obtain **3d** as pale yellow solid (0.363 g, 95%; m. p.  $162 \pm 2$  °C). For NMR quality sample we purified 0.070 g of it by column chromatography (30% EtOAc in hexane).  $^1\text{H}$ -NMR (300 MHz) in  $d_6\text{-DMSO}$ :  $\delta$  6.78-6.72 (m, 3ArH), 7.16-7.12 (m, 1ArH), 7.25-7.23 (m, 2ArH), 7.88 (s, 1ArH), 8.05-8.02 (m, 1ArH), 8.20 (s, 1NH), 9.50 (s, 1NH), 9.99 (s, 1OH).  $^{13}\text{C}$ -NMR (75 MHz) in  $d_6\text{-DMSO}$ :  $\delta$  114.9, 117.1, 119.2, 119.6, 120.5, 122.3, 122.6, 124.6, 127.9, 131.2, 142.1, 146.2, 152.8. MALDI-TOF:  $m/z$  calcd for  $\text{C}_{13}\text{H}_{11}\text{BrKN}_2\text{O}_2$   $[\text{M}+\text{K}]^+$ : 344.96; found: 344.99.

#### ***1-(2-methoxyphenyl)-3-(3-trifluoromethyl)phenyl)urea (2e):***

To a well stirred solution of *m*-trifluoromethylaniline (0.400 g, 2.48 mmol) in DCM (10ml), 2-methoxyphenyl isocyanate (0.370 g, 2.48 mmol) was added and kept for stirring at room temperature for 1 hour (checked by TLC). The solid thus obtained was filtered through a sintered funnel and partitioned between 5%  $\text{NaHCO}_3$  and EtOAc for the removal of residual carbamaic acid. The organic portion was then dried over  $\text{Na}_2\text{SO}_4$  and concentrated under reduced pressure. We obtained **2e** as a white solid (0.788 g, 87%; m. p.  $140 \pm 2$  °C). For NMR quality sample we purified 0.070 g of it by column chromatography (35% EtOAc in hexane).  $^1\text{H}$  NMR (300 MHz) in  $\text{CDCl}_3$ :  $\delta$  3.81 (s, 3H), 7.07-6.86 (m, 3ArH), 7.40-7.26 (m, 4ArH), 7.64-7.56 (m, 1ArH, 1NH), 8.05 (dd,  $J = 1.5, 7.8$  Hz, 1NH).  $^{13}\text{C}$ -NMR (75 MHz) in  $\text{CDCl}_3$ :  $\delta$  55.6, 110.4, 116.6 (q,  $J = 3.75$  Hz, for  $\text{CF}_3\text{-}o\text{C}'$ ), 119.9 (q,  $J = 4.50$  Hz, for  $\text{CF}_3\text{-}o\text{C}''$ ), 120.5, 121.2, 123.1, 123.8, 127.4, 129.5, 131.4 (q,  $J = 32.25$  Hz, for  $\text{CF}_3\text{-}ipso\text{C}$ ), 139.0, 148.9, 153.2. MALDI-TOF:  $m/z$  calcd for  $\text{C}_{15}\text{H}_{13}\text{F}_3\text{KN}_2\text{O}_2$   $[\text{M}+\text{K}]^+$ : 349.06; found: 348.09.

#### ***1-(2-hydroxyphenyl)-3-(3-trifluoromethyl)phenyl)urea (3e):***

To **2e** (0.400g, 1.29 mmol) in DCM (5 ml),  $\text{BBr}_3$  (0.356 g, 1.42 mmol) was added and kept for stirring room temperature for 3 hours (checked by TLC). The DCM was removed under reduced pressure and the solid thus obtained was partitioned between EtOAc and 5% aqueous  $\text{NaHCO}_3$ . The organic layer was then washed with dried over  $\text{Na}_2\text{SO}_4$  to obtain **3e** as white solid (0.358 g,

94%; m. p.  $144 \pm 2$  °C). For NMR quality sample we purified 0.070 g of it by column chromatography (30% EtOAc in hexane).  $^1\text{H}$ -NMR in (300 MHz) in  $\text{CDCl}_3 + \text{d}_6\text{-DMSO}$ :  $\delta$  6.98-6.79 (m, 3ArH), 7.21 (d,  $J = 7.8$  Hz, 1ArH), 7.38 (t,  $J = 8.1$  Hz, 1ArH), 7.58 (d,  $J = 8.1$  Hz, 1ArH), 7.90-8.20 (m, 2ArH), 8.23-8.17 (m, 1OH), 9.19 (s, 1NH), 9.34 (s, 1NH).  $^{13}\text{C}$ -NMR (75 MHz) in  $\text{CDCl}_3 + \text{d}_6\text{-DMSO}$ :  $\delta$  110.2, 114.8 (q,  $J = 3.75$  Hz, for  $\text{CF}_3\text{-oC}'$ ), 118.1 (q,  $J = 3.75$  Hz, for  $\text{CF}_3\text{-oC}''$ ), 119.7, 119.8, 120.9, 121.3, 122.8, 127.4, 129.1, 130.7 (q,  $J = 16.5$  Hz, for  $\text{CF}_3\text{-ipsoC}$ ), 140.4, 146.3, 153.4. MALDI-TOF:  $m/z$  calcd for  $\text{C}_{14}\text{H}_{11}\text{F}_3\text{KN}_2\text{O}_2$   $[\text{M}+\text{K}]^+$ : 335.04; found: 334.98.

#### ***1-(4-Cyanophenyl)-3-(2-methoxyphenyl)urea (2f):***

To a well stirred solution of *p*-cyanoaniline (0.400g, 3.38 mmol) in DCM (10 ml), 2-methoxyphenyl isocyanate (0.504 g, 3.38 mmol) was added and kept for stirring at room temperature for 2 hour (checked by TLC). The solid thus obtained was filtered through a sintered funnel and partitioned between 5%  $\text{NaHCO}_3$  and EtOAc for the removal of residual carbamaic acid. The organic portion was then dried over  $\text{Na}_2\text{SO}_4$  and concentrated under reduced pressure. We obtained **2f** as a white solid (0.886 g, 98%; m. p.  $184 \pm 2$  °C). For NMR quality sample we purified 0.070 g of it by column chromatography (35% EtOAc in hexane).  $^1\text{H}$  NMR (300 Hz) in  $\text{d}_6\text{-DMSO}$ :  $\delta$  3.89 (s, 3H), 7.06-6.89 (m, 3ArH), 7.66-7.61 (m, 2ArH), 7.78-7.72 (m, 2ArH), 8.11 (dd,  $J = 1.5, 7.8$  Hz, 1ArH), 8.39 (s, 1NH), 9.81 (s, 1NH).  $^{13}\text{C}$  NMR (75 MHz) in  $\text{d}_6\text{-DMSO}$ :  $\delta$  55.3, 103.6, 111.3, 118.2, 119.0, 119.8, 121.0, 122.9, 128.5, 133.8, 144.7, 148.3, 152.4. MALDI-TOF:  $m/z$  calcd for  $\text{C}_{15}\text{H}_{13}\text{KN}_3\text{O}_2$   $[\text{M}+\text{K}]^+$ : 306.07; found: 306.12.

#### ***1-(4-Cyanophenyl)-3-(2-hydroxyphenyl)urea (3f):***

To **2f** (0.400 g, 1.49 mmol) in DCM (5 ml),  $\text{BBr}_3$  (0.411 g, 1.64 mmol) was added and kept for stirring room temperature for 3 hours (checked by TLC). The DCM was removed under reduced pressure and the solid thus obtained was partitioned between EtOAc and 5% aqueous  $\text{NaHCO}_3$ . The organic layer was then washed with dried over  $\text{Na}_2\text{SO}_4$  to obtain **3f** as white solid (0.341 g, 90%; m. p.  $192 \pm 2$  °C). For NMR quality sample we purified 0.070 g of it by column chromatography (30% EtOAc in hexane).  $^1\text{H}$ -NMR (300 MHz) in  $\text{d}_6\text{-DMSO}$ :  $\delta$  6.87-6.73 (m, 3ArH), 7.64-7.61 (m, 2ArH), 7.75-7.72 (m, 2ArH), 8.04 (d,  $J = 7.5$  Hz, 1ArH), 8.32 (bs, 1NH), 9.81 (bs, 1NH), 10.04 (s, 1OH).  $^{13}\text{C}$  NMR (75 MHz) in  $\text{d}_6\text{-DMSO}$ :  $\delta$  103.5, 114.9, 118.2, 119.2, 119.6, 119.8, 122.8, 127.7, 133.8, 144.9, 146.3, 152.5. MALDI-TOF:  $m/z$  calcd for  $\text{C}_{14}\text{H}_{11}\text{KN}_3\text{O}_2$   $[\text{M}+\text{K}]^+$ : 292.05; found: 291.98.

#### ***1-(2-methoxyphenyl)-3-(4-nitrophenyl)urea (2g) :***

To a well stirred solution of *p*-nitrophenyl isocyanate (0.400g, 2.43 mmol) in DCM (10 ml), *o*-anisidine (0.299 g, 2.43 mmol) was added and kept for stirring at room temperature for 1 hour

(checked by TLC). The solid thus obtained was filtered through a sintered funnel and partitioned between 5% NaHCO<sub>3</sub> and EtOAc for the removal of residual carbamaic acid. The organic portion was then dried over Na<sub>2</sub>SO<sub>4</sub> and concentrated under reduced pressure. We obtained **2g** as a yellow solid (0.658 g, 94%; m. p. 176±2 °C). For NMR quality sample we purified 0.070 g of it by column chromatography (35% EtOAc in hexane). <sup>1</sup>H NMR (300 MHz) in d<sub>6</sub>-DMSO: δ 3.89 (s, 3H), 7.07-6.89 (m, 3ArH), 7.74-7.67 (m, 2ArH), 8.12 (dd, J = 1.5, 7.8Hz, 1NH), 8.24-8.18 (m, 2ArH), 8.45 (s, 1NH). <sup>13</sup>C-NMR (75 MHz) in d<sub>6</sub>-DMSO: δ 56.3, 111.3, 117.7, 119.1, 121.1, 123.1, 125.7, 128.4, 141.4, 146.9, 148.4, 152.3. MALDI-TOF: m/z calcd for C<sub>14</sub>H<sub>13</sub>KN<sub>3</sub>O<sub>4</sub> [M+K]<sup>+</sup>: 326.05; found: 325.98.

***1-(2-Hydroxyphenyl)-3-(4-nitrophenyl)urea (3g) :***

To **2g** (0.400 g, 1.39 mmol) in DCM (5 ml), BBr<sub>3</sub> (0.383 g, 1.53 mmol) was added and kept for stirring room temperature for 3 hours (checked by TLC). The DCM was removed under reduced pressure and the solid thus obtained was partitioned between EtOAc and 5% aqueous NaHCO<sub>3</sub>. The organic layer was then washed with dried over Na<sub>2</sub>SO<sub>4</sub> to obtain **3g** as yellow solid (0.354 g, 93%; m. p. 171±2 °C). For NMR quality sample we purified 0.070 g of it by column chromatography (30% EtOAc in hexane). <sup>1</sup>H-NMR (300 MHz) in d<sub>6</sub>-DMSO: δ 6.88-6.77 (m, 3ArH), 7.68 (d, J = 9.3 Hz, 2ArH), 8.05 (d, J = 7.5 Hz, 1ArH), 8.20 (d, J = 9 Hz, 2ArH), 8.39 (s, 1NH), 10.03 (s, 1NH), 10.08 (s, 1OH). <sup>13</sup>C-NMR (75 MHz) in d<sub>6</sub>-DMSO: δ 114.5, 117.2, 118.8, 119.2, 122.5, 125.3, 127.1, 140.9, 145.9, 146.6, 151.9. MALDI-TOF: m/z calcd for C<sub>13</sub>H<sub>11</sub>KN<sub>3</sub>O<sub>4</sub> [M+K]<sup>+</sup>: 312.04; found: 311.99.

***(R)-1-(2-methoxyphenyl)-3-(1-phenylethyl)urea (2h):***

To a well stirred solution of (R)-methylbenzyl amine (0.400 g, 3.30 mmol) in DCM (10 ml), 2-methoxyphenyl isocyanate (0.492 g, 3.30 mmol) was added and kept for stirring at room temperature for 1 hour (checked by TLC). The solid thus obtained was filtered through a sintered funnel and partitioned between 5% NaHCO<sub>3</sub> and EtOAc for the removal of residual carbamaic acid. The organic portion was then dried over Na<sub>2</sub>SO<sub>4</sub> and concentrated under reduced pressure. We obtained **2h** as a white solid (0.848 g, 95%; m. p. 138±2 °C). For NMR quality sample we purified 0.070 g of it by column chromatography (45% EtOAc in hexane). <sup>1</sup>H NMR (300MHz) in CDCl<sub>3</sub>: δ 1.51 (d, J = 6.6 Hz, 3H), 3.75 (s, 3H), 4.95-4.92 (m, 1H, 1NH), 6.82-6.79 (m, 2ArH), 7.00-6.88 (m, 2ArH), 7.31-7.24 (m, 1ArH), 7.40-7.33 (m, 4ArH), 8.04-8.01 (m, 1NH). <sup>13</sup>C-NMR (75 MHz) in CDCl<sub>3</sub>: δ 23.2, 50.4, 55.6, 110.1, 119.4, 121.2, 124.4, 126.1, 127.4, 128.5, 128.7, 143.8, 148.0, 154.8. MALDI-TOF: m/z calcd for C<sub>16</sub>H<sub>18</sub>KN<sub>2</sub>O<sub>2</sub> [M+K]<sup>+</sup>: 309.10; found: 308.07.

***(R)-1-(2-Hydroxyphenyl)-3-(1-phenylethyl)urea (3h):***

To **2h** (0.400 g, 1.48 mmol) in DCM (5 ml), BBr<sub>3</sub> (0.408 g, 1.63 mmol) was added and kept for stirring room temperature for 2 hours (checked by TLC). The DCM was removed under reduced pressure and the solid thus obtained was partitioned between EtOAc and 5% aqueous NaHCO<sub>3</sub>. The organic layer was then washed with dried over Na<sub>2</sub>SO<sub>4</sub> to obtain **3h** as white solid (0.354 g, 93%; m. p. 111±2 °C). For NMR quality sample we purified 0.070 g of it by column chromatography (45% EtOAc in hexane). <sup>1</sup>H-NMR (300 MHz) in CDCl<sub>3</sub>: δ 1.45 (d, J = 6.9 Hz, 3H), 4.84 (p, J = 6.6 Hz, 1H), 5.45 (d, J = 6.0 Hz, 1NH), 6.68-6.63 (m, 2ArH), 6.75 (dt, J = 1.5, 6.9 Hz, 1ArH), 6.95 (dd, J = 4.5, 8.1 Hz, 1ArH), 7.02 (dt, J = 1.5, 6.9 Hz, 1ArH), 7.36-7.25 (m, 4ArH), 9.25 (s, 1NH). <sup>13</sup>C-NMR (75 MHz) in CDCl<sub>3</sub> + d<sub>6</sub>-DMSO: δ 22.3, 49.0, 117.2, 119.2, 120.0, 123.2, 125.5, 126.5, 127.2, 127.9, 143.9, 146.9, 156.1. MALDI-TOF: m/z calcd for C<sub>15</sub>H<sub>16</sub>KN<sub>2</sub>O<sub>2</sub> [M+K]<sup>+</sup>: 295.09; found: 295.01.

***(S)-1-(2-methoxyphenyl)-3-(1-phenylethyl)urea (2i):***

To a well stirred solution of (R)-methylbenzyl amine (0.400 g, 3.30 mmol) in DCM (10 ml), 2-methoxyphenyl isocyanate (0.492 g, 3.30 mmol) was added and kept for stirring at room temperature for 1 hour (checked by TLC). The solid thus obtained was filtered through a sintered funnel and partitioned between 5% NaHCO<sub>3</sub> and EtOAc for the removal of residual carbamaic acid. The organic portion was then dried over Na<sub>2</sub>SO<sub>4</sub> and concentrated under reduced pressure. We obtained **2i** as a white solid (0.812 g, 90%; m. p. 132±2 °C). For NMR quality sample we purified 0.070 g of it by column chromatography (45% EtOAc in hexane). <sup>1</sup>H NMR (300 MHz) in CDCl<sub>3</sub>: δ 1.50 (d, J = 6.6 Hz, 3H), 3.75 (s, 3H), 4.93 (q, J = 6.9 Hz, 1H), 6.98-6.79 (m, 4ArH), 7.40-7.23 (m, 6ArH), 8.05-8.02 (m, 1NH). <sup>13</sup>C NMR in CDCl<sub>3</sub> (75 MHz): δ 23.2, 50.3, 55.6, 110.1, 119.4, 121.2, 122.4, 126.1, 127.3, 128.6, 128.7, 143.9, 148.0, 154.8. MALDI-TOF: m/z calcd for C<sub>16</sub>H<sub>18</sub>KN<sub>2</sub>O<sub>2</sub> [M+K]<sup>+</sup>: 309.10; found: 308.16.

***(S)-1-(2-Hydroxyphenyl)-3-(1-phenylethyl)urea (3i):***

To **2i** (0.400 g, 1.48 mmol) in DCM (5 ml), BBr<sub>3</sub> (0.408 g, 1.63 mmol) was added and kept for stirring room temperature for 2 hours (checked by TLC). The DCM was removed under reduced pressure and the solid thus obtained was partitioned between EtOAc and 5% aqueous NaHCO<sub>3</sub>. The organic layer was then washed with dried over Na<sub>2</sub>SO<sub>4</sub> to obtain **3i** as white solid (0.352 g, 90%; m. p. 106±2 °C). For NMR quality sample we purified 0.070 g of it by column chromatography (45% EtOAc in hexane). <sup>1</sup>H-NMR (300 MHz) in CDCl<sub>3</sub>: δ 1.43 (d, J = 6.9 Hz, 3H), 4.84 (p, J = 6.9 Hz, 1H), 5.56-5.53 (m, 1NH), 6.78-6.63 (m, 3ArH), 7.04-6.92 (m, 2ArH), 7.35-7.23 (m, 4ArH), 9.30 (s, 1NH). <sup>13</sup>C-NMR (75 MHz) in CDCl<sub>3</sub> + d<sub>6</sub>-DMSO: δ 22.7, 49.7, 118.7, 119.8, 121.1, 124.4, 126.1, 127.1, 127.4, 128.5, 144.1, 148.1, 156.9. MALDI-TOF: m/z calcd for C<sub>15</sub>H<sub>16</sub>KN<sub>2</sub>O<sub>2</sub> [M+K]<sup>+</sup>: 295.09; found: 295.13.

***Morpholine-4-carboxylic acid (2-methoxy-phenyl)amide (2j):***

To a well stirred solution of morpholine (0.400 g, 4.59 mmol) in DCM (10 ml), 2-methoxyphenyl isocyanate (0.684 g, 4.59 mmol) was added and kept for stirring at room temperature for 10 min (checked by TLC). The solid thus obtained was filtered through a sintered funnel and partitioned between 5% NaHCO<sub>3</sub> and EtOAc for the removal of residual carbamaic acid. The organic portion was then dried over Na<sub>2</sub>SO<sub>4</sub> and concentrated under reduced pressure. We obtained **2j** as a off-white solid (1.041 g, 96%; m. p. 64±2 °C). For NMR quality sample we purified 0.070 g of it by column chromatography (30% EtOAc in hexane). <sup>1</sup>H NMR (300 MHz) in CDCl<sub>3</sub>: δ 3.50 (t, J = 4.8 Hz, 4H), 3.76 (t, J = 4.5 Hz, 4H), 3.88 (s, 3H), 6.89-6.84 (m, 1ArH), 7.00-6.93 (m, 2ArH), 7.10 (s, 1ArH), 8.16-8.13 (m, 1NH). <sup>13</sup>C-NMR (75 MHz) in CDCl<sub>3</sub>: δ 44.1, 55.7, 66.5, 109.7, 119.1, 121.2, 122.3, 128.5, 147.6, 154.8. MALDI-TOF: m/z calcd for C<sub>12</sub>H<sub>16</sub>KN<sub>2</sub>O<sub>3</sub> [M+K]<sup>+</sup>: 275.08; found: 274.97.

***Morpholine-4-carboxylic acid (2-hydroxy-phenyl)amide (3j):***

To **2j** (0.400 g, 1.69 mmol) in DCM (5 ml), BBr<sub>3</sub> (0.465 g, 1.86 mmol) was added and kept for stirring room temperature for 3 hours (checked by TLC). The DCM was removed under reduced pressure and the solid thus obtained was partitioned between EtOAc and 5% aqueous NaHCO<sub>3</sub>. The organic layer was then washed with dried over Na<sub>2</sub>SO<sub>4</sub> to obtain **3j** as white solid (0.361 g, 96%; m. p. 118±2 °C). For NMR quality sample we purified 0.070 g of it by column chromatography (45% EtOAc in hexane). <sup>1</sup>H-NMR (300 MHz) in CDCl<sub>3</sub>: δ 3.49 (t, J = 4.8 Hz, 4H), 3.74 (t, J = 5.1 Hz, 4H), 6.60 (bs, 1NH), 6.87-6.82 (m, 1ArH), 7.02-6.95 (m, 2ArH), 7.08 (dt, J = 1.5, 7.2 Hz, 1ArH). <sup>13</sup>C-NMR (75 MHz) in CDCl<sub>3</sub>: δ 44.3, 66.3, 119.4, 120.5, 122.4, 126.1, 126.3, 148.8, 156.2. MALDI-TOF: m/z calcd for C<sub>11</sub>H<sub>14</sub>KN<sub>2</sub>O<sub>3</sub> [M+K]<sup>+</sup>: 261.06; found: 260.99.

***Piperidine-1-carboxylic acid (2-methoxy-phenyl)amide (2k):***

To a well stirred solution of piperidine (0.400g, 4.69 mmol) in DCM (10 ml), 2-methoxyphenyl isocyanate (0.277g, 4.69 mmol) was added and kept for stirring at room temperature for 10 min (checked by TLC). The solid thus obtained was filtered through a sintered funnel and partitioned between 5% NaHCO<sub>3</sub> and EtOAc for the removal of residual carbamaic acid. The organic portion was then dried over Na<sub>2</sub>SO<sub>4</sub> and concentrated under reduced pressure. We obtained **2k** as a off-white solid (0.979 g, 89%; m. p. 62±2 °C). For NMR quality sample we purified 0.070 g of it by column chromatography (20% EtOAc in hexane). <sup>1</sup>H NMR (300MHz) in CDCl<sub>3</sub>: δ 1.67-1.61 (m, 6H), 3.48-3.46 (m, 4H), 3.87 (s, 3H), 6.87-6.83 (m, 1ArH), 7.02-6.89 (m, 2ArH), 7.12 (bs, 1NH), 8.19-8.12 (m, 1ArH). <sup>13</sup>C-NMR (75MHz) in CDCl<sub>3</sub>: δ 24.5, 25.7,

45.1, 55.8, 109.7, 119.0, 121.2, 121.7, 129.1, 147.6, 154.7. MALDI-TOF:  $m/z$  calcd for  $C_{13}H_{18}KN_2O_2$   $[M+K]^+$ : 273.10; found: 273.06.

***Piperidine-1-carboxylic acid (2-hydroxy-phenyl)amide (3k):***

To **2k** (0.400 g, 1.71 mmol) in DCM (5 ml),  $BBr_3$  (0.471 g, 1.88 mmol) was added and kept for stirring at room temperature for 3 hours (checked by TLC). The DCM was removed under reduced pressure and the solid thus obtained was partitioned between EtOAc and 5% aqueous  $NaHCO_3$ . The organic layer was then washed with dried over  $Na_2SO_4$  to obtain **3k** as white solid (0.357 g, 95%; m. p.  $80 \pm 2$  °C). For NMR quality sample we purified 0.070 g of it by column chromatography (25% EtOAc in hexane).  $^1H$ -NMR (300 MHz) in  $CDCl_3$ :  $\delta$  1.65 (s, 6H), 3.48 (d,  $J = 5.7$  Hz, 4H), 6.52 (s, 1NH), 6.89-6.79 (m, 2ArH), 7.09-6.99 (m, 2ArH).  $^{13}C$ -NMR (75 MHz) in  $CDCl_3$ :  $\delta$  24.1, 25.5, 45.5, 119.1, 120.2, 122.3, 125.6, 126.9, 148.9, 156.2. MALDI-TOF:  $m/z$  calcd for  $C_{12}H_{16}KN_2O_2$   $[M+K]^+$ : 259.09; found: 259.01.

***1-Adamantan-1-yl-3-(2-methoxy-phenyl)-urea (2l):***

To a well stirred solution of 1-Adamantanylamine (0.100g, 0.66 mmol) in DCM (3 ml), 2-methoxyphenyl isocyanate (0.098 g, 0.66 mmol) was added and kept for stirring at room temperature for 30 min (checked by TLC). The solid thus obtained was filtered through a sintered funnel and partitioned between 5%  $NaHCO_3$  and EtOAc for the removal of residual carbamic acid. The organic portion was then dried over  $Na_2SO_4$  and concentrated under reduced pressure. We obtained **2l** as white hygroscopic solid (0.185 g, 93%). For NMR quality sample we purified 0.070 g of it by column chromatography (20% EtOAc in hexane).  $^1H$  NMR (300MHz) in  $CDCl_3$ :  $\delta$  1.70 (s, 6H), 2.13 (s, 3H), 2.19 (s, 6H), 6.07 (s, 1ArH), 6.97 (dd,  $J = 8.4$ , 12 Hz, 2ArH), 7.20-7.14 (m, 1ArH), 7.54 (bs, 2NH).  $^{13}C$  NMR (75MHz) in  $CDCl_3$ :  $\delta$  29.6, 36.2, 41.6, 55.5, 55.7, 111.54, 120.9, 123.5, 126.4, 178.3. HRMS (ESI+):  $m/z$  calcd for  $C_{18}H_{25}N_2O_2$   $[M+H]^+$ : 301.1916; found: 301.1915.

***1-Adamantan-1-yl-3-(2-hydroxy-phenyl)-urea (3l):***

To **2l** (0.100 g, 0.33 mmol) in DCM (5 ml),  $BBr_3$  (0.082 g, 0.33 mmol) was added and kept for stirring at room temperature for 4 hours (checked by TLC). The DCM was removed under reduced pressure and the solid thus obtained was partitioned between EtOAc and 5% aqueous  $NaHCO_3$ . The organic layer was then washed with dried over  $Na_2SO_4$  to obtain **3l** as white solid (0.002 g, 2%) and free amine (**1l**) with comp **4**. Comp. **3l** was obtained by column chromatography (55% EtOAc in hexane).  $^1H$ -NMR (300 MHz) in  $CDCl_3$ :  $\delta$  1.63 (s, 6H), 2.04 (s, 3H), 2.17 (s, 6H), 7.07-6.88 (m, 3ArH), 7.86 (s, 1ArH, 1OH), 8.45 (s, 1NH), 9.35 (s, 1NH). HRMS (ESI+):  $m/z$  calcd for  $C_{17}H_{23}N_2O_2$   $[M+H]^+$ : 287.1760; found: 287.1758.

***1-Cyclohexyl-3-(2-methoxy-phenyl)-urea (2m):***

To a well stirred solution of Cyclohexylamine (0.100g, 1.00 mmol) in DCM (3 ml), 2-methoxyphenyl isocyanate (0.149 g, 1.00 mmol) was added and kept for stirring at room temperature for 10 min (checked by TLC). The solid thus obtained was filtered through a sintered funnel and partitioned between 5% NaHCO<sub>3</sub> and EtOAc for the removal of residual carbamaic acid. The organic portion was then dried over Na<sub>2</sub>SO<sub>4</sub> and concentrated under reduced pressure. We obtained **2m** as colourless liquid (0.243 g, 97%). For NMR quality sample we purified 0.070 g of it by column chromatography (20% EtOAc in hexane). <sup>1</sup>H NMR (300MHz) in CDCl<sub>3</sub>: δ 1.38-1.12 (m, 6H), 1.63 (s, 3H), 2.04 (t, J = 3 Hz, 2H), 3.84-3.82 (m, 3H), 4.24 (s, 1H), 6.05 (s, 1ArH), 6.96 (s, 2ArH), 7.20 (s, 1ArH), 7.54 (s, 1NH). <sup>13</sup>C-NMR (75MHz) in CDCl<sub>3</sub>: δ 24.7, 25.4, 53.9, 55.7, 112.1, 121.0, 124.6, 125.4, 127.3, 152.3, 179.0. HRMS (ESI+): m/z calcd for C<sub>14</sub>H<sub>21</sub>N<sub>2</sub>O<sub>2</sub> [M+H]<sup>+</sup>: 249.1603; found: 249.1598.

***1-Cyclohexyl-3-(2-hydroxy-phenyl)-urea (3m):***

To **2m** (0.150 g, 0.60 mmol) in DCM (5 ml), BBr<sub>3</sub> (0.149 g, 0.60 mmol) was added and kept for stirring at room temperature for 2 hours (checked by TLC). The DCM was removed under reduced pressure and the solid thus obtained was partitioned between EtOAc and 5% aqueous NaHCO<sub>3</sub>. The organic layer was then washed with dried over Na<sub>2</sub>SO<sub>4</sub> to obtain **3m** as colourless liquid (0.137 g, 97%). For NMR quality sample we purified 0.070 g of it by column chromatography (35% EtOAc in hexane). <sup>1</sup>H-NMR (300 MHz) in d<sub>6</sub>-DMSO: δ 1.41-1.17 (m, 6H), 1.74 (d, J = 9.3 Hz, 2H), 1.97 (d, J = 8.4 Hz, 2H), 3.55-3.51 (m, 1H), 6.95 (t, J = 7.8 Hz, 1ArH), 7.09 (t, J = 7.5 Hz, 1ArH), 7.22 (d, J = 7.8 Hz, 1ArH), 7.31 (d, J = 7.8 Hz, 1H), 7.86 (d, J = 7.8 Hz, 1NH). <sup>13</sup>C-NMR (75 MHz) in d<sub>6</sub>-DMSO: δ 25.0, 25.7, 29.5, 32.9, 52.0, 108.8, 115.7, 120.4, 124.0, 143.9, 148.3, 162.1. HRMS (ESI+): m/z calcd for C<sub>13</sub>H<sub>19</sub>N<sub>2</sub>O<sub>2</sub> [M+H]<sup>+</sup>: 235.1447; found: 235.1449.

***1-(3,7-Dimethyl-octa-2,6-dienyl)-3-(2-methoxy-phenyl)-urea (2n):***

To a well stirred solution of Geranylamine (0.100g, 0.65 mmol) in DCM (3 ml), 2-methoxyphenyl isocyanate (0.097 g, 0.65 mmol) was added and kept for stirring at room temperature for 10 min (checked by TLC). The solid thus obtained was filtered through a sintered funnel and partitioned between 5% NaHCO<sub>3</sub> and EtOAc for the removal of residual carbamaic acid. The organic portion was then dried over Na<sub>2</sub>SO<sub>4</sub> and concentrated under reduced pressure. We obtained **2n** as colourless liquid (0.189 g, 96%). For NMR quality sample we purified 0.070 g of it by column chromatography (20% EtOAc in hexane). <sup>1</sup>H NMR (300MHz) in CDCl<sub>3</sub>: δ 1.57 (s, 3H), 1.65 (s, 6H), 2.02 (s, 4H), 3.84 (d, J = 3 Hz, 3H), 4.22 (s, 2H), 5.03 (s,

1H), 5.22 (s, 1H), 6.05 (s, 1ArH), 6.96 (d, J = 5.4 Hz, 2ArH), 7.32-7.19 (m, 1ArH, 1NH), 7.59 (s, 1NH). <sup>13</sup>C-NMR (75MHz) in CDCl<sub>3</sub>: δ 16.5, 17.7, 25.7, 26.3, 39.4, 43.6, 55.7, 112.0, 118.9, 120.7, 123.5, 123.7, 124.6, 127.3, 131.8, 140.9, 152.3, 180.1. HRMS (ESI<sup>+</sup>): m/z calcd for C<sub>18</sub>H<sub>27</sub>N<sub>2</sub>O<sub>2</sub> [M+H]<sup>+</sup>: 302.2072; found: 302.2077.

***1-(3,7-Dimethyl-octa-2,6-dienyl)-3-(2-hydroxy-phenyl)-urea (3n):***

To **2n** (0.070 g, 0.23 mmol) in DCM (5 ml), BBr<sub>3</sub> (0.058 g, 0.23 mmol) was added and kept for stirring at room temperature for 2 hours (checked by TLC). The DCM was removed under reduced pressure and the solid thus obtained was partitioned between EtOAc and 5% aqueous NaHCO<sub>3</sub>. The organic layer was then washed with dried over Na<sub>2</sub>SO<sub>4</sub> to obtain **1n** and **4** (confirmed by GC).

***1-(4-Fluoro-benzyl)-3-(2-methoxy-phenyl)-urea (2o):***

To a well stirred solution of *p*-Fluorobenzylamine (0.100g, 0.80 mmol) in DCM (3 ml), 2-methoxyphenyl isocyanate (0.118 g, 0.80 mmol) was added and kept for stirring at room temperature for 10 min (checked by TLC). The solid thus obtained was filtered through a sintered funnel and partitioned between 5% NaHCO<sub>3</sub> and EtOAc for the removal of residual carbamaic acid. The organic portion was then dried over Na<sub>2</sub>SO<sub>4</sub> and concentrated under reduced pressure. We obtained **2o** as white hygroscopic solid (0.202 g, 92%). For NMR quality sample we purified 0.070 g of it by column chromatography (30% EtOAc in hexane). <sup>1</sup>H NMR (300MHz) in CDCl<sub>3</sub>: δ 3.81 (s, 3H), 4.85 (d, J = 5.4 Hz, 2H), 6.33 (bs, 1ArH), 7.04-6.93 (m, 4ArH), 7.33-7.20 (m, 3ArH), 7.62 (bs, 1NH). <sup>13</sup>C-NMR (75MHz) in CDCl<sub>3</sub>: δ 48.7, 55.7, 112.1, 115.6 (d, J = 21.75 Hz), 121.1, 125.1 (d, J = 26.25 Hz), 128.0, 129.4 (d, J = 8.25 Hz), 133.2, 152.7, 162.3 (d, J = 244.50 Hz), 163.1, 181.0. HRMS (ESI<sup>+</sup>): m/z calcd for C<sub>15</sub>H<sub>15</sub>FN<sub>2</sub>O<sub>2</sub> [M+H]<sup>+</sup>: 275.1196; found: 275.1199.

***1-(4-Fluoro-benzyl)-3-(2-hydroxy-phenyl)-urea (3o):***

To **2o** (0.100 g, 0.36 mmol) in DCM (5 ml), BBr<sub>3</sub> (0.091 g, 0.36 mmol) was added and kept for stirring at room temperature for 2 hours (checked by TLC). The DCM was removed under reduced pressure and the solid thus obtained was partitioned between EtOAc and 5% aqueous NaHCO<sub>3</sub>. The organic layer was then washed with dried over Na<sub>2</sub>SO<sub>4</sub> to obtain **3o** as hygroscopic solid (0.90 g, 95%). <sup>1</sup>H-NMR (300 MHz) in d<sub>6</sub>-DMSO: δ 4.7 (d, J = 5.4 Hz, 2H), 6.77 (t, J = 7.2 Hz, 1ArH), 6.87 (d, J = 7.8 Hz, 1ArH), 6.99 (t, J = 7.5 Hz, 1ArH), 7.16 (t, J = 8.7 Hz, 2ArH), 7.38 (q, J = 5.7 Hz, 2ArH), 7.72 (d, J = 7.8 Hz, 1ArH), 8.23 (s, 1OH), 8.99 (s, 1NH), 9.77 (1NH). <sup>13</sup> C-NMR (75 MHz) in d<sub>6</sub>-DMSO: δ 46.9, 115.2 (d, J = 21.75 Hz), 116.1, 119.1, 126.2, 126.7, 129.7 (d, J = 8.25 Hz), 135.8, 161.5 (d, J = 255.75 Hz), 181.2. HRMS (ESI<sup>+</sup>): m/z calcd for C<sub>14</sub>H<sub>14</sub>N<sub>2</sub>O<sub>2</sub> [M+H]<sup>+</sup>: 261.1039; found: 261.1037.

***2-[3-(2-Methoxy-phenyl)-ureido]-3-phenyl-propionic acid methyl ester (2p):***

To a well stirred solution of Phenylalanine(OMe) (0.584g, 3.26 mmol) in DCM (10 ml), 2-methoxyphenyl isocyanate (0.480 g, 3.26 mmol) was added and kept for stirring at room temperature for 20 min (checked by TLC). The solid thus obtained was filtered through a sintered funnel and partitioned between 5% NaHCO<sub>3</sub> and EtOAc for the removal of residual carbamaic acid. The organic portion was then dried over Na<sub>2</sub>SO<sub>4</sub> and concentrated under reduced pressure. We obtained **2p** as white solid (0.995 g, 93%; m. p. 139±2 °C). For NMR quality sample we purified 0.100 g of it by column chromatography (30% EtOAc in hexane). <sup>1</sup>H NMR (300MHz) in CDCl<sub>3</sub>: δ 3.17 (dd, J = 5.4, 13.8 Hz, 1H), 3.38 (dd, J = 6, 13.8 Hz, 1H), 5.43-5.36 (m, 1H), 6.56 (d, J = 6.9 Hz, 1ArH), 6.85 (t, J = 7.8 Hz, 1ArH), 6.93 (d, J = 8.4 Hz, 1ArH), 7.05-7.00 (m, 3ArH), 7.29-7.16 (m, 3ArH, 1NH), 7.60 (s, 1NH). <sup>13</sup>C-NMR (75MHz) in CDCl<sub>3</sub>: δ 37.5, 52.4, 55.6, 111.9, 121.0, 124.4, 124.9, 127.2, 127.7, 128.6, 129.1, 129.3, 135.7, 152.2, 172.0, 179.9. HRMS (ESI+): m/z calcd for C<sub>18</sub>H<sub>21</sub>N<sub>2</sub>O<sub>4</sub> [M+H]<sup>+</sup>: 329.1501; found: 329.1503.

***2-[3-(2-Hydroxy-phenyl)-ureido]-3-phenyl-propionic acid methyl ester (3p):***

To **2p** (0.160 g, 0.49 mmol) in DCM (5 ml), BBr<sub>3</sub> (0.124 g, 0.49 mmol) was added and kept for stirring at room temperature for 3 hours (checked by TLC). The DCM was removed under reduced pressure and the solid thus obtained was partitioned between EtOAc and 5% aqueous NaHCO<sub>3</sub>. The organic layer was then washed with dried over Na<sub>2</sub>SO<sub>4</sub> to obtain **1p** and **4** (confirmed by GC).

***2-[3-(2-Methoxy-phenyl)-ureido]-3-methyl-butyric acid methyl ester (2q):***

To a well stirred solution of Valine(OMe) (0.136g, 1.16 mmol) in DCM (10 ml), 2-methoxyphenyl isocyanate (0.173 g, 1.16 mmol) was added and kept for stirring at room temperature for 20 min (checked by TLC). The solid thus obtained was filtered through a sintered funnel and partitioned between 5% NaHCO<sub>3</sub> and EtOAc for the removal of residual carbamaic acid. The organic portion was then dried over Na<sub>2</sub>SO<sub>4</sub> and concentrated under reduced pressure. We obtained **2q** as white hygroscopic solid (0.293 g, 95%). For NMR quality sample we purified 0.100 g of it by column chromatography (60% EtOAc in hexane). <sup>1</sup>H NMR (300MHz) in CDCl<sub>3</sub>: δ 0.95-0.91 (m, 6H), 2.32-2.26 (m, 1H), 3.75 (d, J = 1.5 Hz, 3H), 3.86 (d, J = 1.5 Hz, 3H), 5.14 (t, J = 4.8 Hz, 1H), 6.68 (d, J = 7.5 Hz, 1ArH), 7.003 (t, J = 8.4 Hz, 2ArH), 7.27-7.23 (m, 1ArH), 7.38 (d, J = 7.8 Hz, 1 NH), 7.72 (bs, 1NH). <sup>13</sup>C-NMR (75MHz) in CDCl<sub>3</sub>: δ 18.4, 31.5, 52.2, 55.7, 62.9, 112.1, 121.1124.6, 125.1, 127.8, 152.4, 172.4, 180.7. HRMS (ESI+): m/z calcd for C<sub>14</sub>H<sub>21</sub>N<sub>2</sub>O<sub>4</sub> [M+H]<sup>+</sup>: 281.1501; found: 281.1495.

***2-[3-(2-Hydroxy-phenyl)-ureido]-3-methyl-butyric acid methyl ester (3q):***

To **2q** (0.100 g, 0.37 mmol) in DCM (5 ml), BBr<sub>3</sub> (0.094 g, 0.37 mmol) was added and kept for stirring at room temperature for 3 hours (checked by TLC). The DCM was removed under reduced pressure and the solid thus obtained was partitioned between EtOAc and 5% aqueous NaHCO<sub>3</sub>. The organic layer was then washed with dried over Na<sub>2</sub>SO<sub>4</sub> to obtain **1q** and **4** (confirmed by GC).

***1-(2-fluorophenyl)-3-(2-methoxyphenyl)urea (2r):***

To a well stirred solution of *o*-fluoroaniline (0.400 g, 3.59 mmol) in DCM (10 ml), 2-methoxyphenyl isocyanate (0.535 g, 3.59 mmol) was added and kept for stirring at room temperature for 45 min (checked by TLC). The solid thus obtained was filtered through a sintered funnel and partitioned between 5% NaHCO<sub>3</sub> and EtOAc for the removal of residual carbamaic acid. The organic portion was then dried over Na<sub>2</sub>SO<sub>4</sub> and concentrated under reduced pressure. We obtained **2r** as a white solid (0.849 g, 92%; m. p. 170±2 °C). For NMR quality sample we purified 0.070 g of it by column chromatography (30% EtOAc in hexane). <sup>1</sup>H NMR in CDCl<sub>3</sub> (300 MHz): δ 3.85 (s, 3H), 6.88 (dd, J = 1.5, 7.8 Hz, 1ArH), 7.14-6.94 (m, 6ArH), 7.24 (s, 1ArH), 8.10-8.06 (m, 1NH), 8.16-8.13 (m, 1NH). <sup>13</sup>C-NMR in CDCl<sub>3</sub> + d<sub>6</sub>-DMSO (75 MHz): δ 55.8, 110.4, 114.6 (d, J = 19.50 Hz), 119.5, 121.0, 121.1, 122.1, 124.3 (d, J = 3.00 Hz), 128.0 (d, J = 9.75 Hz), 128.9, 148.2, 152.5 (d, J = 240.00 Hz), 153.1. MALDI-TOF: m/z calcd for C<sub>14</sub>H<sub>13</sub>FKN<sub>2</sub>O<sub>2</sub> [M+K]<sup>+</sup>: 299.06; found: 299.11.

***1-(2-fluorophenyl)-3-(2-Hydroxyphenyl)urea (3r):***

To **2r** (0.400 g, 1.54 mmol) in DCM (5 ml), BBr<sub>3</sub> (0.423 g, 1.69 mmol) was added and kept for stirring room temperature for 3 hours (checked by TLC). The DCM was removed under reduced pressure and the solid thus obtained was partitioned between EtOAc and 5% aqueous NaHCO<sub>3</sub>. The organic layer was then washed with dried over Na<sub>2</sub>SO<sub>4</sub> to obtain **3r** as white solid (0.363 g, 96%; m. p. 162±2 °C). For NMR quality sample we purified 0.070 g of it by column chromatography (35% EtOAc in hexane). <sup>1</sup>H-NMR in CDCl<sub>3</sub> + d<sub>6</sub>-DMSO (300 MHz): δ 6.84-6.77 (m, 1ArH), 6.91-6.86 (m, 2ArH), 7.05-6.92 (m, 1ArH), 7.11-7.06 (m, 2ArH), 7.76 (d, J = 7.5 Hz, 1ArH), 8.26-8.20 (m, 1ArH), 8.71 (s, 1NH), 8.91 (d, J = 1.5 Hz, 1NH), 9.40 (s, 1OH). <sup>13</sup>C-NMR in CDCl<sub>3</sub> + d<sub>6</sub>-DMSO (75 MHz): δ 113.8 (d, J = 18.75 Hz), 115.1, 118.8, 119.3, 120.1, 121.3 (d, J = 7.50 Hz), 122.1, 123.4 (d, J = 3.00 Hz), 126.7, 145.9, 151.6 (d, J = 240.75 Hz), 152.8. MALDI-TOF: m/z calcd for C<sub>13</sub>H<sub>11</sub>FKN<sub>2</sub>O<sub>2</sub> [M+K]<sup>+</sup>: 285.04; found: 284.98.

### ***1-(3-fluorophenyl)-3-(2-methoxyphenyl)urea (2s) :***

To a well stirred solution of *m*-fluoroaniline (0.400 g, 3.59 mmol) in DCM (10 ml), 2-methoxyphenyl isocyanate (0.535 g, 3.59 mmol) was added and kept for stirring at room temperature for 30 min (checked by TLC). The solid thus obtained was filtered through a sintered funnel and partitioned between 5% NaHCO<sub>3</sub> and EtOAc for the removal of residual carbamaic acid. The organic portion was then dried over Na<sub>2</sub>SO<sub>4</sub> and concentrated under reduced pressure. We obtained **2s** as a white solid (0.923 g, 92%; m. p. 118±2 °C). For NMR quality sample we purified 0.070 g of it by column chromatography (30% EtOAc in hexane). <sup>1</sup>H NMR (300 MHz) in CDCl<sub>3</sub>: δ 3.77 (s, 3H), 6.72 (t, J = 8.1 Hz, 1ArH), 7.04-6.84 (m, 4ArH), 7.22-7.14 (m, 2ArH), 7.50 (bs, 1NH), 8.02 (d, J = 7.8 Hz, 1NH). <sup>13</sup>C-NMR (75 MHz) in CDCl<sub>3</sub>: δ 55.5, 107.2 (d, J = 25.5 Hz), 110.4, 115.3 (d, J = 3.00 Hz), 120.9, 121.0, 123.7, 127.5, 130.0, 140.2 (d, J = 10.5 Hz), 149.1, 153.6, 163.1 (d, J = 242.25 Hz). MALDI-TOF: m/z calcd for C<sub>14</sub>H<sub>13</sub>FN<sub>2</sub>O<sub>2</sub> [M+K]<sup>+</sup>: 299.06; found: 299.01.

### ***1-(3-fluorophenyl)-3-(2-Hydroxyphenyl)urea (3s):***

To **2s** (0.400 g, 1.54 mmol) in DCM (5 ml), BBr<sub>3</sub> (0.423 g, 1.69 mmol) was added and kept for stirring room temperature for 3 hours (checked by TLC). The DCM was removed under reduced pressure and the solid thus obtained was partitioned between EtOAc and 5% aqueous NaHCO<sub>3</sub>. The organic layer was then washed with dried over Na<sub>2</sub>SO<sub>4</sub> to obtain **3s** as white solid (0.359 g, 95%; m. p. >200 °C). For NMR quality sample we purified 0.070 g of it by column chromatography (35% EtOAc in hexane). <sup>1</sup>H-NMR (300 MHz) in CDCl<sub>3</sub> + d<sub>6</sub>-DMSO: δ 6.66 (dt, J = 1.8, 8.4 Hz, 1ArH), 6.96-6.78 (m, 3ArH), 7.11-7.06 (m, 1ArH), 7.28-7.15 (m, 1ArH), 7.57-7.45 (m, 1ArH), 7.83 (d, J = 7.2 Hz, 1ArH), 8.22 (bs, 1NH), 9.12 (bs, 1NH). <sup>13</sup>C-NMR (75 MHz) in CDCl<sub>3</sub> + d<sub>6</sub>-DMSO: δ 104.9 (d, J = 26.25 Hz), 107.7 (d, J = 21.00 Hz), 113.2 (d, J = 2.25 Hz), 115.3, 119.2 (d, J = 12.00 Hz), 122.3, 126.9, 129.1, 140.9 (d, J = 11.25 Hz), 145.8, 153.0, 162.4 (d, J = 240.75 Hz). MALDI-TOF: m/z calcd for C<sub>13</sub>H<sub>11</sub>FN<sub>2</sub>O<sub>2</sub> [M+K]<sup>+</sup>: 285.04; found: 284.96.

### ***1-(3-Chlorophenyl)-3-(2-methoxyphenyl)urea (2t):***

To a well stirred *o*-chloroaniline (0.400 g, 3.13 mmol) in DCM (10ml), 2-methoxyphenyl isocyanate (0.467 g, 3.13 mmol) was added and kept for stirring at room temperature for 30 min (checked by TLC). The solid thus obtained was filtered through a sintered funnel and partitioned between 5% NaHCO<sub>3</sub> and EtOAc for the removal of residual carbamaic acid. The organic portion was then dried over Na<sub>2</sub>SO<sub>4</sub> and concentrated under reduced pressure. We obtained **2t** as a white solid (0.807 g, 93%; m. p. 126±2 °C). For NMR quality sample we purified 0.070 g of it

by column chromatography (30% EtOAc in hexane). <sup>1</sup>H-NMR (300MHz) in CDCl<sub>3</sub>: δ 3.83 (s, 3H), 6.87 (dd, J = 1.2, 7.8 Hz, 1ArH), 7.07-6.94 (m, 4ArH), 7.26-7.17 (m, 2ArH), 7.31 (bs, 1NH), 7.46-7.45 (m, 1ArH), 8.04 (dd, J = 1.8, 8.1 Hz, 1NH). <sup>13</sup>C (75 MHz) in d<sub>6</sub>-DMSO: δ 56.3, 111.2, 116.8, 117.7, 118.9, 121.0, 121.8, 122.6, 128.8, 130.9, 133.7, 141.8, 148.2, 152.7. MALDI-TOF: m/z calcd for C<sub>14</sub>H<sub>13</sub>ClKN<sub>2</sub>O<sub>2</sub> [M+K]<sup>+</sup>: 315.03; found: 315.09.

***1-(3-Chlorophenyl)-3-(2-hydroxyphenyl)urea (3t):***

To **2t** (0.400 g, 1.52 mmol) in DCM (5 ml), BBr<sub>3</sub> (0.418 g, 1.67 mmol) was added and kept for stirring at room temperature for 3 hours (checked by TLC). The DCM was removed under reduced pressure and the solid thus obtained was partitioned between EtOAc and 5% aqueous NaHCO<sub>3</sub>. The organic layer was then washed with dried over Na<sub>2</sub>SO<sub>4</sub> to obtain **3t** as white solid (0.341 g, 90%; m. p. 152±2 °C). For NMR quality sample we purified 0.070 g of it by column chromatography (30% EtOAc in hexane). <sup>1</sup>H-NMR (300MHz) in CDCl<sub>3</sub> + d<sub>6</sub>-DMSO: δ 6.94-6.77 (m, 4ArH), 7.26-7.16 (m, 2ArH), 7.69 (d, J = 1.8 Hz, 1ArH), 7.92-7.89 (m, 1ArH), 8.17 (s, 1NH), 9.10 (s, 1NH), 9.41 (s, 1OH). <sup>13</sup>C-NMR (75 MHz) in CDCl<sub>3</sub> + d<sub>6</sub>-DMSO: δ 114.6, 115.6, 117.3, 118.8, 118.8, 120.8, 121.8, 126.8, 128.9, 133.3, 140.4, 145.4, 152.5. MALDI-TOF: m/z calcd for C<sub>13</sub>H<sub>11</sub>ClKN<sub>2</sub>O<sub>2</sub> [M+K]<sup>+</sup>: 301.02; found: 300.97.

***1-(2-methoxyphenyl)-3-(2-trifluoromethyl)phenyl)urea (2u):***

To a well stirred solution of *o*-trifluoromethylaniline (0.400 g, 2.48 mmol) in DCM (10ml), 2-methoxyphenyl isocyanate (0.370 g, 2.48 mmol) was added and kept for stirring at room temperature for 1.5 hour (checked by TLC). The solid thus obtained was filtered through a sintered funnel and partitioned between 5% NaHCO<sub>3</sub> and EtOAc for the removal of residual carbamaic acid. The organic portion was then dried over Na<sub>2</sub>SO<sub>4</sub> and concentrated under reduced pressure. We obtained **2u** as a white solid (0.570 g, 74%; m. p. 164±2 °C). For NMR quality sample we purified 0.070 g of it by column chromatography (35% EtOAc in hexane). <sup>1</sup>H NMR (300 Hz) in CDCl<sub>3</sub>: δ 3.87 (s, 3H), 6.92-6.86 (m, 2ArH), 7.11-6.96 (m, 3ArH), 7.20 (t, J = 7.5 Hz, 1ArH), 7.57 (q, J = 8.1 Hz, 2ArH), 7.98 (dd, J = 1.5, 7.8 Hz, 1NH), 8.06 (d, J = 8.1 Hz, 1NH). <sup>13</sup>C NMR (75 MHz) in CDCl<sub>3</sub> + d<sub>6</sub>-DMSO: δ 55.5, 110.2, 119.7, 120.7 (q, J = 5.25 Hz, for CF<sub>3</sub>-*o*C'), 121.0, 122.1, 123.0, 125.6 (q, J = 5.25 Hz, for CF<sub>3</sub>-*o*C''), 126.0, 128.5, 132, 136.4, 148.2, 153.2. MALDI-TOF: m/z calcd for C<sub>15</sub>H<sub>13</sub>F<sub>3</sub>KN<sub>2</sub>O<sub>2</sub> [M+K]<sup>+</sup>: 349.06; found: 348.98.

***1-(2-hydroxyphenyl)-3-(2-trifluoromethyl)phenyl)urea (3u):***

To **2u** (0.400g, 1.29 mmol) in DCM (5 ml), BBr<sub>3</sub> (0.356 g, 1.42 mmol) was added and kept for stirring room temperature for 3 hours (checked by TLC). The DCM was removed under reduced pressure and the solid thus obtained was partitioned between EtOAc and 5% aqueous NaHCO<sub>3</sub>. The organic layer was then washed with dried over Na<sub>2</sub>SO<sub>4</sub> to obtain **3u** as white solid (0.370 g, 97%; m. p. 122±2 °C). For NMR quality sample we purified 0.070 g of it by column

chromatography (30% EtOAc in hexane). <sup>1</sup>H-NMR (300 MHz) in CDCl<sub>3</sub>: δ 6.74 (s, 1ArH), 6.74 (bs, 1ArH), 6.92-6.87 (m, 2ArH), 7.17-7.01 (m, 3ArH), 7.31-7.26 (m, 1ArH), 7.66-7.57 (m, 1ArH, 1NH), 7.97-7.94 (m, 1NH). <sup>13</sup>C-NMR (75 MHz) in d<sub>6</sub>-DMSO: δ 117.3, 119.8, 121.0, 123.5, 124.0, 125.8 (q, J = 5.25 Hz, for CF<sub>3</sub>-oC), 125.9, 127.1, 132.3, 136.2, 147.4, 154.5. MALDI-TOF: m/z calcd for C<sub>14</sub>H<sub>11</sub>F<sub>3</sub>KN<sub>2</sub>O<sub>2</sub> [M+K]<sup>+</sup>: 335.04; found: 335.08.

#### ***3H-Benzooxazol-2-one (4):***

<sup>1</sup>H-NMR (300 MHz) in CDCl<sub>3</sub>: δ 7.24-7.08 (m, 4ArH). <sup>13</sup>C-NMR (75 MHz) in CDCl<sub>3</sub>: δ 110.2, 122.8, 124.2, 129.4, 143.9, 156.1. HRMS (ESI<sup>+</sup>): m/z calcd for C<sub>7</sub>H<sub>6</sub>NO<sub>2</sub> [M+H]<sup>+</sup>: 136.0399; found: 136.0399.

#### ***1-(3-Methoxyphenyl)-3-(o-tolyl)urea (5):***

To a well stirred solution of o-toluidine (0.400 g, 3.73 mmol) in DCM (10 ml), 3-methoxyphenyl isocyanate (0.556 g, 3.73 mmol) was added and kept for stirring at room temperature for 15 min (checked by TLC). The solid thus obtained was filtered through a sintered funnel and partitioned between 5% NaHCO<sub>3</sub> and EtOAc for the removal of residual carbamaic acid. The organic portion was then dried over Na<sub>2</sub>SO<sub>4</sub> and concentrated under reduced pressure. We obtained 1-(3-Methoxyphenyl)-3-(o-tolyl)urea as a white solid (0.928 g, 97%; m. p. 173±2 °C). For NMR quality sample we purified 0.070 g of it by column chromatography (30% EtOAc in hexane). <sup>1</sup>H-NMR (300MHz) in d<sub>6</sub>-DMSO: δ 2.24 (s, 3H), 3.73 (s, 3H), 6.55 (dd, J = 2.4, 8.4 Hz, 1ArH), 6.97-6.92 (m, 2ArH), 7.21-7.12 (m, 4ArH), 7.83 (d, J = 8.1 Hz, 1ArH), 7.90 (s, 1NH), 9.03 (s, 1NH). <sup>13</sup>C-NMR (75 MHz) in d<sub>6</sub>-DMSO: δ 18.4, 55.4, 104.2, 107.7, 110.8, 121.6, 123.2, 126.7, 128.0, 130.1, 130.7, 137.9, 141.6, 153.1, 160.2. MALDI-TOF: m/z calcd for C<sub>15</sub>H<sub>16</sub>KN<sub>2</sub>O<sub>2</sub> [M+K]<sup>+</sup>: 295.09; found: 294.04.

#### ***1-(3-Hydroxyphenyl)-3-(o-tolyl)urea (7):***

To a 1-(3-methoxyphenyl)-3-(o-tolyl)urea (0.400 g, 1.56 mmol) in DCM (5 ml), BBr<sub>3</sub> (0.431 g, 1.72 mmol) was added and kept for stirring room temperature for 3 hours (checked by TLC). The DCM was removed under reduced pressure and the solid thus obtained was partitioned between EtOAc and 5% aqueous NaHCO<sub>3</sub>. The organic layer was then washed with dried over Na<sub>2</sub>SO<sub>4</sub> to obtain 1-(3-Hydroxyphenyl)-3-(o-tolyl)urea as white solid (0.356 g, 94%; m. p. 167±2 °C). For NMR quality sample we purified 0.070 g of it by column chromatography (35% EtOAc in hexane). <sup>1</sup>H-NMR in d<sub>6</sub>-DMSO (300 MHz): δ 2.05 (s, 3H), 6.42 (dd, J = 1.8, 7.8 Hz, 1ArH), 6.85 (dd, J = 1.2, 8.1 Hz, 1ArH), 6.99 (dt, J = 1.2, 7.5 Hz, 1ArH), 7.13-7.08 (m, 2ArH), 7.25-7.17 (m, 2ArH), 7.91-7.89 (m, 1ArH, 1NH), 8.97 (s, 1NH), 9.39 (s, 1OH). <sup>13</sup>C-NMR (75 MHz) in d<sub>6</sub>-DMSO: δ 18.4, 105.5, 109.2, 109.4, 121.3, 123.0, 126.6, 127.8, 130.0, 130.6, 137.9, 141.4, 153.0, 158.2. MALDI-TOF: m/z calcd for C<sub>14</sub>H<sub>14</sub>KN<sub>2</sub>O<sub>2</sub> [M+K]<sup>+</sup>: 281.07; found: 281.02.

***1-(4-methoxyphenyl)-3-(o-tolyl)urea (6):***

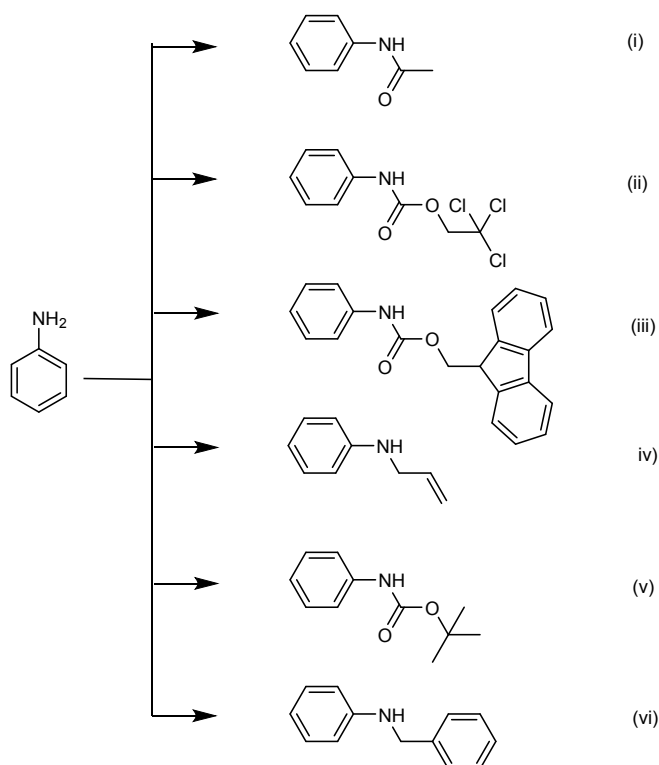
To a well stirred solution of *o*-toulidine (0.400 g, 3.73 mmol) in DCM (10 ml), 4-methoxyphenyl isocyanate (0.556 g, 3.73 mmol) was added and kept for stirring at room temperature for 10 min (checked by TLC). The solid thus obtained was filtered through a sintered funnel and partitioned between 5% NaHCO<sub>3</sub> and EtOAc for the removal of residual carbamaic acid. The organic portion was then dried over Na<sub>2</sub>SO<sub>4</sub> and concentrated under reduced pressure. We obtained 1-(4-Methoxyphenyl)-3-(*o*-tolyl)urea as a white solid (0.937 g, 98%; m. p. 168±2 °C). For NMR quality sample we purified 0.070 g of it by column chromatography (30% EtOAc in hexane). <sup>1</sup>H-NMR (300 MHz) in d<sub>6</sub>-DMSO: δ 2.30 (s, 3H), 3.78 (s, 3H), 6.96-6.91 (m, 2ArH), 7.00 (dd, J = 0.9, 7.2 Hz, 1ArH), 7.24-7.17 (m, 2ArH), 7.45-7.40 (m, 2ArH), 7.92-7.88 (m, 1ArH, 1NH), 8.89 (s, 1NH). <sup>13</sup>C-NMR (75MHz) in d<sub>6</sub>-DMSO: δ 18.4, 55.6, 114.5, 120.2, 121.3, 122.9, 126.6, 127.7, 130.6, 133.4, 138.1, 153.3, 154.8. MALDI-TOF: m/z calcd for C<sub>15</sub>H<sub>16</sub>KN<sub>2</sub>O<sub>2</sub> [M+K]<sup>+</sup>: 295.09; found: 294.14.

***1-(4-Hydroxyphenyl)-3-(o-tolyl)urea (8):***

To a well stirred 1-(4-Methoxyphenyl)-3-(*o*-tolyl)urea (0.400g, 1.56 mmol) in DCM (5 ml), BBr<sub>3</sub> (0.431 g, 1.72 mmol) was added and kept for stirring room temperature for 3 hours (checked by TLC). The DCM was removed under reduced pressure and the solid thus obtained was partitioned between EtOAc and 5% aqueous NaHCO<sub>3</sub>. The organic layer was then washed with dried over Na<sub>2</sub>SO<sub>4</sub> to obtain 1-(4-Hydroxyphenyl)-3-(*o*-tolyl)urea as white solid (0.364 g, 96%; m. p. 183±2 °C). For NMR quality sample we purified 0.070 g of it by column chromatography (35% EtOAc in hexane). <sup>1</sup>H NMR in d<sub>6</sub>-DMSO (300 MHz): δ 2.29 (s, 3H), 6.77-6.73 (m, 2ArH), 6.98 (t, J = 6.6 Hz, 1ArH), 7.23-7.16 (m, 2ArH), 7.31-7.27 (m, 2ArH), 7.83 (s, 1NH), 7.91 (d, J = 8.1 Hz, 1ArH), 8.76 (s, 1NH), 9.12 (s, 1OH). <sup>13</sup>C-NMR (75 MHz) in d<sub>6</sub>-DMSO: δ 18.4, 115.7, 120.6, 121.1, 122.7, 126.6, 127.5, 130.6, 131.8, 138.2, 152.9, 153.3. MALDI-TOF: m/z calcd for C<sub>14</sub>H<sub>14</sub>KN<sub>2</sub>O<sub>2</sub> [M+K]<sup>+</sup>: 281.07; found: 281.13.

### Synthesis of N-protected aniline derivatives for stability studies:

All the N-protected derivatives were synthesized by reported methods available in literature.



#### Synthesis of Ac-aniline (i):

Aniline (0.5 g, 5.37 mmol) was dissolved in DCM and to that Triethylamine (2.24 mL, 16.1 mmol) was added and cooled to 10 °C. To that Acetyl chloride (0.46 mL, 6.44 mmol) was added and stirred at room temperature. After reaction completion by TLC, quenched with water and extracted with DCM (3X100 mL). And the collected organic phase washed with water and brine. Dried over Sodium sulphate and evaporated to give the product as a colorless solid (0.61 g, 84.1 %). <sup>1</sup>H-NMR (300 MHz) in CDCl<sub>3</sub>: δ 2.17 (s, 3H), 7.10 (t, J = 7.5 Hz, 1ArH), 7.31 (t, J = 8.1 Hz, 2ArH), 7.50 (d, J = 7.8 Hz, 2ArH).

#### Synthesis of Troc-aniline (ii):

Aniline (0.5 g, 5.37 mmol) was dissolved in DCM and to that Triethylamine (2.24 mL, 16.1 mmol) was added and cooled to 10 °C. To that 2, 2, 2-trichloroethoxycarbonyl chloride (0.89

mL, 6.44 mmol) was added and stirred at room temperature. After reaction completion by TLC, quenched with water and extracted with DCM (3X100 mL). And the collected organic phase washed with water and brine. Dried over Sodium sulphate and evaporated to give the product as a colorless solid (0.122 g, 86.8 %). <sup>1</sup>H-NMR (300 MHz) in CDCl<sub>3</sub>: δ 4.83 (s, 2H), 7.12 (t, J = 7.2 Hz, 1ArH), 7.35 (t, J = 8.4 Hz, 2ArH), 7.43 (d, J = 7.8 Hz, 2ArH).

#### Synthesis of Fmoc-aniline (iii):

Aniline (0.5 g, 5.37 mmol) and Sodium bicarbonate (0.9 g, 10.7 mmol) were dissolved in water/1, 4-Dioxane mixture (1:1, 5 mL) and cooled to 10 °C, then 9-Fluorenylmethyl chloroformate (1.53 g, 5.9 mmol) was added and stirred at room temperature for 6 hours. After completion of reaction by TLC volatiles evaporated and diluted with water and partitioned with ethylacetate (3X100 mL). Combined organic layers washed with water followed by brine. Dried over Sodium sulphate and evaporated. Purified by column chromatography to give the product as white solid (1.2 g, 71 %). <sup>1</sup>H-NMR (300 MHz) in CDCl<sub>3</sub>: δ 4.28 (t, J = 6.6 Hz, 1H), 4.55 (d, J = 6.6 Hz, 2H), 7.07 (t, J = 7.5 Hz, 1ArH), 7.45-7.28 (m, 8ArH), 7.62 (d, J = 7.5 Hz, 2ArH), 7.79 (d, J = 7.5 Hz, 2ArH).

#### Synthesis of Allyl-aniline (iv):

Aniline (0.5 g, 5.37 mmol) was dissolved in Acetone and to that Potassium carbonate (1.48 g, 10.7 mmol) was added and stirred at room temperature. To that Allyl bromide (0.51 mL, 5.9 mmol) was added and maintained at 60 °C. After reaction completion volatiles evaporated and the crude was partitioned between water and ethyl acetate (3X100 mL). Combined organic layer was washed with water and brine. Purification through column chromatography using hexane ethyl acetate yielded product as a clear liquid (0.48 g, 67.1 %). <sup>1</sup>H-NMR (300 MHz) in CDCl<sub>3</sub>: δ 3.91 (d, J = 4.8 Hz, 2H), 5.17-5.13 (m, 2H), 5.88-5.49 (m, 1H), 6.78-6.61 (m, 3ArH), 7.24-7.13 (m, 2ArH).

#### Synthesis of Boc-aniline (v):

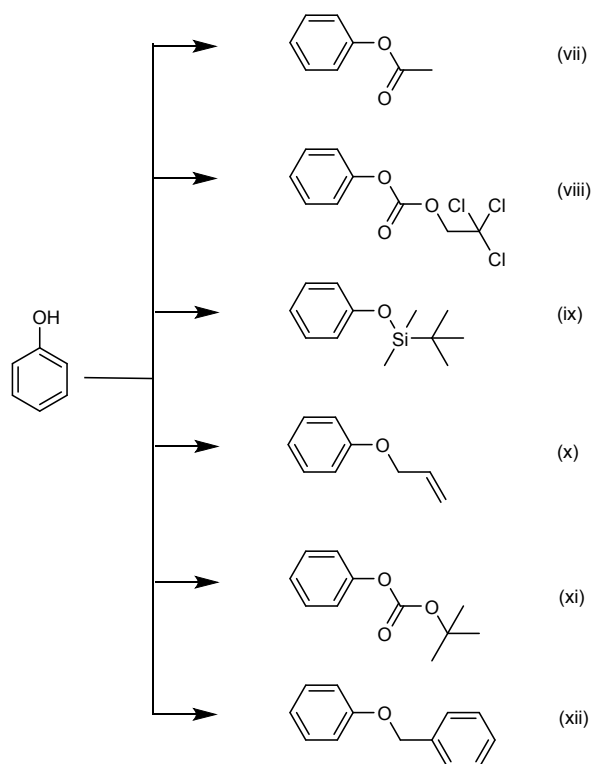
Aniline (0.5 g, 5.37 mmol) was dissolved in THF and to that DMAP (0.032 g, 0.26 mmol) was added followed by Boc anhydride (1.28 mL, 5.91 mmol) and refluxed. After completion of reaction volatiles evaporated the crude was partitioned between water and ethyl acetate (3X100 mL). Combined organic layer was washed with water and brine. Purification through column chromatography using hexane ethyl acetate yielded product as an off white solid (0.82 g, 80.4 %). <sup>1</sup>H-NMR (300 MHz) in CDCl<sub>3</sub>: δ 1.44 (s, 9H), 7.38-7.24 (m, 5ArH).

### Synthesis of Bn-aniline (vi):

Aniline (0.5 g, 5.37 mmol) was dissolved in Acetone and to that Potassium carbonate (1.48 g, 10.7 mmol) was added and stirred at room temperature. To that Benzyl bromide (0.51 mL, 5.9 mmol) was added and maintained at 60 °C. After reaction completion volatiles evaporated and the crude was partitioned between water and ethyl acetate (3X100 mL). Combined organic layer was washed with water and brine. Purification through column chromatography using hexane ethyl acetate yielded product as a clear liquid (0.48 g, 67.1 %). <sup>1</sup>H-NMR (300 MHz) in CDCl<sub>3</sub>: δ 4.64 (s, 2H), 6.77-6.61 (m, 2ArH), 7.48-7.12 (m, 8ArH). The NMR shows presence of certain amount of benzyl bromide.

### Synthesis of O-protected Phenol derivatives for stability studies:

All the N-protected derivatives were synthesized by reported methods available in literature.



### Synthesis of Ac-phenol (vii):

Phenol (0.5 g, 5.31 mmol) was dissolved in DCM and to that Triethylamine (2.22 mL, 15.93 mmol) was added and cooled to 10 °C. To that Acetyl chloride (0.45 mL, 6.37 mmol) was added and stirred at room temperature. After reaction completion by TLC, quenched with water and extracted with DCM (3X100 mL). And the collected organic phase washed with 5 % Sodium

bicarbonate, water and brine successively. Dried over Sodium sulphate and evaporated to give the product as a clear liquid (0.68 g, 94.1 %). <sup>1</sup>H-NMR (300 MHz) in CDCl<sub>3</sub>: δ 2.30 (s, 3H), 7.09 (d, J = 8.4 Hz, 2ArH), 7.26-7.20 (m, 1ArH), 7.38 (t, J = 8.1 Hz, 2ArH).

#### Synthesis of Troc-phenol (viii):

Phenol (0.5 g, 5.31 mmol) was dissolved in DCM and to that triethylamine (2.22 mL, 15.93 mmol) was added and cooled to 10 °C. To that 2, 2, 2-trichloroethoxycarbonyl chloride (0.88 mL, 6.37 mmol) was added and stirred at room temperature. After reaction completion by TLC, quenched with water and extracted with DCM (3X100 mL). And the collected organic phase washed with 5 % Sodium bicarbonate, water and brine successively. Dried over Sodium sulphate and evaporated to give the product as a colorless solid (1.31 g, 91.6 %). <sup>1</sup>H-NMR (300 MHz) in CDCl<sub>3</sub>: δ 4.88 (s, 2H), 7.31-7.21 (m, 3ArH), 7.42 (t, J = 8.1 Hz, 2ArH).

#### Synthesis of TBS-phenol (ix):

Phenol (0.5 g, 5.31 mmol) was dissolved in DMF (1 mL) to that imidazole (0.9 g, 13.28 mmol) was added and stirred at room temperature. After 10 minutes tert-Butyldimethylchlorosilane (0.96 g, 6.37 mmol) was added and stirred at room temperature for 6 hours. After completion of reaction by TLC quenched with water and partitioned with ethylacetate (3X100 mL). Combined organic layers washed with water followed by brine. Dried over Sodium sulphate and evaporated to give the product as colorless liquid (0.89 g, 80.9 %). <sup>1</sup>H-NMR (300 MHz) in CDCl<sub>3</sub>: δ 0.19 (s, 6H), 0.98 (s, 9H), 6.85 (d, J = 8.7 Hz, 2ArH), 6.94 (t, J = 7.2 Hz, 1ArH), 7.25-7.20 (m, 2ArH).

#### Synthesis of Allyl-phenol (x):

Phenol (0.5 g, 5.31 mmol) was dissolved in Acetone and to that Potassium carbonate (1.47 g, 10.6 mmol) was added and stirred at room temperature. To that Allyl bromide (0.51 mL, 5.8 mmol) was added and maintained at 60 °C. After reaction completion volatiles evaporated and the crude was partitioned between water and ethyl acetate (3X100 mL). Combined organic layer was washed with water and brine. Purification through column chromatography using hexane ethyl acetate yielded product as a clear liquid (0.66 g, 92.7%). <sup>1</sup>H-NMR (300 MHz) in CDCl<sub>3</sub>: δ 4.55-4.53 (m, 2H), 5.28 (dd, J = 1.5, 10.5 Hz, 1H), 5.42 (dd, J = 1.8, 17.4 Hz, 1H), 6.13-6.0 (m, 1H), 6.97-6.91 (m, 3ArH), 7.31-7.25 (m, 2ArH).

#### Synthesis of Boc-phenol (xi):

Phenol (0.5 g, 5.31 mmol) was dissolved in THF and to that DMAP (0.032 g, 0.27 mmol) was added followed by Boc anhydride (1.27 mL, 5.8 mmol) and refluxed. After completion of reaction volatiles evaporated the crude was partitioned between water and ethyl acetate (3X100 mL). Combined organic layer was washed with water and brine. Purification through column

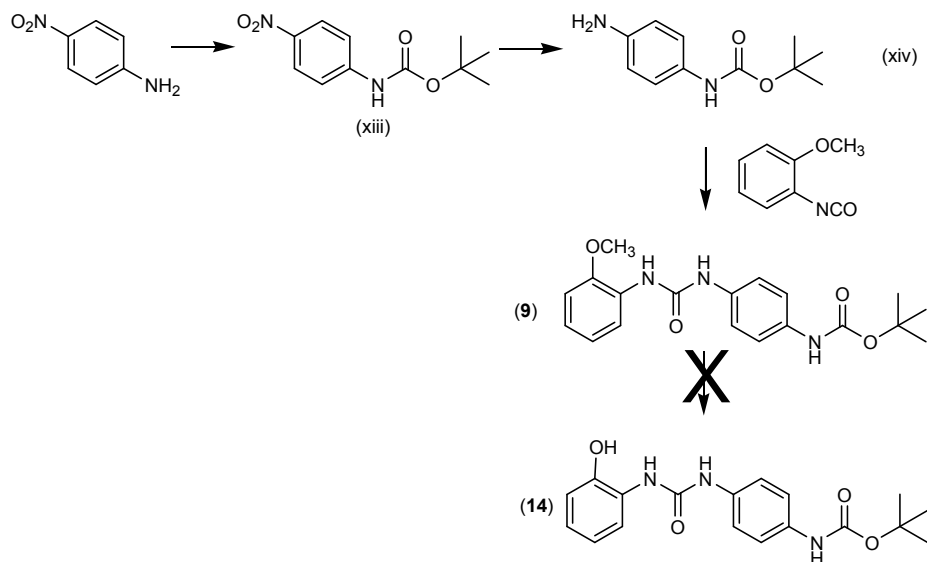
chromatography using hexane ethyl acetate yielded product as colorless liquid (0.91 g, 88.3%).  $^1\text{H-NMR}$  (300 MHz) in  $\text{CDCl}_3$ :  $\delta$  1.56 (s, 9H), 7.26-7.15 m, 3ArH), 7.40-7.35 (m, 2ArH).

Synthesis of **Benzyl-phenol (xii)**:

Phenol (0.5 g, 5.31 mmol) was dissolved in Acetone and to that Potassium carbonate (1.47 g, 10.6 mmol) was added and stirred at room temperature. To that Benzyl bromide (0.51 mL, 5.8 mmol) was added and maintained at 60 °C. After reaction completion volatiles evaporated and the crude was partitioned between water and ethyl acetate (3X100 mL). Combined organic layer was washed with water and brine. Purification through column chromatography using hexane ethyl acetate yielded product as a clear liquid (0.91 g, 93.0%).  $^1\text{H-NMR}$  (300 MHz) in  $\text{CDCl}_3$ :  $\delta$  5.05 (s, 2H), 6.98 (dd,  $J = 0.6, 6.6$  Hz, 3ArH), 7.45-7.22 (m, 7ArH).

### Synthesis of target molecules for the orthogonal stability study:

All these molecules with two different amine protecting groups were synthesized following the reported protocols as shown in the following schemes.



#### Synthesis of (xiii):

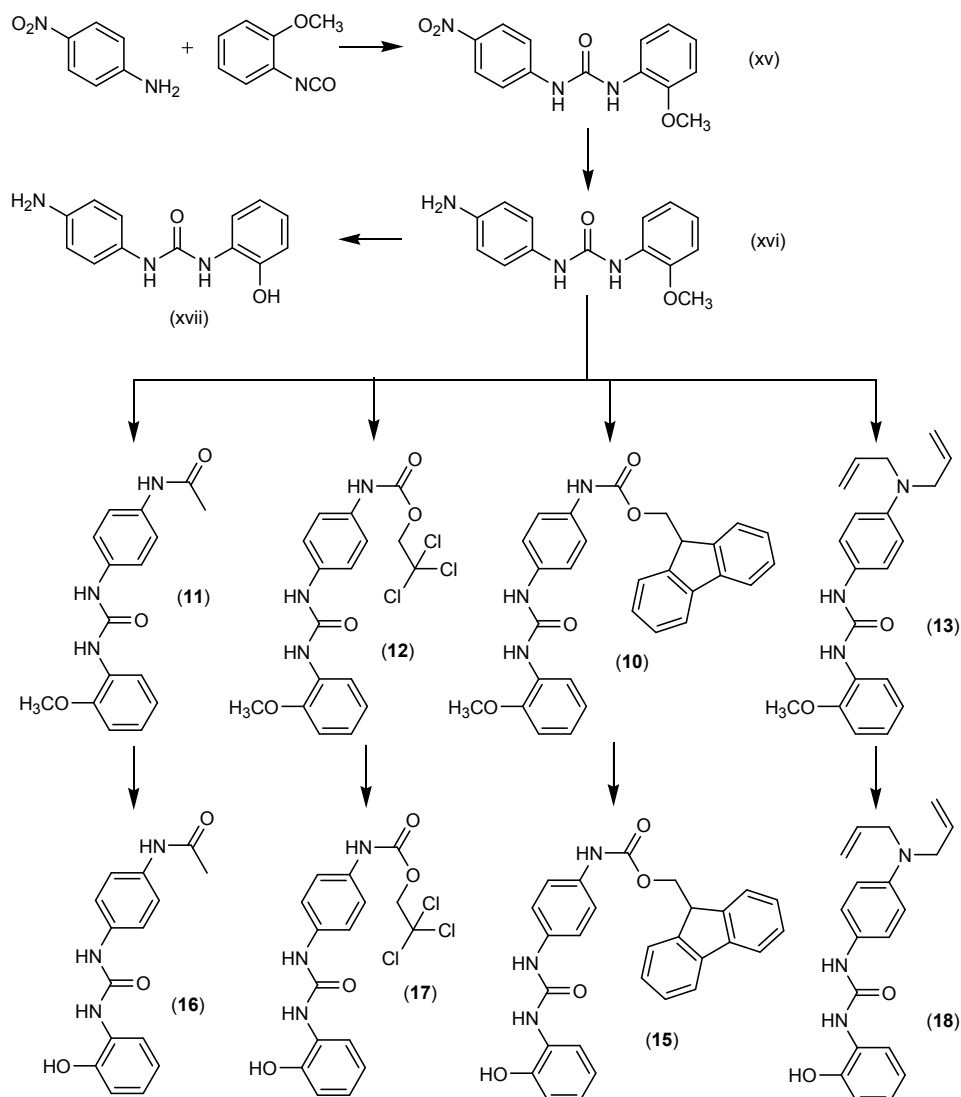
4-Nitroaniline (1g, 7.2 mmol) was dissolved in THF and to that DMAP (0.044g, 0.36 mmol) was added and stirred for 10 minutes. Then Boc anhydride (1.73 mL, 7.92 mmol) and maintained at 70 °C for 6 hours. After completion of reaction volatiles evaporated the crude was partitioned between water and ethyl acetate (3X100 mL). Combined organic layer was washed with water and brine. Purification through column chromatography using hexane ethyl acetate yielded product as pale yellow solid (1.56 g, 91.2%).

#### Synthesis of (xiv):

Compound **xiii** (1 g, 4.2 mmol) was dissolved in ethanol and anhydrous Sodiumsulfide (0.982 g, 12.6 mmol) and maintained at 50 °C for 1 hour. After completion of reaction by TLC volatiles evaporated and partitioned between water and ethylacetate (3X100 mL). Combined organic layer was washed with water and brine. It was then evaporated to get the product as a pale brown solid (0.73 g, 83.4 %).

### Synthesis of compound **9**:

Compound **xiv** (0.5 g, 2.4 mmol) was dissolved in DCM and to that was added 2-methoxyphenyl isocyanate (0.32 mL, 2.4 mmol). And the mass was allowed to stir at room temperature for 8 hours. After completion of reaction by TLC hexane was added and stirred for 30 minutes then filtered and dried to give the product as an off white solid (0.76 g, 88.6 %, m. p.: >200 °C). <sup>1</sup>H-NMR (300MHz) in CDCl<sub>3</sub>: δ 1.52 (s, 9H), 3.81 (s, 3H), 6.49 9bs, 1ArH), 6.78 (bs, 1ArH), 6.87-6.84 (m, 1ArH), 7.03-6.93 (m, 2ArH), 7.20 (bs, 1NH), 7.34-7.29 (m, 3ArH), 8.10 (dd, J = 1.8, 7.8 Hz, 1NH). MALDI-TOF: m/z calcd for C<sub>19</sub>H<sub>23</sub>KN<sub>3</sub>O<sub>4</sub> [M+K]<sup>+</sup>: 396.13; found: 396.06.



#### Synthesis of (xv):

4-Nitroaniline (2g, 14.5 mmol) was dissolved in DCM and to that was added 2-methoxyphenyl isocyanate (2.16 mL, 14.5 mmol). And the mass was allowed to stir at room temperature for 8 hours. After completion of reaction by TLC hexane was added and stirred for 30 minutes then filtered and dried to give the product as yellow solid (3.89 g, 93.5 %).

#### Synthesis of (xvi):

Compound **xv** (2 g, 6.96 mmol) was dissolved in a mixture of THF/Methanol (8:2) 100 mL and maintained at 10-15 °C. To that 1 mL of water was added. Then Nickel chloride hexahydrate (0.083g, 0.35 mmol) was added and after 15 minutes Sodium borohydride (0.79 g, 20.9 mmol) was added in 2 lots. After reaction completion volatiles evaporated and the crude was dissolved in a mixture of water and ethyl acetate and filtered through celite and partitioned with ethyl acetate (3X200 mL). Washed with water, brine and dried over sodium sulfate. Evaporated and purified by column chromatography hexane ethylacetate to give the product as a pale brown solid (1.32 g, 73.7 %).

#### Synthesis of (xvii):

Compound **xvi** (0.2 g, 0.77 mmol) was suspended in DCM and Borontribromide (0.93 mL, 0.93 mmol) 1 M solution was added and stirred at room temperature for 6 hours. After completion of reaction by TLC, quenched with water and neutralized with solid sodium bicarbonate. Extracted three times with DCM and evaporated to give the product as a pale brown solid (0.135 g, 72.2 %).

#### Synthesis of compound 10:

Compound **xvi** (0.35 g, 1.36 mmol) was dissolved in a mixture of 1, 4-Dioxane and water (1:1, 10 ml). To that was added Sodium bicarbonate (0.228 g, 2.72 mmol). Then Fmoc chloride (0.352 g, 1.36 mmol) was added and stirred at room temperature for 4 hours. After completion of reaction by TLC, volatiles evaporated and diluted with water and extracted using ethyl acetate (3X100). Combined organic layer was washed with water and brine. Evaporated and purified by column chromatography to give the product as a pale yellow solid (0.53 g, 81.3 %, m. p.: >200 °C). <sup>1</sup>H-NMR (300MHz) in d<sub>6</sub>-DMSO: δ 3.88 (s, 3H), 4.31 (t, J = 6.3 Hz, 1H), 4.47, (d, J = 6 Hz, 2H), 6.91 (p, J = 7.5 Hz, 1ArH), 7.02-7.00 (m, 1ArH), 7.46-7.34 (m, 8ArH), 7.76 (d, J = 6.9 Hz, 2ArH), 7.92 (d, J = 7.5 Hz, 2ArH), 8.18-8.11 (m, 1ArH, 1NH), 9.21 (bs, 1NH). MALDI-TOF: m/z calcd for C<sub>29</sub>H<sub>25</sub>KN<sub>3</sub>O<sub>4</sub> [M+K]<sup>+</sup>: 518.15; found: 518.07.

#### Synthesis of compound 11:

Compound **xvi** (0.35 g, 1.36 mmol) was dissolved in DCM and to that was added triethylamine (0.57 mL, 4.1 mmol). Then maintained at 10-15 °C and acetyl chloride (0.107 g, 1.36 mmol) was added and stirred at room temperature for 4 hours. After completion of reaction by TLC, quenched with 10 % Sodium bicarbonate and partitioned with DCM (3X100 mL) and water. Combined organic layer washed with water followed by brine and evaporated. Purified by column chromatography using ethyl acetate in hexanes to obtain the product as an off white solid (0.36 g, 88.5 %, m. p.: >200 °C). <sup>1</sup>H-NMR (300MHz) in d<sub>6</sub>-DMSO: δ 2.02(s, 3H), 3.88 (s, 3H), 7.03-6.86 (m, 3ArH), 7.36 (d, J = 9 Hz, 2ArH), 7.48 (d, J = 9 Hz, 2ArH), 8.13 (dd, J = 1.8, 7.8 Hz, 1ArH), 8.19 (s, 1NH), 9.24 (s, 1NH), 9.83 (s, 1NH). MALDI-TOF: m/z calcd for C<sub>16</sub>H<sub>17</sub>KN<sub>3</sub>O<sub>3</sub> [M+K]<sup>+</sup>: 338.09; found: 338.03.

#### Synthesis of compound 12:

Compound **xvi** (0.35 g, 1.36 mmol) was dissolved in DCM and to that was added triethylamine (0.57 mL, 4.1 mmol). Then maintained at 10-15 °C and 2,2,2-trichloroethoxycarbonyl chloride (0.288 g, 1.36 mmol) was added and stirred at room temperature for 4 hours. After completion of reaction by TLC, quenched with 10 % Sodium bicarbonate and partitioned with DCM (3X100 mL) and water. Combined organic layer washed with water followed by brine and evaporated. It was then purified by column chromatography using ethyl acetate in hexanes to yield the product as an off white solid (0.42 g, 71.4 %, m. p.: >200 °C). <sup>1</sup>H-NMR (300MHz) in d<sub>6</sub>-DMSO: δ 3.88 (s, 3H), 4.93 (s, 2H), 7.03-6.86 (m, 3ArH), 7.39 (s, 4ArH), 8.13 (dd, J = 1.8, 7.8 Hz, 1ArH), 8.19 (s, 1NH), 9.26 (s, 1NH), 10.03 (bs, 1NH). MALDI-TOF: m/z calcd for C<sub>17</sub>H<sub>16</sub>Cl<sub>3</sub>KN<sub>3</sub>O<sub>4</sub> [M+K]<sup>+</sup>: 469.98; found: 469.94.

#### Synthesis of compound 13:

Compound **xvi** (0.35 g, 1.36 mmol) was dissolved in Acetonitrile and to that Potassium carbonate (0.563 g, 4.1 mmol) was added. Then allyl bromide (0.165 g, 1.36 mmol) was added and maintained at 70 °C. After completion of reaction by TLC, volatiles evaporated and diluted with water and extracted with ethyl acetate (3X100). Combined organic layer washed with water and brine. Evaporated and purified by column chromatography to give the product as a pale brown solid (0.37 g, 80.6 %, m. p.: 140 °C). <sup>1</sup>H-NMR (300MHz) in CDCl<sub>3</sub>: δ 7.75 (s, 3H), 3.93 (d, J = 4.8 Hz, 4H), 5.18 (td, J = 1.2, 14.1 Hz, 4H), 5.92-5.80 (m, 2H), 6.24 (s, 1NH), 6.69 (d, J = 9 Hz, 2ArH), 6.83-6.80 (m, 1ArH), 6.99-6.92 (m, 2ArH), 7.18-7.14 (m, 3ArH), 8.16 (dd, J = 4.5, 7.2 Hz, 1NH). MALDI-TOF: m/z calcd for C<sub>20</sub>H<sub>23</sub>KN<sub>3</sub>O<sub>2</sub> [M+K]<sup>+</sup>: 376.14; found: 376.07.

<sup>1</sup>H-NMR for 1-(4-Amino-phenyl)-3-(2-methoxy-phenyl)-urea:

<sup>1</sup>H-NMR (300MHz) in CDCl<sub>3</sub> + d<sub>6</sub>-DMSO: δ 3.89 (s, 3H), 6.64 (d, J = 8.7 Hz, 2ArH), 6.97-6.85 (m, 3ArH), 7.21 (d, J = 8.7 Hz, 2ArH), 7.89 (s, 1NH), 8.23-8.20 (m, 1ArH), 8.47 (s, 1NH). HRMS (ESI+): m/z calcd for C<sub>14</sub>H<sub>16</sub>N<sub>3</sub>O<sub>2</sub> [M+H]<sup>+</sup>: 258.1243; found: 258.1241.

Synthesis of compound 15:

Compound **10** (0.2 g, 0.42 mmol) was suspended in DCM and Borontribromide (0.625 mL, 0.63 mmol) 1 M solution was added and stirred at room temperature for 6 hours. After completion of reaction by TLC, quenched with water and neutralized with solid sodium bicarbonate. Extracted three times with DCM and evaporated and purified by column chromatography (ethyl acetate in hexane) to give the product as a pale brown solid (0.170 g, 58.0 %, m. p.: >200 °C). <sup>1</sup>H-NMR (300MHz) in CDCl<sub>3</sub> + d<sub>6</sub>-DMSO: δ 4.23 (t, J = 7.5 Hz, 1H), 4.49 (d, J = 6.9 Hz, 2H), 6.96-6.77 (m, 3ArH), 7.44-7.31 (m, 7ArH), 7.70 (t, J = 6.9 Hz, 3ArH), 7.78 (d, J = 7.2 Hz, 2ArH), 8.14 (s, 1ArH), 8.74 (s, 1NH), 8.88 (bs, 1OH), 9.52 (s, 1NH). MALDI-TOF: m/z calcd for C<sub>28</sub>H<sub>23</sub>KN<sub>3</sub>O<sub>4</sub> [M+K]<sup>+</sup>: 504.13; found: 504.08.

Synthesis of compound 16:

Compound **11** (0.2 g, 0.67 mmol) was suspended in DCM and Borontribromide (1.00 mL, 1.00 mmol) 1 M solution was added and stirred at room temperature for 6 hours. After completion of reaction by TLC, quenched with water and neutralized with solid sodium bicarbonate. Extracted three times with DCM and evaporated and purified by column chromatography (ethyl acetate in hexane) to give the product as a pale brown solid (0.115 g, 60.2 %, m. p.: 190 °C). <sup>1</sup>H-NMR (300MHz) in CDCl<sub>3</sub> + d<sub>6</sub>-DMSO: δ 2.21 (s, 3H), 6.84-6.77 (m, 1ArH), 6.88 (d, J = 3.6 Hz, 2 ArH), 7.38 (d, J = 8.7 Hz, 2ArH), 7.49 (d, J = 8.7 Hz, 2ArH), 7.70 (d, J = 7.8 Hz, 1ArH), 8.13 (s, 1NH), 8.78 (s, 1NH), 9.23 (s, 1OH), 9.49 (s, 1NH). MALDI-TOF: m/z calcd for C<sub>15</sub>H<sub>15</sub>NaN<sub>3</sub>O<sub>3</sub> [M+Na]<sup>+</sup>: 308.10; found: 308.03.

Synthesis of compound 17:

Compound **12** (0.2 g, 0.46 mmol) was suspended in DCM and Borontribromide (0.69 mL, 0.69 mmol) 1 M solution was added and stirred at room temperature for 6 hours. After completion of reaction by TLC, quenched with water and neutralized with solid sodium bicarbonate. Extracted three times with DCM and evaporated and purified by column chromatography (ethyl acetate in hexane) to give the product as a pale brown solid (0.120 g, 62.5 %, m. p.: 190 °C). <sup>1</sup>H-NMR (300MHz) in CDCl<sub>3</sub> + d<sub>6</sub>-DMSO: δ 4.84 (s, 2H), 6.88-6.79 (m, 4ArH), 7.47-7.37 (m, 3ArH, 1NH), 7.79 (d, J = 7.5 Hz, 1ArH), 8.14 (s, 1NH), 8.86 (s, 1OH), 9.47 (d, J = 4.3 Hz, 1NH). MALDI-TOF: m/z calcd for C<sub>16</sub>H<sub>14</sub>Cl<sub>3</sub>KN<sub>3</sub>O<sub>4</sub> [M+K]<sup>+</sup>: 455.97; found: 455.89.

### Synthesis of compound 18:

Compound **13** (0.2 g, 0.59 mmol) was suspended in DCM and Borontribromide (0.89 mL, 0.89 mmol) 1 M solution was added and stirred at room temperature for 6 hours. After completion of reaction by TLC, quenched with water and neutralized with solid sodium bicarbonate. Extracted three times with DCM and evaporated and purified by column chromatography (ethyl acetate in hexane) to give the product as a pale brown solid (0.135 g, 71.0 %, m. p.: 112 °C). <sup>1</sup>H-NMR (300MHz) in CDCl<sub>3</sub>: δ 3.95 (d, J = 4.5 Hz, 4H), 5.22-5.16 (m, 4H), 7.92-5.80 (m, 2H), 6.60-6.49 (m, 2NH), 6.81-6.69 (m, 4ArH), 7.16-7.00 (m, 4ArH). MALDI-TOF: m/z calcd for C<sub>19</sub>H<sub>21</sub>KN<sub>3</sub>O<sub>2</sub> [M+K]<sup>+</sup>: 362.13; found: 362.04.

### <sup>1</sup>H-NMR for 1-(4-Amino-phenyl)-3-(2-hydroxy-phenyl)-urea:

<sup>1</sup>H-NMR (300MHz) in CDCl<sub>3</sub> + d<sub>6</sub>-DMSO: δ 6.67 (d, J = 8.4 Hz, 2ArH), 6.88 (d, J = 4.2 Hz, 2ArH), 7.22 (d, J = 8.7 Hz, 2ArH), 7.71-7.56 (m, 2ArH), 8.15-8.06 (m, 2H-NH<sub>2</sub>), 8.41 (s, 1NH), 8.91 (s, OH), 9.65 (s, 1NH). HRMS (ESI<sup>+</sup>): m/z calcd for C<sub>13</sub>H<sub>23</sub>N<sub>3</sub>O<sub>2</sub> [M+Na]<sup>+</sup>: 266.0905; found: 266.0901.

### **General procedure for Boc deprotection:**

The Boc compound **9** (0.1 g, 0.28 mmol) was dissolved in THF (0.5 mL) and to that 5 % aqueous HCl (0.5 mL) was added and stirred at room temperature for 3 hours. After that reaction basified with saturated Sodium bicarbonate and extracted with ethyl acetate. Off white solid obtained (0.065 g, 91.0 %).

### **General procedure for Fmoc deprotection (10 & 15):**

The Fmoc compound **10** (0.1 g, 0.21 mmol) was dissolved in THF and to that piperidine (20 µL) was added and stirred at room temperature for 2 hours. After that time quenched with water and extracted with ethyl acetate to give the product as an off white solid (0.052 g, 97.0 %).

The Fmoc compound **15** (0.1 g, 0.22 mmol) was dissolved in THF and to that piperidine (20 µL) was added and stirred at room temperature for 2 hours. After that time quenched with water and extracted with ethyl acetate to give the product as an off white solid (0.042 g, 78.0 %).

### **General procedure for acetyl deprotection (11 & 16):**

The acetyl compound **11** (0.1 g, 0.33 mmol) was dissolved in THF (0.5 mL) and to that 5%aqueous HCl (0.5 mL) was added and maintained at 70 °C for 6 hours. After that the reaction mass was quenched with saturated Sodium bicarbonate and extracted with ethyl acetate to give the product as an off white solid (0.076 g, 90.0 %).

The acetyl compound **16** (0.1 g, 0.35 mmol) was dissolved in THF (0.5 mL) and to that 5% aqueous HCl (0.5 mL) was added and maintained at 70 °C for 6 hours. After that the reaction mass was quenched with saturated Sodium bicarbonate and extracted with ethyl acetate to give the product as an off white solid (0.079 g, 93.2 %).

#### **General procedure for Troc deprotection (12 & 17):**

The troc compound **12** (0.1 g, 0.23 mmol) was dissolved in Acetic acid (0.5 mL). To that zinc dust (5 mg) was added and stirred at room temperature for 6 hours. After that quenched with water and basified with Sodium bicarbonate. Thereafter, it was extracted with ethyl acetate to obtain the product as an off white solid (0.056 g, 95.0 %).

The troc compound **17** (0.1 g, 0.24 mmol) was dissolved in Acetic acid (0.5 mL). To that zinc dust (5 mg) was added and stirred at room temperature for 6 hours. After that it was quenched with water and basified with Sodium bicarbonate. Thereafter, it was extracted with ethyl acetate to obtain the product as an off white solid (0.055 g, 94.0 %).

#### **General procedure for diallyl deprotection (13 & 18):**

The diallyl compound **13** (0.1 g, 0.3 mmol) was dissolved in THF 0.5 mL and to that Palladium acetate (0.007 g) was added followed by N, N –dimethylbarbituric acid (30 mg) was added and maintained at 70 °C for 4 hours, after that quenched with saturated ammonium chloride and extracted with ethyl acetate to give the product as an off white solid (0.073 g, 95.0 %).

The diallyl compound **18** (0.1 g, 0.31 mmol) was dissolved in THF 0.5 mL and to that Palladium acetate (0.007 g) was added followed by N, N –dimethylbarbituric acid (30 mg) was added and maintained at 70 °C for 4 hours, after that quenched with saturated ammonium chloride and extracted with ethyl acetate to give the product as an off white solid (0.071 g, 94.0 %).

#### ***1-(4-Hydroxy-phenyl)-3-(2-methoxy-phenyl)-urea (20):***

To a well stirred solution of *p*-Aminophenol (0.200 g, 1.80 mmol) in 3 ml THF and 3 ml DCM (1:1), 2-methoxyphenyl isocyanate (0.268 g, 1.8 mmol) was added and kept for stirring at room temperature for 3.5 h (checked by TLC). The solid thus obtained was filtered through a sintered funnel and partitioned between 5% NaHCO<sub>3</sub> and EtOAc for the removal of residual carbamaic acid. The organic portion was then dried over Na<sub>2</sub>SO<sub>4</sub> and concentrated under reduced pressure. We obtained **20** as a white solid (0.464 g, 98%; m. p. 150±2 °C). For NMR quality sample we purified 0.070 g of it by column chromatography (40% EtOAc in hexane). <sup>1</sup>H-NMR in CDCl<sub>3</sub> + d<sub>6</sub>-DMSO (300 MHz): δ 3.78 (s, 3H), 6.99-6.87 (m, 4ArH), 7.20-7.09 (m, 3ArH), 8.19 (s, 1OH), 8.30 (d, J = 5.7 Hz, 1ArH), 8.62 (s, 1NH), 9.10 (s, 1NH). <sup>13</sup>C-NMR in CDCl<sub>3</sub> + d<sub>6</sub>-DMSO (75

MHz):  $\delta$  55.7, 110.6, 116.2, 120.2, 123.9, 125.5, 127.3, 127.5, 150.7, 156.4, 179.3. HRMS (ESI+):  $m/z$  calcd for  $C_{14}H_{15}N_2O_3$   $[M+H]^+$ : 259.1083; found: 259.1081.

***1-(2-Hydroxy-ethyl)-3-(2-methoxy-phenyl)-urea (22):***

To a well stirred solution of ethanolamine (0.050 g, 0.80 mmol) in 3 ml DCM, 2-methoxyphenyl isocyanate (0.119 g, 0.80 mmol) was added and kept for stirring at room temperature for 3.5 h (checked by TLC). The solid thus obtained was filtered through a sintered funnel and partitioned between 5%  $NaHCO_3$  and EtOAc for the removal of residual carbamaic acid. The organic portion was then dried over  $Na_2SO_4$  and concentrated under reduced pressure. We obtained **22** as a white solid (0.166 g, 95%; m. p.  $90 \pm 2$  °C). For NMR quality sample we purified 0.070 g of it by column chromatography (75% EtOAc in hexane).  $^1H$ -NMR in  $CDCl_3$  (300 MHz):  $\delta$  2.45 (bs, 1OH), 3.86 (s, 4H), 3.85 (s, 3H), 6.65 (s, 1ArH), 7.02-6.96 (m, 2ArH), 7.27-7.21 (m, 1ArH), 7.23 (d,  $J = 6.9$  Hz, 1NH), 7.70 (bs, 1NH).  $^{13}C$ -NMR in  $CDCl_3$  (75 MHz):  $\delta$  55.8, 61.7, 112.1, 121.2, 125.0, 127.8, 152.5, 181.1. HRMS (ESI+):  $m/z$  calcd for  $C_{10}H_{15}N_2O_3$   $[M+H]^+$ : 211.1083; found: 211.1087.

***4-[3-(2-Methoxy-phenyl)-ureido]-butyric acid (24):***

To a well stirred solution of GABA (0.080 g, 0.78 mmol) in 3 ml pyridine, 2-methoxyphenyl isocyanate (0.116 g, 0.78 mmol) was added and kept for stirring at room temperature for 3.5 h (checked by TLC). The reaction mass was partitioned between saturated  $NaHCO_3$  and EtOAc for the removal. The organic portion was then dried over  $Na_2SO_4$  and concentrated under reduced pressure. We obtained **24** as a dense liquid (0.180 g, 92%). For NMR quality sample we purified 0.070 g of it by column chromatography (80% EtOAc in hexane).  $^1H$ -NMR in  $d_6$ -DMSO (300 MHz):  $\delta$  1.75 (p,  $J = 7.2$  Hz, 2H), 2.26 (t,  $J = 7.5$  Hz, 2H), 3.45 (d,  $J = 5.7$  Hz, 2H), 3.81 (s, 3H), 7.16-6.88 (m, 3ArH), 7.80 (d,  $J = 6.9$  Hz, 1ArH), 7.88 (s, 1NH), 8.88 (s, 1NH), 12.10 (bs, 1COOH).  $^{13}C$ -NMR in  $d_6$ -DMSO (75 MHz):  $\delta$  24.6, 31.6, 43.6, 56.0, 111.9, 120.3, 126.0, 127.9, 174.7, 181.0. HRMS (ESI+):  $m/z$  calcd for  $C_{12}H_{16}N_2NaO_4$   $[M+H]^+$ : 275.1008; found: 275.1003.