Electronic Supplementary Material (ESI) for CrystEngComm.

Supporting Information

The impact of modular substitution on crystal packing: The tale of two ureas

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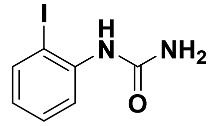
1. Synthesis

1.1 Synthesis of 2-iodophenylurea (3a):


3a

In a 500 ml flask 2-iodoaniline (9.13 mmol) was dissolved in 5 mL of aqueous HCl (2M). 200 mL of water was added to completely dissolve the solid. In another beaker KNCO (13.69 mmol) was dissolved in a minimum volume of water and was dropwise added to the above solution and the reaction mixture was diluted by adding 300 ml of water. After stirring at room temperature for 4 h, a white precipitate was filtered and washed with hot water (20 ml × 3 times). The compound was dried under vacuum, washed with toluene (20 ml × 3 times) and dried under vacuum to yield 2-iodophenylurea (**3a**) in 38%. 3a was crystallized from a 1:1 mixture of ethanol:ethyl acetate.

^{1}H NMR (500 MHz, DMSO-d_6, 298K) $\delta = 7.78$ (ddd, $J_{\text{H-H}} = 12.3$ Hz, 8.3 Hz, 1.4 Hz, 2H, Ar, C*H*), 7.62 (s, 1H, N*H*), 7.28 (t, $J_{\text{H-H}} = 7.8$ Hz, 1H, Ar, C*H*), 6.76 (t, $J_{\text{H-H}} = 7.5$ Hz, 1H, Ar, C*H*), 6.35 (s, 2H, NH_2). **^{13}C NMR** (125 MHz, DMSO-d_6, 298K) $\delta = 155.8$ (s, *C*O), 140.6 (s, Ar, quat), 138.7 (s, Ar, *C*H), 128.4 (s, Ar, *C*H), 124.4 (s, Ar, *C*H), 122.8 (s, Ar, *C*H), 90.8 (s, Ar-I). **IR** (cm^{-1}): 3430 (NH$_2$), 3298 (NH$_2$), 3200 (NH), 1698 (C=O). **ESI-MS** (+ve) (For $C_7H_7IN_2O$) m/z = 262.96 [M+H]$^+$, 284.94 [M+Na]$^+$. **Mp** = 140°C.

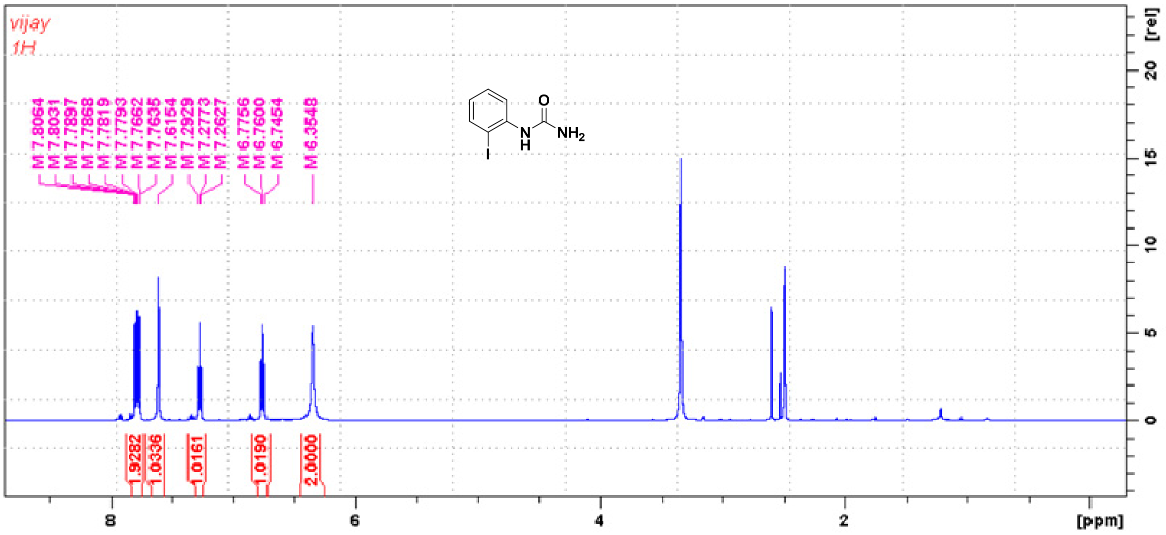


Figure S1. ^{1}H NMR (in DMSO-d_6) of 1-(2-iodophenyl)urea (**3a**).

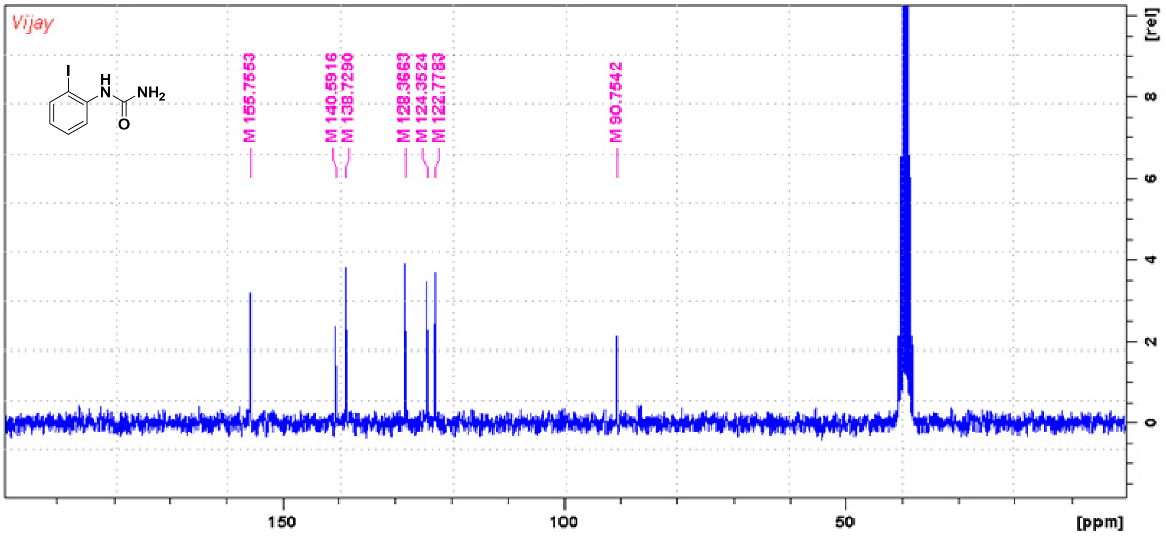


Figure S2. ^{13}C NMR (in DMSO-d$_6$) of 1-(2-iodophenyl)urea (**3a**).

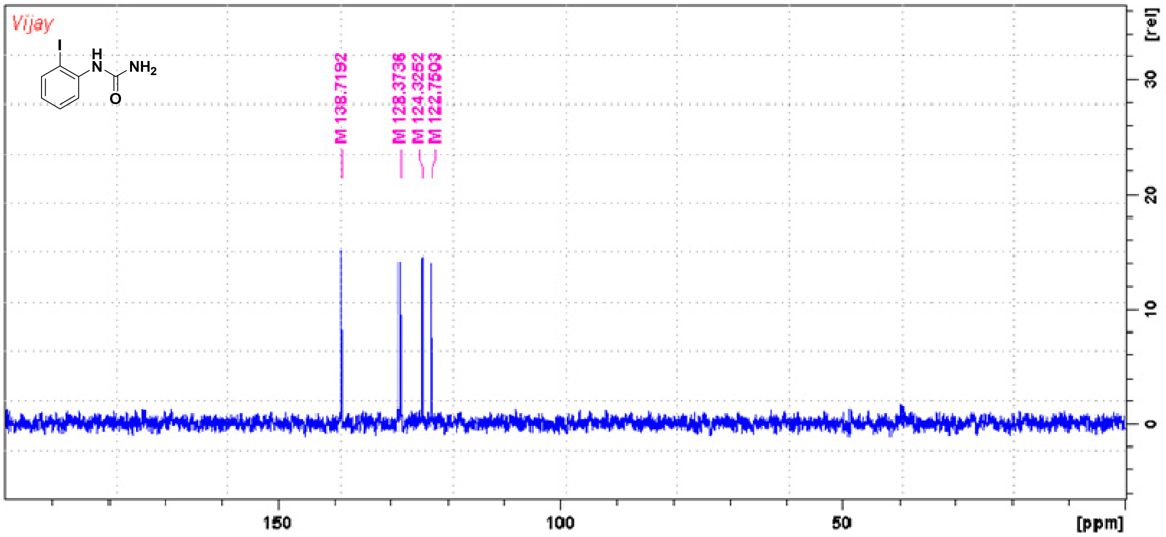


Figure S3. DEPT-135 NMR (in DMSO-d$_6$) of 1-(2-iodophenyl)urea (**3a**).

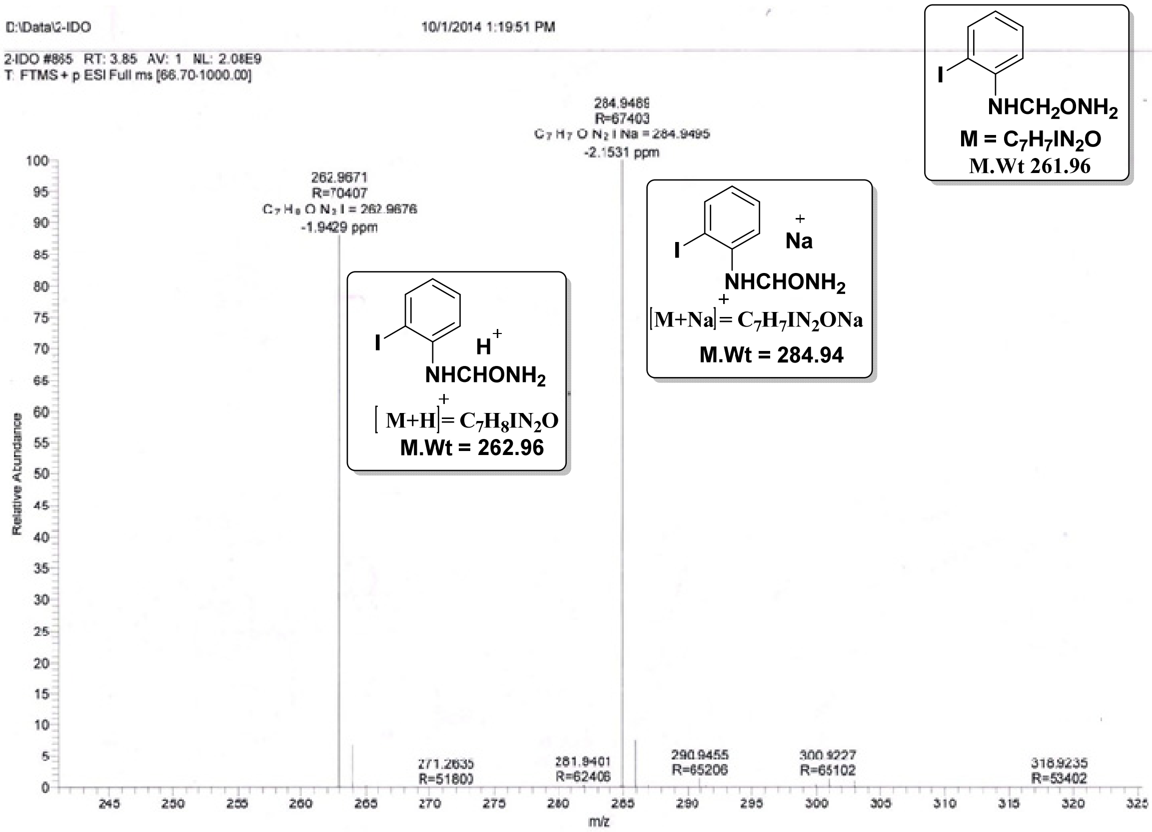
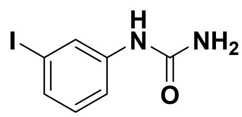


Figure S4. ESI-MS (+ve mode) spectra of 1-(2-iodophenyl)urea (**3a**).

1.2 Synthesis of 3-iodophenylurea (3b):



3b

In a 500 ml flask 3-iodoaniline (4.5 mmol) was dissolved in 10 mL aqueous hydrochloric acid (2M). 200 mL of water was added to completely dissolve the solid. In another beaker KNCO (10.04 mmol) was dissolved in a minimum volume of water and was dropwise added to the above solution and the reaction mixture was diluted by adding 300 ml of water. After stirring at room temperature for 6 h, a white precipitate was filtered and washed with hot water (20 ml × 3 times). The compound was dried under vacuum, washed with toluene (20 ml × 3 times) and dried under vacuum to obtain 3-iodophenylurea (**3b**) in 64% yield. The 3-iodophenyurea was crystallized from a 1:1 mixture of ethanol and ethyl acetate.

^{1}H NMR (500 MHz, DMSO-d$_6$, 298K) δ = 8.66 (s, 1H, N*H*), 7.98 (s, 1H, Ar, C*H*), 7.24 (q, $J_{\text{H-H}}$ = 6.7 Hz, 2H, Ar, C*H*), 6.99 (t, $J_{\text{H-H}}$ = 8.00 Hz, 1H, Ar, C*H*), 5.94 (s, 2H, N*H*$_2$). **^{13}C NMR** (125 MHz, THF-d$_8$, 298K) δ = 157.2 (s, *C*O), 143.3 (s, Ar, quat), 131.2 (s, Ar, *C*H), 131.0 (s, Ar, *C*H), 127.8 (s, Ar, *C*H), 118.3 (s, Ar, *C*H), 94.8 (s, Ar-I). **IR** (cm^{-1}): 3429

(NH_2), 3295 (NH_2), 3203 (NH), 1698 (C=O). **ESI-MS** (+ve) (For $C_7H_7IN_2O$) m/z = 262.96 $[M+H]^+$, 284.94 $[M+Na]^+$. **Mp** = 165°C.

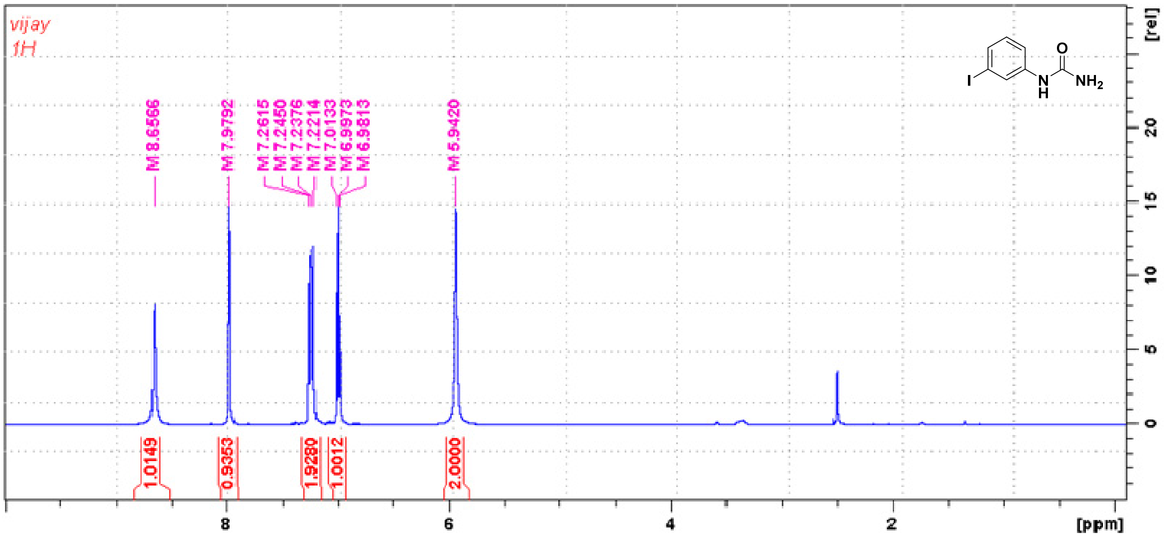


Figure S5. ^1H NMR (in DMSO-d_6) of 1-(3-iodophenyl)urea (**3b**).

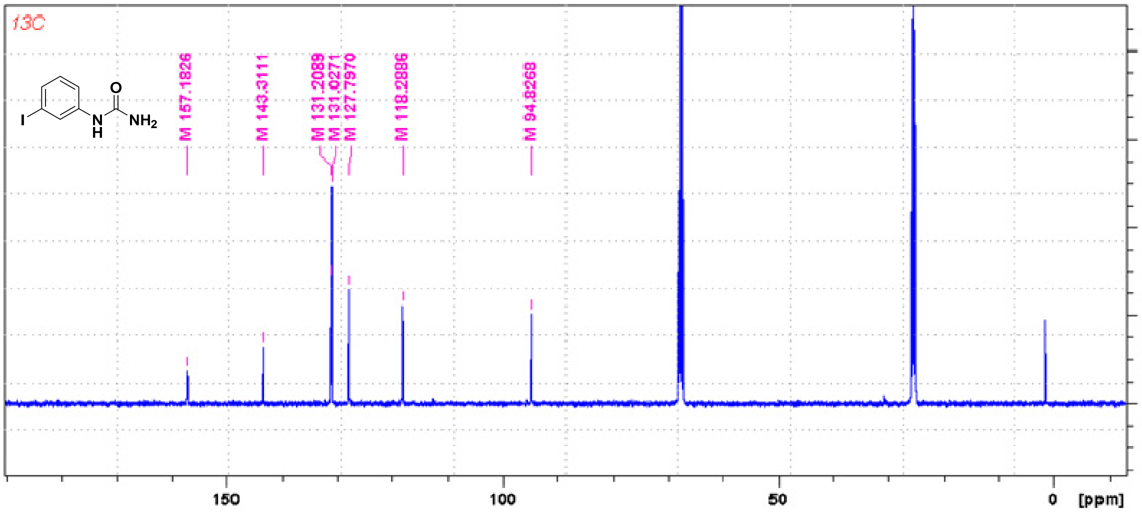


Figure S6. ^{13}C NMR (in THF-d_8) of 1-(3-iodophenyl)urea (**3b**).

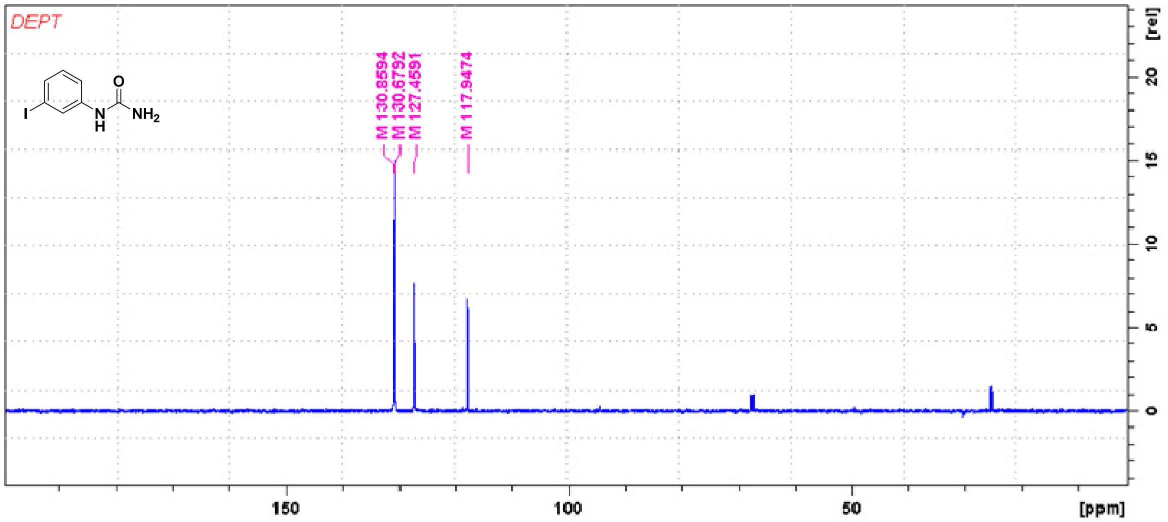


Figure S7. DEPT-135 (in THF-d$_8$) spectrum of 1-(3-iodophenyl)urea (**3b**).

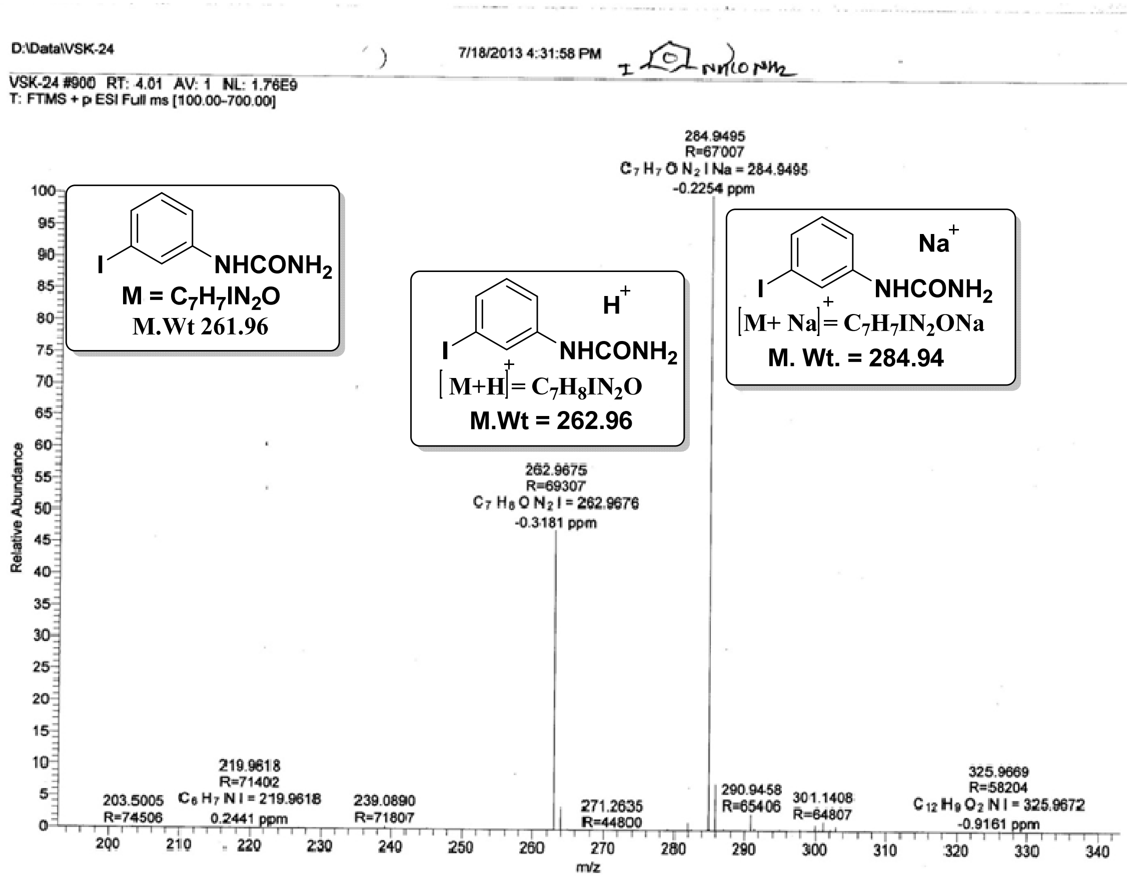
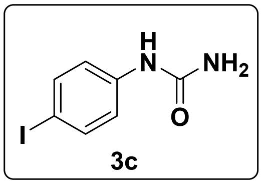


Figure S8. ESI-MS (+ve mode) spectra of 1-(3-iodophenyl)urea (**3b**).

1.3 Synthesis of 1-(4-iodophenyl)urea (3c):

In a 1lit flask 4-iodoaniline (22.83 mmol) was dissolved in 15 mL of dilute (2M) aqueous hydrochloric acid. 200 mL of water was added to completely dissolve



3c

the solid. In another beaker KNCO (45.66 mmol) was dissolved in a minimum volume of water and was dropwise added to the above solution and the reaction mixture was diluted by adding 300 ml of water. After stirring at room temperature for 6 h, a white precipitate was filtered and washed with hot water (20 ml × 3 times). The compound was dried under vacuum, washed with toluene (20 ml × 3 times) and dried under vacuum to obtain 1-(4-iodophenyl)urea (**3c**) in excellent yield (72%). 3c was crystallized from ethanol:ethyl acetate (1:1) mixture.

^{1}**H NMR** (500 MHz, DMSO-d_6, 298K) δ = 8.7 (s, 1H, N*H*), 7.52 (s, 2H, Ar, C*H*), 7.26 (s, 2H, Ar, C*H*), 5.93 (s, 2H, N*H*$_2$). ^{13}**C NMR** (125 MHz, DMSO-d_6, 298K) δ = 155.8 (s, *C*O), 140.5 (s, Ar, quat), 137.1 (s, Ar, *C*H), 120.0 (s, Ar, *C*H), 83.6 (s, Ar-I). **IR** (cm^{-1}): 3423 (NH_2), 3303 (NH_2), 3259 (NH), 1654 (C=O). **ESI-MS** (+ve) (For $C_7H_7IN_2O$) m/z = 262.96 $[M+H]^+$, 284.94 $[M+Na]^+$. **Mp** = 220^{o}C.

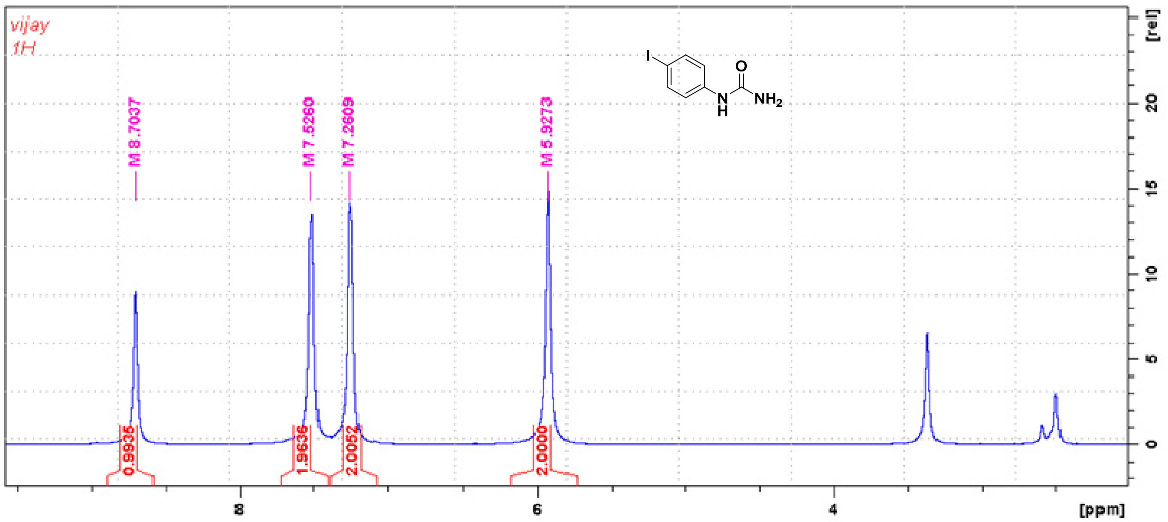


Figure S9. ^{1}H NMR (in DMSO-d_6) of 1-(4-iodophenyl)urea (**3c**).

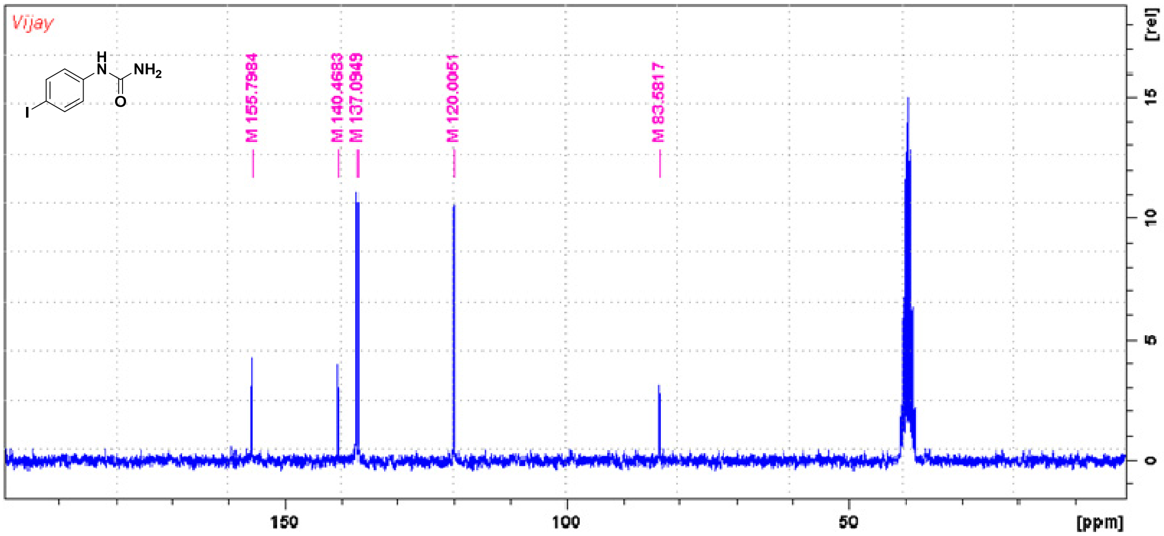


Figure S10. ^{13}C NMR (in DMSO-d$_6$) of 1-(4-iodophenyl)urea (**3c**).

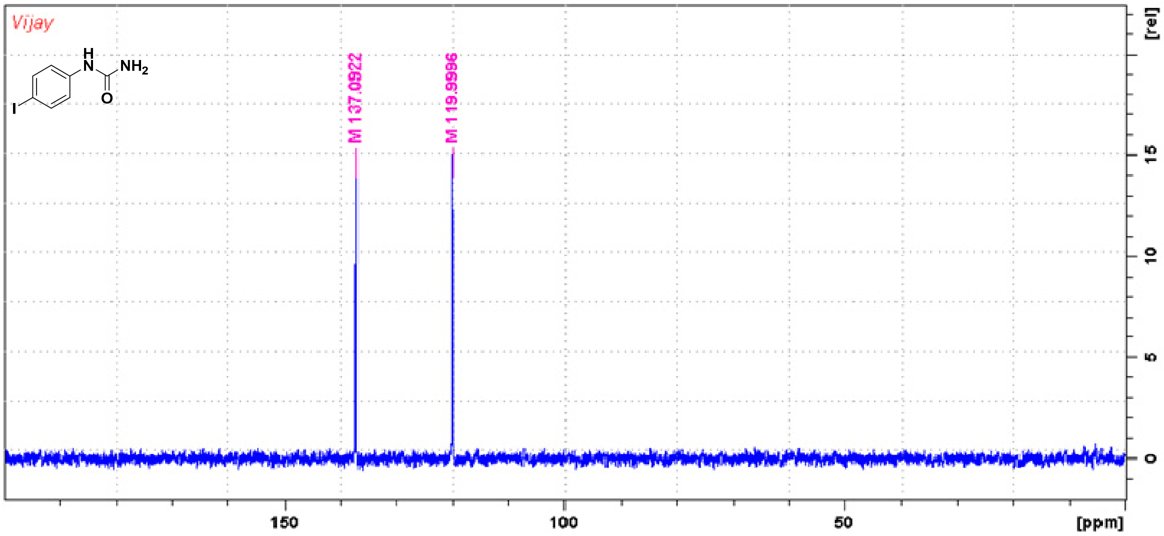


Figure S11. DEPT-135 NMR (in DMSO-d$_6$) of 1-(4-iodophenyl)urea (**3c**).

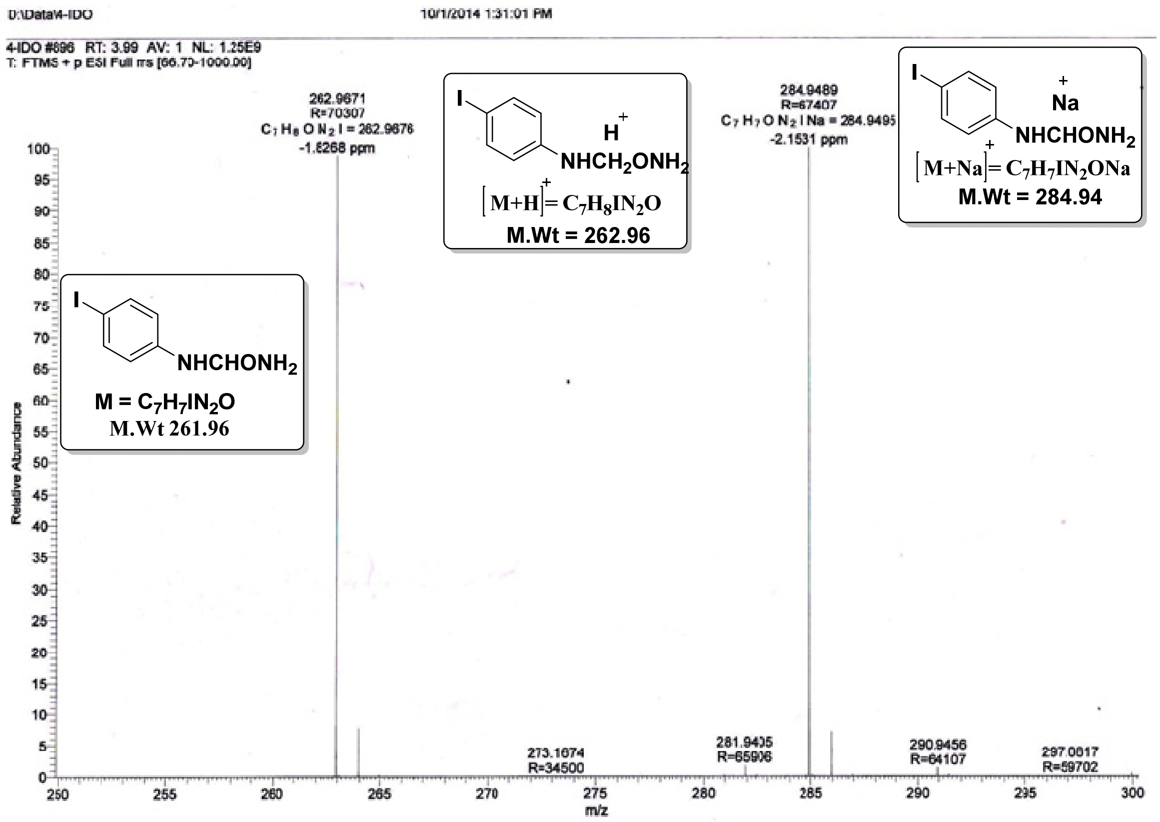
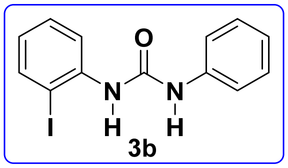


Figure S12. ESI-MS (+ve mode) spectra of 1-(4-iodophenyl)urea (**3c**).

1.4 1-(2-iodophenyl)-3-phenylurea (3d):



3b

A 10 ml dichloromethane solution of 2-Iodoaniline (9.13 mmol) was taken in a 100 ml Schlenk flask and kept at 0°C. Phenyl isocyanate (10.04 mmol) was added dropwise to the reaction mixture with constant stirring at 0°C. After that the reaction mixture was allowed to warm to room temperature and was stirred overnight. The progress of the reaction was monitored by TLC. The volatiles were evaporated under reduced pressure and the product was purified by silica gel column chromatography (ethyl acetate : petroleum ether (10:90)) to yield 81% of **3d**. This compound was crystallized from a DMF:ethyl acetate (1:1) mixture at room temperature.

^{1}**H NMR** (500 MHz, DMSO-d$_6$, 298K) δ = 9.44 (s, 1H, N*H*), 7.90 (s, 1H, N*H*), 7.86 (dd, $J_{\text{H-H}}$ = 7.95 Hz, 1.14Hz, 1H, Ar, C*H*), 7.83 (dd, $J_{\text{H-H}}$ = 7.92 Hz, 1.12Hz, 1H, Ar, C*H*), 7.50 (s, 1H, Ar, C*H*), 7.48 (s, 1H, Ar, C*H*),7.34 (s, 1H, Ar, C*H*), 7.30 (td, 8.6Hz, 1.3Hz, 2H, Ar, C*H*), 6.98 (t, J_{H-H} = 7.28 Hz, 1H, Ar, C*H*), 6.83 (td, 7.65Hz, 1.2Hz, 1H, Ar, C*H*). **^{13}C NMR** (500 MHz, DMSO-d_6, 298K) δ = 152.3 (s, quat, C=O), 139.8 (s, quat, Ar), 139.6 (s, quat, Ar), 138.9 (s, Ar), 128.8 (s, Ar), 128.5 (s, Ar), 125.0 (s, Ar), 123.0 (s, Ar), 122.0 (s, Ar), 118.2 (s, Ar), 91.3 (s, quat, Ar, C-*I*). **IR** (cm^{-1}): 3284 (NH), 1644 (C=O). **ESI-MS** (+ve) (Cal. For $C_{13}H_{11}N_2OI$) m/z = 338.99 $[M+H]^+$, 360.98 $[M+Na]^+$. **Mp** = 190 °C.

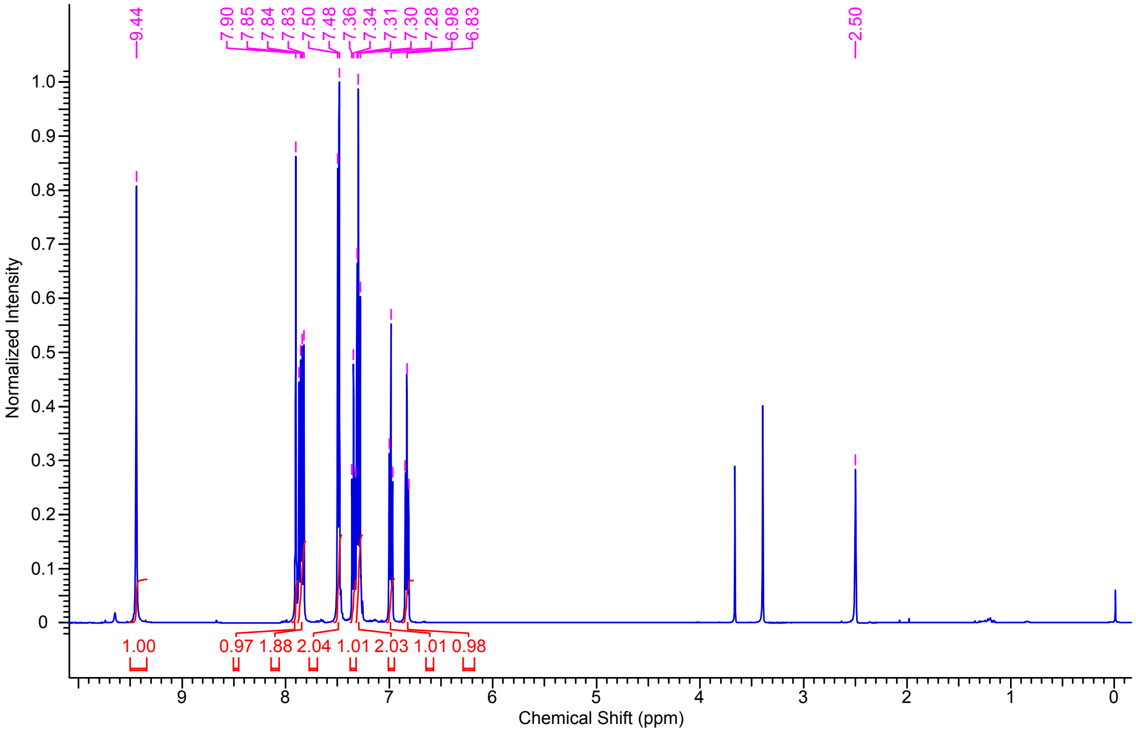


Figure S13. ^{1}H-NMR spectrum of 1-(2-iodophenyl)-3-phenylurea (**3d**) in DMSO-d_6.

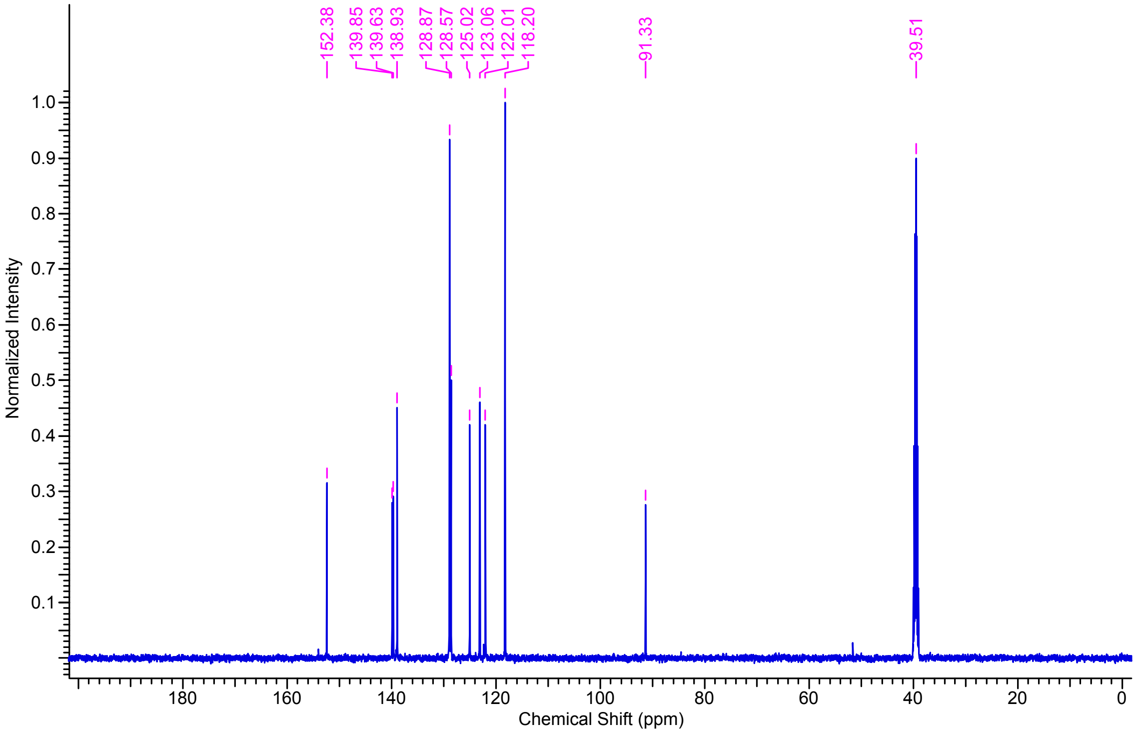


Figure S14. ^{13}C-NMR spectrum of 1-(2-iodophenyl)-3-phenylurea (**3d**) in DMSO-d$_6$.

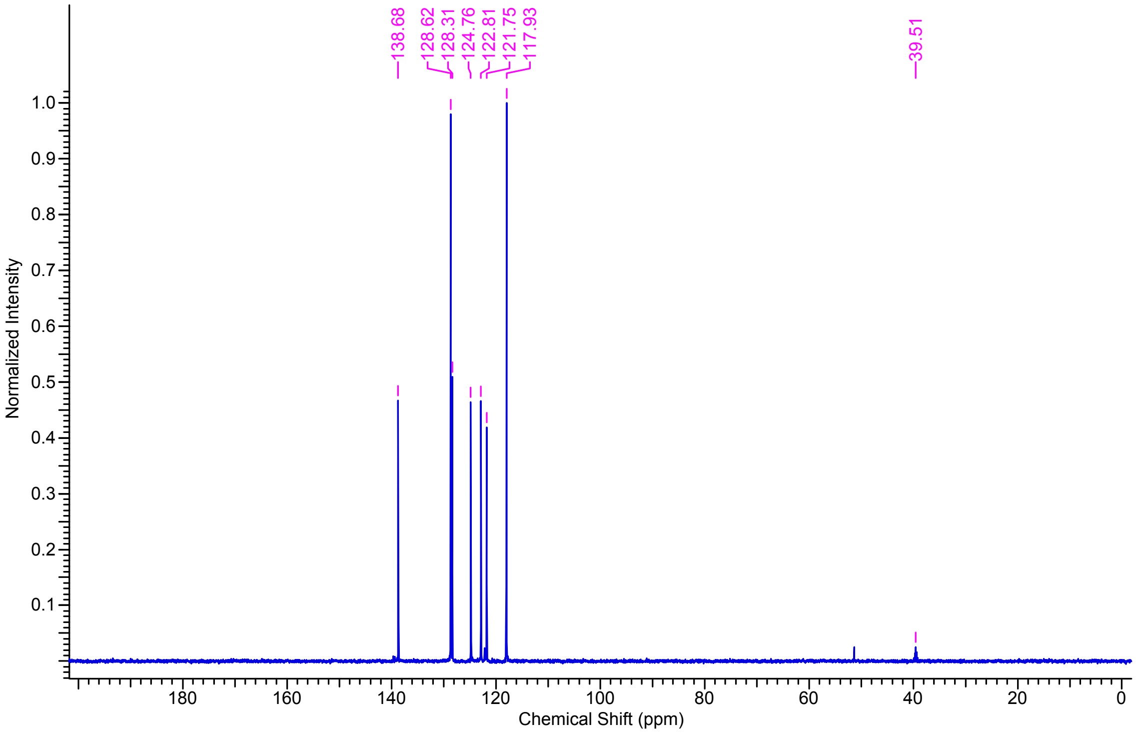


Figure S15. ^{13}C-NMR spectrum of 1-(2-iodophenyl)-3-phenylurea (**3d**)in DMSO-d$_6$.

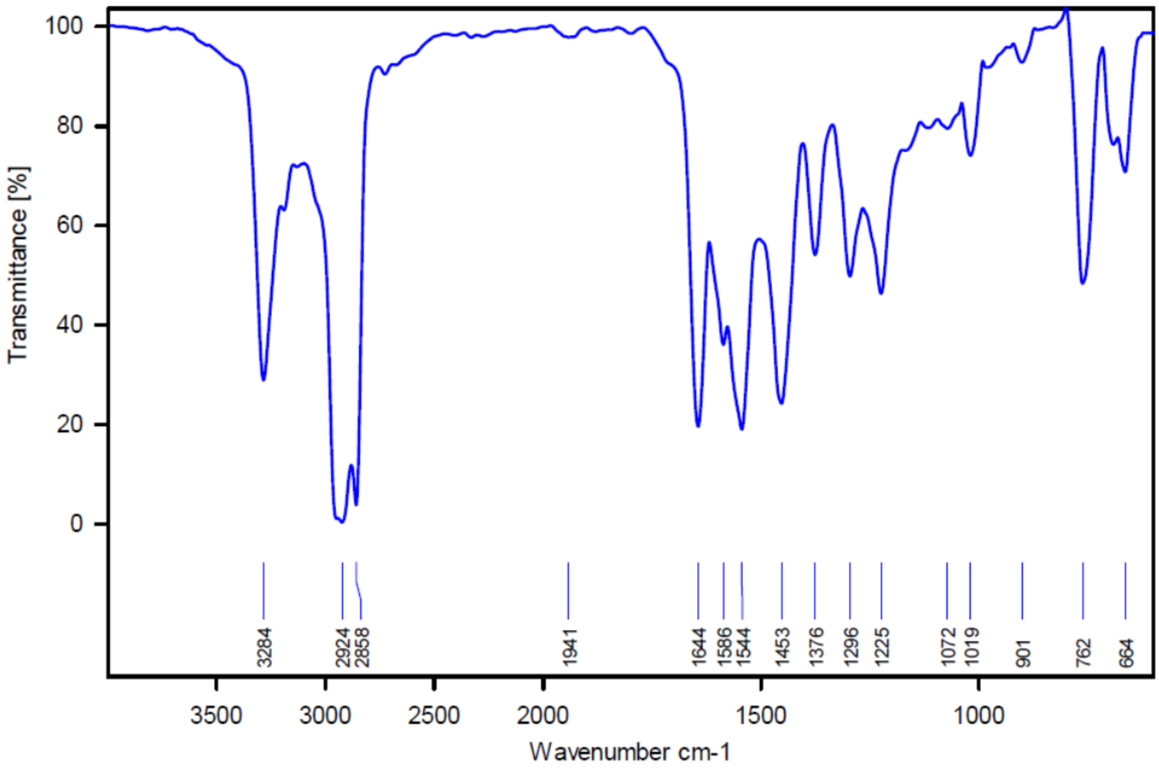


Figure S16. IR spectrum of 1-(2-iodophenyl)-3-phenylurea (**3d**).

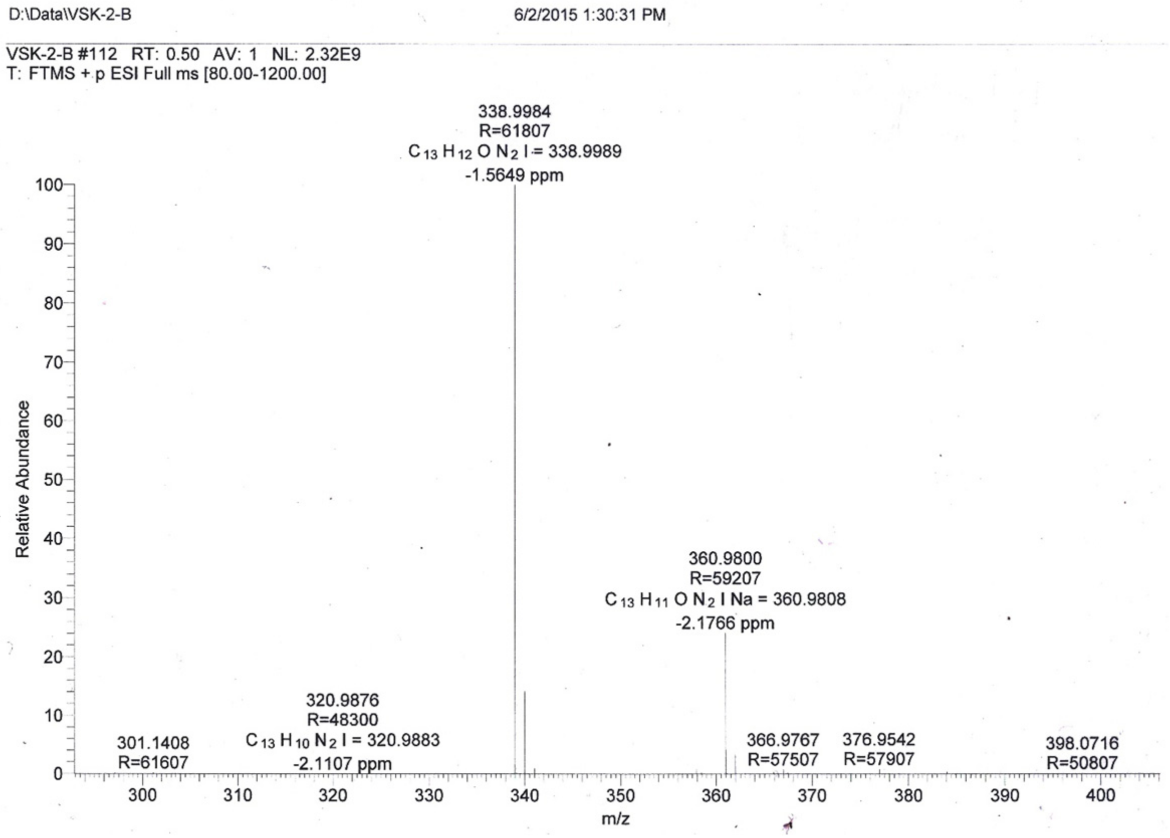
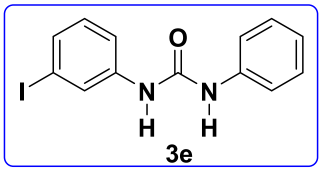


Figure S17. ESIMS (+ve mode) spectrum of 1-(2-iodophenyl)-3-phenylurea (**3d**).

1.5 1-(3-iodophenyl)-3-phenylurea (3e):



3e

In a 100 ml flask, 20 ml DCM was taken and 3-Iodoaniline (9.13 mmol) was dissolved. The reaction mixture was cooled to 0°C and phenyl isocyanate (10.04 mmol) was dropwise added to the reaction mixture with constant stirring. The reaction mixture allowed to warm to room temperature and stirred it for 2 h. The progress of the reaction was monitored by TLC. Volatiles were evaporated under reduced pressure and the product was purified by silica gel column chromatography (ethyl acetate : petroleum ether (40:60)) in 86% yield. This compound was crystallized from a DMF : ethyl acetate (1:1) mixture at room temperature.

^{1}H NMR (200 MHz, DMSO-d$_6$, 298K) δ = 8.75 (s, 1H, N*H*), 8.67 (s, 1H, N*H*), 7.97 (d, 1.8Hz, 1H, C*H*), 7.42 (s, 1H, Ar, C*H*), 7.39 (s, 1H, Ar, C*H*), 7.27-7.22 (m, 4H, Ar, C*H*), 7.03 (t, $J_{\text{H-H}}$ = 8.32 Hz 1H, Ar, C*H*), 6.94 (t, $J_{\text{H-H}}$ = 7.33 Hz, 1H, Ar, C*H*). **^{13}C NMR** (100 MHz, DMSO-d$_6$, 298K) δ = 152.4 (s, quat, C=O), 141.2 (s, quat, Ar), 139.4 (s, quat, Ar), 130.8 (s, Ar), 130.3(s, Ar), 128.8 (s, Ar), 126.3 (s, Ar), 122.1 (s, Ar), 118.4 (s, Ar), 117.5 (s, Ar), 94.8 (s, quat, Ar). **IR** (cm^{-1}): 3295 (NH), 1631 (C=O). **ESI-MS** (+ve) (Cal. For $C_{13}H_{11}N_2OI$) m/z = 338.99 [M+H]$^+$, 360.98 [M+Na]$^+$. **Mp** = 195°C.

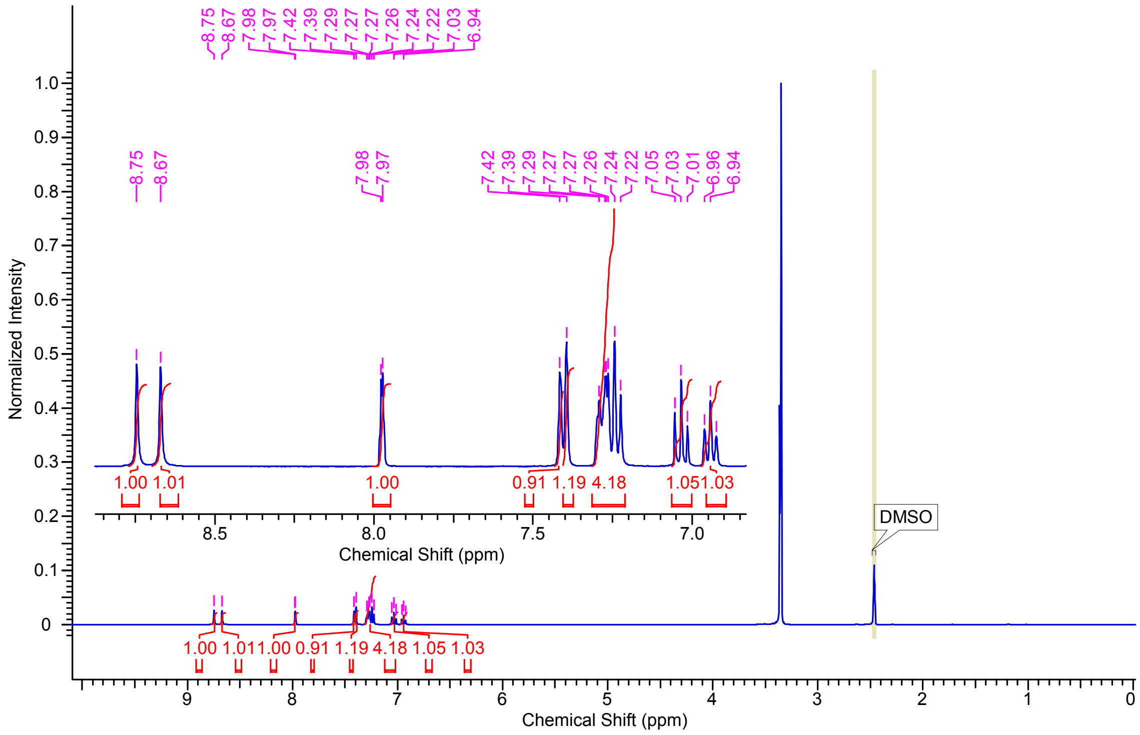


Figure S18. ^{1}H-NMR spectrum of 1-(3-iodophenyl)-3-phenylurea (**3e**) in DMSO-d$_6$.

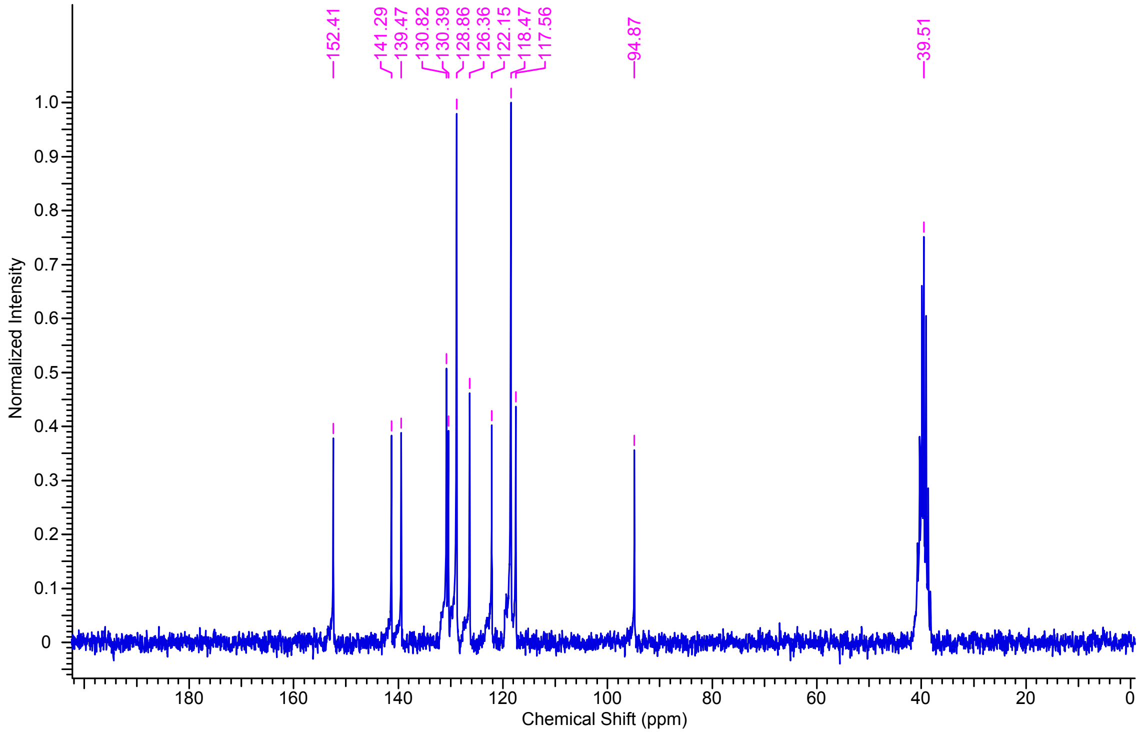


Figure S19. ^{13}C-NMR spectrum of 1-(3-iodophenyl)-3-phenylurea (**3e**) in DMSO-d$_6$.

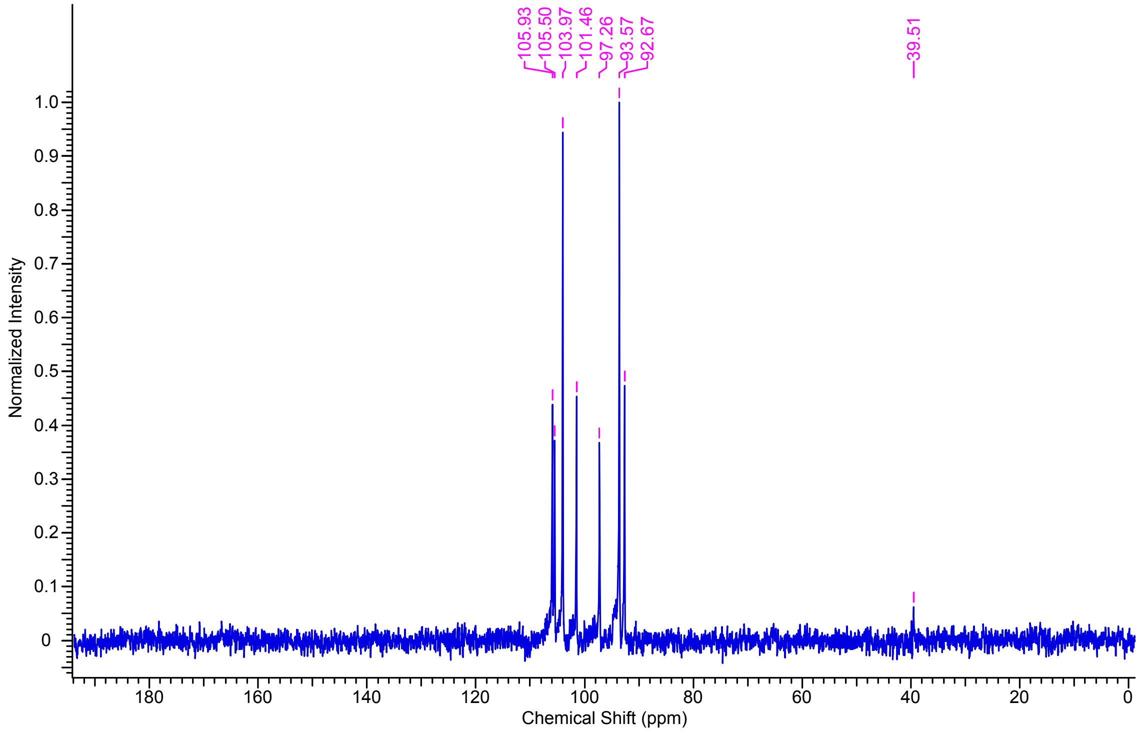


Figure S20. ^{13}C-NMR (DEPT) spectrum of 1-(3-iodophenyl)-3-phenylurea (**3e**) in DMSO-d$_6$.

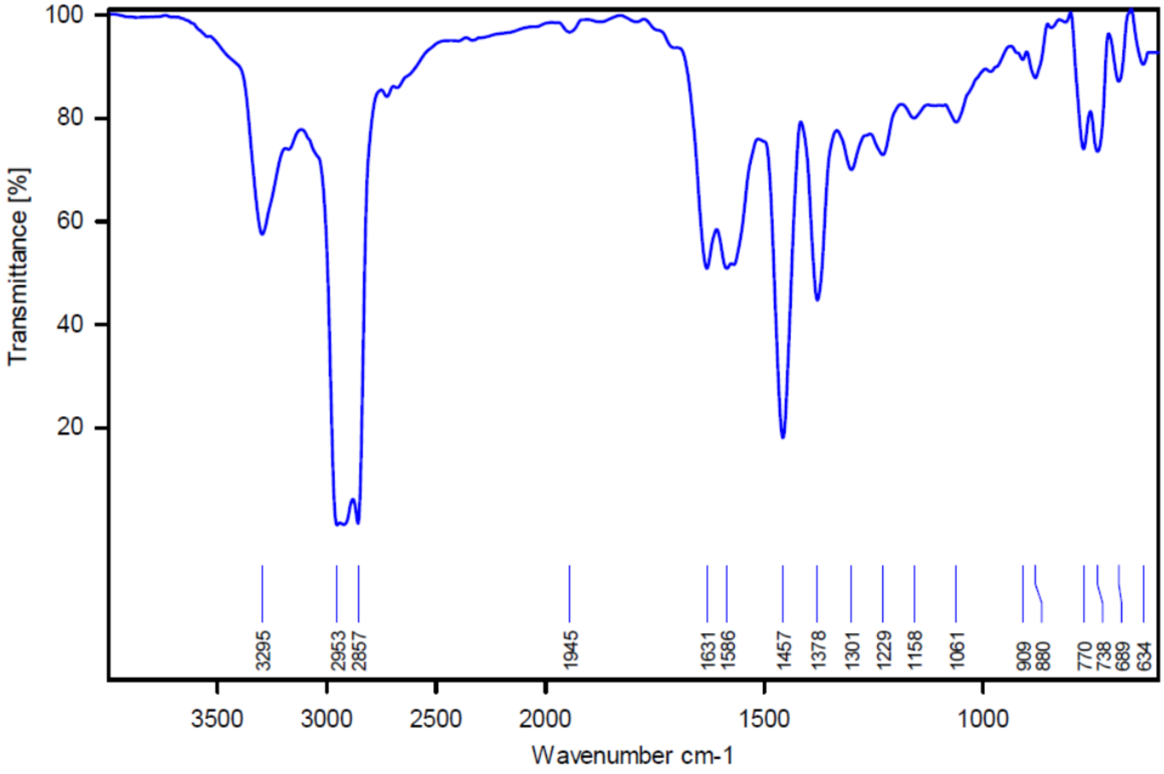


Figure S21. IR spectrum of 1-(3-iodophenyl)-3-phenylurea (**3e**).

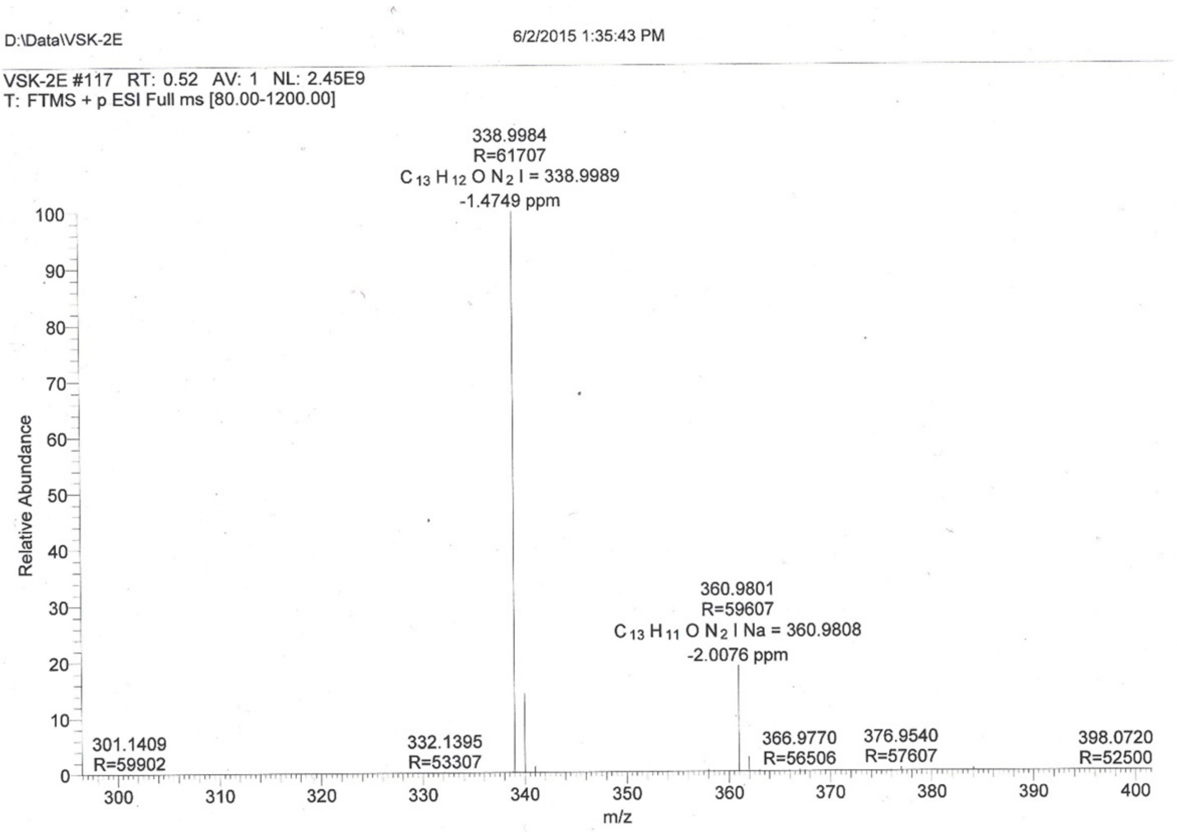
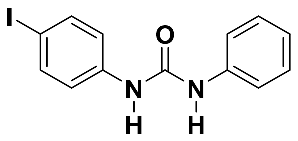


Figure S22. ESIMS (+ve mode) spectrum of 1-(3-iodophenyl)-3-phenylurea (**3e**).

1.6 1-(4-iodophenyl)-3-phenylurea (3f):

In a 100 ml flask, DCM (20 ml) solution of 4-Iodoaniline (9.13 mmol) was taken and the reaction mixture was cooled to 0°C. Phenyl isothiocyanate (10.04 mmol) was added dropwise to the reaction mixture with constant stirring. After that the reaction mixture allowed to warm to room temperature and was stirred for 4 h. The progress of the reaction was monitored by TLC. Volatiles were evaporated from the reaction mixture by reducing pressure and the product was purified by silica gel column chromatography (ethyl acetate : petroleum ether (30:70)) in 90% yield. This compound was crystallized form a 1:1 mixture of DMF and ethyl acetate at room temperature.



3f

^{1}H NMR (400MHz, DMSO-d$_{6,}$ 298K) δ = 8.79 (s, 1H, N*H*), 8.70 (s, 1H, N*H*), 7.60 (d, $^{J}_{\text{H-H}}$ = 8.66 Hz, 2H, C*H*), 7.46 (d, $^{J}_{\text{H-H}}$ = 7.66Hz, 2H, C*H*), 7.33 (d, $J_{\text{H-H}}$ = 8.66 Hz, 2H, C*H*), 7.28 (t, $^{J}_{\text{H-H}}$ = 7.66 Hz, 2H, C*H*), 6.98 (t, $J_{\text{H-H}}$ = 7.34 Hz, 1H, C*H*). **^{13}C NMR** (100 MHz, 298K, DMSO-d_6) δ = 152.3 (s, quat, C=O), 139.6 (s, quat, Ar), 139.5 (s, quat, Ar), 137.3 (s, Ar, *C*H), 128.3 (s, Ar, *C*H), 121.8 (s, Ar, *C*H), 120.4 (s, Ar, *C*H), 118.3 (s, Ar, *C*H), 84.6 (s, quat, Ar). **IR** (cm^{-1}): 3300 (NH), 1632 (C=O). **ESI-MS** (+ve) (Cal. For $C_{13}H_{11}N_2OI$) m/z = 338.99 $[M+H]^+$, 360.98 $[M+Na]^+$. **Mp**= 150°C.

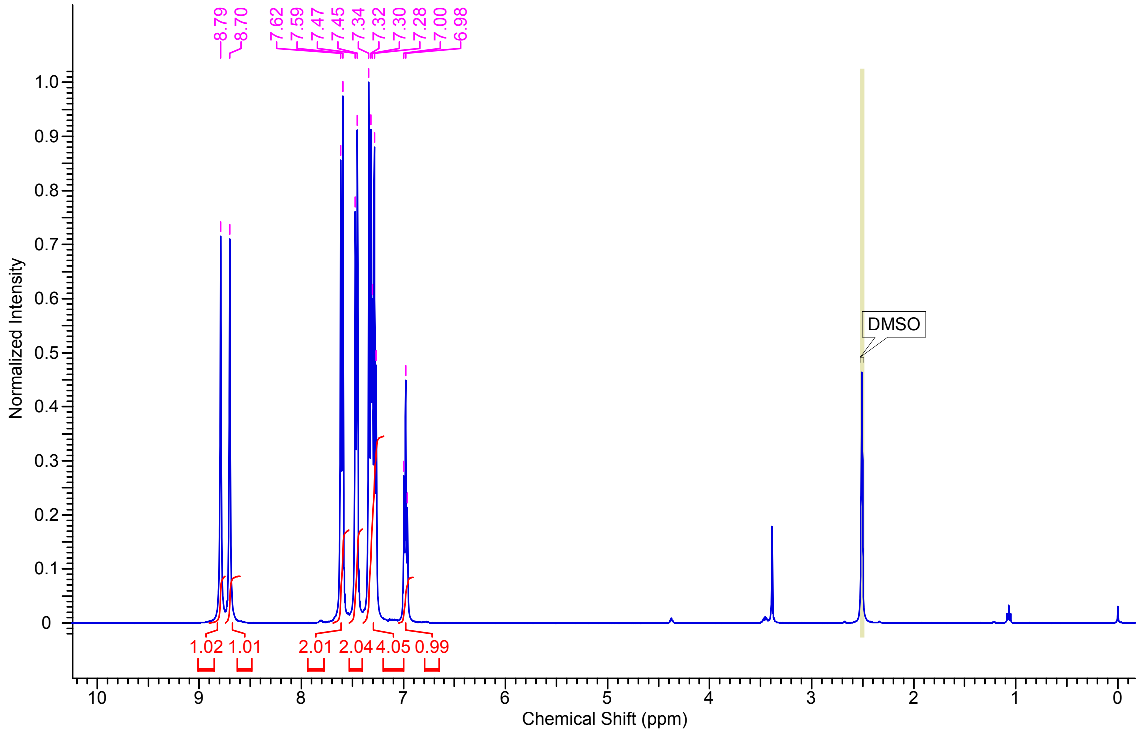


Figure S23. ^{1}H-NMR spectrum of 1-(4-iodophenyl)-3-phenylurea (**3f**) in DMSO-d_6.

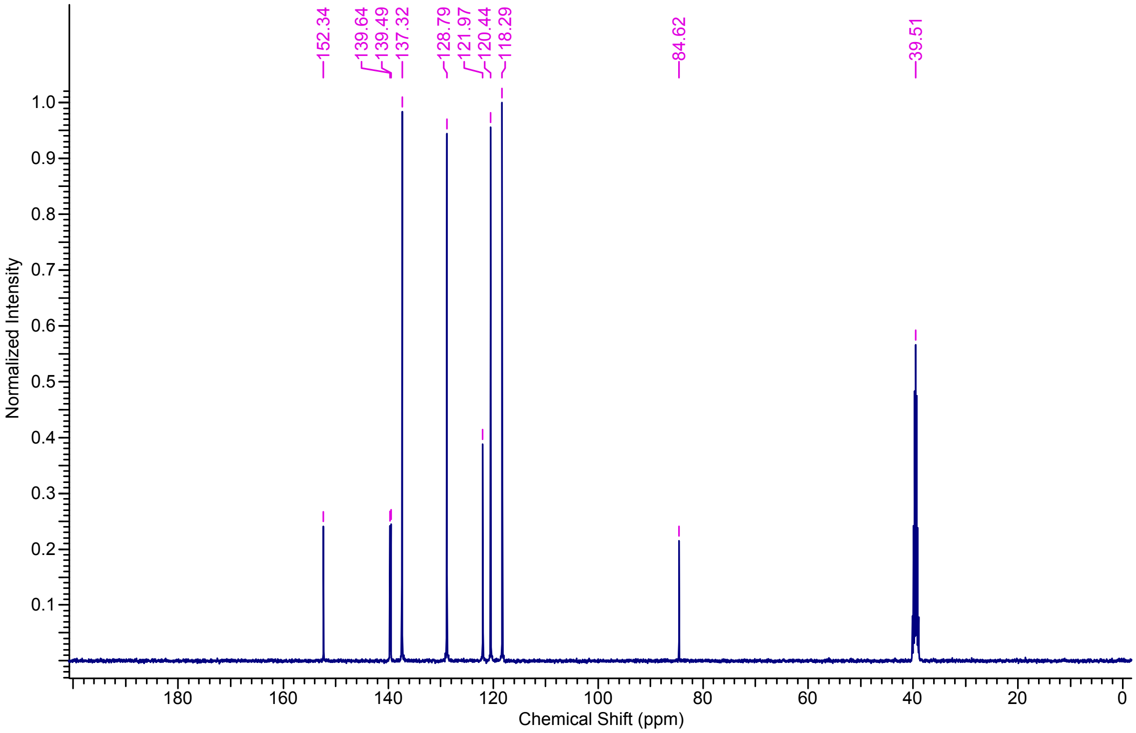


Figure S24. ^{13}C-NMR spectrum of 1-(4-iodophenyl)-3-phenylurea (**3f**) in DMSO-d$_6$.

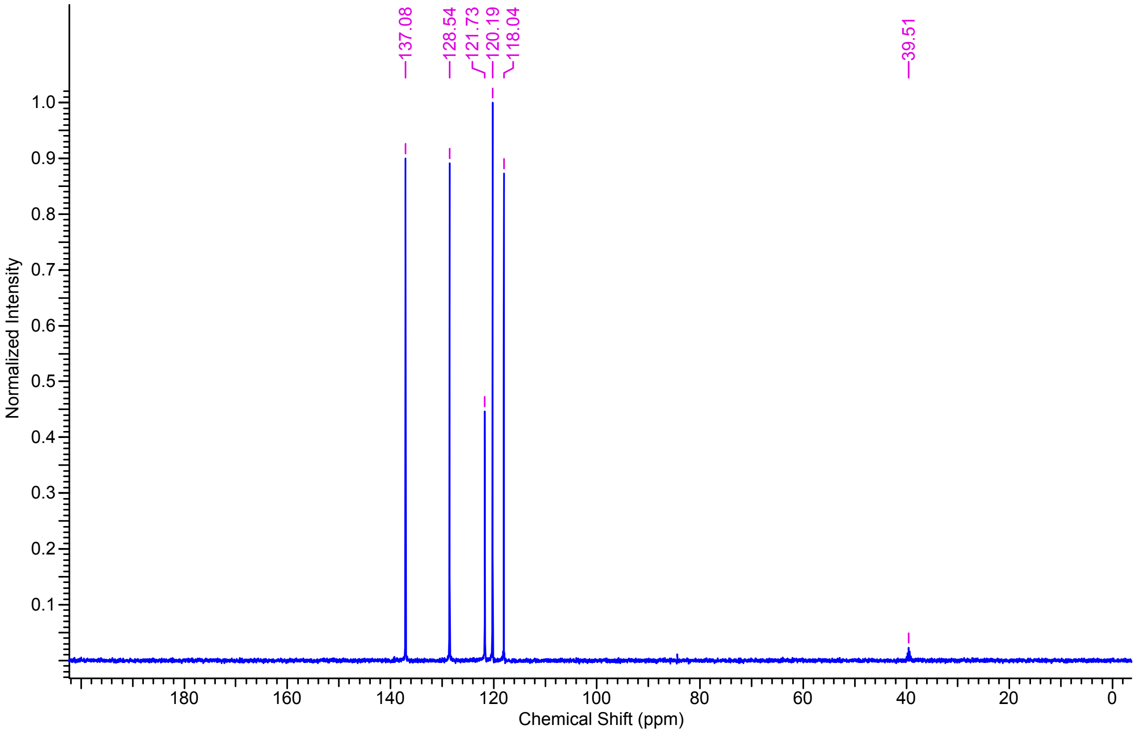


Figure S25. ^{13}C-NMR (DEPT) spectrum of 1-(4-iodophenyl)-3-phenylurea (**3f**) in DMSO-d$_6$.

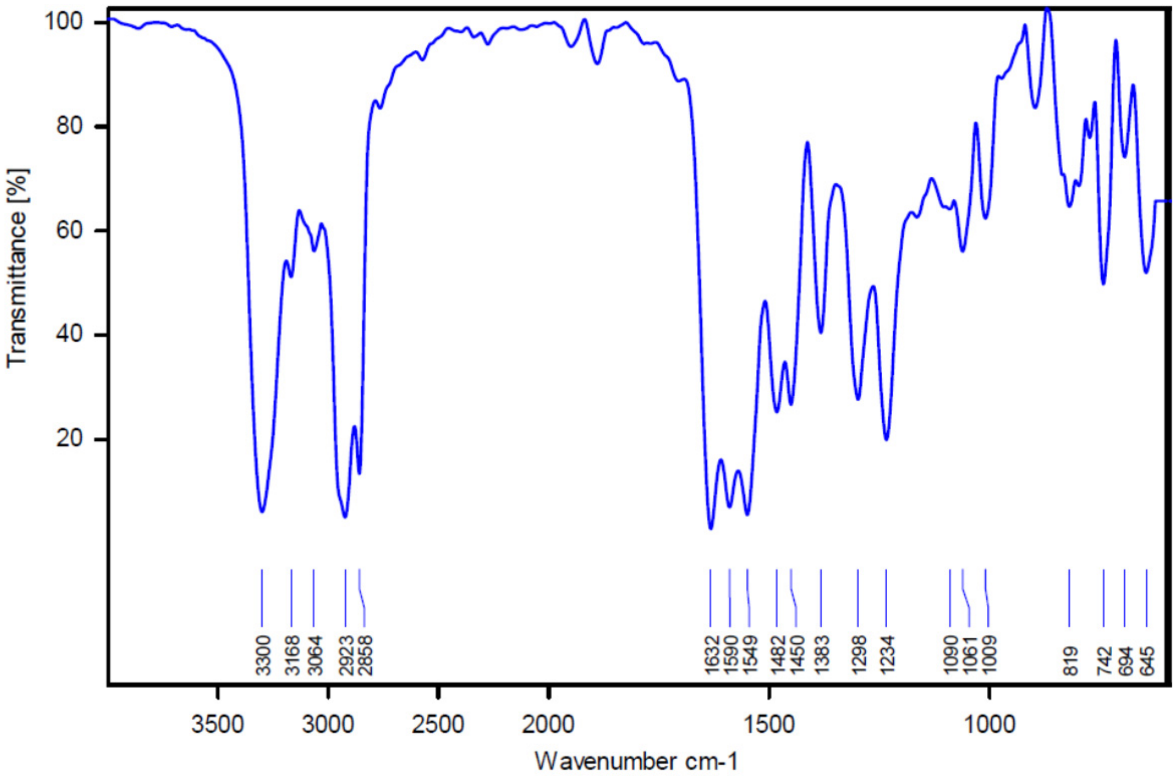


Figure S26. IR spectrum of 1-(4-iodophenyl)-3-phenylurea (**3f**).

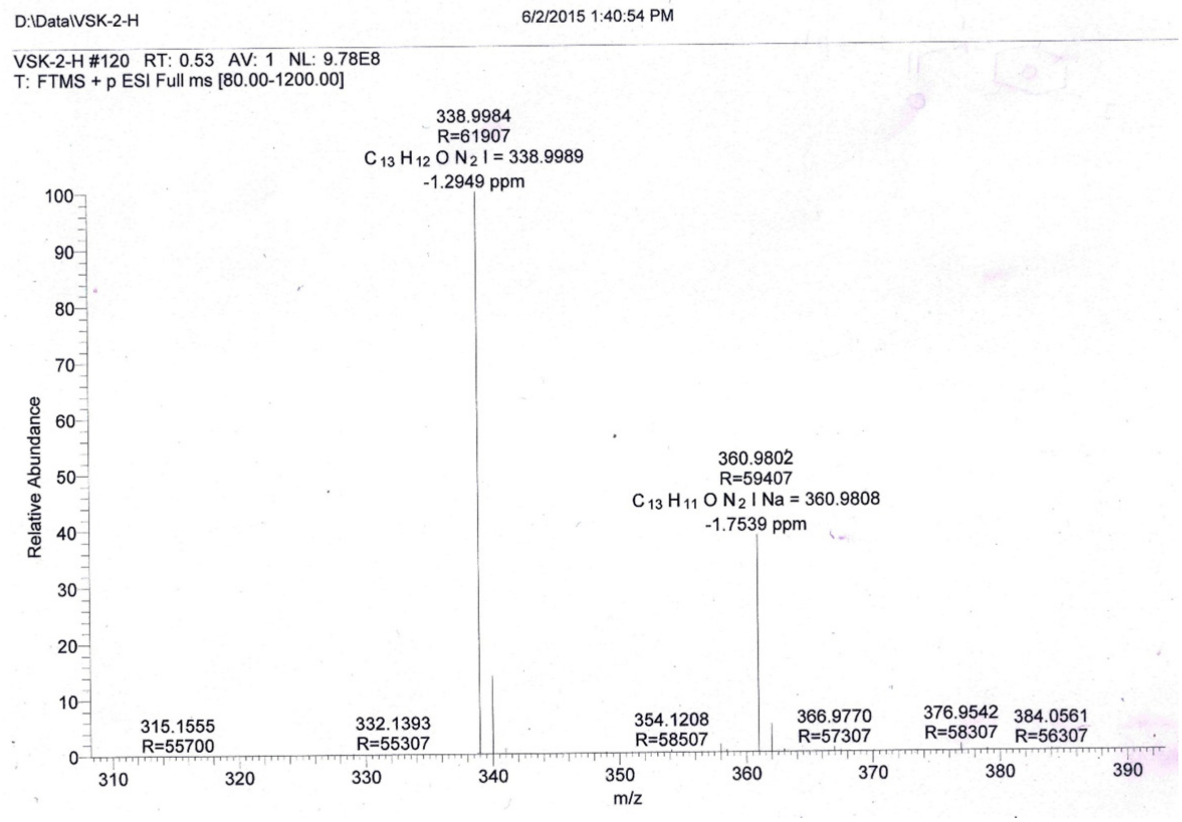
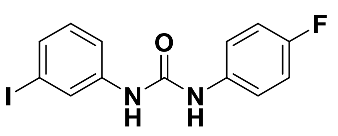


Figure S27. ESI-MS (+ve mode) spectrum of 1-(4-iodophenyl)-3-phenylurea (**3f**).

1.7 Synthesis of 1-(4-fluorophenyl)-3-(3-iodophenyl)urea (3g):

20 ml dichloromethane was taken in a 100 ml flask and 3- Iodoaniline (10.2 mmol) was dissolved in it. The reaction mixture was then cooled to 0°C and phenyl isothiocyanate (7.29 mmol) was added dropwise to the reaction mixture with constant stirring. The reaction mixture was allowed to warm to room temperature and was stirred for 4 h. The progress of the reaction was monitored by TLC. Solvent was evaporated under reduced pressure and the product was purified by column chromatography (ethyl acetate : petroleum ether (60:40)) in 81% yield. **3g** was crystallized from a 1:1 mixture of DMF and ethyl acetate at room temperature.



3g

^{1}**H NMR** (500 MHz, , DMSO-d$_6$, 298K): δ = 8.78 (s, 1H, N*H*), 8.75(s, 1H, N*H*), 8.01 (s, 1H, Ar, C*H*), 7.46 (q, $J_{\text{H-H}}$ = 7.26 Hz, 2H, Ar, C*H*), 7.32 (q, $J_{\text{H-H}}$ = 8.98 Hz, 2H, Ar, C*H*), 7.12 (t, $J_{\text{H-H}}$ = 7.10 Hz, 2H, Ar, C*H*), 7.06 (t, $J_{\text{H-H}}$ = 7.05 Hz, 1H, Ar, C*H*). ^{13}**C NMR** (125 MHz, DMSO-d$_6$, 298K): δ = 158.4 (s, quat, C=S), 152.4 (s, quat, Ar), 141.2 (s, quat, Ar), 135.7 (s, quat, Ar), 130.7 (s, Ar, CH), 130.3 (s, Ar, CH), 126.3 (s, Ar, CH), 120.2 (d, Ar, CH), 117.5 (s, Ar, CH), 115.2 (s, Ar, CH), 94.7 (s, quat, Ar, C-I). **IR (cm^{-1}):** 3300 (NH), 1632 (C=O). **ESI-MS** (+ve) (Cal. For $C_{13}H_{11}N_2OFI$) m/z = 356.98 [M+H]$^+$, 378.97 [M+Na]$^+$. **Mp** = 210^{o}C.

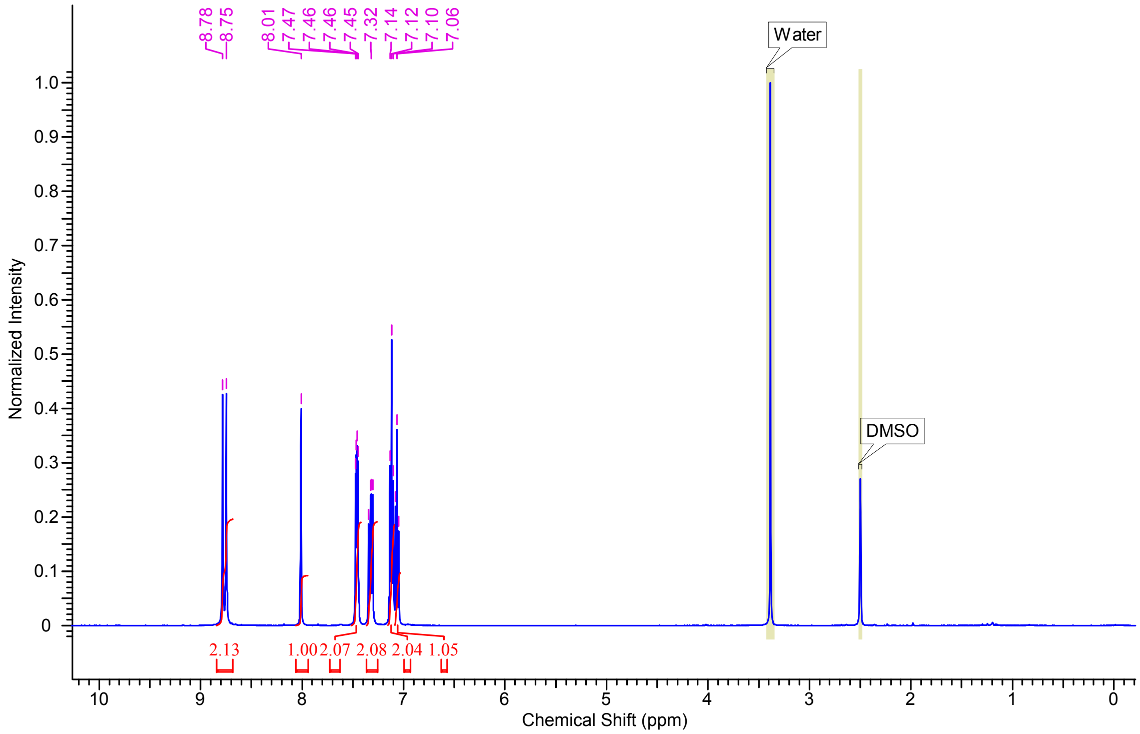


Figure S28. ^{1}H-NMR spectrum of 1-(4-fluorophenyl)-3-(3-iodophenyl)urea (**3g**) in DMSO-d_6.

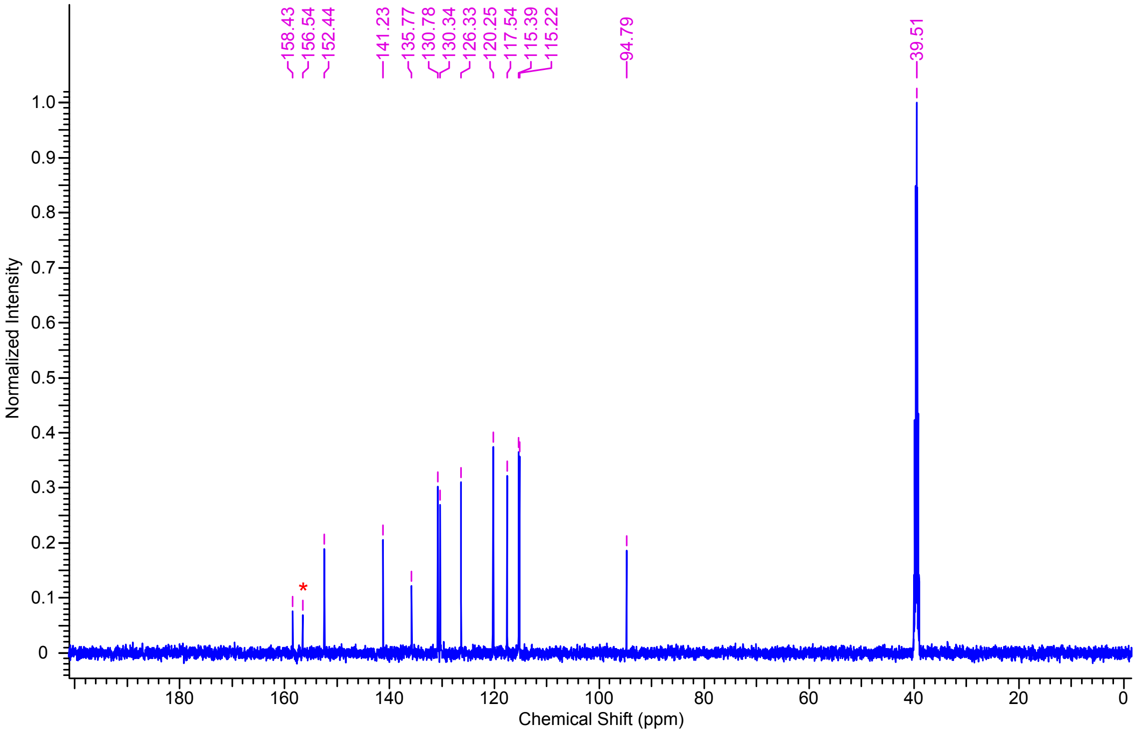


Figure S29. ^{13}C-NMR spectrum of 1-(4-fluorophenyl)-3-(3-iodophenyl)urea (**3g**) in DMSO-d$_6$.(* impurity)

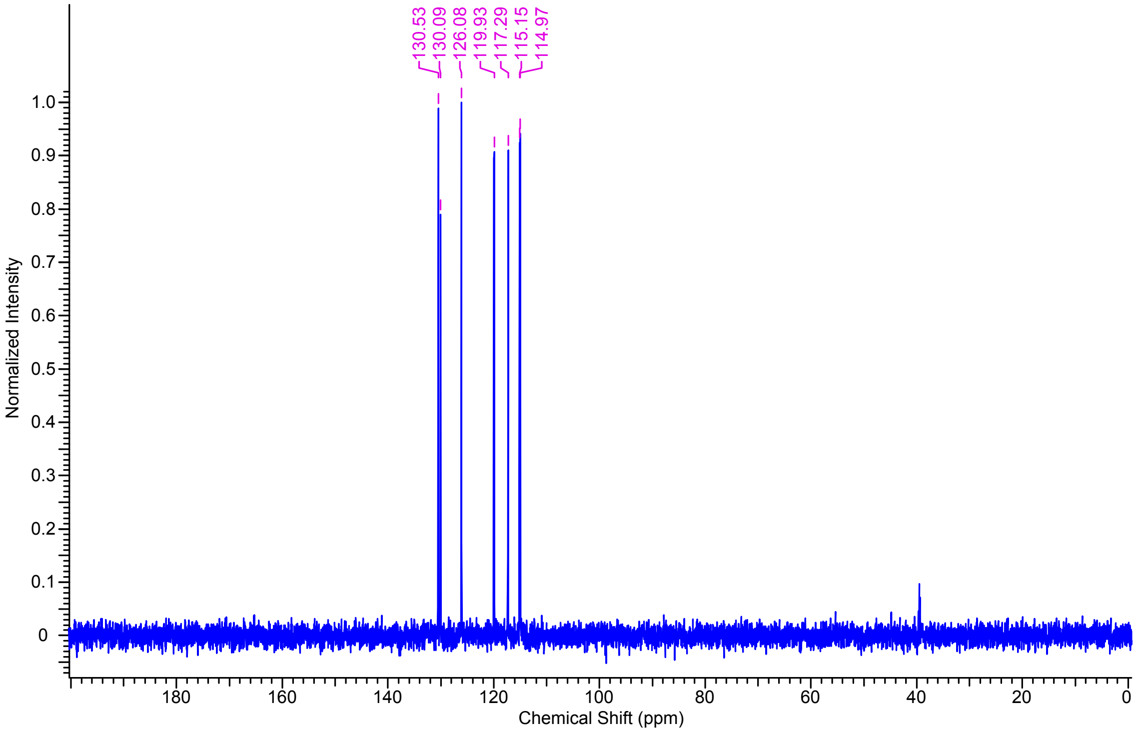


Figure S30. ^{13}C-NMR spectrum of 1-(4-fluorophenyl)-3-(3-iodophenyl)urea (**3g**) in DMSO-d_6.

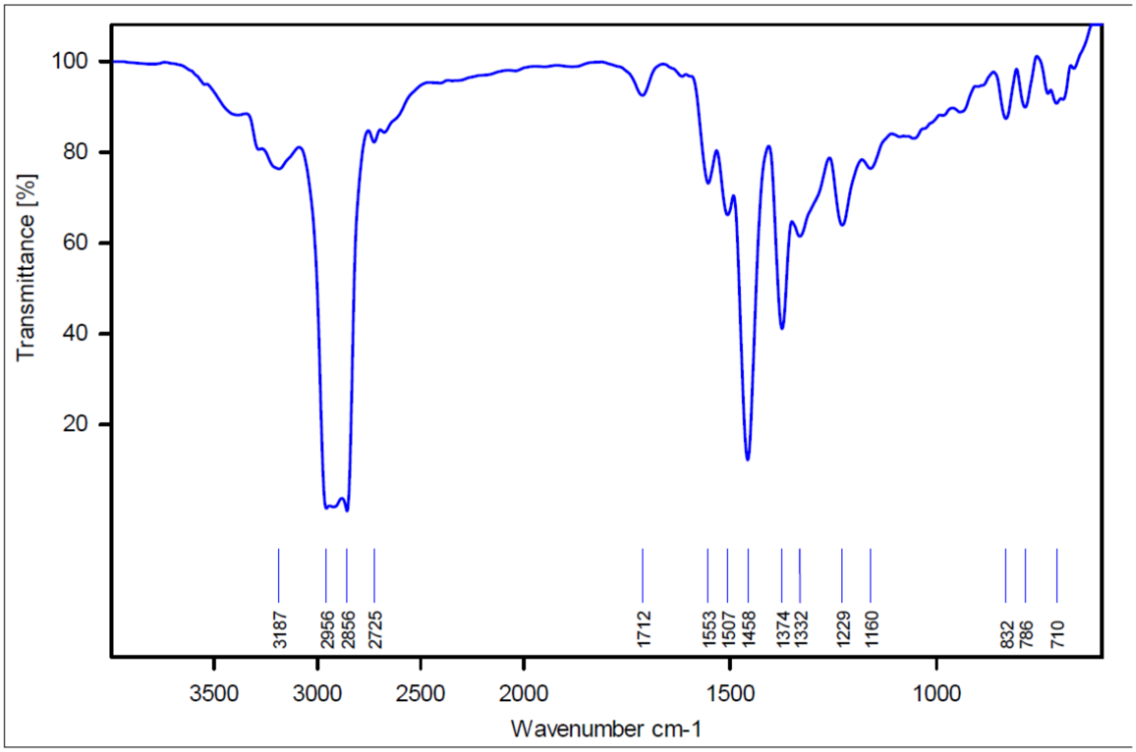


Figure S31. IR spectrum of 1-(4-fluorophenyl)-3-(3-iodophenyl)urea (**3g**).

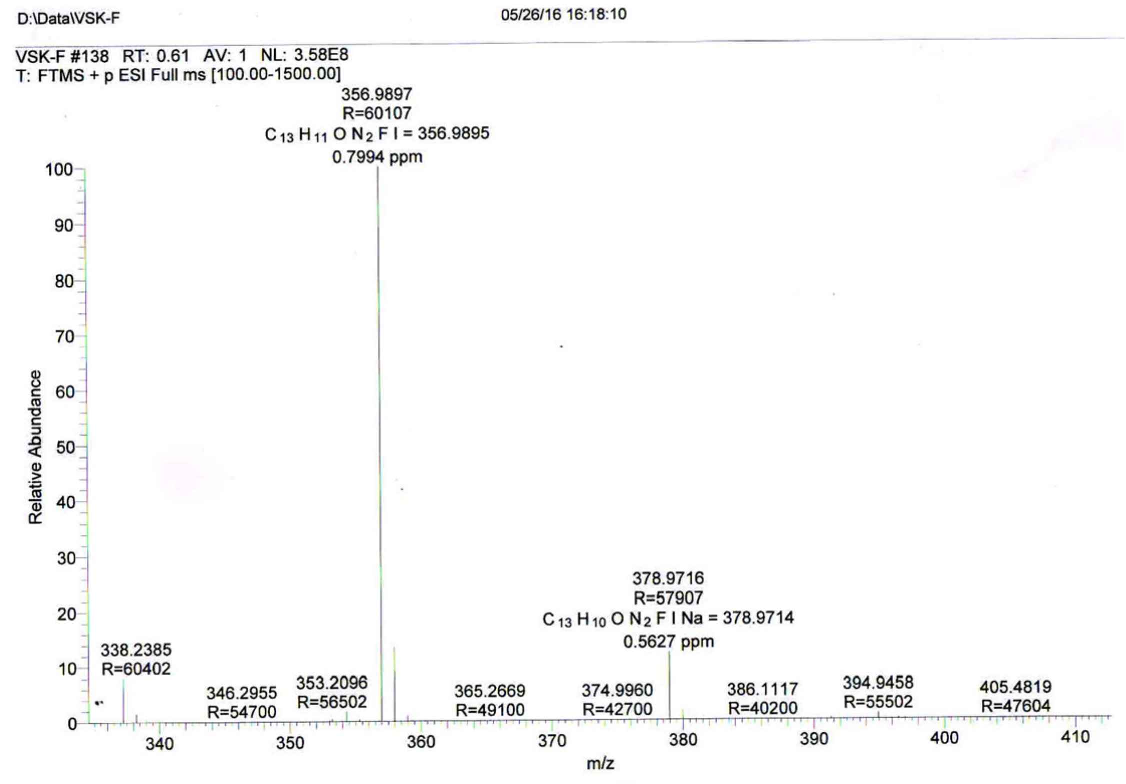
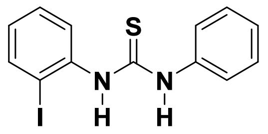


Figure S32. ESI-MS (+ve mode) spectrum of 1-(4-fluorophenyl)-3-(3-iodophenyl)urea (**3g**).

1.8 1-(2-iodophenyl)-3-phenylthiourea (3h):



3c

In 100 ml round bottom flask, DCM (20 ml) and 2-Iodoaniline (9.13 mmol) was added the reaction mixture was cooled to 0°C. Phenyl isothiocyanate (10.04 mmol) was added dropwise to reaction mixture with constant stirring. After that the reaction mixture allowed to warm to room temperature and was stirred overnight. The progress of the reaction was monitored by TLC. Volatiles were evaporated under reduced pressure and the product was purified by column chromatography (ethyl acetate : petroleum ether (10:90)) in 62% yield. **3h** was crystallized from a 1:1 mixture of DMF:ethyl acetate at room temperature.

^{1}H NMR (400MHz, DMSO-d$_{6,}$ 298K) δ = 9.93 (s, 1H, N*H*), 9.33 (s, 1H, N*H*), 7.88 (d, $^{J}{}_{\text{H-H}}$ = 7.96 Hz, 1H, Ar, C*H*), 7.56 (d, $^{J}{}_{\text{H-H}}$ = 7.71Hz, 2H, Ar, C*H*), 7.33-7.44 (m, 4H, Ar, C*H*), 7.15 (t, $^{J}{}_{\text{H-H}}$ = 7.20 Hz, 1H, Ar, C*H*), 7.02 (t, $J_{\text{H-H}}$ = 6.57 Hz, 1H, Ar, C*H*). **^{13}C NMR** (100MHz, DMSO-d$_{6,}$ 298K) δ = 180.2 (s, quat, C=S), 141.1 (s, quat, Ar), 139.7 (s, quat, Ar), 138.9 (s, Ar), 128.9 (s, Ar), 128.5 (s, Ar), 128.5 (s, Ar), 128.2 (s, Ar), 124.6 (s, Ar), 123.8 (s, Ar), 99.6 (s, quat, Ar, C-*I*). **IR** (cm^{-1}): 3289 (NH), 1588 (C=S). **ESI-MS** (+ve) (Cal. For $C_{13}H_{11}N_2SI$) m/z = 354.97 [M+H]$^{+}$, 376.95 [M+Na]$^{+}$. **Mp** = 160°C.

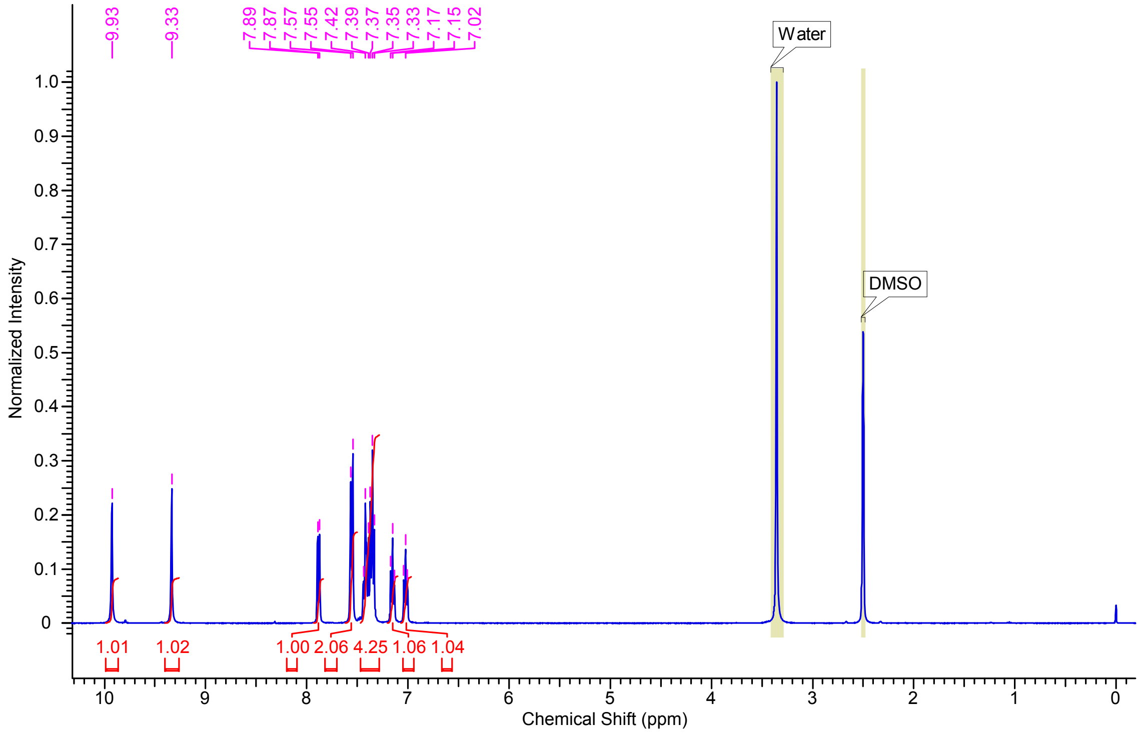


Figure S33. ^{1}H-NMR spectrum of 1-(2-iodophenyl)-3-phenylthiourea (**3h**)in DMSO-d$_6$.

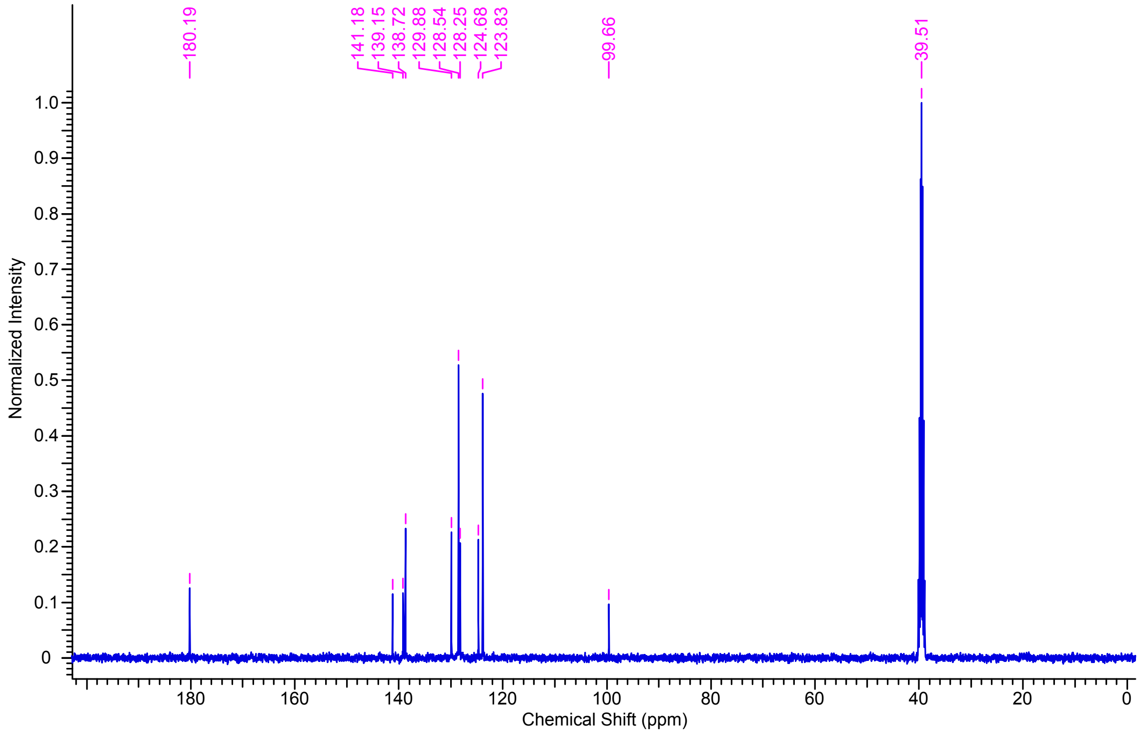


Figure S34. ^{13}C-NMR spectrum of 1-(2-iodophenyl)-3-phenylthiourea (**3h**)in DMSO-d$_6$.

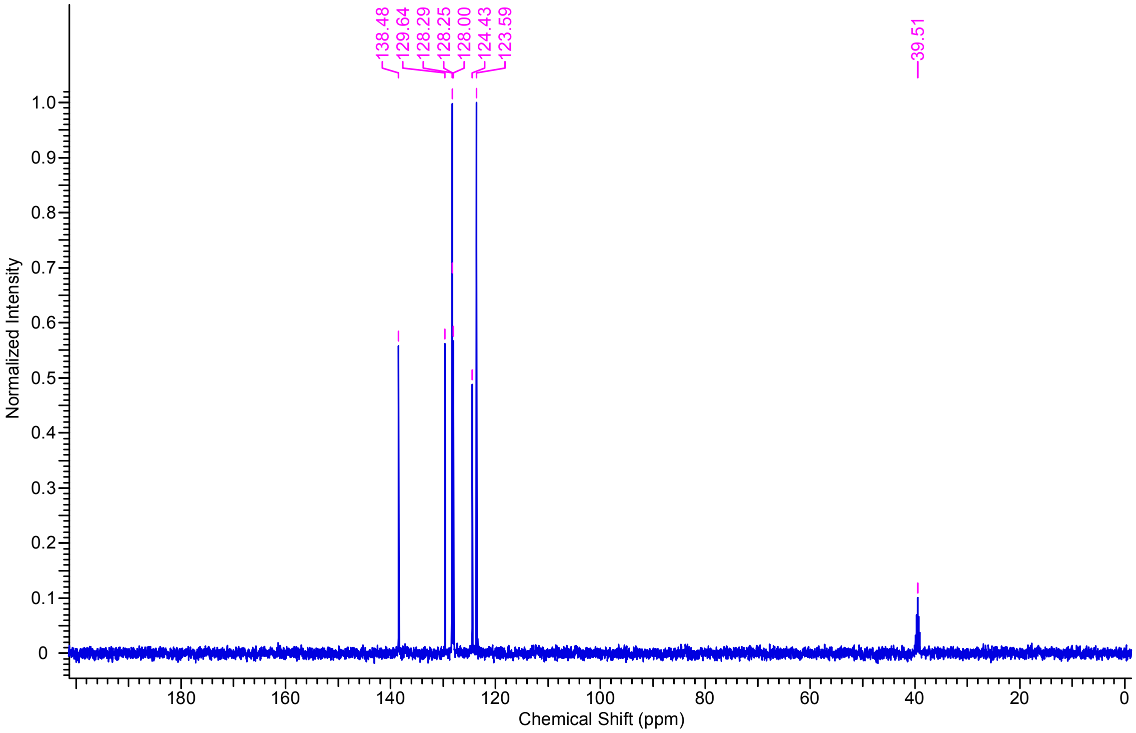


Figure S35. ^{13}C-NMR (DEPT) spectrum of 1-(2-iodophenyl)-3-phenylthiourea (**3h**) in DMSO-d$_6$.

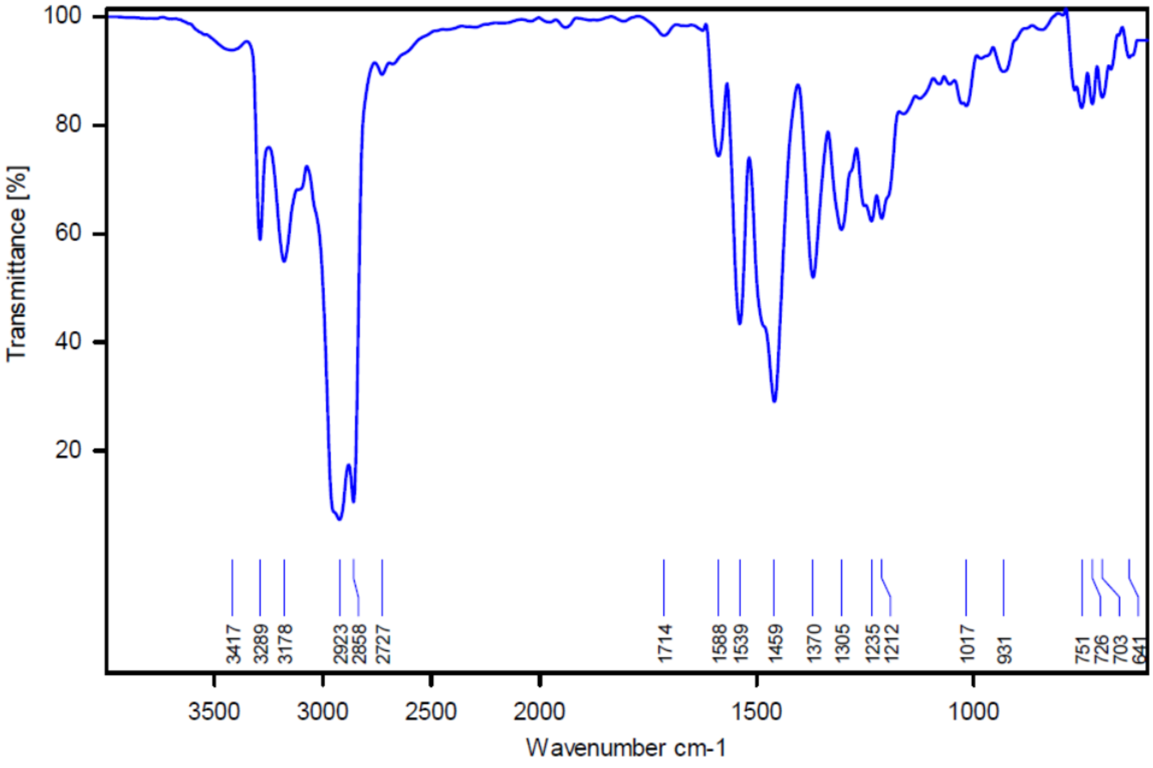


Figure S36. IR spectrum of 1-(2-iodophenyl)-3-phenylthiourea (**3h**).

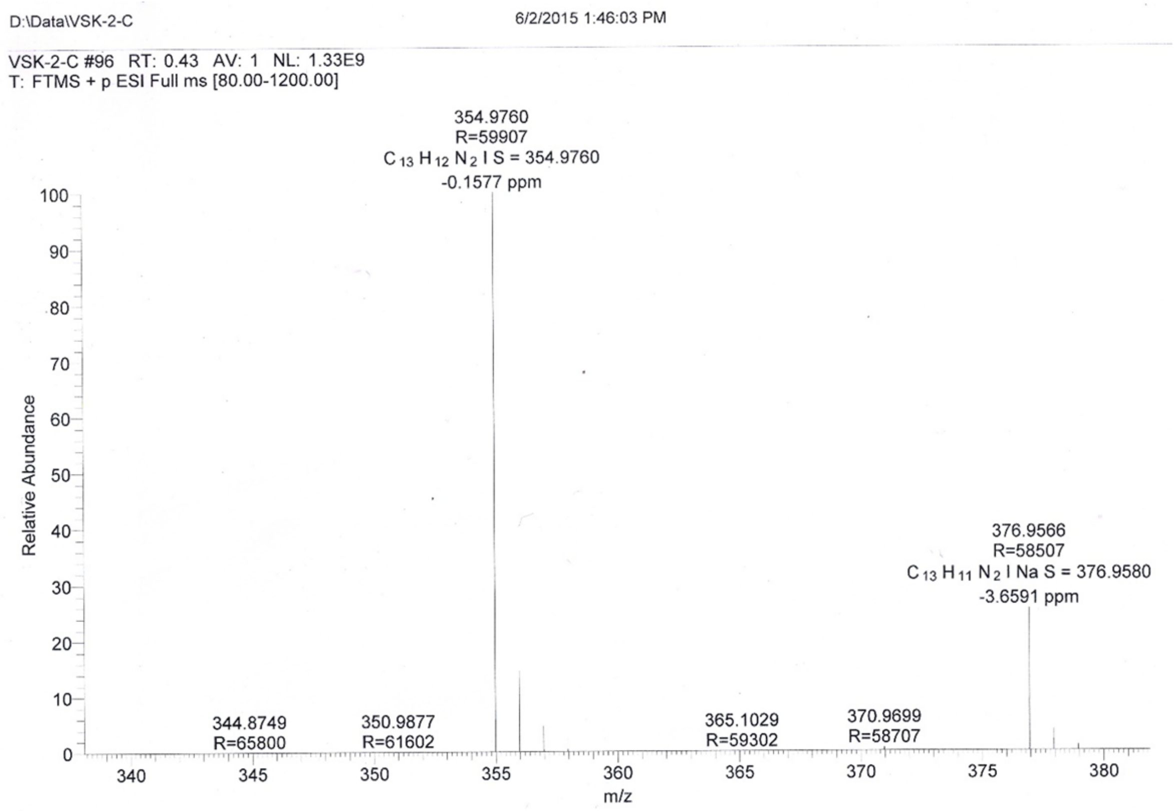
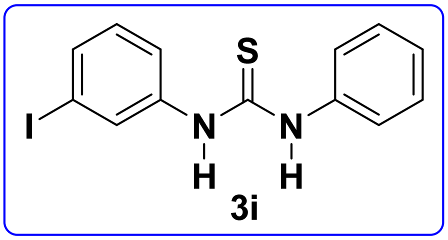


Figure S37. ESIMS (+ve mode) spectrum of 1-(2-iodophenyl)-3-phenylthiourea (**3h**).

1.10 1-(3-iodophenyl)-3-phenylthiourea (3i):

In a 100 ml round bottom flask, 25 ml DCM and 3-Iodoaniline (16.62 mmol) were added amd the flask was cooled to 0°C. Phenyl isothiocyanate (18.28 mmol) was added dropwise to the reaction mixture with constant stirring. After that the reaction mixture was allowed to warm to room temperature and was stirred for 18 h. The progress of the reaction was monitored by TLC. After completion of reaction, solvent was evaporated from the reaction mixture and the product was purified by column chromatography (ethyl acetate : petroleum ether (10:90)) in 94% yield. **3i** was crystallized from a 1:1 mixture of THF:ethyl acetate (1:1) at room temperature.



3i

^{1}**H NMR** (400 MHz, DMSO-d$_6$, 298K) δ = 9.95 (s, 1H, N*H*), 9.86 (s, 1H, N*H*), 7.97 (s, 1H, Ar, C*H*), 7.48 (d, $J_{H\text{-}H}$ = 7.57 Hz, 4H, Ar, C*H*), 7.35 (t, $J_{H\text{-}H}$ = 7.58, 2H, Ar, C*H*), 7.14 (q, $J_{H\text{-}}$

$_H$ = 7.34 Hz, 2H, Ar, C*H*). **^{13}C NMR** (100 MHz, DMSO-d_6, 298K) δ = 179.5 (s, quat, C=S), 141.0 (s, quat, Ar), 139.1 (s, quat, Ar), 132.7 (s, Ar), 131.7 (s, Ar), 130.3 (s, Ar), 128.5 (s, Ar), 124.6 (s, Ar), 123.3 (s, Ar), 122.9 (s, Ar), 93.8 (s, quat, Ar). **IR** (cm^{-1}): 3323 (NH), 1577 (C=S). ESI-MS (+ve) (Cal. For $C_{13}H_{11}N_2SI$) m/z = 354.97[M+H]$^+$, 376.95[M+Na]$^+$. **Mp** =110°C.

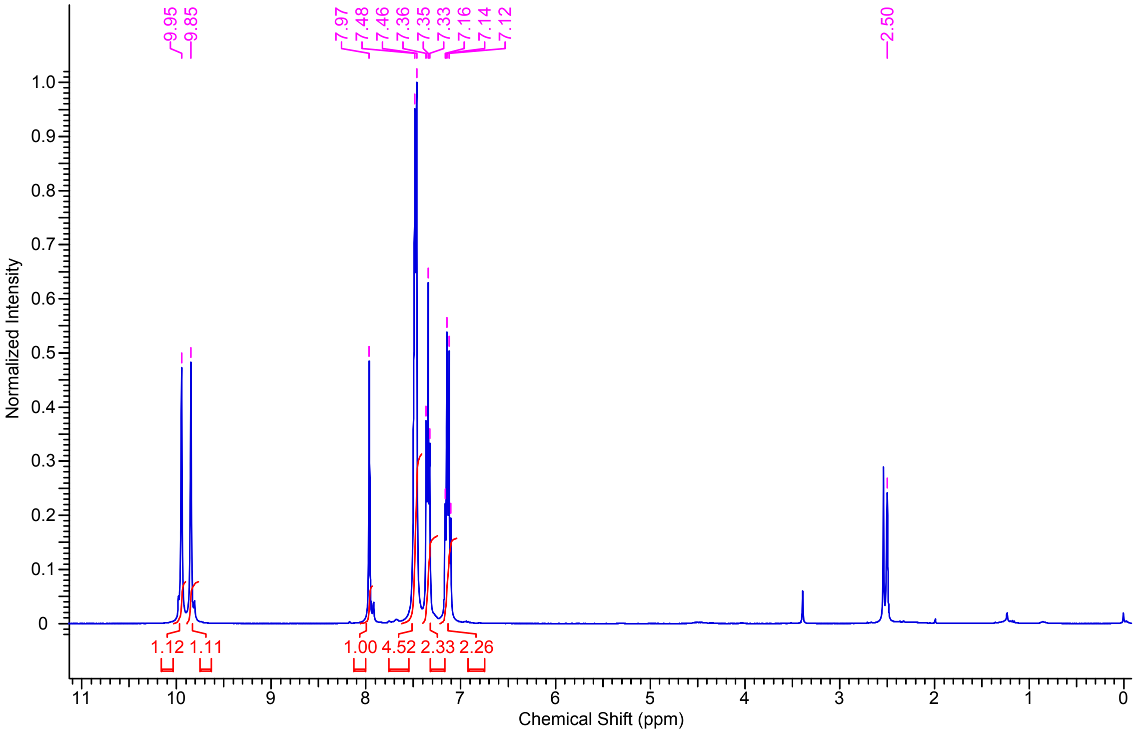


Figure S38. ^{1}H-NMR Spectra of 1-(3-iodophenyl)-3-phenylthiourea (3i) in DMSO-d_6.

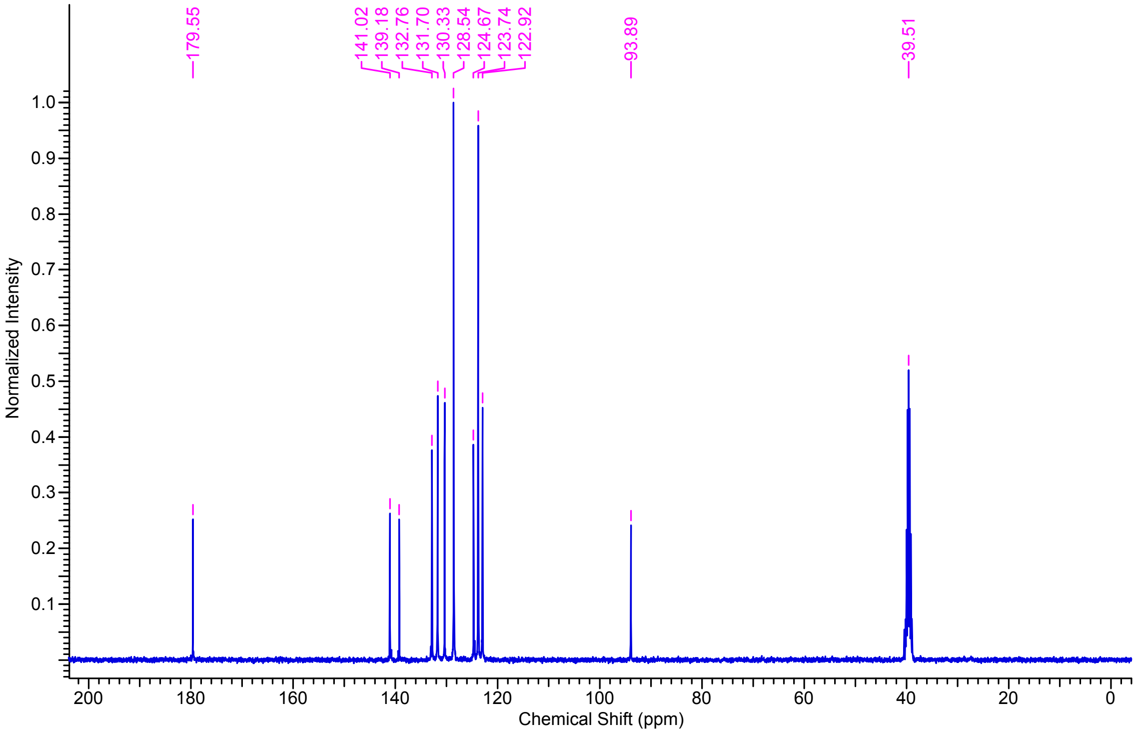


Figure S39. ^{13}**C-NMR Spectra of 1-(3-iodophenyl)-3-phenylthiourea (3i) in DMSO-d$_6$.**

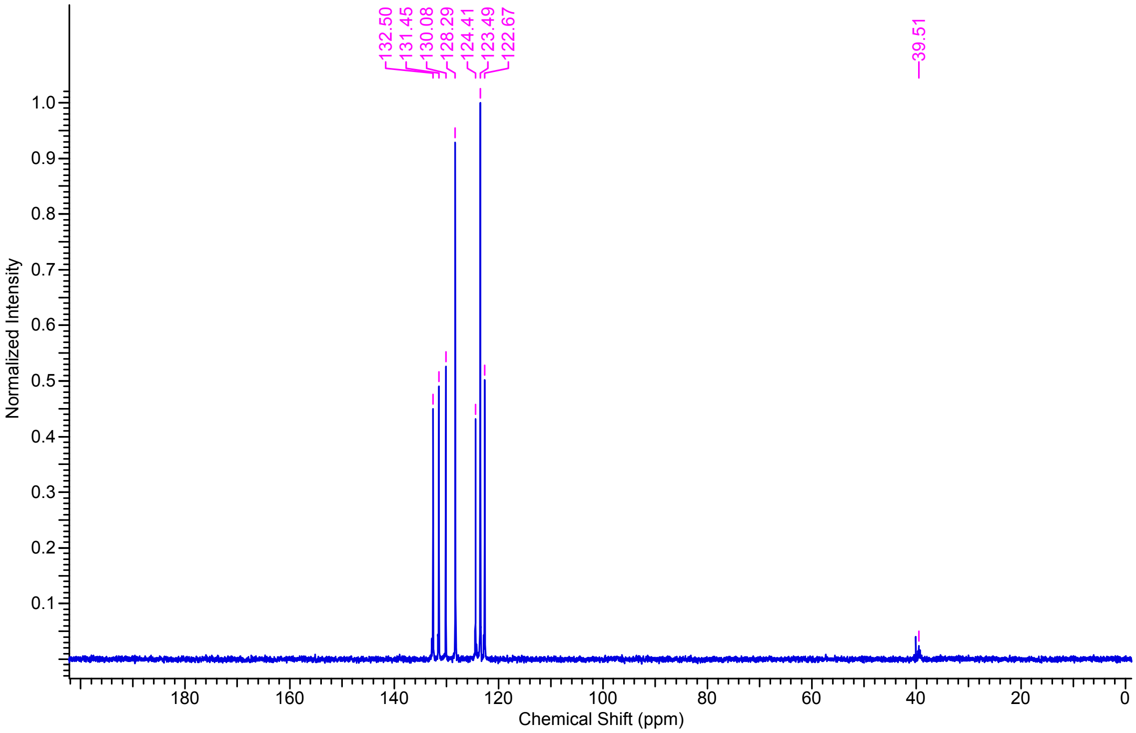


Figure S40. ^{13}C-NMR (DEPT) spectrum of 1-(3-iodophenyl)-3-phenylthiourea (**3i**) in DMSO-d$_6$.

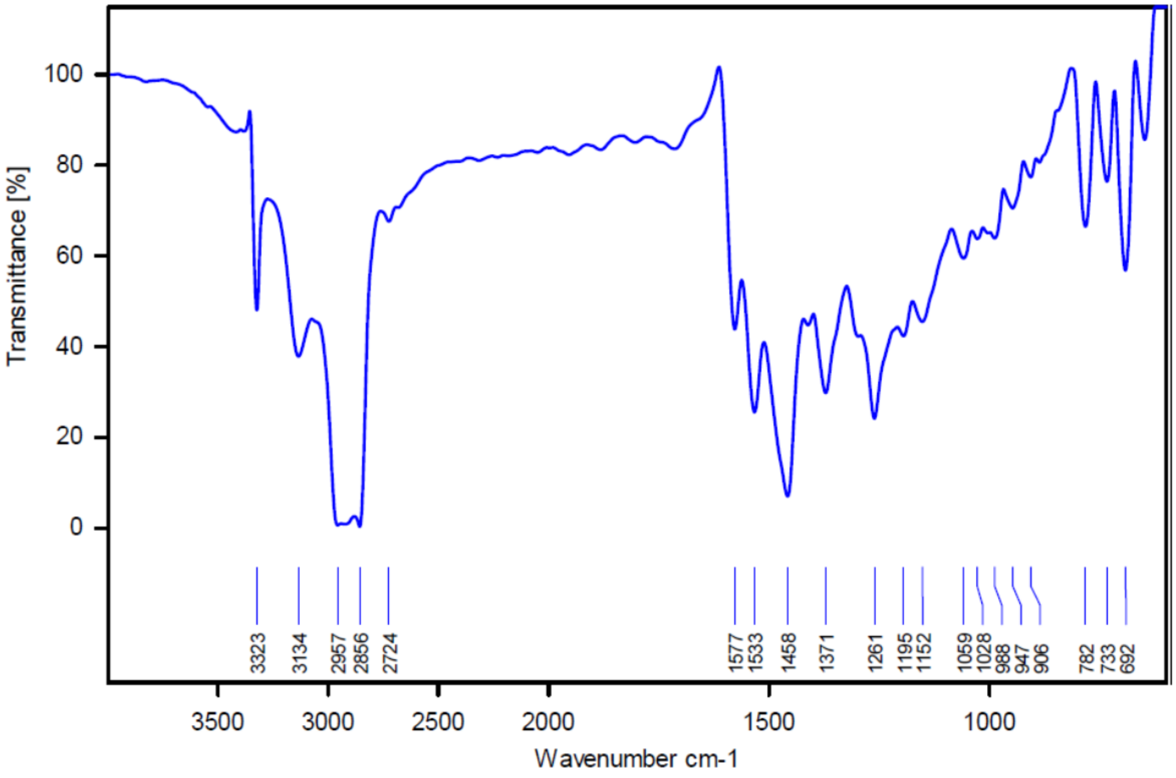


Figure S41. IR spectrum of 1-(3-iodophenyl)-3-phenylthiourea (**3i**).

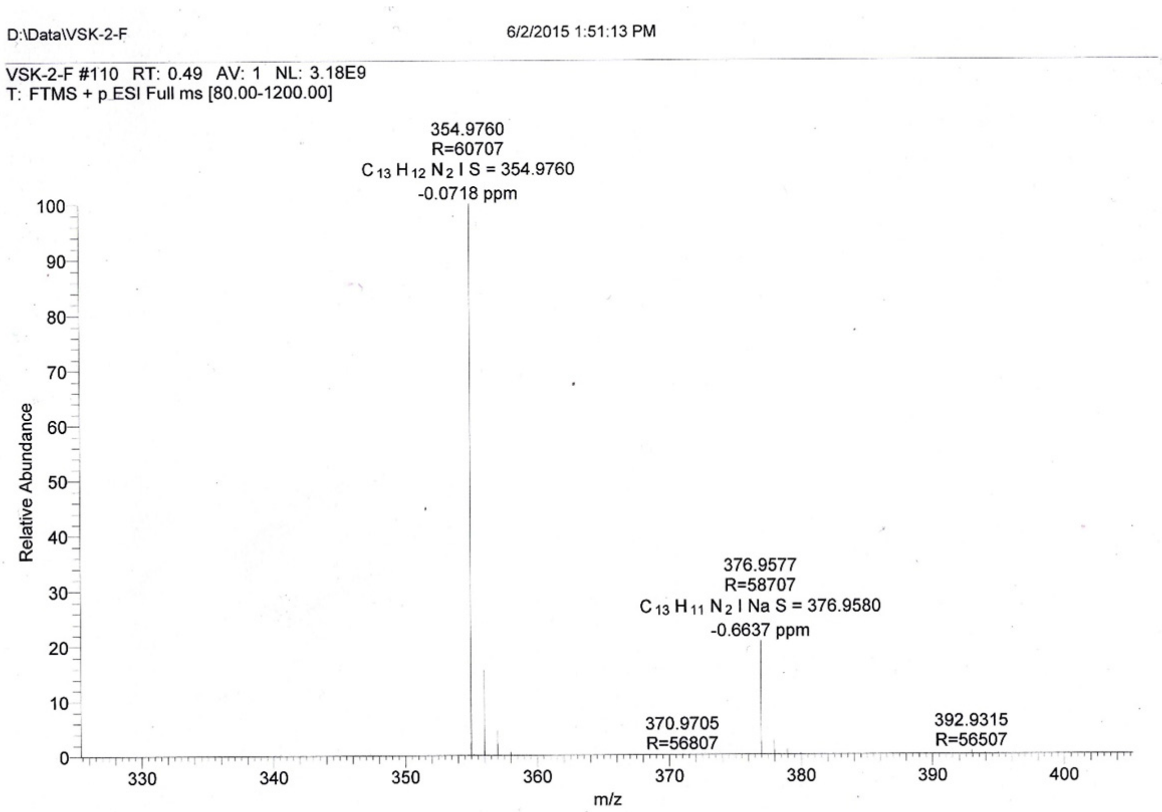
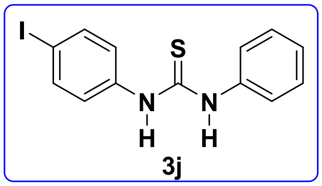


Figure S42. ESI-MS (+ve mode) spectrum of 1-(3-iodophenyl)-3-phenylthiourea (**3i**).

1.9 1-(4-iodophenyl)-3-phenylthiourea (3j):



3j

In a 100 ml round bottom flask, 40 ml DCM and 4-Iodoaniline (9.13 mmol) were added and the resulting solution was cooled to 0°C. Phenyl isothiocyanate (10.04 mmol) was added dropwise to the reaction mixture with constant stirring. The reaction mixture was allowed to warm to room temperature and was stirred for 4 h. The progress of the reaction was monitored by TLC. Solvent was evaporated and the product was purified by column chromatography (ethyl acetate:pet. ether (30:70)) in 90% yield. This compound was crystallized in combination of DMF:ethyl acetate (1:1) at room temperature.

^{1}H NMR (500 MHz, DMSO-d$_6$, 298 K) δ = 8.78 (s, 1H, N*H*), 8.69 (s, 1H, N*H*), 7.61 (d, 2H, J_{H-H} = 8.31 Hz, 2H, Ar, C*H*), 7.45 (d, J_{H-H} = 7.99 Hz, 2H, Ar, C*H*), 7.27-7.33 (m, 4H, Ar, C*H*), 6.98 (t, J_{H-H} = 7.20 Hz, 1H, Ar, C*H*). **^{13}C NMR** (50 MHz, DMSO-d$_6$, 298K) δ = 179.4 (s, quat, C=S), 139.4 (s, quat, Ar), 139.3 (s, quat, Ar), 137.0 (s, Ar), 128.5 (s, Ar), 125.7 (s, Ar), 124.6 (s, Ar), 123.7 (s, Ar), 88.5 (s, quat, Ar, C-*I*). **IR** (cm^{-1}): 3199 (NH), 1587 (C=S). **ESI-MS** (+ve) (Cal. For $C_{13}H_{11}N_2SI$) m/z = 354.97 $[M+H]^+$, 376.95 $[M+Na]^+$. **Mp** = 140°C.

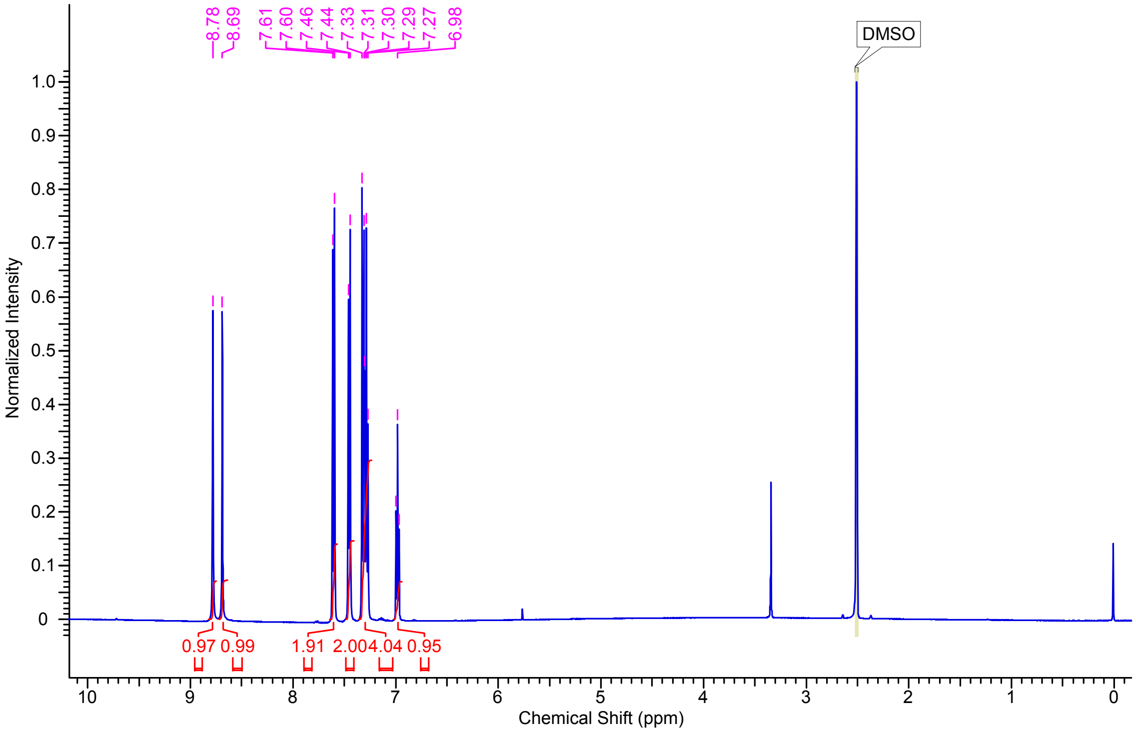


Figure S43. ^{1}H-NMR spectrum of 1-(4-iodophenyl)-3-phenylthiourea (**3j**) in DMSO-d_6.

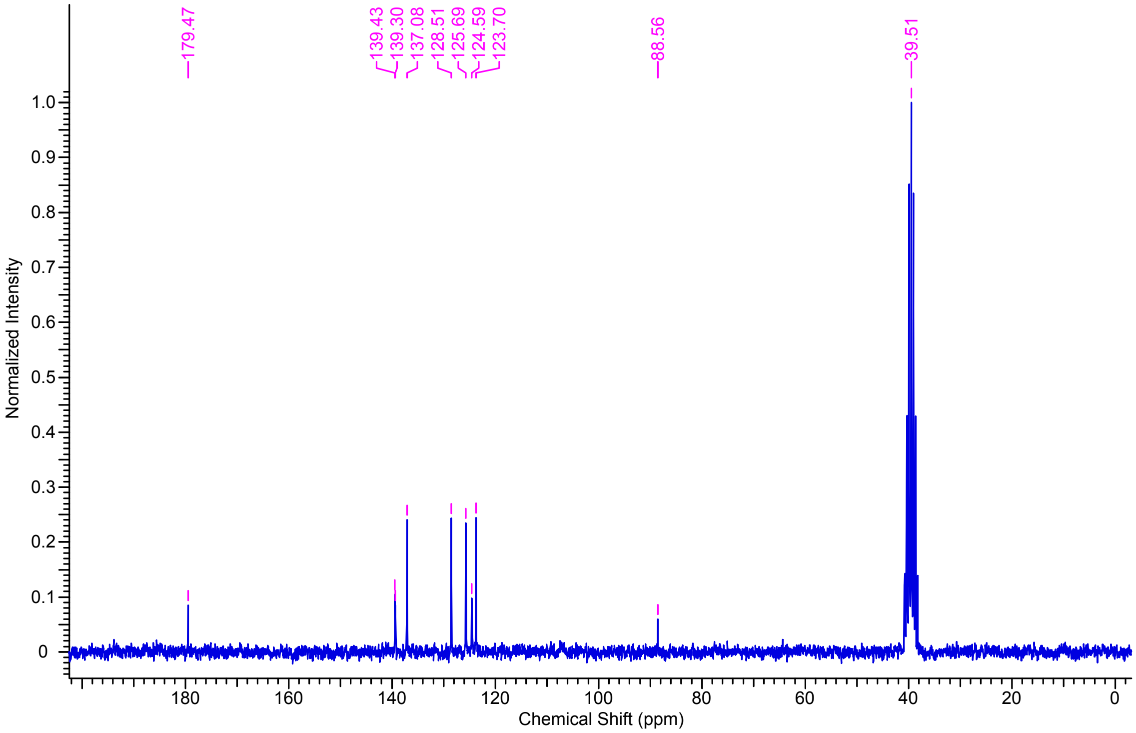


Figure S44. ^{13}C-NMR spectrum of 1-(4-iodophenyl)-3-phenylthiourea (**3j**) in DMSO-d_6.

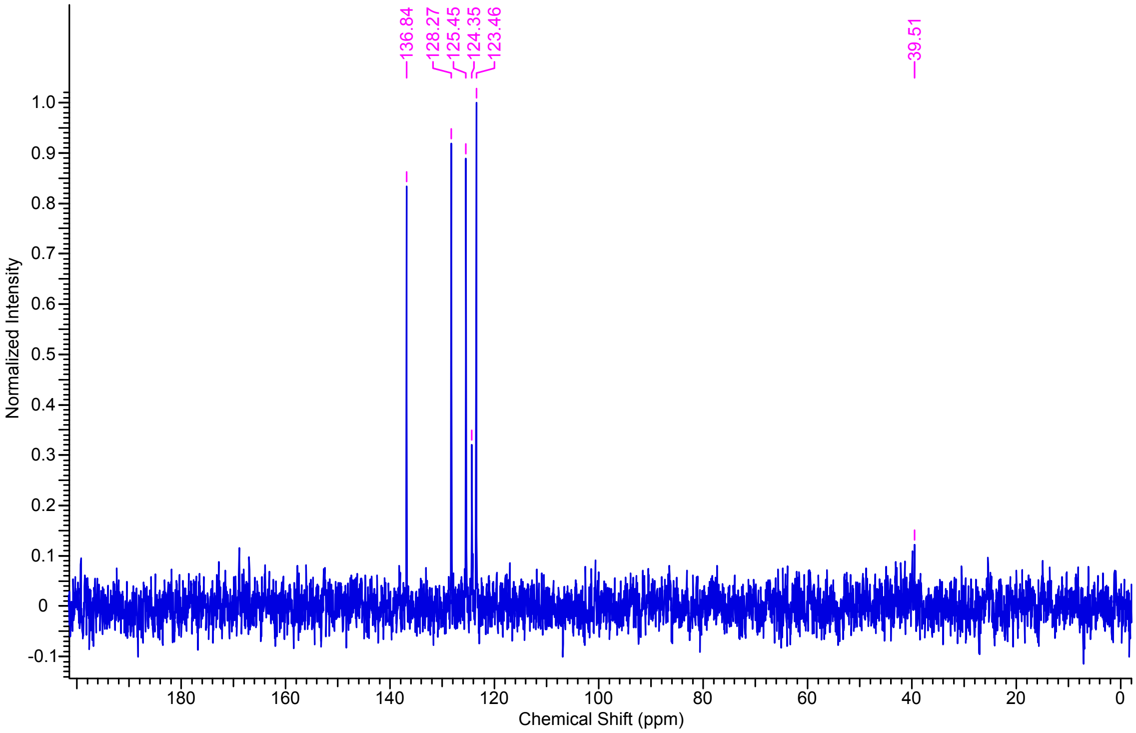


Figure S45. ^{13}C-NMR (DEPT) spectrum of 1-(4-iodophenyl)-3-phenylthiourea (**3j**) in DMSO-d_6.

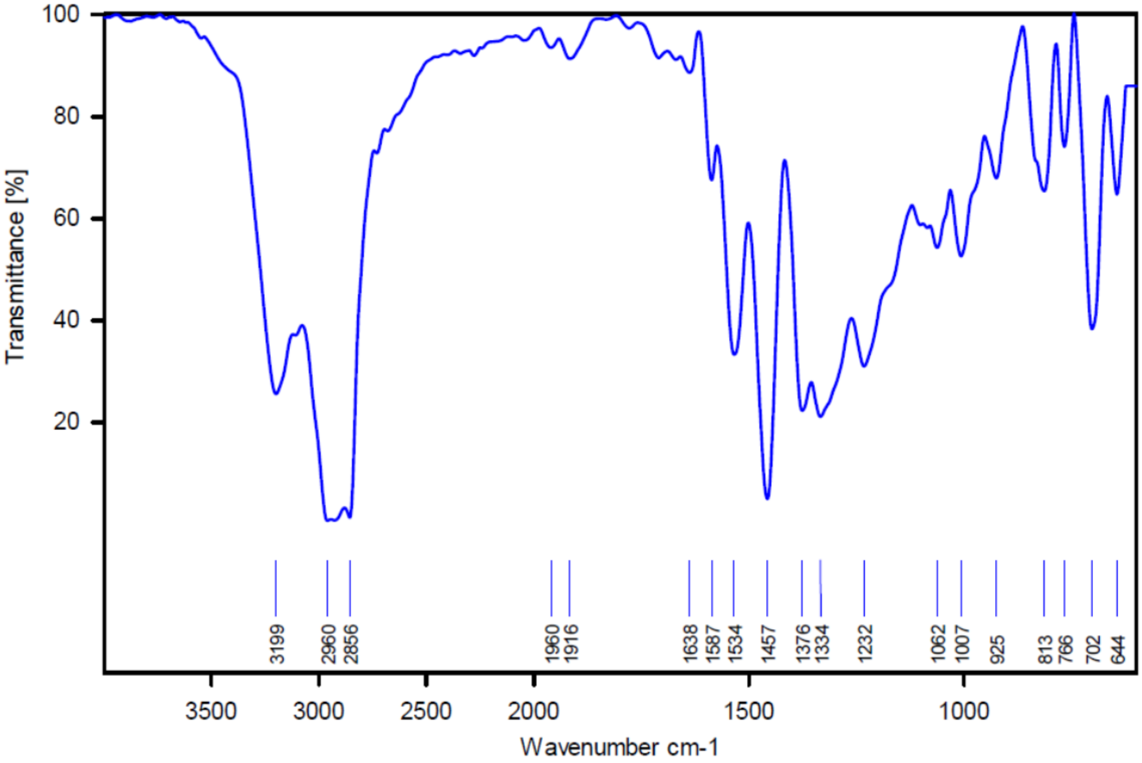


Figure S46. IR spectrum of 1-(4-iodophenyl)-3-phenylthiourea (**3j**).

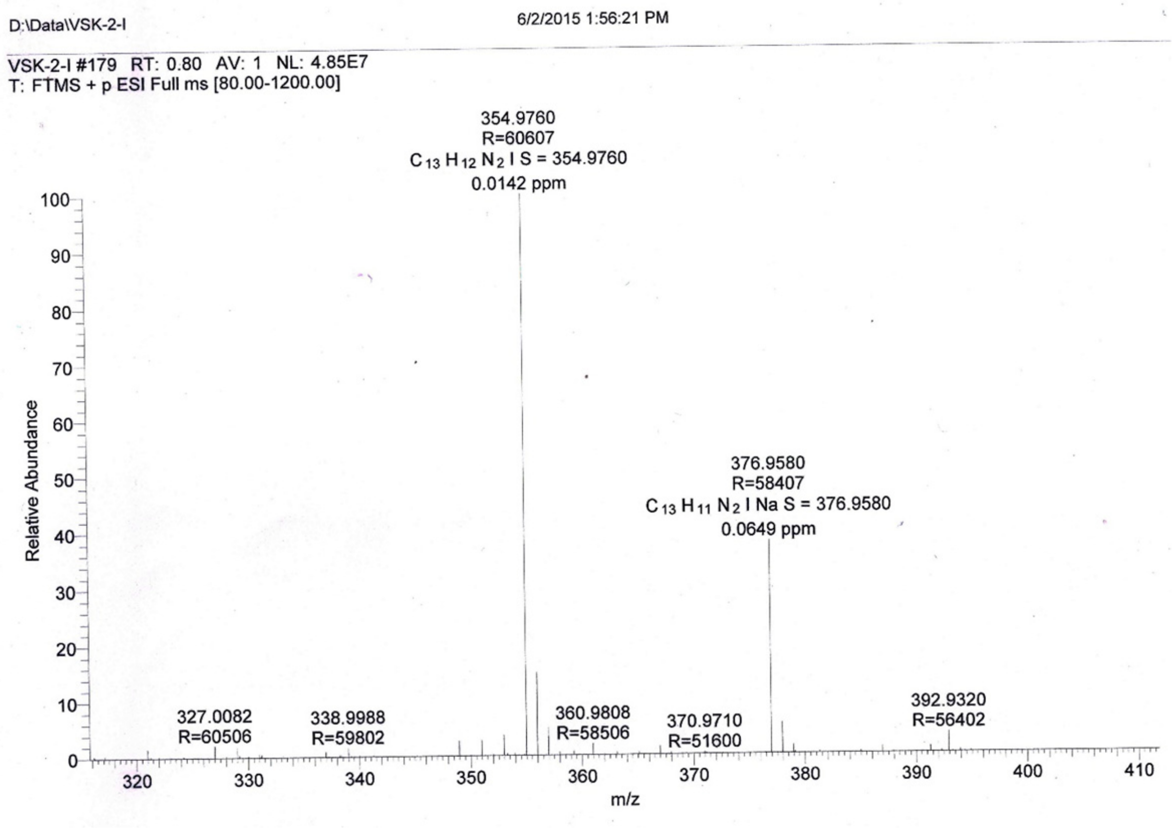
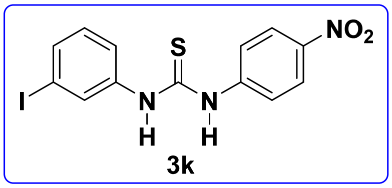


Figure S47. ESIMS (+ve mode) spectrum of 1-(4-iodophenyl)-3-phenylthiourea (**3j**).

1.12 1-(3-iodophenyl)-3-(4-nitrophenyl)thiourea (3k):



3k

In a 100 ml round bottom flask, DCM (15 ml) and 3-Iodoaniline (2.77 mmol) were added and the reaction mixture was cooled to 0°C. 1-isothiocyanato-4-nitrobenzene (3.8 mmol) was added dropwise to the reaction mixture with constant stirring. After that the reaction mixture was allowed to warm to room temperature and was stirred for 4 h. The progress of the reaction was monitored by TLC. Volatiles were evaporated under reduced pressure and the product was purified by silica gel column chromatography (ethyl acetate : petroleum ether (60:40)) in 80% yield. **3k** was crystallized from a 1:1 mixture of DMF:ethyl acetate at room temperature.

^{1}**H NMR** (500 MHz, , DMSO-d$_6$, 298K): δ = 10.50 (s, 1H, N*H*), 10.30 (s, 1H, N*H*), 8.23 (d, 2H, $J_{\text{H-H}}$ = 9.16 Hz, Ar, C*H*), 7.95 (s, 1H, Ar, C*H*), 7.83 (d, $J_{\text{H-H}}$ = 9.16 Hz, 2H, Ar, C*H*), 7.52 (d, $J_{\text{H-H}}$ = 7.60 Hz, 1H, Ar, C*H*), 7.50 (d, $J_{\text{H-H}}$ = 7.85 Hz, 1H, Ar, C*H*), 7.17 (t, $J_{\text{H-H}}$ = 7.93 Hz, 1H, Ar, C*H*). ^{13}**C NMR** (125 MHz, DMSO-d$_{6,}$ 298K): δ = 179.3 (s, quat, C=S), 145.9 (s, quat, Ar), 142.4 (s, quat, Ar), 140.4 (s, quat, Ar), 133.4 (s, Ar, CH), 131.8 (s, Ar, CH), 130.5 (s, Ar, CH), 124.4 (s, Ar, CH), 123.0 (s, Ar*, CH*), 121.7 (s, Ar, CH), 93.9 (s, quat, Ar, C-*I*). **IR** (cm^{-1}): 3216 (NH), 3154 (NH), 1576 (C=S). **ESI-MS** (+ve) (Cal. For $C_{13}H_{10}N_3O_2SI$) m/z = 399.96 $[M+H]^+$. **Mp** = 150°C.

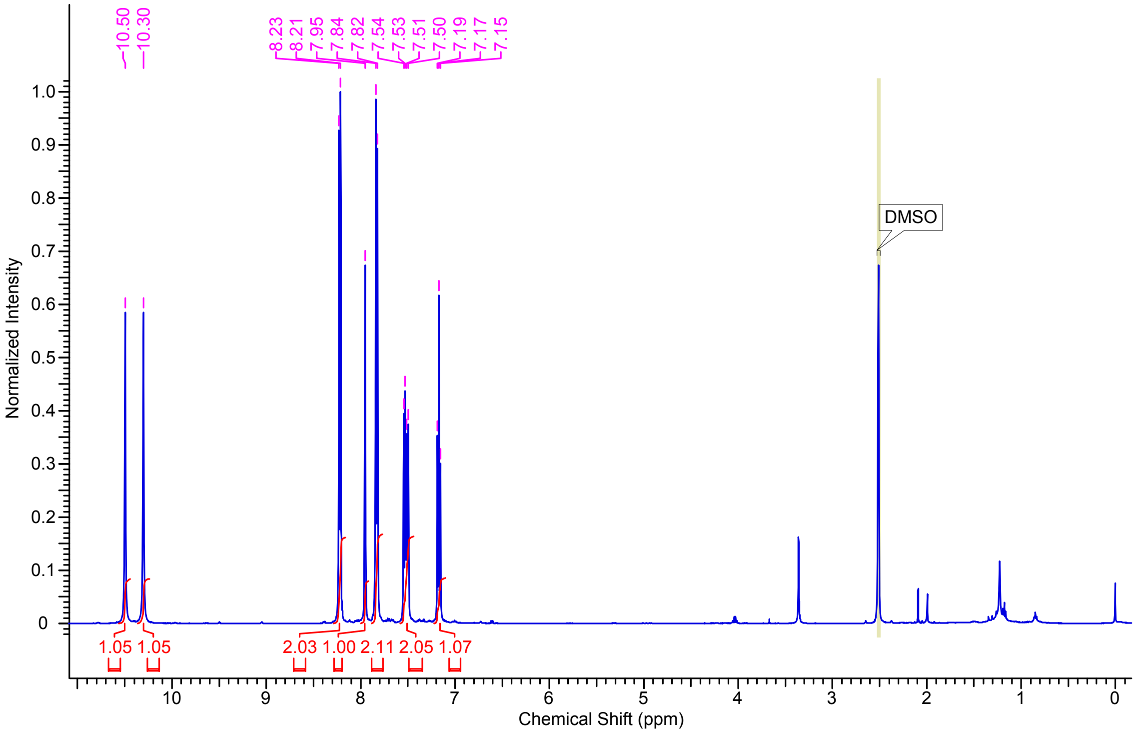


Figure S48. ^{1}H-NMR spectrum of 1-(3-iodophenyl)-3-(4-nitrophenyl)thiourea (**3k**) in DMSO-d$_6$.

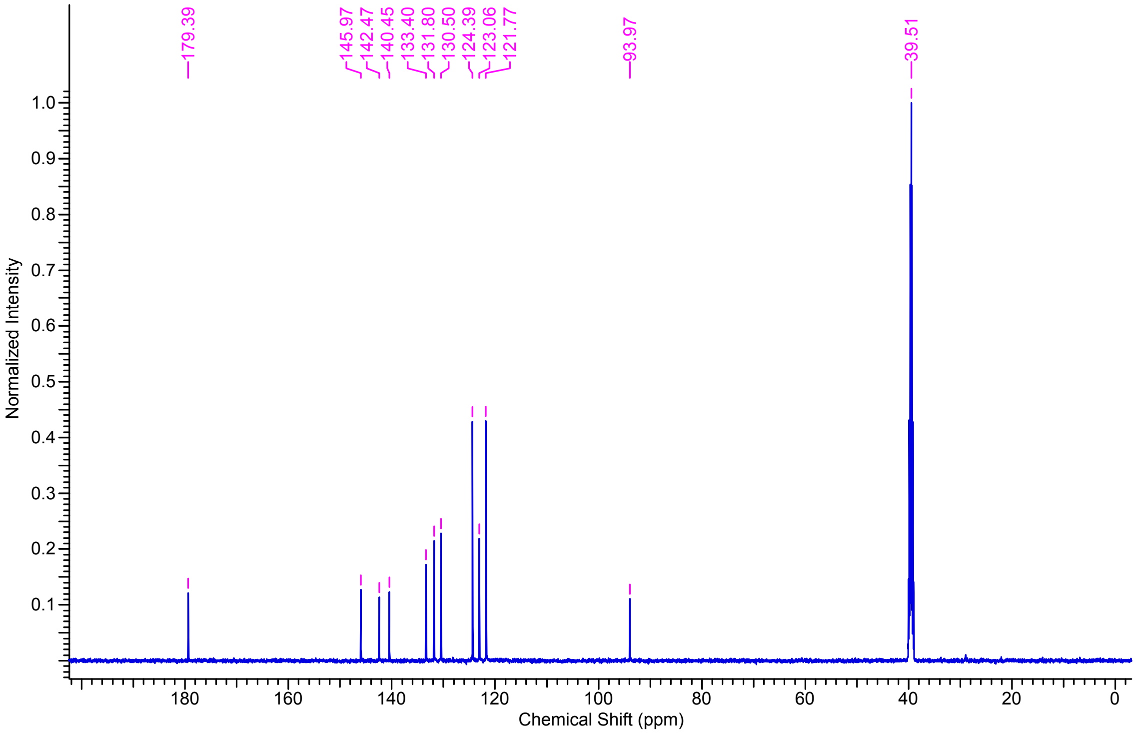


Figure S49. ^{13}C-NMR spectrum of 1-(3-iodophenyl)-3-(4-nitrophenyl)thiourea (**3k**) in DMSO-d$_6$.

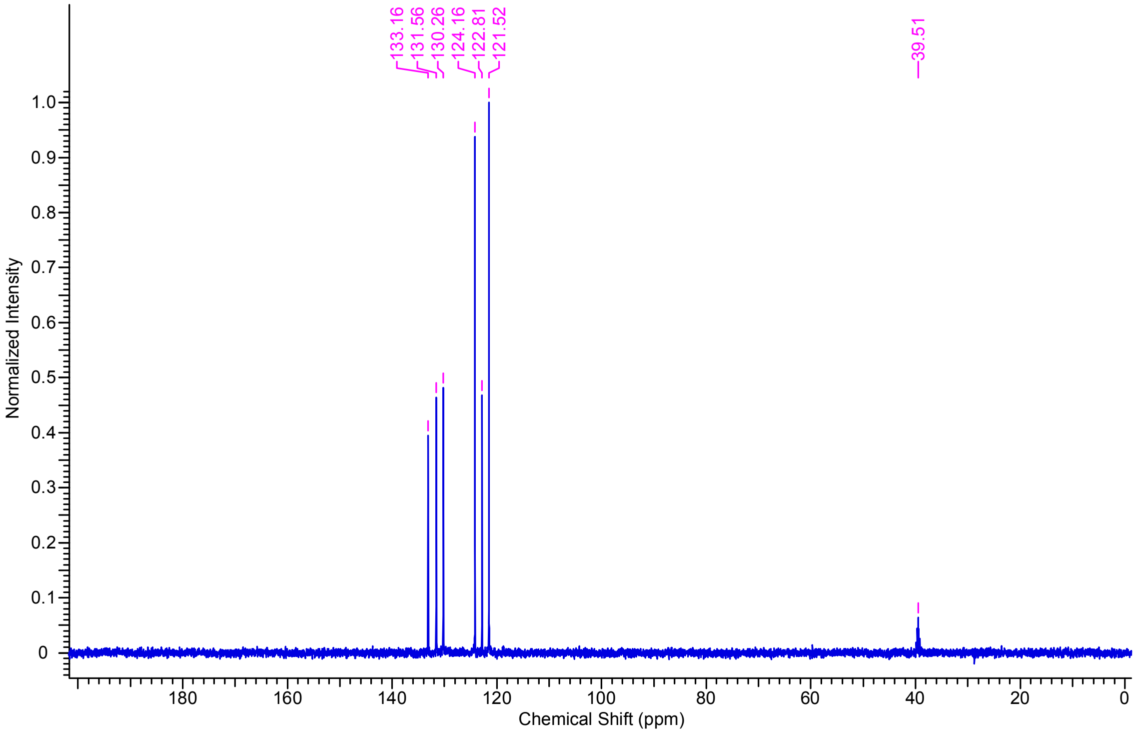


Figure S50. ^{13}C-NMR (DEPT) spectrum of 1-(3-iodophenyl)-3-(4-nitrophenyl)thiourea (**3k**) in DMSO-d_6.

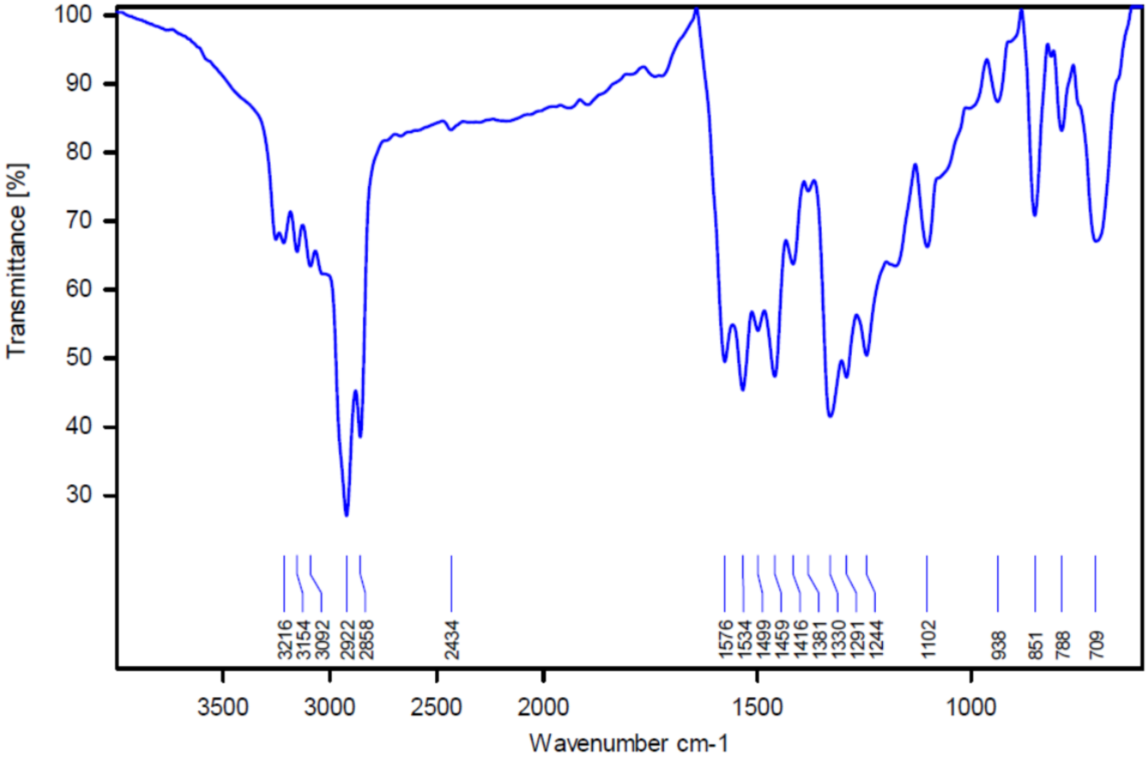


Figure S51. IR spectrum of 1-(3-iodophenyl)-3-(4-nitrophenyl)thiourea (**3k**).

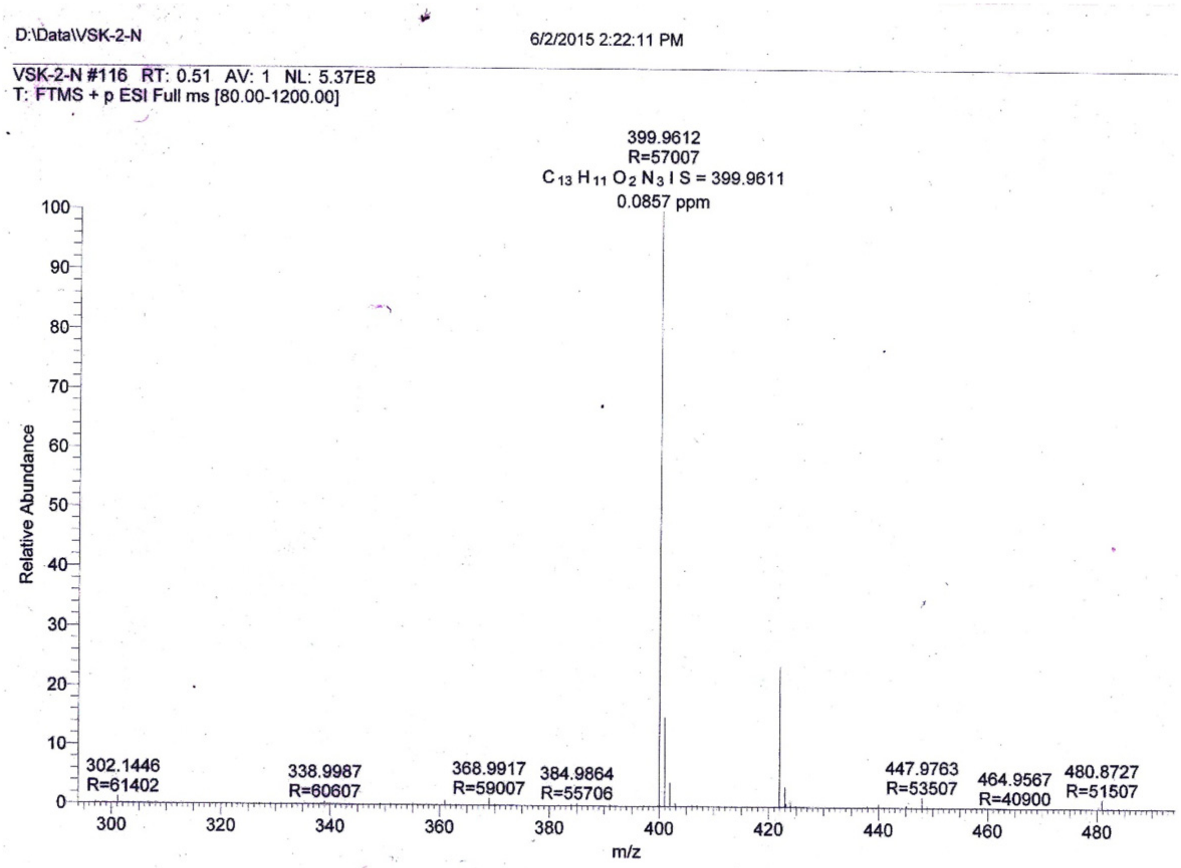
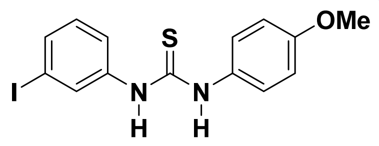


Figure S52. ESIMS (+ve mode) spectrum of 1-(3-iodophenyl)-3-(4-nitrophenyl)thiourea (**3k**).

1.13 1-(3-iodophenyl)-3-(4-methoxyphenyl)thiourea (3l):



3l

In a 100 ml round bottom flask, DCM (15 ml) and 3-Iodoaniline (4.24 mmol) were added and the reaction mixture was cooled to 0°C. 1-isothiocyanato-4-methoxybenzene (3.03 mmol) was added dropwise to reaction solution with constant stirring at 0°C. After that the reaction mixture was allowed to warm to room temperature and was stirred for 18 h. The progress of the reaction was monitored by TLC. The solvent was evaporated and the product was purified by column chromatography (ethyl acetate : petroleum ether (15:85)) in 94% yield. **3l** was crystallized from DMF:ethyl acetate (1:1) solution at room temperature.

^{1}H NMR (500 MHz, DMSO-d$_6$, 298K) δ = 9.76 (s, 1H, N*H*), 9.68 (s, 1H, N*H*), 7.95 (s, 1H, Ar, C*H*), 7.46 (d, $J_{\text{H-H}}$ = 7.6 Hz, 2H Ar, C*H*), 7.32 (d, $J_{\text{H-H}}$ = 9.0 Hz, 2H, Ar, C*H*), 7.11 (t, $J_{\text{H-H}}$ = 7.6 Hz, 1H, Ar, C*H*), 6.92 (d, $J_{\text{H-H}}$ = 8.5 Hz, 2H, C*H*), 3.75 (s, 3H, OCH_3). **^{13}C NMR** (125

MHz, DMSO-d_6, 298K): δ = 179.7 (s, quat, C=S), 156.7 (s, quat, Ar, *C-OMe*), 141.1 (s, quat, Ar), 132.6 (s, Ar, CH), 131.6 (s, Ar, CH), 131.7 (s, Ar, CH), 130.2(s, Ar, CH), 126.1 (s, Ar, CH), 122.9 (s, Ar, *CH*), 113.7 (s, quat, Ar), 93.8 (s, quat, Ar, C-I), 55.2 (s, OCH_3). **IR** (cm^{-1}): 3199 (NH), 1587 (C=S). **ESI-MS** (+ve) (Cal. For $C_{14}H_{13}N_2OSI$) m/z = 384.98 $[M+H]^+$, 406.96 $[M+Na]^+$. **Mp** = 105°C.

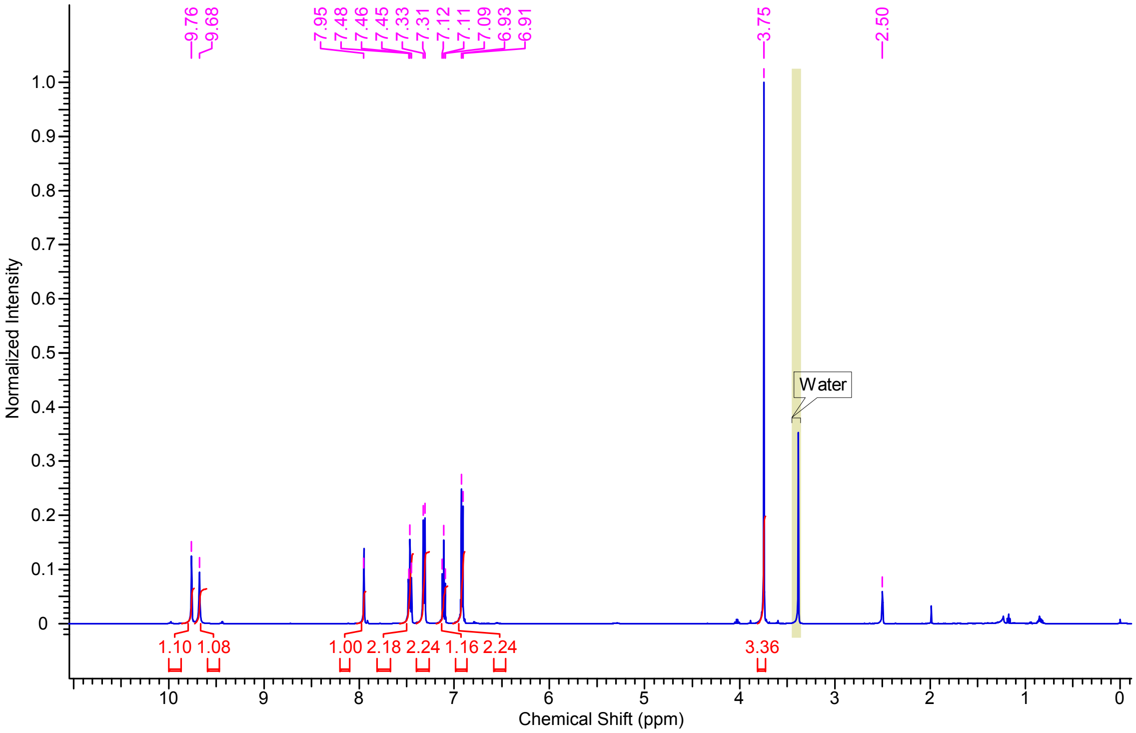


Figure S53. ^{1}H-NMR spectrum of 1-(3-iodophenyl)-3-(4-methoxyphenyl)thiourea (**3l**) in DMSO-d_6.

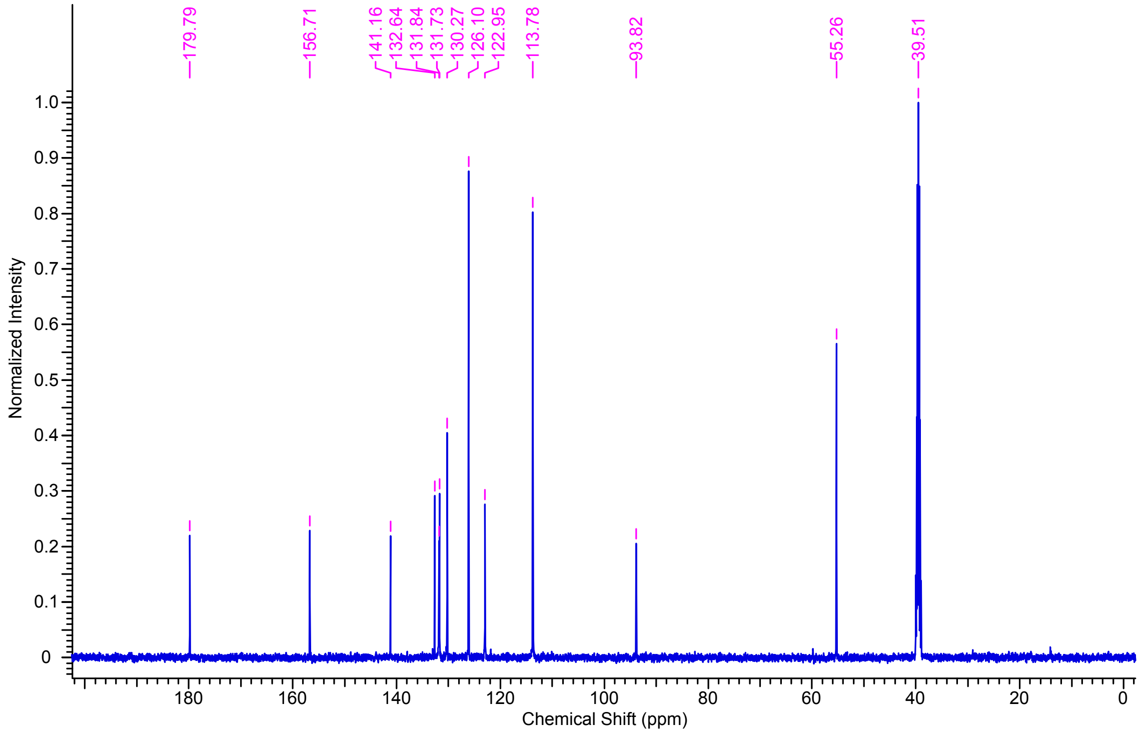


Figure S54. ^{13}C-NMR spectrum of 1-(3-iodophenyl)-3-(4-methoxyphenyl)thiourea (**3l**) in DMSO-d$_6$.

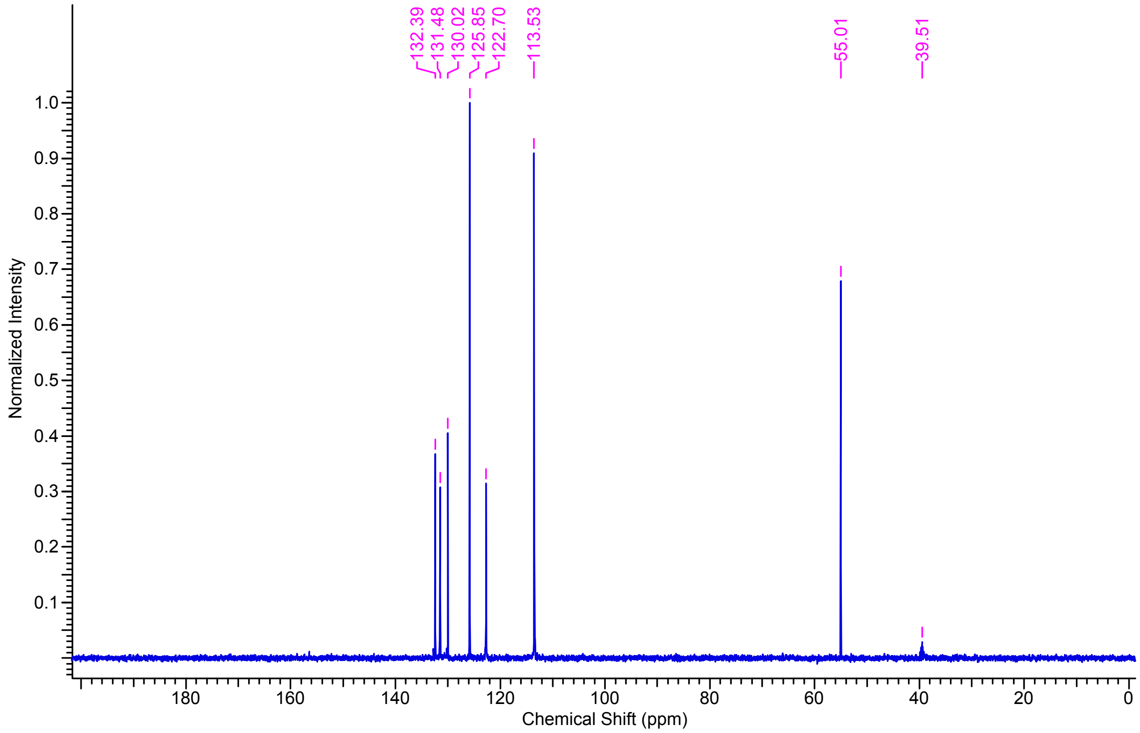


Figure S55. ^{13}C-NMR spectrum of 1-(3-iodophenyl)-3-(4-methoxyphenyl)thiourea (**3l**) in DMSO-d$_6$.

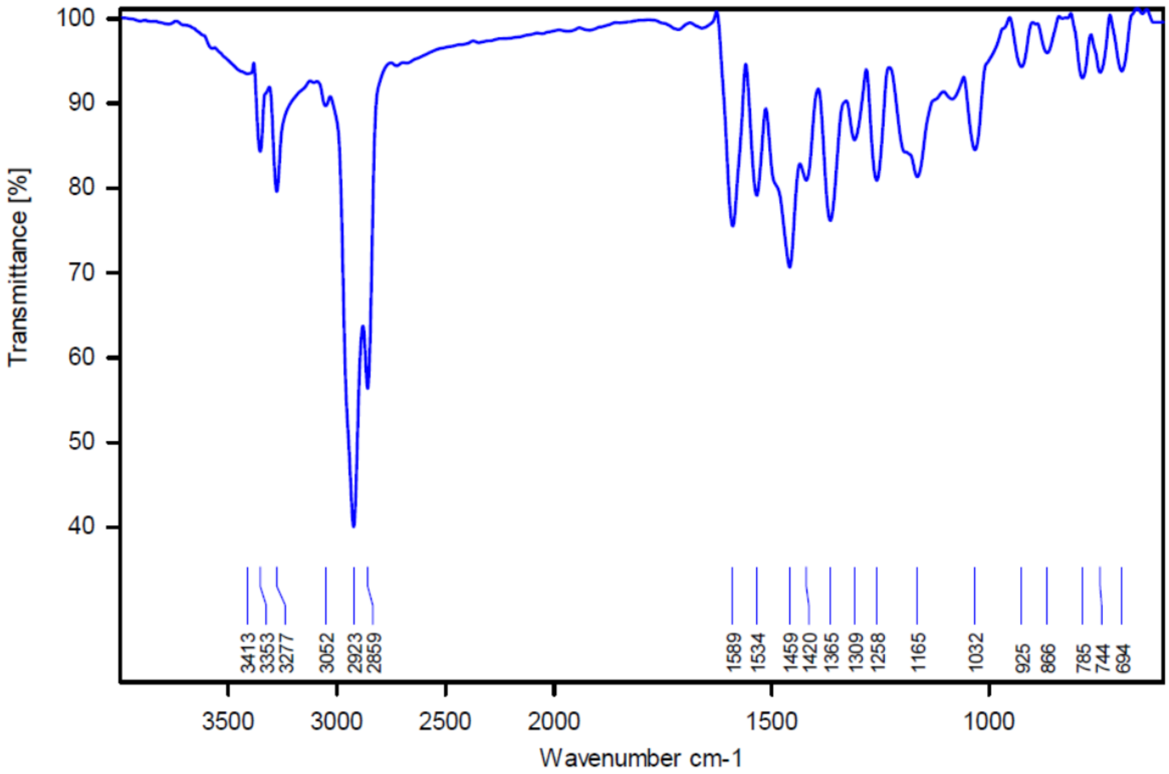


Figure S56. IR spectrum of 1-(3-iodophenyl)-3-(4-methoxyphenyl)thiourea (**3l**).

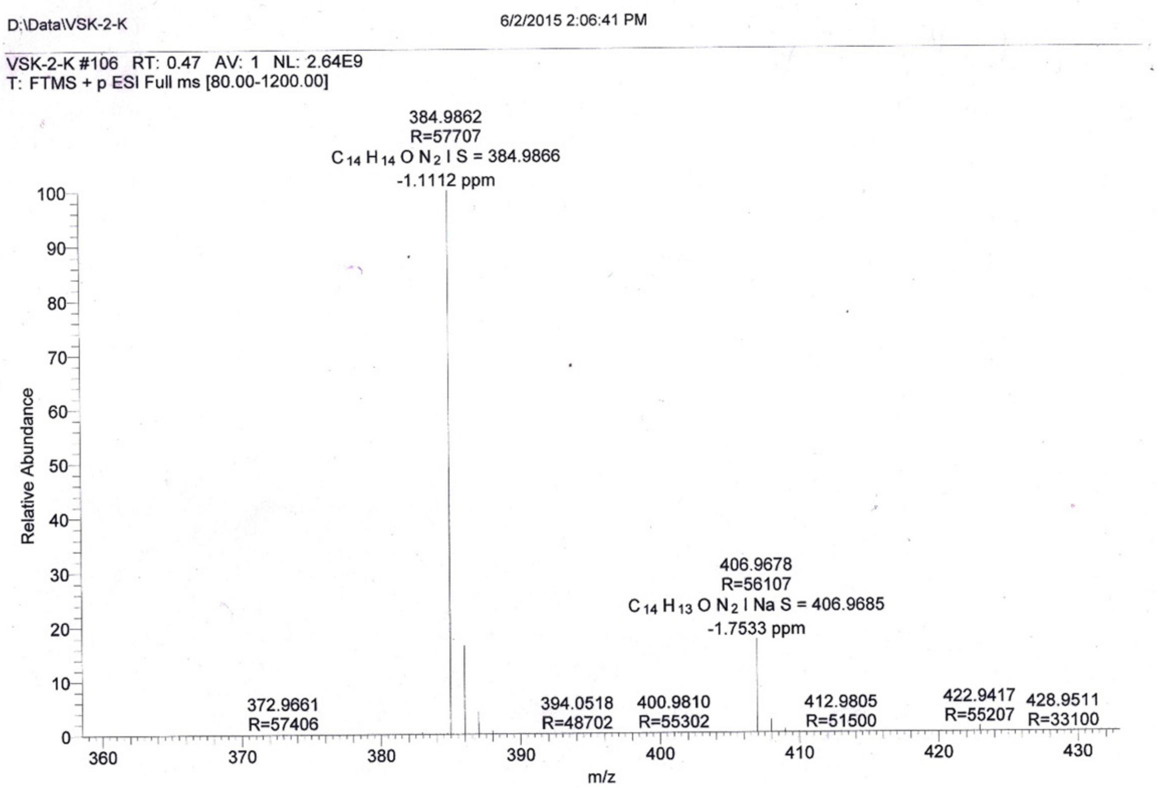
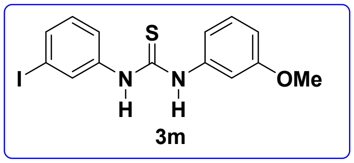


Figure S57. ESI-MS (+ve mode) spectrum of 1-(3-iodophenyl)-3-(4-methoxyphenyl)thiourea (**3l**).

1.11 1-(3-iodophenyl)-3-(3-methoxyphenyl)thiourea (3m):



3-Iodoaniline (4.24 mmol) was dissolved in 15 ml of DCM in a 100 ml of round bottom flask and the solution was cooled to 0°C. 1-isothiocyanato-3-methoxybenzene (3.03 mmol) was added dropwise to the reaction mixture with constant stirring. After that the reaction mixture was allowed to warm to room temperature and was stirred for 18 r. The progress of the reaction was monitored by TLC. The volatiles were evaporated under reduced pressure and the product was purified by silica gel column chromatography (ethyl acetate : petroleum ether (15:85)) in 94% yield. **3m** was crystallized from a 1:1 mixture of DMF:ethyl acetate at room temperature.

^{1}H NMR (400 MHz, DMSO-d$_6$, 298K) δ = 9.95 (s, 1H, N*H*), 9.04 (s, 1H, N*H*), 7.95 (s, 1H, Ar, C*H*), 7.48 (d, 2H, $J_{\text{H-H}}$ = 8.07 Hz, Ar, C*H*), 7.25 (t, $J_{\text{H-H}}$ = 8.07 Hz, 1H, Ar, C*H*), 7.16 (s, 1H, Ar, C*H*),7.13 (t, $J_{\text{H-H}}$ = 8.32 Hz,1H, Ar, C*H*), 7.02 (d, $J_{\text{H-H}}$ = 8.00 Hz, 1H, Ar, C*H*), 6.73 (d, $J_{\text{H-H}}$ = 7.68 Hz, 1H, Ar, C*H*), 3.75 (s, 3H, *OCH*$_3$). **^{13}C NMR** (100 MHz, DMSO-d$_6$, 298K) δ = 179.3 (s, quat, C=S), 159.3 (s, quat, Ar, *C-OMe*), 140.9 (s, quat, Ar), 140.2 (s, quat, Ar), 132.8(s, Ar), 131.7(s, Ar), 130.3 (s, Ar), 129.3 (s, Ar), 122.9 (s, Ar), 115.6 (s, Ar), 110.0 (s, Ar), 109.3 (s, Ar), 93.8 (s, quat, Ar, *C-I*), 55.1 (s, Ar, *OCH*$_3$). **IR** (cm^{-1}): 3190 (NH), 1580 (C=S). **ESI-MS** (+ve) (Cal. For $C_{14}H_{13}N_2OSI$) m/z = 384.98 $[M+H]^+$, 406.96 $[M+Na]^+$. **Mp** = 115°C.

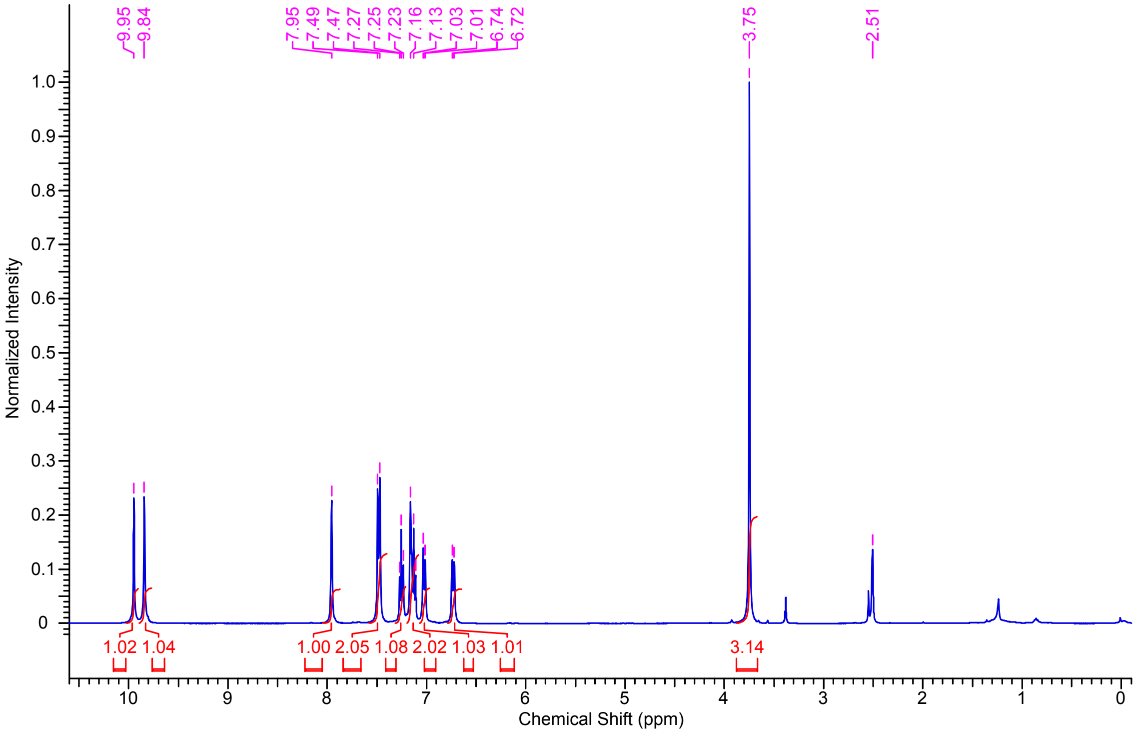


Figure S58. ^{1}H-NMR spectrum of 1-(3-iodophenyl)-3-(3-methoxyphenyl)thiourea (**3m**) in DMSO-d$_6$.

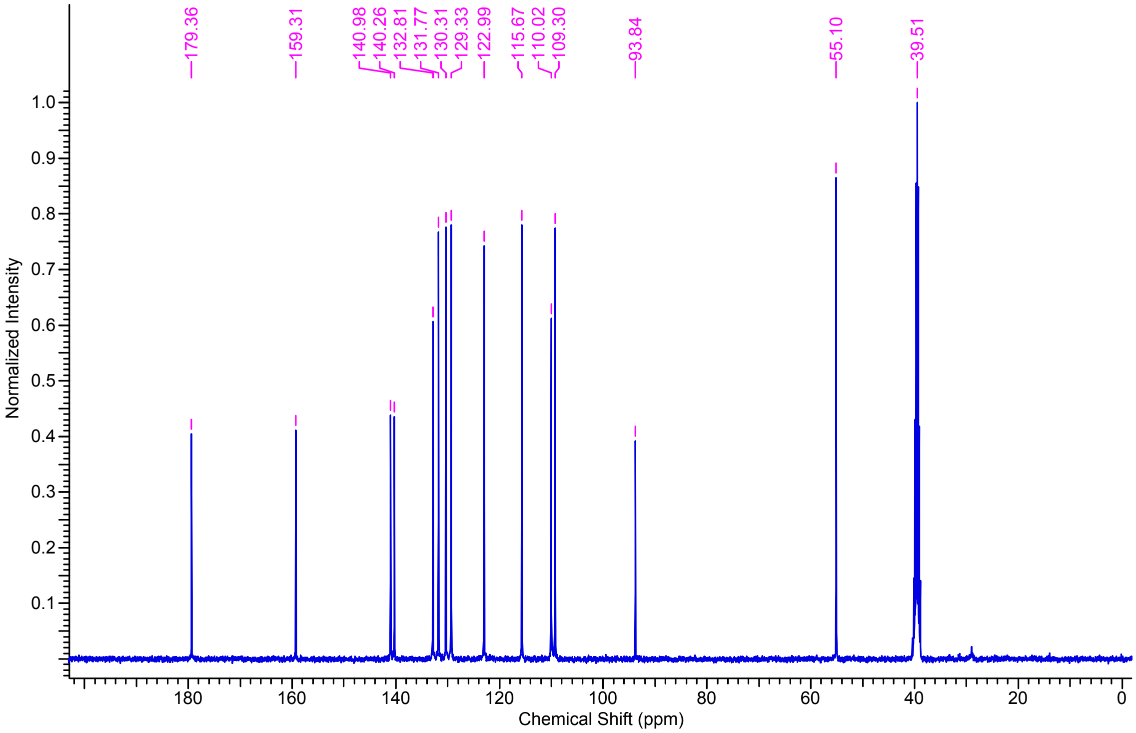


Figure S59. ^{13}C-NMR spectrum of 1-(3-iodophenyl)-3-(3-methoxyphenyl)thiourea (**3m**) in DMSO-d$_6$.

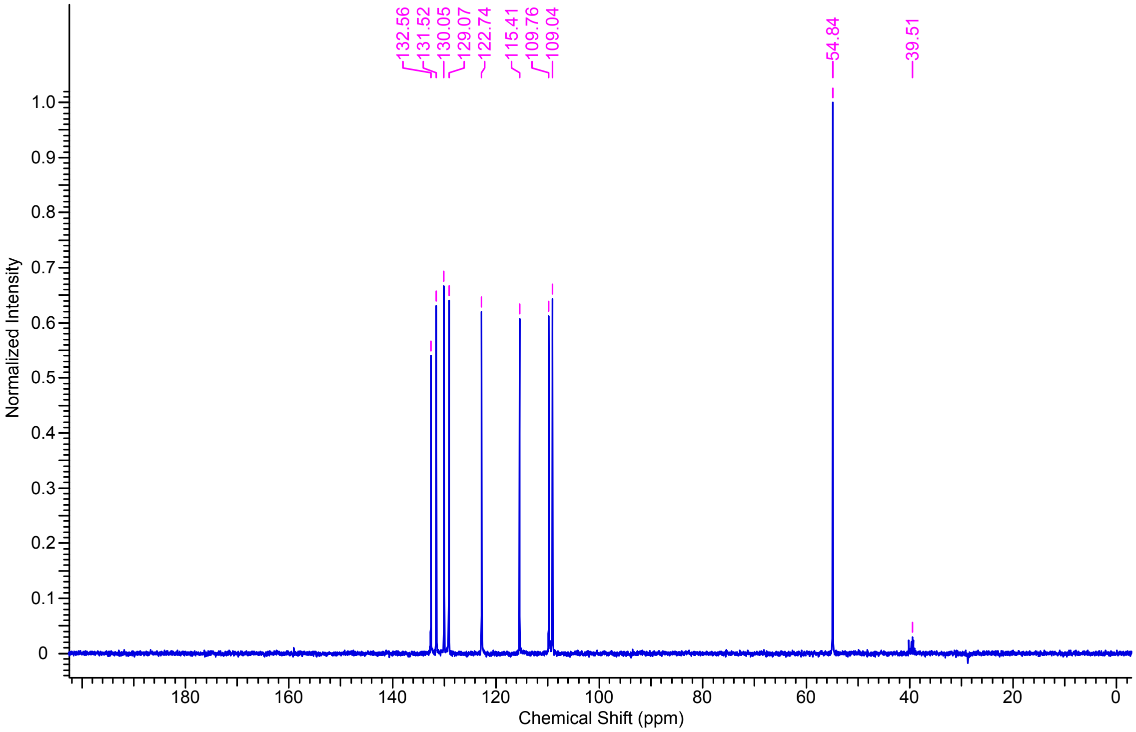


Figure S60. ^{13}C-NMR (DEPT) spectrum of 1-(3-iodophenyl)-3-(3-methoxyphenyl)thiourea (**3m**) in DMSO-d$_6$.

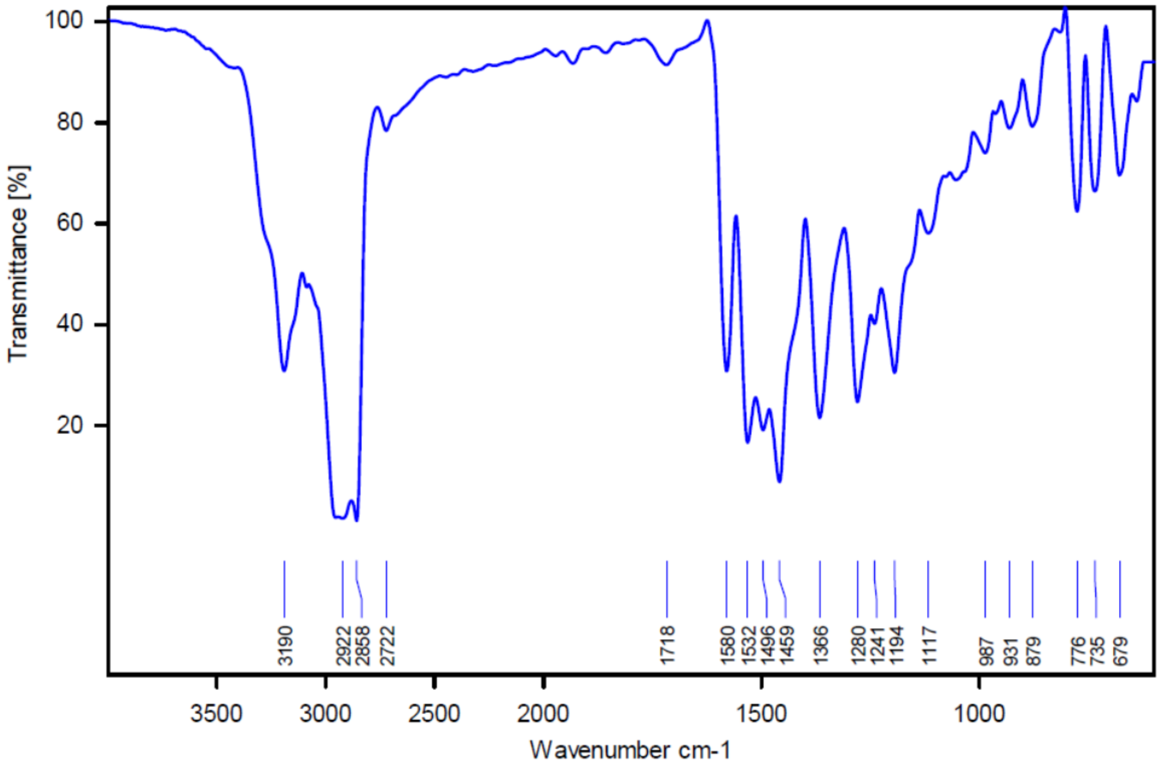


Figure S61. IR spectrum of 1-(3-iodophenyl)-3-(3-methoxyphenyl)thioure (**3m**).

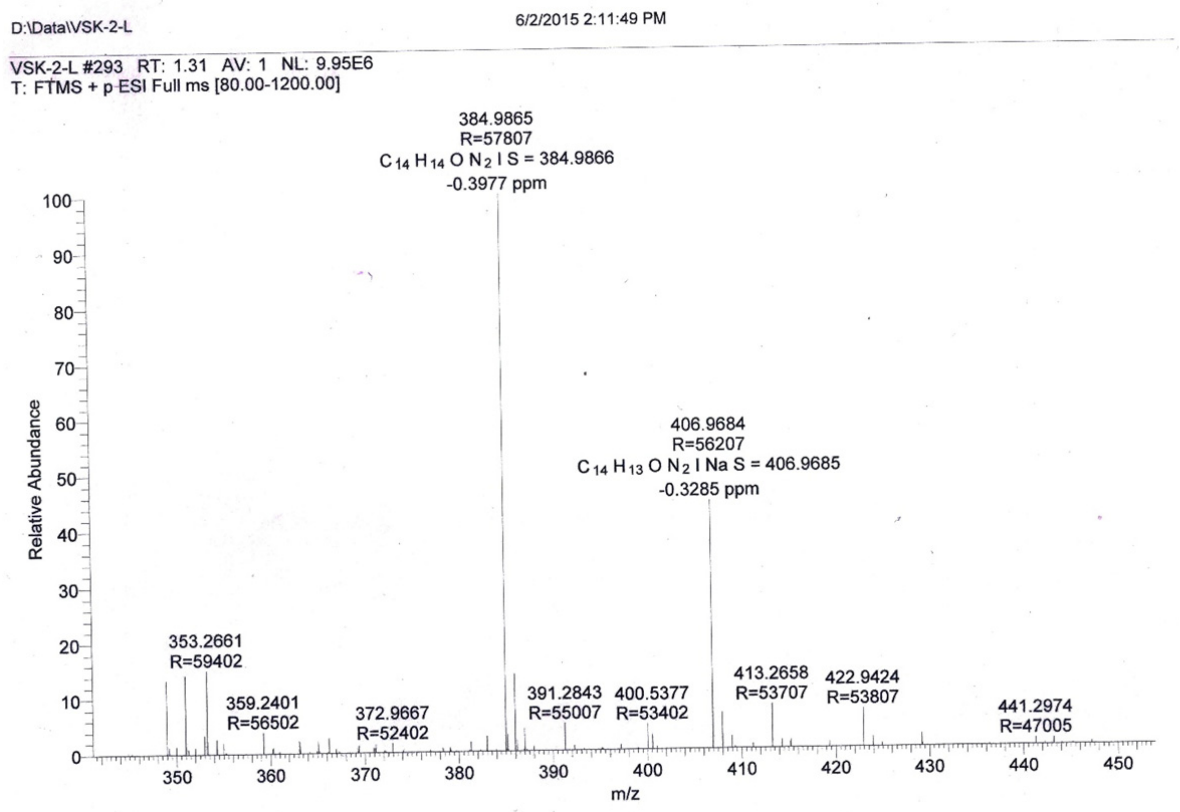
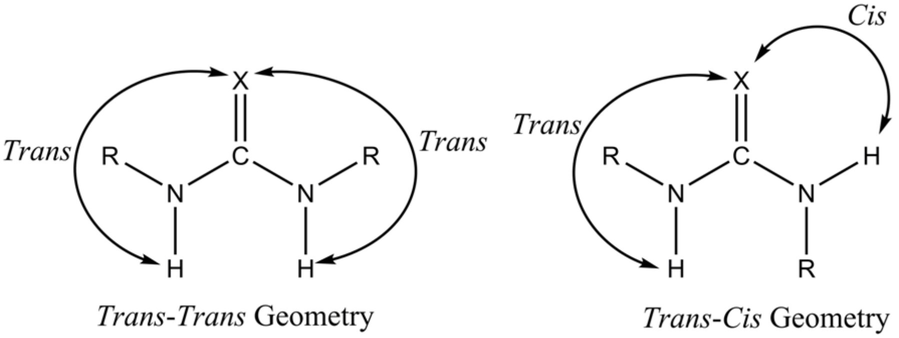


Figure S62. ESIMS (+ve mode) spectrum of 1-(3-iodophenyl)-3-(3-methoxyphenyl)thioure (**3m**).

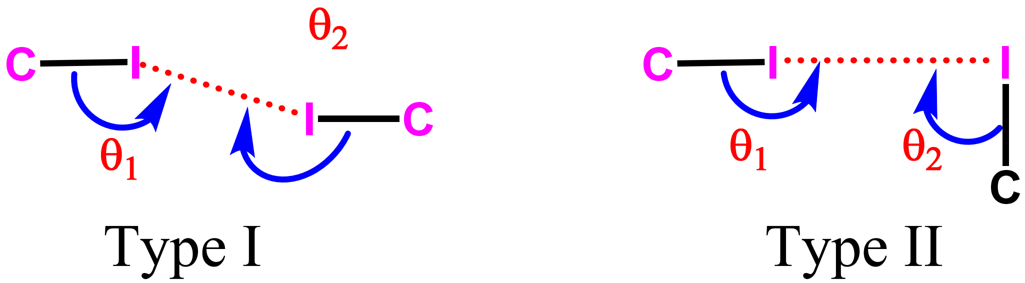
2. *Trans-Trans* and *Trans-Cis* motifs



X = O or S; R = any substituent

Figure S63. Geometrical representations of *Trans-Trans* and *Trans-Cis* motifs in urea and thiourea derivatives

3. Halogen bonding motif

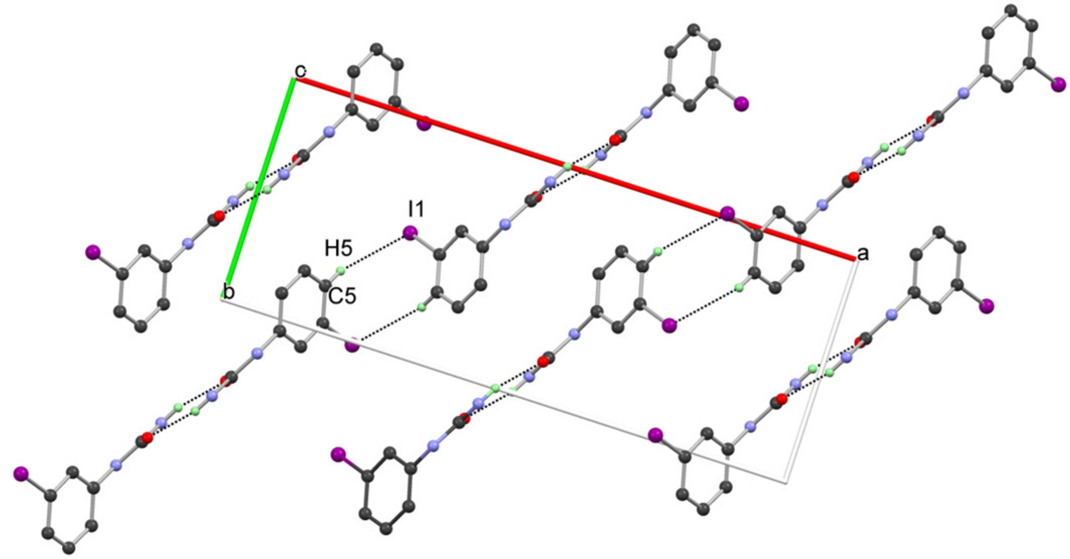


Type I

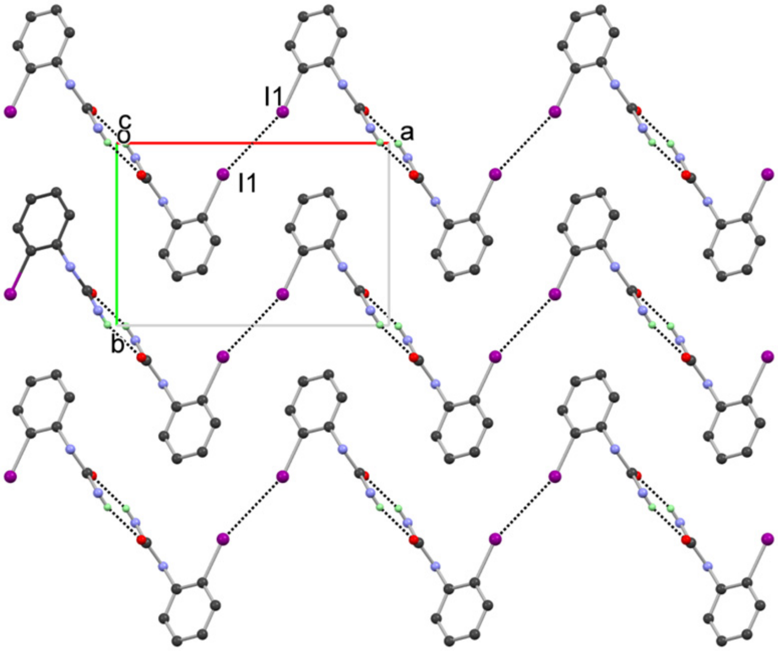
Type II

Figure S64. Types of halogen bonding motifs

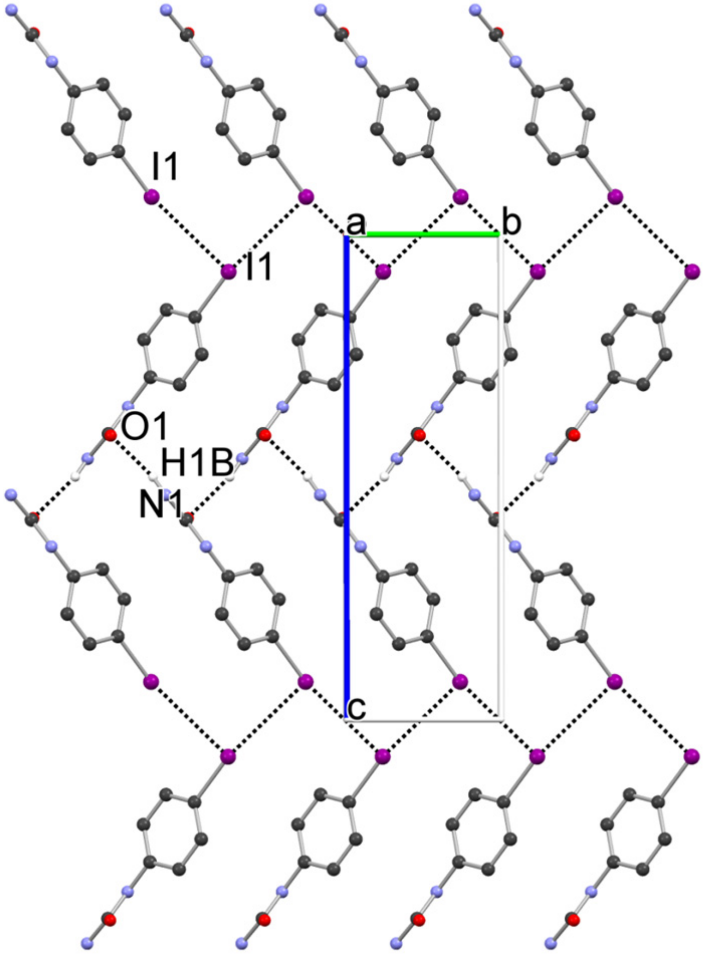
4. View of molecular packing along 3rd direction:



(a)

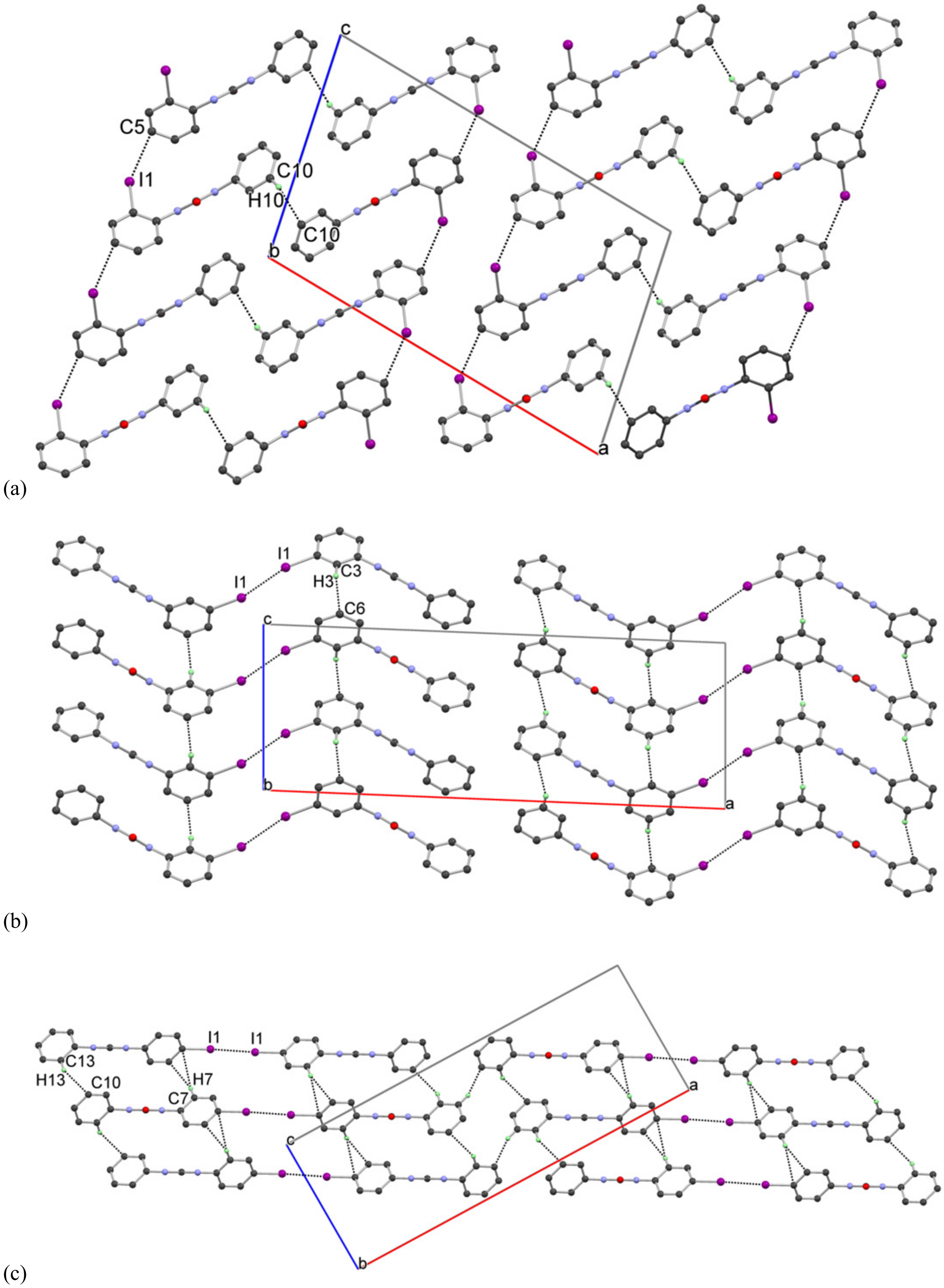


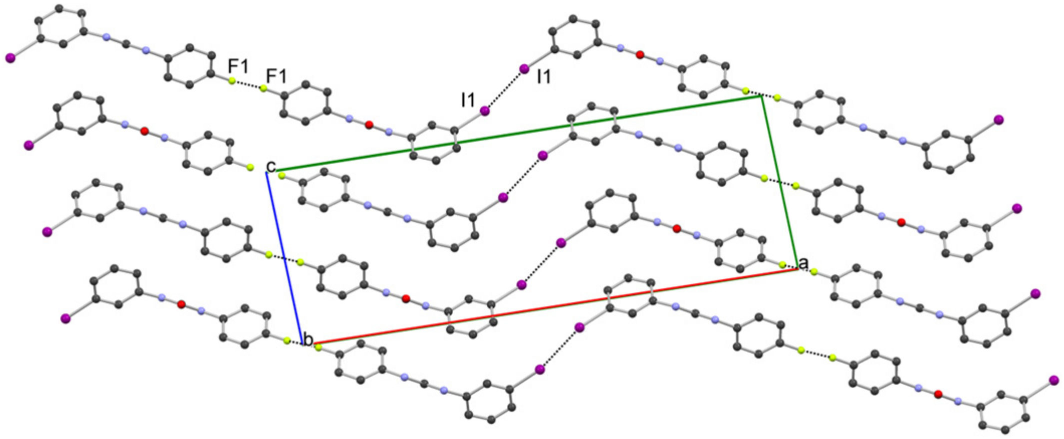
(b)



(c)

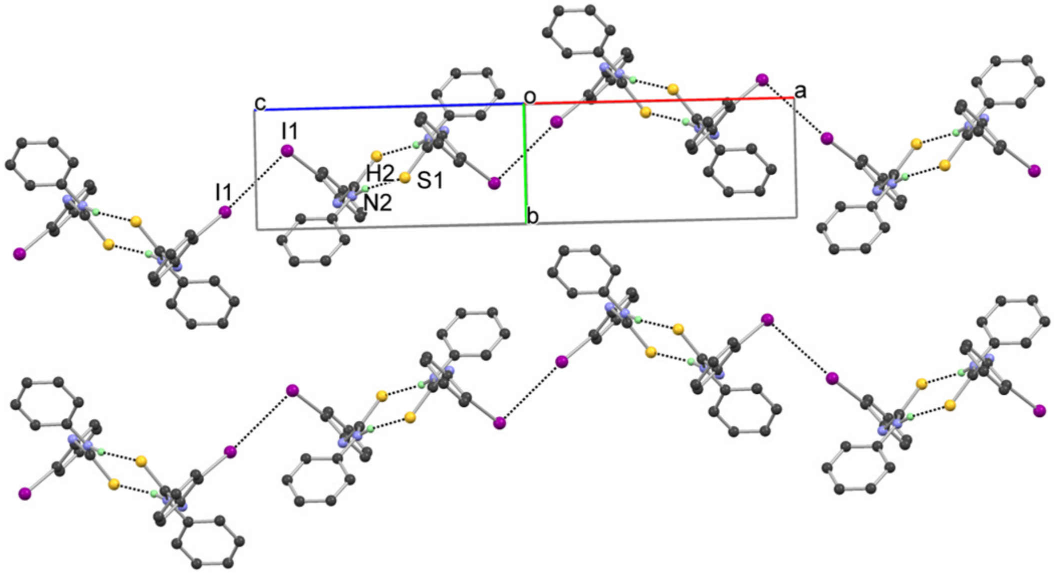
Figure S65. Molecular packing in crystals of (a) **3a**, (b) **3b** and (c) **3c** along the third direction.


c
C5
I1
C10
H10
C10
b
a
(a)
I1
I1
C3
H3
C6
c
b
a
(b)
I1
I1
C13
H13
C10
H7
C7
a
c
b
(c)

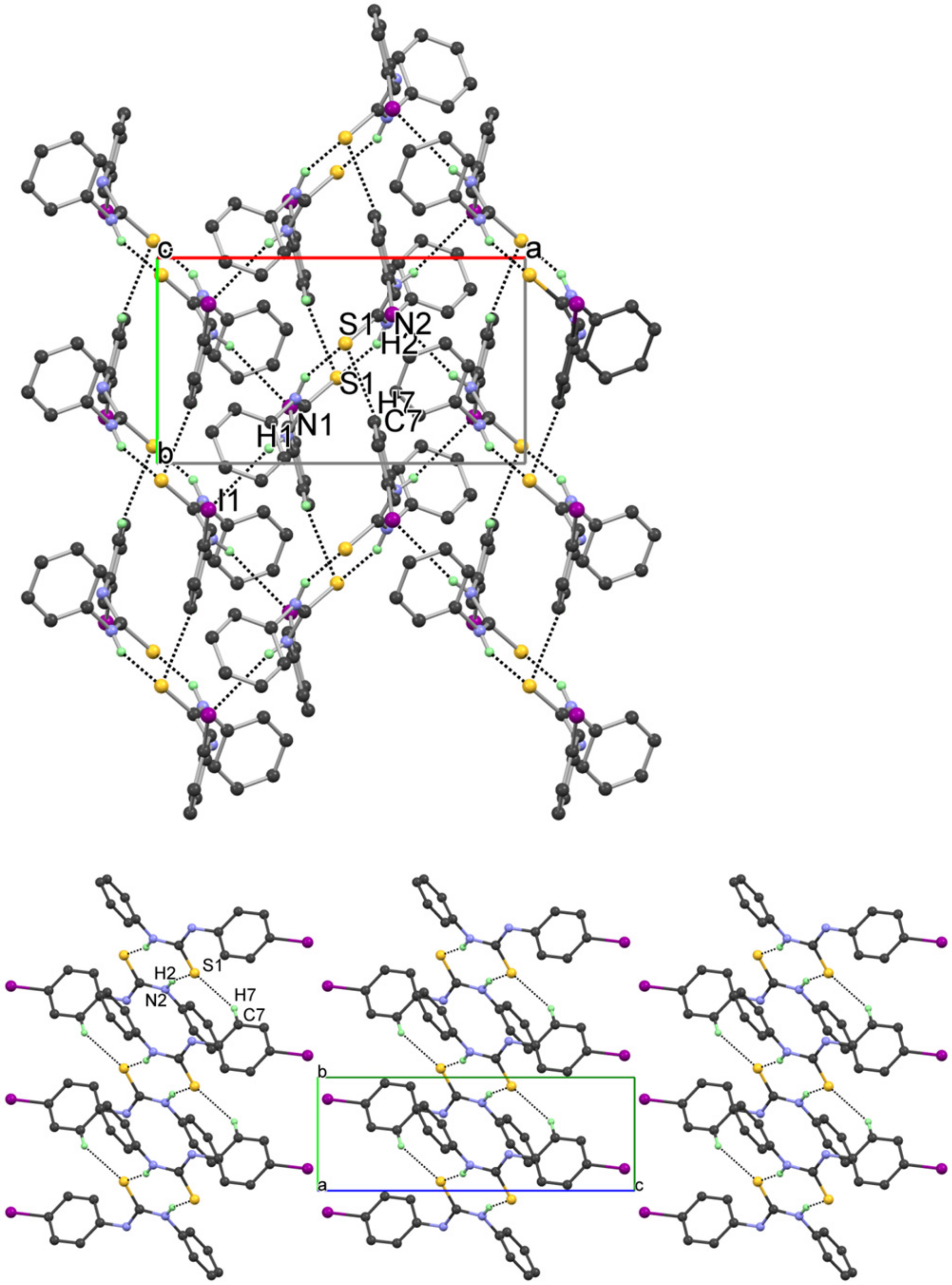


(d)

Figure S66. Molecular packing in crystals of (a) **3d**, (b) **3e**, (c) **3f** and (d) **3g** along the third direction.



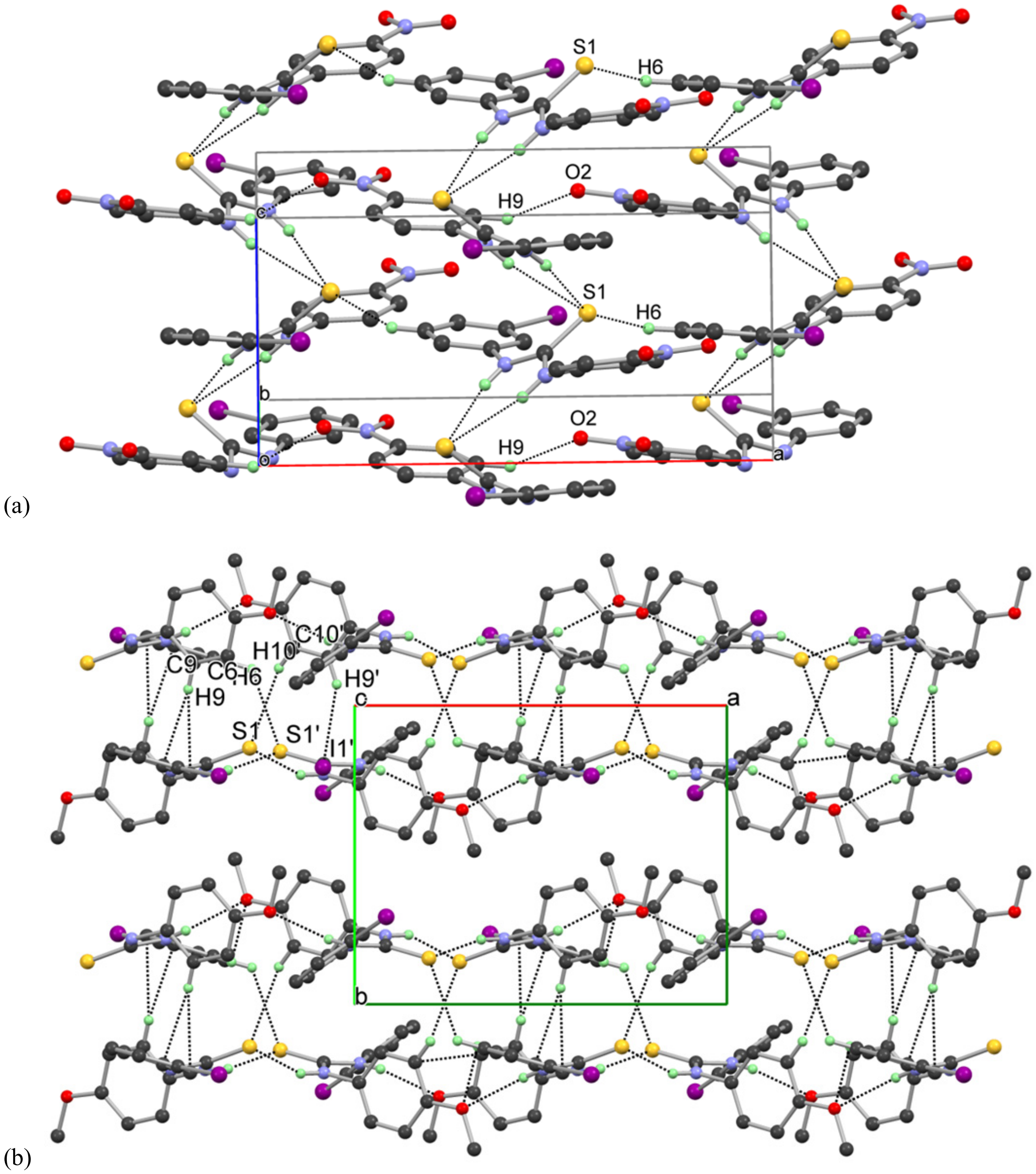
(a)

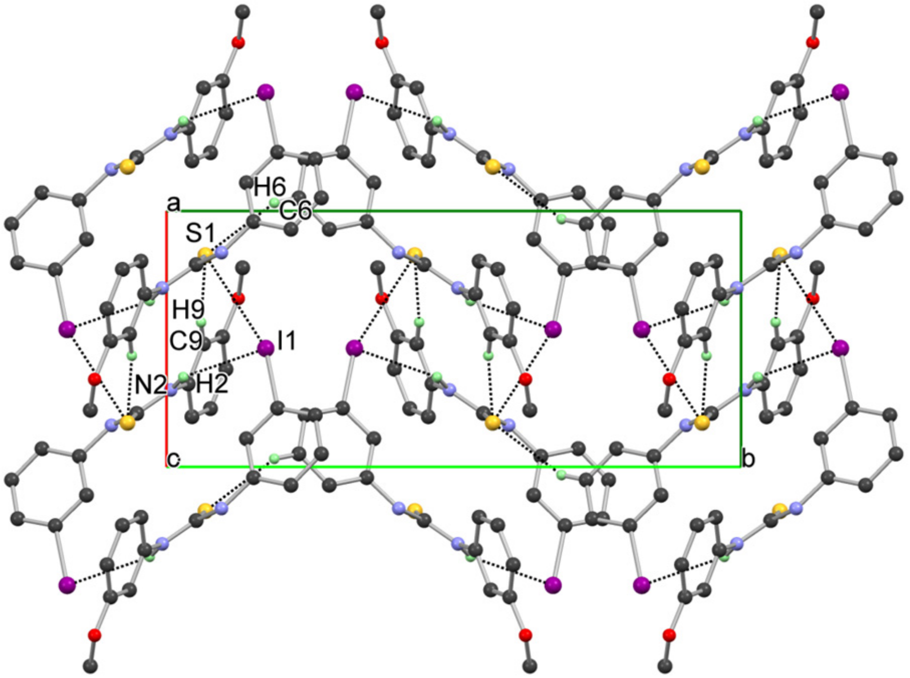


(b)

(c)

Figure S67. Molecular packing in crystals of (a) **3h**, (b) **3i** and (c) **3j** along the third direction.

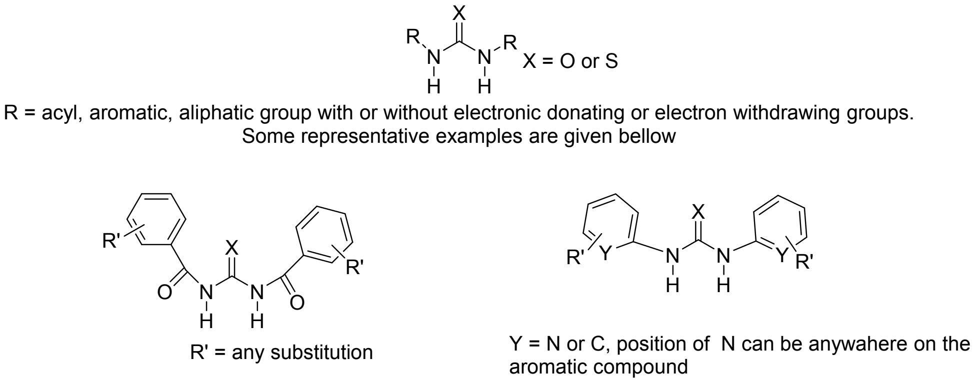

S1
H6
H9
O2
S1
H6
H9
O2
c
b
o
a
(a)
C10'
C9
C6
H10'
H6
H9'
H9
S1
S1'
I1'
c
a
b
(b)



(c)

Figure S68. Molecular packing in crystals of (a) **3k**, (b) **3l** and (c) **3m** along the third direction.

5. CSD Search Criteria



X = O or S

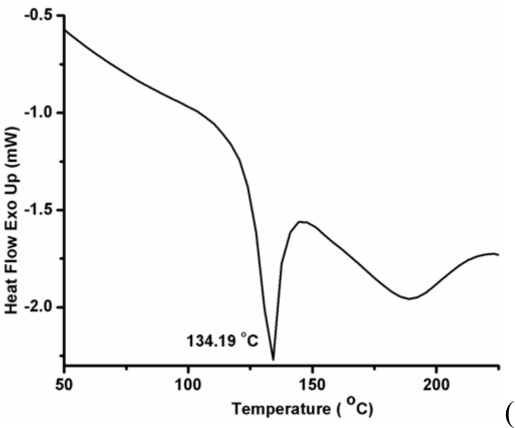
R = acyl, aromatic, aliphatic group with or without electronic donating or electron withdrawing groups.
Some representative examples are given bellow

R' = any substitution

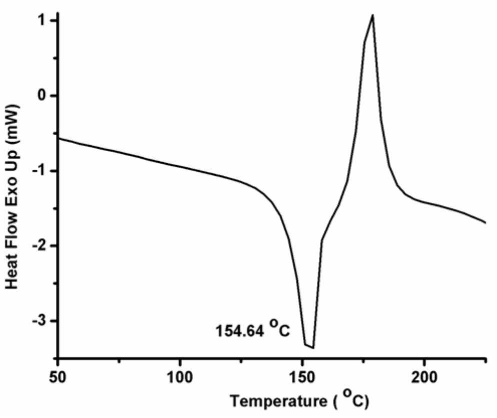
Y = N or C, position of N can be anywahere on the aromatic compound

Figure S69. Criteria applied in CSD search.

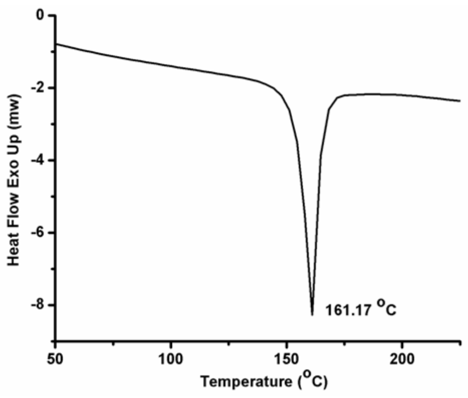
6. Differential Scanning Calorimetry Studies



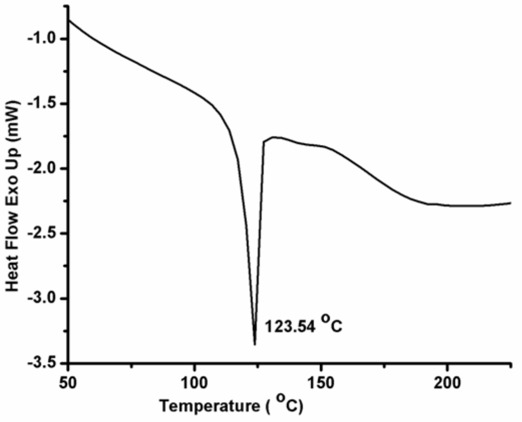
(3a)



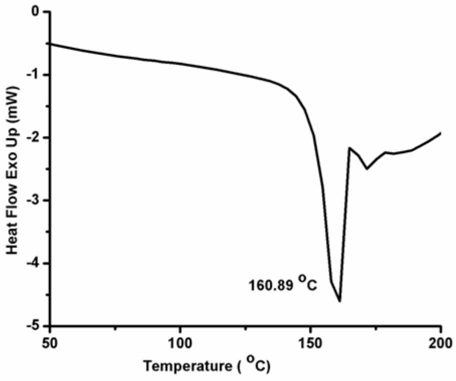
(3b)



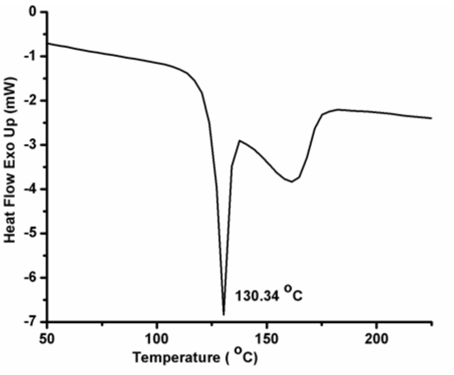
(3c)



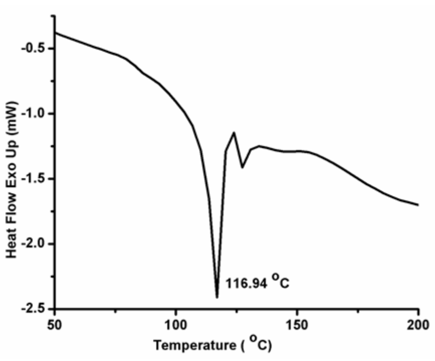
(3d)



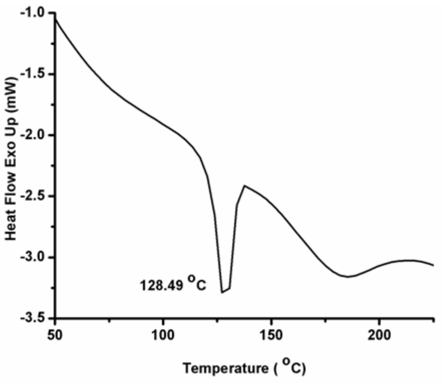
(3e)



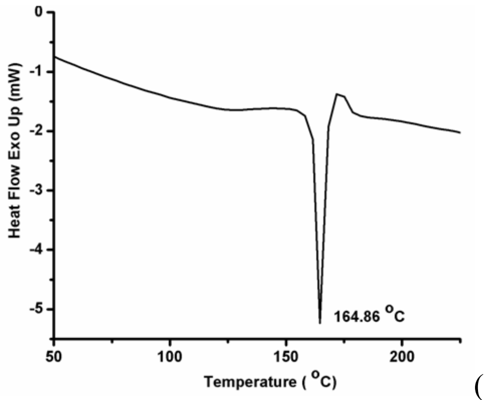
(3f)



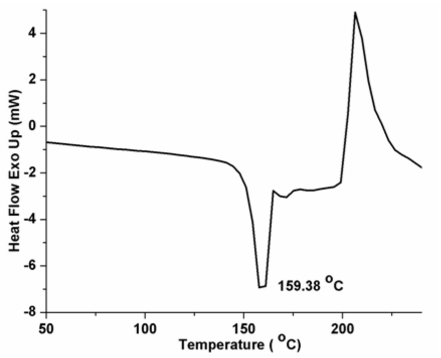
(**3g**)



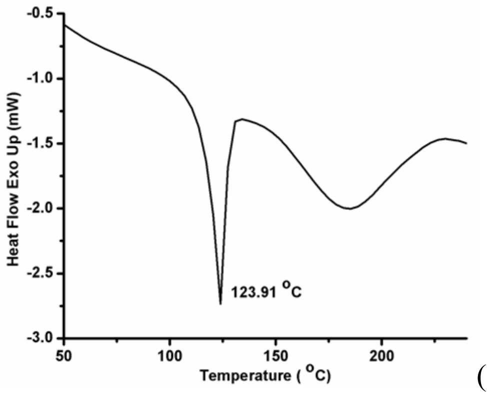
(**3h**)



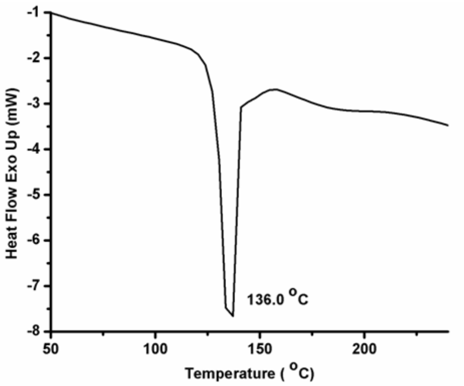
(**3i**)



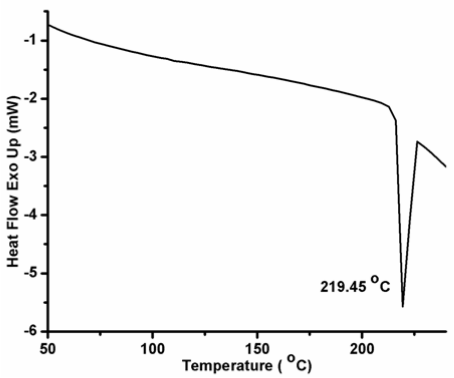
(**3j**)



(**3k**)



(**3l**)



(**3m**)

Figure S70: DSC profiles of compounds **3a-3m**.