

# ***Supporting Information***

## **Continuous Recycling of Homogeneous Pd/Cu Catalysts For Cross-Coupling Reactions**

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1. General Information
2. Synthesis of catalyst
3. Organic synthetic procedure
4. NMR of synthesized compounds

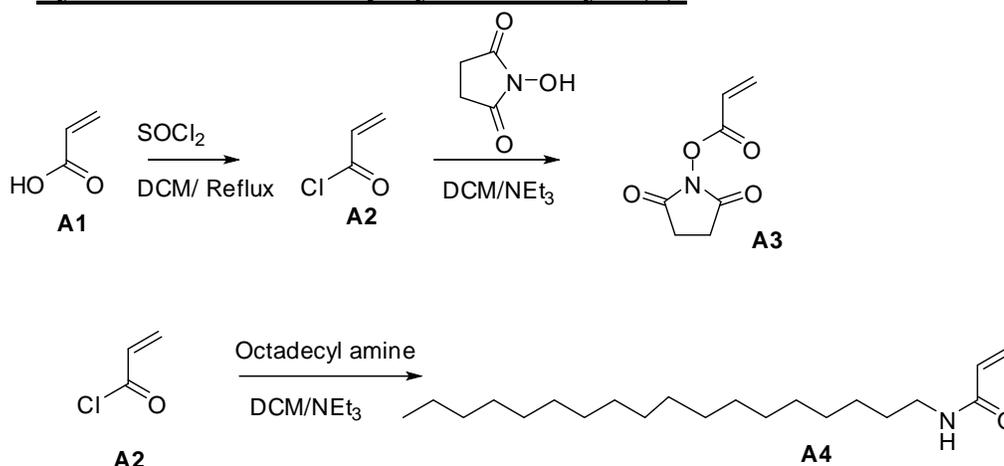
## 1. General Considerations

PFA (id = 500, 800  $\mu\text{m}$ ) tubings, T-junction, were purchased from Upchurch Scientific. Common organic solvents were purchased from Daejung chemicals, Korea. Unless otherwise specified all reagents and chemicals were purchased from Sigma Aldrich and/or Alfa Aesar, and were used without further purification.  $^1\text{H}$  NMR and  $^{13}\text{C}$  NMR spectra were recorded on a Bruker 600MHz. Chemical shifts are reported in units of parts per million (ppm) relative to the signal (0.00 ppm) for internal tetramethylsilane for solutions in  $\text{CDCl}_3$ . The compounds were fully characterized by their Mass-spectra,  $^1\text{H}$ , and  $^{13}\text{C}$  NMR data. All the compounds have been collected under stabilized condition ( $\approx 10$ -15min. for stable condition). Optimization yields were average of at least two experiments. All XPS measurements were taken in a Sigma probe (ThermoVG) using a monochromatic Al-K $\alpha$  X-ray source at 100 W. The thermal degradation processes and stabilities of the catalyst were investigated using a thermo gravimetric analyzer (SDT Q600 TGA/SDTA851 with *water* software) under a nitrogen atmosphere with a heating rate of 1  $^\circ\text{C}/\text{min}$  from 50 to 500 $^\circ\text{C}$ . Molecular weights of the polymers were estimated by gel permeation chromatography (GPC, Waters) using PS standards and a refractive index detector in THF solvent. Wide angle X-ray diffractograms of the synthetic samples were recorded using Rigaku D/max 2500/PC X-ray diffractometer with Cu K $\alpha$  (1.54056) radiation.

**Important Note:** It should be noted that all the tubing were filled with DMF before the start the continuous flow synthesis to achieve fast stabilized condition and to remove the air from HPLC pump.

## 2. Synthesis of catalyst

### Method S1. Synthesis of block copolymer catalyst (I).



**Scheme S1.** Synthesis of monomers for block copolymer synthesis.

#### S1.1. Synthesis of acryloyl chloride (A2).

Acrylic acid (A1) (5.25 g, 5 mL, 69.38 mmol) was dissolved in 20 mL anhydrous dichloromethane. Thionyl chloride (1 molar equivalent) was added drop wise to this solution while stirring under N<sub>2</sub> atm and the reaction mixture was allowed to heat to reflux for 4 h. After the completion of reaction, the solvent was distilled out first in 39 °C and then acryloyl chloride in 73 °C. Pale yellow liquid was obtained in 81% yield.

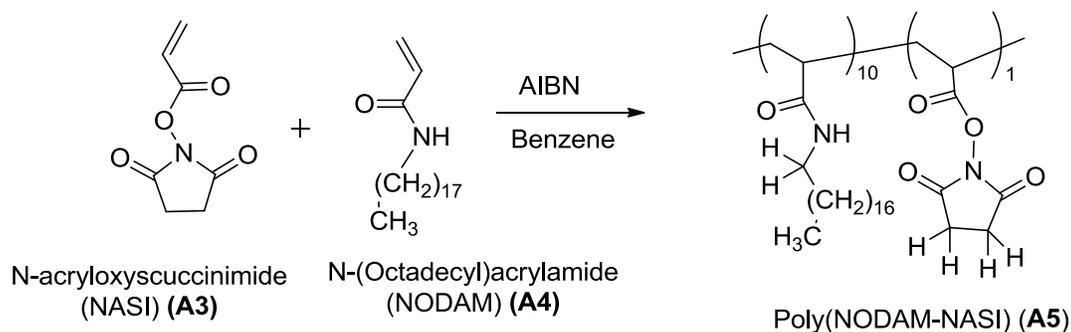
#### S1.2. Synthesis of N-acryloxysuccinimide (A3).

Acryloyl chloride (4.25 mL, 1.2 eq.) was added dropwise to a stirred solution of N-hydroxysuccinimide (5.0 g, 86.9 mmol) and TEA (triethylamine) (7.3 mL, 1.2 eq.) in chloroform (60 mL) at 0 °C. After 4 h, the solution was extracted with deionized water and the organic phase was dried over Na<sub>2</sub>SO<sub>4</sub>. The solution was concentrated and the crude product was recrystallized from hexane/ethyl acetate (8:1). The crystals were filtered and washed with hexane/ethyl acetate (4:1), and then dried. A white solid in 62% yield have been collected.

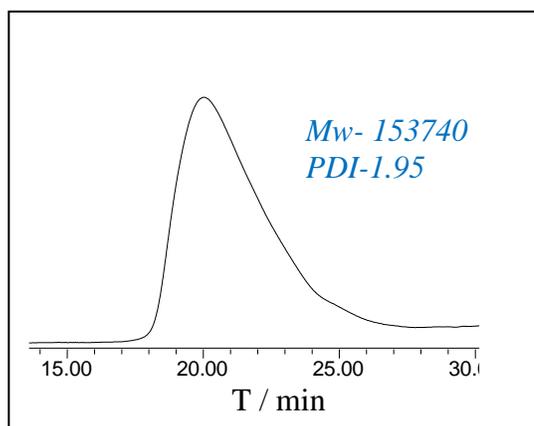
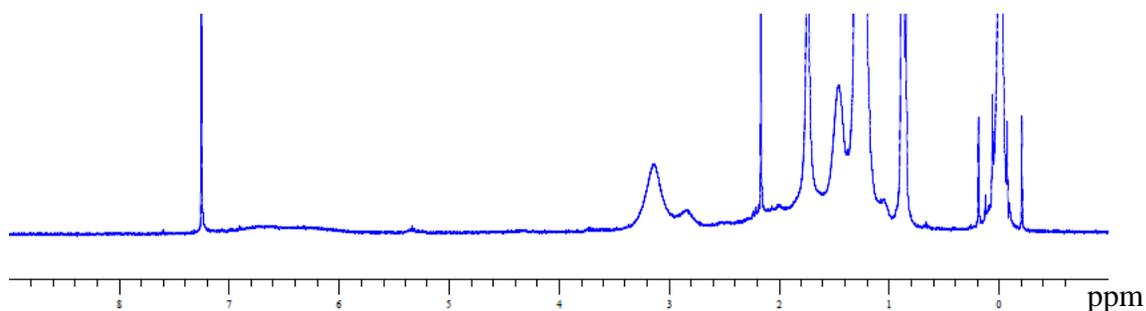
### S1.3. Synthesis of N-octadecylacrylamide (A4).

N-octadecylacrylamide were synthesized by drop-wise addition of acryloyl chloride to the appropriate octadecan-1-amine in dry THF at 0 °C with stirring for 12 h. Excess triethylamine was added to neutralize the generated hydrochloric acid. The product was extracted in ethyl acetate, the organic phase was dried over Na<sub>2</sub>SO<sub>4</sub>, and the solvent was evaporated under reduced pressure. The crude material was purified using silica gel column chromatography using EtOAc/Hexane.

### S1.4. Synthesis of Poly(N-octadecyl-acrylamide-co-N-acryloxysuccinimide) (PNODAM-c-PNASI) (A5).

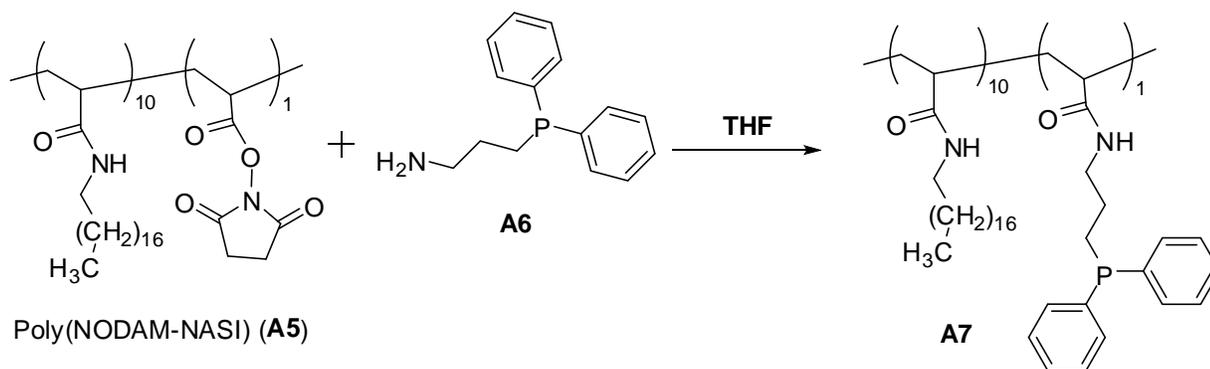


16.15 g (50 mmol) of N-octadecylacrylamide (NIPAM) (A4) and 0.845 mg (5 mmol) of N-acryloxysuccinimide (NASI) (A3) were dissolved in 80 ml of benzene at 65 °C under nitrogen. A solution of azobisisobutyronitrile 20 mg (AIBN) in 2 ml of benzene was added to this solution. The reaction mixture was stirred at 65 °C for 20 h. The solvent was then removed by rotary evaporator under vacuum. The synthesized (PNODAM-c-PNASI) (A5) was the isolated (6 g) by successive precipitation from THF solution into hexane. The dried polymer was characterized by GPC, and <sup>1</sup>H NMR (Fig. S1).



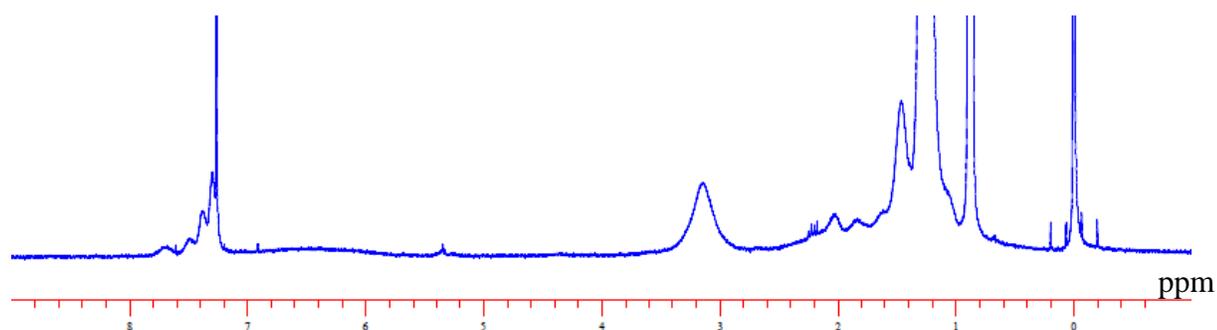
**Fig. S1.**  $^1\text{H}$  NMR and GPC of block copolymer **A5**.

**S1.5. Synthesis of phosphine modified block-copolymer (**A7**).**



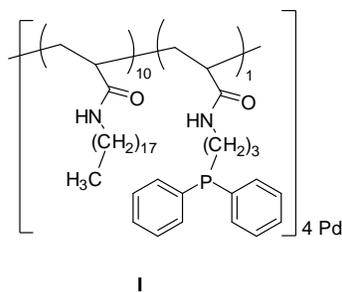
5 g of PNODAM-c-PNASI (**A5**) was dissolved in 75 ml of THF. Then 0.8g of 3-aminopropyl

diphenylphosphine in 10 ml of THF was added under N<sub>2</sub>. The mixture was stirred at room temperature for 5 h and excess of aqueous ammonia was added to quench any unreacted succinamide groups. The mixture was again stirred for 5 h at room temperature. The polymer (**A7**) was then isolated by precipitation using excess hexane and repeated twice the same procedure. Then the dried polymer was characterized by <sup>1</sup>H-NMR (Fig. S2).



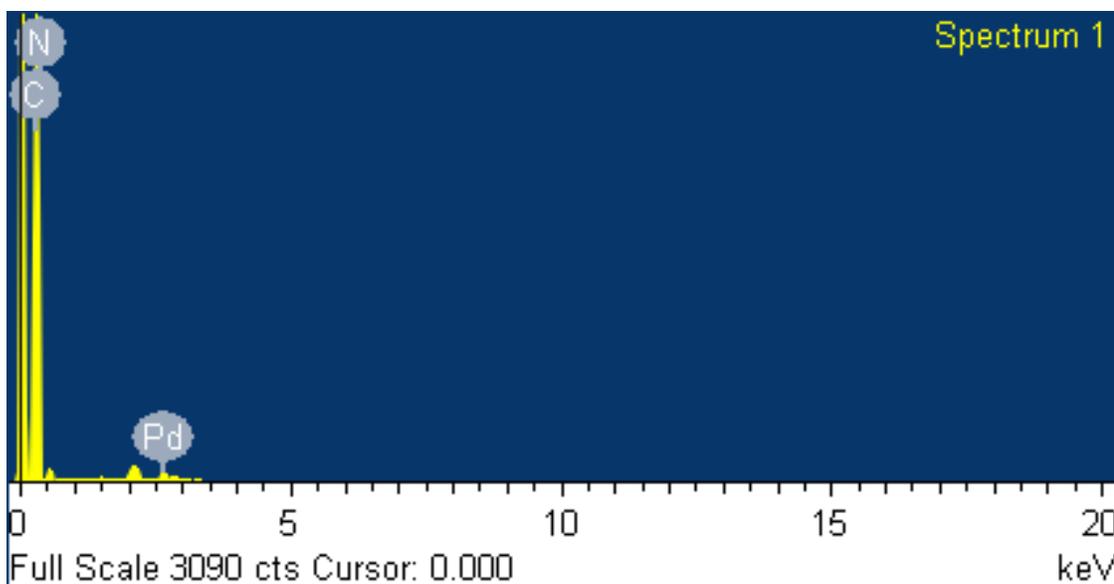
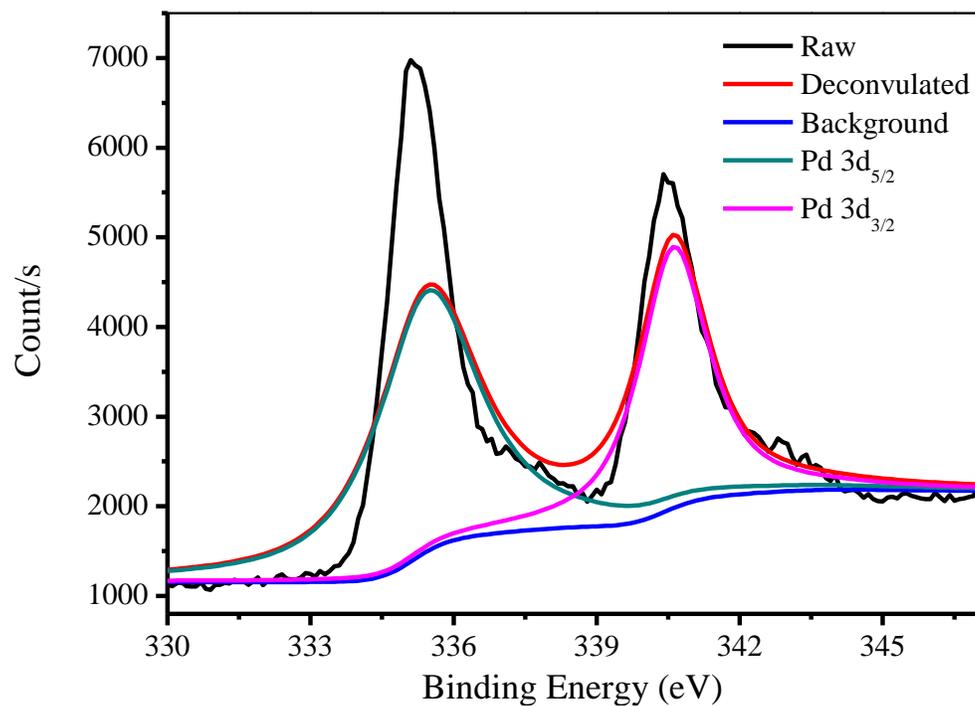
**Fig. S2.** <sup>1</sup>H NMR of block copolymer **A7**.

### **S1.6. Loading of Pd-catalyst on phosphine functionalized block copolymer as catalyst (**I**).**



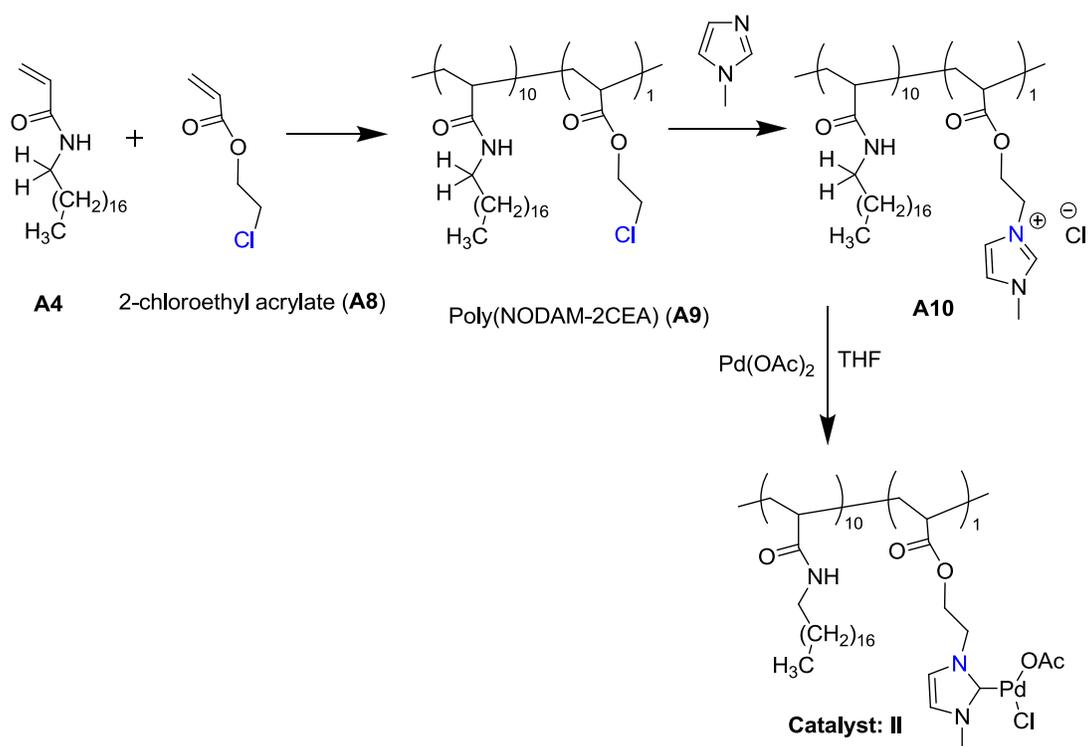
Polymer **A7** (2 g) was dissolved in 60 mL of 90:10 THF: H<sub>2</sub>O under N<sub>2</sub>. A solution of Pd(0)(dba)<sub>2</sub> (200 mg, 0.088 mmol) in 25 ml of the same solvent was separately prepared under N<sub>2</sub>. And the Pd precatalyst solution was added to the polymer solution using double tipped needle and N<sub>2</sub> pressure. The solution mixture was allowed to stir for further 1 h, then hexane was added to the polymer solution to precipitate the catalyst (**I**) as a solid. Finally the polymer catalyst was dried under vacuum and store

under N<sub>2</sub> for further use. Pd metal has been confirmed and quantify by EDX, XPS and ICP-AES analysis. In order to estimate the amount of Pd loaded on polymer, a known amount of polymer was digested by nitric acid and sulfuric acid mixture and diluted with water, which was analyzed by ICP-AES. The amount 0.51mg/g of Pd was found.



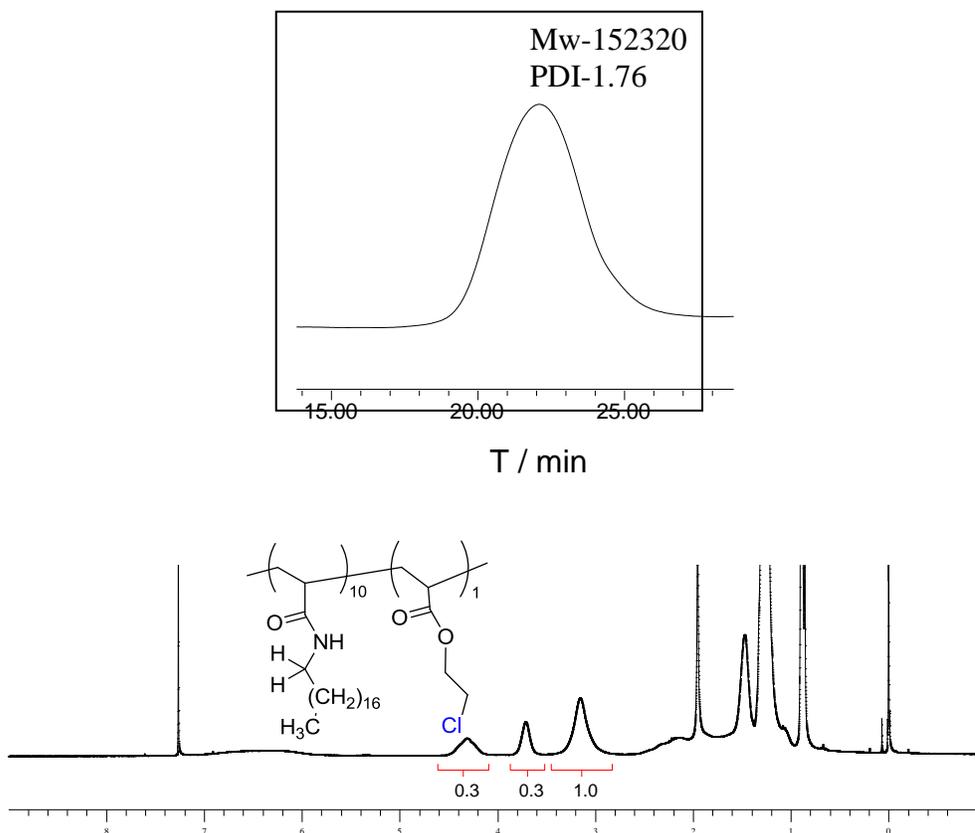
**Fig. S3.** XPS and EDX spectra for palladium characterization in catalyst (I).

## Method S2. Synthesis of block copolymer catalyst (II).



### S2.1. Synthesis of block copolymer Poly (NODAM-2CEA) (A9).

16.15 g (50mmol) of N-octadecylacrylamide (NIPAM) (**A4**) and 0.670 g (5 mmol) of 2-chloroethyl acrylate (2CEA) (**A8**) were dissolved in 100 ml of toluene in Schenk tube. A solution of azobisisobutyronitrile (AIBN) 20 mg in 10 ml of toluene was added to this solution. The reaction mixture was stirred at 75 °C for 18 h under nitrogen atmosphere. The solvent was then removed by rotary evaporator under vacuum. The synthesized Poly(NODAM-2CEA) (**A9**) was isolated (8 g) by successive precipitation from THF solution into hexane. The polymer has been characterized by GPC and  $^1\text{H-NMR}$  analysis.

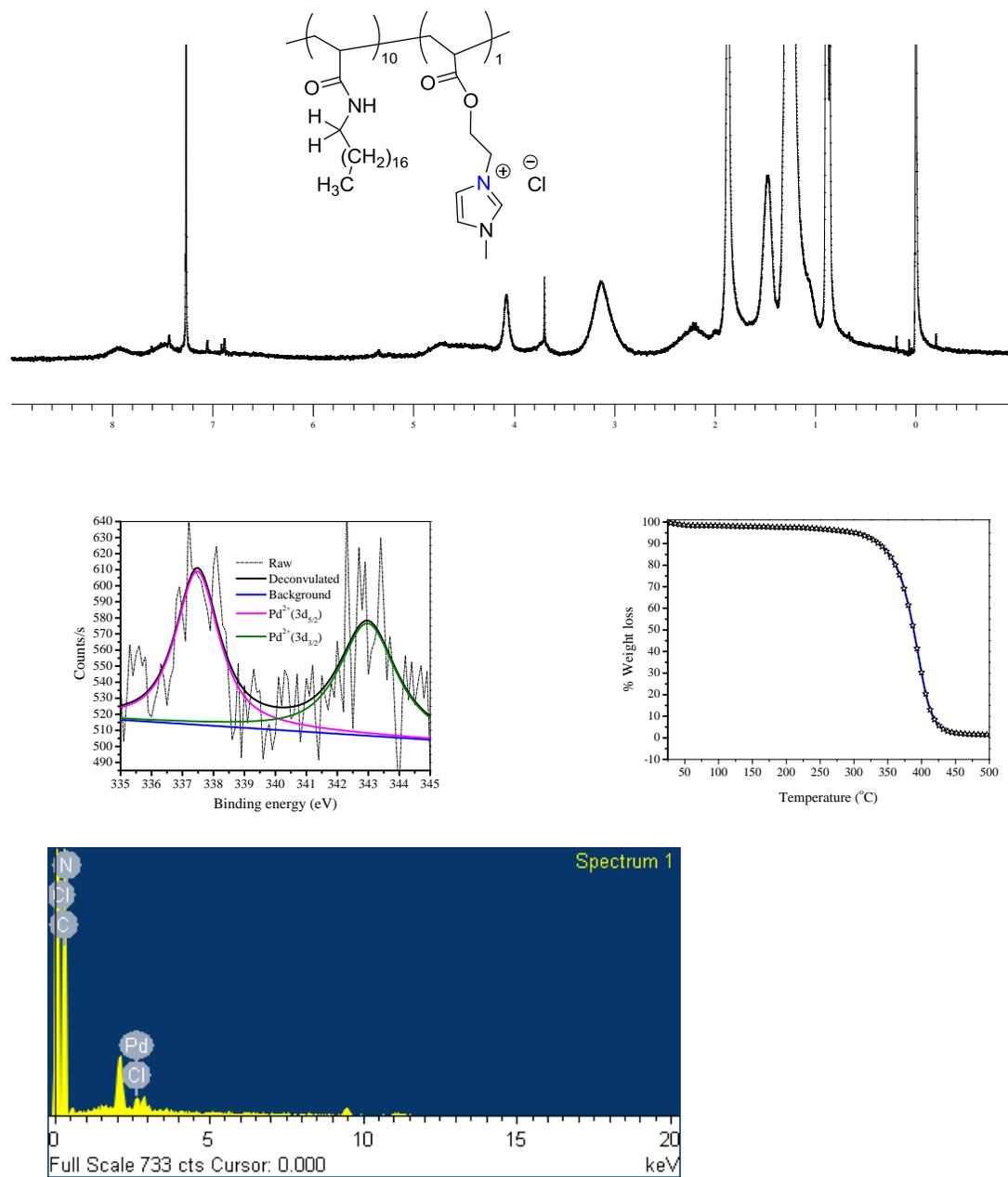


**Fig. S4.** GPC and  $^1\text{H}$  NMR analysis for **A9**.

### S2.2. Experimental Procedure for thermomorphic block-copolymer supported N-heterocyclic carbene (NHC) Palladium Catalyst (II).

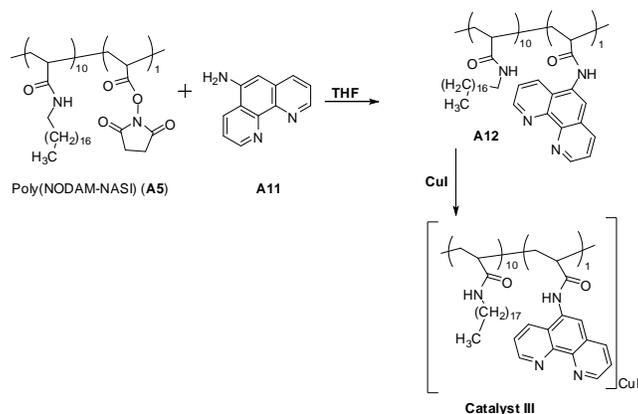
A mixture of Poly(NODAM-2CEA) (**A9**) 5 g, 1-(methyl) imidazole (1 g) was stirred in THF (80 ml) at 70 °C for 24 h. After cooling to room temperature, the reaction mixture was evaporated by rotary evaporator under vacuum. The synthesized polymer (**A10**) was isolated (6 g) by successive precipitation from THF solution into excess of hexane. The polymer has been characterized by  $^1\text{H}$ -NMR. The synthesized polymer (**A10**) and  $\text{Pd}(\text{OAc})_2$  (5 equiv) was mixed and stirred in THF at 50 °C for 4 h. After increasing the temperature to 70 °C, the mixture was stirred for a further 1 h. The synthesized catalyst (**II**) was then isolated (3 g) by successive precipitation from THF solution into excess of hexane. The polymer was then dried under reduced pressure. In order to estimate the amount of Pd loaded on polymer, a known amount of polymer was digested by nitric acid and sulfuric acid

mixture and diluted with water, which was analyzed by ICP-AES. The amount 0.5mg/g of Pd was found.



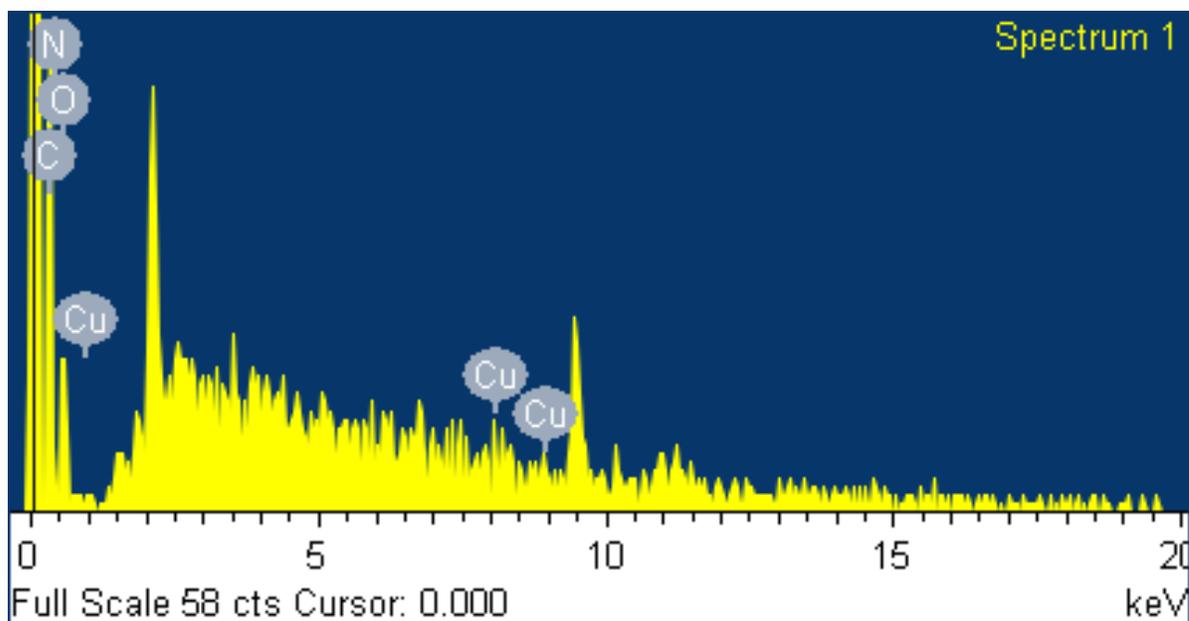
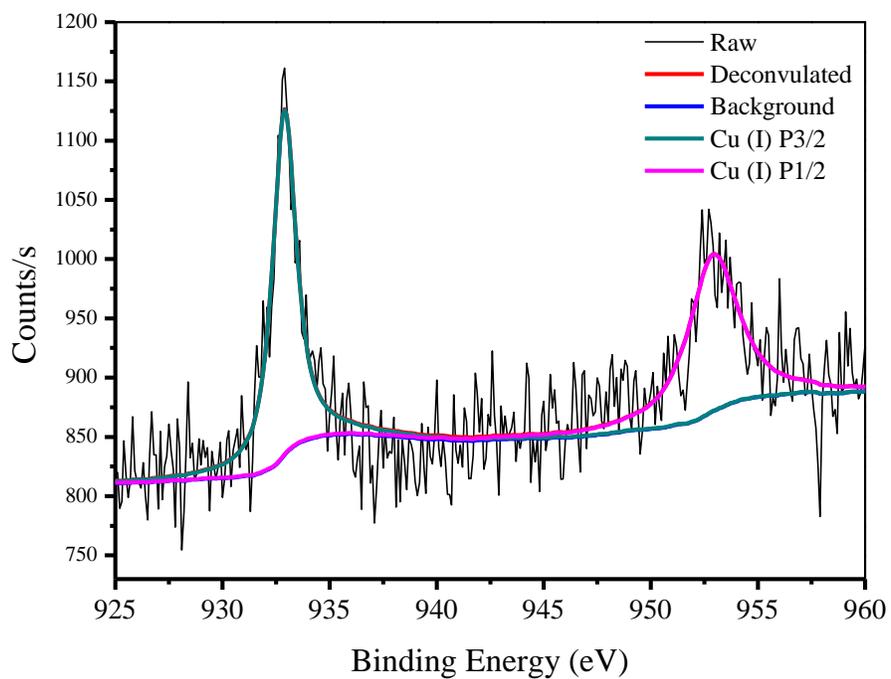
**Fig. S5.**  $^1\text{H}$  NMR (A10), XPS, TGA and EDX spectra for palladium characterization in catalyst (II).

## Method S3. Thermomorphic block-copolymer synthesis of catalyst III for click chemistry application (III).

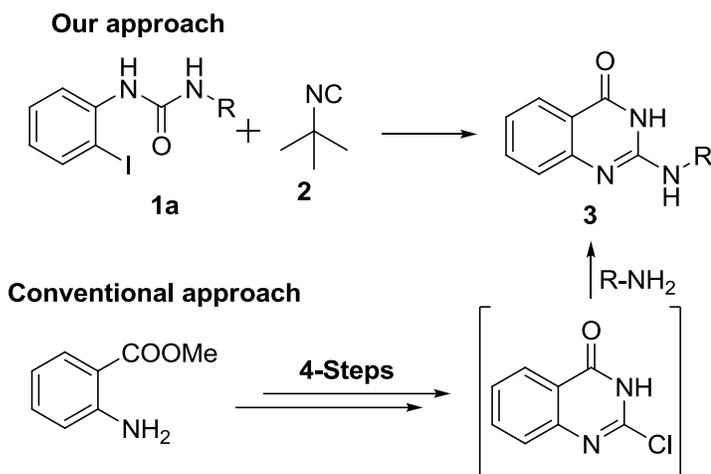


### S3.1. Experimental procedure for the synthesis of catalyst (III).

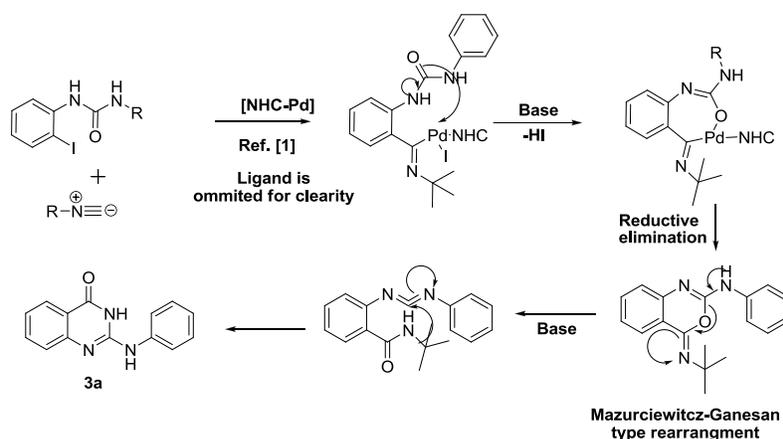
5 g of PNODAM-co-PNASI (A5) was dissolved in 75 ml of THF. Then 1g of 5-amino-1,10-phenanthroline (A11) in 10 ml of THF was added under N<sub>2</sub>. The mixture was stirred at reflux for overnight and excess of aqueous ammonia was added to quench the reaction. The mixture was again stirred at room temperature for 5 h. The polymer (A12) was then isolated by precipitation in the excess hexane. The transformation has been confirmed by <sup>1</sup>H-NMR. The synthesized polymer (A12) and CuI (3 equiv to amino-1,10-phenanthroline) was mixed and stirred in DMSO-THF (80:20) at room temperature for 4h. The synthesized catalyst (III) was then isolated (3.2 g) by successive precipitation from THF solution into excess of hexane. The polymer was then dried under reduced pressure and we found that about 0.40 mg/g Cu has been immobilized as confirmed by ICP-AES using the aforementioned digestion procedure. Copper was further confirmed by XPS and EDX (Fig. S6).



**Fig. S6.** XPS and EDX spectra for copper characterization in catalyst (III).



**Fig. S7.** Highly concise and cascade approach for the synthesis of substituted 2-aminoquinazolinones under TMS system.

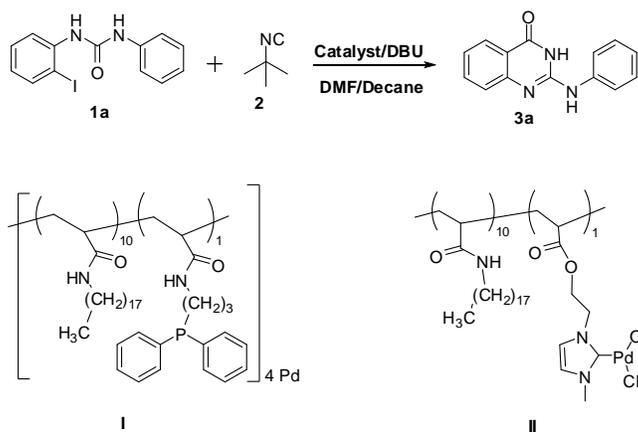


**Fig. S8.** Plausible mechanism pathway for the isocyanide insertion.<sup>(1)</sup>

### Synthesis of Urea derivatives (1a-1g).

Phenylisocyanate derivatives (16.0 mmol, 1 eq.) was dissolved in dichloromethane (25 mL). 2-iodo aniline (1.2 eqv) was added, followed by triethylamine (1.1 eq.) and the resulting solution was stirred overnight. A precipitate was formed, filtered and washed with cold dichloromethane to get pure product. Urea (**1a-1g**) were obtained as a white solid and confirmed by <sup>1</sup>H and <sup>13</sup>C NMR.

### Method S4. Batch Optimization studies for the isocyanide insertion in urea for the synthesis of quinazolinone (3a).



#### S4.1. Synthesis of quinazolinone (**3a**) under batch condition and reuse of catalyst **I** and **II**.

**Table S1.** Optimization studies for the synthesis of **3a** with Pd catalysts.<sup>a</sup>

Entry	Catalyst	Catalyst loading (mol%)	Reaction time (h)	Yield (%) <sup>b</sup>
1 <sup>c</sup>	PdOAc <sub>2</sub>	5	15	66
2 <sup>c</sup>	Pd(PPh <sub>3</sub> ) <sub>4</sub>	5	15	38
3	Catalyst I	1	12	69
4	Catalyst II	1	12	81
5	Catalyst II	0.5	12	83
6 <sup>d</sup>	Catalyst II	0.5	12	56
7 <sup>e</sup>	Catalyst II	0.5	6	85
8 <sup>f</sup>	Catalyst II	0.5	6	81

<sup>a</sup>Isocyanide (1

mmol), Urea (1 mmol), DBU (1.5 mmol) as base in DMF, Pd catalyst in decane in the case of catalyst **I**, **II**, DMF/decane (0.1 molar each)

as the solvent at 80°C. <sup>b</sup> Isolated yield. <sup>c</sup> DMF was used as solvent for the reaction. <sup>d</sup> NEt<sub>3</sub> has been used as base. <sup>e</sup> Reaction has been

carried out at 110°C. <sup>f</sup> Reaction has been carried out at 130°C.

A 50 mL Schlenk tube was charged with urea (1 mmol), isocyanide (1 mmol), and DBU (1.5 mmol) in DMF and Pd catalyst (**I**, **II**) (0.5 mol%) in decane. Please note that, in the case of Pd(OAc)<sub>2</sub> and Pd(PPh<sub>3</sub>)<sub>4</sub> as a catalyst experiments has been carried under DMF only. Vacuum was applied and the flask was back-filled with N<sub>2</sub>. The reaction mixture was stirred at appropriate temperature (Please refer Table S1) in N<sub>2</sub> atmosphere. As the DMF and decane layers were separated by cooling down, and the

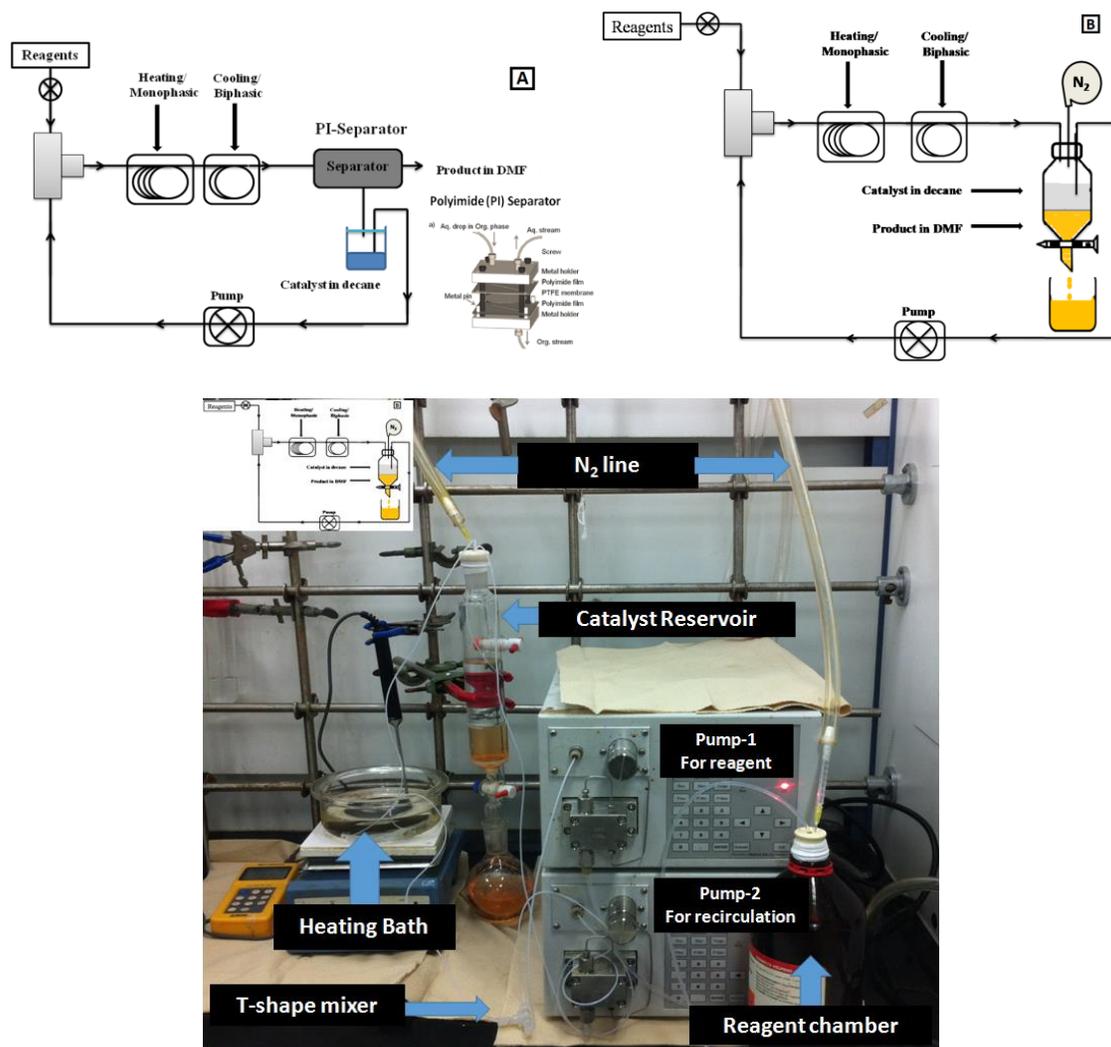
bottom DMF layer has been taken out by syringe. The obtained DMF layer was concentrated and worked up by ethyl acetate and water. The ethyl acetate layer was dried on Na<sub>2</sub>SO<sub>4</sub> and concentrated under vacuum to obtain **3a** in pure form, and the off-white solid **3a** (84%) was recrystallized in MeOH. The remaining decane layer was taken out in gas tight syringe and transfer in to new Schlenk tube, which was already charged with urea (1 mmol), isocyanide (1 mmol), and DBU (1.5 mmol) in DMF. The aforementioned procedure was used for reutilization of catalyst (**II**). After the continuous four recycle, 85, 88, 85, 80% yield was obtained respectively using simple aqueous-organic work-up.

**Important note:** The yields were obtained from averaging two independent experiments.

### **Method S5. Mechanistic study of catalyst.**

To evaluate whether the catalyst is actually functioning through palladium nanoparticles or bonded to NHC during the course of the reaction, a control experiment have been performed. We conducted a test with the use of catalyst **II**. Under the usual batch condition reagents and catalyst was dissolved in DMF and decane respectively and heated at 110°C and stopped the reaction before the substrate was completely consumed (After 2.5 h). After cooling down the separated DMF layer (without decane and NHC-Pd) was again heated for additional 6 h. However, upon the further heating of a catalyst-free solution for 6 h, no progress was observed. This experiment indicates that the catalyst is not a precatalyst for the formation of naked Pd NPs and it is homogeneous (ligand-protected) Pd species during the course of the reaction. This phenomenon was further confirmed by corresponding ICP-AES analysis of DMF layer, where no Pd was observed (< 0.1 ppm).

### **Method S6. Continuous flow Synthesis of quinazolinone utilizing polyimide separator and reservoir (3a).**



**Fig. S9.** Continuous flow polymer supported Pd/Cu catalyzed reactions and its recirculation using either of membrane separator or reservoir under TMS condition. **A:** An attempt for continuous recirculation using membrane separator; **B:** General figure for microfluidic loop system for recirculation of catalyst using reservoir; **C:** The employed continuous recirculation setup.

**Table S2.** Optimized synthesis of quinazolinone products in microfluidic system <sup>a</sup>

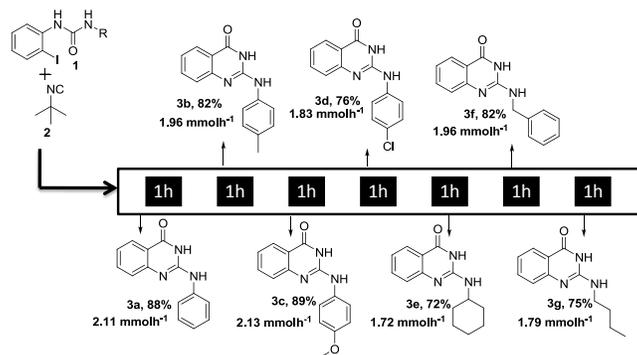
Entry	Res. time (min)	Product/Yield (%) <sup>b</sup>
1	4.08 <sup>[c]</sup>	<b>3a</b> /38
2	8.2 <sup>[d]</sup>	<b>3a</b> /88
3	6.5 <sup>[e]</sup>	<b>3a</b> /59
4	8.5 <sup>[f]</sup>	<b>3a</b> /86

<sup>a</sup>Reaction conditions: urea (0.1M), isocyanide (0.1 M), and DBU (0.15 M) in DMF and NHC-Pd catalyst (0.5mM). <sup>b</sup>Isolated yield on 1 mmol scale. <sup>c</sup>Flow rates for 4.08 min res. time: 800  $\mu$ L/min (DMF stream) and 800  $\mu$ L/min (deacne stream); PFA capillary (id = 800  $\mu$ m; length = 13.0 m). <sup>d</sup>Flow rates for 8.2 min res. time: 400  $\mu$ L/min (DMF stream) and 400  $\mu$ L/min (deacne stream); PFA capillary (id = 800  $\mu$ m; length = 13.0 m). <sup>e</sup>Flow rates for 6.5 min res. time: 500  $\mu$ L/min (DMF stream) and 500  $\mu$ L/min (deacne stream); PFA capillary (id = 800  $\mu$ m; length = 13.0 m). <sup>f</sup>Flow rates for 8.5 min res. time: 150  $\mu$ L/min (DMF stream) and 150  $\mu$ L/min (deacne stream); PFA capillary (id = 800  $\mu$ m; length = 13.0 m).

= 500  $\mu\text{m}$ ; length = 13.0 m).

A solution of urea (**1a**) (0.1 M), isocyanide (**2**) (0.1 M), DBU (0.15 M as a base) in DMF was taken in a reagent bottle and the solution of NHC-Pd catalyst (0.5 mg Pd is present in 1 g of polymer accordingly, 50 ml of 0.5 mM solution has been prepared under  $\text{N}_2$ ) in decane was taken in reservoir under  $\text{N}_2$ . With the help of T-mixer and the PFA tubing (id = 800 $\mu\text{m}$ , length = 13 m, total volume = 6.5 ml) both streams were allowed (400  $\mu\text{lmin}^{-1}$ ) to pass through the heating bath (temperature 110 $^\circ\text{C}$ ) for 8.2 min. The flow rate of DMF solution and decane kept identical to maintain the stoichiometry 1:1 of solvents. After the reaction, the DMF-decane phase was collected in catalyst reservoir. Due to density difference between DMF (944.0  $\text{kg/m}^3$ ) and decane (730.00  $\text{kg/m}^3$ ), DMF layer was collected in the bottom side whereas decane layer remain the upper side. This decane layer from the upper side was again recirculated via HPLC pump (see fig. S9-B) for catalyst recirculation. This setup ran for 18 h continuously under stable condition and DMF stream was collected by just opening the tab to calculate the yield (Yield was calculated after every 3 h) and to detect metal leaching via ICP-AES. The reaction crude was diluted with ethyl acetate, the organic layer was washed with water and brine, concentrated in vacuum. And the obtained crude was purified by recrystallization in MeOH. During the run of 18 h, 40 mmol of product has been collected with the amount of only 0.025 mmol of NHC-Pd catalyst with the average yield of 81.8%, which resulted in to the TON of 1308 and TOF of 73.8  $\text{h}^{-1}$ . However in the attempt to separate DMF and decane layer via PTFE membrane separator, we have observed the biphasic solution in the product layer, which indicated the insufficient separation of DMF and decane by membrane separator, ultimately resulted in poor reproducibility after several attempts.

**Method S7. Synthesis of chemical library of quinazolinone under thermomorphic condition with reagent switch.**

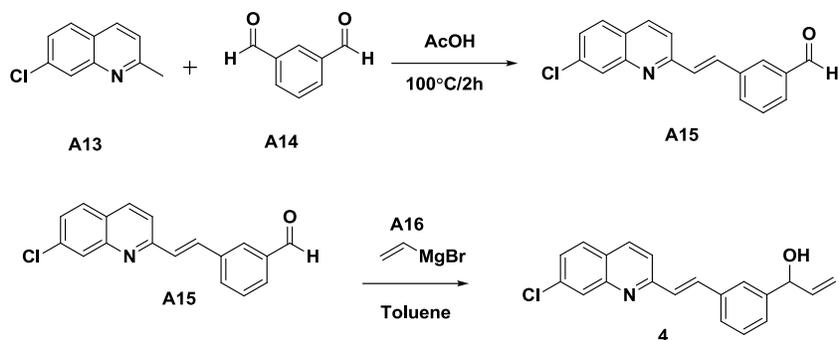


**Fig. S10.** Chemical library via continuous flow approach.

A solution of urea (**1a**) (0.1 M), isocyanide (**2**) (0.1 M), DBU (0.15 M as a base) in DMF was taken in a reagent bottle and the solution of NHC-Pd catalyst (0.5mg Pd is present in 1 gm of polymer accordingly, 50 ml of 0.5 mM solution has been prepared) in decane was taken in reservoir. With the help of T-mixer and the PFA tubing (13 m, total volume = 6.5 ml) both streams (400  $\mu\text{min}^{-1}$ ) were allowed to pass through the heating bath (temperature 110°C) for 8.2 min. The flow rate of DMF solution and decane kept identical to maintain the stoichiometry 1:1 of solvents. After the reaction, DMF-decane phase collected in catalyst reservoir. Due to density difference between DMF (944.00 kg/m<sup>3</sup>) and decane (730.00 kg/m<sup>3</sup>), DMF layer was collected in the bottom side whereas decane layer remain the upper side. This decane layer from the upper side was again recirculated via HPLC pump (see fig. S9-B) for catalyst recirculation. This setup ran for 1 h continuously under stable condition and DMF stream was collected by just opening the tab to calculate the yield and to detect metal leaching via ICP-AES. In the next step the fresh DMF layer was passed in the system to wash the tubing for 15 min. and the same system was repeated six times with different reagents to collect seven types of products in total. The reaction crude was diluted with ethyl acetate, the organic layer was washed with water and brine, concentrated in vacuum. And the obtained crude was purified by recrystallization in MeOH to render the yield of **3a** (88%) **3b** (82%) **3c** (89%) **3d** (76%), **3e** (72%), **3f** (82%), **3g** (75%) respectively.

## **Method S8. Synthesis of intermediate in the production of Merck's LTD4**

## antagonist “Singulair” under thermomorphic condition using NHC-Pd catalyst.



Scheme for the synthesis of intermediate 4.

**Synthesis of (E)-3-(2-(7-chloroquinolin-2-yl)vinyl)benzaldehyde (A15).** A solution of 7-chloroquinoline (A13) (50.0 g, 0.275 mol, 1.0 eq), isophthalaldehyde (A14) (56.77 g, 0.423 mol, 1.5 eq), in acetic acid (100 ml) were heated at 100°C for 2 hr. The reaction mixture was allowed to cool to room temperature. The precipitated crude solid was filtered and washed with 100 ml methanol. The wet crude product was charged to 1000 ml ethyl acetate and heated to reflux with stirring for 2 hrs. The solution was filtered in hot and was then concentrated under vacuum to ~150.0 ml. The resultant slurry was cooled below 20°C and stirred at same temperature for 2 hrs. The solid was then filtered, washed with chilled ethyl acetate and dried at 55-60°C under vacuum for 5.0 hours in 65.4% of yield (A15).

**Synthesis of (E)-1-(3-(2-(7-chloroquinolin-2-yl)vinyl)phenyl)prop-2-en-1-ol (4).** A suspension of monoaldehyde (A15) (20.0 g, 0.0681 mol) in toluene (160.0 mL) at 0°C was degassed by purging three times with vacuum and nitrogen. Vinylmagnesium bromide (1.0 M in THF, 72.0 mL, 0.072 mol) was added dropwise over 35 min while the internal temperature was maintained at 30°C. The reaction mixture was stirred at 0-5°C for 1 h and quenched by slowly adding 10% aqueous ammonium acetate (160.0 mL). This two-phase mixture was stirred for 1 h to ensure the solvolysis of the magnesium salts. The separated organic layer was washed with water and concentrated in vacuo and purified by silica gel chromatography (EtOAc/ hexane (50:50) in 88% isolated yield of 4.

**S8.1. Batch synthesis of intermediate in the production of Merck’s LTD4 antagonist “Singulair” under**

thermomorphic condition using NHC-Pd catalyst.

A 50 mL Schlenk tube was charged with allylic alcohol (**4**) (0.5 M), methyl 2-iodobenzoate (**5**) (0.5 M), NEt<sub>3</sub> (0.75 M as a base) in DMF and NHC-Pd catalyst (0.1 mol%) in decane. Vacuum was applied and the flask was back-filled with N<sub>2</sub>. The reaction mixture was stirred at 110°C in N<sub>2</sub> atmosphere for 5h. After cooling down, the DMF and decane layers were separated and the bottom DMF layer has been taken out by syringe. The obtained DMF layer was concentrated and worked up by ethyl acetate and water. The ethyl acetate layer was dried on Na<sub>2</sub>SO<sub>4</sub> and concentrated under vacuum to obtain the concentrated in vacuum. And the obtained crude was purified by column chromatography in 86% yield. In the continuous three recycle test, 86, 88, 91% yields of (**6**) were obtained.

S8.2. Continuous flow synthesis of important intermediate in the production of Merck's LTD4 antagonist "Singulair" under thermomorphic condition.

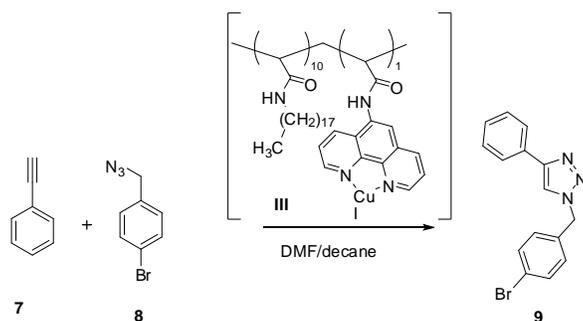
A solution of allylic alcohol (**4**) (0.5 M), methyl 2-iodobenzoate (**5**) (0.5 M), NEt<sub>3</sub> (0.75 M as a base) in DMF was taken in one syringe and the solution of NHC-Pd catalyst (0.5mg Pd is present in 1 gm of polymer accordingly, 50ml of 0.5mM solution has been prepared, 0.1 mol% Pd) in decane was taken in reservoir. With the help of T-mixer and the PFA tubing (id = 800 μm, length = 13 m, total volume = 6.5 ml), both streams (250 μlmin<sup>-1</sup>) were allowed to pass through the heating bath (temperature 110 °C) for 13.06 min. The flow rate of DMF solution and decane kept identical to maintain the stoichiometry 1:1 of solvents. After the reaction, the DMF-decane phase collected in catalyst reservoir. Due to density difference between DMF (944.00 kg/m<sup>3</sup>) and decane (730.00 kg/m<sup>3</sup>), DMF layer was collected in the bottom side whereas decane layer remain the upper side. This decane layer from the upper side was again recirculated via HPLC pump (see fig. S9-B) for catalyst recirculation. This setup ran for 6 h continuously under stable condition (our attempts for run more than 6 h has been failed by plausible deactivation of catalyst, however no significant leaching of catalyst was observed in ICP-AES analysis) and after every 2 h the DMF stream was collected by just opening the tab to calculate the yield and to detect metal leaching via ICP-AES. The reaction crude was diluted with ethyl acetate, the organic layer was washed with water and brine, concentrated in vacuum. And the obtained crude was purified by

column chromatography in 5 % of MeOH (in DCM) as an eluent. During the run of 6 h, 16.75 g product has been collected with 82 % overall yield.

## **Method S9. Synthesis of Huisgen 1,3-dipolar cycloaddition reaction under thermomorph condition using copper catalyst.**

### **S9.1. Batch synthesis of Huisgen 1,3-dipolar cycloaddition reaction under thermomorph condition using copper catalyst.**

A 50 mL Schlenk tube was charged with phenyl acetylene (**7**) (1 mmol), 4-bromobenzyl azide (**8**) (1 mmol) in DMF and Cu catalyst (**III**) (0.5 mol%) in decane. Vacuum was applied and the tube was back-filled with N<sub>2</sub>. The reaction mixture was stirred (5 h) at 120°C in N<sub>2</sub> atmosphere. After cooling down, the DMF and decane layers were separated and the bottom DMF layer has been taken out by syringe. The obtained DMF layer was concentrated and worked up by ethyl acetate and water. The ethyl acetate layer was dried on Na<sub>2</sub>SO<sub>4</sub> and concentrated under vacuum to obtain the concentrated in vacuum, and the obtained crude was purified by column chromatography in 92% yield. The remaining decane layer was taken out in gas tight syringe and transfer in to new Schlenk tube, which was already charged with reagents in DMF. The aforementioned procedure was used for reutilization of catalyst (**III**). The reaction crude was diluted with ethyl acetate, the organic layer was washed with water and brine, concentrated in vacuum. And the obtained crude was purified by column chromatography in 1% of MeOH (in DCM) as an eluent. After the continuous three recycle test, 92, 95, 94% yields of triazole (**9**) were obtained.



**Fig. S11.** Click reaction in batch condition under TMS system.

**S9.2. Continuous flow synthesis of Huisgen 1,3-dipolar cycloaddition reaction under thermomorphic condition using copper catalyst.**

**Table S3.** Optimization studies for the synthesis of **9** with Cu catalysts.<sup>[a]</sup>

Entry	Res. time (min)	Product/Yield (%) <sup>[b]</sup>
1	4.08 <sup>[c]</sup>	<b>9</b> /56
2	8.2 <sup>[d]</sup>	<b>9</b> /91
3	6.5 <sup>[e]</sup>	<b>9</b> /93

<sup>[a]</sup>Reaction conditions: phenyl acetylene (0.1M) (**7**), 4-bromobenzyl azide (0.1M) (**8**), in DMF and Cu catalyst (0.5mM) . <sup>[b]</sup>Isolated yield on 1 mmol scale. <sup>[c]</sup>Flow rates for 4.08 min res. time: 800  $\mu$ L/min (DMF stream) and 800  $\mu$ L/min (decane stream); PFA capillary (id = 800  $\mu$ m; length = 13.0 m) <sup>[d]</sup>Flow rates for 8.2 min res. time: 400  $\mu$ L/min (DMF stream) and 400  $\mu$ L/min (decane stream); PFA capillary (id = 800  $\mu$ m; length = 13.0 m). <sup>[e]</sup>Flow rates for 6.5 min res. time: 500  $\mu$ L/min (DMF stream) and 500  $\mu$ L/min (decane stream); PFA capillary (id = 800  $\mu$ m; length = 13.0 m).

A solution of phenyl acetylene (**7**) (0.1 M), 4-bromobenzyl azide (**8**) (0.1 M) in DMF was taken reagent bottle under N<sub>2</sub> and the solution of copper block copolymer catalyst (**III**) (0.40 mg Cu is present in 1 gm of polymer accordingly, 50 ml of 0.5 mM solution has been prepared) in decane was taken in reservoir. With the help of T-mixer and the PFA tubing (13 m, total volume = 6.5 ml), both streams (500  $\mu$ L/min) were allowed to pass through the heating bath (temperature 120 °C) for 6.5 min. The flow rate of DMF solution and decane kept identical to maintain the stoichiometry 1:1 of solvents. After the reaction the DMF-decane phase collected in catalyst reservoir. Due to density difference between DMF (944.00 kg/m<sup>3</sup>) and decane (730.00 kg/m<sup>3</sup>), the DMF layer was collected in bottom side whereas the decane layer remain the upper side. This decane layer from the upper side was again recirculated via HPLC pump (see fig. S9-B) for catalyst recirculation. This setup ran for 10 h continuously under stable condition and after every 2.5 h DMF stream was collected for yield calculation and to detect metal leaching via ICP-AES. The reaction crude was diluted with ethyl acetate, the organic layer was washed with water and brine, concentrated in vacuum. And the obtained crude was purified by column chromatography in 1% of MeOH (in DCM) as an eluent. During the run of 10 h, 9.38 g product has been collected with 88% overall yields of triazole (**9**).

#### 4. NMR of synthesized compounds:

##### Characterization data for the synthesized compounds.

**2,5-dioxopyrrolidin-1-yl acrylate (A3).**  $^1\text{H}$  NMR (600 MHz,  $\text{CDCl}_3$ ):  $\delta$  2.80-2.85 (m, 4H), 6.20-6.23 (dd,  $J = 11.0$  Hz, 1.0 Hz, 1H), 6.40 (dd,  $J = 17.5$  Hz, 11.0 Hz, 1H), 6.66 (dd,  $J = 17.5$  Hz, 1.0 Hz, 1H),  $^{13}\text{C}$  NMR (150 MHz,  $\text{CDCl}_3$ ):  $\delta$  25.6, 122.9, 136.2, 161.1, 169.2.

**N-octadecylacrylamide (A4).**  $^1\text{H}$  NMR (600 MHz,  $\text{CDCl}_3$ ):  $\delta$  0.89-0.91 (m, 3H), 1.27-1.33 (m, 30H), 1.54-1.56 (m, 2H), 3.32-3.36 (m, 2H), 5.63-5.65 (m, 1H), 5.69 (s, 1H), 6.06-6.15 (m, 1H), 6.26 (dd,  $J = 15.4$  Hz, 1.7 Hz, 1H),  $^{13}\text{C}$  NMR (300 MHz,  $\text{CDCl}_3$ ):  $\delta$  14.1, 22.6, 26.9, 29.3-29.6, 31.9, 39.6, 126.0, 131.0, 165.4.

**1-(2-Iodophenyl)-3-phenylurea (1a).** Mass (EI):  $m/z = 337$  ( $\text{M}^+$ );  $^1\text{H}$  NMR (DMSO, 600MHz)  $\delta$ : 6.84 (t,  $J = 6.6$  Hz, 1H), 6.98 (t,  $J = 7.2$  Hz, 1H), 7.29 (t,  $J = 7.8$  Hz, 2H), 7.34 (t,  $J = 6.6$  Hz, 1H), 7.47 (d,  $J = 7.2$  Hz, 2H), 7.84 (d,  $J = 7.2$  Hz, 2H), 7.89 (s, 1H), 9.42 (s, 1H);  $^{13}\text{C}$  NMR (DMSO, 150MHz)  $\delta$ : 91.8, 118.6, 122.4, 123.5, 125.5, 129.0, 129.3, 139.3, 140.0, 140.3, 152.8.

**1-(2-Iodophenyl)-3-p-tolylurea (1b).** Mass (EI):  $m/z = 352$  ( $\text{M}^+$ );  $^1\text{H}$  NMR (DMSO, 600MHz)  $\delta$ : 2.25 (s, 3H), 6.82 (td,  $J = 1.8$  Hz, 6.2 Hz, 1H), 7.10 (d,  $J = 8.4$  Hz, 2H), 7.33-7.37 (m, 3H), 7.83-7.86 (m, 3H), 9.33 (s, 1H);  $^{13}\text{C}$  NMR (DMSO, 150MHz)  $\delta$ : 20.8, 91.6, 118.7, 123.3, 125.3, 129.0, 129.7, 131.3, 137.4, 139.3, 140.3, 152.8.

**1-(2-Iodophenyl)-3-(4-methoxyphenyl)urea (1c).** Mass (EI):  $m/z = 368$  ( $\text{M}^+$ );  $^1\text{H}$  NMR (DMSO, 600MHz)  $\delta$ : 3.73 (s, 3H), 6.81 (td,  $J = 1.2$  Hz, 6.6 Hz, 1H), 6.85 (d,  $J = 9.0$  Hz, 2H), 7.33 (td,  $J = 1.2$  Hz, 7.2 Hz, 1H), 7.36 (d,  $J = 9.0$  Hz, 2H) 7.80 (s, 1H), 7.82 (m, 2H), 9.27 (s, 1H);  $^{13}\text{C}$  NMR (DMSO, 150MHz)  $\delta$ : 55.6, 91.5, 114.5, 120.4, 123.2, 125.2, 129.0, 133.0, 139.3, 140.4, 152.9, 155.0.

**1-(4-Chlorophenyl)-3-(2-iodophenyl)urea (1d).** Mass (EI):  $m/z = 371$  ( $\text{M}^+$ );  $^1\text{H}$  NMR (DMSO, 600MHz)  $\delta$ : 6.85 (t,  $J = 1.2$  Hz, 6.6 Hz, 1H), 7.34 (m, 3H), 7.50 (m, 2H), 7.82 (m, 2H) 7.92 (s, 1H), 9.55 (s, 1H);  $^{13}\text{C}$  NMR (DMSO, 150MHz)  $\delta$ : 92.0, 120.1, 123.6, 126.7, 125.9, 129.0, 129.1, 139.0, 139.4, 140.1, 152.7.

**1-Cyclohexyl-3-(2-iodophenyl)urea (1e).** Mass (EI):  $m/z = 344$  ( $M^+$ );  $^1\text{H}$  NMR (DMSO, 600MHz)  $\delta$ : 1.16-1.23 (m, 3H), 1.28-1.34 (m, 2H), 1.53-1.55 (m, 1H), 1.66-1.69 (m, 2H), 1.81-1.83 (m, 2H), 3.47-3.49 (m, 1H), 6.86-6.88 (m, 1H), 7.06 (d,  $J = 7.2$  Hz, 1H), 7.25 (t,  $J = 7.2$  Hz, 1H), 7.53 (dd,  $J = 1.2$  Hz, 6.6 Hz, 1H), 7.75 (s, 1H), 8.09 (dd,  $J = 1.2$  Hz, 6.6 Hz, 1H);  $^{13}\text{C}$  NMR (DMSO, 150MHz)  $\delta$ : 24.7, 25.7, 33.3, 48.2, 112.2, 121.6, 123.3, 128.3, 132.7, 138.4, 154.3.

**1-Benzyl-3-(2-iodophenyl)urea (1f).** Mass (EI):  $m/z = 352$  ( $M^+$ );  $^1\text{H}$  NMR (DMSO, 600MHz)  $\delta$ : 4.31 (d,  $J = 5.4$  Hz, 2H), 6.76 (td,  $J = 1.2$  Hz, 7.8 Hz, 1H), 7.27-7.37 (m, 6H), 7.51(t, 1H), 7.67 (s, 1H), 7.79 (dd,  $J = 1.2$  Hz, 7.8 Hz), 7.85 (dd,  $J = 1.2$  Hz, 8.4 Hz, 1H);  $^{13}\text{C}$  NMR (DMSO, 150MHz)  $\delta$ : 43.3, 90.9, 122.8, 124.7, 127.3, 127.7, 128.8, 128.9, 139.3, 140.4, 140.9, 155.4.

**1-Butyl-3-(2-iodophenyl)urea (1g).** Mass (EI):  $m/z = 318$  ( $M^+$ );  $^1\text{H}$  NMR (DMSO, 600MHz)  $\delta$ : 0.90-0.92 (m, 3H), 1.32-1.35 (m, 2H), 1.42-1.44 (m, 2H), 3.08-3.11 (m, 2H), 6.73 (td,  $J = 1.2$ Hz, 7.8Hz, 1H), 7.02 (m, 1H), 7.27 (t,  $J = 1.2$ Hz, 7.8Hz, 1H), 7.51 (s, 1H), 7.77 (dd,  $J = 1.2$ Hz, 7.8Hz, 1H), 7.83 (dd,  $J = 1.2$ Hz, 7.8Hz, 1H);  $^{13}\text{C}$  NMR (DMSO, 150MHz)  $\delta$ : 14.1, 20.0, 32.1, 39.2, 90.6, 122.5, 124.5, 128.9, 139.2, 141.1, 155.3.

**2-(Phenylamino)quinazolin-4(3H)-one (3a).** Mass (EI):  $m/z = 237$  ( $M^+$ );  $^1\text{H}$  NMR ( $\text{CDCl}_3$ , 600MHz)  $\delta$ : 7.04 (t,  $J = 7.2$  Hz, 1H), 7.23 (t,  $J = 7.2$  Hz, 1H), 7.35 (t,  $J = 7.8$  Hz, 2H), 7.41 (d,  $J = 11.4$  Hz, 1H), 7.65 (td,  $J = 1.2$  Hz, 7.2 Hz, 1H), 7.77 (d,  $J = 7.8$  Hz, 2H), 7.98 (dd,  $J = 1.2$  Hz, 7.8 Hz, 1H), 8.49 (s, 1H), 9.30 (s, 1H);  $^{13}\text{C}$  NMR ( $\text{CDCl}_3$ , 150MHz)  $\delta$ : 118.8, 119.7, 122.9, 123.4, 125.4, 126.4, 129.3, 134.9, 139.5, 148.2, 150.2, 162.1.

**2-(p-Tolylamino)quinazolin-4(3H)-one (3b).** Mass (EI):  $m/z = 251$  ( $M^+$ );  $^1\text{H}$  NMR ( $\text{CDCl}_3$ , 600MHz)  $\delta$ : 2.28 (s, 3H), 7.15 (d,  $J = 8.4$  Hz, 1H), 7.20 (t,  $J = 7.2$  Hz, 1H), 7.37 (d,  $J = 8.4$  Hz, 2H), 7.61-7.65 (m, 3H), 7.95 (d,  $J = 7.8$  Hz, 1H), 8.54 (s, 1H), 10.78 (s, 1H);  $^{13}\text{C}$  NMR ( $\text{CDCl}_3$ , 150MHz)  $\delta$ : 20.9, 118.7, 119.2, 123.3, 125.7, 126.3, 129.7, 131.9, 134.9, 136.8, 147.9, 150.6, 162.7.

**2-((4-Methoxyphenyl)amino)quinazolin-4(3H)-one (3c).** Mass (EI):  $m/z = 267$  ( $M^+$ );  $^1\text{H}$  NMR ( $\text{CDCl}_3$ , 600MHz)  $\delta$ : 3.76 (s, 3H), 6.94 (d,  $J = 9.0$ Hz, 2H), 7.19 (t,  $J = 7.2$ Hz, 1H), 7.34 (d,  $J = 7.8$  Hz,

1H), 7.62-7.64 (m, 3H), 7.95 (d,  $J = 7.2$  Hz, 1H), 8.46 (s, 1H), 10.7 (s, 1H);  $^{13}\text{C}$  NMR ( $\text{CDCl}_3$ , 150MHz)  $\delta$ : 55.7, 114.5, 118.6, 121.8, 123.1, 125.6, 126.3, 132.3, 134.8, 148.2, 150.7, 155.5, 162.1.

**2-(4-Chlorophenylamino)quinazolin-4(3H)-one (3d).** Mass (EI):  $m/z = 271$  ( $\text{M}^+$ );  $^1\text{H}$  NMR ( $\text{CDCl}_3$ , 600MHz)  $\delta$ : 7.27 (t,  $J = 7.2$  Hz, 1H), 7.43-7.45 (m, 3H), 7.67 (td,  $J = 1.2$  Hz, 7.2 Hz, 1H), 7.75 (d,  $J = 8.4$  Hz, 2H), 7.99 (dd,  $J = 1.2$  Hz, 7.8 Hz, 1H), 9.45 (s, 1H);  $^{13}\text{C}$  NMR ( $\text{CDCl}_3$ , 150MHz)  $\delta$ : 118.5, 122.3, 124.0, 124.3, 126.5, 127.4, 129.3, 135.1, 137.7, 148.3, 161.9.

**2-(Cyclohexylamino)quinazolin-4(3H)-one (3e).** Mass (EI):  $m/z = 243$  ( $\text{M}^+$ );  $^1\text{H}$  NMR ( $\text{CDCl}_3$ , 600MHz)  $\delta$ : 1.22-1.27 (m, 3H), 1.33-1.39 (m, 2H), 1.55-1.57 (m, 1H), 1.67-1.69 (m, 2H), 1.91-1.93 (m, 2H), 3.82 (b, s, 1H), 6.15 (d,  $J = 7.2$  Hz, 1H), 7.07 (t,  $J = 7.8$  Hz, 1H), 7.23 (d,  $J = 8.4$  Hz, 1H), 7.53-7.56 (m, 1H), 7.86 (d,  $J = 7.8$  Hz, 1H), 10.59 (s, 1H);  $^{13}\text{C}$  NMR ( $\text{CDCl}_3$ , 150MHz)  $\delta$ : 24.6, 25.6, 32.8, 48.7, 117.8, 121.9, 125.0, 126.3, 134.6, 150.1, 151.7, 162.3.

**2-(Benzylamino)quinazolin-4(3H)-one (3f).** Mass (EI):  $m/z = 251$  ( $\text{M}^+$ );  $^1\text{H}$  NMR ( $\text{CDCl}_3$ , 600MHz)  $\delta$ : 4.5 (s, 2H), 6.88 (s, 1H), 7.10-7.12 (m, 1H), 7.25 (t,  $J = 7.8$  Hz, 2H), 7.34-7.58 (m, 6H), 7.89 (s,  $J = 7.2$  Hz, 1H), 11.03 (s, 1H);  $^{13}\text{C}$  NMR ( $\text{CDCl}_3$ , 150MHz)  $\delta$ : 44.0, 118.0, 122.1, 125.1, 126.3, 127.4, 127.8, 128.8, 128.9, 129.0, 129.3, 134.5, 134.6, 139.7, 151.0, 151.4, 162.3.

**2-(Butylamino)quinazolin-4(3H)-one (3g).** Mass (EI):  $m/z = 217$  ( $\text{M}^+$ );  $^1\text{H}$  NMR ( $\text{CDCl}_3$ , 600MHz)  $\delta$ : 0.87-0.91 (m, 3H), 1.31-1.39 (m, 2H), 1.50-1.55 (m, 2H), 3.31-3.34 (m, 2H), 6.59 (s, 1H), 7.08 (t,  $J = 7.2$  Hz, 1H), 7.24 (d,  $J = 7.8$  Hz, 1H), 7.54 (td,  $J = 1.2$  Hz, 8.4 Hz, 1H), 7.8 (dd, 1.2 Hz, 7.8 Hz, 1H), 10.9 (s, 1H);  $^{13}\text{C}$  NMR ( $\text{CDCl}_3$ , 150MHz)  $\delta$ : 13.9, 19.5, 29.5, 38.9, 117.8, 121.8, 125.0, 126.4, 134.5, 151.2, 151.6, 162.3.

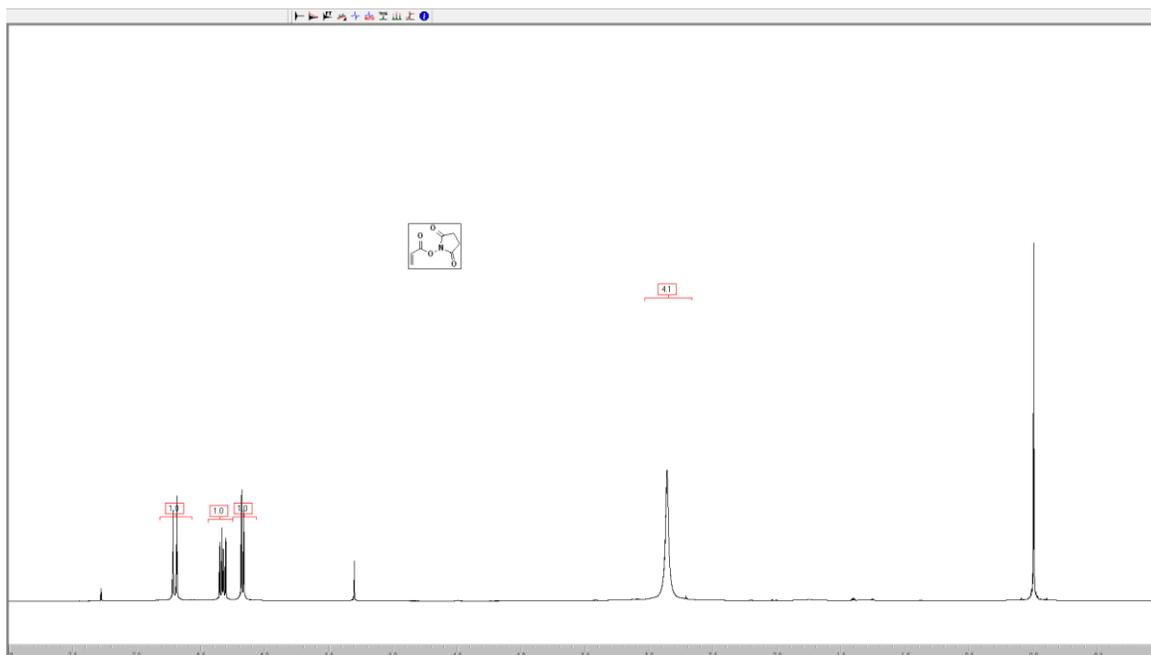
**(E)-3-(2-(7-Chloroquinolin-2-yl)vinyl)benzaldehyde (A15).** Mass (EI):  $m/z = 293$  ( $\text{M}^+$ );  $^1\text{H}$  NMR ( $\text{CDCl}_3$ , 600MHz)  $\delta$ : 7.58-7.69 (m, 3H), 7.87-8.09 (m, 6H), 8.27 (s, 1H), 8.41 (d,  $J = 16.8$  Hz, 1H), 10.08 (s, 1H).

**(E)-1-(3-(2-(7-Chloroquinolin-2-yl)vinyl)phenyl)prop-2-en-1-ol (4).** Mass (EI):  $m/z = 321$  ( $\text{M}^+$ );  $^1\text{H}$  NMR ( $\text{CDCl}_3$ , 600MHz)  $\delta$ : 5.09 (d,  $J = 10.2$  Hz, 1H), 5.13-5.15 (m, 1H), 5.30 (d,  $J = 16.8$  Hz, 1H), 5.60 (d,  $J = 4.2$  Hz, 1H), 5.98-6.04 (ddd,  $J = 16.8$  Hz, 5.4 Hz, 10.2 Hz, 1H), 7.33 (d,  $J = 7.2$  Hz, 1H),

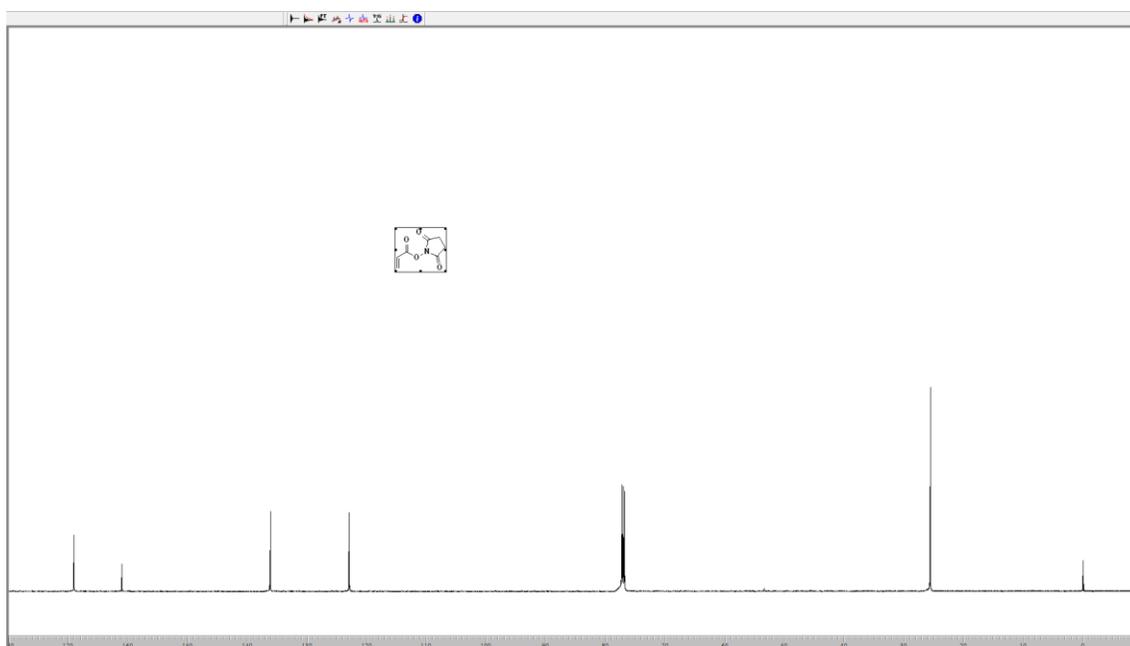
7.39 (t,  $J = 7.2$  Hz, 1H), 7.45 (d,  $J = 16.2$  Hz, 1H), 7.58-7.62 (m, 2H), 7.71 (s, 1H), 7.87 (d,  $J = 16.2$  Hz, 1H), 7.93 (d,  $J = 8.4$  Hz, 1H), 7.99-8.02 (m, 2H), 8.39 (d,  $J = 8.4$  Hz, 1H);  $^{13}\text{C}$  NMR ( $\text{CDCl}_3$ , 150MHz)  $\delta$ : 73.7, 114.0, 120.8, 125.5, 126.0, 126.4, 127.1, 127.3, 127.7, 128.7, 129.2, 130.2, 134.8, 135.5, 136.3, 137.0, 142.3, 145.4, 148.5, 157.2.

**Drug intermediate (E)-methyl 2-(3-(3-(2-(7-chloroquinolin-2-yl)vinyl)phenyl)-3-oxopropyl)benzoate (6).** Mass (EI):  $m/z = 455$  ( $\text{M}^+$ );  $^1\text{H}$  NMR ( $\text{CDCl}_3$ , 600MHz)  $\delta$ : 3.26 (t,  $J = 7.2$  Hz, 2H), 3.41 (t,  $J = 7.2$  Hz, 2H), 3.84 (s, 3H), 7.36 (t,  $J = 7.8$  Hz, 1H), 7.47 (d,  $J = 7.8$  Hz, 1H), 7.53 (t,  $J = 7.2$  Hz, 1H), 7.57-7.63 (m, 3H), 7.84 (d,  $J = 7.8$  Hz, 1H), 7.93-8.02 (m, 6H), 8.34 (s, 1H), 8.41 (d,  $J = 8.4$  Hz, 1H);  $^{13}\text{C}$  NMR ( $\text{CDCl}_3$ , 150MHz)  $\delta$ : 28.8, 31.1, 52.5, 120.8, 126.1, 126.8, 127.3, 127.5, 127.7, 128.4, 129.81, 129.85, 129.9, 130.2, 130.6, 131.6, 132.0, 132.7, 134.6, 134.8, 137.1, 137.6, 143.0, 148.5, 157.1, 167.7, 199.4.

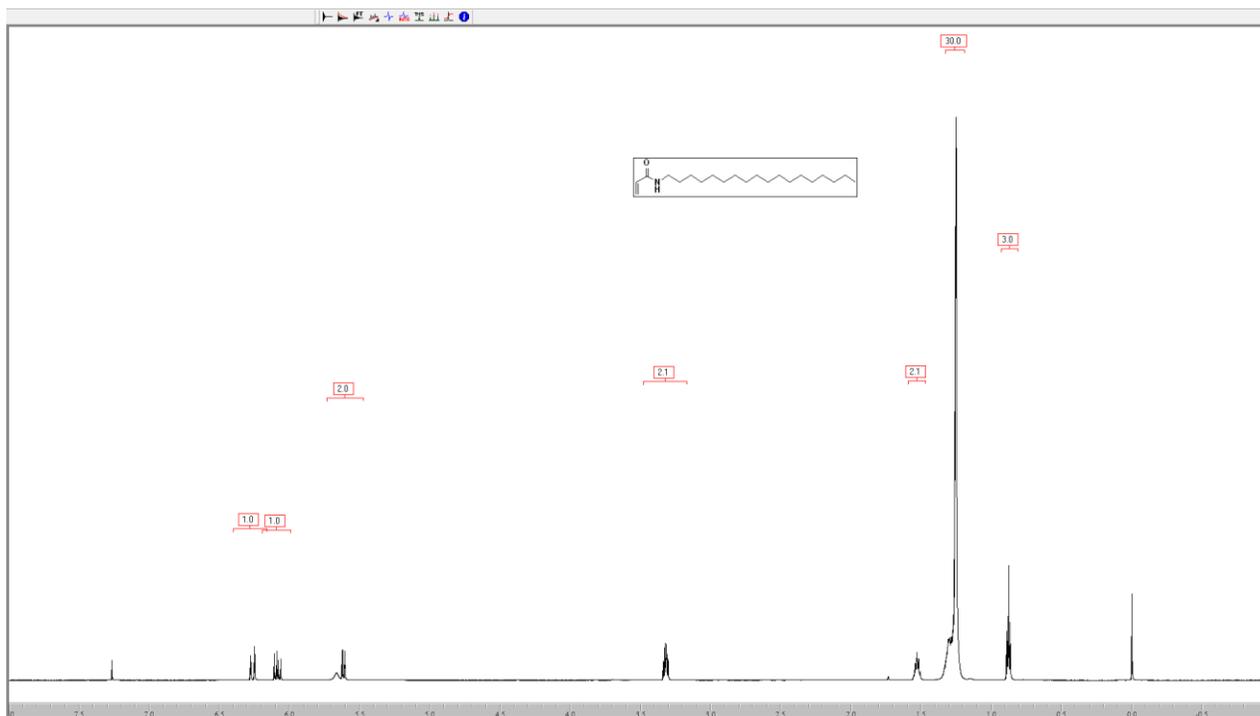
**1-(4-Bromobenzyl)-4-phenyl-1H-1,2,3-triazole (9).** Mass (EI):  $m/z = 313$  ( $\text{M}^+$ );  $^1\text{H}$  NMR ( $\text{DMSO-d}_6$ , 600MHz)  $\delta$ : 5.48 (s, 2H), 7.13-7.16 (m, 2H), 7.29-7.43 (m, 3H), 7.46-7.51 (m, 2H), 7.68 (s, 1H), 7.77-7.80 (m, 2H);  $^{13}\text{C}$  NMR ( $\text{CDCl}_3$ , 150MHz)  $\delta$ : 53.4, 119.5, 122.8, 125.6, 128.2, 128.8, 129.5, 130.3, 132.2, 133.7, 148.2.



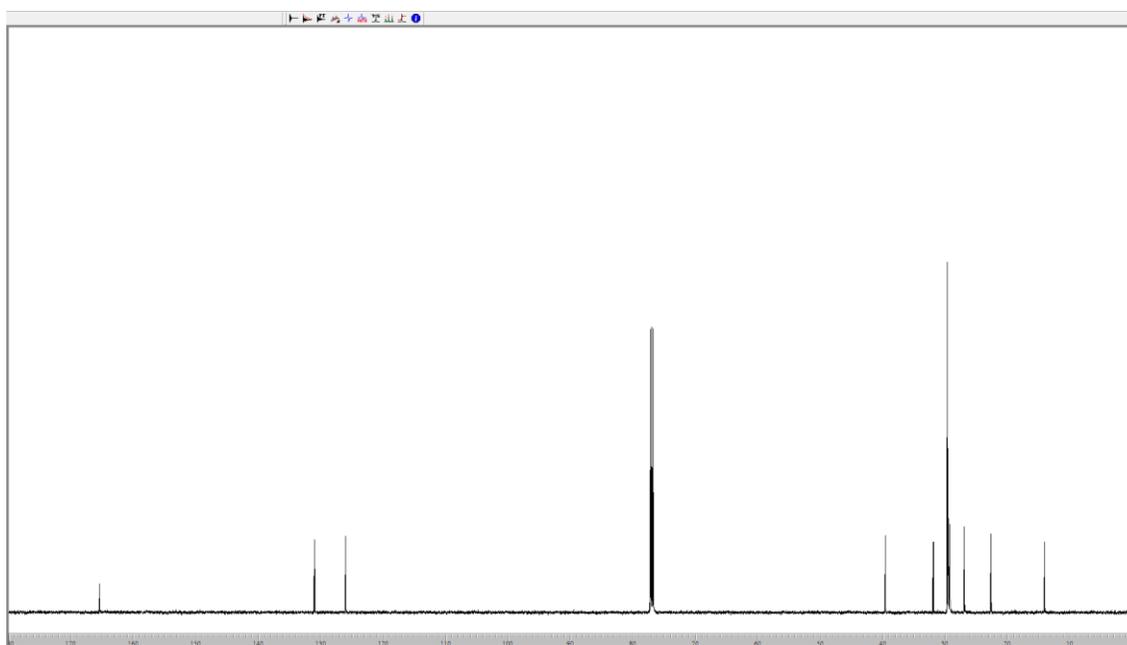
**$^1\text{H}$  NMR of 2,5-dioxopyrrolidin-1-yl acrylate (A3).**



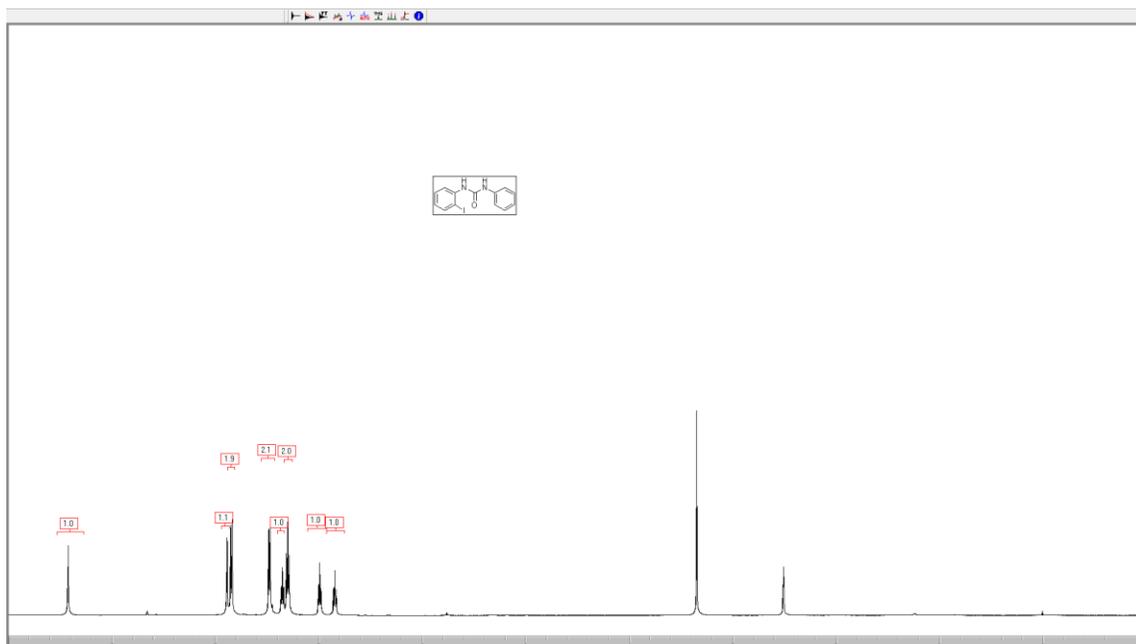
**$^{13}\text{C}$  NMR of 2,5-dioxopyrrolidin-1-yl acrylate (A3).**



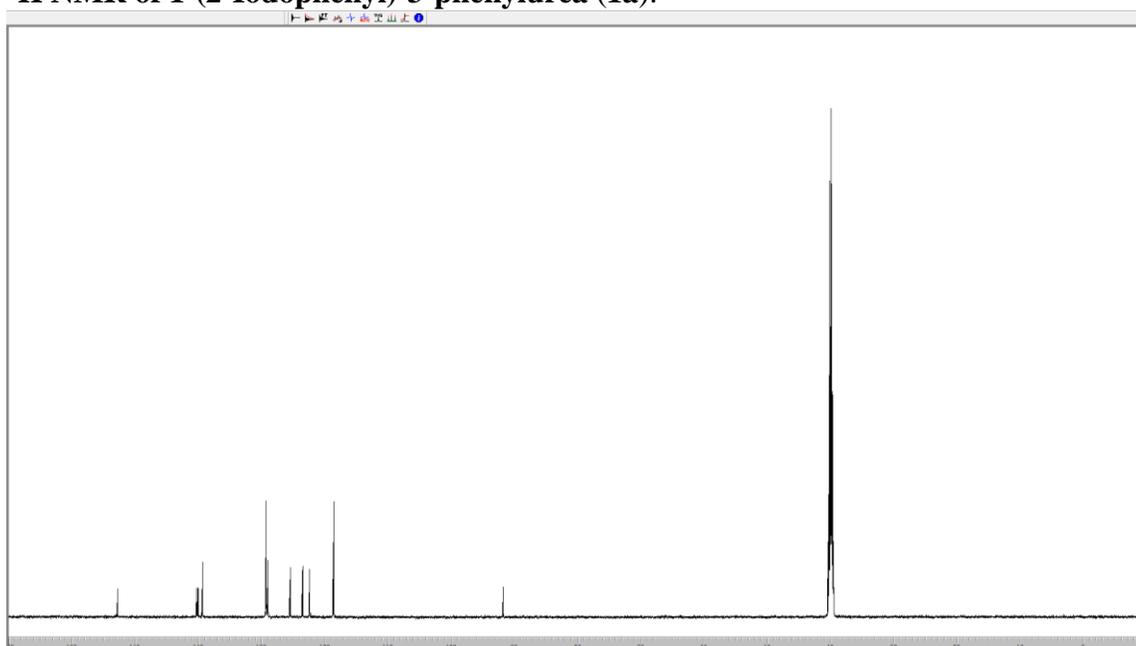
**<sup>1</sup>H NMR of N-octadecylacrylamide (A4).**



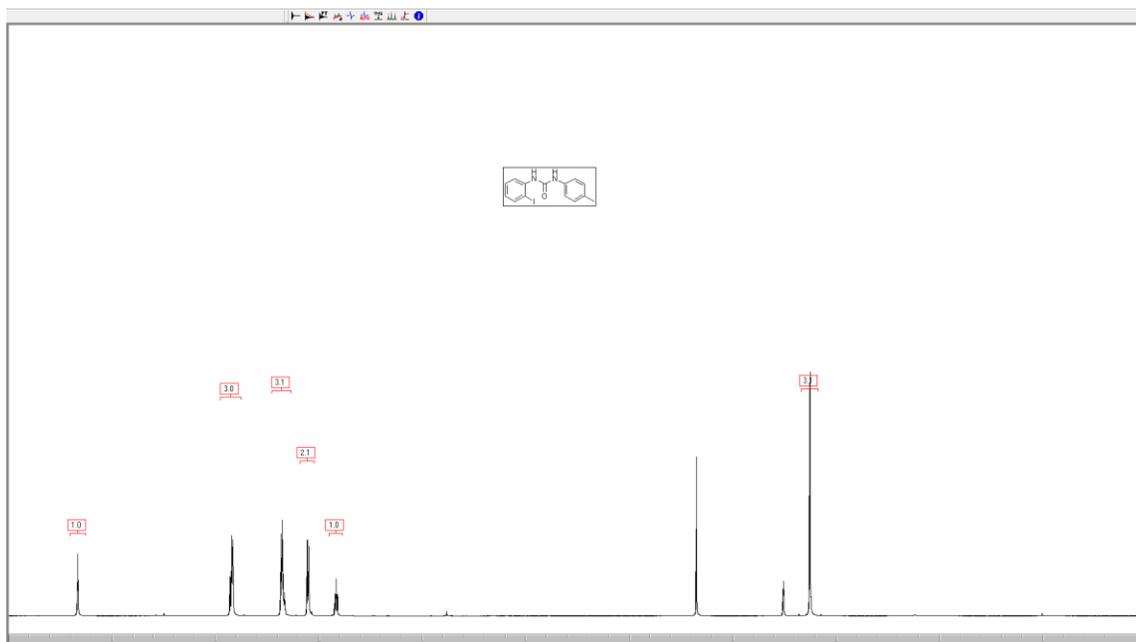
**<sup>13</sup>C NMR of N-octadecylacrylamide (A4).**



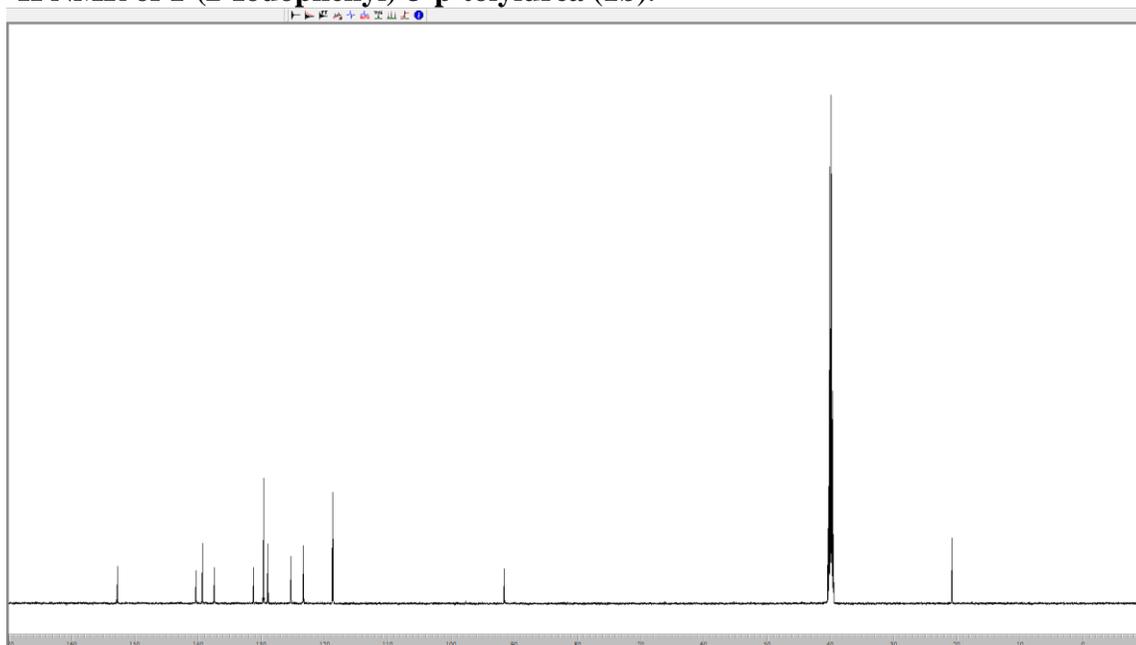
**<sup>1</sup>H NMR of 1-(2-Iodophenyl)-3-phenylurea (1a).**



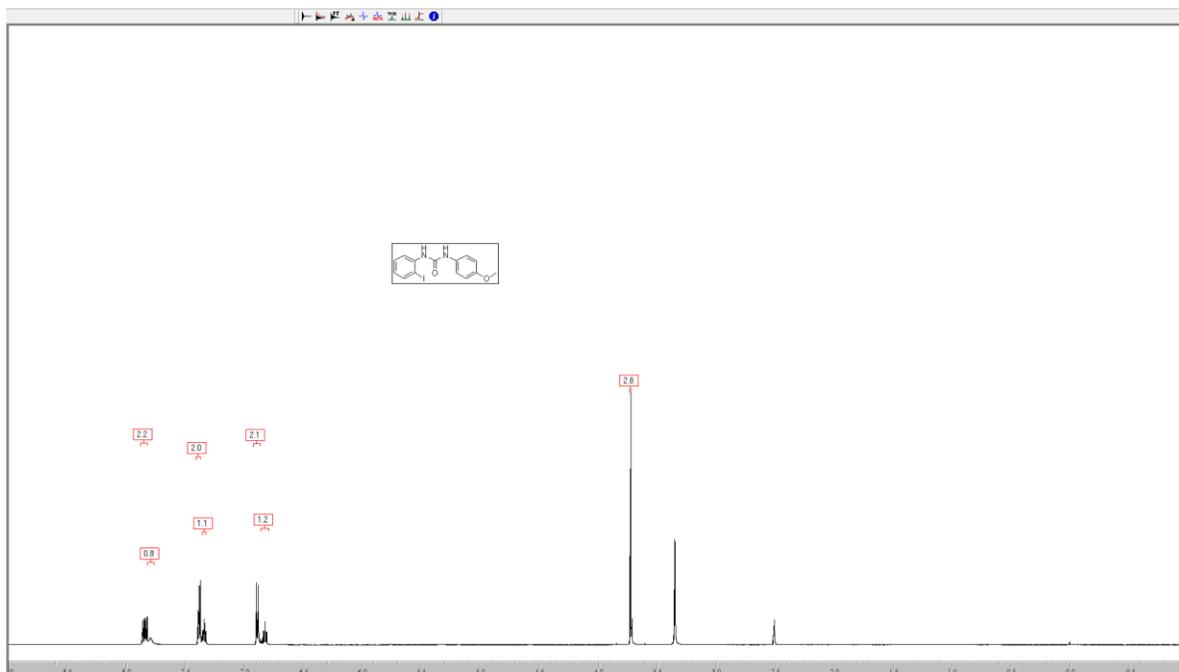
**<sup>13</sup>C NMR of 1-(2-Iodophenyl)-3-phenylurea (1a).**



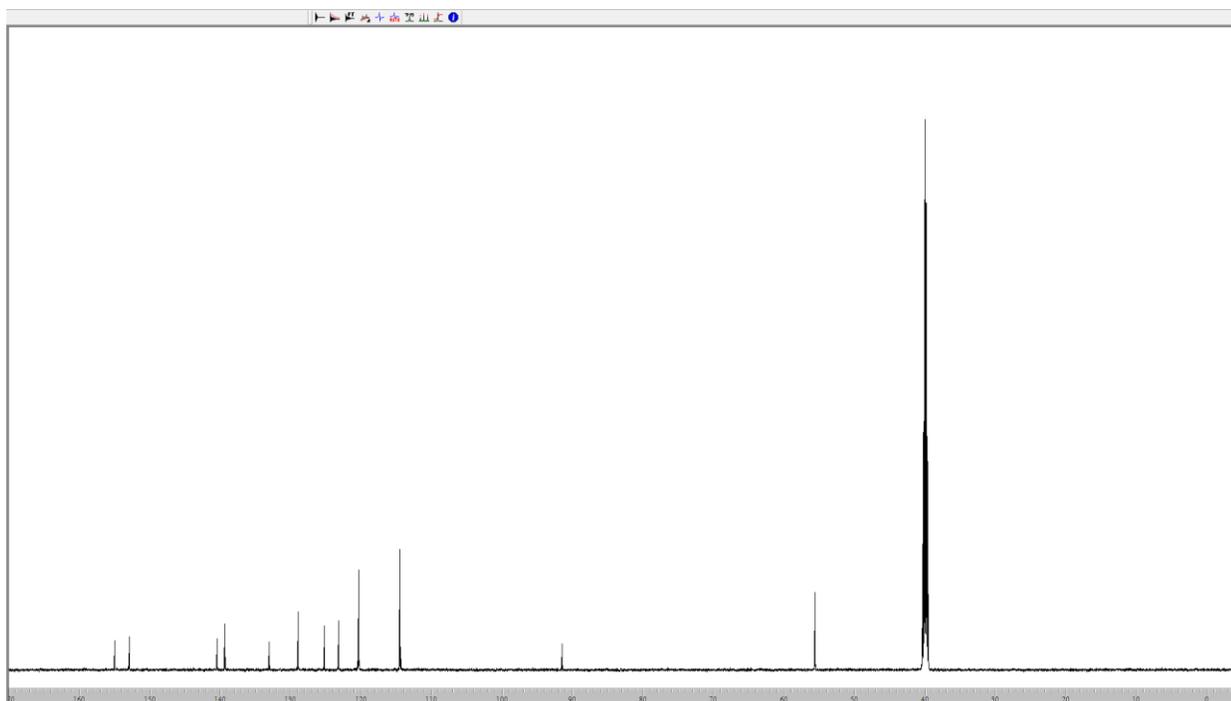
**<sup>1</sup>H NMR of 1-(2-Iodophenyl)-3-p-tolylurea (1b).**



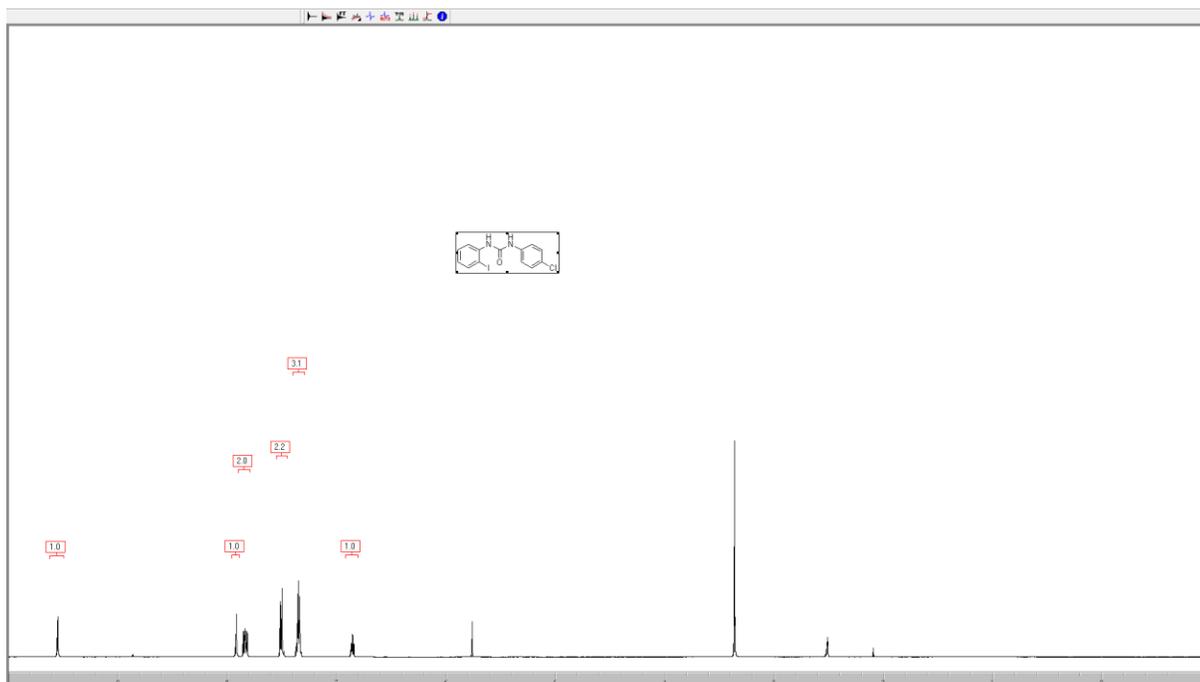
**<sup>13</sup>C NMR of 1-(2-Iodophenyl)-3-p-tolylurea (1b).**



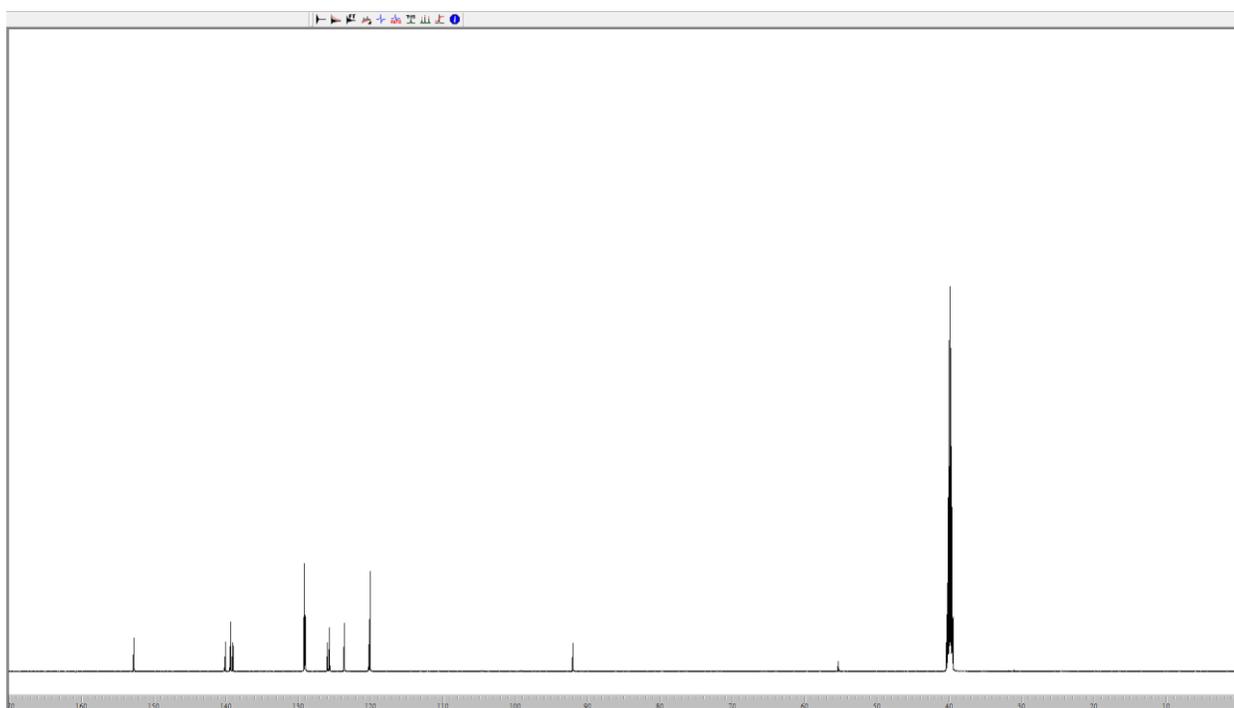
**<sup>1</sup>H NMR of 1-(2-Iodophenyl)-3-(4-methoxyphenyl)urea (1c).**



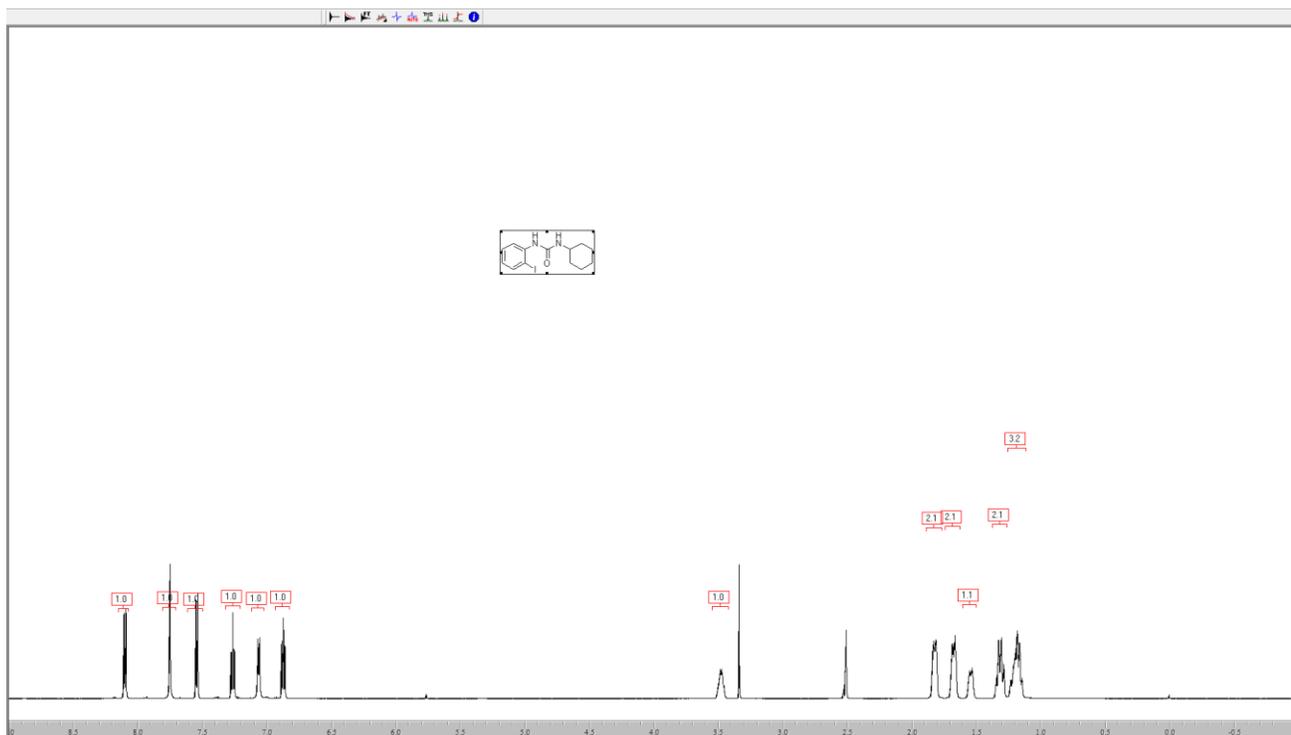
**<sup>13</sup>C NMR of 1-(2-Iodophenyl)-3-(4-methoxyphenyl)urea (1c).**



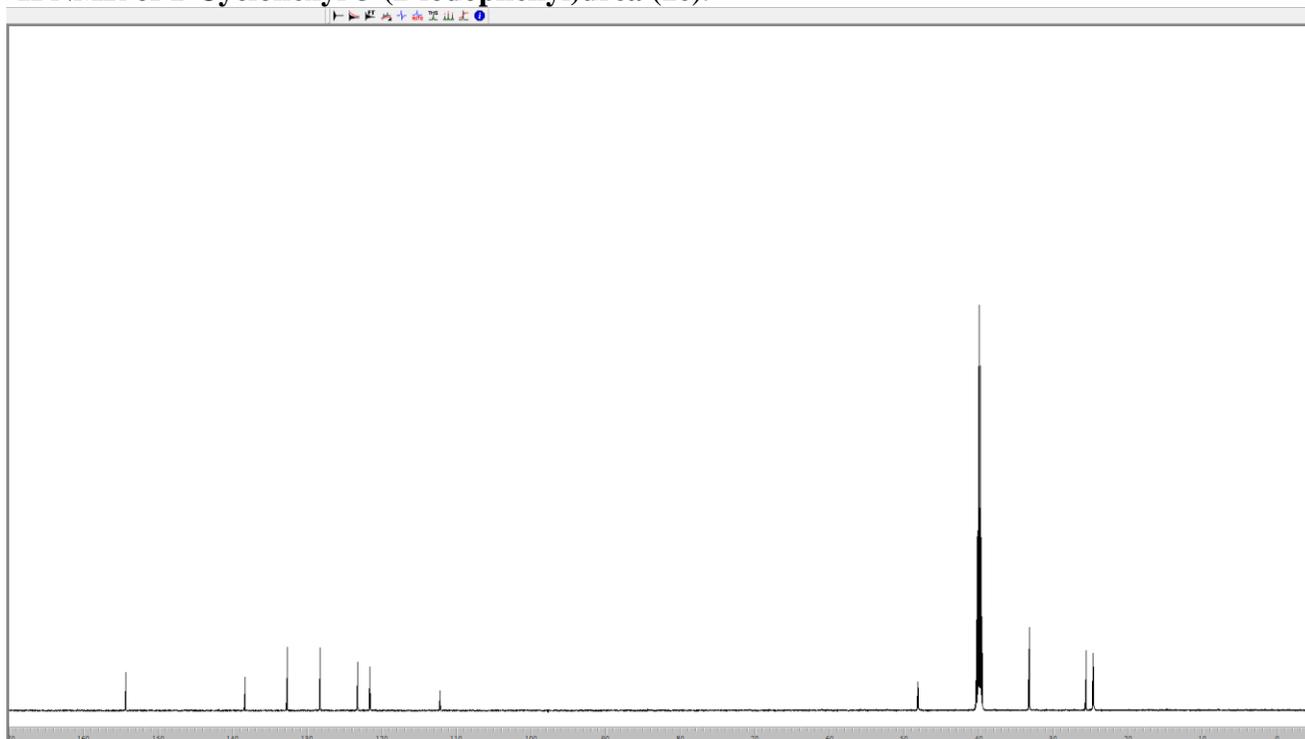
**<sup>1</sup>H NMR of 1-(4-Chlorophenyl)-3-(2-iodophenyl)urea (1d).**



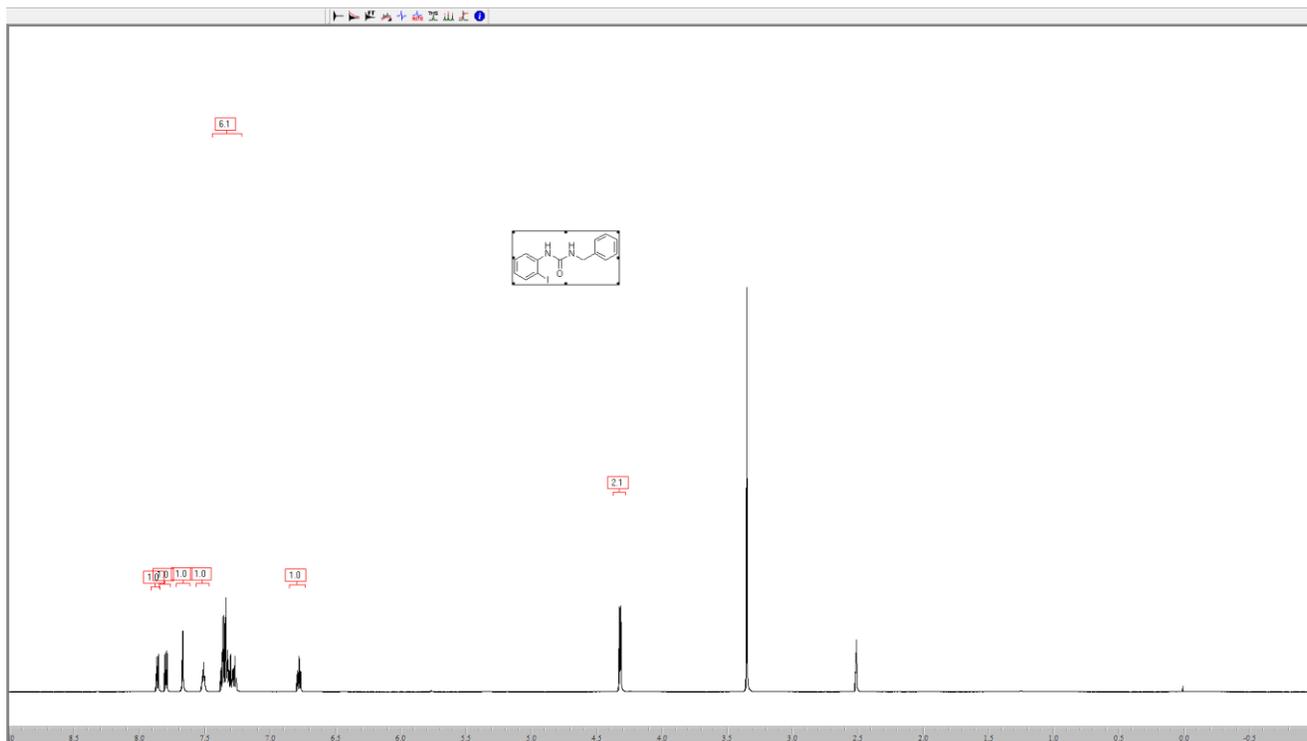
**<sup>13</sup>C NMR of 1-(4-Chlorophenyl)-3-(2-iodophenyl)urea (1d).**



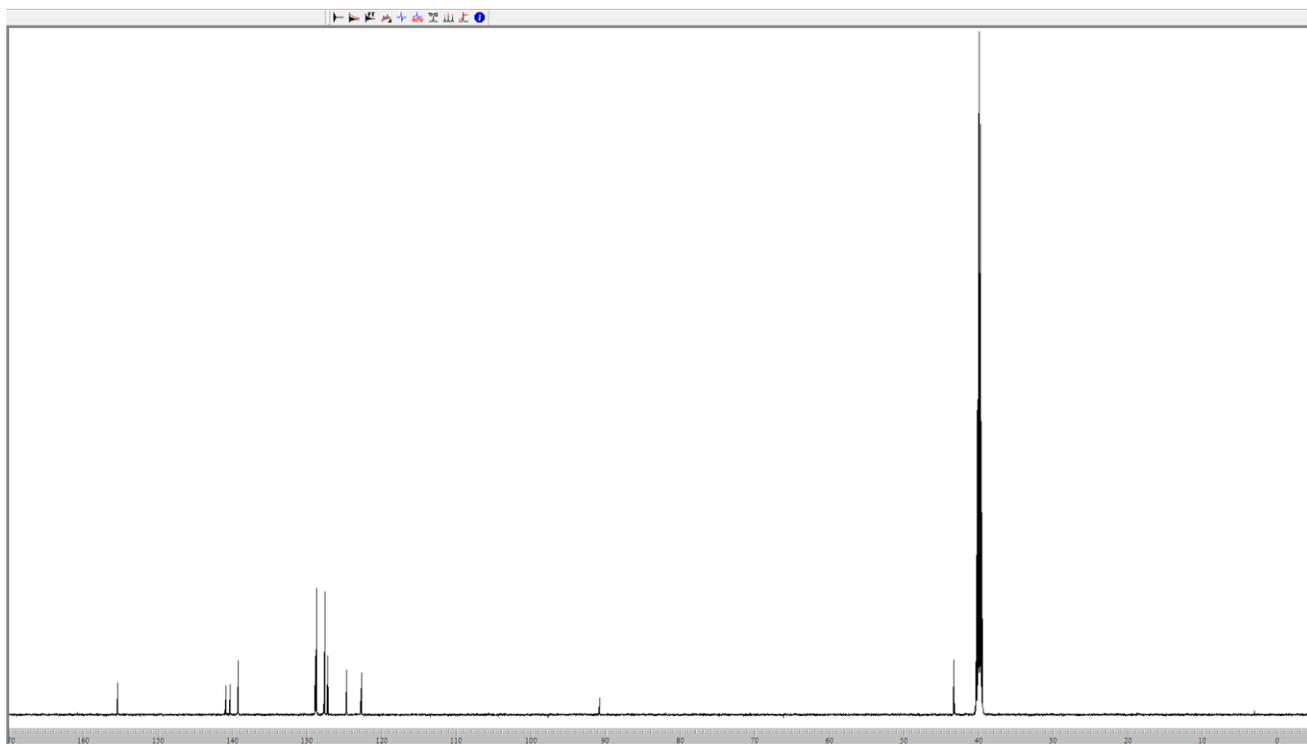
**<sup>1</sup>H NMR of 1-Cyclohexyl-3-(2-iodophenyl)urea (1e).**



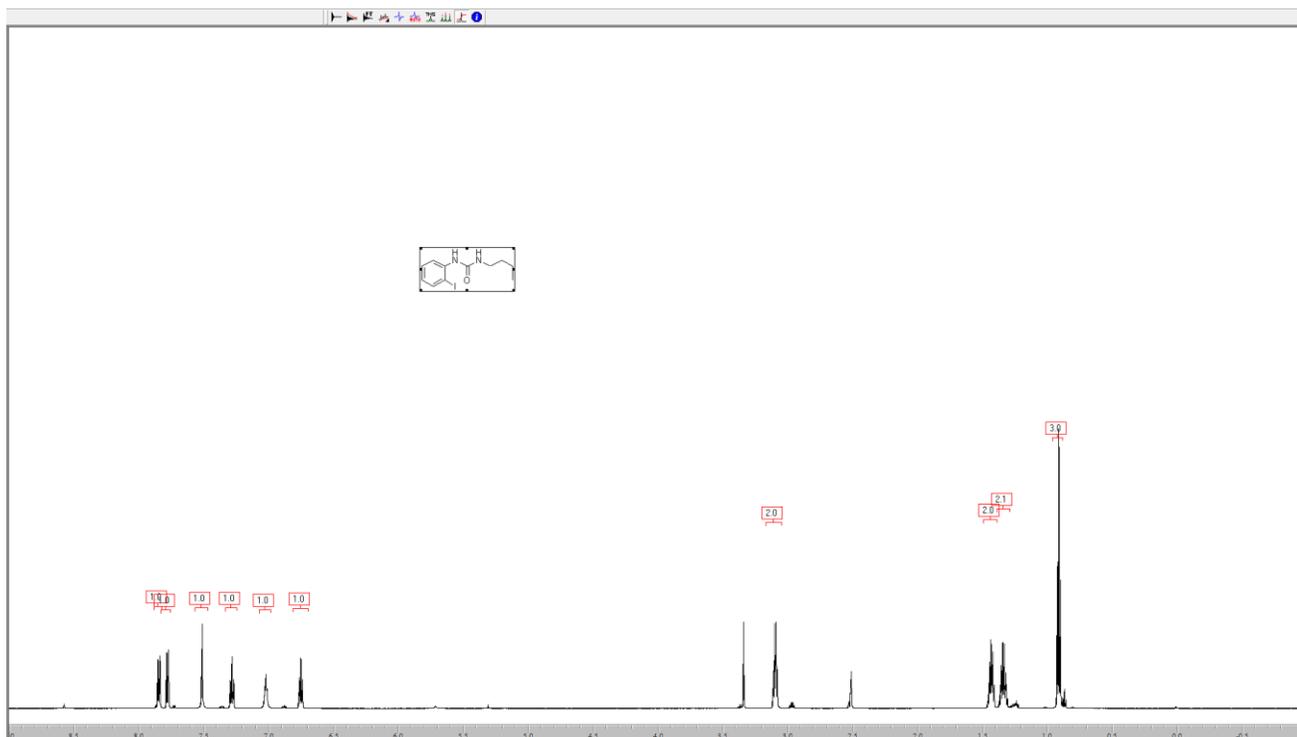
**<sup>13</sup>C NMR of 1-Cyclohexyl-3-(2-iodophenyl)urea (1e).**



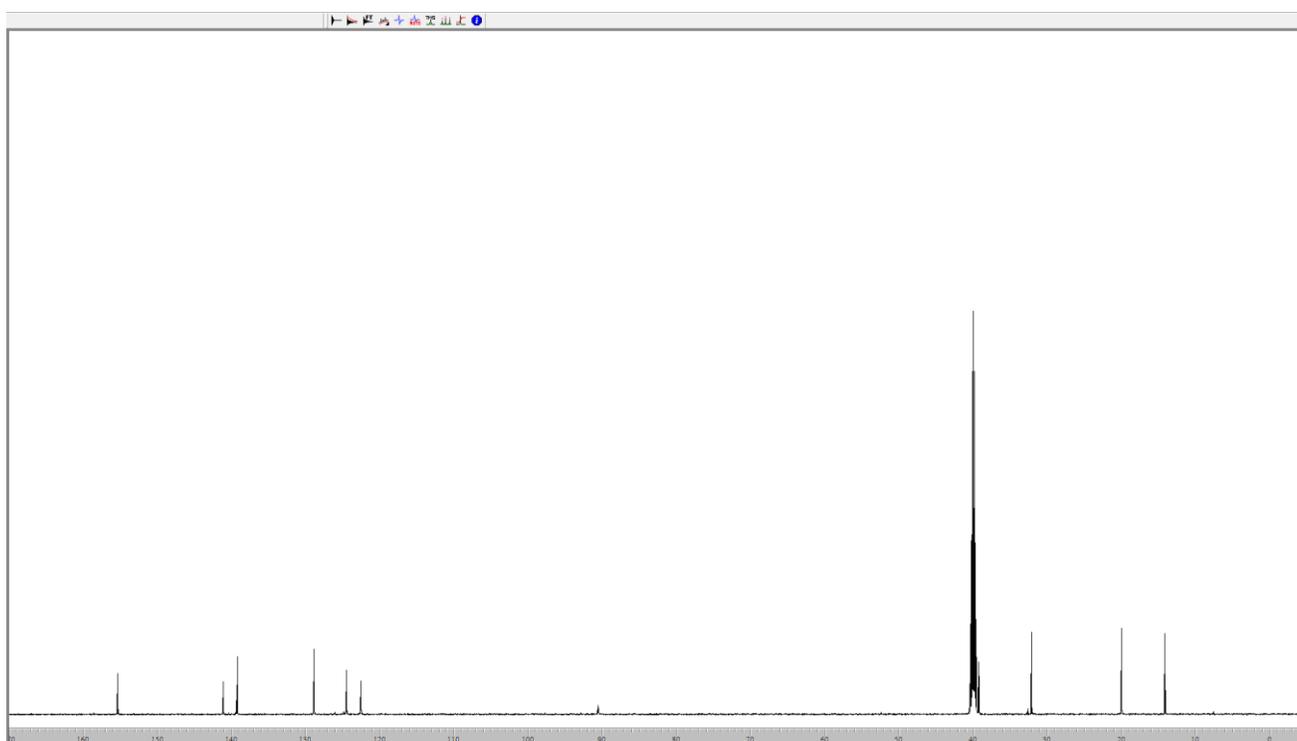
<sup>1</sup>H NMR of 1-Benzyl-3-(2-iodophenyl)urea (1f).



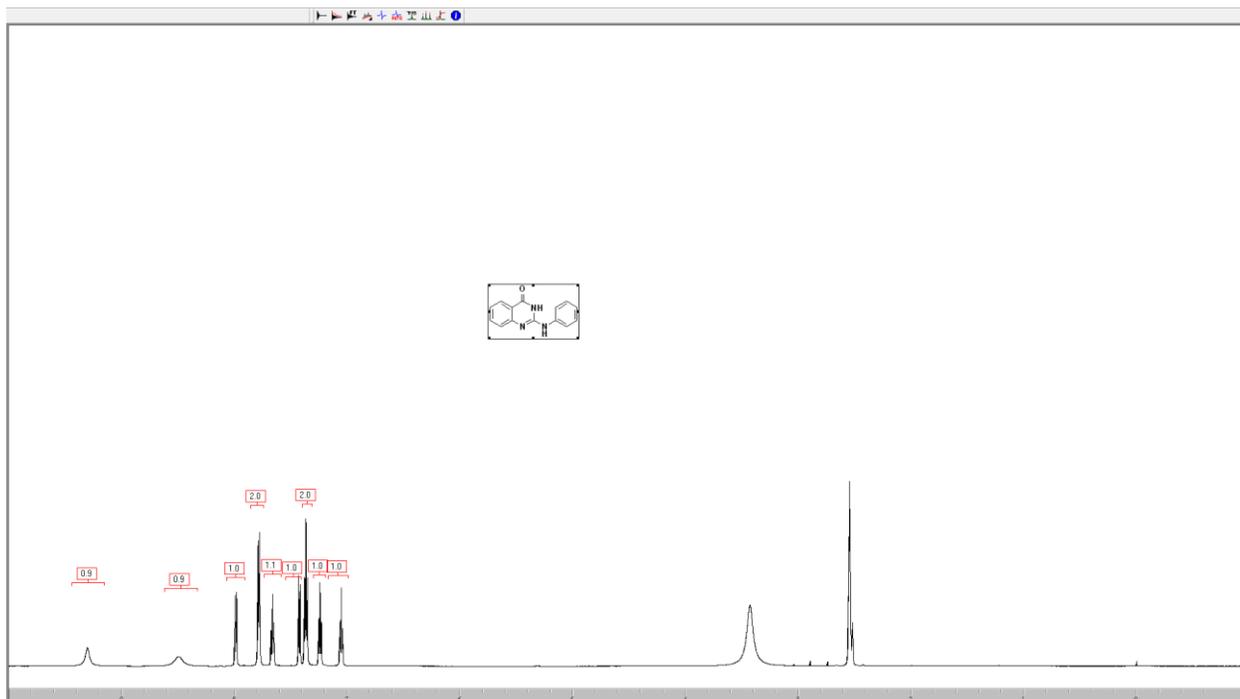
<sup>13</sup>C NMR of 1-Benzyl-3-(2-iodophenyl)urea (1f).



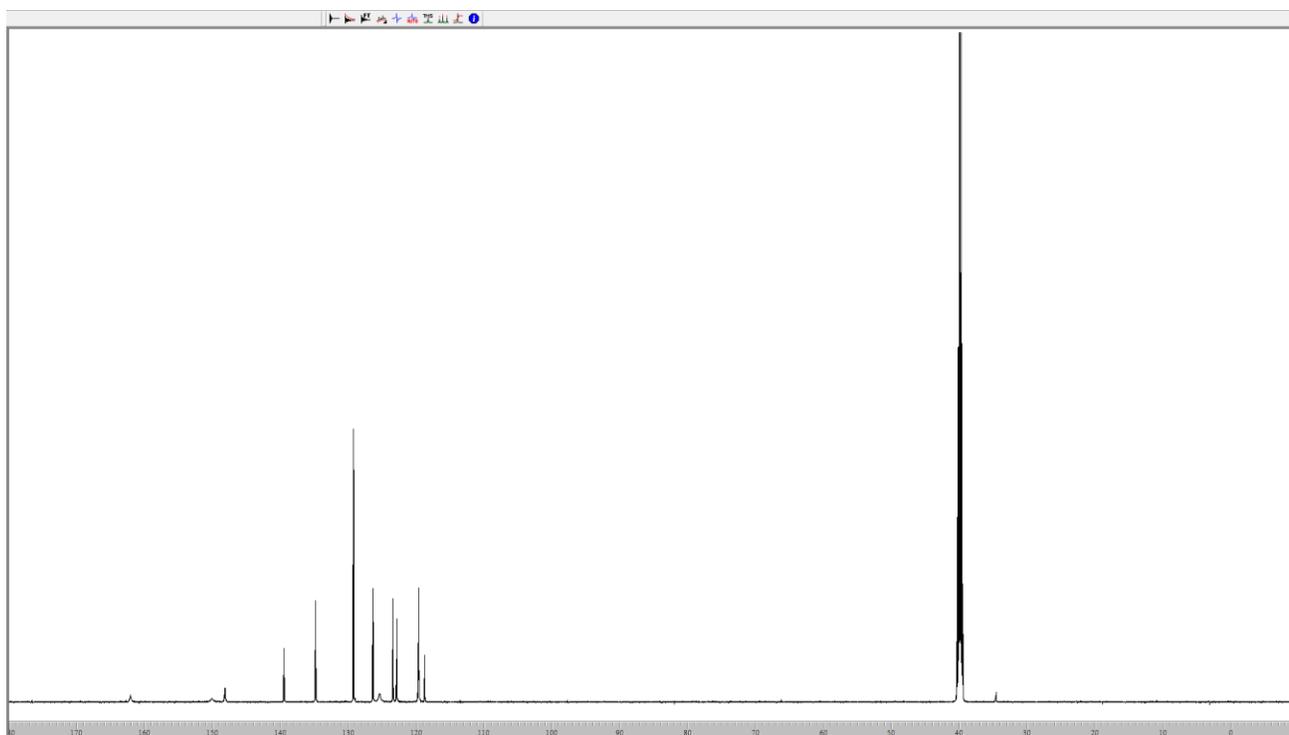
**<sup>1</sup>H NMR of 1-Butyl-3-(2-iodophenyl)urea (1g).**



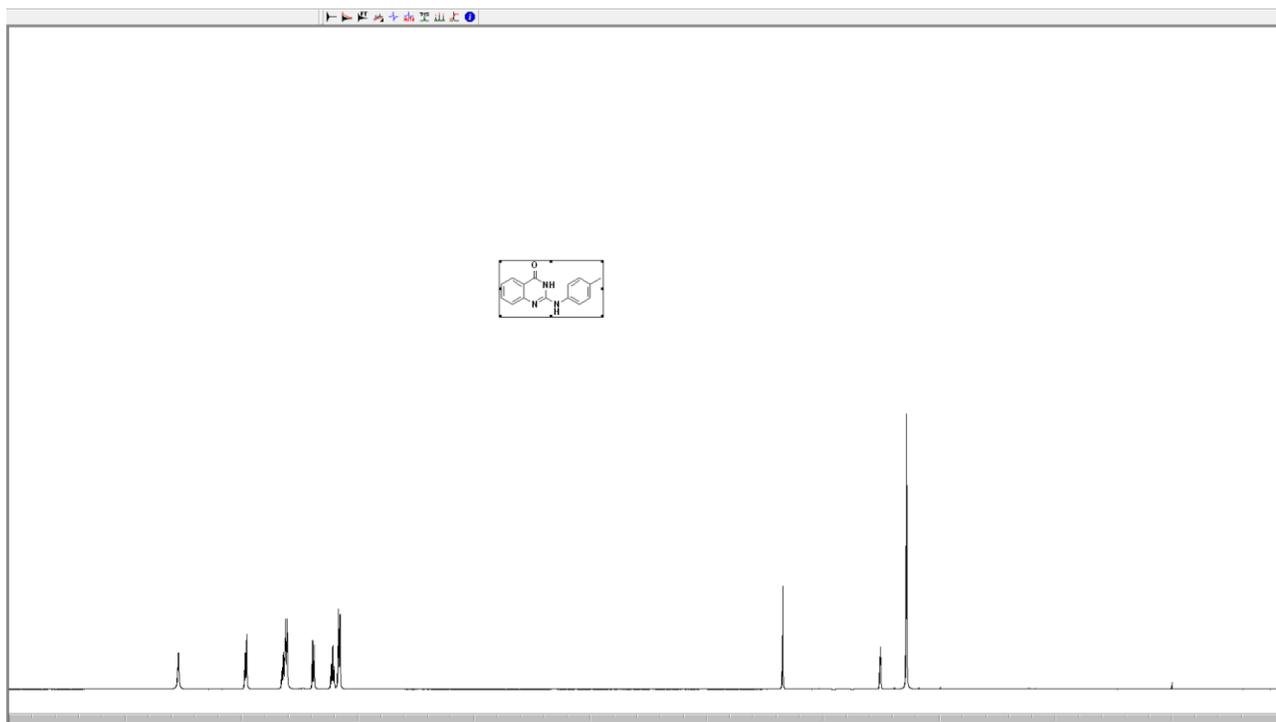
**<sup>13</sup>C NMR of 1-Butyl-3-(2-iodophenyl)urea (1g).**



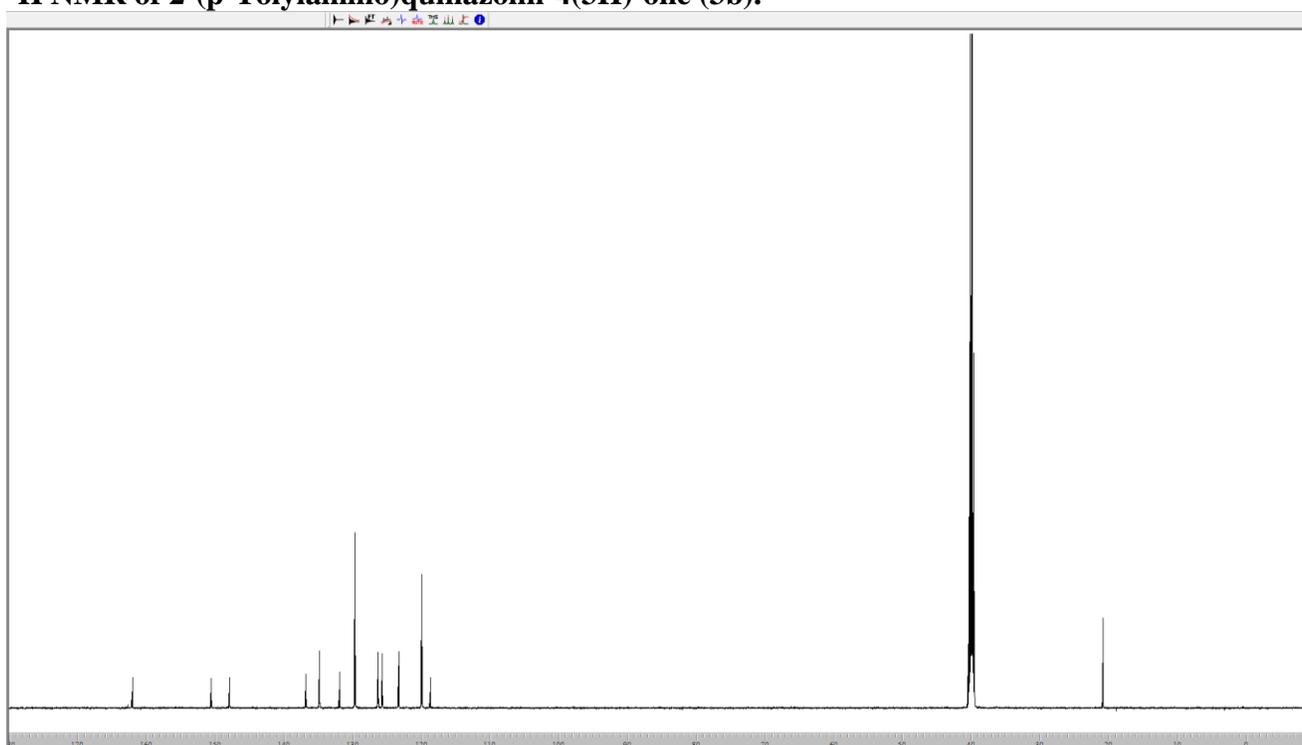
**<sup>1</sup>H NMR of 2-(Phenylamino)quinazolin-4(3H)-one (3a).**



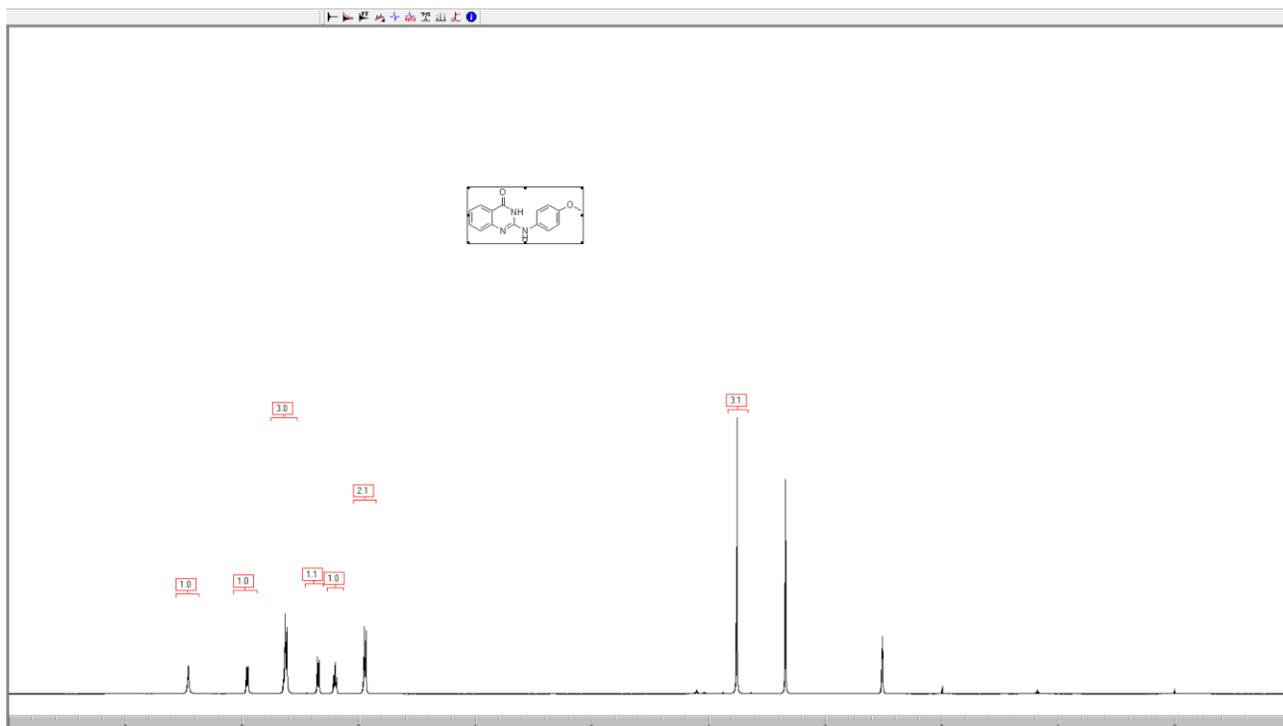
**<sup>13</sup>C NMR of 2-(Phenylamino)quinazolin-4(3H)-one (3a).**



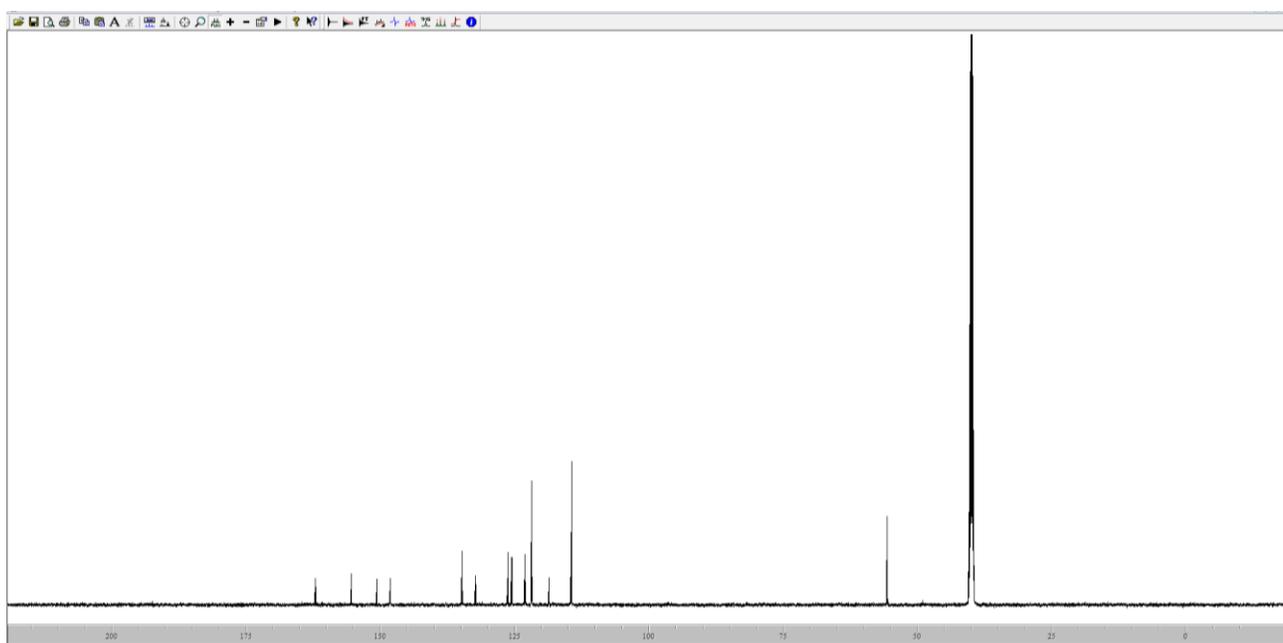
**<sup>1</sup>H NMR of 2-(p-Tolylamino)quinazolin-4(3H)-one (3b).**



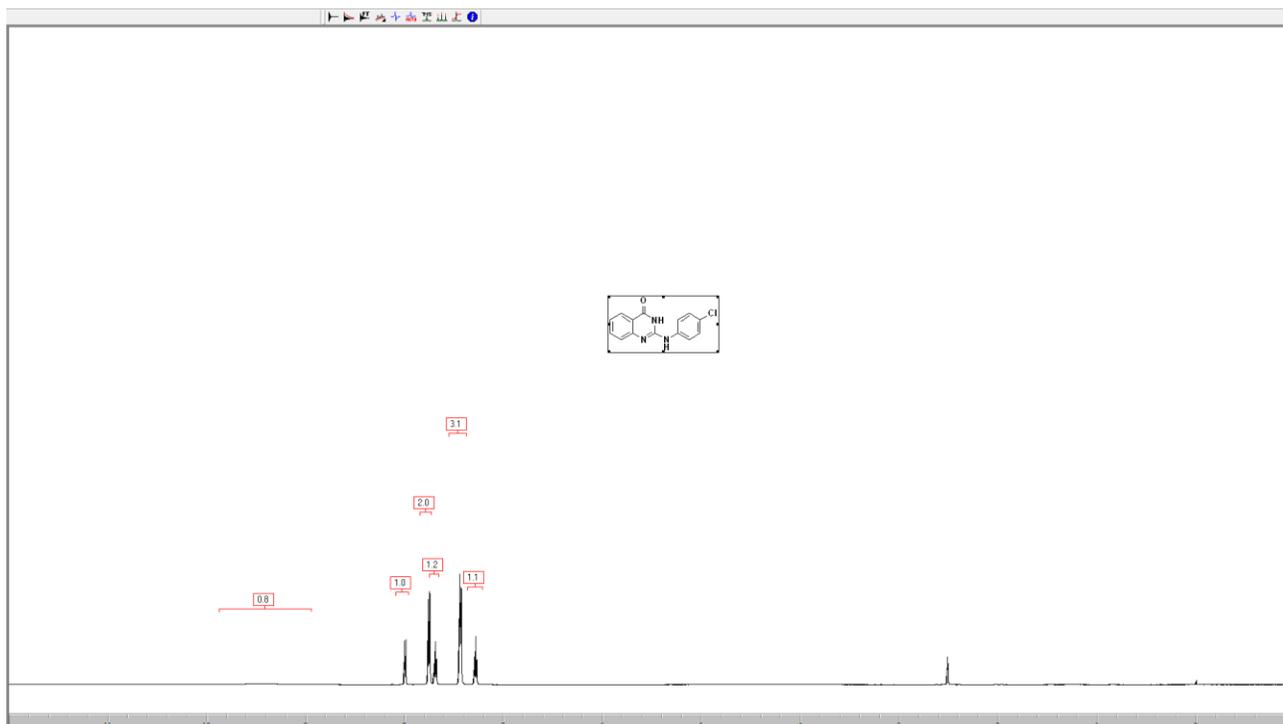
**<sup>13</sup>C NMR of 2-(p-Tolylamino)quinazolin-4(3H)-one (3b).**



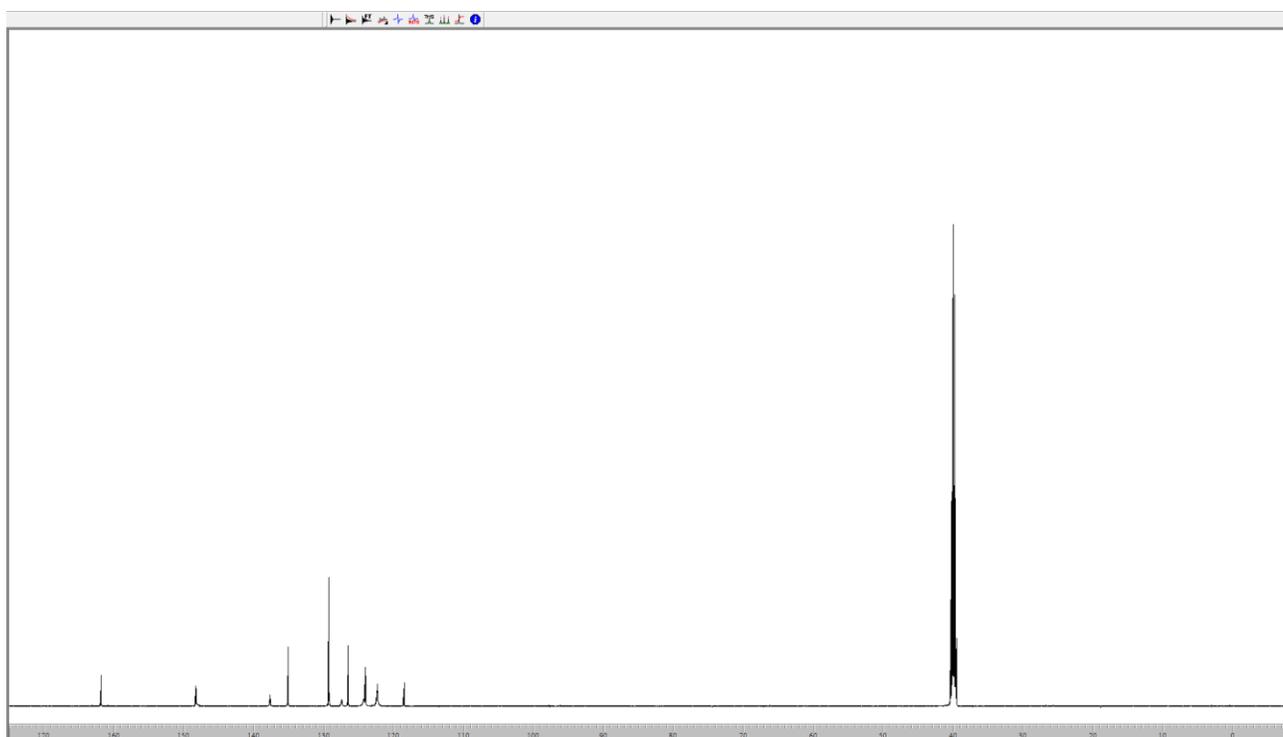
**<sup>1</sup>H NMR of 2-((4-Methoxyphenyl)amino)quinazolin-4(3H)-one (3c).**



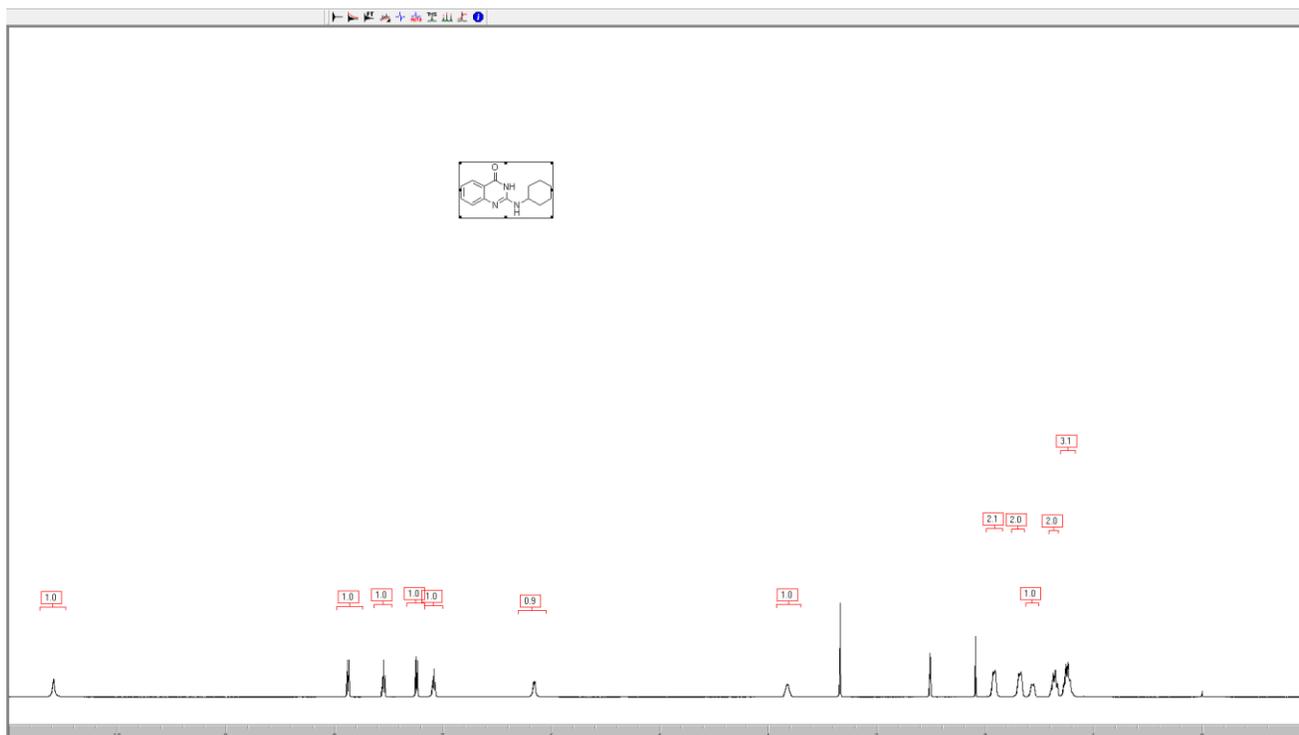
**<sup>13</sup>C NMR of 2-((4-Methoxyphenyl)amino)quinazolin-4(3H)-one (3c).**



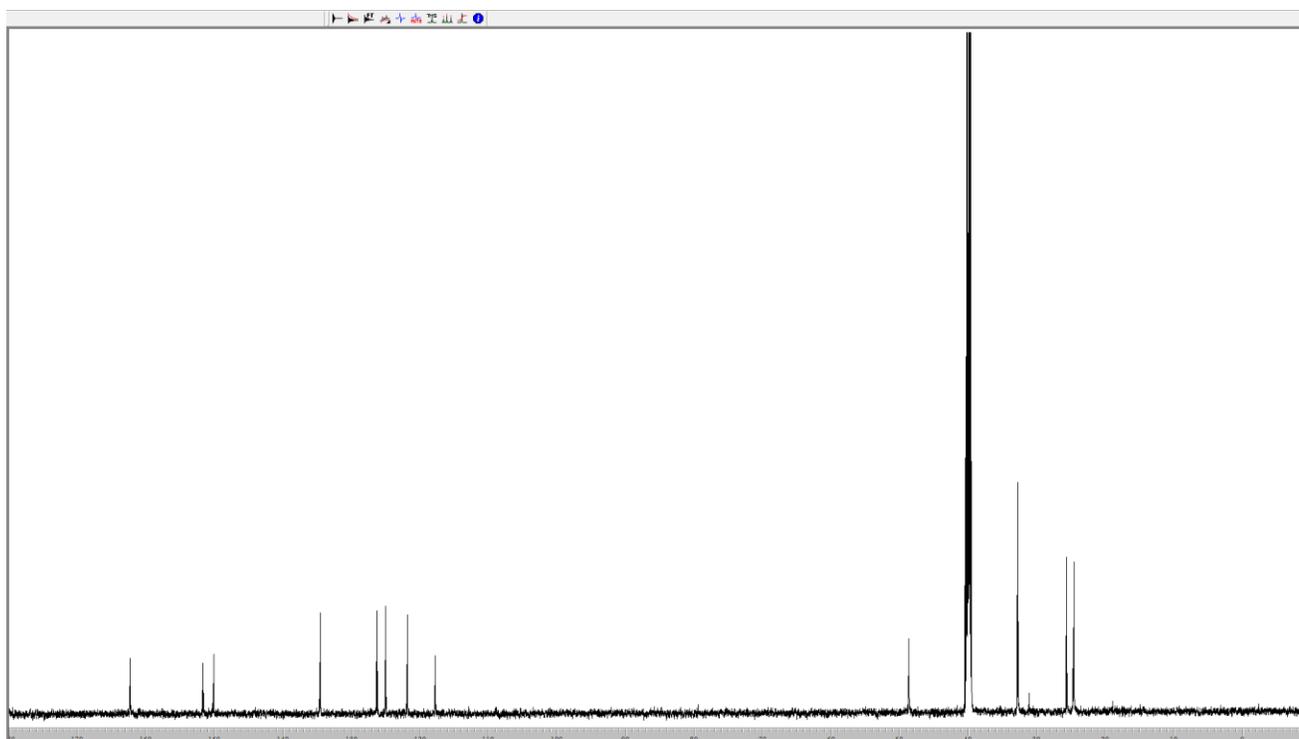
**<sup>1</sup>H NMR of 2-(4-Chlorophenylamino)quinazolin-4(3H)-one (3d).**



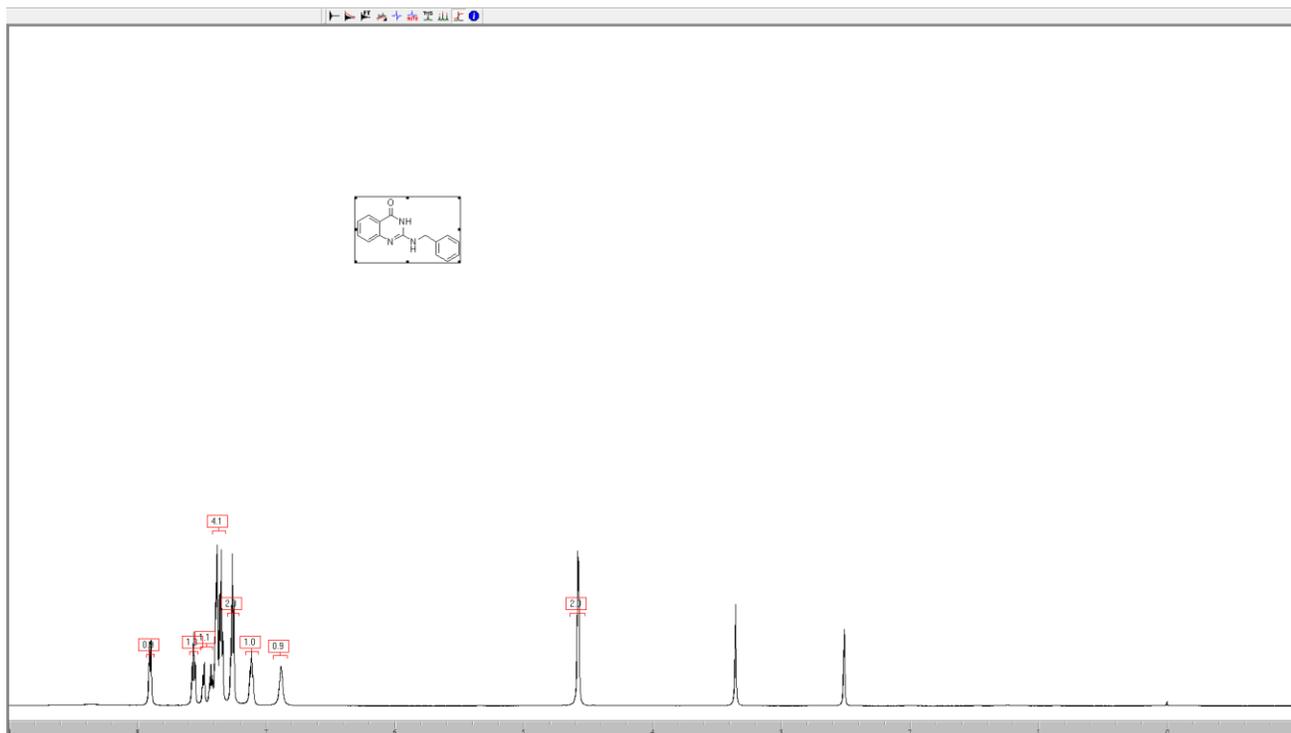
**<sup>13</sup>C NMR of 2-(4-Chlorophenylamino)quinazolin-4(3H)-one (3d).**



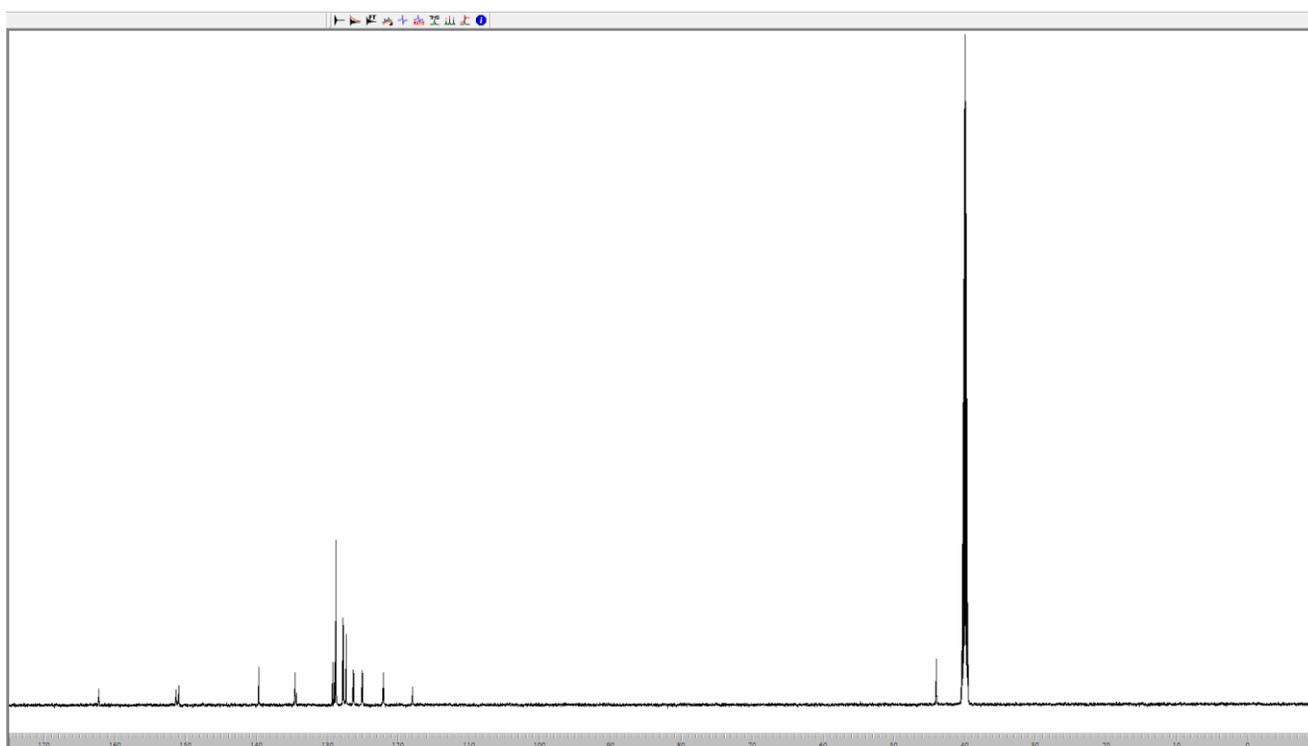
**<sup>1</sup>H NMR of 2-(Cyclohexylamino)quinazolin-4(3H)-one (3e).**



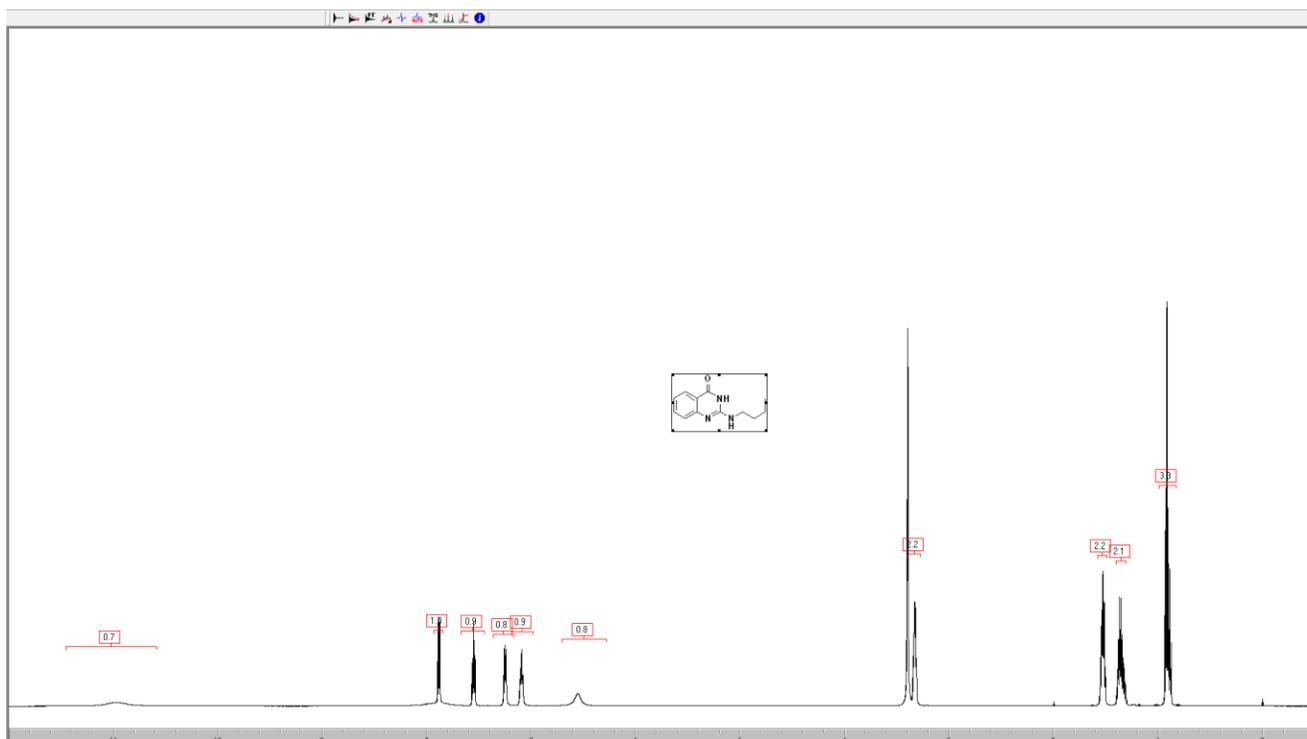
**<sup>13</sup>C NMR of 2-(Cyclohexylamino)quinazolin-4(3H)-one (3e).**



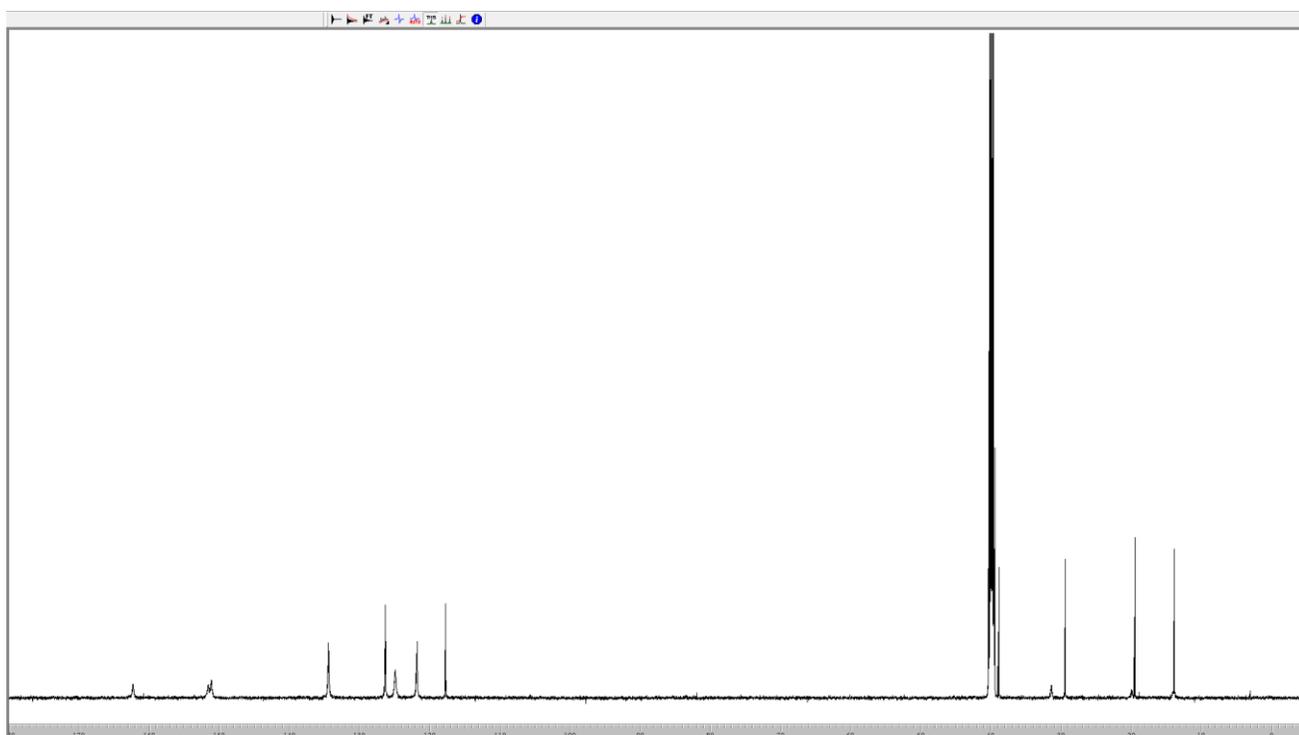
**<sup>1</sup>H NMR of 2-(Benzylamino)quinazolin-4(3H)-one (3f).**



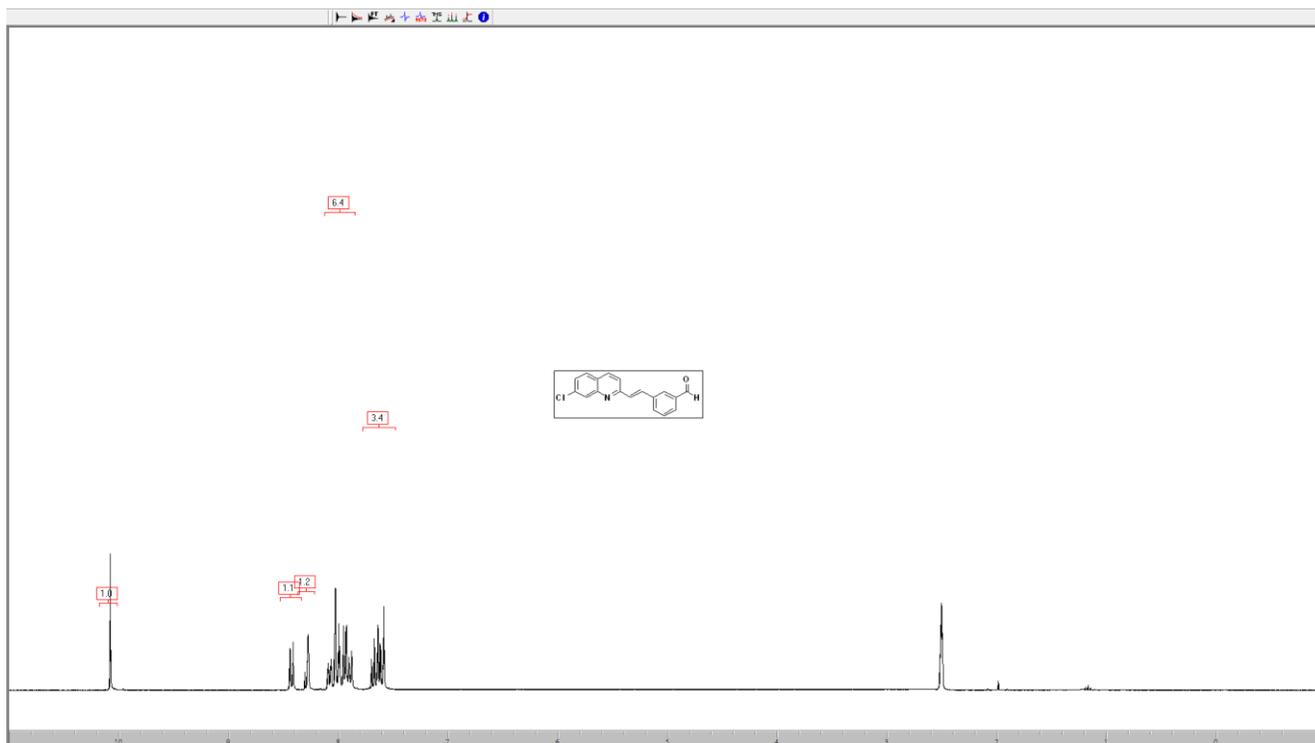
**<sup>13</sup>C NMR of 2-(Benzylamino)quinazolin-4(3H)-one (3f).**



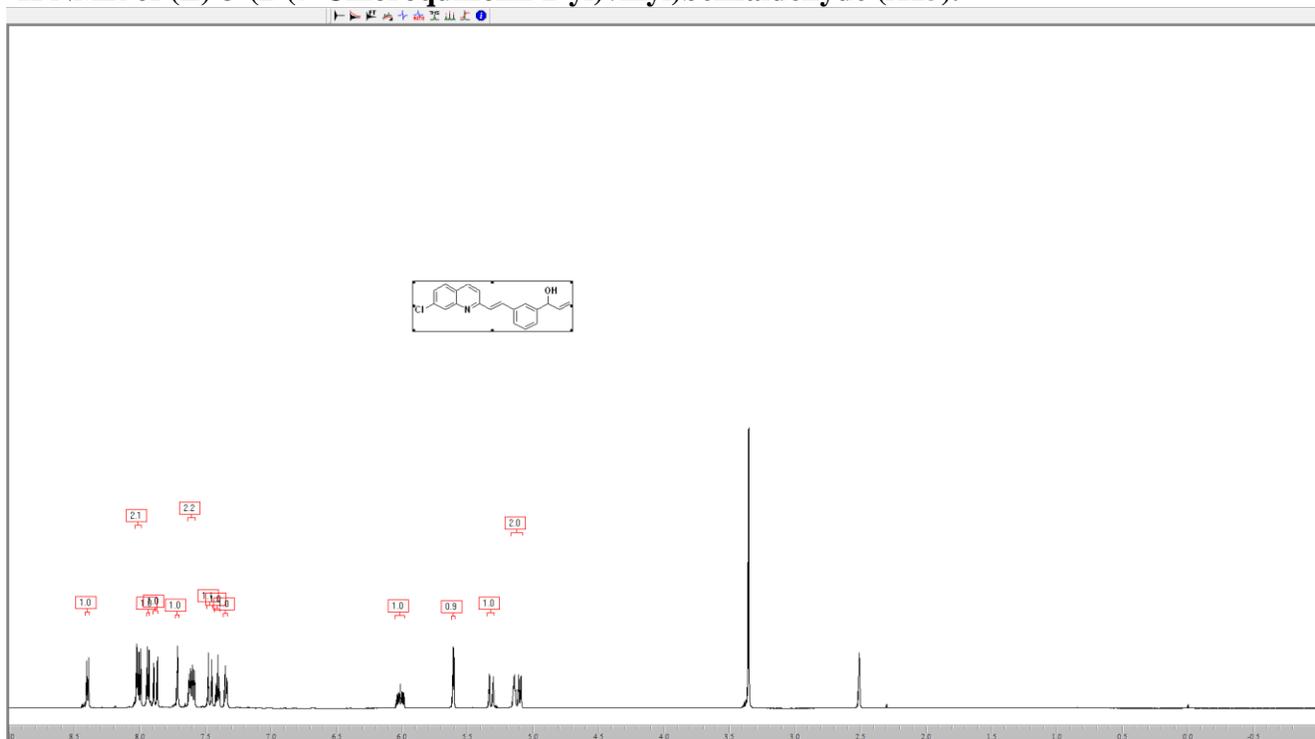
**<sup>1</sup>H NMR of 2-(Butylamino)quinazolin-4(3H)-one (3g).**



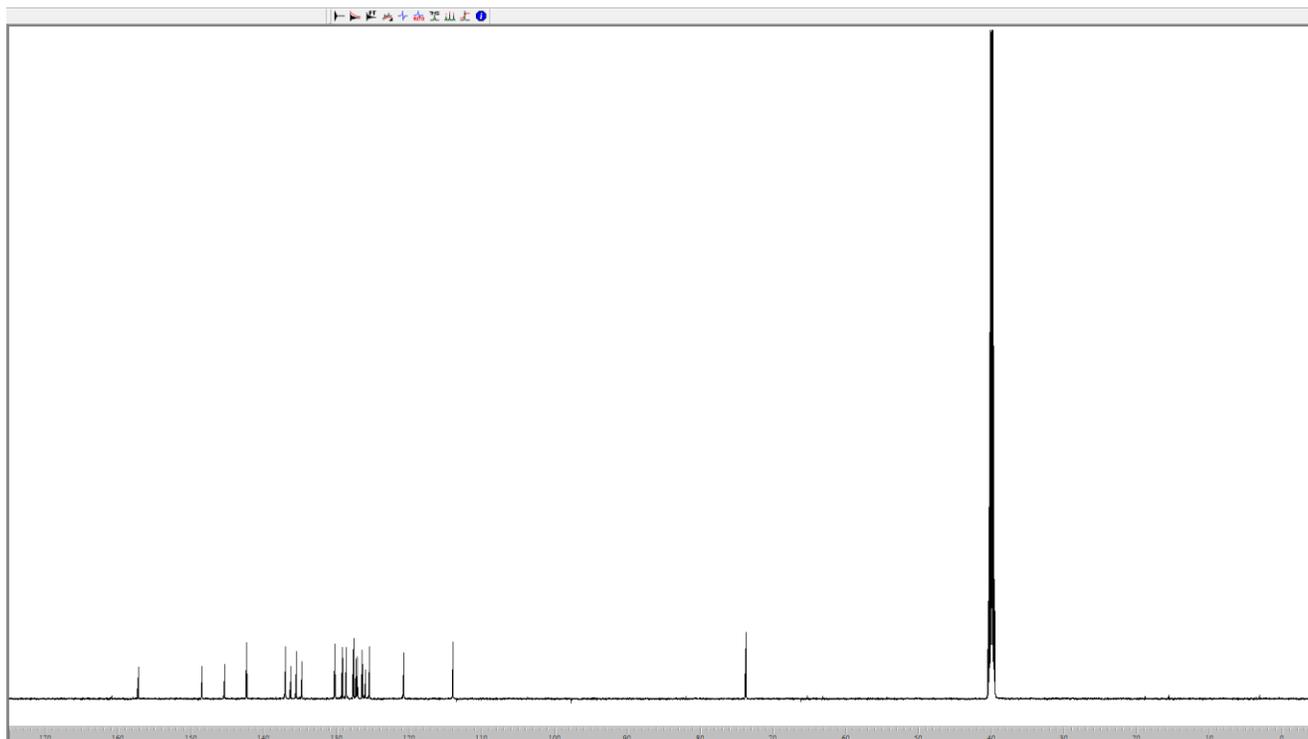
**<sup>13</sup>C NMR of 2-(Butylamino)quinazolin-4(3H)-one (3g).**



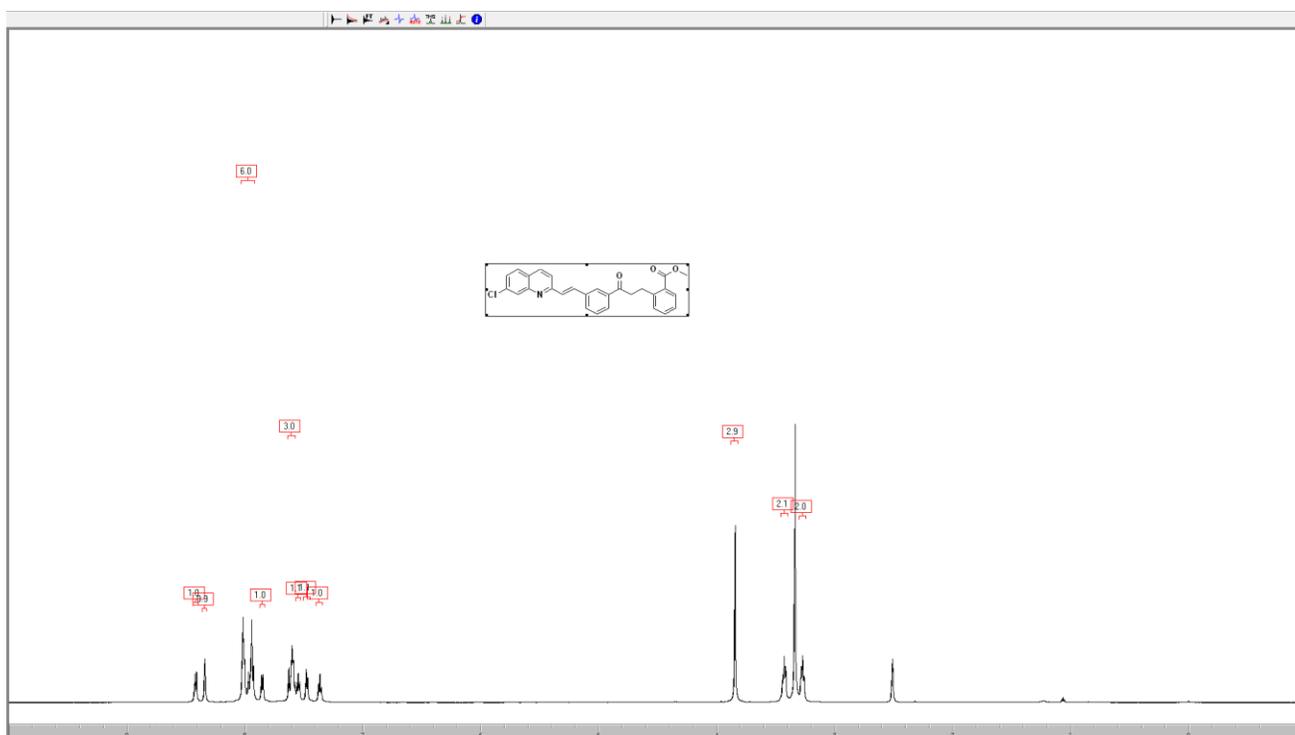
**<sup>1</sup>H NMR of (E)-3-(2-(7-Chloroquinolin-2-yl)vinyl)benzaldehyde (A15).**



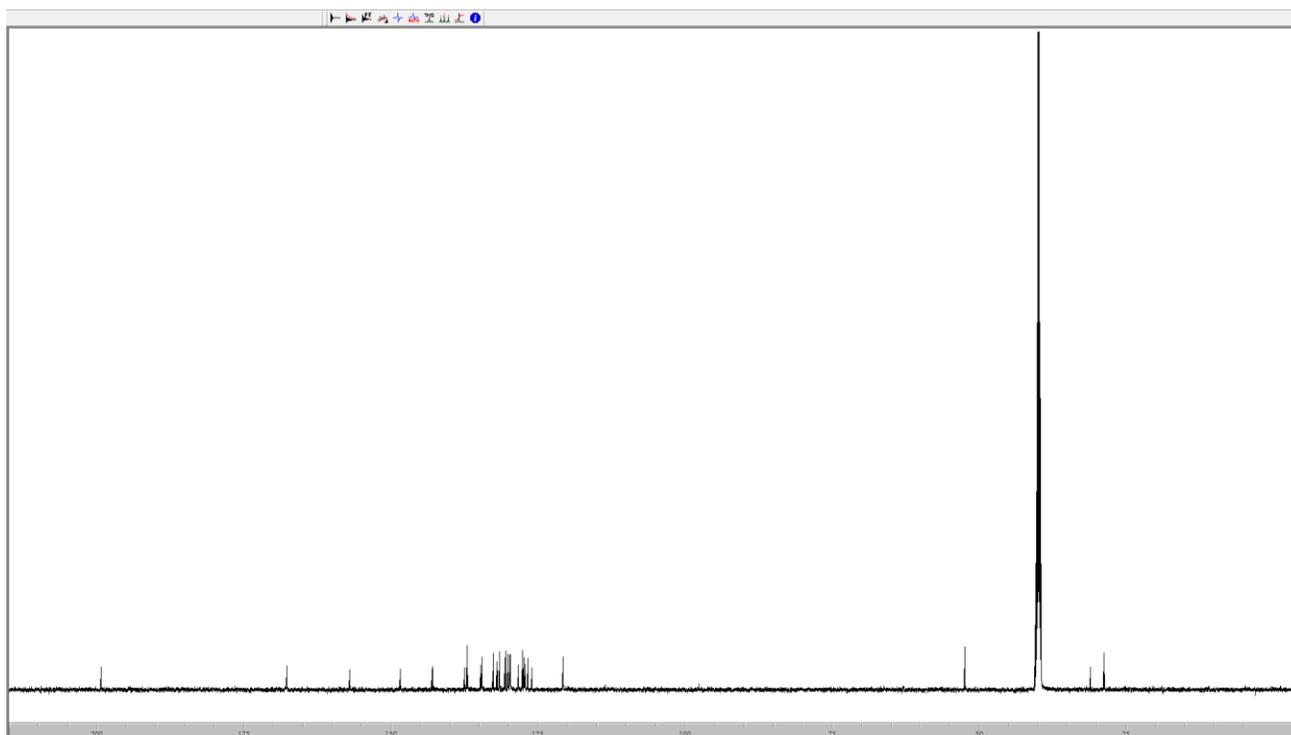
**<sup>1</sup>H NMR of (E)-1-(3-(2-(7-Chloroquinolin-2-yl)vinyl)phenyl)prop-2-en-1-ol (4).**



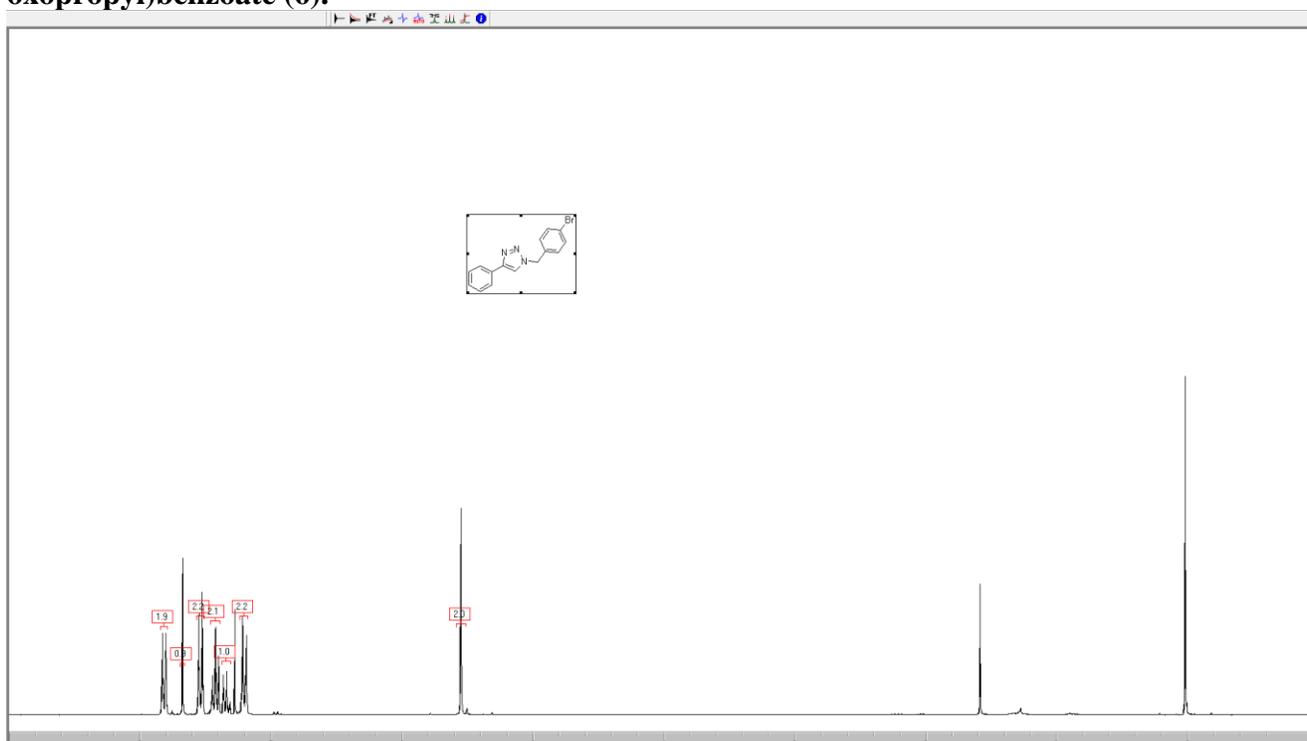
<sup>13</sup>C NMR of (E)-1-(3-(2-(7-Chloroquinolin-2-yl)vinyl)phenyl)prop-2-en-1-ol (4).



<sup>1</sup>H NMR of drug intermediate (E)-methyl 2-(3-(3-(2-(7-chloroquinolin-2-yl)vinyl)phenyl)-3-oxopropyl)benzoate (6).



**<sup>13</sup>C NMR of drug intermediate (E)-methyl 2-(3-(3-(2-(7-chloroquinolin-2-yl)vinyl)phenyl)-3-oxopropyl)benzoate (6).**



**<sup>1</sup>H NMR of 1-(4-Bromobenzyl)-4-phenyl-1H-1,2,3-triazole (9).**

Reference

(1) Tyagi, V.; Khan, S.; Giri, A.; Gouniyal, H.; Sridhar, B.; Chauhan, P. M. S. *Org. Lett.* **2012**, *14*,

3126.