Supporting Information

A rapid and scalable method for visible light-induced bromination of uracil derivatives in falling film looping photoreactor

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Materials and Methods

Reagents and Instruments

Reagents and solvents:

All commercially available reagents and solvents were purchased from companies as follows: water: Milli-Q; HPLC grade acetonitrile: Merck; N-Bromosuccinimide: TCI; 6-chloro-3-methyluracil: TCI; 1-methyl-6-aminouracil: Sigma; 6-methyluracil: TCI; 2-aminopyrimidine: TCI; 2,4-diamino-6-chloropyrimidine: TCI; 2-amino-4-chloro-6-methylpyrimidine: TCI; Hexane, Ethyl acetate: SRL; $CDCl_3$ & DMSO-d_6: Cambridge isotope laboratories. Reagents were used directly without purification. All the solvents were purified before use. Thin layer chromatography (TLC) was performed on Merck silica gel 60 F_{254}. Products were purified by column chromatography by using 100-200 mesh silica gel from Merck.

The NMR spectra were recorded in $CDCl_3$ and DMSO-d_6 solvent. Data reported as s = singlet, d = doublet, t = triplet, q = quartet, dd = doublet of doublets, dt = doublet of triplets; coupling constant in Hz: integration.

Instruments:

The reaction mixture was evaporated under reduced pressure on a Buchi rotary evaporator. The NMR yield and isolated products were quantified and characterized via NMR spectroscopy using a Bruker 500 MHz & 400 MHz FT-NMR spectrometer. Peristaltic pumps were bought from Kamoer (KHM-SW3S40). High-resolution mass spectrometry (HRMS) of compounds were analysed on XEVO G2-XS QTOF mass spectrometer. Single crystal-XRD was performed using a Bruker D8 Venture Diffractometer.

Equipment	Model	Suppliers
1) Rotavapor	Rotavapor R-100	BUCHI
2) Peristaltic pump	KHM-SW3S40	Kamoer
3) 500 MHz NMR spectrometer	ECZ500R/S1	JEOL
4) UV-VIS Spectrophotometer	UV-1780	Shimadzu

Falling film looping photoreactor design and concept

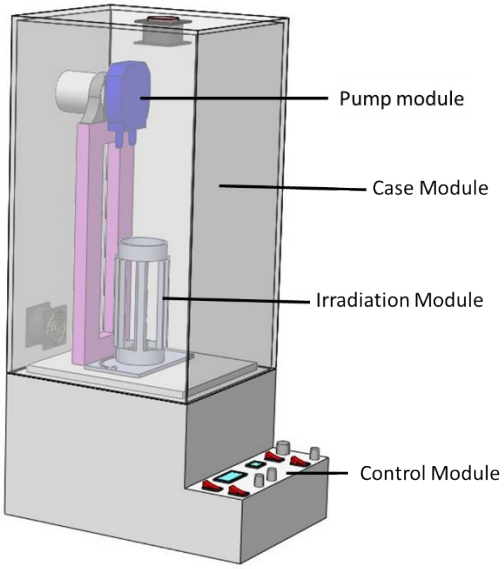


Figure S1: Falling film looping photoreactors

The falling film looping photoreactor was designed and developed by our group. It is designed to carry out small-scale laboratory reactions in batch mode and looping falling film mode. It enables researchers to optimize a lab-scale reaction with respect to different photon fluxes and space velocities. One can scale up the reaction with almost the same optimized laboratory condition and efficiency with this optimization. It has five main modules:

1) Reactor module: It is a specially designed glassware made up of borosilicate glass of thickness 1.5 mm. The neck portion of the glassware is designed to function as a distributor for the reaction solution using an integrated spillway. The reaction solution is pumped up from the bottom, distributed through the four inlet holes into the grove at the neck, and finally overflows through the inside surface of the glassware, making a thin film. During the reaction, this looping operation continues with a specific space velocity. We have three reactor modules (1XA, 2XA, 4XA) for consecutive scale-up processes. This can further be scaled up according to need.

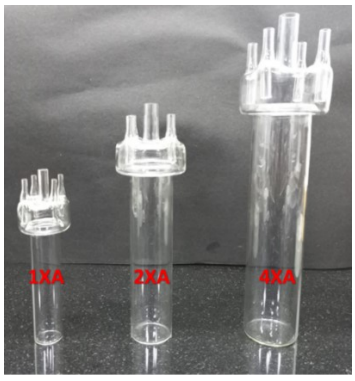


Figure S2: 1XA, 2XA and 4XA reactor module

2) **Irradiation Module:** Three different irradiation modules have been developed in the three different-sized reactor modules. It consists of several single LED strips mounted on a heat sink. The circuit diagram for each irradiation module has been kept similar for maintaining similar photon fluxes with the applied current. 1×A reactor module contains 5 LED strips and each strip contains 8 LEDs. Similarly, 2×A and 4×A irradiation module contains 7 and 10 LED strips, each containing 13 and 16 LEDs, respectively. This also can be scaled up or down according to need.

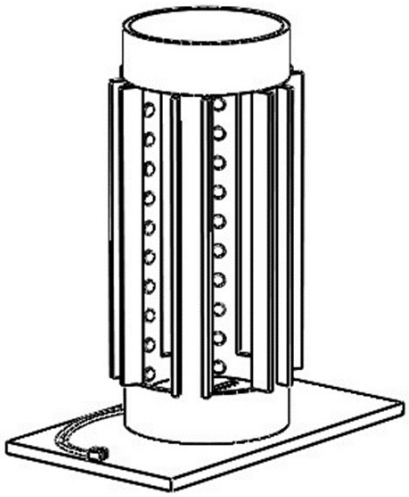


Figure S3: Irradiation module.

3) **Pump Module:** Kamoer (KHM-SW3S40) peristaltic pumps were used for the looping operations. It is mounted on a pump stand, which allows to adjust the position of the pump height according to the reactor module.
4) **Controller Module:** It contains all the switches, controllers, and display units, allowing easy and simple laboratory operations. A 12 V, 10 A DC power supply was used for the main operation.

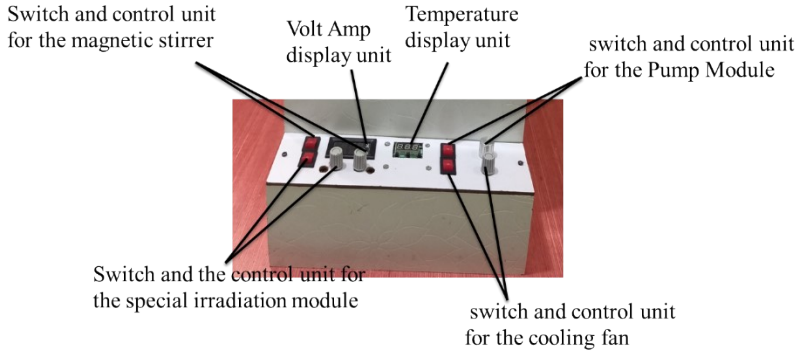


Figure S4: Controller module

5) Case Module

A case module is used to protect the eyes of the users from high-energy visible light. The case module also has cooling fans and a cooling coil to maintain the operating temperature.

All the detailed information about the reactor regarding the design, dimensions, circuit diagram and photonic characterization are available in our published research article.[1] Any detail regarding reactor design will also be provided upon request.

Photon-flux and photonic characteristics:

The instrument is equipped with well-characterized irradiation modules. The emitted optical power, emission spectrum and geometrical optical properties were experimentally determined and reported earlier. The optical properties of the different reactor modules in terms of total radiant power and photon flux were also determined and reported. One can easily set the required photon flux from these reported values (See Table S1) by applying a specific current to the irradiation module.

Table S1: Optical properties of the falling film looping photoreactors

reactor module	wetted surface A / cm²	number of LEDs	electrical current / A	current per LED / mA	total photon flux / µmol · s⁻¹	total radiant power P/ W	irradiance E / mW · cm²
1×A	78.5	40	1	71-77	21	4.71	60.1
		40	2	143-154	38	8.56	109.0
		40	2.5	179-192	46	10.32	131.4
2×A	179.1	91	5	177-183	102	22.81	127.4
4×A	314.2	160	10	185-189	185	41.27	131.4

Optimization with respect to temperature in the dark condition

0.6 mmol uracil derivatives and 2.2 equivalent NBS (1.32mmol) were dissolved in 1 mL solvents in a round bottom flask. The flask was placed in hot oil bath and desired temperature was set. The reaction was allowed to continue for 15 hours in dark condition. The reaction was monitored by thin layer chromatography (TLC). After the complete consumption of the starting material, the reaction is stopped and the solvent is evaporated under reduced pressure. It was purified by column chromatography using ethyl acetate/hexane mixture and separated yields were measured.

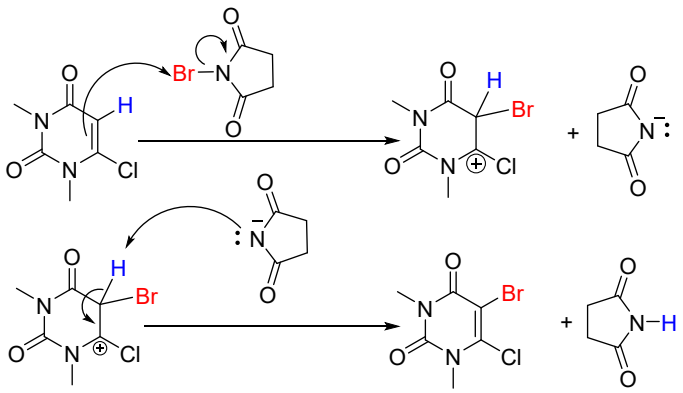
Table S2: Optimization with respect to temperature

Entry	Solvents[b]	Temperature	Time (h)	Yield (%)[c]
1	CH_3CN	45-50°C	15h	66*
1	CH_3CN	75-80°C	15h	65*
1	DMF	45-50°C	15h	41*

1	DMF	75-80^{o}C	15h	43*

Reaction condition: 1 (0.6 mmol) and NBS were taken in solvents. [a]Volume of solvent: 1 mL, [a]Pure product was isolated by silica-gel column chromatography, *Starting material was not consumed.

Reaction mechanism in dark condition



In the absence of light

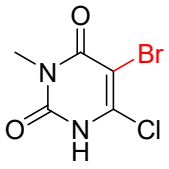
Scheme S1: Proposed reaction mechanism in dark

Synthesis procedure, ^{1}H-NMR and ^{13}C-NMR data

General procedure for the synthesis of compound 1a-h, 2a-e and 3a-c

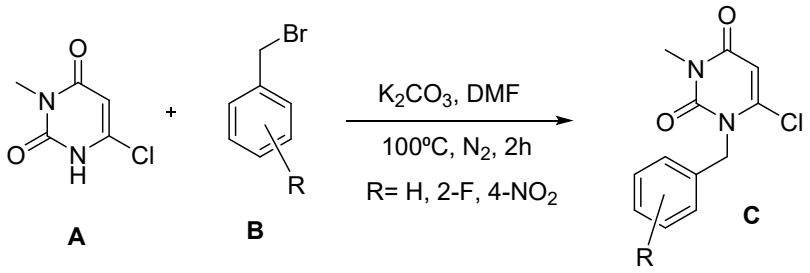
0.6 mmol uracil derivatives and 2.2 equivalent NBS (1.32mmol) were dissolved in 1 mL solvent (acetonitrile). A constant photon flux of 46 µmol · s^{-1} was applied and corresponding time-dependent reaction monitoring was performed by TLC. After the complete consumption of the starting material, the reaction is stopped and the solvent is evaporated under reduced pressure. It was purified by column chromatography using ethyl acetate/hexane mixture and separated yields were measured.

5-bromo-6-chloro-3-methyl pyrimidine-2,4(1H,3H)-dione (1a)



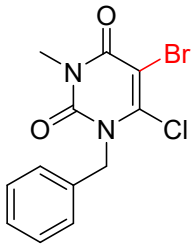
White solid (120.5 mg, 84% yield), eluent: hexane/ethyl acetate (1:1), **^{1}H-NMR** (400 MHz, DMSO-d_6) δ: 12.80 (s, 1H), 3.13 (s, 3H); **^{13}C-NMR** (101 MHz, DMSO-d_6) δ: 159.33, 150.00, 143.39, 95.60, 28.63. **HRMS (ESI):** calculated for $C_5H_5BrClN_2O_2$ $[M+H]^+$: 238.9223; found: 238.9235

General procedure for the synthesis of starting material from 6-chloro-3-methyluracil



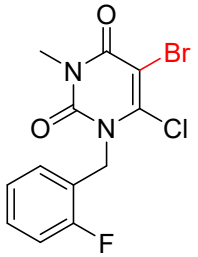
Compound **C** was synthesized using previously reported method. [2] 6-chloro-3-methyluracil (**A**, 2mmol, 1equiv.) and potassium carbonate (8mmol, 4 equiv.) was dissolved in 10ml DMF. Subsequently, benzyl bromide derivatives (**B**, 8mmol, 4 equiv.) was added to it. The resulting solution was stirred at 100^{o}C under N_2 atmosphere for 2h. Next, the reaction mixture was passed through Celite and rinsed with the dichloromethane. The resulted filtrate was concentrated under reduced pressure and crude product (**C**) was purified through column chromatography using ethyl acetate/hexane (4:1) solvent ratio. Further, the isolated product was used for bromination reaction.

1-benzyl-5-bromo-6-chloro-3-methylpyrimidine-2,4(1H,3H)-dione (1b)



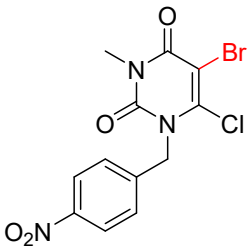
White solid (162.4 mg, 82% yield), eluent: hexane/ethyl acetate (4:1), **^{1}H-NMR** (400 MHz, DMSO-d_6) δ 7.36 – 7.25 (m, 5H), 5.29 (s, 2H), 3.25 (s, 3H). **^{13}C-NMR** (101 MHz, DMSO-d_6) δ 158.18, 150.66, 145.32, 136.31, 129.07, 127.96, 127.02, 98.33, 51.67, 30.00. **HRMS (ESI):** calculated for $C_{12}H_{11}BrClN_2O_2$ $[M+H]^+$: 328.9692; found: 328.9684

5-bromo-6-chloro-1-(2-fluorobenzyl)-3-methylpyrimidine-2,4(1H,3H)-dione (1c)



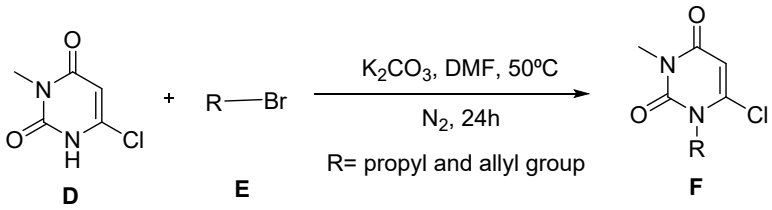
White solid (173.3 mg, 83% yield), eluent: hexane/ethyl acetate (4:1), **^{1}H-NMR** (400 MHz, DMSO-d_6) δ 7.33 (dt, *J* = 14.4, 6.7 Hz, 2H), 7.19 (dt, *J* = 15.0, 9.1 Hz, 2H), 5.31 (s, 2H), 3.24 (s, 3H). **^{13}C-NMR** (101 MHz, DMSO-d_6) δ 161.03, 158.21, 150.57, 145.08, 130.09, 128.55, 123.30, 115.73, 98.57, 46.17, 29.98. **HRMS (ESI):** calculated for $C_{12}H_{10}BrClFN_2O_2$ $[M+H]^+$: 346.9598; found: 346.9592

5-bromo-6-chloro-3-methyl-1-(4-nitrobenzyl)pyrimidine-2,4(1H,3H)-dione (1d)



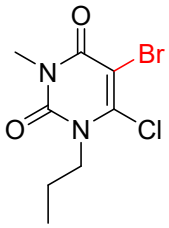
White solid (177.8 mg, 79% yield), eluent: hexane/ethyl acetate (4:1), **^{1}H-NMR** (400 MHz, DMSO-d_6) δ: 8.17 (d, *J* = 8.8 Hz, 2H), 7.58 (d, *J* = 8.8 Hz, 2H), 5.39 (s, 2H), 3.23 (s, 3H). **^{13}C-NMR** (101 MHz, DMSO-d_6) δ: 158.31, 150.67, 147.31, 145.00, 144.11, 128.14, 124.18, 98.63, 51.34, 30.02; **HRMS (ESI):** calculated for $C_{12}H_{10}BrClN_3O_4$ [M+H] $^+$: 373.9543; found: 373.9551

General procedure for the synthesis of starting material from 6-chloro-3-methyluracil



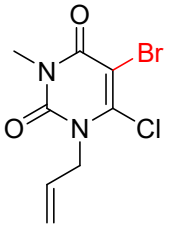
Compound **F** was synthesized using modified method of previous one.[2] 6-chloro-3-methyluracil (**D**, 2mmol, 1equiv.) and potassium carbonate (10mmol, 5 equiv.) was dissolved in 10ml DMF. Subsequently, propyl/allyl bromide (**E**, 10mmol, 5 equiv.) was added to it. The resulting solution was stirred at 50^{o}C under N_2 atmosphere for 24h. Next, the reaction mixture was passed through Celite and rinsed with the dichloromethane. The resulted filtrate was concentrated under reduced pressure and crude product (**F**) was purified through column chromatography using ethyl acetate/hexane (4:1) solvent ratio. Further, the separated product was employed in the bromination reaction.

5-bromo-6-chloro-3-methyl-1-propylpyrimidine-2,4(1H,3H)-dione (1e)



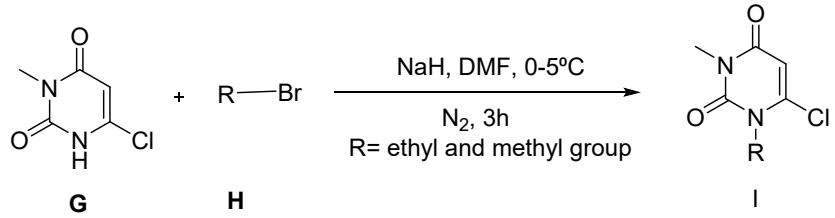
White solid (143.8 mg, 85% yield), eluent: hexane/ethyl acetate (4:1), **^{1}H-NMR** (400 MHz, DMSO-d_6) δ: 4.01 – 3.95 (t, 2H), 3.20 (s, 3H), 1.61 (dt, *J* = 12.9, 6.5 Hz, 2H), 0.88 (t, *J* = 7.5 Hz, 3H); **^{13}C-NMR** (101 MHz, DMSO-d_6) δ: 158.12, 150.11, 145.27, 97.68, 50.50, 29.77, 21.77, 11.17; **HRMS (ESI):** calculated for $C_8H_{11}BrClN_2O_2$ [M+H] $^+$: 280.9692; found: 280.9686

1-allyl-5-bromo-6-chloro-3-methylpyrimidine-2,4(1H,3H)-dione (1f)



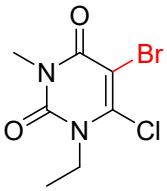
White solid (142.8 mg, 85% yield), eluent: hexane/ethyl acetate (4:1), **^{1}H-NMR** (500 MHz, DMSO-d_6) δ: 4.68 – 4.61 (m), 4.49 (t, J = 7.0 Hz), 4.04 (dd, J = 11.1, 5.8 Hz), 3.93 (dd, J = 11.1, 5.8 Hz), 3.19 (s); **^{13}C-NMR** (126 MHz, DMSO-d_6) δ: 158.09, 150.33, 145.07, 98.62, 53.15, 50.16, 36.46, 29.92; **HRMS (ESI):** calculated for $C_8H_9BrClN_2O_2$ [M+H] $^+$: 278.9536; found: 278.9532

General procedure for the synthesis of starting material from 6-chloro-3-methyluracil



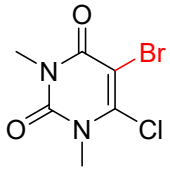
6-chloro-3-methyluracil (**G**, 2mmol, 1equiv.) and sodium hydride (8mmol, 4equiv.) was dissolved in 10ml DMF. Subsequently, ethyl/methyl bromide (**H**, 8mmol, 4equiv.) was added to it. The resulting solution was stirred at 0-5ºC under N_2 atmosphere for 3h. Next, the reaction mixture was passed through Celite and resulted filtrate was concentrated under reduced pressure and crude product (**I**) was purified through column chromatography using ethyl acetate/hexane (3.5:1.5) solvent ratio. [3] Further, the separated product was employed in the bromination reaction.

5-bromo-6-chloro-1-ethyl-3-methylpyrimidine-2,4(1H,3H)-dione (1g)



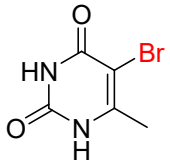
White solid (133.5 mg, 83% yield), eluent: hexane/ethyl acetate (4:1), **^{1}H-NMR** (500 MHz, DMSO-d_6) δ: 4.06 (q, *J* = 7.1 Hz, 2H), 3.18 (s, 3H), 1.17 (t, *J* = 7.1 Hz, 3H); **^{13}C-NMR** (126 MHz, DMSO-d_6) δ: 158.19, 149.98, 145.20, 97.66, 44.66, 29.78, 13.93; **HRMS (ESI)**: calculated for $C_7H_9BrClN_2O_2$ $[M+H]^+$: 266.9536; found: 266.9538.

5-bromo-6-chloro-1,3-dimethylpyrimidine-2,4(1H,3H)-dione (1h)



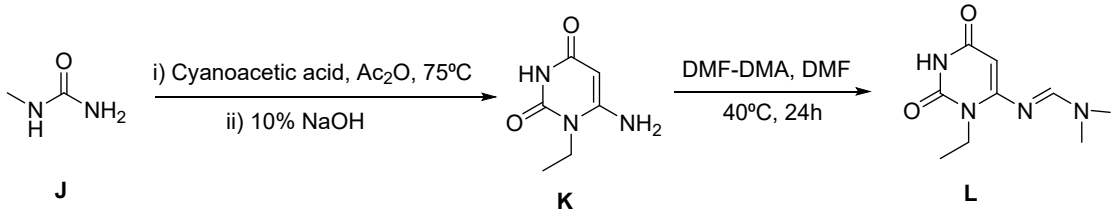
White solid (132.1 mg, 87% yield), eluent: hexane/ethyl acetate (3.5:1.5), **^{1}H-NMR** (500 MHz, DMSO-d_6) δ: 3.18 (s, 3H), 3.18 (s, 3H); **^{13}C-NMR** (126 MHz, DMSO-d_6) δ: 163.37, 163.11, 150.10, 60.42, 30.45, 30.31; **HRMS (ESI):** calculated for $C_6H_7BrClN_2O_2$ $[M+H]^+$: 252.9379; found: 252.9371

5-bromo-6-methylpyrimidine-2,4(1H,3H)-dione (2a)



White solid (95.9 mg, 78% yield), eluent: hexane/ethyl acetate (7:3), **^{1}H-NMR** (400 MHz, DMSO-d_6) δ: 11.38 (s, 1H), 11.25 (s, 1H), 2.19 (s, 3H); **^{13}C-NMR** (101 MHz, DMSO-d_6) δ: 160.43, 151.81, 150.68, 95.44, 19.93. **HRMS (ESI):** calculated for $C_5H_5BrN_2NaO_2$ $[M+Na]^+$: 226.9432; found: 226.9517

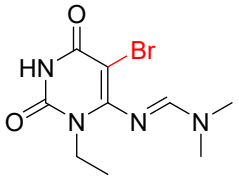
General procedure for the synthesis of starting material (L)



Procedure for K: a mixture of N-ethylurea (J, 10 mmol), cyanoacetic acid (10.1 mmol) and 5 ml of acetic anhydride were heated at 75°C for two hours. The resulted mixture was cooled and added 50 ml of diethyl ether and allowed to stand for 2 hours in an ice-bath. The resulted precipitate was filtered off and gradually washed with diethyl ether. Resultant air dried precipitate was dissolved in water/ethanol (2:1) and continuously added the 10% aqueous NaOH solution. The mixture was continuously stirred at 85°C and aminouracil precipitate gradually separated out. Finally, the obtained crude product (A) was filtered off, washed with water and dried in vacuum oven.[4]

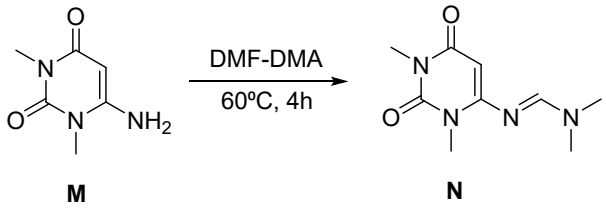
Procedure for L: a mixture of 1-ethyl-6-aminouracil (K, 1mmol, 1equiv.) and DMF-DMA (1.5mmol, 1.5equiv.) was dissolved in 1ml of DMF. The resulting mixture was heated at 40-50°C for 24h in an oil bath. Following this time, excess DMF is dried in vacuum oven and diethyl was added. The obtained white precipitated (K) was filtered off, washed with diethyl ether and dried in vacuum oven.[5]

(E)-N'-(5-bromo-3-ethyl-2,6-dioxo-1,2,3,6-tetrahydropyrimidin-4-yl)-N, N-dimethylformimidamide (2b)



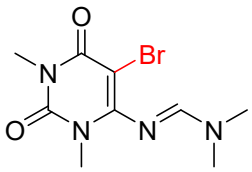
Brown, solid (140.5 mg, 81% yield), eluent: 100% ethyl acetate **^{1}H-NMR** (500 MHz, DMSO-d_6) δ: 11.44 (s, 1H), 8.64 (s, 1H), 3.60 (dd, J = 13.9, 7.1 Hz, 2H), 3.21 (s, 6H), 1.06 (t, J = 7.2 Hz, 3H); **^{13}C-NMR** (126 MHz, DMSO-d_6) δ: 160.02, 155.35, 150.23, 136.58, 86.92, 30.04, 14.28; **HRMS (ESI):** calculated for $C_9H_{14}BrN_4O_2$ $[M+H]^+$: 289.0300; found: 289.0313

General procedure for the synthesis of starting material (N)



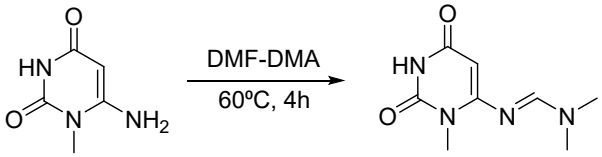
A 25ml round bottom flask was filled with 1,3-dimethyl-6-aminouracil (M, 1mmol) and flask was dipped in an oil bath. Then, 1ml of DMF-DMA was added dropwise and stirred at 60°C for 4 hours. After this time, cooled the reaction mixture and further the obtained precipitate was recrystallized in ethanol.[6]

(E)-N'-(5-bromo-1,3-dimethyl-2,6-dioxo-1,2,3,6-tetrahydropyrimidin-4-yl)-N,N-dimethylformimidamide (2c)



Reddish brown, solid (157.8 mg, 91% yield), eluent: 100% ethyl acetate, **^{1}H-NMR** (400 MHz, DMSO-d_6) δ: 7.93 (s, 1H), 3.26 (s, 3H), 3.20 (s, 3H), 3.11 (s, 3H), 3.00 (s, 3H); **^{13}C-NMR** (101 MHz, DMSO-d_6) δ: 159.51, 157.59, 157.13, 151.15, 82.39, 40.56, 34.47, 31.87, 29.19; **HRMS (ESI):** calculated for $C_9H_{14}BrN_4O_2$ $[M+H]^+$: 289.0300; found: 289.0308

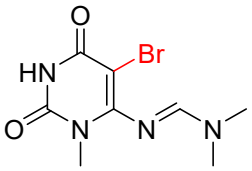
General procedure for the synthesis of starting material (E)-N,N-dimethyl-N'-(3-methyl-2,6-dioxo-1,2,3,6-tetrahydropyrimidin-4-yl)formimidamide (P)



O **P**

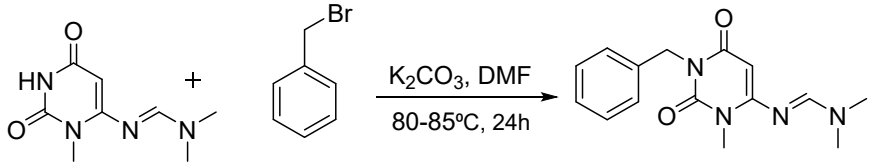
A mixture of 1-methyl-6-aminouracil (**O**, 1mmol, 1equiv.) and DMF-DMA (2mmol, 2equiv.) was dissolved in 5ml of DMF. The resulting mixture was heated at 40-50^{o}C for 24h in an oil bath. Following this time, excess DMF and DMF-DMA was filtered off, washed with diethyl ether and crude product was dried in vacuum oven.[7]

(E)-N'-(5-bromo-3-methyl-2,6-dioxo-1,2,3,6-tetrahydropyrimidin-4-yl)-N,N-dimethylformimidamide (2d)



Darkish brown, solid (140.2 mg, 85% yield), eluent: 100% ethyl acetate **^{1}H-NMR** (400 MHz, DMSO-d_6) δ: 11.25 (s, 1H), 7.93 (s, 1H), 3.18 (s, 3H), 3.10 (s, 3H), 2.99 (s, 3H); **^{13}C-NMR** (101 MHz, DMSO-d_6) δ: 160.00, 158.53, 157.55, 150.85, 82.68, 40.53, 34.45, 30.87; **HRMS (ESI):** calculated for $C_8H_{12}BrN_4O_2$ $[M+H]^+$: 275.0144; found: 275.0137.

General procedure for the synthesis of starting material (S)

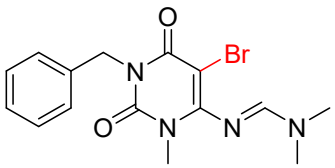


Q **R** **S**

A mixture of **Q** (1mmol, 1equiv.), **R** (10mmol, 10 equiv.) and K_2CO_3 (2.2mmol, 2.2equiv.) were dissolved in .5ml DMF. The resultant mixture was immersed in an oil bath and stirred at 80-85^{o}C for 24h. The excess

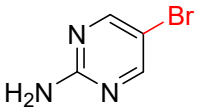
solvent and aryl halide were evaporated. Finally, water was added to the residue and precipitated was filtered off and washed with the diethyl ether. The obtained product (**S**) was dried under vacuum oven.[5]

(E)-N'-(1-benzyl-5-bromo-3-methyl-2,6-dioxo-1,2,3,6-tetrahydropyrimidin-4-yl)-N,N-dimethylformimidamide (2e)



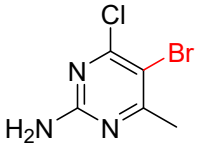
Pale yellow, solid (199.3 mg, 91% yield), eluent: hexane/ethyl acetate (1:1), **^{1}H-NMR** (400 MHz, DMSO-d_6) δ 7.89 (s, 1H), 7.29 – 7.18 (m, 5H), 4.98 (s, 2H), 3.23 (s, 3H), 3.05 (s, 3H), 2.96 (s, 3H); **^{13}C-NMR** (101 MHz, DMSO-d_6) δ 163.06, 159.42, 157.60, 151.13, 137.77, 128.75, 127.96, 127.61, 82.39, 45.23, 34.47, 31.96, 29.92; **HRMS (ESI):** calculated for $C_{15}H_{18}BrN_4O_2$ $[M+H]^+$: 365.0613; found: 365.0615

5-bromopyrimidin-2-amine (3a)



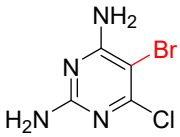
Light pink, solid (75.2 mg, 72% yield), eluent: hexane/ethyl acetate (1:1), **^{1}H-NMR** (400 MHz, DMSO-d_6) δ: 8.30 (s, 2H), 6.86 (s, 2H); **^{13}C-NMR** (101 MHz, DMSO-d_6) δ: 162.42, 158.55, 105.62; **HRMS (ESI):** calculated for $C_4H_5BrN_3$ $[M+H]^+$: 173.9667; found: 173.9673, Spectroscopic data matched with ref. 8

5-bromo-4-chloro-6-methylpyrimidin-2-amine (3b)



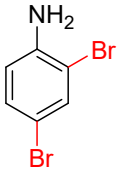
White solid (105.2 mg, 79% yield), eluent: hexane/ethyl acetate (3:2), **^{1}H-NMR** (400 MHz, DMSO-d_6) δ 6.77 (s, 2H), 2.33 (s, 3H); **^{13}C-NMR** (101 MHz, DMSO-d_6) δ 169.51, 161.11, 159.59, 104.52, 25.44; **HRMS (ESI):** calculated for $C_5H_6BrClN_3$ $[M+H]^+$: 221.9434; found: 221.9425

5-bromo-6-chloropyrimidine-2,4-diamine (3c)



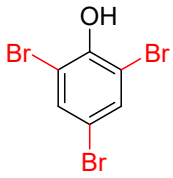
White solid (107 mg, 80% yield), eluent: hexane/ethyl acetate (1:1), **^{1}H-NMR** (400 MHz, DMSO-d_6) δ: 7.02 (s, 1H), 6.53 (s, 1H); ^{13}C-NMR (101 MHz, DMSO-d_6) δ:162.46, 161.50, 157.63, 86.74; **HRMS (ESI):** calculated for $C_5H_5BrClN_4$ $[M+H]^+$: 222.9386; found: 222.9391

2,4-dibromoaniline (4a)



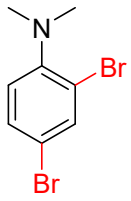
Yield: 96.4 mg, 64%; **^{1}H-NMR** (400 MHz, $CDCl_3$) δ 7.52 (s, 1H), 7.19 (d, J = 8.5 Hz, 1H), 6.62 (d, J = 8.5 Hz, 1H), 4.06 (s, 2H); **^{13}C-NMR** (101 MHz, $CDCl_3$) δ 143.28, 134.46, 131.19, 116.76, 109.61. Spectroscopic data matched with ref. 9

2,4,6-tribromophenol (4b)



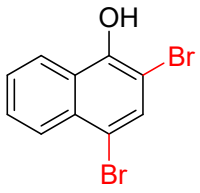
Yield: 142.9 mg, 72%; **^{1}H-NMR** (400 MHz, $CDCl_3$) δ 7.59 (s, 2H), 5.87 (s, 1H); **^{13}C-NMR** (101 MHz, $CDCl_3$) δ 148.95, 134.24, 112.72, 110.42. Spectroscopic data matched with ref. 10

2,4-dibromo-N,N-dimethylaniline (4c)



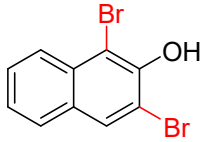
Yield: 128.9 mg, 77%; **^{1}H-NMR** (400 MHz, $CDCl_3$) δ 7.68 (s, 1H), 7.36 (d, *J* = 10.9 Hz, 1H), 6.94 (d, *J* = 8.6 Hz, 1H), 2.78 (s, 6H); **^{13}C-NMR** (101 MHz, $CDCl_3$) δ 151.15, 136.04, 131.01, 121.64, 119.69, 115.36, 44.11. Spectroscopic data matched with ref. 11

2,4-dibromonaphthalen-1-ol (4d)



Yield: 115.9 mg, 64%; (400 MHz, $CDCl_3$) δ 8.25 (d, *J* = 8.4 Hz, 1H), 8.13 (d, *J* = 8.3 Hz, 1H), 7.79 (s, 1H), 7.63 (t, *J* = 7.0 Hz, 1H), 7.56 (t, *J* = 7.5 Hz, 1H), 5.97 (s, 1H); **^{13}C-NMR** (101 MHz, $CDCl_3$) δ 148.18, 131.89, 131.11, 128.17, 127.15, 126.95, 125.09, 122.81, 113.35, 103.20.

1,3-dibromonaphthalen-2-ol (4e)



Yield: 112.3 mg, 62%; **^{1}H-NMR** (400 MHz, $CDCl_3$) δ 7.90 (dd, *J* = 16.5, 5.4 Hz, 2H), 7.61 (dd, *J* = 12.6, 5.5 Hz, 2H), 7.27 (s, 1H), 5.93 (s, 1H); **^{13}C-NMR** (101 MHz, $CDCl_3$) δ 150.91, 131.05, 130.61, 130.09, 128.40, 127.23, 118.29, 106.13.

UV-Visible absorption spectra of NBS in different solvents:

235 mg of NBS (equal to the reaction concentration) was dissolved separately in 1 mL of 8 different solvents and absorption data were taken within the 200 nm to 800 nm range. Finally, these absorption data were compared with the normalized spectrum of the used white LEDs. [1]

Table S3: NBS in 1 mL of different solvents

Entry	Solvent	Volume Taken (mL)	NBS taken (mg)
1	CH_3CN	1	235
2	CH_3OH	1	235
3	CH_3CH_2OH	1	235
4	CH_3COOEt	1	235
5	$CHCl_3$	1	235
6	DMF	1	235
7	H_2O	1	235

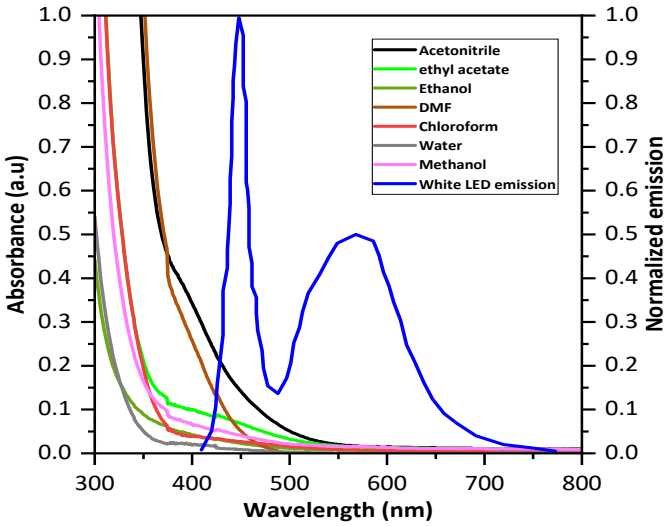


Figure S5: Absorption spectra of NBS in reaction concentration and in different solvents and normalized spectra of used LED

Reaction monitoring with BHT and TEMPO

Three different glassware were taken. The first glassware dissolved 0.6 mmol of 6-chloro-3-methyluracil (1a) and 2.2 equivalent NBS in 1 mL acetonitrile. The second glassware dissolved 0.6 mmol of 6-chloro-3-methyluracil (1a), 2.2 equivalent NBS and 2 equivalent BHT in 1 mL acetonitrile. In the third glassware, 0.6 mmol of 6-chloro-3-methyluracil, 2.2 equivalent NBS and 2 equivalent TEMPO were dissolved in 1 mL acetonitrile. A constant photon flux of 46 µmol · s^{-1} was applied for 1.5 hours and corresponding time-dependent reaction monitoring was performed by TLC. After 1.5 hours, it was observed that no products were formed in the presence of TEMPO and BHT, but the reaction was completed in the first glassware where no TEMPO and BHT were present (Figure S6).

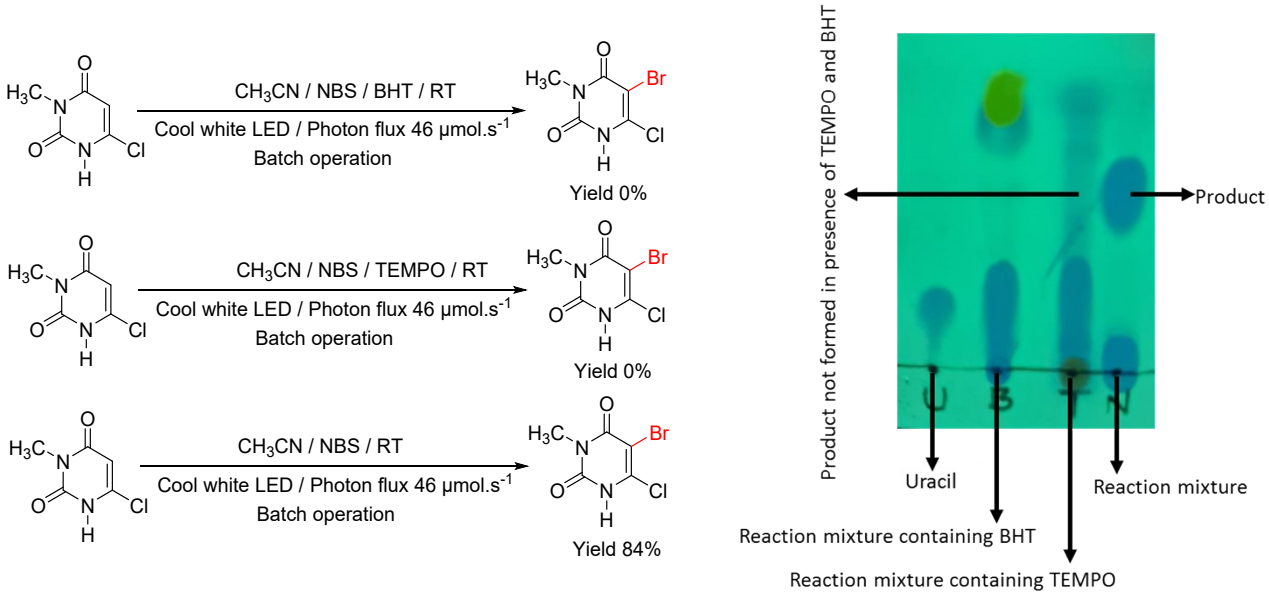
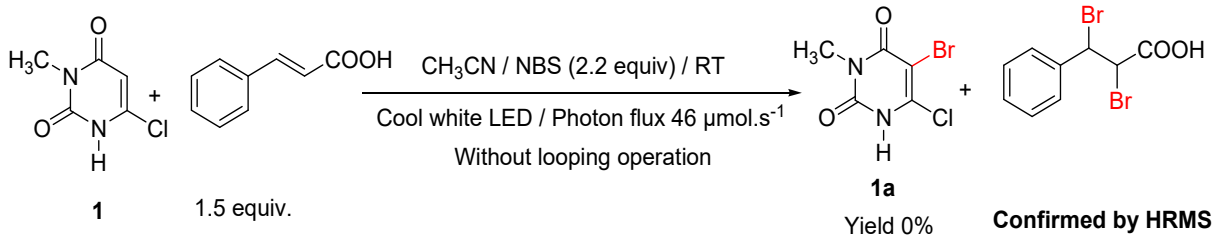


Figure S6: Reaction monitoring with BHT and TEMPO

General procedure for competitive inhibition reaction in presence of cinnamic acid:

A mixture of 6-chloro-3-methyluracil (**1**, 1 equiv., 0.6 mmol), cinnamic acid (1.5 equiv., 0.9 mmol) and NBS (2.2 equiv., 1.32 mmol) were dissolved in 1 mL acetonitrile. A constant photon flux of 46 µmol.s^{-1} was applied for 2hours. After 2h, no product (**1a**) spot was obtained on TLC. However, HRMS data of the raw reaction mixture suggested dibromo product of cinnamic acid. **HRMS** (**ESI**) data of dibromo cinnamic acid, Calculated $C_9H_9Br_2O_2$ $[M + H]^+$ = 306.8969; found: 306.9667.



Scheme S2: Competitive reaction in the presence of cinnamic acid.

Comparison of the absorbance data of the reaction mixture at different time interval with respect to molecular bromine:

0.6 mmols of 6-chloro-3-methyl uracil and 2.2 equivalent NBS were dissolved in 1 mL solvent (acetonitrile). A constant photon flux of 46 µmol · s-1 was applied and corresponding time-dependent absorbance were taken by UV-visible spectrophotometer. For this 10 µL of the reaction mixture were dissolved in 3 mL of

carbon tetrachloride (CCl_4) and corresponding absorbance data were taken. Then molecular bromine was dissolved in CCl4 and absorbance data were taken and compared with the literature. Finally, pure product which is 5-bromo-6-chloro-3-methyl uracil was dissolved in acetonitrile and 10 µL of that solution were dissolved in 3mL of CCl_4 and absorbance data was taken. All these absorbance data were compared which proved that molecular bromine was formed during the reaction in presence light.

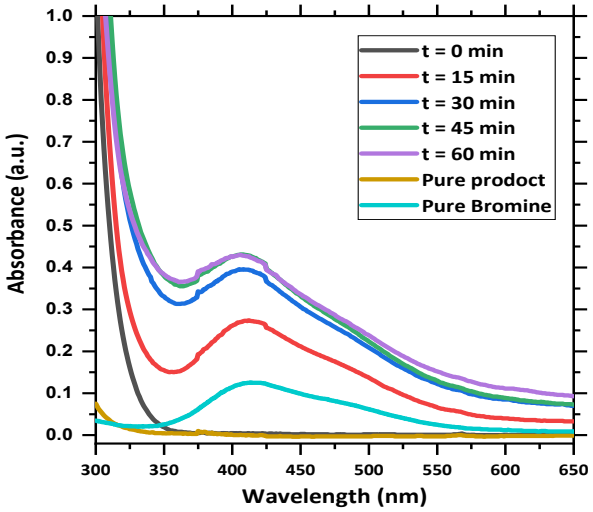


Figure S7. Comparison of the absorbance data of the reaction mixture at different time interval and pure product with respect to molecular bromine.

GC-MS analysis of the reaction for detection of molecular bromine:

0.6 mmols of 6-chloro-3-methyl uracil and 2.2 equivalent of NBS were dissolved in 1 mL solvent (acetonitrile) and a constant photon flux of 46 µmol · s-1 was applied for 15 minutes. Then 50 µL of reaction mixture was taken out and diluted with 1000 µL of carbon tetrachloride (CCl_4). Finally, it was introduced to GC-MS instruments for the detection of molecular bromine by the following methodology.

Instrument details: Shimadzu: GCMS-TQ™ 8040 NX

Column: SH-I-1MS (Crossbond 100% dimethyl polysiloxane), 30 meter, 0.25 mmID, 0.25 um df.

Temperature: 40-120^{o}C

Solvents: Carbon tetrachloride (CCl_4)

Column flow rate: 1.56 mL/min.

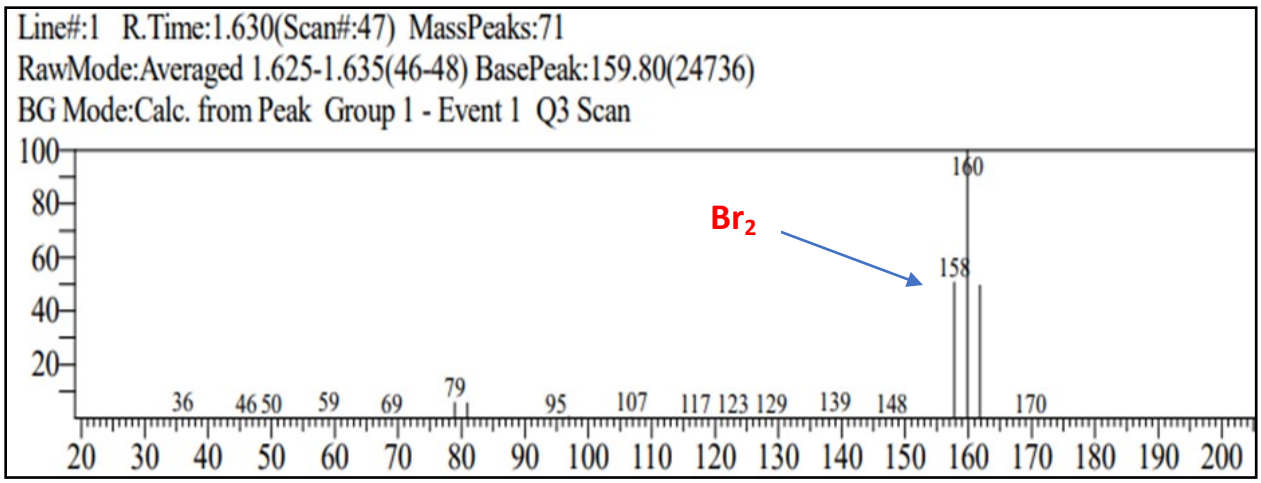


Figure S8: GC-MS spectra of reaction mixture for molecular bromine detection

Reaction optimization with respect to different photon flux for gradual scale-up reaction:

In an oven-dried 1XA reactor module, 960 mg of 6-chloro-3methyluracil (6 mmol) was taken. 2.2 equivalent of NBS were added and dissolved in 10 mL of acetonitrile. A constant photon flux of 21 µmol.s^{-1} were set by adjusting the volt and ampere. A falling film looping space velocity (S) was set to 15 min^{-1}. The cooling fan was started, and TLC performed corresponding time-dependent reaction monitoring. The Same procedure was performed separately by changing only the photon flux to 38 µmol.s^{-1} and 46 µmol.s^{-1} respectively. After each reaction was completed, the NMR as well as separated yield were taken.

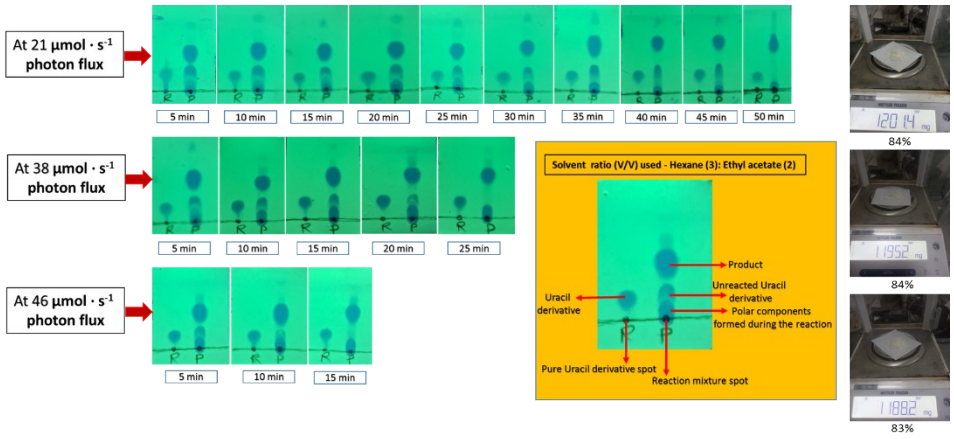


Figure S9: Time-dependent reaction monitoring with respect to different photon flux and corresponding separated yield

NMR yield determination:

After the reaction was completed, the reaction mixture was dried entirely by reduced pressure. This crude reaction mixture was then partially purified by column chromatography, eluting it with ethyl acetate and hexane in the ratio of 2:3. The solvent was run until the product came out from the column, including some impurities. It was made sure that no product was left in the column. For this, some impurity was allowed

to enter into the product. In this process, unreacted uracil derivative, NBS and polar product formed during the reaction were mostly removed. Finally, the mixture was dried, and the residue was dissolved in 10 mL of acetonitrile. From this solution, 200 µL was taken out and evaporated to dryness under reduced pressure. To this residue, a measured amount of 1,3,5-trimethoxybenzene was added and the mixture was completely dissolved in 600 µL DMSO-d6 and ^{1}H NMR were taken at 16 scan rate. The following equation calculated the yield:

$$\frac{n_p}{n_{is}} = \frac{I_p}{N_p} \times \frac{N_{is}}{I_{is}}$$

n_p= no of moles of product
n_{is}= no of moles of internal standard
I_p= peak integration value corresponds to the product
N_p= no of H atom corresponds to I_p
I_{is}= peak integration value corresponds to internal standard=1
N_{is}= no of H atom corresponds to I_{is} = 9 (1,3,5-trimethoxybenzene)

1,3,5-trimethoxy benzene has a characteristic peak at ppm 3.6, corresponding to 9 protons. Our product has a characteristic peak at ppm 3.1, corresponding to 3 protons. These two peaks are used to determine the % yield.

Reactor condition:

Experiment 1: current = 1 A, total radiant power = 4.71 W, irradiance = 60.1 mW.cm^{-2}, total photon flux = 21 µmol.s^{-1}, space velocity = 15 min^{-1}, reaction volume = 10 mL, temperature = 25-28^{o}C.

Experiment 2: current = 2 A, total radiant power = 8.56 W, irradiance = 109 mW.cm^{-2}, total photon flux = 38 µmol.s^{-1}, space velocity = 15 min^{-1}, reaction volume = 10 mL, temperature = 25-28^{o}C.

Experiment 3: current = 2.5 A, total radiant power = 10.32 W, irradiance = 131.4 mW.cm^{-2}, total photon flux = 46 µmol.s^{-1}, space velocity = 15 min^{-1}, reaction volume = 10 mL, temperature = 25-28^{o}C.

Table S4: NMR yield after completion of the reaction at different photon flux

Entry	*Applied photon flux (µmol.s^{-1})*	*Time needed (min)*	*Reactor module*	*Weight of internal standard taken (mg)*	n_{is}	I_{is}	N_{is}	I_p	N_p	*% yield*
1	21	50	1XA	34.6	0.21	1	9	0.17	3	89
2	38	25	1XA	34.9	0.21	1	9	0.17	3	89
3	46	15	1XA	34.6	0.21	1	9	0.16	3	84

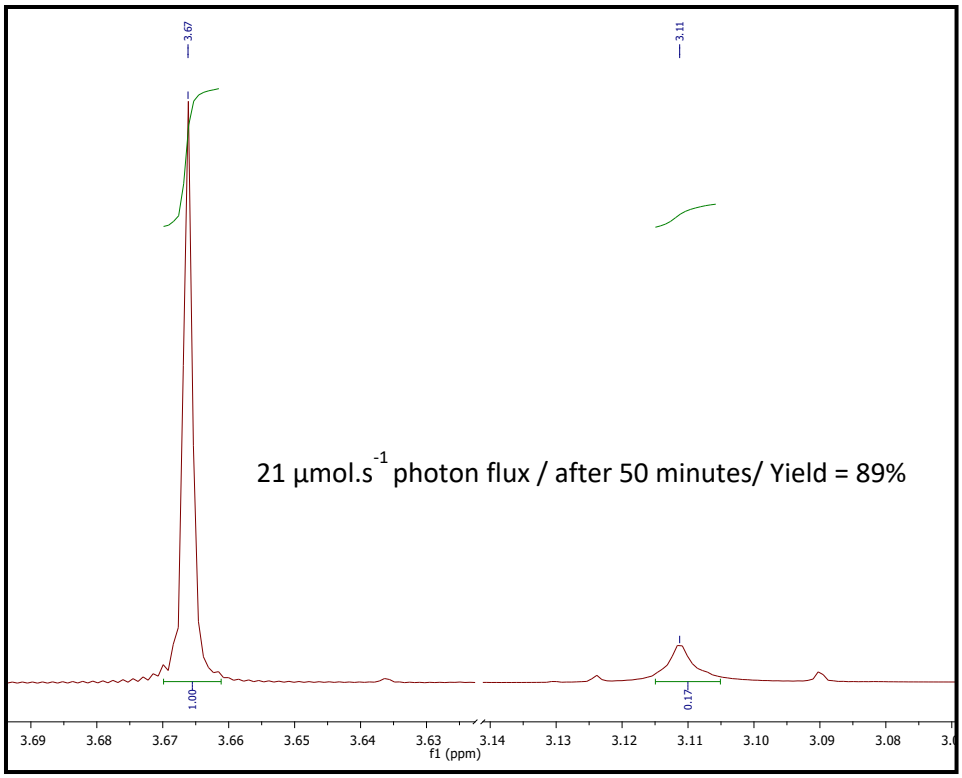


Figure S10: NMR spectra of the reaction mixture after 50 minutes of reaction at 21 µmol.s^{-1} photon flux

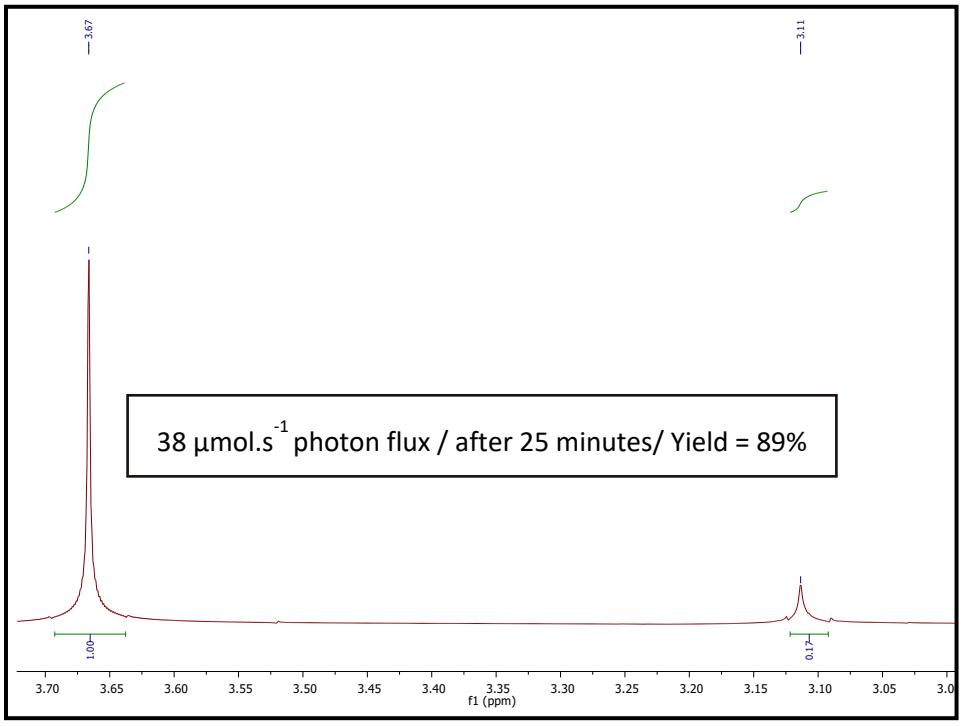


Figure S11: NMR spectra of the reaction mixture after 25 minutes of reaction at 38 µmol.s^{-1} photon flux

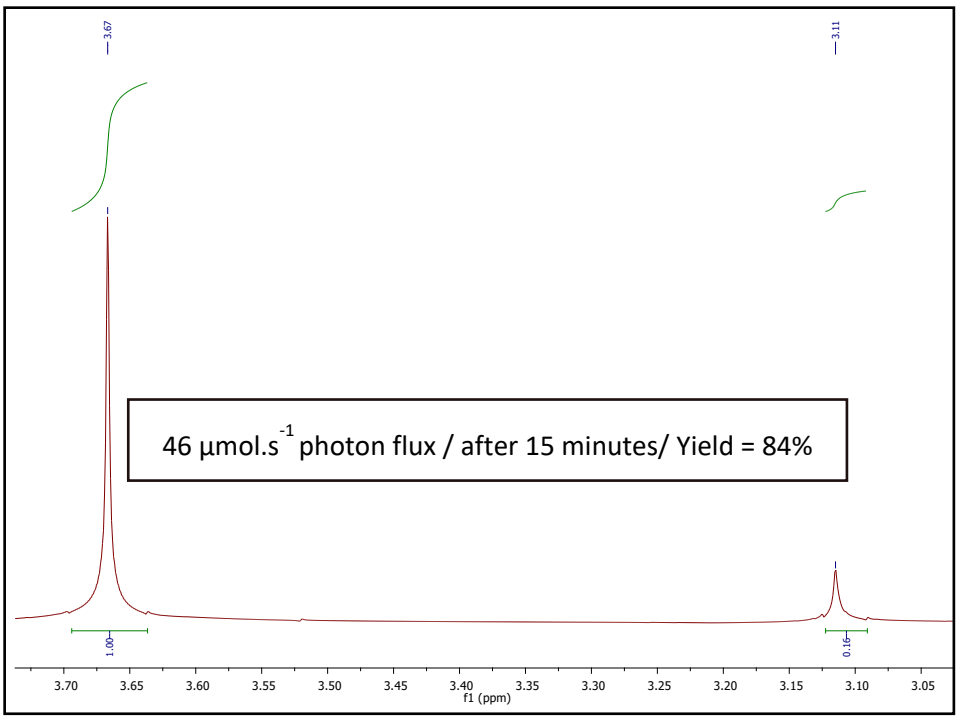


Figure S12: NMR spectra of the reaction mixture after 15 minutes of reaction at 46 µmol.s^{-1} photon flux

Gradual scale-up by using the above-optimized condition:

NMR Yield determination:

Time-dependent product yield was calculated using NMR spectroscopy for the entire scale-up process. For NMR yield calculation, sampling was done in every 3 min time interval. For each sampling, an exact 1 mL of reaction mixture was taken out from the reaction mixture. These reaction mixtures were completely dried by reduced pressure. These crude reaction mixtures were then partially purified by column chromatography by eluting them with ethyl acetate and hexane in the ratio of 2:3. The solvent was run until the entire product came out from the column, including some impurities. It was made sure that no product was left in the column. For this reason, some impurity was allowed to enter into the product. In this process unreacted uracil derivatives, NBS and other impurities formed during the reaction were mostly removed. Finally, the mixtures were dried, and the residue was dissolved in 1 mL of acetonitrile. From this solution, 333 µL were taken out and evaporated to dryness under reduced pressure. To this residue, a known amount (see Table S4) of 1,3,5-trimethoxybenzene was added and the mixture were completely dissolved in 600 µL DMSO-d_6 and ^{1}H NMR were taken at 16 scan rate. The following equation was used to calculate the NMR yield:

$$\frac{n_p}{n_{is}} = \frac{I_p}{N_p} \times \frac{N_{is}}{I_{is}}$$

n_p= no of mmoles of product
n_{is}= no of mmoles of internal standard
I_p= peak integration value corresponds to the product

N_p= no of H atom corresponds to I_p=3
I_{is}= peak integration value corresponds to internal standard=1
N_{is}= no of H atom corresponds to I_{is} =9 (1,3,5-trimethoxybenzene)

1,3,5-trimethoxy benzene has a characteristic peak at ppm 3.6, corresponding to 9 protons. Our product has a characteristic peak at ppm 3.1, corresponding to 3 protons. These two peaks are used to determine the % yield.

0.96 g scale reaction:

In an oven-dried 1XA reactor module, 6 mmol (0.96 g) of 6-chloro-3-methyluracil and 2.2 equivalent of NBS were taken, and 10 mL of acetonitrile were added. The peristaltic pump was set with a space velocity of 15 min^{-1}. A constant photon flux of 46 µmol · s^{-1} was applied for 15 mins. NMR yield were taken in every 3 min time interval.

Figure S13: Red colored reaction mixture after the completion of reaction in 1XA reactor module

Reactor condition: current = 2.5 A, total radiant power = 10.32 W, irradiance = 131.4 $mW.cm^{-2}$, total photon flux = 46 µmol.s^{-1}, space velocity = 15 min^{-1}, reaction volume = 10 mL, temperature = 25-28^{o}C.

Table S5: Time studies of the 0.96 g scale bromination reaction of 6-chloro-3-methyl-uracil

Entry	*Time (min)*	*Weight of internal standard taken (mg)*	n_{is}	I_{is}	N_{is}	I_p	N_p	*% yield*
1	0	-	-	-	-	-	-	0
2	3	34.7	0.21	1	9	0.04	3	13
3	6	34.6	0.21	1	9	0.07	3	22
4	9	34.6	0.21	1	9	0.23	3	72
5	12	34.7	0.21	1	9	0.30	3	94
6	15	34.6	0.21	1	9	0.29	3	92

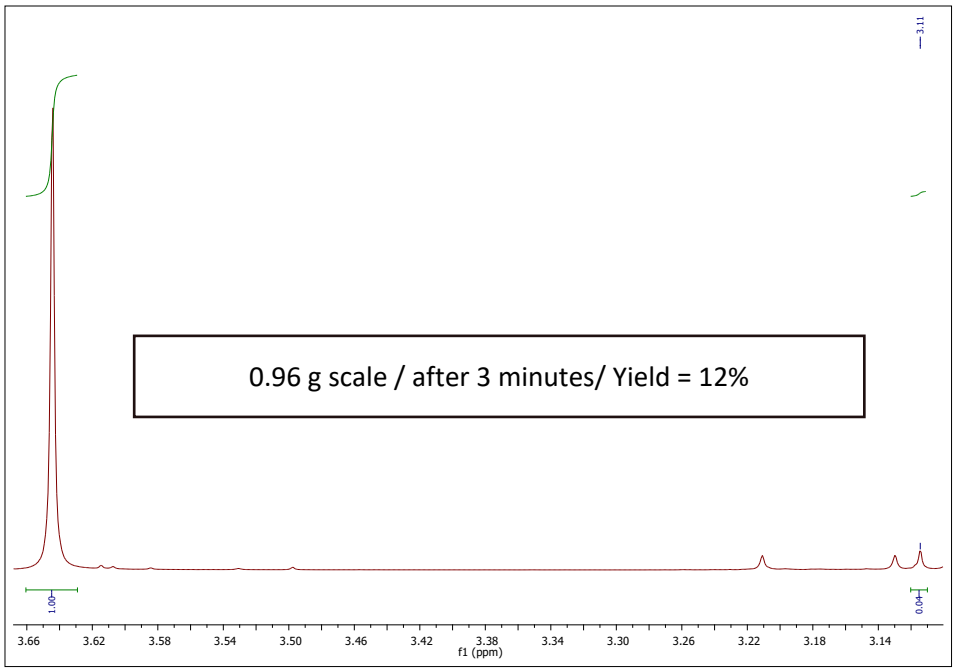


Figure S14: NMR spectra of the reaction mixture obtained after 3 min of reaction

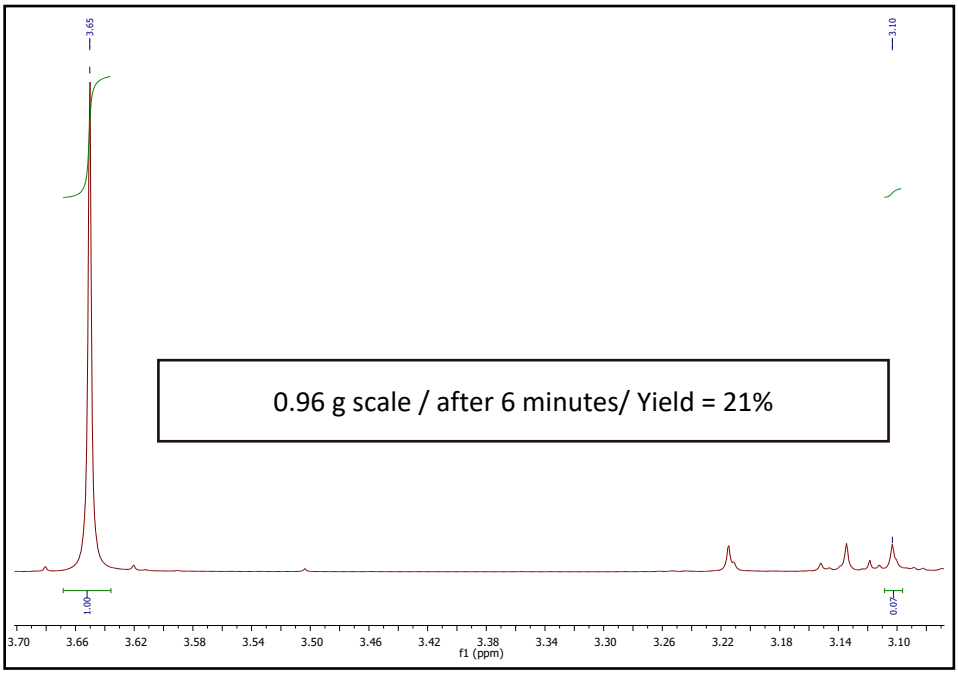


Figure S15: NMR spectra of the reaction mixture obtained after 6 min of reaction

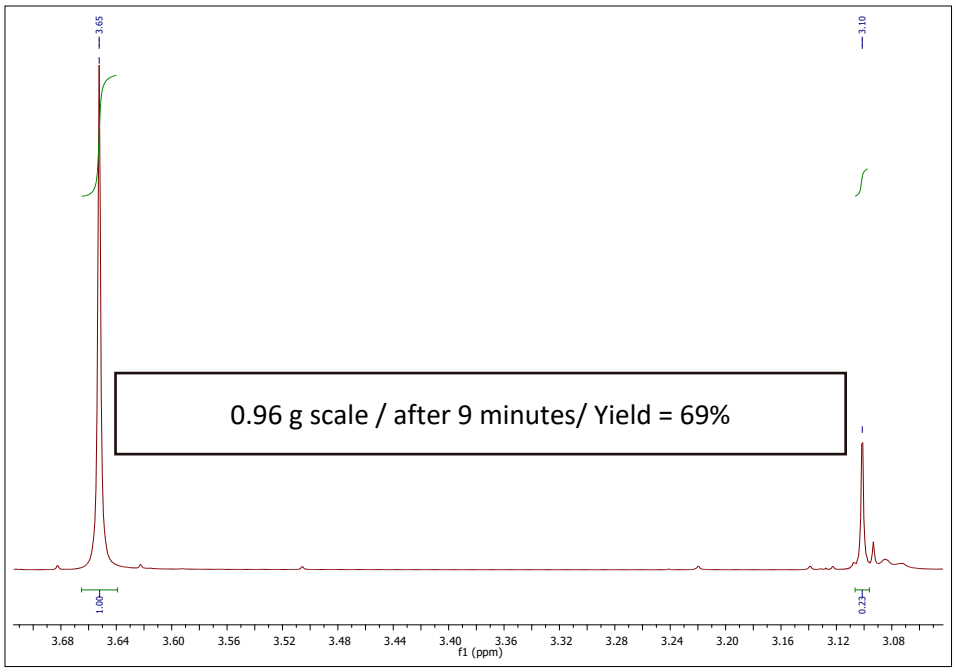


Figure S16: NMR spectra of the reaction mixture obtained after 9 min of reaction

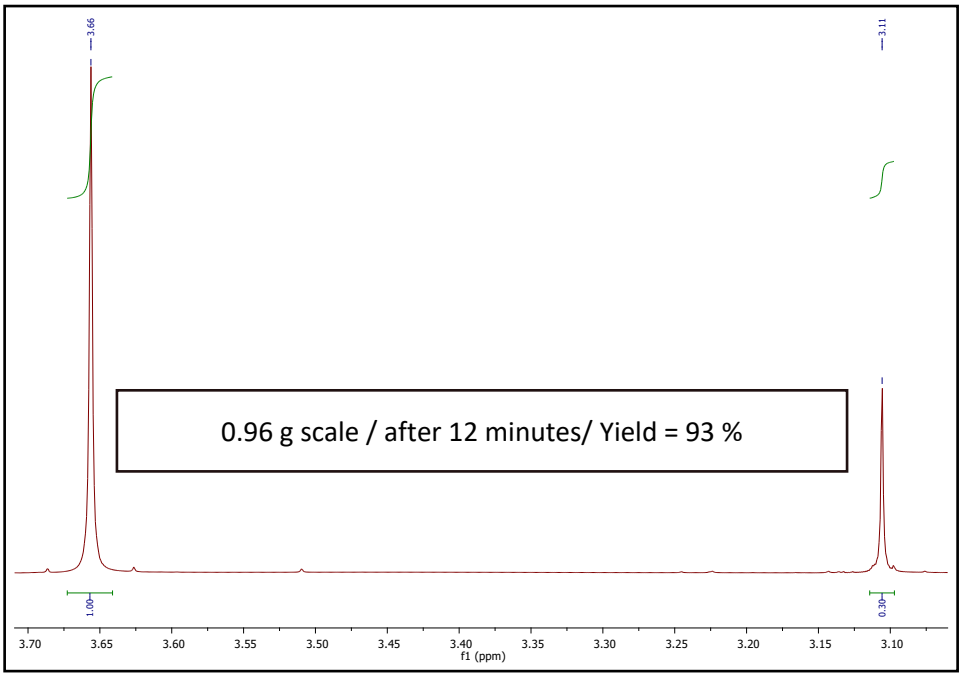


Figure S17: NMR spectra of the reaction mixture obtained after 12 min of reaction

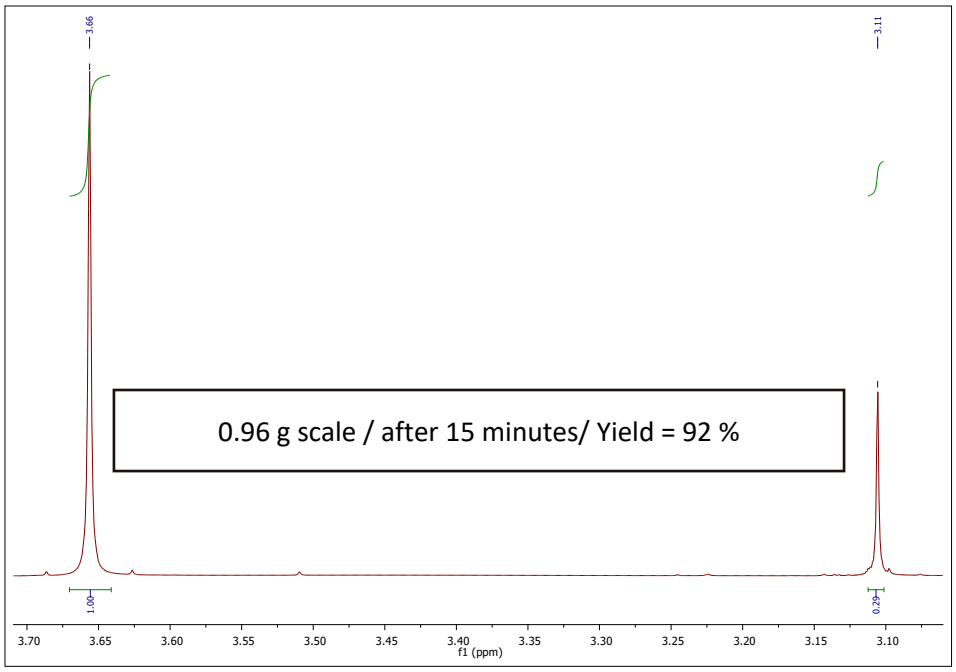


Figure S18: ^{1}H NMR spectra of the reaction mixture obtained after 15 min of reaction

4.8 g scale reaction:

In a dry 2XA reactor module, 30 mmol (4.8 g) of 6-chloro-3-methyluracil and 2.2 equivalent of NBS were taken and 50 mL of acetonitrile was added. The peristaltic pump was set with a space velocity of 15 min^{-1}. A constant photon flux of 102 µmol · s^{-1} was applied for 15 mins. NMR yield were taken in every 3 min time interval.

Reactor condition: current = 5 A, total radiant power = 22.81 W, irradiance = 127.4 $mW.cm^{-2}$, total photon flux = 102 $\mu mol.s^{-1}$, space velocity = 15 min^{-1}, reaction volume = 50 mL, temperature = 25-28°C.

Table S6: Time studies of the 4.8 g scale bromination reaction of 6-chloro-3-methyluracil

Entry	*Time (min)*	*Weight of internal standard taken (mg)*	n_{is}	I_{is}	N_{is}	I_p	N_p	*% yield*
1	0	-	-	-	-	-	-	0
2	3	34.6	0.21	1	9	0.04	3	13
3	6	34.6	0.21	1	9	0.07	3	22
4	9	34.6	0.21	1	9	0.23	3	69
5	12	34.4	0.20	1	9	0.31	3	93
6	15	34.6	0.21	1	9	0.29	3	92

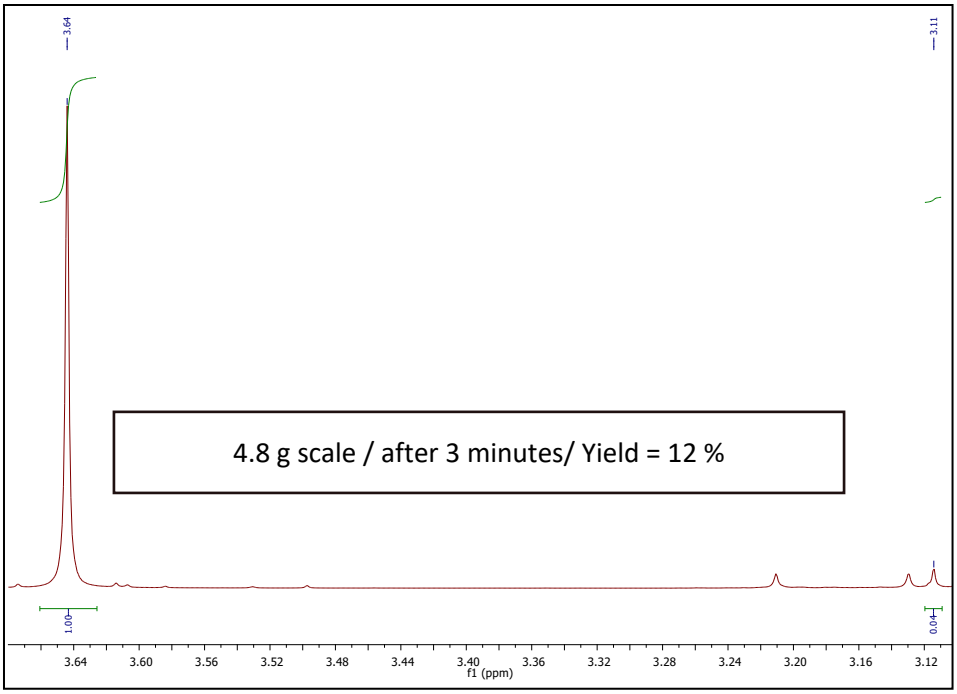


Figure S19: NMR spectra of the reaction mixture obtained after 3 min for 4.8 g scale reaction

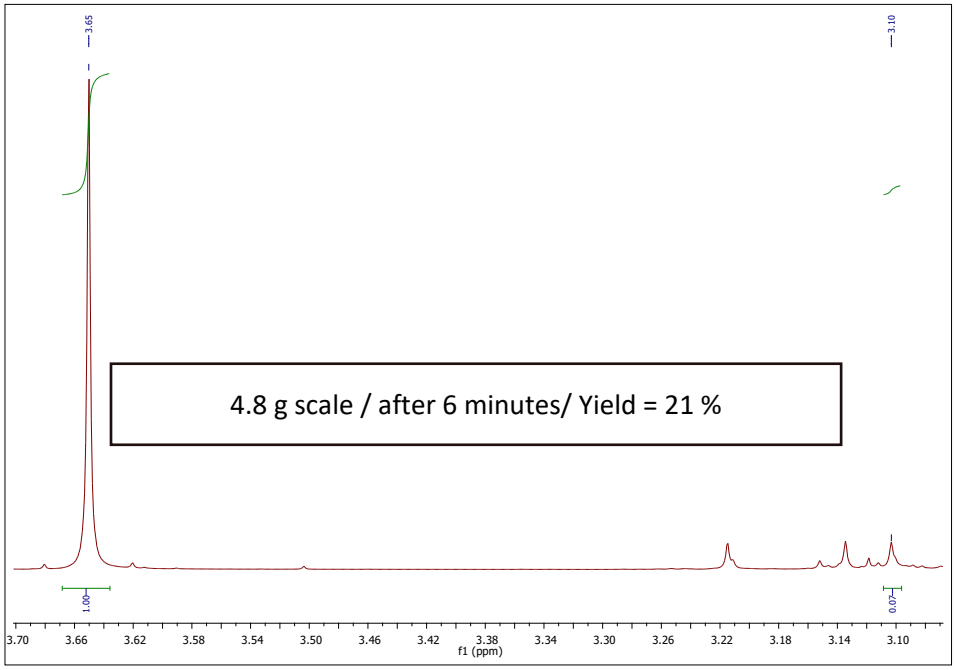


Figure S20: NMR spectra of the reaction mixture obtained after 6 min for 4.8 g scale reaction

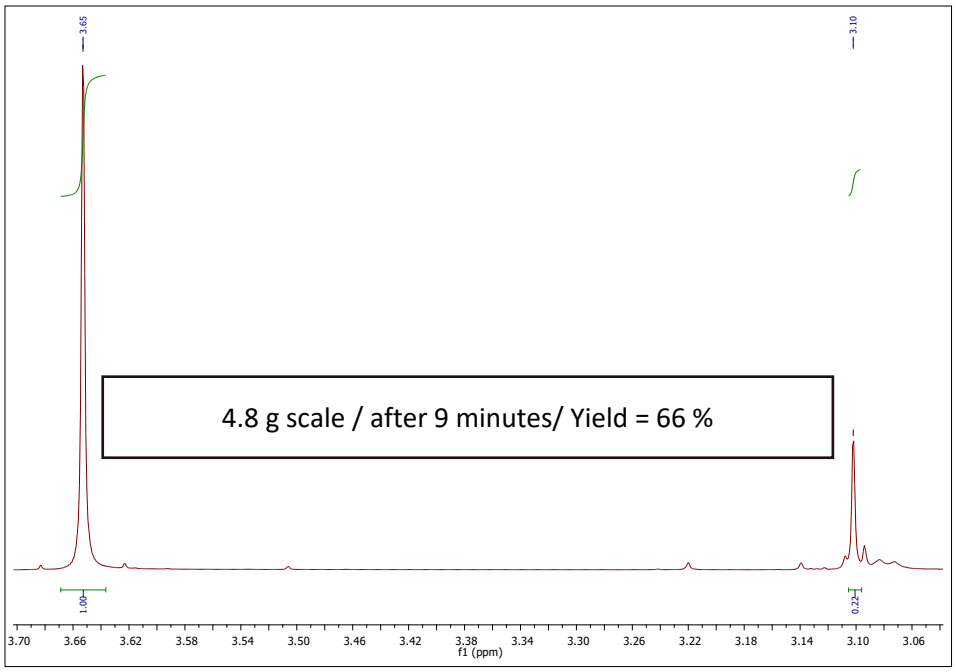


Figure S21: NMR spectra of the reaction mixture obtained after 9 min for 4.8 g scale reaction

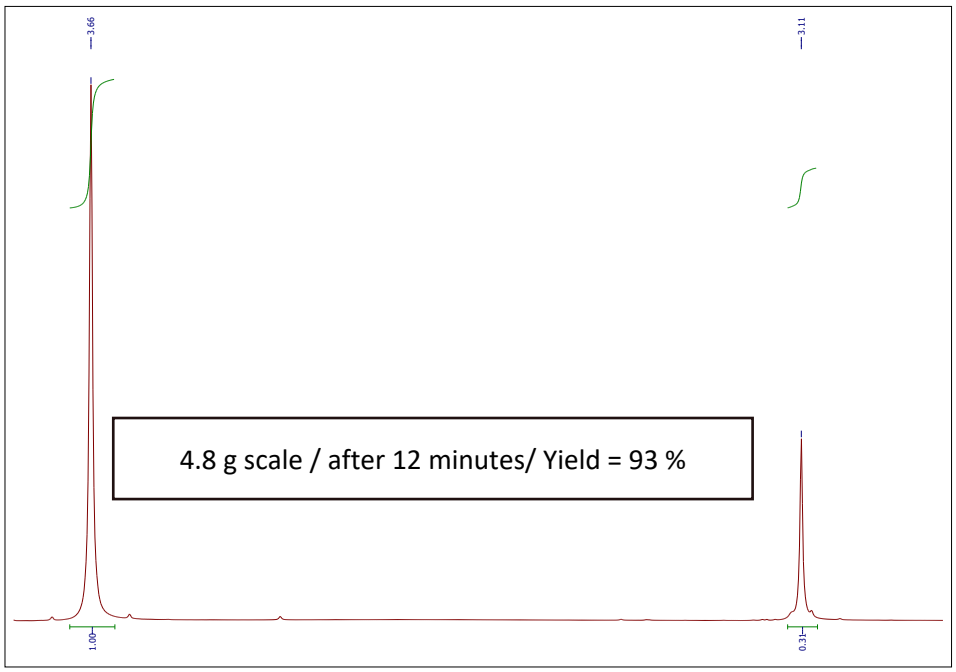


Figure S22: NMR spectra of the reaction mixture obtained after 12 min for 4.8 g scale reaction

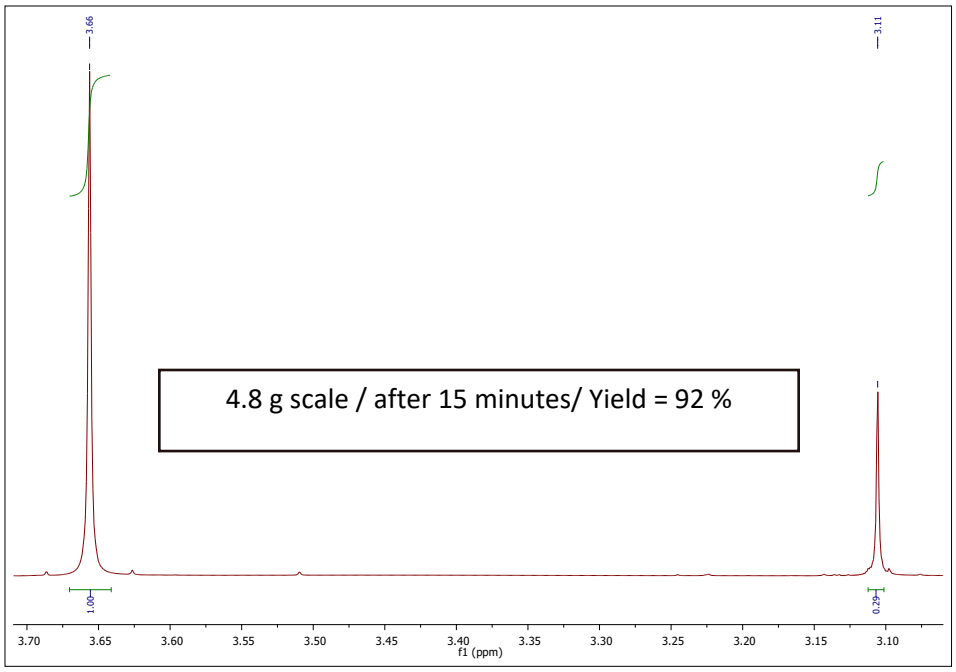


Figure S23: ^{1}H NMR spectra of the reaction mixture obtained after 15 min for 4.8 g scale reaction

9.6 g scale reaction:

In an oven-dried 4XA reactor module, 60 mmol (9.6 g) of 6-chloro-3-methyluracil and 2.2 equivalent of NBS were taken and 100 mL of acetonitrile were added. The peristaltic pump was set with a space velocity of 15 min^{-1}. A constant photon flux of 185 µmol · s^{-1} was applied for 15 mins. NMR yield were taken in every 3 min time interval.

Reactor condition: current = 10 A, total radiant power = 41.27 W, irradiance = 131.4 $mW.cm^{-2}$, total photon flux = 185 $\mu mol.s^{-1}$, space velocity = 15 min^{-1}, reaction volume = 100 mL, temperature = 25-28°C.

Table S7: Time studies of the 9.6 g scale bromination reaction of 6-chloro-3-methyluracil

Entry	*Time (min)*	*Weight of internal standard taken (mg)*	n_{is}	I_{is}	N_{is}	I_p	N_p	*% yield*
1	0	-	-	-	-	-	-	0
2	3	34.7	0.21	1	9	0.04	3	13
3	6	34.6	0.21	1	9	0.11	3	35
4	9	34.7	0.21	1	9	0.23	3	72
5	12	34.6	0.21	1	9	0.30	3	94
6	15	34.6	0.21	1	9	0.29	3	92

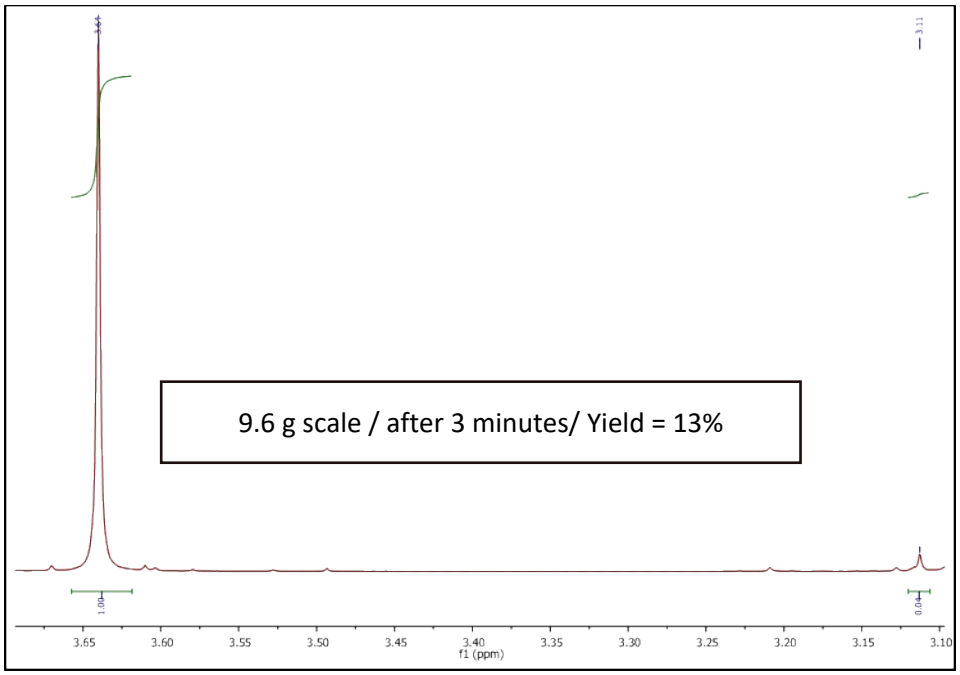


Figure S24: NMR spectra of the reaction mixture obtained after 3 min for 9.6 g scale reaction

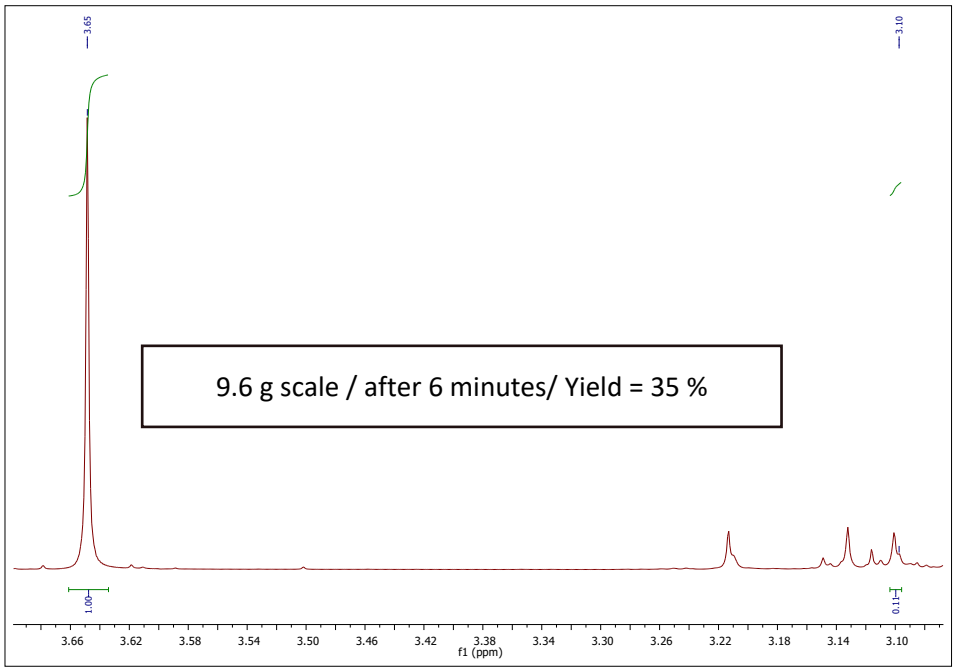


Figure S25: NMR spectra of the reaction mixture obtained after 6 min for 9.6 g scale reaction

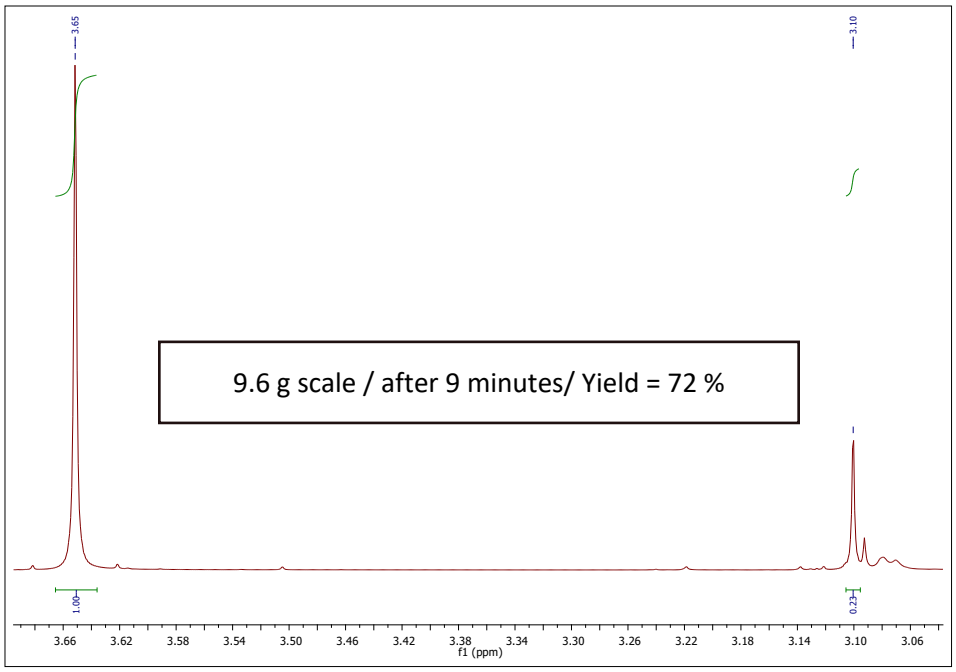


Figure S26: NMR spectra of the reaction mixture obtained after 9 min for a 9.6 g scale reaction

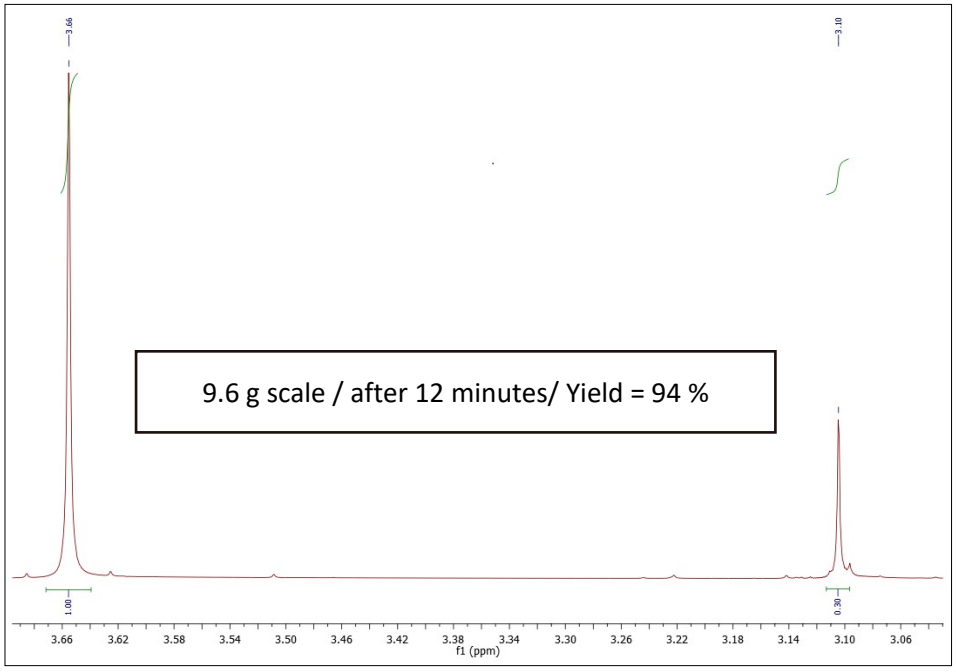


Figure S27: NMR spectra of the reaction mixture obtained after 12 min for 9.6 g scale reaction

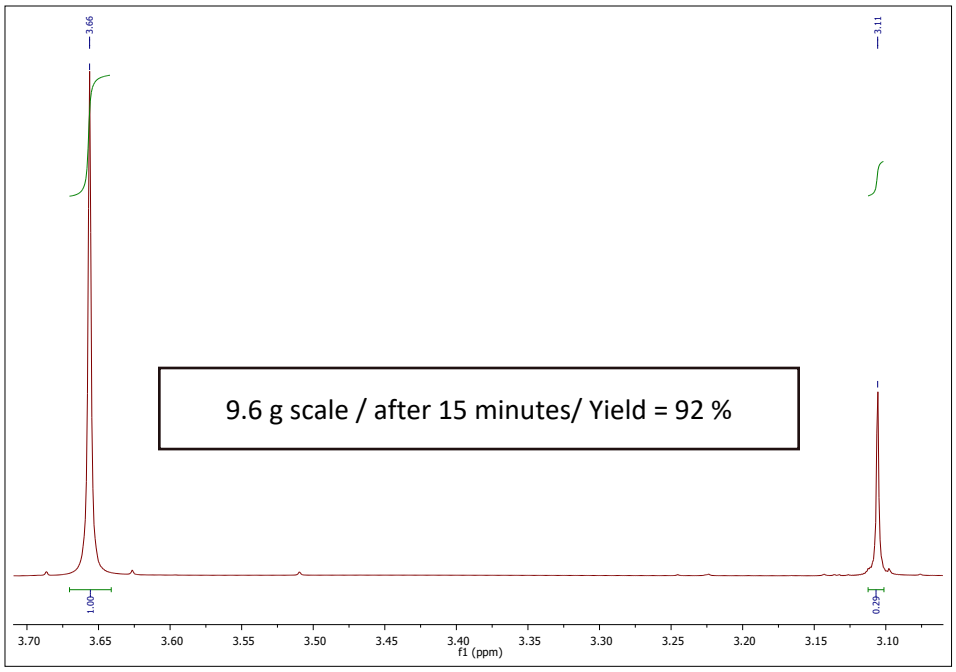


Figure S28: ^{1}H NMR spectra of the reaction mixture obtained after 15 min for 9.6 g scale reaction

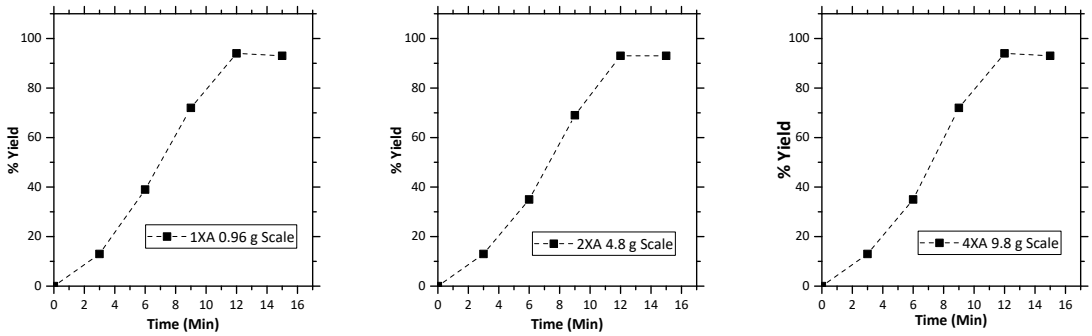


Figure S29: Time dependent product yield at different scale.

Performance indicator:

Photochemistry itself is a diversified field and thus each sub area has different performance indicators. So the choice of performance indicators is very important for the comparison between photochemical systems. We have used three most important performance indicators along with other standard data reporting protocols for the comparability, reproducibility of experimental result across different photochemical systems. These performance indicators are:

(1) Reaction rate (r) $= \frac{\Delta n}{\Delta t}$

Where, $\Delta n =$ no of moles of educt or product and $\Delta t =$ reaction time

(2) Space time yield (STY) $$= \frac{\Delta n}{\Delta t \,.\, V}$$

Where, $\Delta n =$ no of moles of product, $\Delta t =$ reaction time and $V =$ reaction volume.

(3) Photonic efficiency $$(\xi_{ext}) = \frac{r}{q_{emitted}}$$

Where, r = reaction rate and $q_{emitted}$ = applied photon flux

Table S8: Time dependent calculation of STY for 0.96 g scale

Entry	Δt (s)	Δn (mol)	V (L)	STY (µmol.L^{-1}.s^{-1})
1	0	0	0	0
2	180	0.78	0.01	0.43
3	360	2.34	0.01	0.65
4	540	4.32	0.01	0.8
5	720	5.64	0.01	0.78
6	900	5.58	0.01	0.61

Table S9: Time dependent calculation of STY for 4.8 g scale

Entry	Δt (s)	Δn (mol)	V (L)	STY (µmol.L^{-1}.s^{-1})
1	0	0	0	0
2	180	3.9	0.05	0.43
3	360	10.5	0.05	0.58
4	540	20.7	0.05	0.76
5	720	27.9	0.05	0.78
6	900	27.9	0.05	0.61

Table S10: Time dependent calculation of STY for 9.6 g scale

Entry	Δt (s)	Δn (mol)	V (L)	STY (µmol.L^{-1}.s^{-1})
1	0	0	0	0
2	180	7.8	0.1	0.43
3	360	21	0.1	0.58
4	540	43.2	0.1	0.8
5	720	56.4	0.1	0.78
6	900	55.8	0.1	0.61

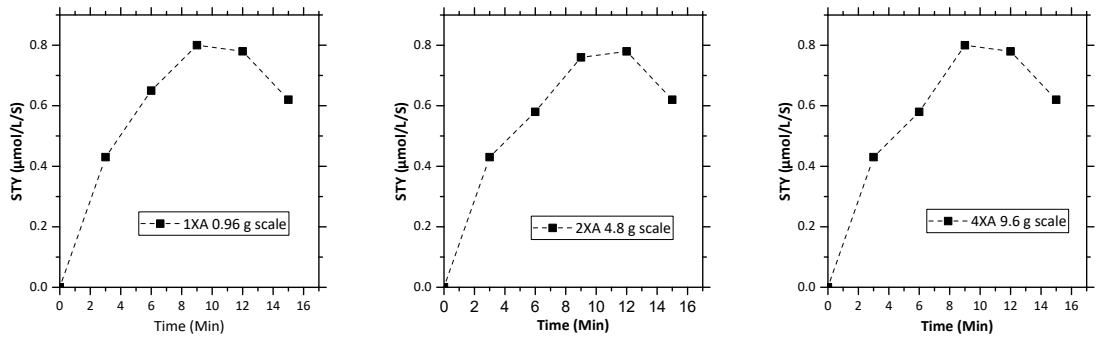


Figure S30: Time dependent STY at different scale

Table S11: Variation of reaction rate with emitted photon flux at different scale

Entry	Reaction scale (g)	$q_{emitted}$ (µmol.s^{-1})	Δt (s)	Δn (mmol)	*r (*µmol.s^{-1}*)*
1	0.96	46	0-900	5.64	6.2
2	4.8	102	0-900	27.9	31
3	9.6	185	0-900	56.4	62

Table S12: variation of reaction rate with reaction scale

Entry	*r (*µmol.s^{-1}*)*	Reaction scale (g)
1	6.2	0.96
2	31	4.8
3	62	9.6

Table S13: Photonic efficiency at different scale of reaction

Entry	Reaction scale (g)	*r (*µmol.s^{-1}*)*	$q_{emitted}$ (µmol.s^{-1})	ξ_{ext}
1	0.96	6.2	46	0.13
2	4.8	31	102	0.30
3	9.6	62	185	0.34

^{1}H-NMR and ^{13}C-NMR spectra

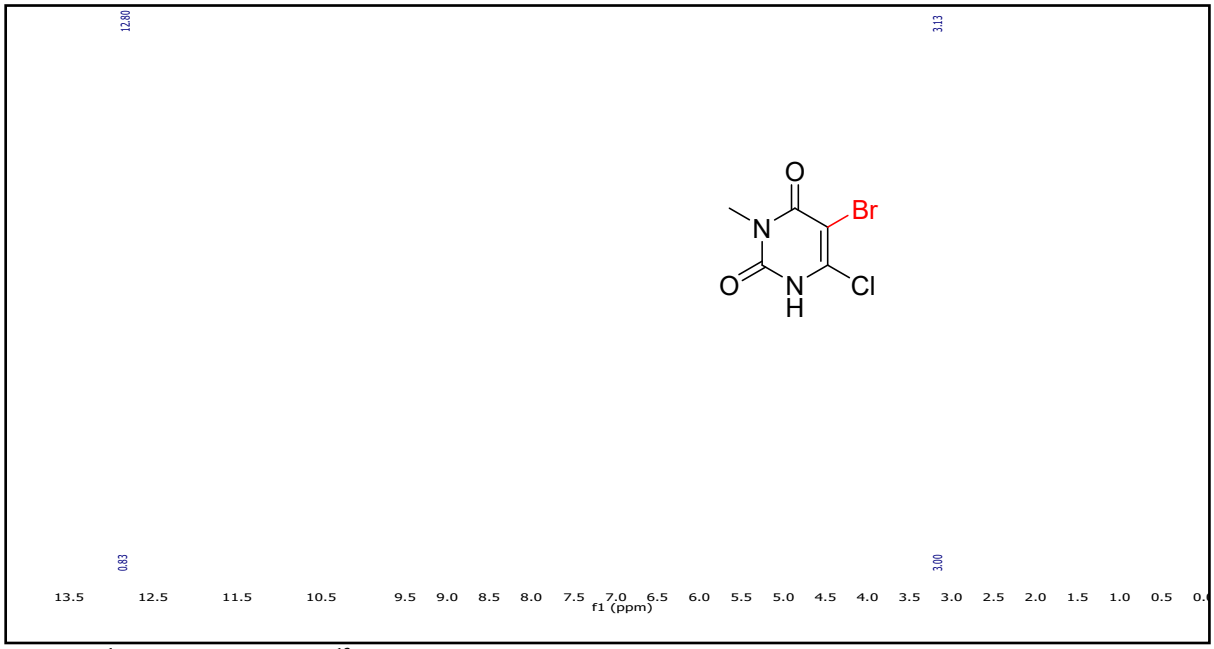
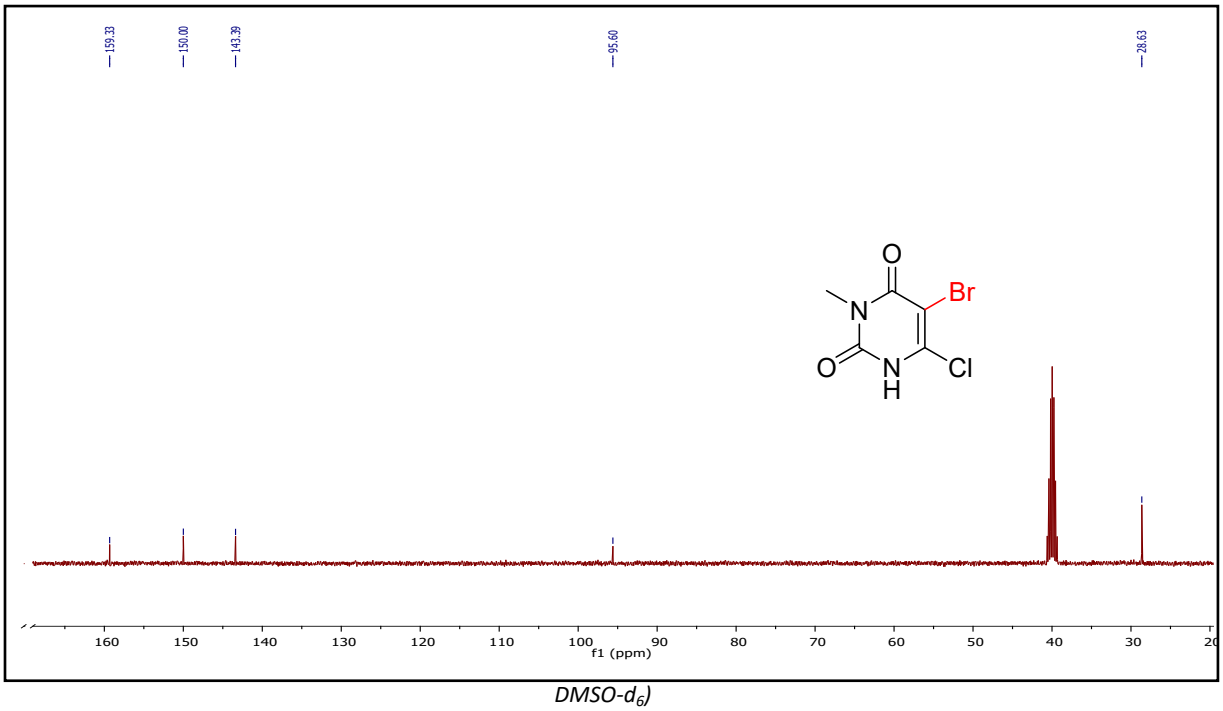


*Figure S31: ^{1}H-NMR (400MHz) and ^{13}C-NMR (101MHz) spectra of 5-bromo-6-chloro-3-methylpyrimidine-2,4(1H,3H)-dione (**1a**,*



DMSO-d_6)

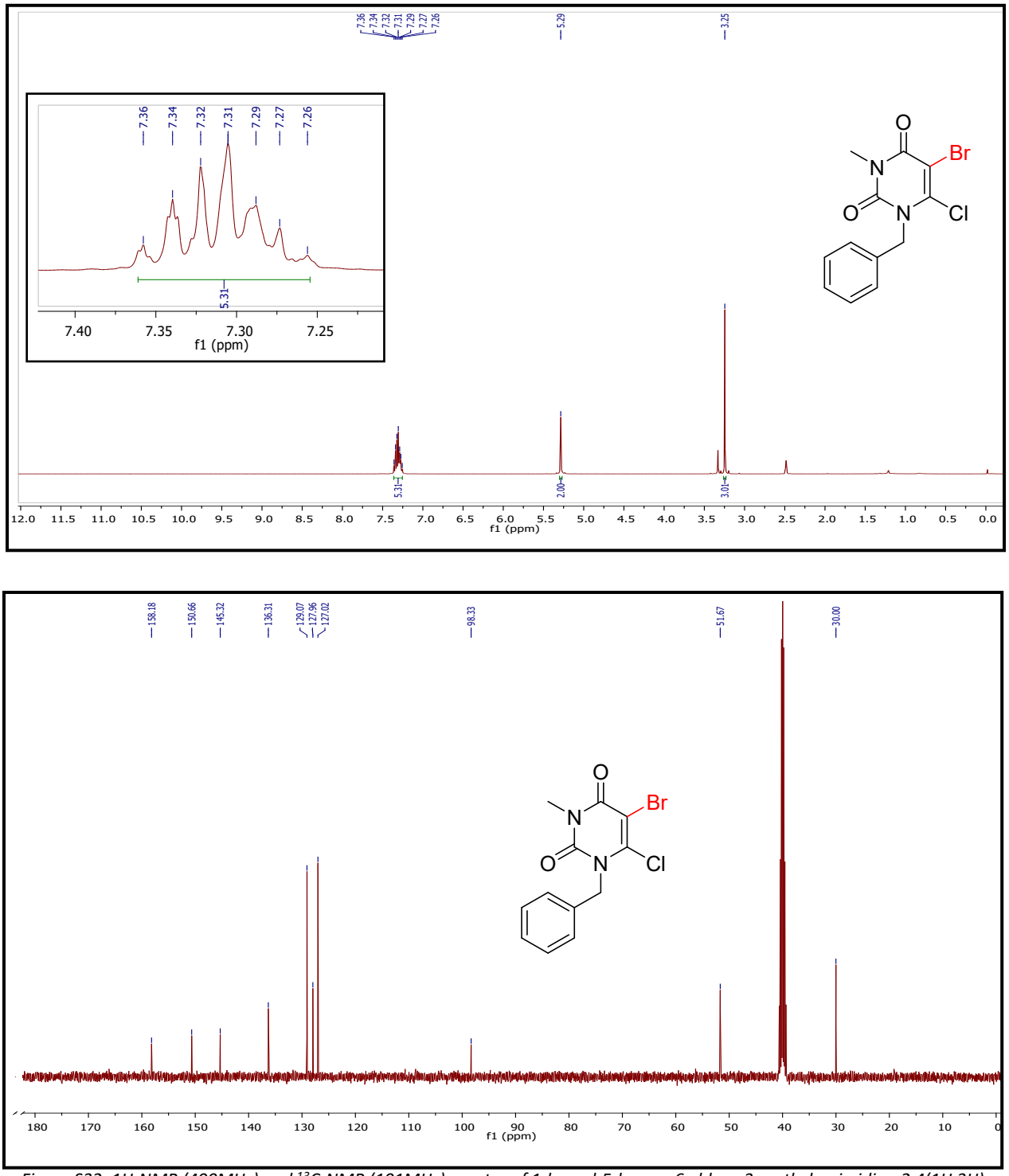
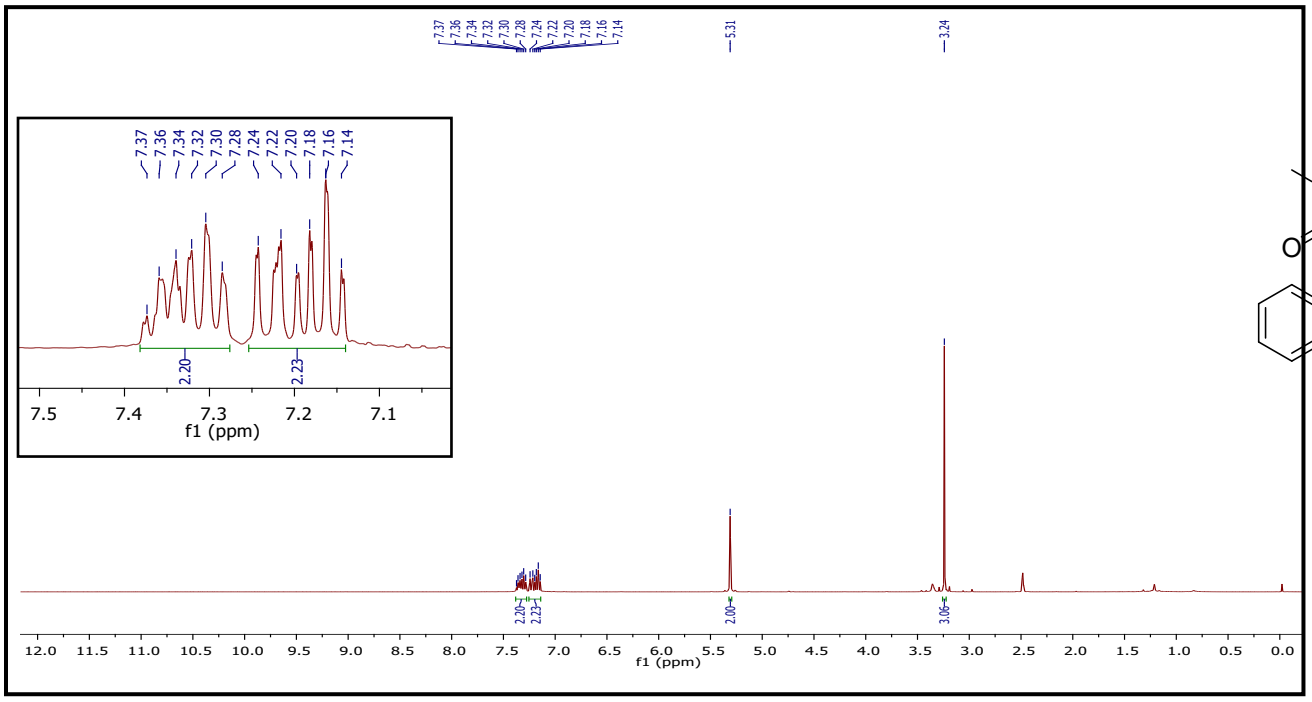


*Figure S32: 1H-NMR (400MHz) and ^{13}C-NMR (101MHz) spectra of 1-benzyl-5-bromo-6-chloro-3-methylpyrimidine-2,4(1H,3H)-dione (**1b**, DMSO-d_6).*



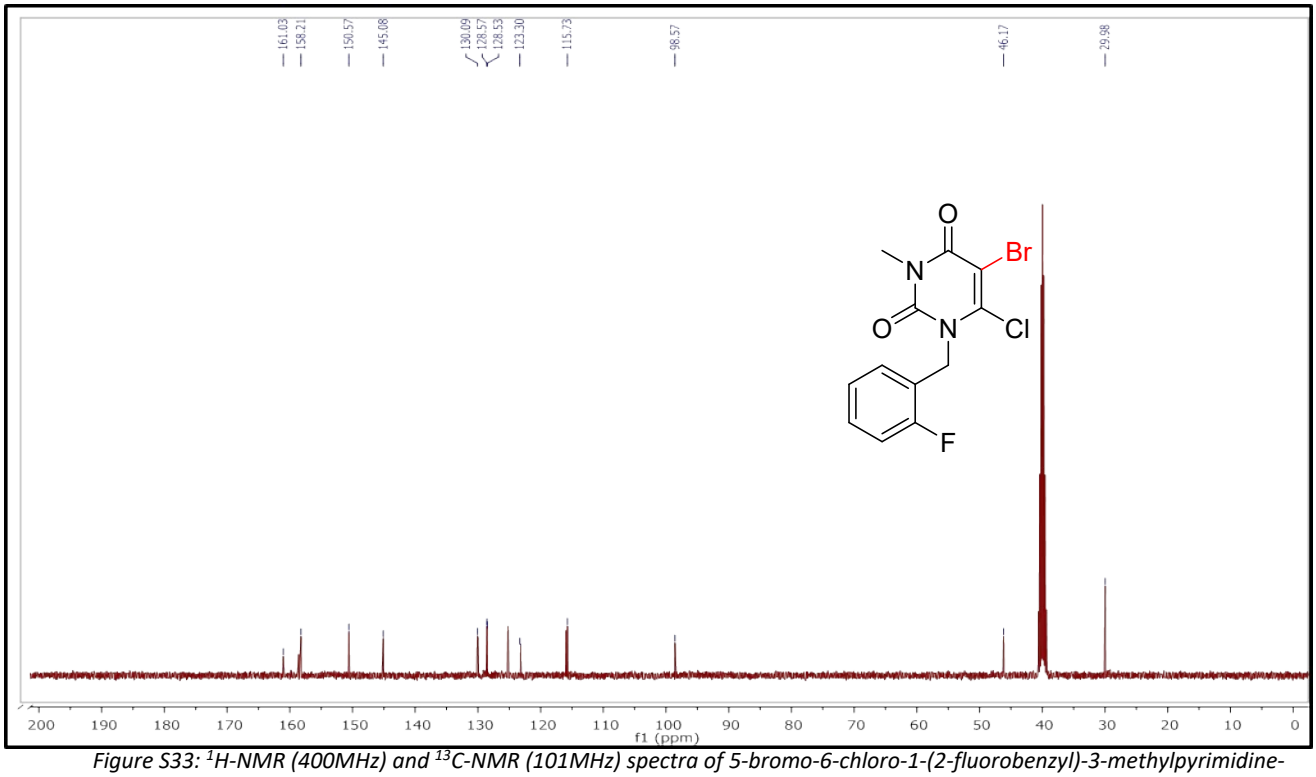
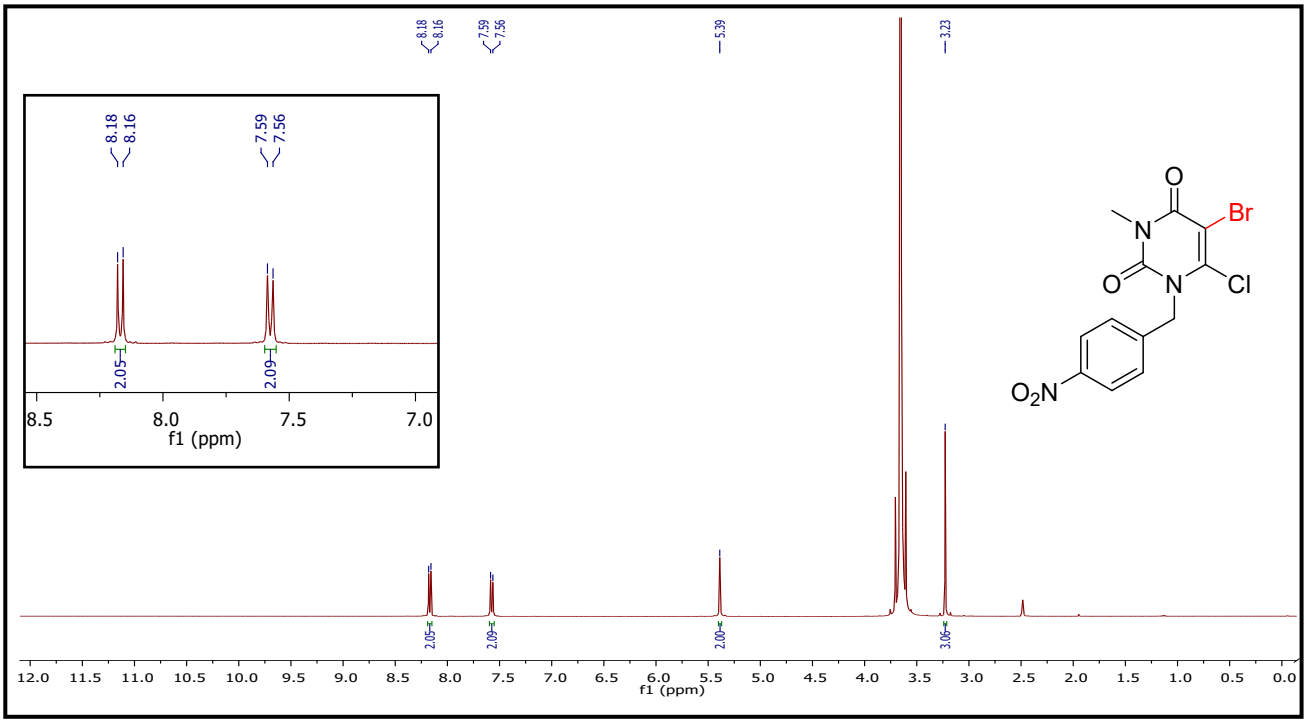


*Figure S33: ^{1}H-NMR (400MHz) and ^{13}C-NMR (101MHz) spectra of 5-bromo-6-chloro-1-(2-fluorobenzyl)-3-methylpyrimidine-2,4(1H,3H)-dione (**1c**, DMSO-d_6)*



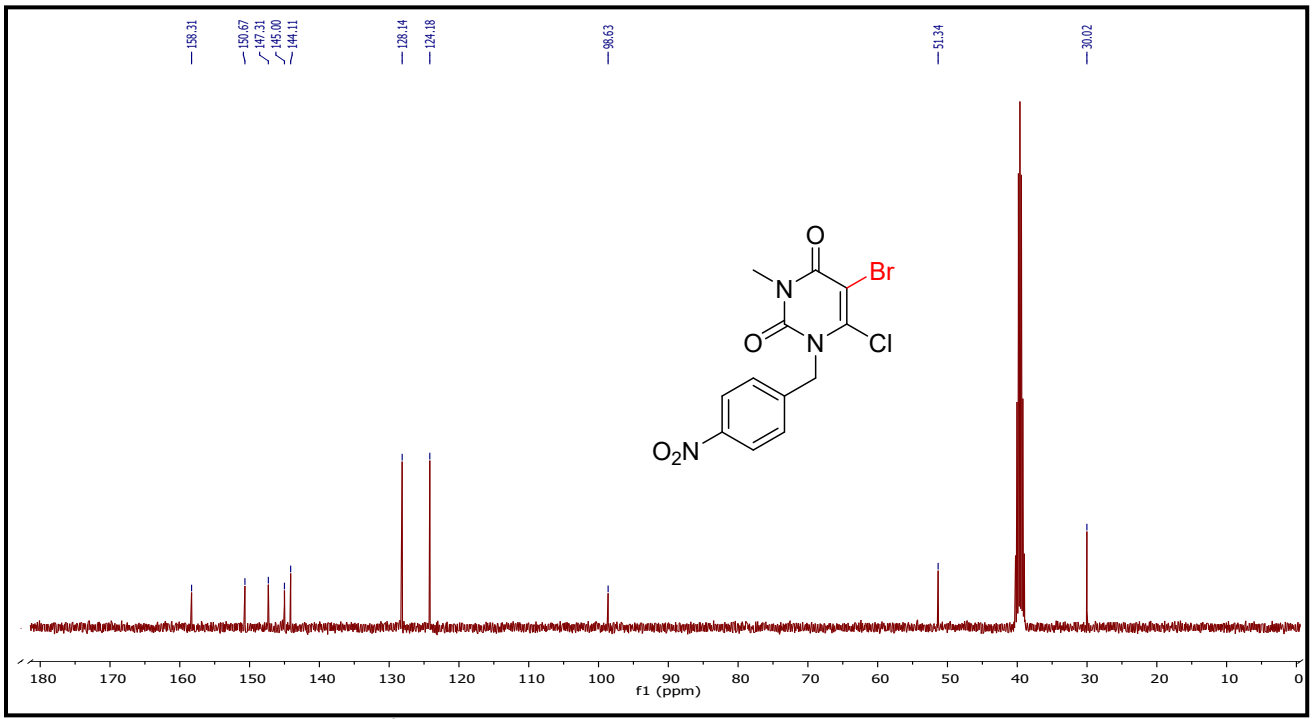


*Figure S34:[1]H-NMR (400MHz) and [13]C-NMR (101MHz) spectra of 5-bromo-6-chloro-3-methyl-1-(4-nitrobenzyl)pyrimidine-2,4(1H,3H)-dione (**1d**, DMSO-d_6).*

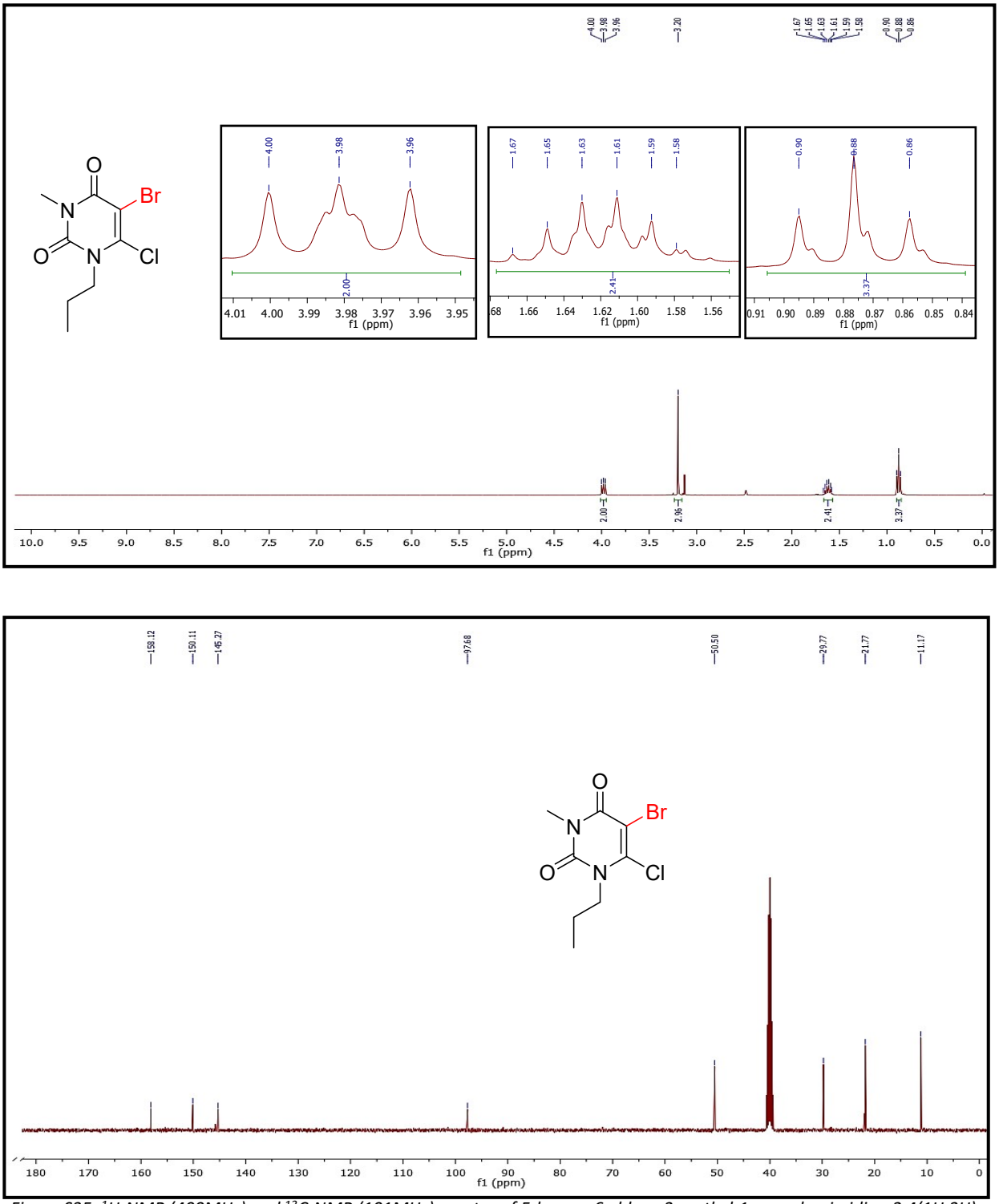
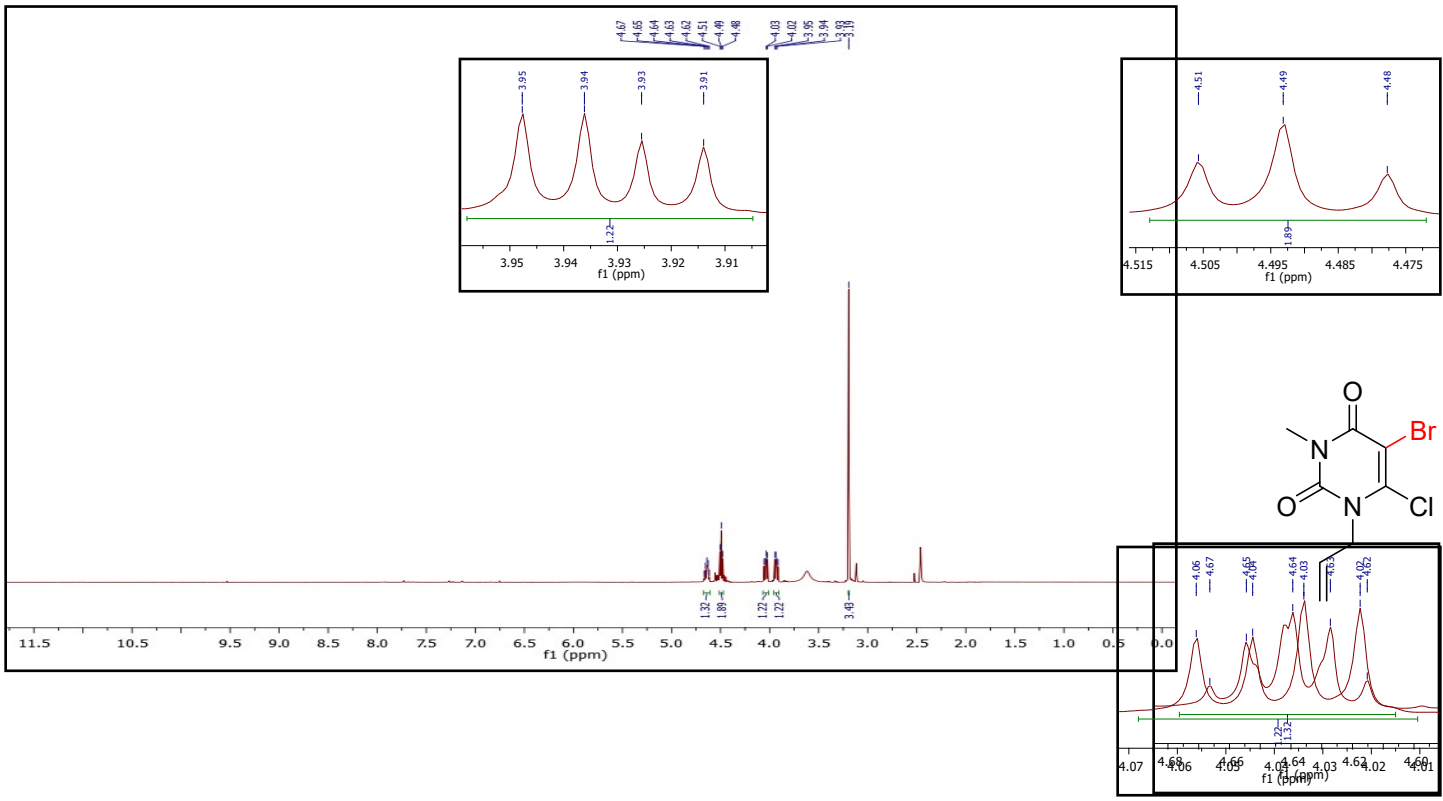


*Figure S35: ^{1}H-NMR (400MHz) and ^{13}C-NMR (101MHz) spectra of 5-bromo-6-chloro-3-methyl-1-propylpyrimidine-2,4(1H,3H)-dione (**1e**, DMSO-d_6).*


f1 (ppm)
Br
Cl
N
O

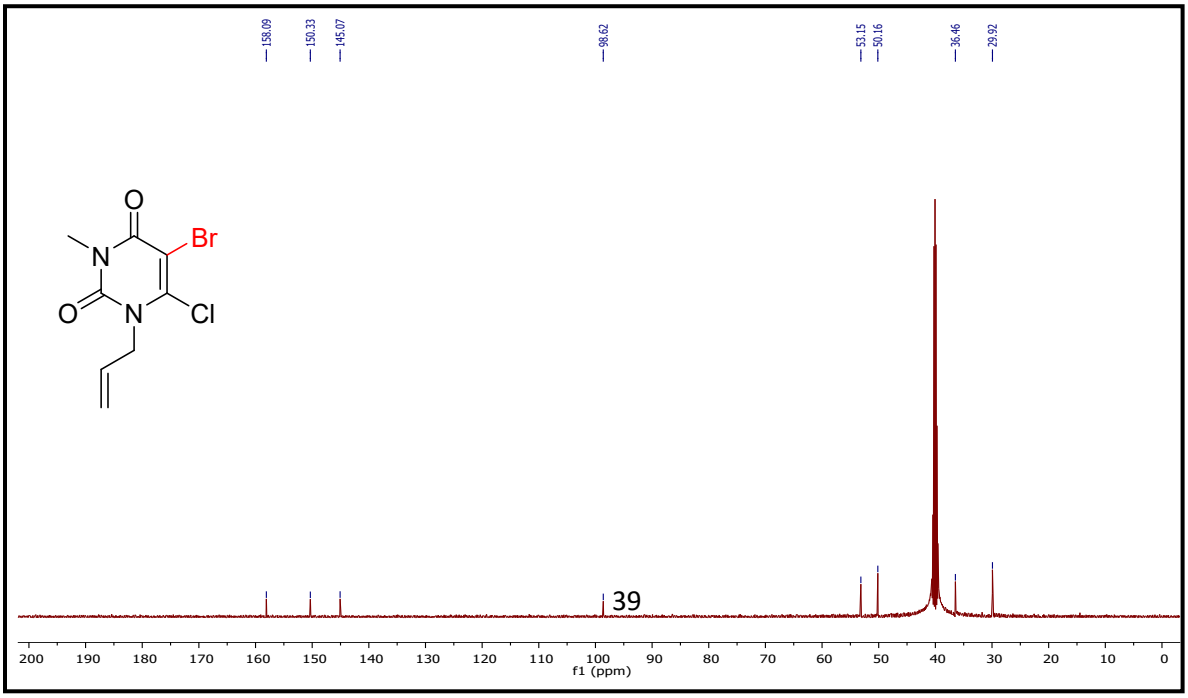
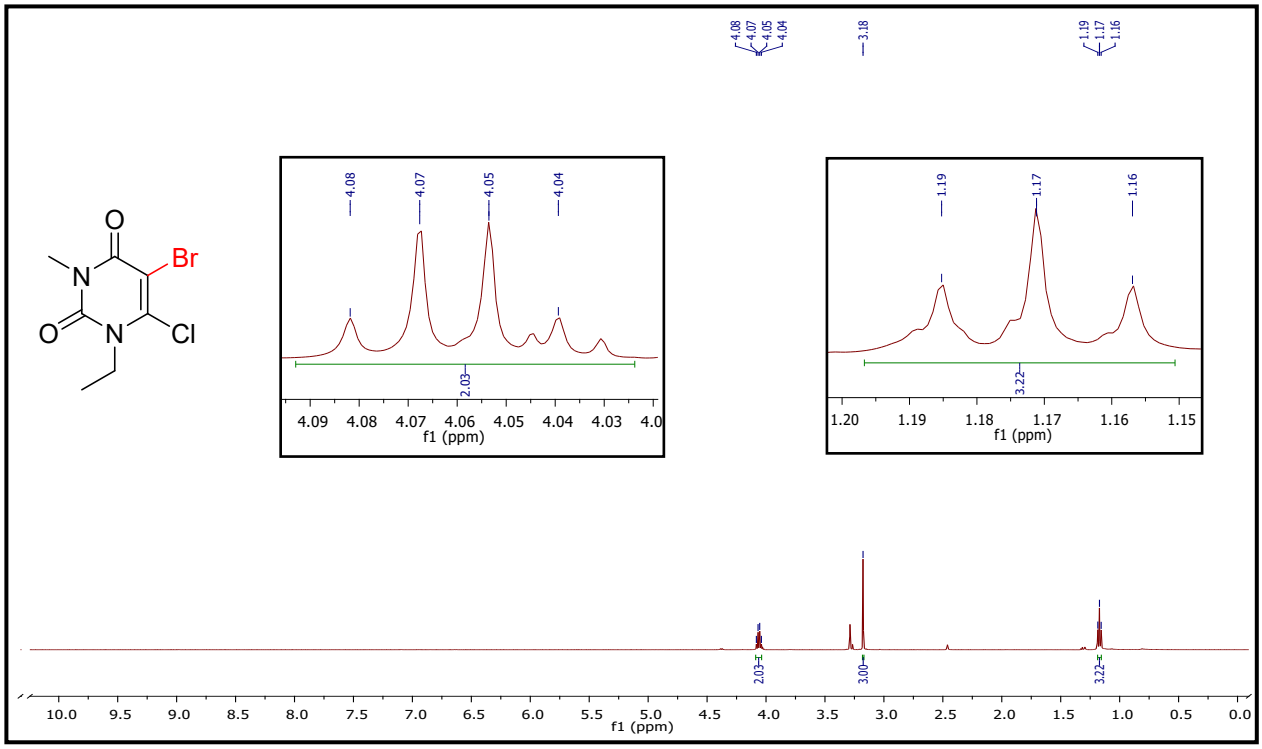

158.09
150.33
145.07
98.62
53.15
50.16
36.46
29.92
f1 (ppm)
Br
Cl
N
O

*Figure S36:[1]H-NMR (500MHz) and [13]C-NMR (126MHz) spectra of 1-allyl-5-bromo-6-chloro-3-methylpyrimidine-2,4(1H,3H)-dione (**1f**, DMSO-d_6)*



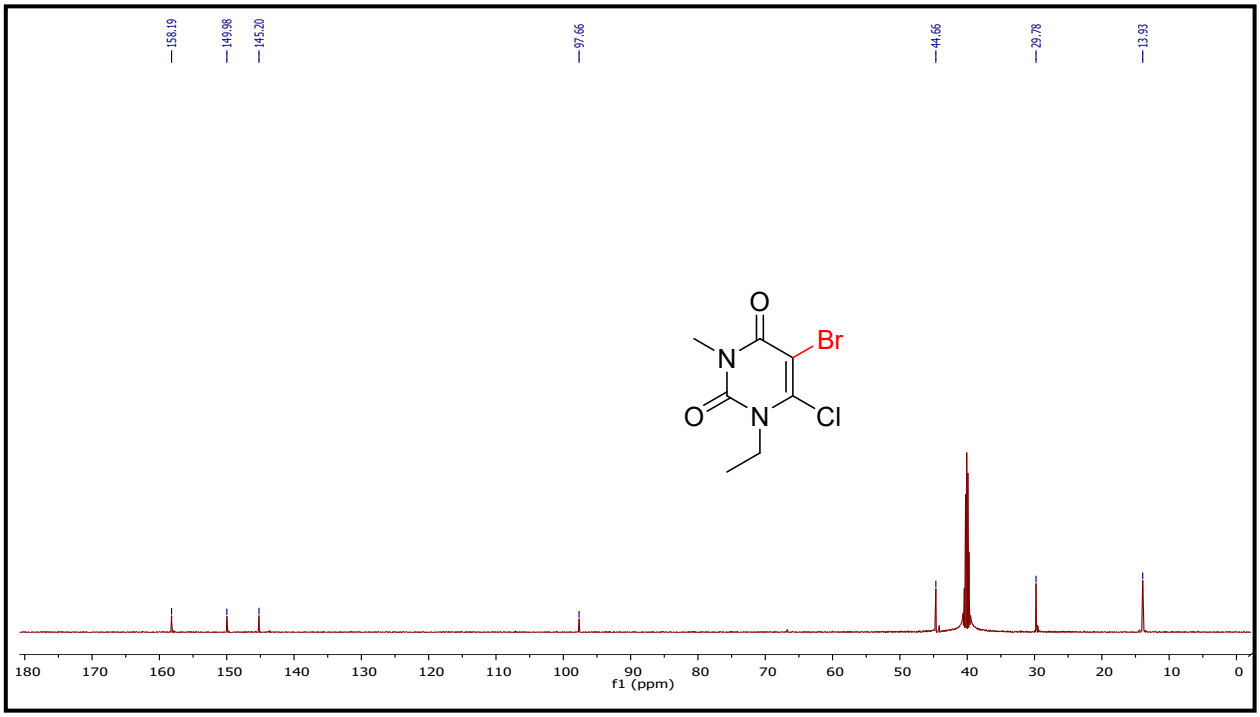
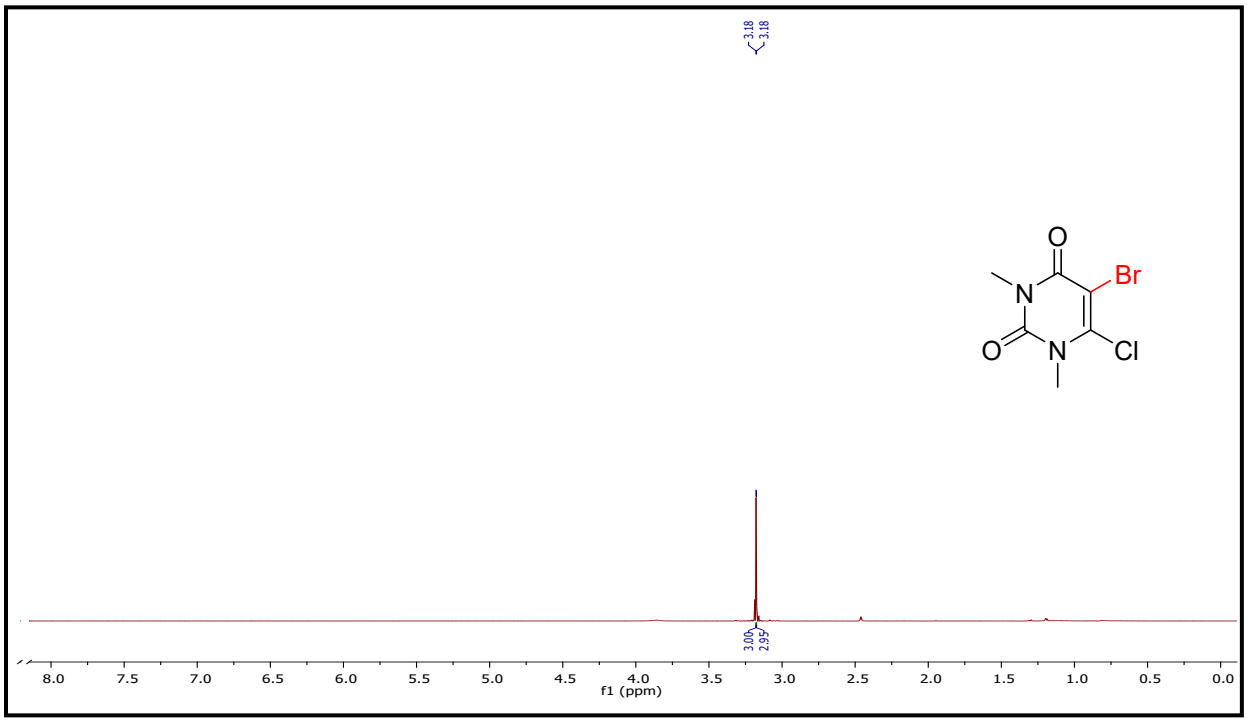


*Figure S37: ^{1}H-NMR (500MHz) and ^{13}C-NMR (126MHz) spectra of 5-bromo-6-chloro-1-ethyl-3-methylpyrimidine-2,4(1H,3H)-dione (**1g**, DMSO-d_6)*



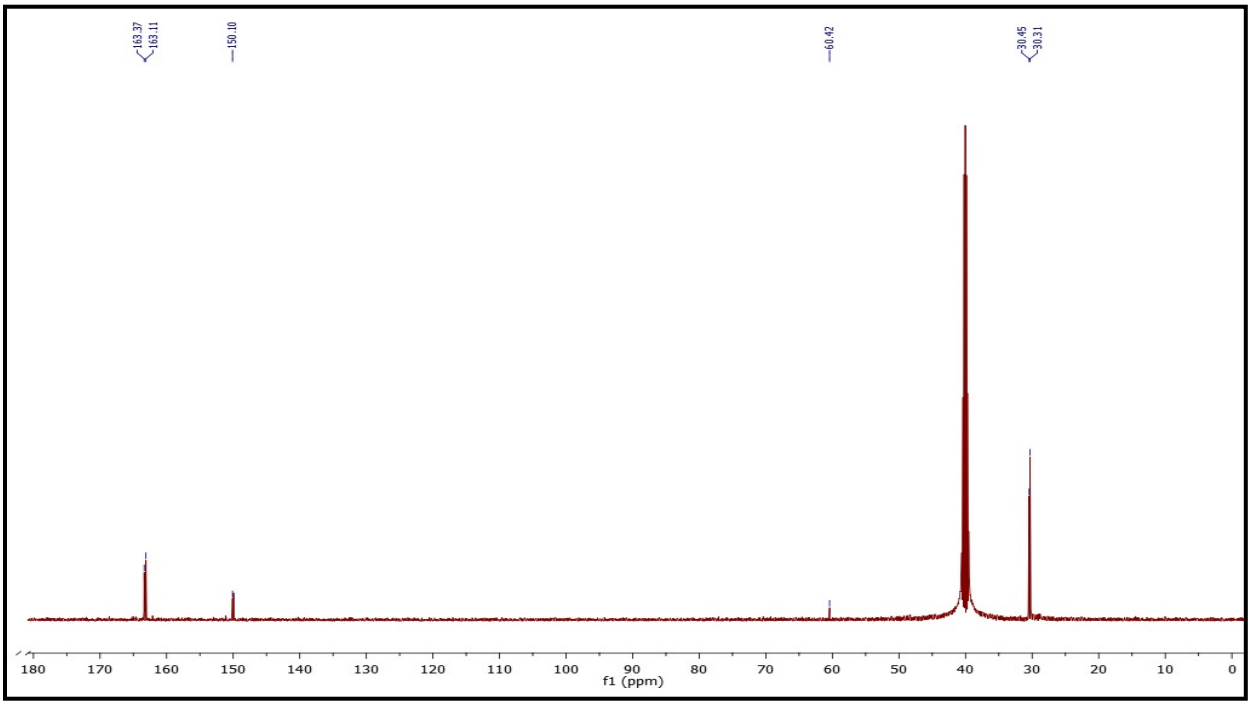
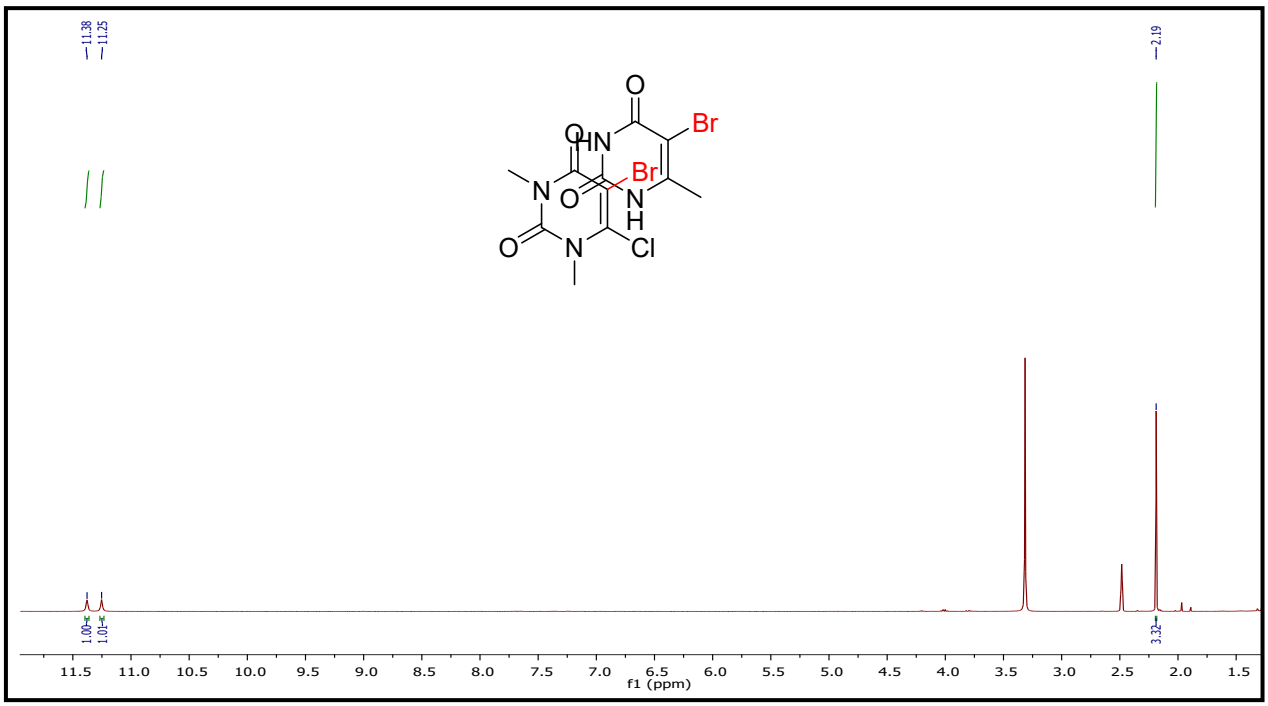


*Figure S38: [1]H-NMR (500MHz) and [13]C-NMR (126MHz) spectra of 5-bromo-6-chloro-1,3-dimethylpyrimidine-2,4(1H,3H)-dione (**1h**, DMSO-d_6)*



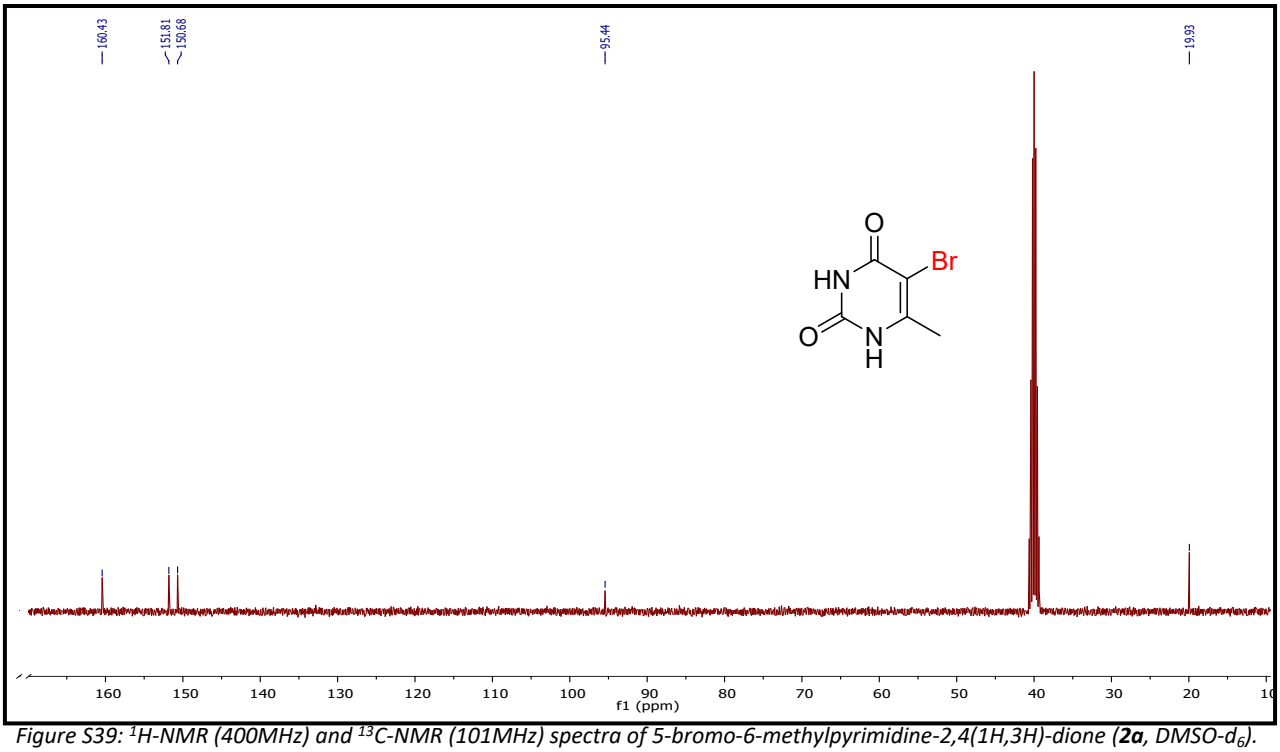
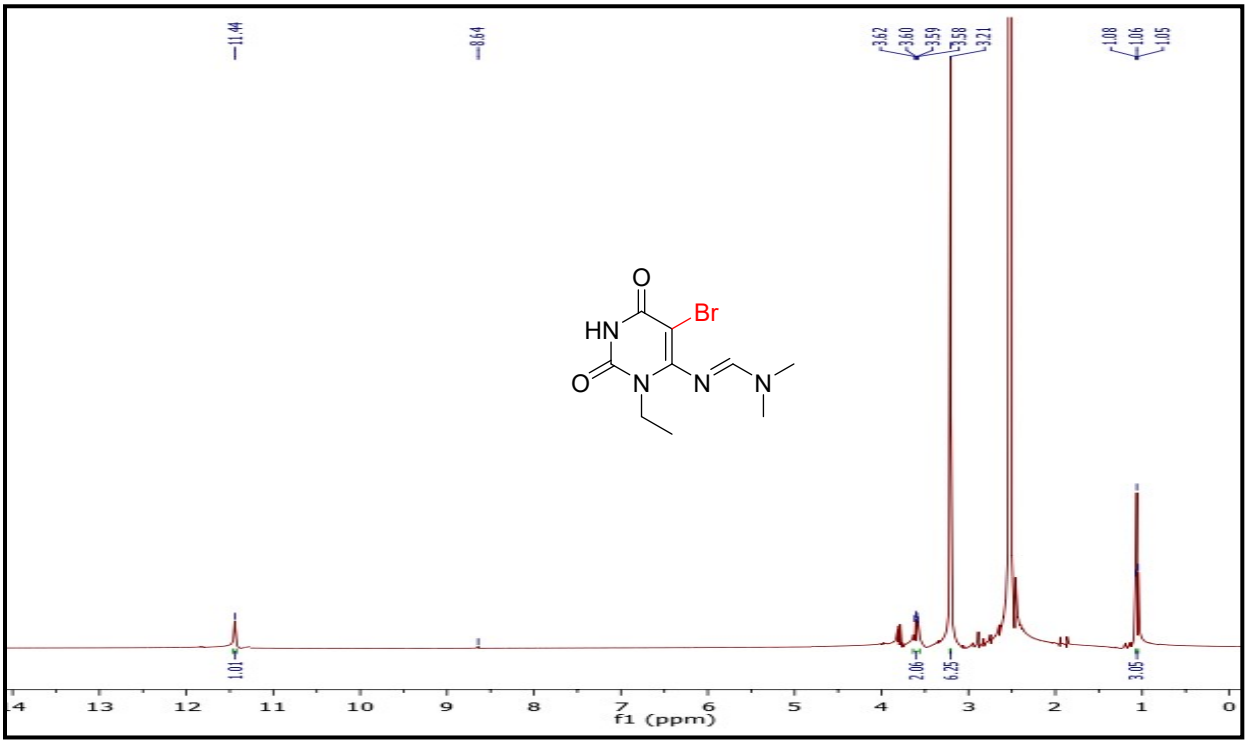
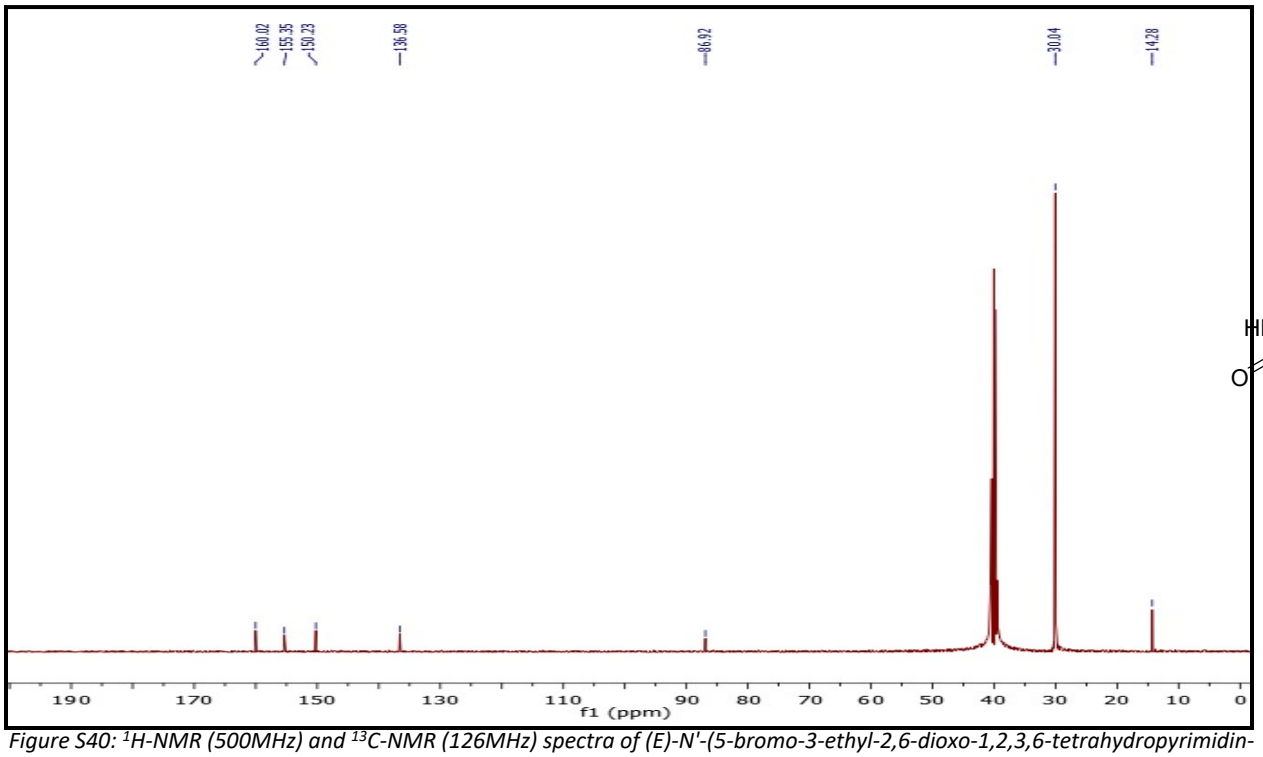


*Figure S39: [1]H-NMR (400MHz) and [13]C-NMR (101MHz) spectra of 5-bromo-6-methylpyrimidine-2,4(1H,3H)-dione (**2a**, DMSO-d_6).*





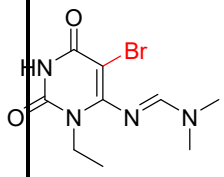
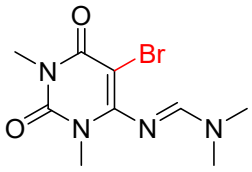
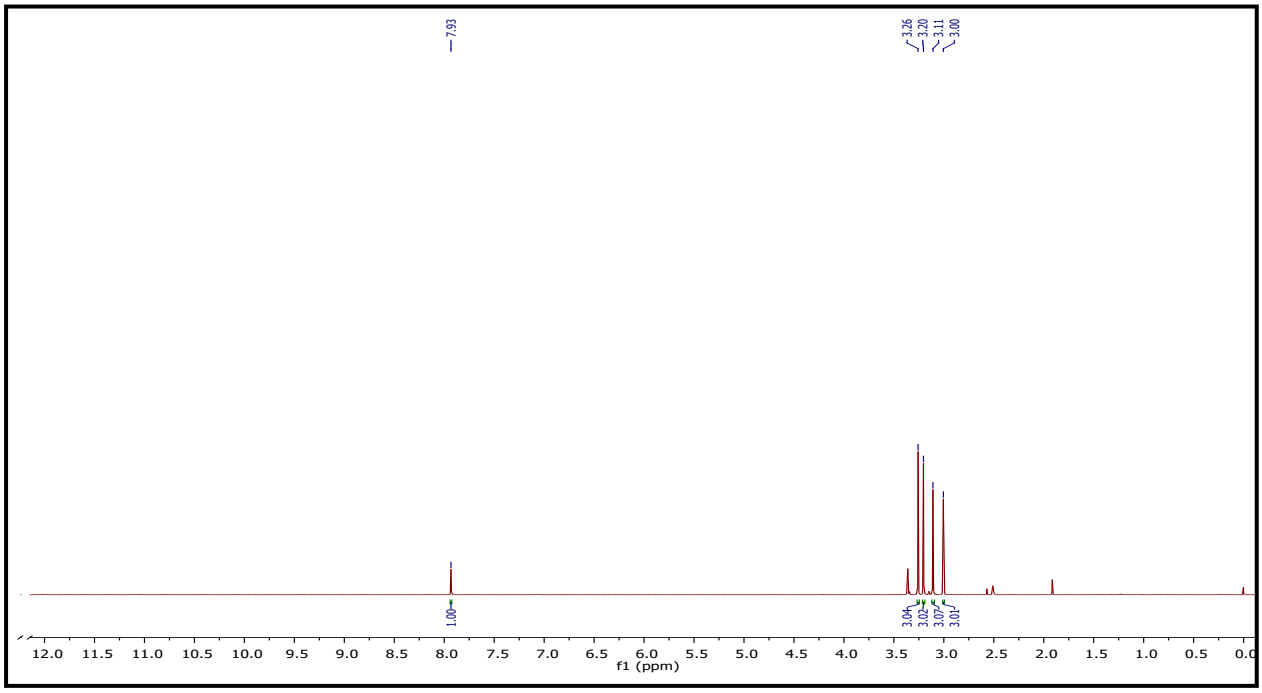


*Figure S40: [1]H-NMR (500MHz) and [13]C-NMR (126MHz) spectra of (E)-N'-(5-bromo-3-ethyl-2,6-dioxo-1,2,3,6-tetrahydropyrimidin-4-yl)-N,N-dimethylformimidamide (**2b**, DMSO-d_6).*





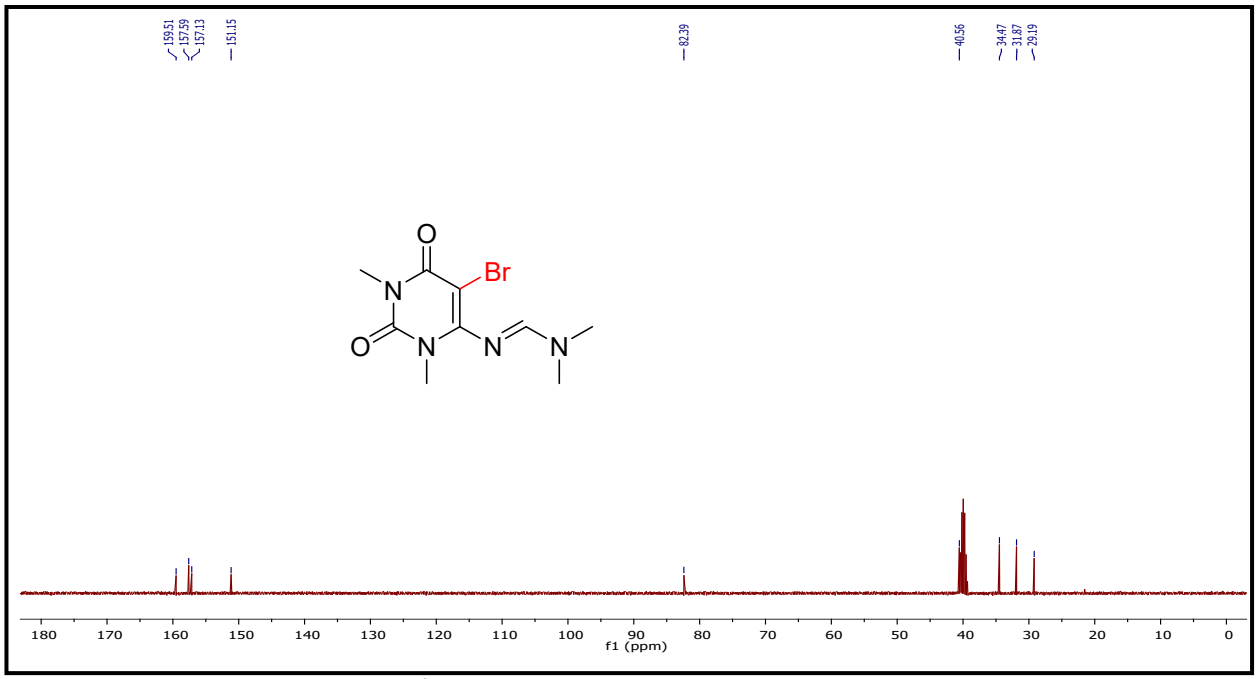


*Figure S41: ^{1}H-NMR (400MHz) and ^{13}C-NMR (101MHz) spectra of (E)-N'-(5-bromo-1,3-dimethyl-2,6-dioxo-1,2,3,6-tetrahydropyrimidin-4-yl)-N,N-dimethylformimidamide(**2c**, DMSO-d_6)*

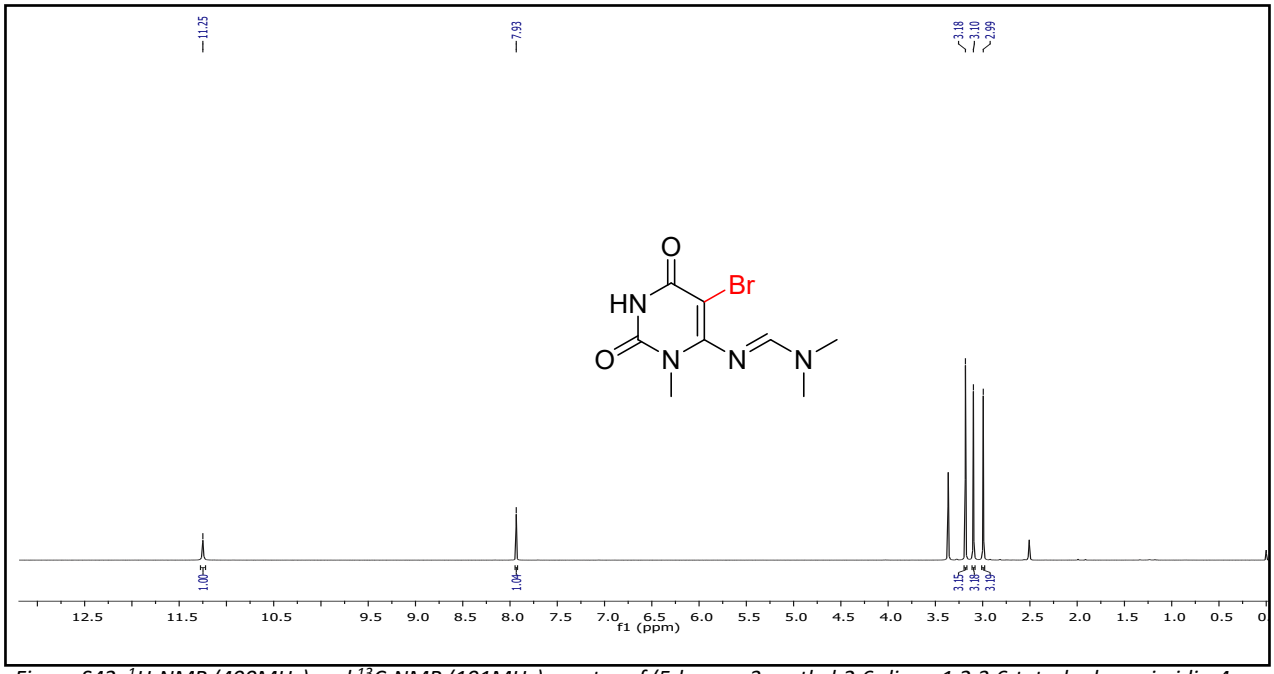
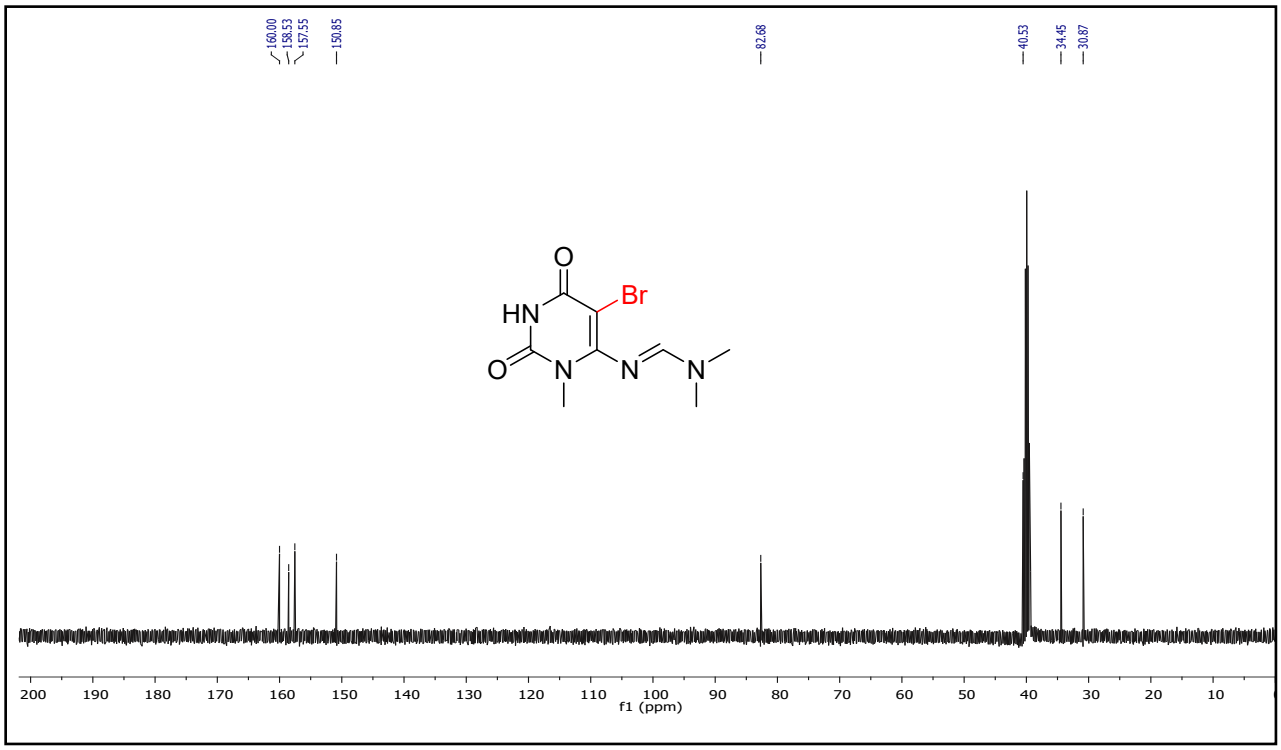


Figure S42: ^{1}H-NMR (400MHz) and ^{13}C-NMR (101MHz) spectra of (5-bromo-3-methyl-2,6-dioxo-1,2,3,6-tetrahydropyrimidin-4-



*yl)-N,N-dimethylformimidamide (**2d**, DMSO-d_6).*

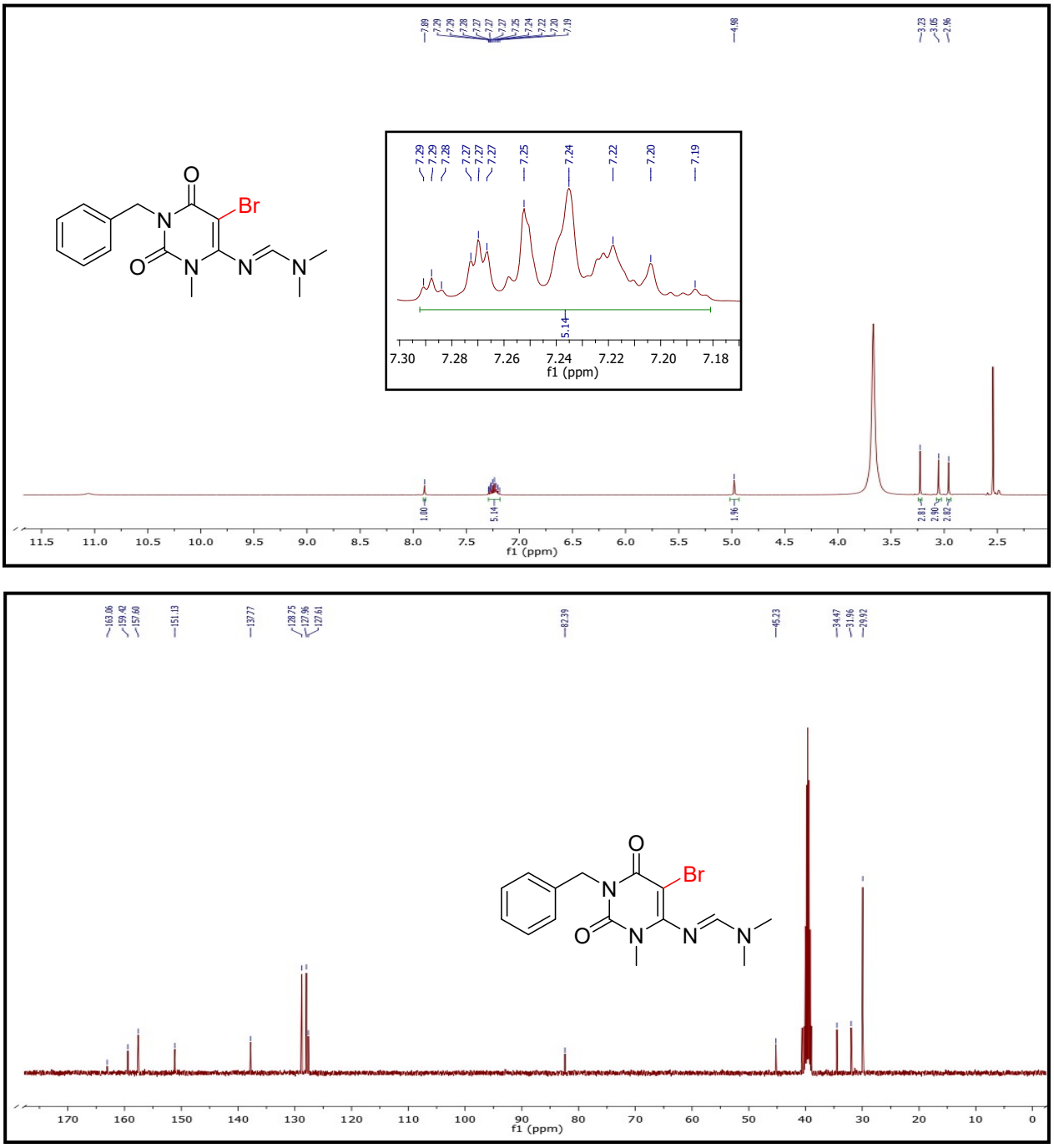


*Figure S43: [1]H-NMR (400MHz) and [13]C-NMR (101MHz) spectra of (E)-N'-(1-benzyl-5-bromo-3-methyl-2,6-dioxo-1,2,3,6-tetrahydropyrimidin-4-yl)-N,N-dimethylformimidamide (**2e**, DMSO-d_6).*

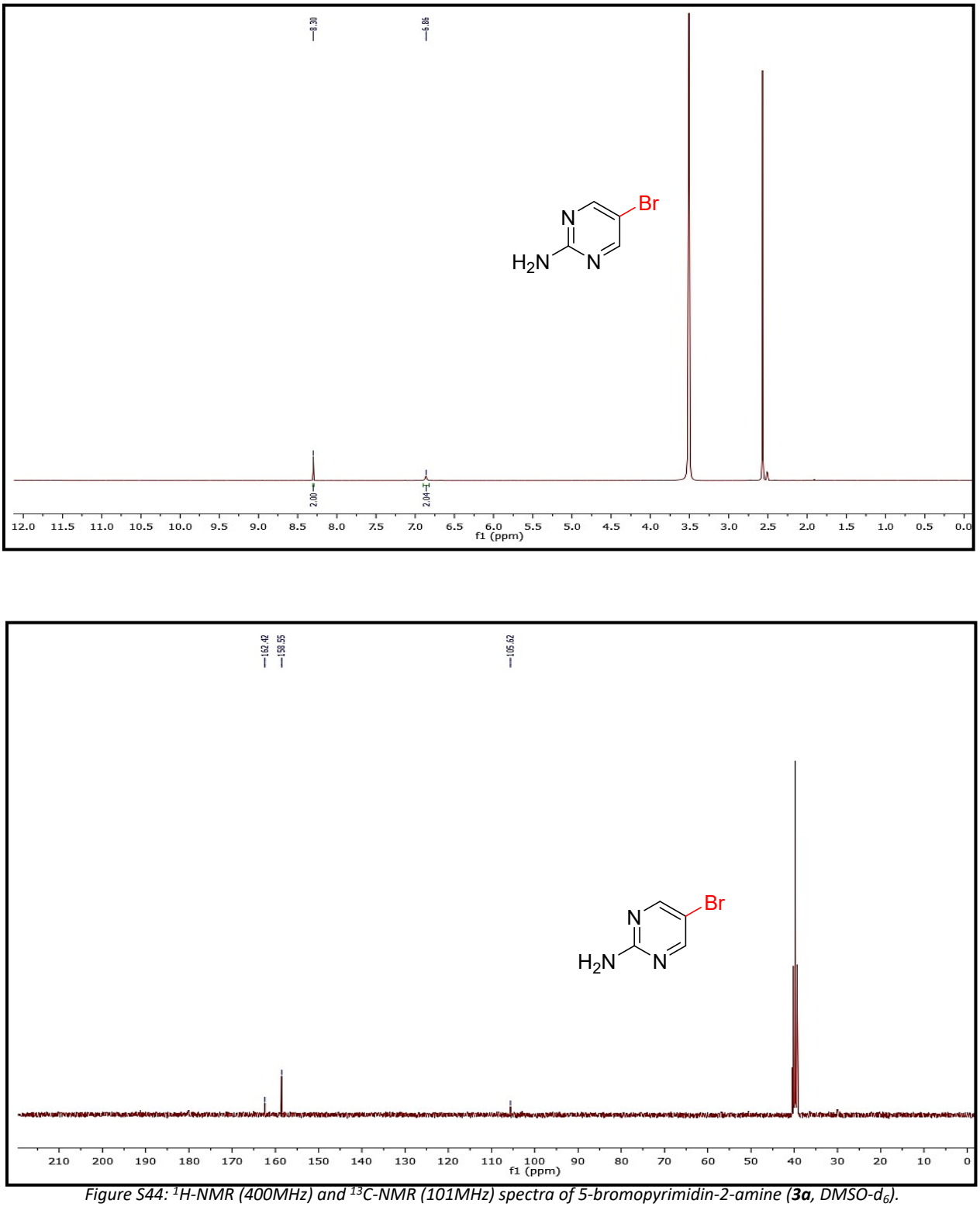
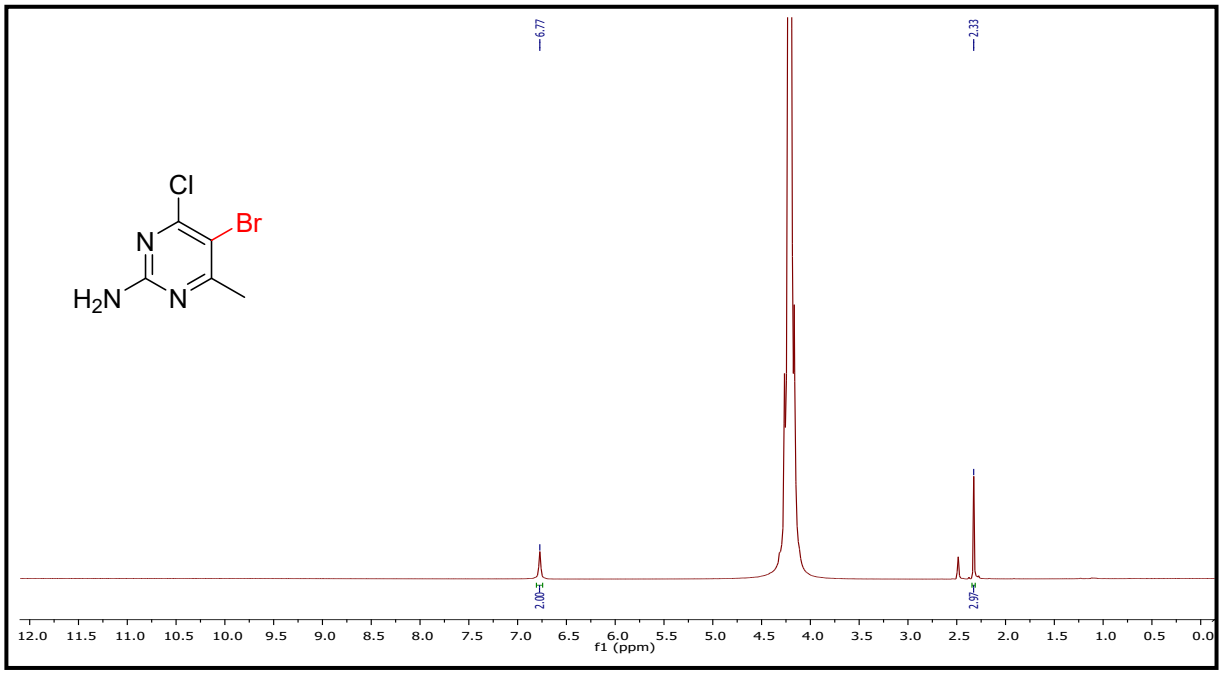


*Figure S44: ^{1}H-NMR (400MHz) and ^{13}C-NMR (101MHz) spectra of 5-bromopyrimidin-2-amine (**3a**, DMSO-d_6).*



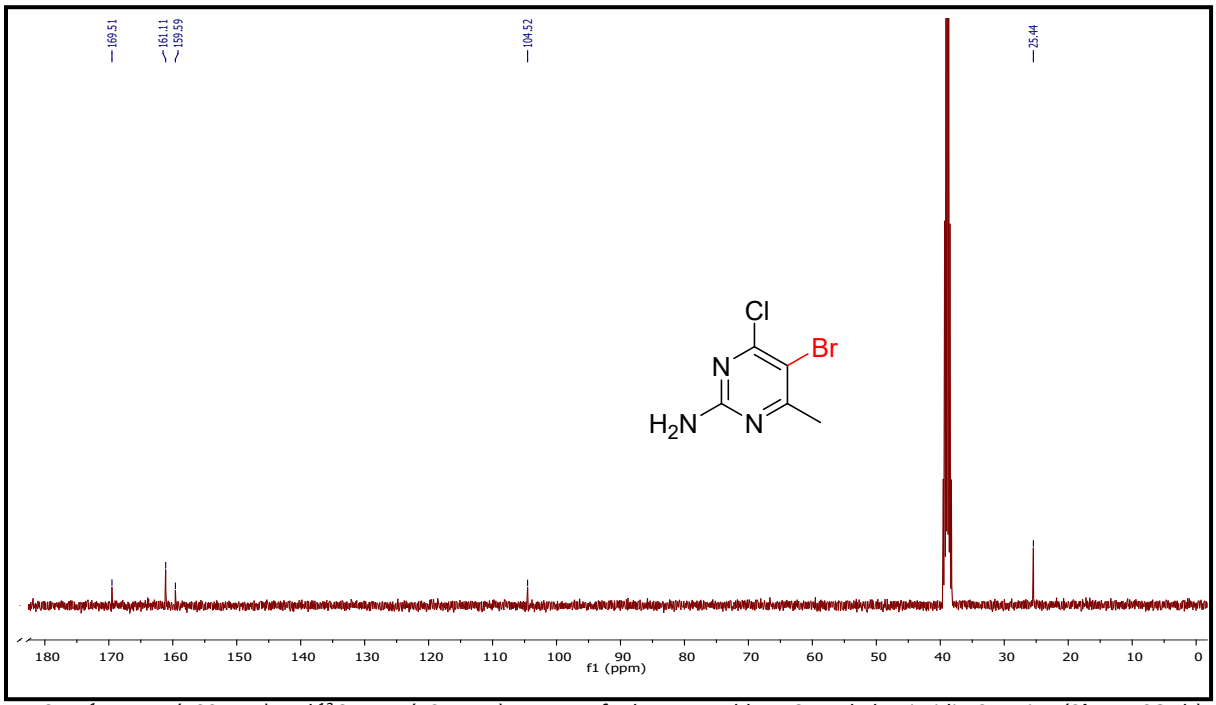
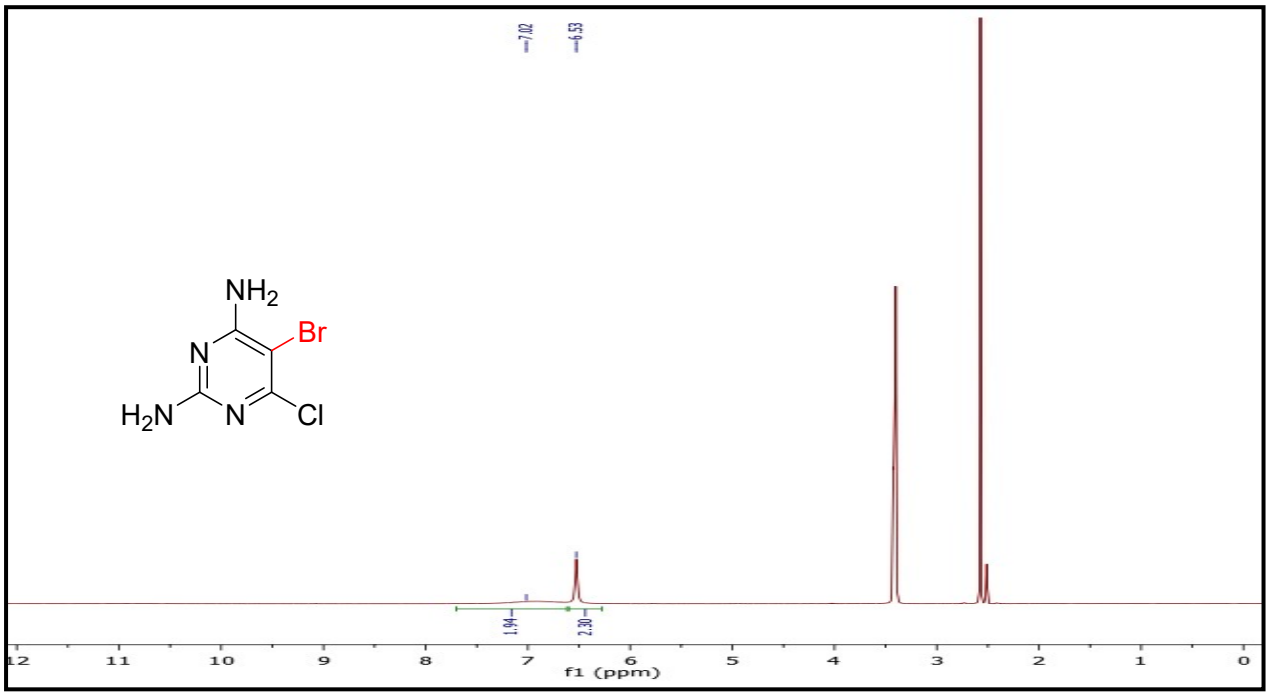


*Figure S45: ^{1}H-NMR (400MHz) and ^{13}C-NMR (101MHz) spectra of 5-bromo-4-chloro-6-methylpyrimidin-2-amine (**3b**, DMSO-d_6)*



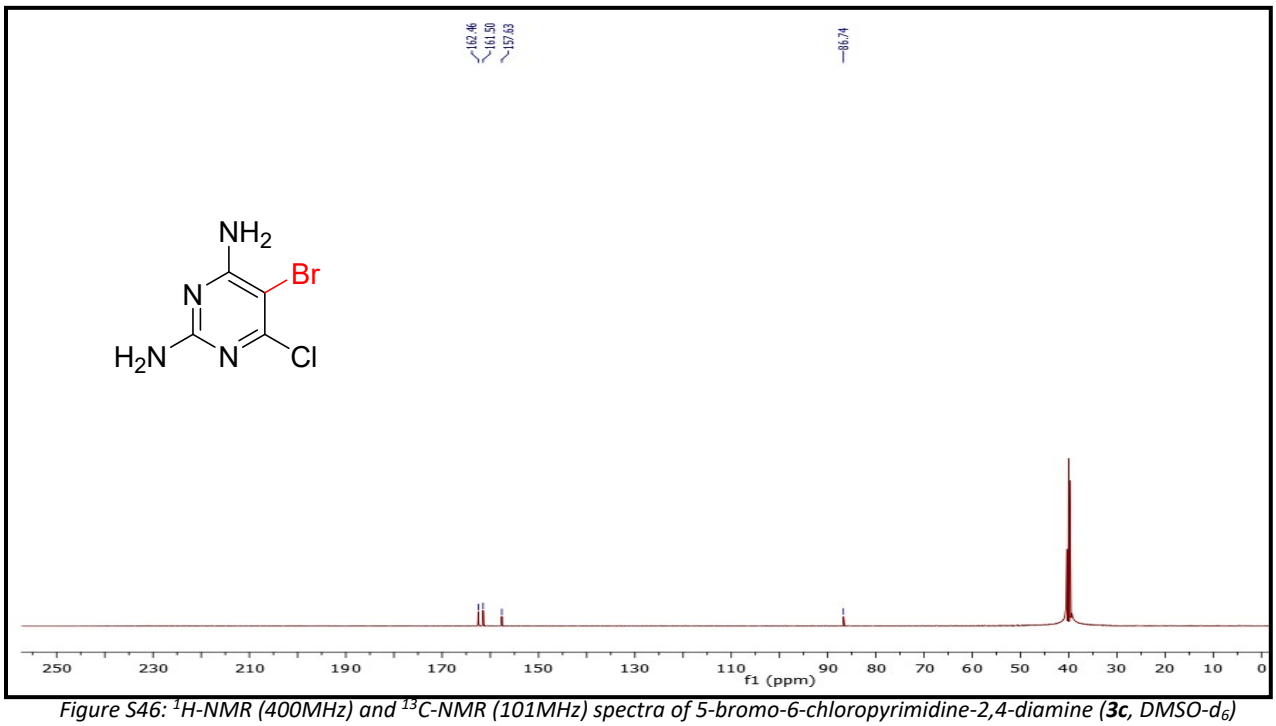
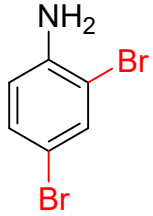
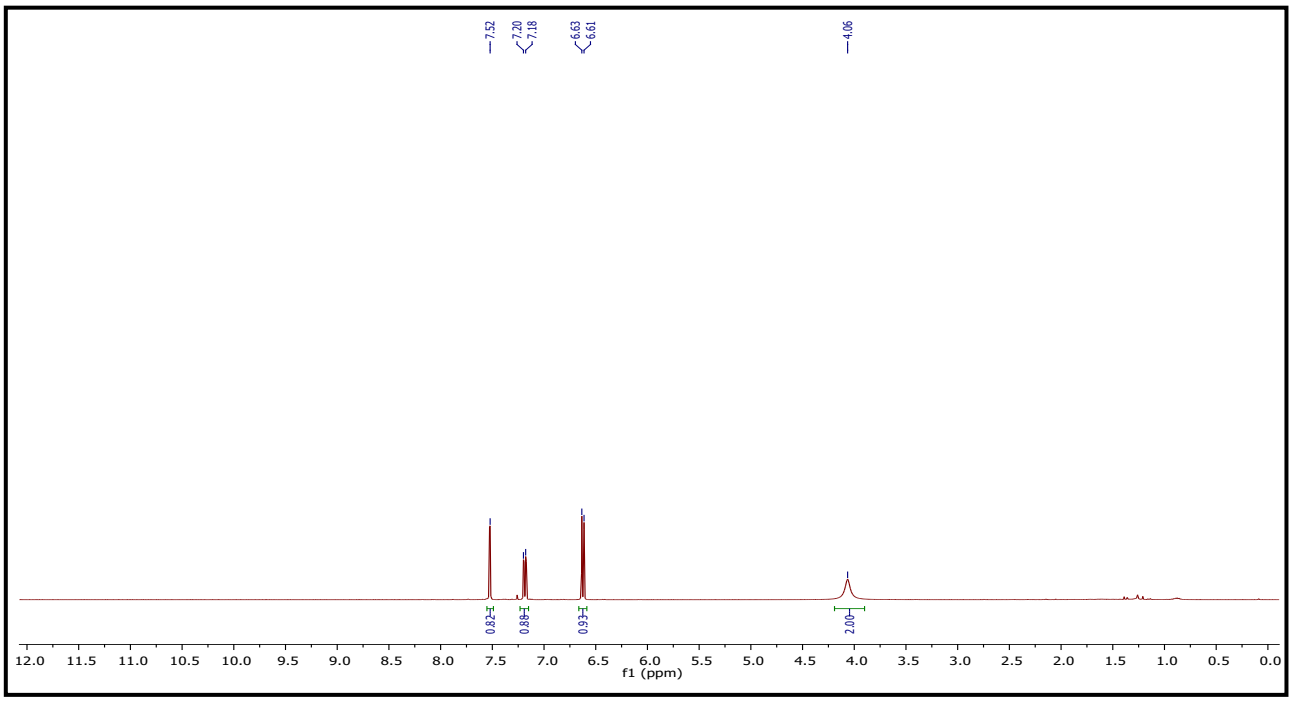


*Figure S46: ^{1}H-NMR (400MHz) and ^{13}C-NMR (101MHz) spectra of 5-bromo-6-chloropyrimidine-2,4-diamine (**3c**, DMSO-d_6)*





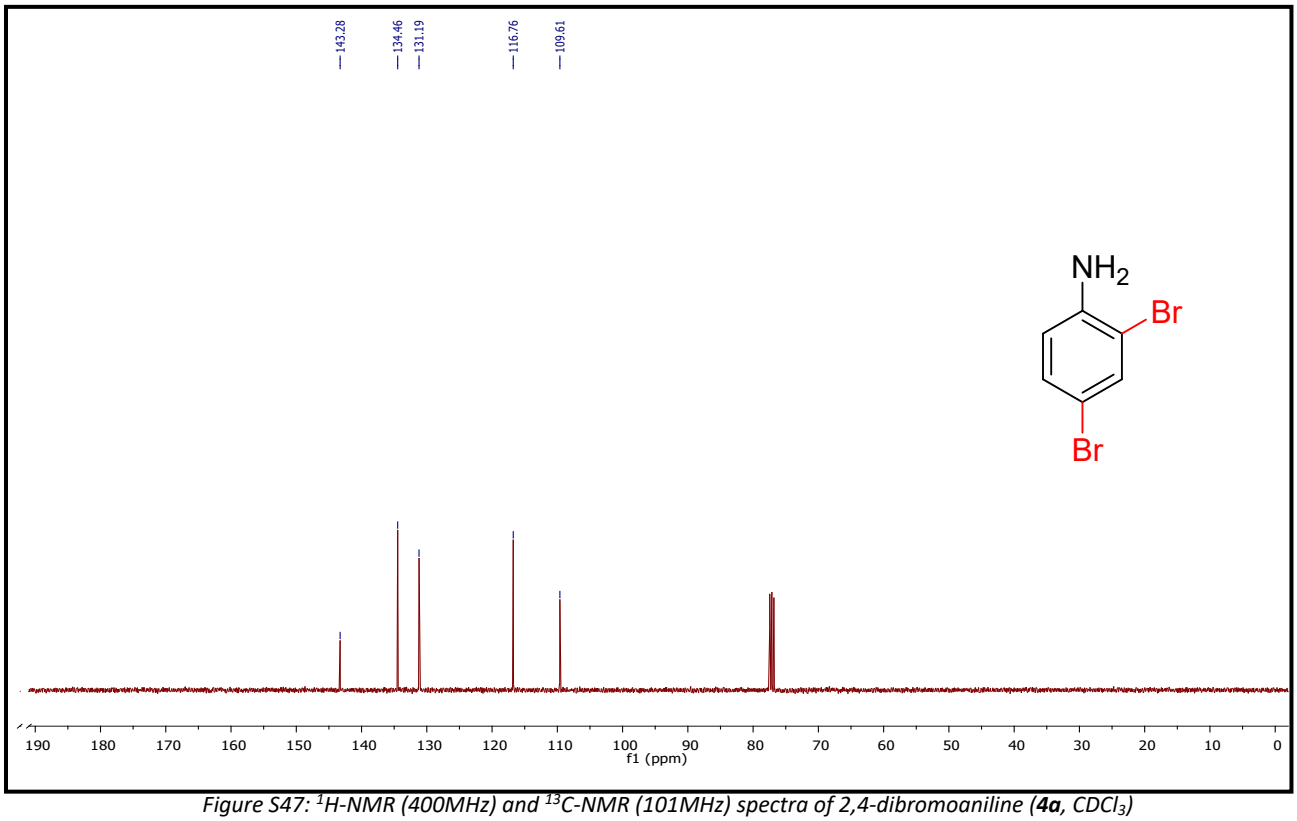
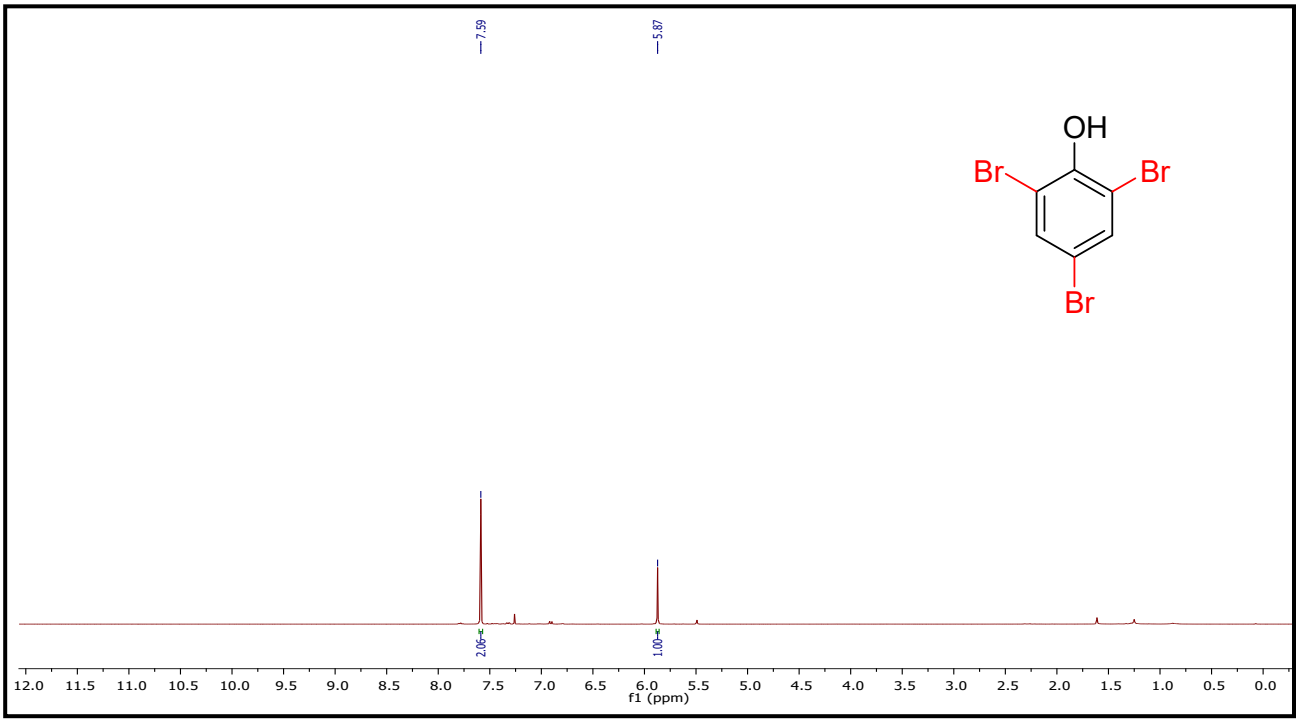


*Figure S47: ^{1}H-NMR (400MHz) and ^{13}C-NMR (101MHz) spectra of 2,4-dibromoaniline (**4a**, $CDCl_3$)*



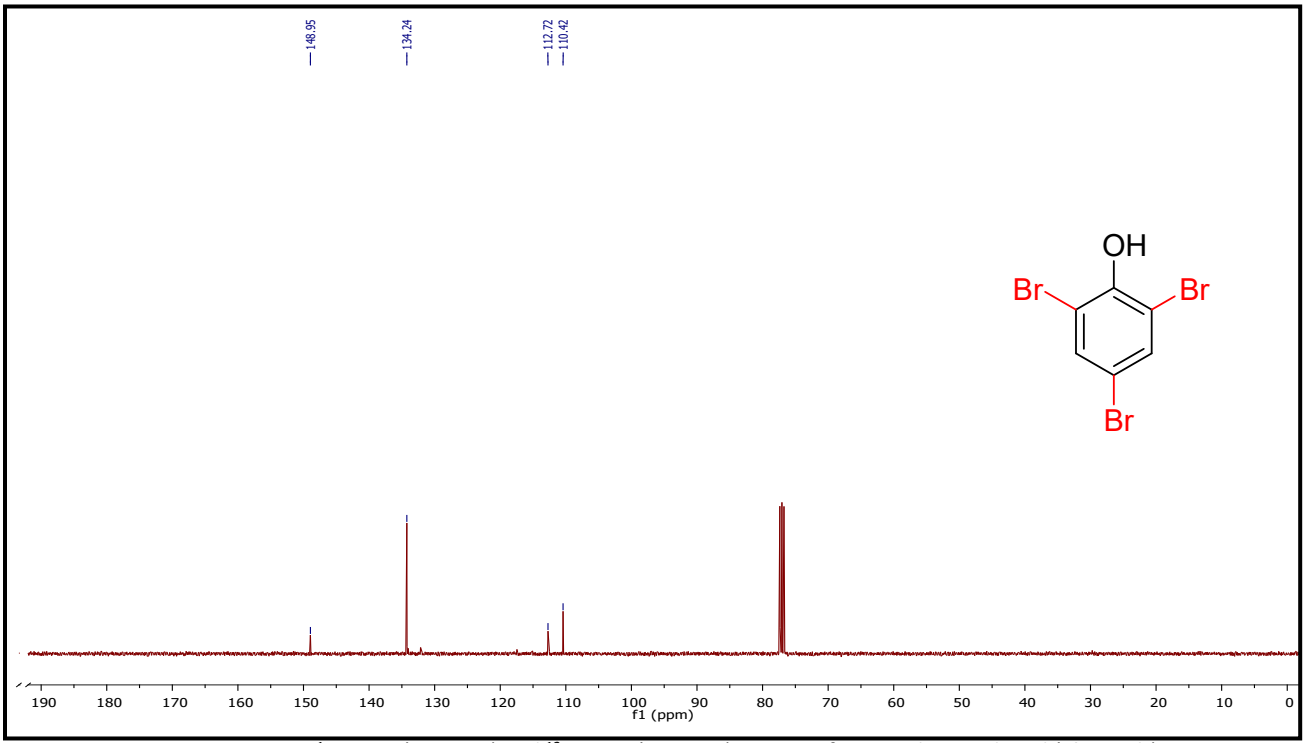
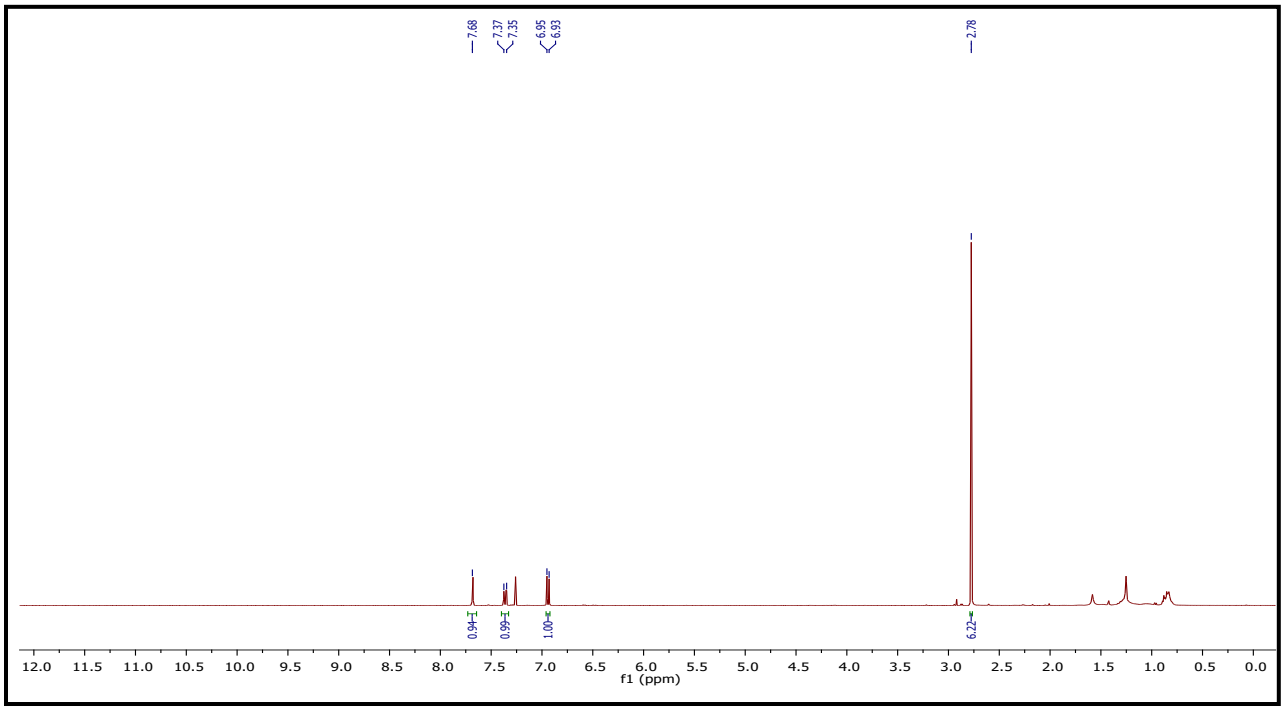


*Figure S48: ^{1}H-NMR (400MHz) and ^{13}C-NMR (101MHz) spectra of 2,4,6-tribromophenol (**4b**, $CDCl_3$)*



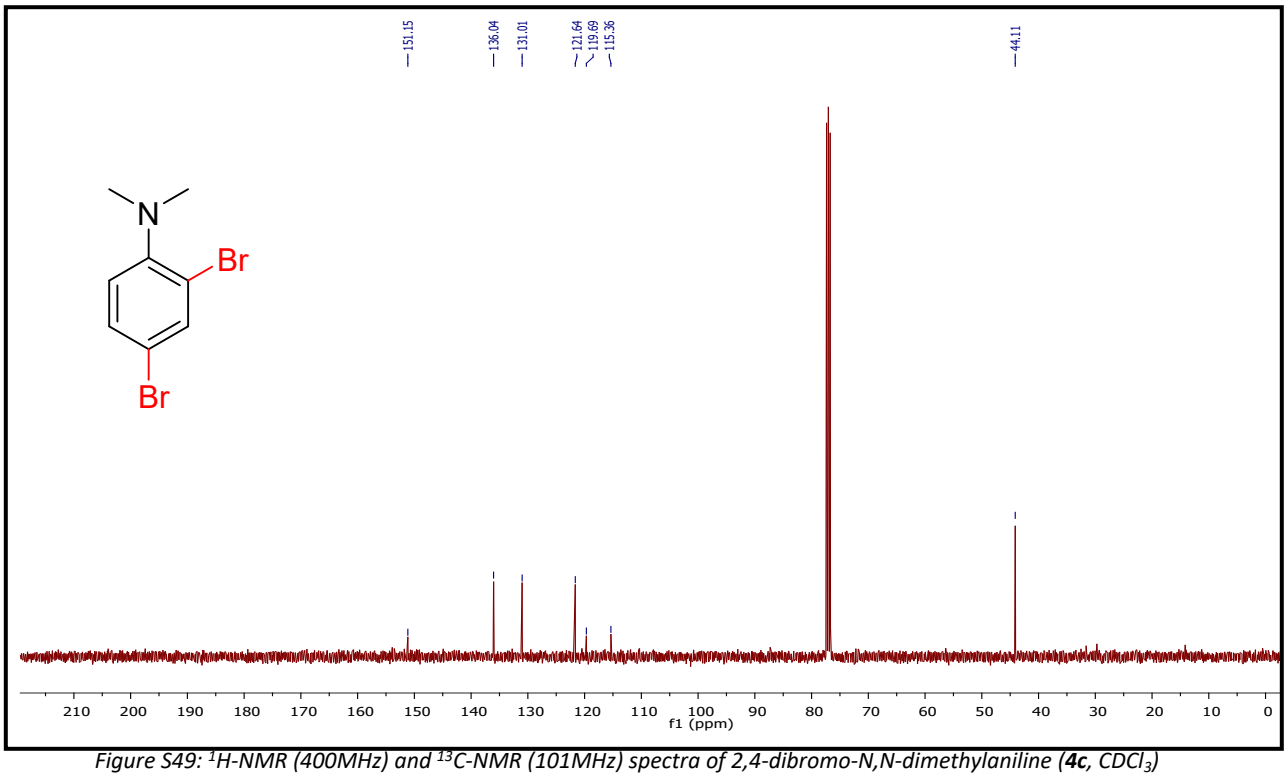


*Figure S49: ^{1}H-NMR (400MHz) and ^{13}C-NMR (101MHz) spectra of 2,4-dibromo-N,N-dimethylaniline (**4c**, $CDCl_3$)*

F

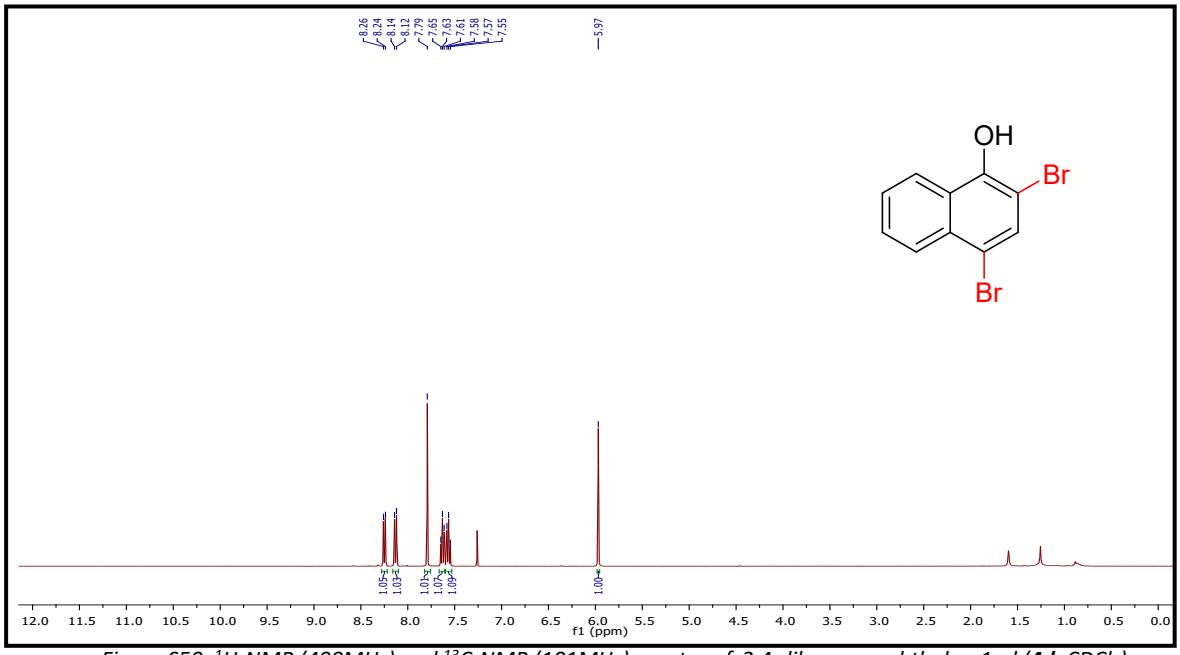


*Figure S50: [1]H-NMR (400MHz) and [13]C-NMR (101MHz) spectra of 2,4-dibromonaphthalen-1-ol (**4d**, $CDCl_3$)*

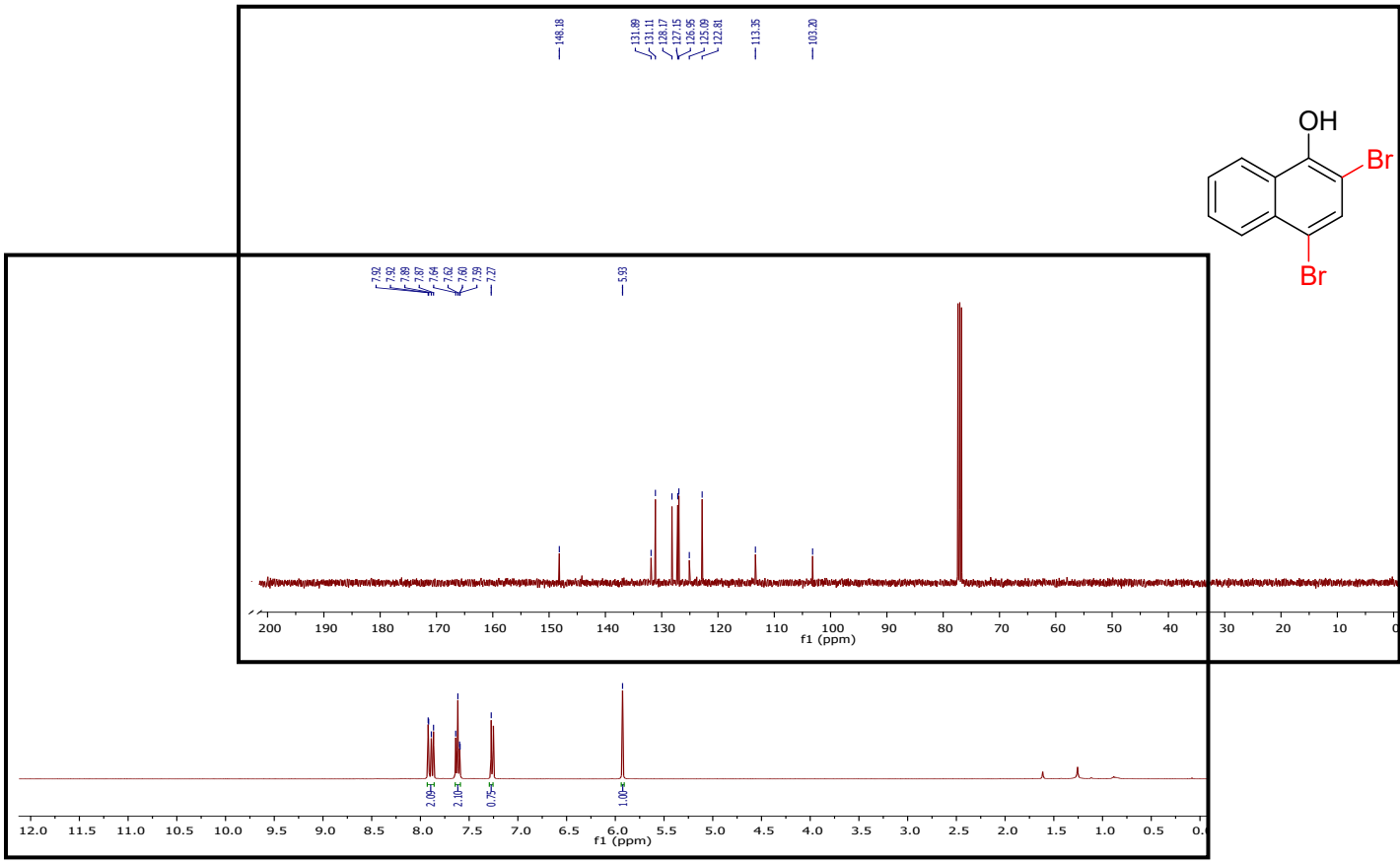
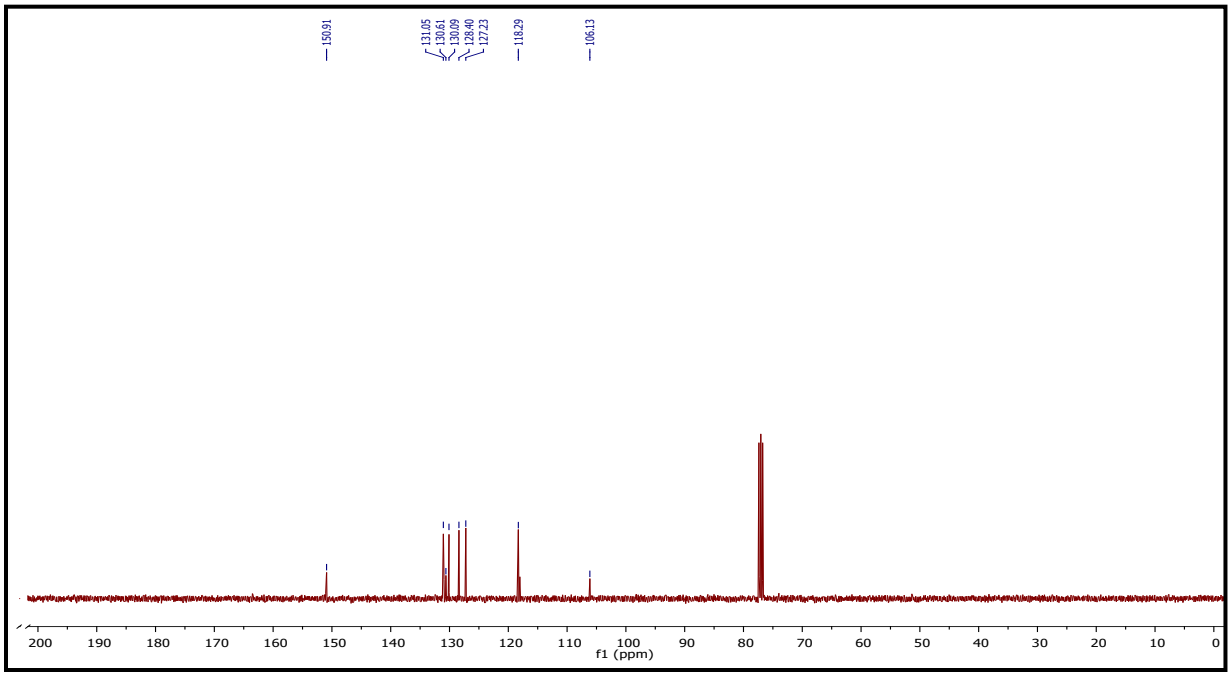


*Figure S51: ^{1}H-NMR (400MHz) and ^{13}C-NMR (101MHz) spectra of 1,3-dibromonaphthalen-2-ol (**4e**, $CDCl_3$)*

Crystal data

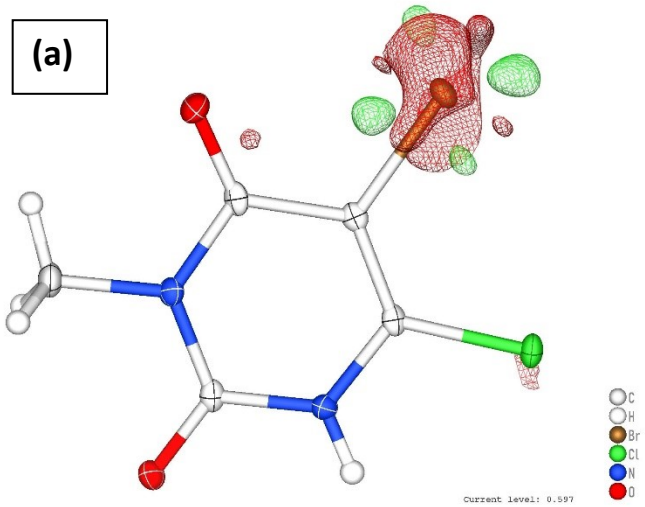
*Table S14: Crystal data of Compound **1a (CCDC = 2380150)***

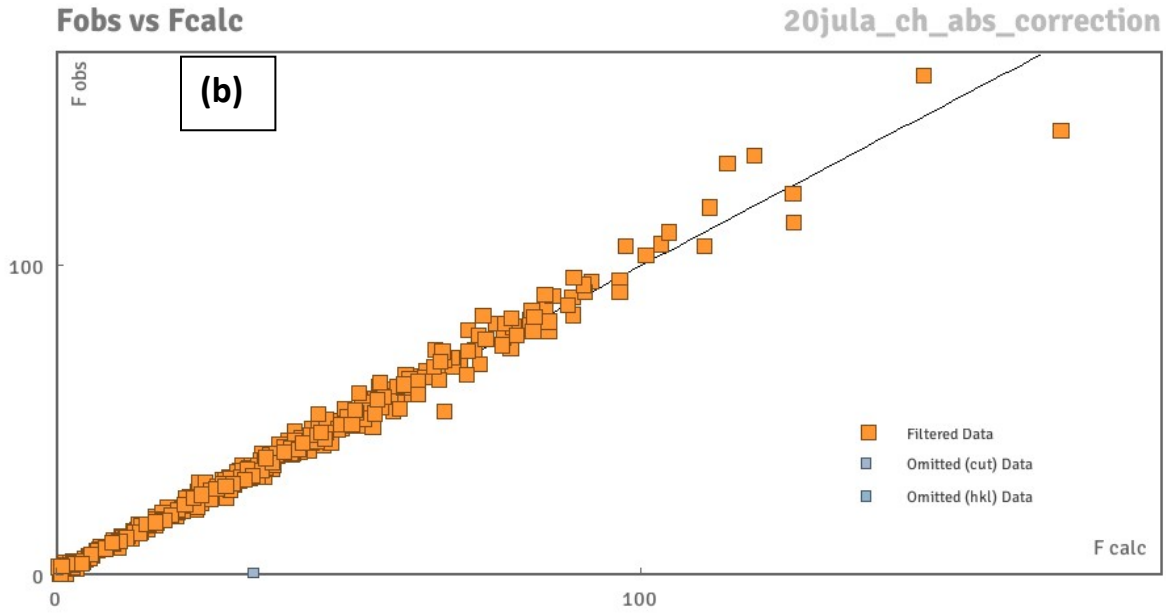
In this case, discrepancies between Fobs and Fcalc can arise due to poor crystal quality or diffraction issues (Figure S52, b). Further absorption correction (Gaussian) and appropriate treatments were applied. As shown in the graph below, the Fobs and Fcalc data are in good agreement, with minor deviations in the reflections (Figure S52, c). These deviations are likely due to random variations during data collection or slight omissions of reflections caused by the beam stop. However, these small deviations do not compromise the data quality or the structural model and remain within the standards set by the IUCr.



Chemical formula	$C_5H_4BrClN_2O_2$
Chemical formula weight	239.46
Temperature	293K
Crystal system	Monoclinic
Space group	P 1 21/c 1
a (Å)	10.9173(7)

b (Å)	8.5748(4)
c (Å)	8.1733(5)
α	90
β	109.345(7)
γ	90
Cell volume	721.93(8)
Cell formula unit (Z)	4
Dx (g/cm^3)	2.203
μ (mm^{-1})	6.007
Crystal size (mm)	0.158 × 0.078 × 0.048
F (000)	464.0
Radiation	Mo Kα (λ = 0.71073)
Data/restraints/parameters	1320/0/102
Final R indexes [I>=2σ (I)]	R1 = 0.0403, wR2 = 0.0963
Final R indexes [all data]	R1 = 0.0414, wR2 = 0.0980




Fobs vs Fcalc
20jula_ch_abs_correction
(b)
F obs
100
0
0
100
Filtered Data
Omitted (cut) Data
Omitted (hkl) Data
F calc

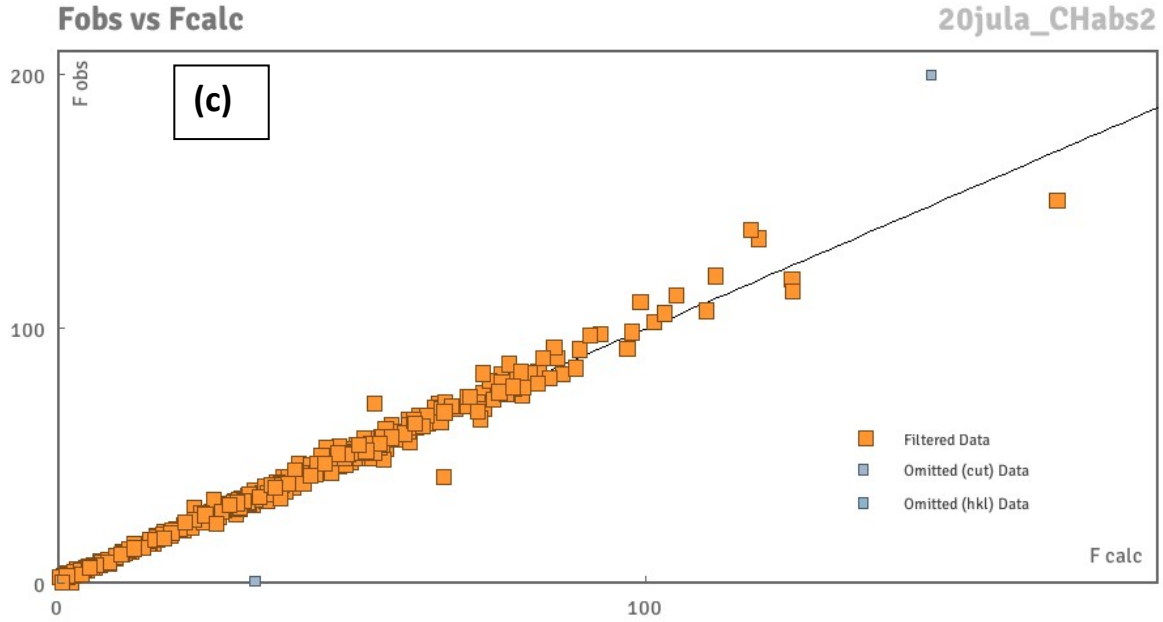

Fobs vs Fcalc
20jula_CHabs2
(c)
F obs
200
100
0
0
100
Filtered Data
Omitted (cut) Data
Omitted (hkl) Data
F calc

*Figure S52: Ellipsoids are drawn of the compound **1a** at the 50% probability level and (**b**) Fobs vs Fcalc plot (before treatment) (**c**) Fobs vs Fcalc plot (after treatment).*

*Table S15: Crystal data of Compound **1g (CCDC = 2348542)***

Chemical formula	$C_7H_8BrClN_2O_2$
Chemical formula weight	267.51
Temperature	293K
Crystal system	Monoclinic
Space group	P 1 21/c 1
a (Å)	4.6708(5)
b (Å)	15.134(10)
c (Å)	13.5776(8)
α	90
β	92.765(7)
γ	90
Cell volume	958.65(13)
Cell formula unit (Z)	4
Dx (g/cm^3)	1.854
μ (mm^{-1})	4.535
Crystal size (mm)	0.1 × 0.09 × 0.085
F (000)	528.0
Radiation	Mo Kα (λ = 0.71073)
Data/restraints/parameters	1759/0/120
Final R indexes [I>=2σ (I)]	R1 = 0.0470, wR2 = 0.0944
Final R indexes [all data]	R1 = 0.0787, wR2 = 0.1076

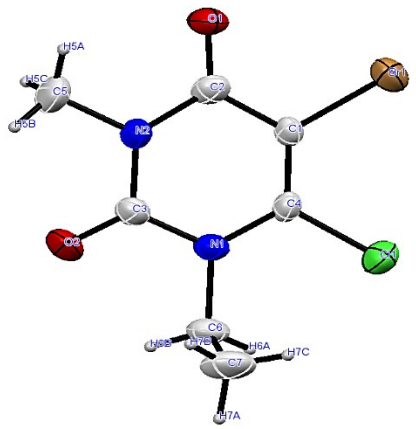


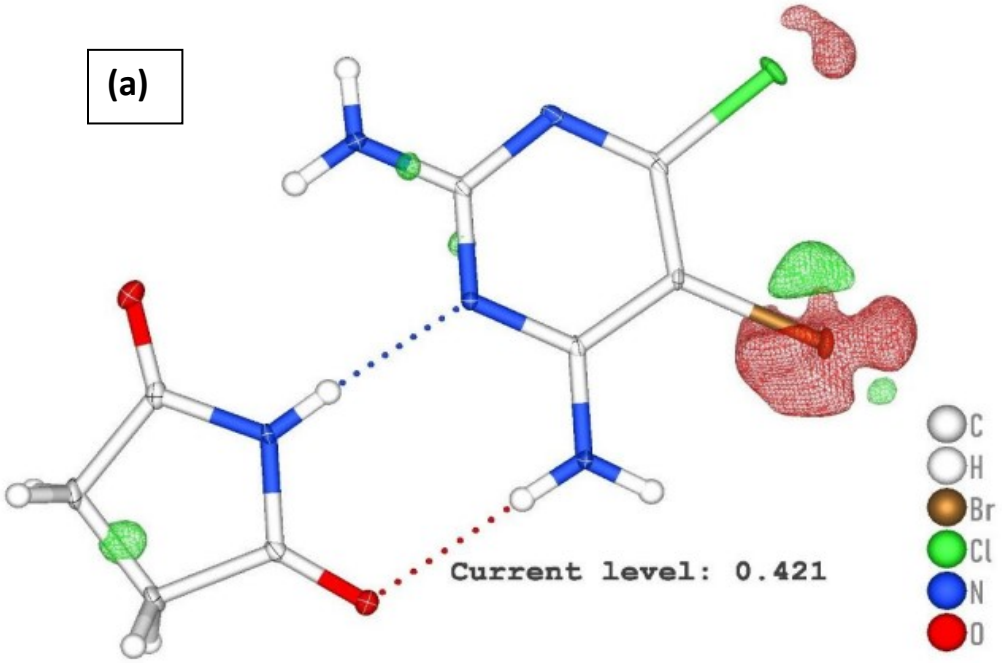
*Figure S53: ORTEP diagram of compound **1g***

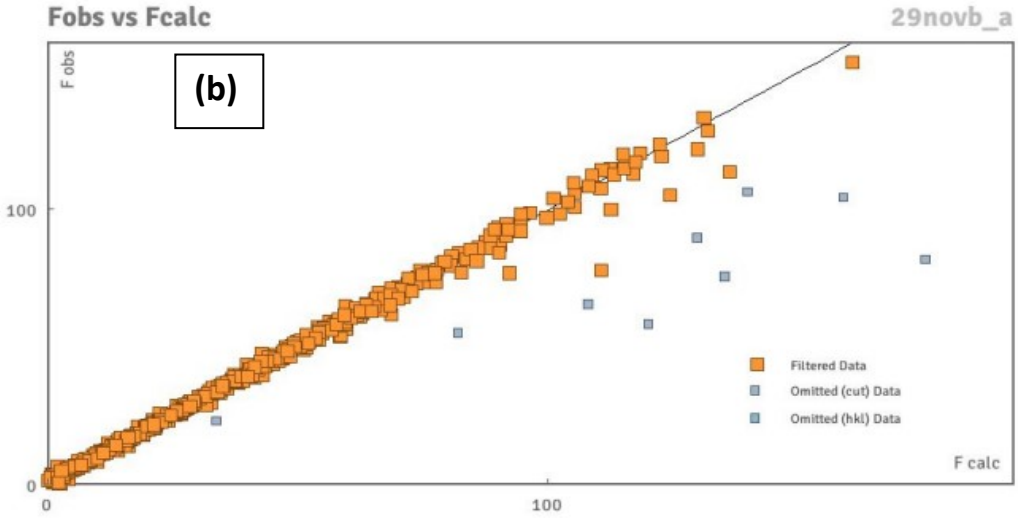
*Table S16: Crystal data of Compound **3c (CCDC = 2329775)***

Product 3c was obtained as a crystalline compound, allowing further characterization by single-crystal X-ray diffraction. Despite our best efforts, we were unable to get the crystal from the pure product. However, the crystal appeared from a crude reaction mixture where succinimide is present as a cocrystal (Figure S54, a). In this case, significant discrepancies between Fobs and Fcalc can arise due to poor crystal quality or diffraction issues (Figure S54, b). To further enhance the quality of the data and reduce the observed discrepancies, we addressed potential extinction issues by incorporating an EXTI command into the .ins file and running a complete refinement cycle. This helped in improving the model, as tested during the refinement process. Additionally, we considered the possibility that some of the large discrepancies between Fobs and Fcalc might be due to improper absorption corrections. As a result, an empirical absorption correction was applied (DIFABS), and we observed a marked improvement in the agreement of the reflections (Figure S54, c). Furthermore, all statistical parameters are suitable for publication, in accordance with IUCr recommendations.

Chemical formula	$C_{32}H_{36}Br_4Cl_4N_{20}O_8$
Chemical formula weight	1290.197
Temperature	273.15K
Crystal system	monoclinic
Space group	$P2_1/n$
a (Å)	7.7958(4)
b (Å)	6.4753(3)
c (Å)	22.4577(12)
α	90
β	90.521(2)
γ	90
Cell volume	1133.62(10)
Cell formula unit (Z)	1
Dx (g/cm^3)	1.890

μ (mm^{-1})	3.859
Crystal size (mm)	0.24 × 0.12 × 0.11
F (000)	640.2
Radiation	Mo Kα (λ = 0.71073)
Data/restraints/parameters	2834/0/154
Goodness-of-fit on F^2	1.038
Final R indexes [I>=2σ (I)]	R_1 = 0.0272, wR_2 = 0.0672
Final R indexes [all data]	R_1 = 0.0282, wR_2 = 0.0678





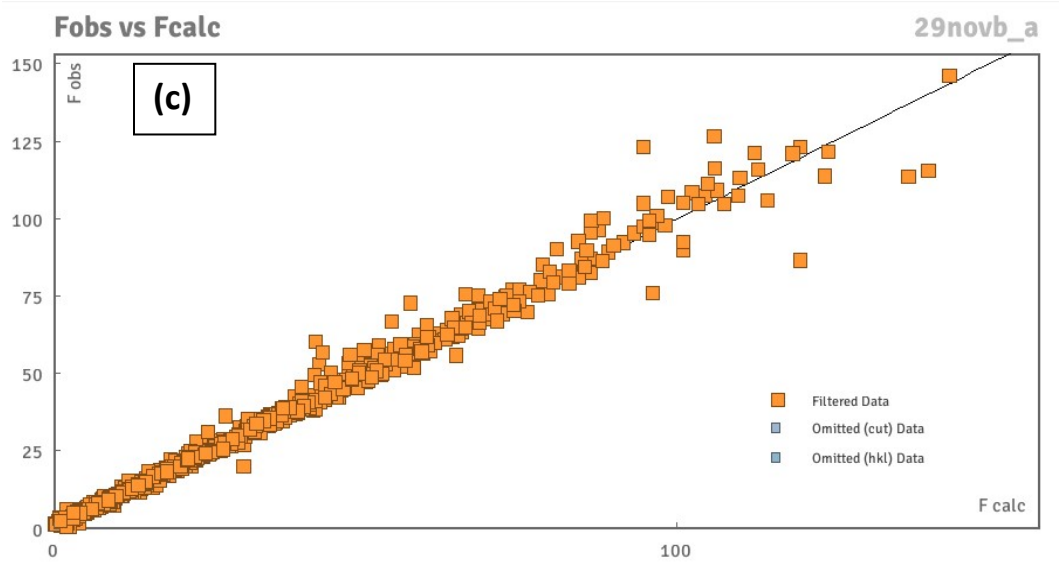


*Figure S54: (**a**) Ellipsoids are drawn of the compound **3c** at the 50% probability level and (**b**) Fobs vs Fcalc plot (before treatment) (c) Fobs vs Fcalc plot (after treatment).*

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