Bioinspired Design of Reagent Allows the Functionalization of C_α–H of α, β-Unsaturated Carbonyl Compounds via Baylis-Hillman Chemistry Under Ambient Conditions

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Supporting information

General Information

Dimethyl sulphoxide (DMSO), distilled water, hexane, ethyl acetate, petroleum ether were purchased from Sigma Aldrich. Acrolein, crotonaldehyde, cinnnamaldehyde, mesityl oxide, chromone, 2(5*H*)-furanone, 4-phenylbut-3-en-2-one, methyl iodide, allylbromide, crotyl bromide, cinnamyl bromide and other reagents were purchased from Sigma Aldrich and Spectrochem, Mumbai. ^{1}H and ^{13}C NMR spectra were recorded on Bruker 500 MHz NMR spectrometer using $CDCl_3$/DMSO-d_6 as a solvent for deuterium locking, 5.0 mm BBO probe with temperature 298K. To avoid the vibration disturbance, pneumatic mode was used to keep the magnet suspended in air (standard Bruker option). Chemical shifts are given in ppm with TMS as an internal reference. *J* values are given in Hertz.

Mass spectra were recorded on Bruker micrOTOF Q II Mass spectrometer. The solutions were made/diluted in ACN-H_2O (3:7) and directly injected to the ESI (electrospray ionization, a soft ionization technique capable to detect the non-covalent adducts)[1] source through Kd Scientific pump. In case of reaction mixtures, aliquots were taken at different reaction times and diluted with ACN-H_2O (3:7) for recording the mass spectra. TLC was performed on glass plates coated with silica gel GF-254 and different combinations of ethyl acetate, hexane and methanol were used to run the plate. Column chromatography was performed with 60-120 mesh silica. Flash chromatography was performed using Biotage Isolera One 2.0.8 model in isocratic mode with ethyl acetate – hexane – petroleum ether as eluent. IR spectral data were recorded on FTIR (VARIAN 660 IR) instrument. Optical rotation was recorded on AT-100 Atago automatic polarimeter.

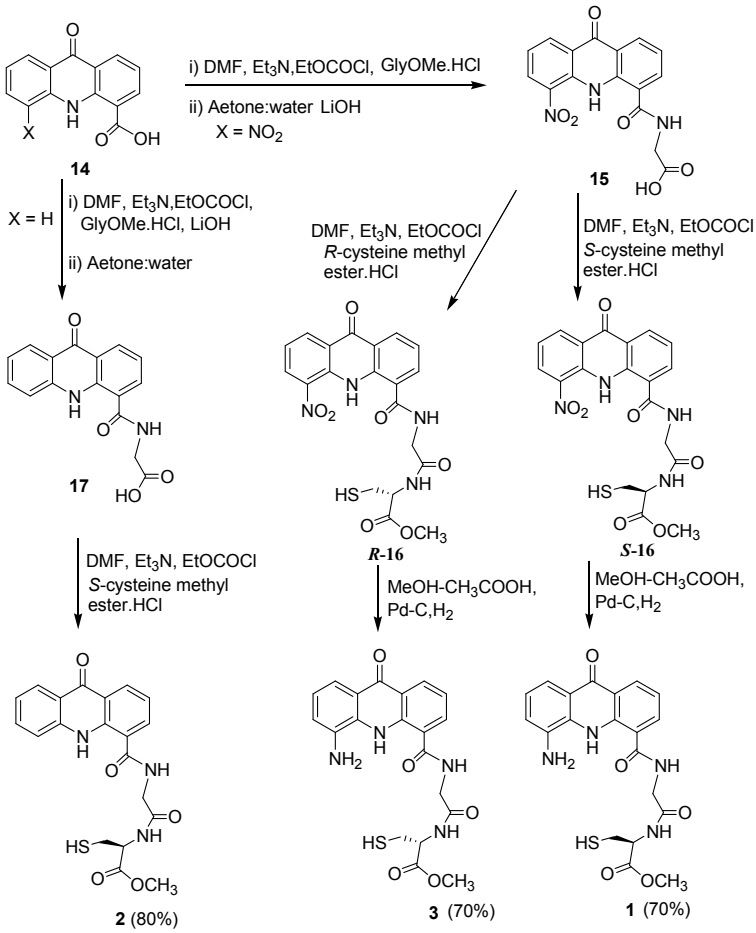
For LC-MS, Dionex Ultimate 3000 system was linked to mass spectrometer. Chirobiotic® T 10 μm reverse phase chiral HPLC column (25 cm x 4.6 mm) was used for ensuring the chiral purity of compounds **9g,h** and **10g,h**. Acetonitrile-water (3:1) was used as eluent. 2 μL of sample (injection volume) was loaded to the column, flow rate was kept 0.2 ml and absorbance was set at 200, 220 and 254 nm. Sodium formate was used as internal calibrant.

Experimental Procedure:

Synthesis of compound 1 – 3. Compounds **1** and **3** were obtained by the sequential coupling of glycine and *S*-cysteine/*R*-cysteine with 5-nitro-9-oxo-9,10-dihydroacridine-4-carboxylic acid (**14**, X = NO_2) in the presence of ethyl chloroformate and triethyl amine as depicted in Scheme S1 (630 mg, 75%), mp 170 ^{o}C, $[\alpha]_D$ -8^{o} for **1** and +11^{o} for **3** (c 1.00, MeOH). ^{1}H NMR (500 MHz, DMSO-d_6, δ): 3.74 (s, OCH_3, 3H), 3.98-4.02 (m, CH_2, 2H), 4.13-4.16 (m, CH_2, 2H), 4.80 (m, CH, 1H), 5.02 (br, NH_2, 2H), 7.37-7.40 (m, ArH, 2H), 7.69-7.78 (m, ArH,

1H), 8.23-8.49 (m, ArH, 3H), 9.26 (br, NH, 1H), 9.50 (br, NH, 1H), 10.54 (br, NH, 1H). ^{13}C NMR (125 MHz, DMSO-d_6, δ): 180.82, 177.18, 170.61, 168.67, 140.83, 134.51, 133.67, 131.16, 126.32, 122.64, 122.51, 120.94, 120.49, 118.89, 55.11, 52.43, 41.67, 30.12. IR (KBr, thin film) ν_{max} (cm^{-1}): 3648 (NH_2), 3620 (NH), 3610 (NH), 3475 (NH), 1745 (CO), 1681 (CO), 1620 (CO), 1578 (CO). HRMS-ESI (*m/z*): $[M+H]^+$ calculated for $C_{20}H_{20}N_4O_5S$, 429.1227; found 429.1215.

Compound **2** was obtained through same sequence of steps but starting from acridone **14** (X =H) (Scheme S1). (850 mg, 81%), mp 175 °C, $[\alpha]_D$ -8° (c 1.00, MeOH). ^{1}H NMR (500 MHz, DMSO-d_6, δ): 3.73 (s, OCH_3, 3H), 3.97-4.20 (m, CH_2, 2H), 4.12-4.16 (m, CH_2, 2H), 4.78-4.83 (m, CH, 1H), 7.41-7.44 (m, Ar H, 2H), 7.71-7.75 (m, Ar H, 2H), 8.23-8.44 (m, Ar H, 3H), 8.53 (br, NH, 1H), 9.50 (br, NH, 1H), 12.14 (br, NH, 1H). ^{13}C NMR (125 MHz, DMSO-d_6, δ): 181.32, 177.15, 170.63, 168.65, 140.82, 134.52, 133.67, 131.18, 126.33, 122.53, 122.62, 120.93, 120.52, 118.87, 55.12, 52.42, 41.64, 29.05. IR (KBr, thin film) ν_{max} (cm^{-1}): 3635 (NH), 3615 (NH), 3465 (NH), 1735 (CO), 1662 (CO), 1625 (CO), 1567 (CO). HRMS-ESI (*m/z*): $[M+H]^+$ calculated for $C_{20}H_{19}N_3O_5S$, 414.1118; found 414.1120.



Scheme S1. Synthesis of compound **1** – **3**.

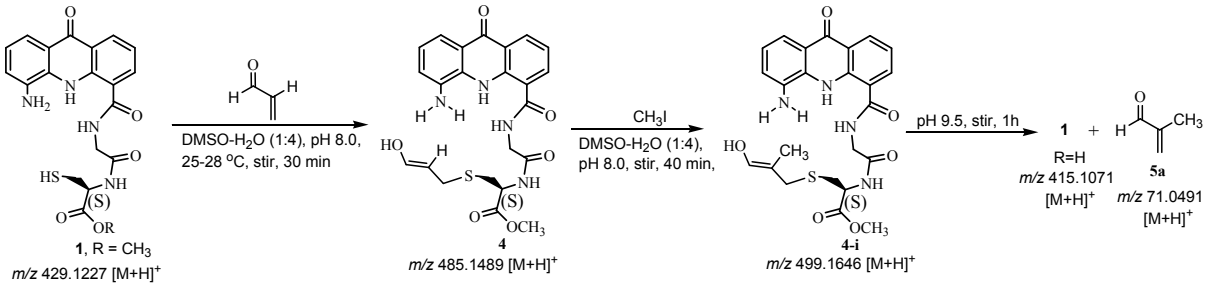
General Procedure. Reaction of compound 1 with α, β-unsaturated carbonyl compound, alkylation of the adduct and release of the product.

(i) Solution of compound **1** and α, β-unsaturated carbonyl compound (1.2 equiv) in 30-50 ml DMSO-distilled H_2O (1:4, v/v) having pH 7.0 was stirred at 25-28 ^oC. Mass spectrum of the reaction mixture showed a new peak corresponding to *m/z* of **1** – **α, β-unsaturated carbonyl compound** adduct but there was no new spot on the thin layer chromatographic (TLC) plate. On changing the pH of the reaction mixture to 8.0, a new spot was observed on TLC plate and the peak corresponding to *m/z* of **1** – **α, β-unsaturated carbonyl compound** adduct was intensified indicating the formation of a covalent adduct (as **4**/**7**).

(ii) Alkylating/acylating agent (1.5 equiv) was added to the above reaction mixture containing adduct of **1** – **α, β-unsaturated carbonyl compound** at pH 8.0 and stirred for 40 min at 25 – 28 ^oC. A new peak developed in the mass spectrum which was indicating the introduction of alkyl/acyl group to the adduct (as **4i-xv**/**7i-iv**).

(iii) After the alkylation/acylation in step ii, pH of the reaction mixture was changed to 9.5 (using 0.1 N NaOH). Within 1h of stirring the reaction mixture, compound **1** (R=H) was formed along with the formation of a new product (HRMS). The reaction mixture was purified through flash chromatography using ethyl acetate – hexane – petroleum ether as eluent to obtain compound **1** (R=H) (75-80%) and the product. Most of the products were obtained as transparent oil after the removal of the organic solvent at low temperature (30 – 40 ^oC). All the oily products were stored in the form of their chloroform/hexane solutions.

2-Methylpropenal (5a).



General procedure was performed on a 5 mmol scale with reagent **1** (R=CH_3) and acrolein in 50 mL of DMSO-H_2O (1:4, v/v) with stirring at 25 – 28 °C keeping the pH of the reaction mixture 8.0 for 30 min (formation of **4**, Figure S4). Then CH_3I was added and the reaction mixture was further stirred for 40 min (formation of **4-i**, Figure S5). Then pH of the reaction mixture was changed to 9.5. After stirring the reaction mixture for 1h, formation of **1** (R=H) and product **5a** was detected (Figure S6). The reaction mixture was washed with $CHCl_3$ (5x25 mL). Chloroform was removed slowly at 40 – 45 °C. The crude residue was purified by flash chromatography to furnish the title compound as a transparent oil (295 mg, 4 mmol, 84%). ^{1}H NMR (500 MHz, $CDCl_3$): δ 2.30 (s, 3H, CH_3), 6.13 (d, *J* =1.2 Hz, 1H, CH_2), 6.14 (d, *J* = 1.2 Hz, 1H, CH_2), 9.76 (s, 1H, CHO). ^{13}C NMR (125 MHz, $CDCl_3$): δ 18.21, 134.43, 143.55, 193.84. HRMS-ESI (*m/z*) found $[M+H]^+$ 71.0485, C_4H_6O requires 71.0491.

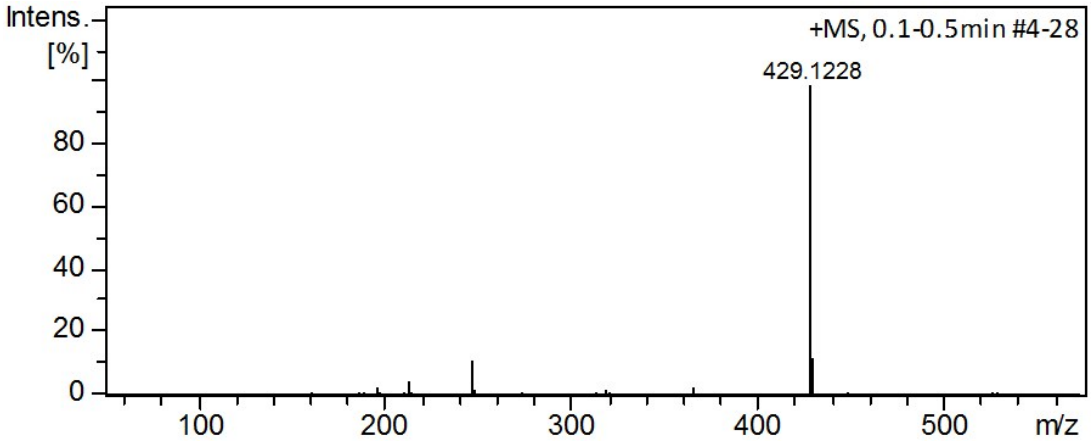


Figure S1. HRMS of reagent **1** (R=CH_3). Peak at *m/z* 429.1228 is corresponding to *m/z* of [**1**+H]$^+$ (calcd *m/z* 429.1224 $[M+H]^+$).

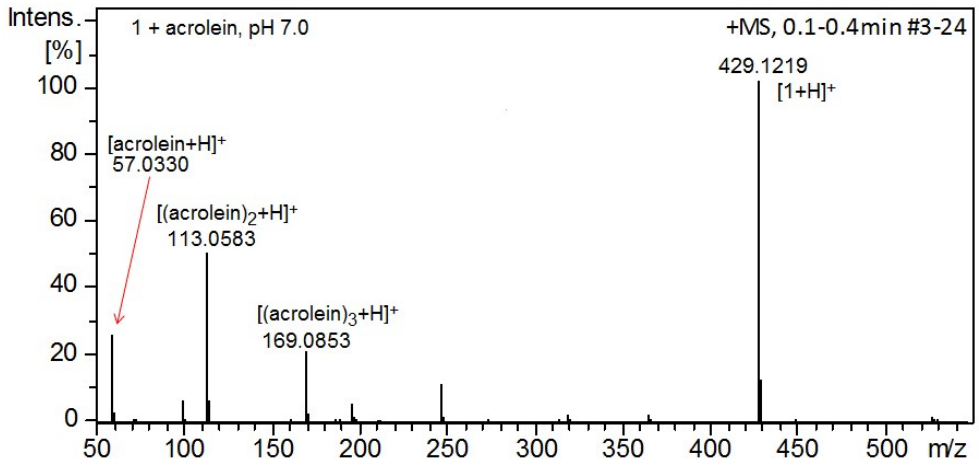


Figure S2. HRMS of **1**+acrolein reaction mixture at pH 7.0.

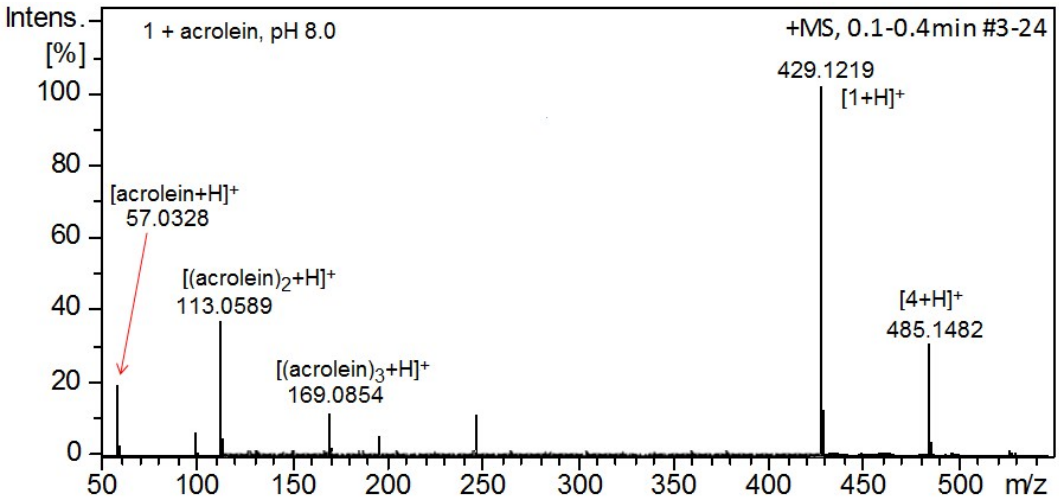


Figure S3. HRMS of the reaction mixture of reagent **1** and acrolein after 10 min of stirring at pH 8.0.

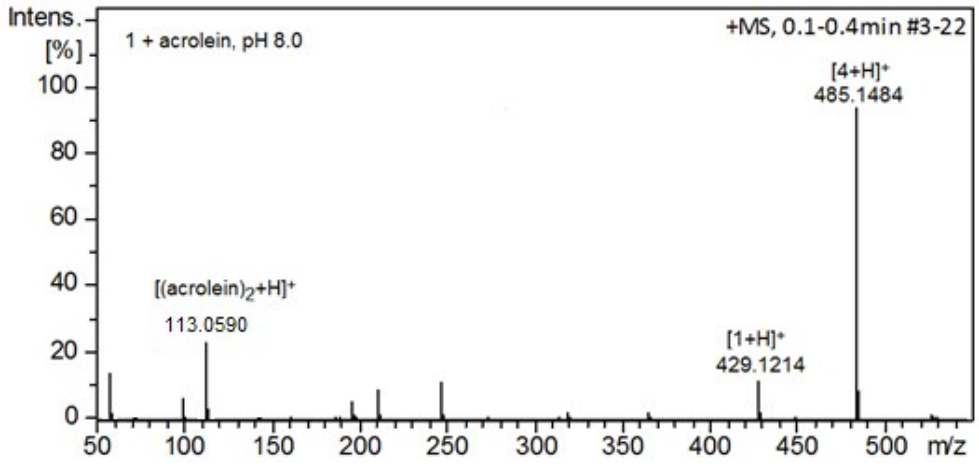


Figure S4. HRMS of the reaction mixture of reagent **1** and acrolein after 30 min of stirring at pH 8.0. Base peak was corresponding to *m/z* of adduct **4** (calcd *m/z* 485.1489 $[M+H]^+$).

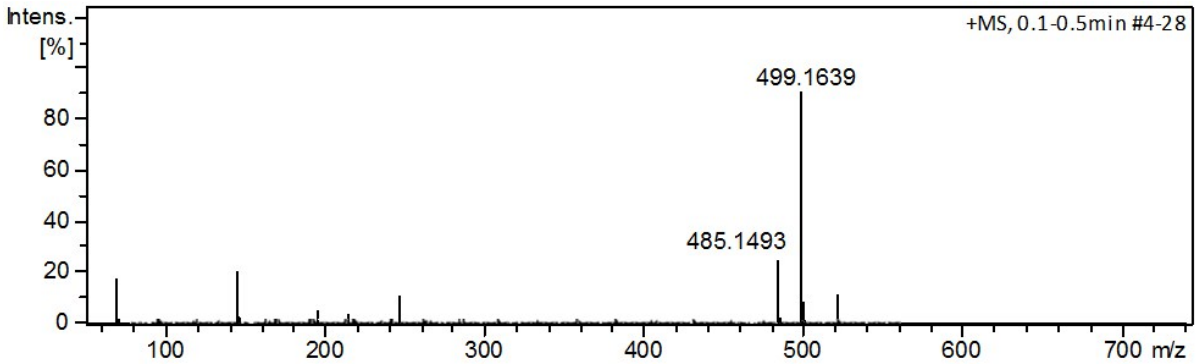


Figure S5. HRMS of the reaction mixture after the addition of CH_3I. pH of the reaction mixture was 8.0. The peak at *m/z* 499.1639 corresponds to mass of species **4-i** (calcd *m/z* 499.1646 $[M+H]^+$).

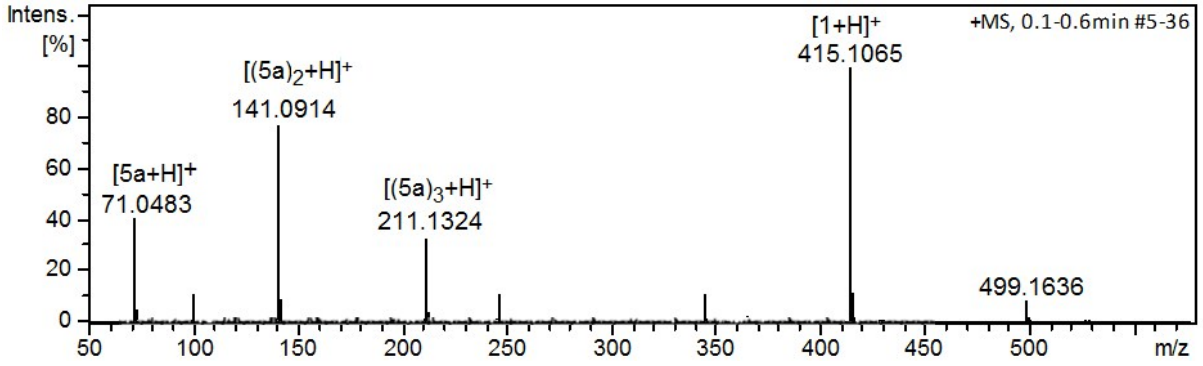
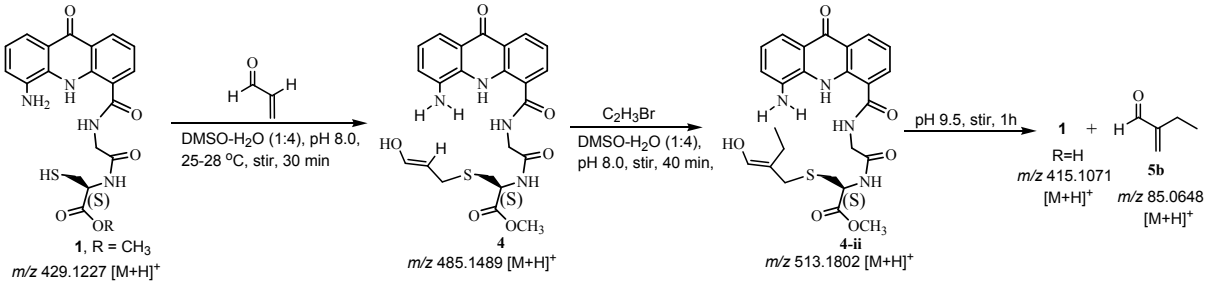


Figure S6. HRMS of the reaction mixture of **1** + acrolein after the addition of CH_3I and change of pH from 8.0 to 9.5 (1h stirring at room temperature). The peaks at *m/z* 71.0483, 141.0914 and 211.1324 clearly indicate the formation of product **5a**, the respective calcd *m/z* is 71.0491, 141.0910 and 211.1329. Reagent **1** (R=H) was also formed (calcd *m/z* 415.1071 $[M+H]^+$).

2-Methylenebutyraldehyde (5b).



General procedure was performed on a 2 mmol scale with reagent **1** (R=CH_3) and acrolein in 30 mL of DMSO-H_2O (1:4, v/v) with stirring at 25 – 28 °C keeping the pH of the reaction mixture 8.0 for 30 min. Then C_2H_5Br was added and the reaction mixture was further stirred for 40 min (Figure S7). Then pH of the reaction mixture was changed to 9.5. After stirring the reaction mixture for 1h, formation of **1** (R=H) and product **5b** was detected (Figure S8). The reaction mixture was washed with $CHCl_3$ (5x25 mL). Chloroform was removed slowly at 40 – 45 °C. The crude residue was purified by flash chromatography to furnish the title compound as a transparent oil (127 mg, 1.5 mmol, 77%). ^{1}H NMR (500 MHz, $CDCl_3$): δ 1.22 (t, *J* = 7.8 Hz, 3H, CH_3), 2.43 (q, J = 7.8 Hz, 2H, CH_2), 6.14 (d, *J*=1.2 Hz, 1H, CH_2), 6.16 (d, *J*=1.2 Hz, 1H, CH_2), 9.81 (s, 1H, CHO). ^{13}C NMR (125 MHz, $CDCl_3$): δ 15.70, 22.33, 135.14, 145.15, 192.84. HRMS-ESI (*m/z*) found $[M+H]^+$ 85.0640, C_5H_8O requires 85.0648.

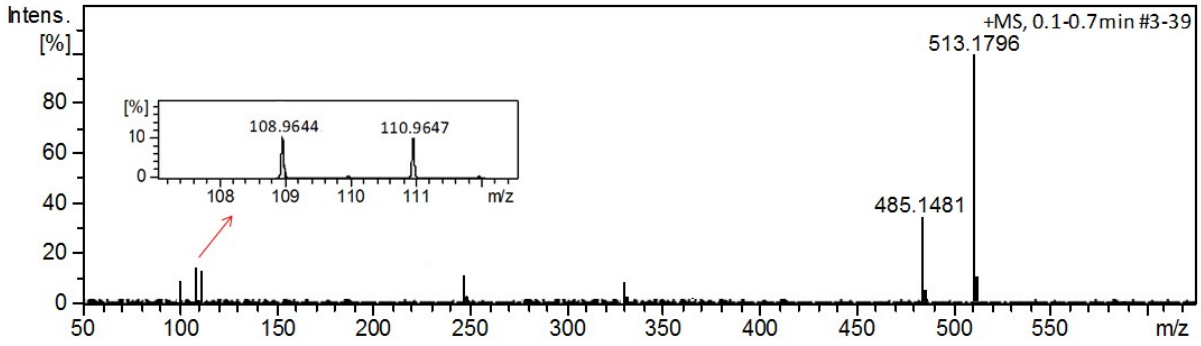


Figure S7. HRMS of the reaction mixture of **4** and ethyl bromide at pH 8.0.

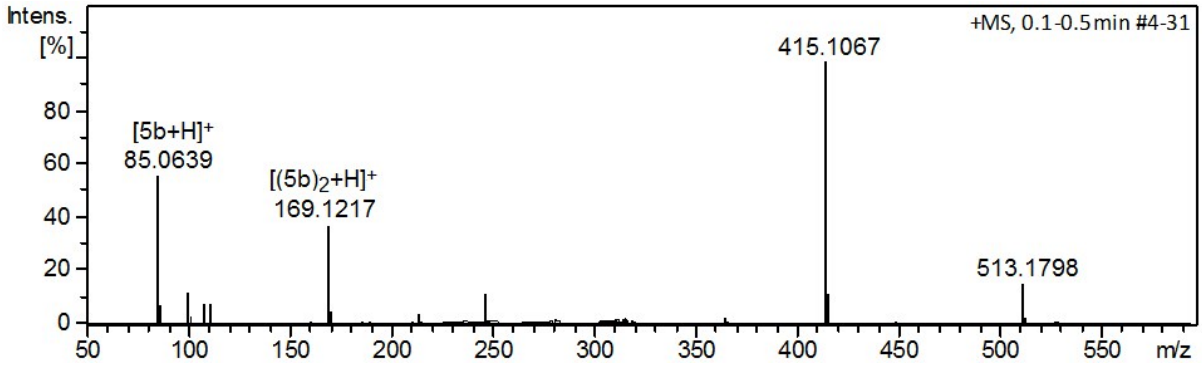
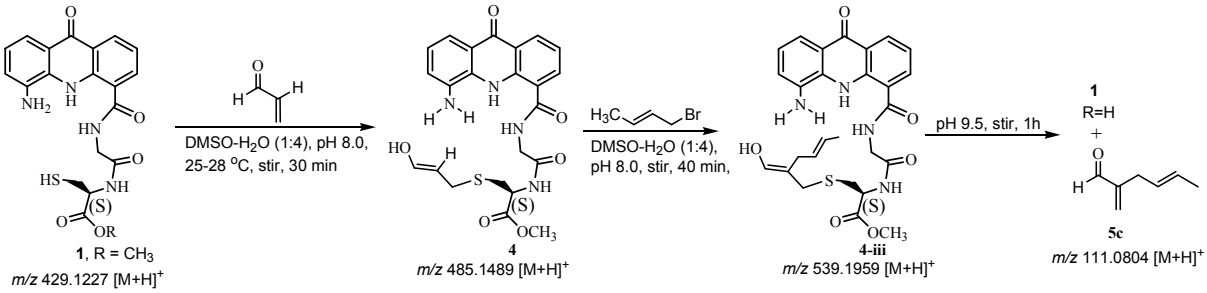


Figure S8. HRMS of the reaction mixture of **4** and ethyl bromide at pH 9.5, after stirring for 1h. Peak at 513.1798 corresponds to *m/z* of species **4-ii** (calcd *m/z* 513.1802 $[M+H]^+$).

2-Methylenehex-4-enal (5c).



General procedure was performed on a 2 mmol scale with reagent **1** (R=CH_3) and acrolein in 30 mL of DMSO-H_2O (1:4, v/v) with stirring at 25 – 28 °C keeping the pH of the reaction mixture 8.0 for 30 min. Then crotyl bromide was added and the reaction mixture was further stirred for 40 min. Then pH of the reaction mixture was changed to 9.5. After stirring the

reaction mixture for 1h, formation of product **5c** and reagent **1** (R=H) was observed (Figure S9). The reaction mixture was washed with $CHCl_3$ (5x25 mL). Chloroform was removed slowly at 40 – 45 ^oC. The crude residue was purified by flash chromatography to furnish the title compound as a transparent oil (178 mg, 1.6 mmol, 80%). ^1H NMR (500 MHz, $CDCl_3$): δ 2.13 (d, *J*=8.5 Hz, 3H, CH_3), 2.73 (d, *J*=8.2 Hz, 2H, CH_2), 5.37-5.42 (m, 1H, CH), 5.46-5.52 (m, 1H, CH), 6.13 (d, *J* = 1.2 Hz, 1H, CH_2), 6.14 (d, *J* = 1.2 Hz, 1H, CH_2), 9.85 (s, 1H, CHO). ^{13}C NMR (125 MHz, $CDCl_3$): δ 19.20, 36.36, 124.76, 125.11, 134.31, 140.31, 193.29. HRMS-ESI (*m/z*) found $[M+H]^+$ 111.0799, $C_7H_{10}O$ requires 111.0804.

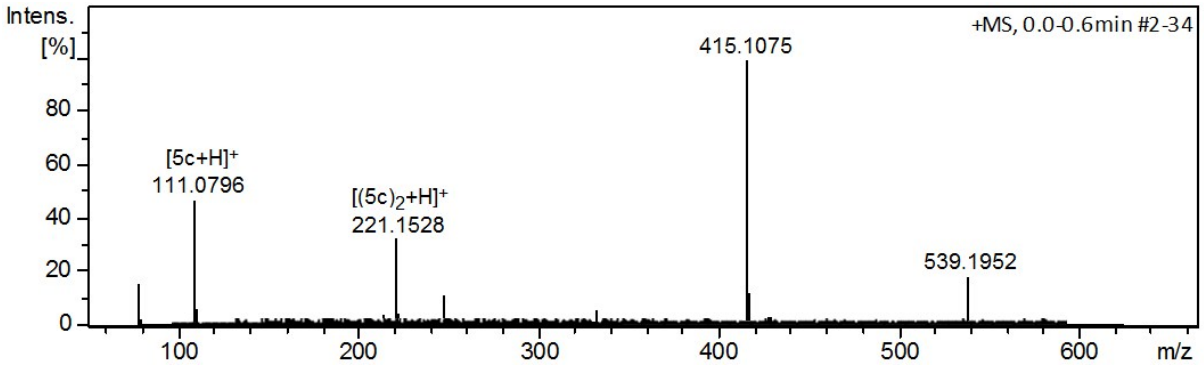
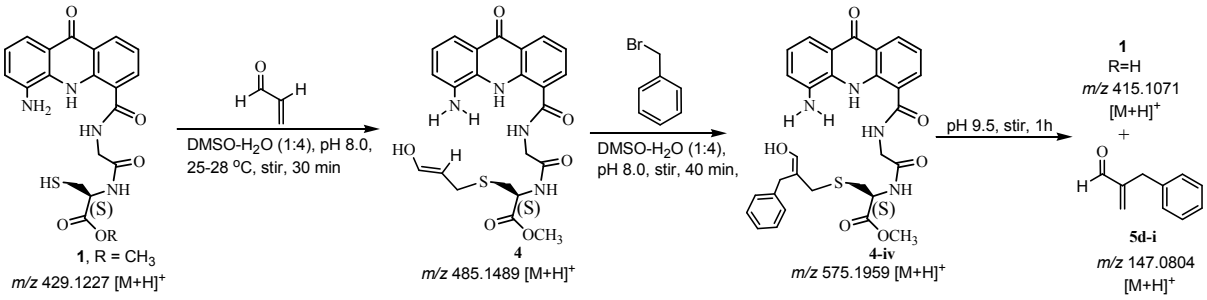


Figure S9. HRMS of the reaction mixture of **4** and crotyl bromide at pH 9.5, after stirring for 1h. Peak at *m/z* 539.1952 corresponds to *m/z* of species **4-iii** (calcd *m/z* 539.1959 $[M+H]^+$). Peak at 111.0796 and 221.1528 correspond to mass of product **5c**, monomer and dimer, respectively (calcd *m/z* 111.0804 and 221.1536 $[M+H]^+$).

2-Benzylpropenal (5d-i).



General procedure was performed on a 1 mmol scale with reagent **1** and acrolein in 20 mL of DMSO-H_2O (1:4, v/v) with stirring at 25 – 28 ^oC keeping the pH of the reaction mixture 8.0 for 30 min. Then benzyl bromide was added and the reaction mixture was further stirred for 40 min. Then the pH of the reaction mixture was changed to 9.5 and after stirring for 1h,

formation of product **5d-i** and reagent **1** (R=H) was detected (Figure S10). The reaction mixture was washed with $CHCl_3$ (5x25 mL). Chloroform was removed slowly at 40 – 45 °C. The crude residue was purified by flash chromatography to furnish the title compound as a transparent oil (105 mg, 0.7 mmol, 70%). ^{1}H NMR (500 MHz, $CDCl_3$): δ 3.53 (s, 2H, CH_2), 6.13 (d, *J* = 1.1 Hz, 1H, CH_2), 6.14 (d, *J* = 1.1 Hz, 1H, CH_2), 7.12-7.22 (m, 2H, ArH), 7.24-7.25 (m, 1H, ArH), 7.48-7.49 (m, 2H, ArH), 9.84 (s, 1H, CHO). ^{13}C NMR (125 MHz, $CDCl_3$): δ 32.07, 125.32, 126.34, 128.51, 129.23, 129.25, 140.23, 143.34, 194.67. HRMS-ESI (*m/z*) found $[M+H]^+$ 147.0801, $C_{10}H_{10}O$ requires 147.0804.

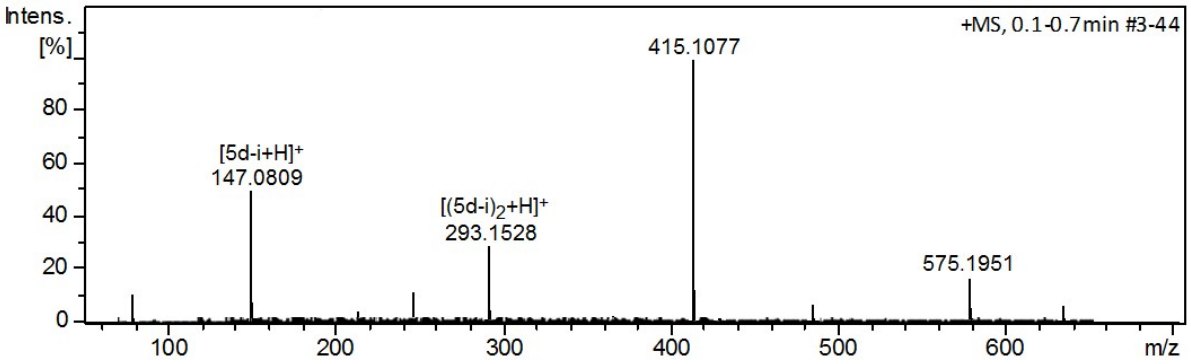
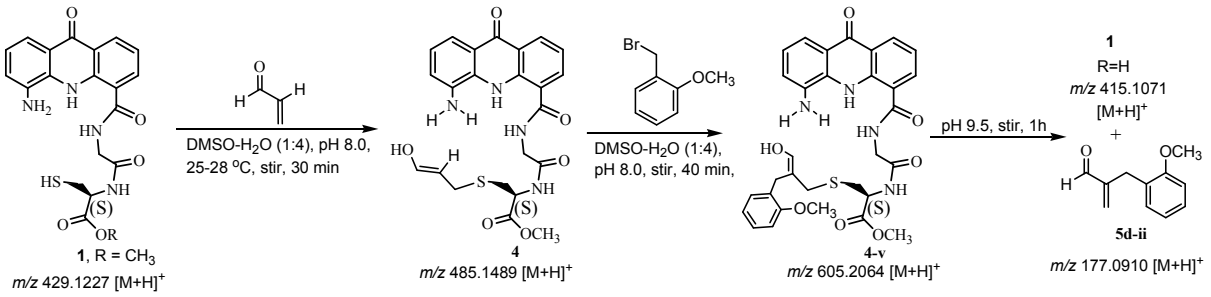


Figure S10. HRMS of the reaction mixture of **4** and benzyl bromide at pH 9.5, after stirring for 1h. Peak at *m/z* 575.1951 corresponds to *m/z* of **4-iv** (calcd *m/z* 575.1959 $[M+H]^+$). Peak at 147.0809 and 293.1528 correspond to mass of product **5d-i**, monomer and dimer, respectively (calcd *m/z* 147.0804 and 293.1536 $[M+H]^+$).

2-(2-Methoxybenzyl)-propenal (5d-ii).



General procedure was performed on a 1 mmol scale with reagent **1** and acrolein in 20 mL of DMSO-H_2O (1:4, v/v) with stirring at 25 – 28 °C keeping the pH of the reaction mixture 8.0 for 30 min. Then 2-methoxybenzyl bromide was added and the reaction mixture was further

stirred for 40 min. Then pH of the reaction mixture was changed to 9.5 and after 1h of stirring, formation of **5d-ii** and **1** (R=H) was observed (Figure S11). The reaction mixture was washed with $CHCl_3$ (5x25 mL). Chloroform was removed slowly at 40 – 45 ^oC. The crude residue was purified by flash chromatography to furnish the title compound as a transparent oil (142 mg, 0.8 mmol, 82%). ^1H NMR (500 MHz, $CDCl_3$): δ 3.55 (s, 2H, CH_2), 3.98 (s, 3H, OCH_3), 6.12 (d, *J* = 1.2 Hz, 1H, CH_2), 6.15 (d, *J* = 1.2 Hz, 1H, CH_2), 6.64-6.65 (m, 2H, ArH), 6.90-7.12 (m, 1H, ArH), 7.14-7.21 (m, 1H, ArH), 9.86 (s, 1H, CHO). ^{13}C NMR (125 MHz, $CDCl_3$): δ 33.19, 53.23, 114.67, 125.32, 126.23, 128.51, 129.23, 129.25, 141.67, 155.21, 194.67. HRMS-ESI (*m/z*) found $[M+H]^+$ 177.0901, $C_{11}H_{12}O_2$ requires 177.0910.

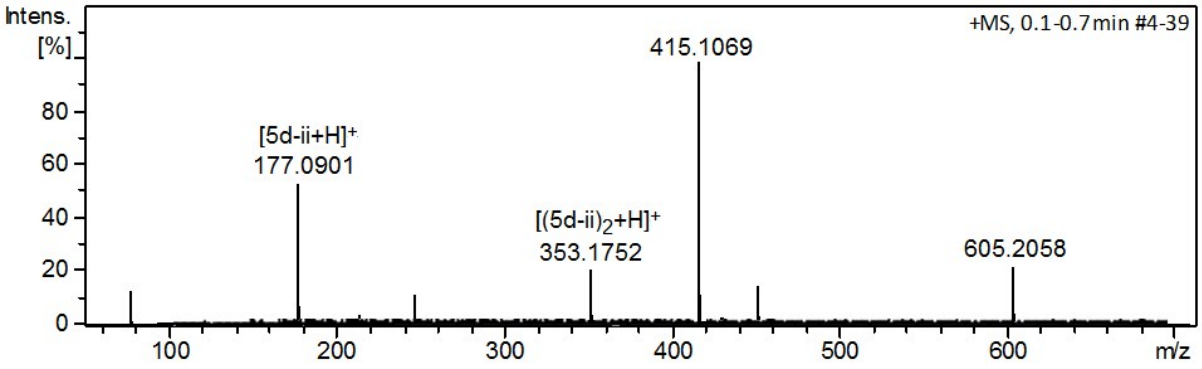
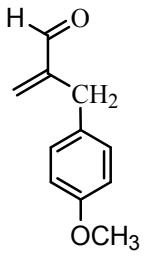


Figure S11. HRMS of the reaction mixture of **4** and 2-methoxybenzyl bromide at pH 9.5, after stirring for 1h. Peak at *m/z* 605.2058 corresponds to **4-v** (calcd *m/z* 605.2064 $[M+H]^+$). Peak at 177.0901 and 353.1752 correspond to mass of product **5d-ii**, monomer and dimer, respectively (calcd *m/z* 177.0910 and 353.1747 $[M+H]^+$).

2-(4-Methoxybenzyl)-propenal (5d-iii).

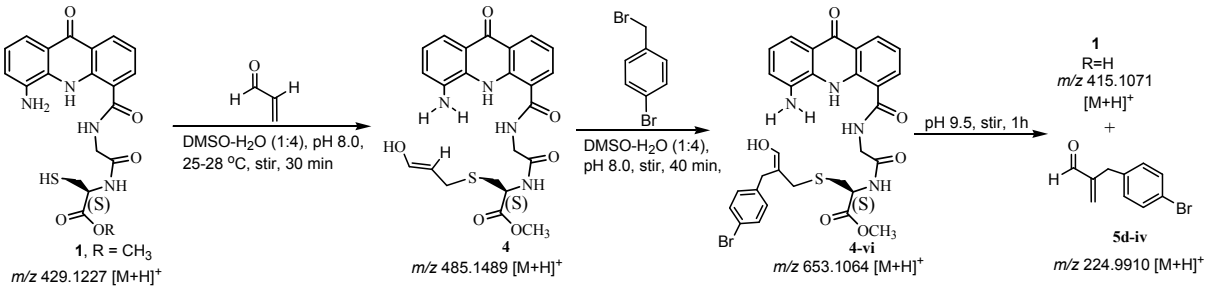


General procedure was performed on a 1 mmol scale with reagent **1** and acrolein in 20 mL of DMSO-H_2O (1:4, v/v) with stirring at 25 – 28 ^oC keeping the pH of the reaction mixture 8.0 for 30 min. Then 4-methoxybenzyl bromide was added and the reaction mixture was further stirred for 40 min. Then pH of the reaction mixture was changed to 9.5 and after 1h of

stirring, formation of the product **5d-iii** and **1** (R=H) was observed. The reaction mixture was washed with $CHCl_3$ (5x25 mL). Chloroform was removed slowly at 40 – 45 ^oC. The crude residue was purified by flash chromatography to furnish the title compound as a transparent oil (150 mg, 0.85 mmol, 85%). ^1H NMR[1] ($CDCl_3$): δ 3.56 (s, 2H, CH_2), 3.98 (s, 3H, OCH_3), 6.12 (d, 1H, *J* = 1.2 Hz, CH_2), 6.15 (d, 1H, *J* = 1.2 Hz, CH_2), 6.64 (d, *J* = 7.5 Hz, 2H, ArH), 6.90 (d, *J* = 7.5 Hz, 2H, ArH), 9.86 (s, 1H, CHO). ^{13}C NMR (125 MHz, $CDCl_3$): δ 32.12, 52.23, 113.52, 125.78, 126.78, 128.51, 130.23, 130.25, 141.72, 155.32, 194.48. HRMS-ESI (*m/z*) found $[M+H]^+$ 177.0895, $C_{11}H_{12}O_2$ requires 177.0910.

1. C. N. Cona, C. V. Ramana, *Chem. Commun*, 2014, **50**, 2152-2154.

2-(4-Bromobenzyl)-propenal (5d-iv).



General procedure was performed on a 1 mmol scale with reagent **1** and acrolein in 20 mL of DMSO-H_2O (1:4, v/v) with stirring at 25 – 28 ^oC keeping the pH of the reaction mixture 8.0 for 30 min. Then 4-bromobenzyl bromide was added and the reaction mixture was further stirred for 40 min. Then pH of the reaction mixture was changed to 9.5 and formation of product **5d-iv** and **1** (R=H) was detected after 1h of stirring (Figure S12). The reaction mixture was washed with $CHCl_3$ (5x25 mL). Chloroform was removed slowly at 40 – 45 ^oC. The crude residue was purified by flash chromatography to furnish the title compound as a transparent oil (190 mg, 0.85 mmol, 87%). ^1H NMR (500 MHz, $CDCl_3$): δ 3.53 (s, 2H, CH_2), 6.13 (d, *J* = 1.2 Hz, 1H, CH_2), 6.14 (d, *J* = 1.2 Hz, 1H, CH_2), 7.19 (d, *J* = 7.5 Hz, 2H, ArH), 7.79 (d, *J* = 7.3 Hz, 2H, ArH), 9.85 (s, 1H, CHO). ^{13}C NMR (125 MHz, $CDCl_3$): δ 34.01, 118.29, 124.93, 126.78, 130.33, 130.75, 137.06, 144.68, 194.97. HRMS-ESI (*m/z*) found $[M+H]^+$ 224.9901, $C_{10}H_9OBr$ requires 224.9910.

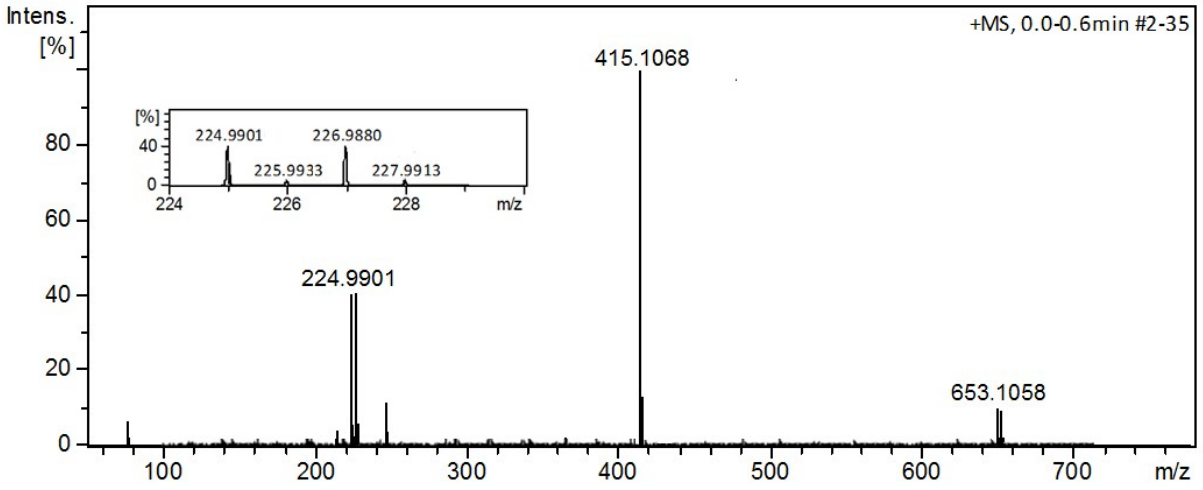
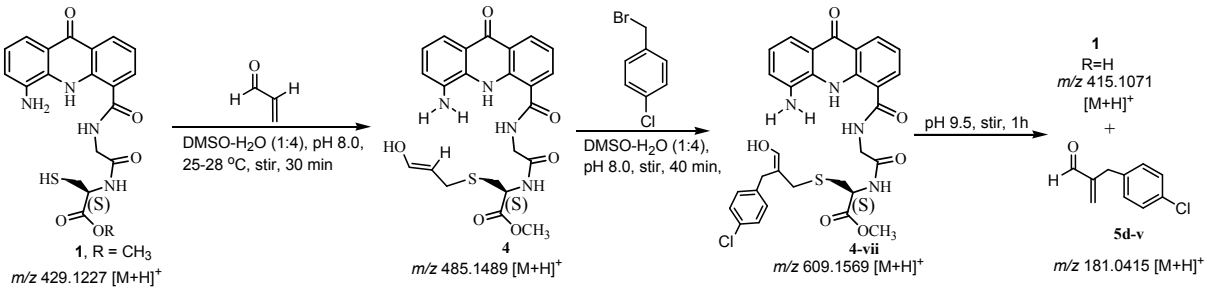


Figure S12. HRMS of the reaction mixture of **4** and 4-bromobenzyl bromide at pH 9.5, after stirring for 1h. Peak at *m/z* 653.1058 corresponds to species **4-vi** (calcd *m/z* 653.1064 $[M+H]^+$). Peak at 224.9901 corresponds to mass of product **5d-iv** (calcd *m/z* 224.9910 $[M+H]^+$).

2-(4-Chlorobenzyl)-propenal (5d-v).



General procedure was performed on a 1 mmol scale with reagent **1** and acrolein in 20 mL of DMSO-H_2O (1:4, v/v) with stirring at 25 – 28 °C keeping the pH of the reaction mixture 8.0 for 30 min. Then 4-chlorobenzyl bromide was added and the reaction mixture was further stirred for 40 min. Then pH of the reaction mixture was changed to 9.5 and product **5d-v** and reagent **1** (R=H) were formed after 1h of stirring (Figure S13). The reaction mixture was washed with $CHCl_3$ (5x25 mL). Chloroform was removed slowly at 40 – 45 °C. The crude residue was purified by flash chromatography to furnish the title compound as a transparent oil (152 mg, 0.85 mmol, 88%). ^{1}H NMR ($CDCl_3$): δ 3.54 (s, 2H, CH_2), 6.13 (d, *J* = 1.2 Hz, 1H, CH_2), 6.14 (d, *J* = 1.2 Hz, 1H, CH_2), 7.29 (d, *J* = 7.5 Hz, 2H, ArH), 7.49 (d, *J* = 7.5 Hz,

2H, ArH), 9.84 (s, 1H, CHO). ^{13}C NMR (125 MHz, $CDCl_3$): δ 35.14, 125.39, 126.91, 129.63, 130.46, 130.88, 137.19, 144.81, 194.10. HRMS-ESI (*m/z*) found $[M+H]^+$ 181.0407, $C_{10}H_9OCl$ requires 181.0415.

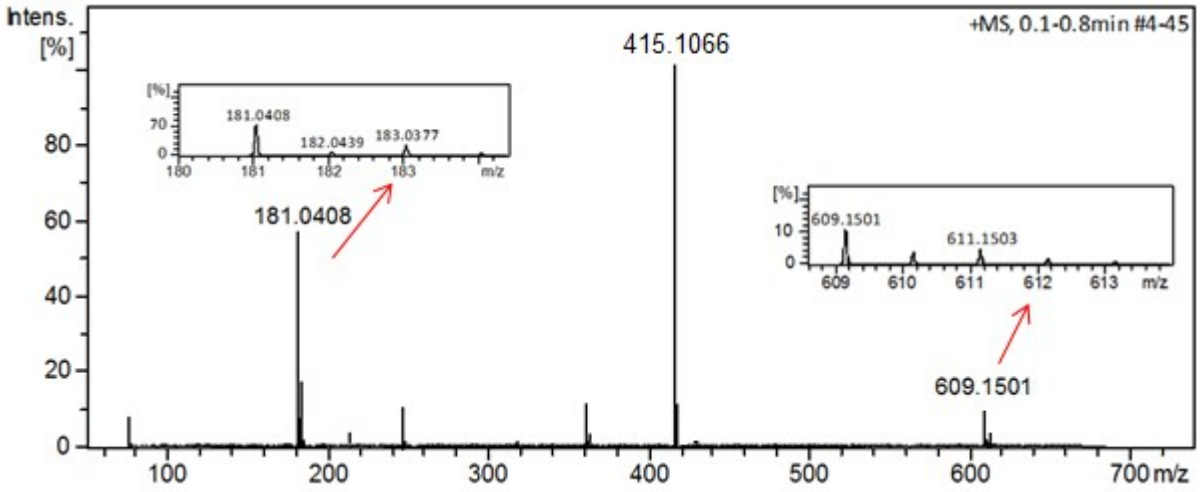
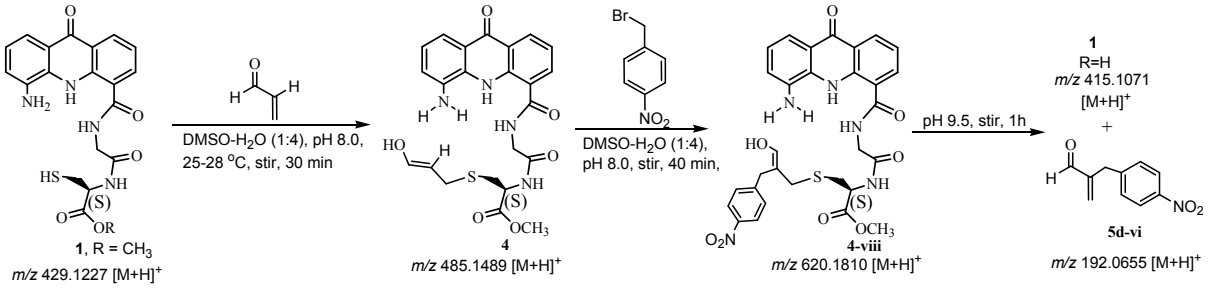


Figure S13. HRMS of the reaction mixture of **4** and 4-chlorobenzyl bromide at pH 9.5, after stirring for 1h. Peak at *m/z* 609.1501 corresponds to species **4d-vii** (calcd *m/z* 609.1569 $[M+H]^+$). Peak at 181.0408 corresponds to mass of product **5d-v** (calcd *m/z* 181.0415 $[M+H]^+$).

2-(4-Nitrobenzyl)-propenal (5d-vi).



General procedure was performed on a 1 mmol scale with reagent **1** and acrolein in 20 mL of DMSO-H_2O (1:4, v/v) with stirring at 25 – 28 °C keeping the pH of the reaction mixture 8.0 for 30 min. Then 4-nitrobenzyl bromide was added and the reaction mixture was further stirred for 40 min. Then pH of the reaction mixture was changed to 9.5 and formation of **5d-vi** and **1** (R=H) was detected after 1h stirring (Figure S14). The reaction mixture was washed with $CHCl_3$ (5x25 mL). Chloroform was removed slowly at 40 – 45 °C. The crude residue

was purified by flash chromatography to furnish the title compound as a transparent oil (105 mg, 0.55 mmol, 55%). ^{1}H NMR (500 MHz, $CDCl_3$): δ 3.56 (s, 2H, CH_2), 6.13 (d, *J* = 1.3 Hz, 1H, CH_2), 6.14 (d, *J* = 1.3 Hz, 1H, CH_2), 7.55 (d, *J* = 7.8 Hz, 2H, ArH), 8.20 (d, *J* = 7.8 Hz, 2H, ArH), 9.85 (s, 1H, CHO). ^{13}C NMR (125 MHz, $CDCl_3$): δ 39.33, 124.97, 125.58, 127.10, 130.65. 131.07, 145.00, 148.49, 152.34, 194.29. HRMS-ESI (*m/z*) found $[M+H]^+$ 192.0648, $C_{10}H_9NO_3$ requires 192.0655.

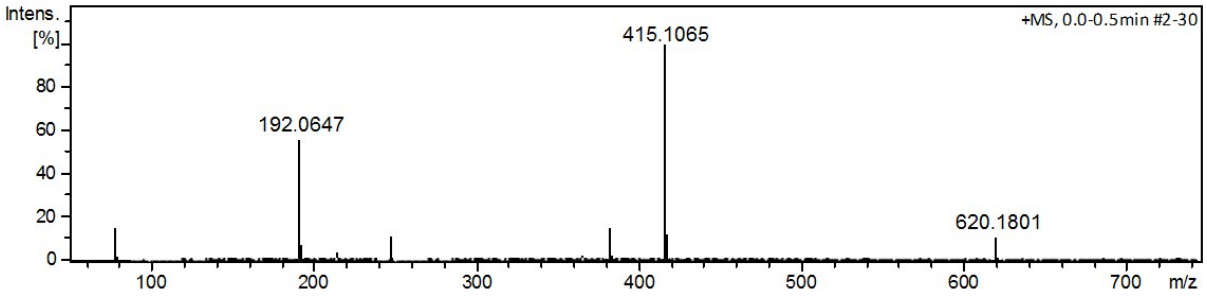
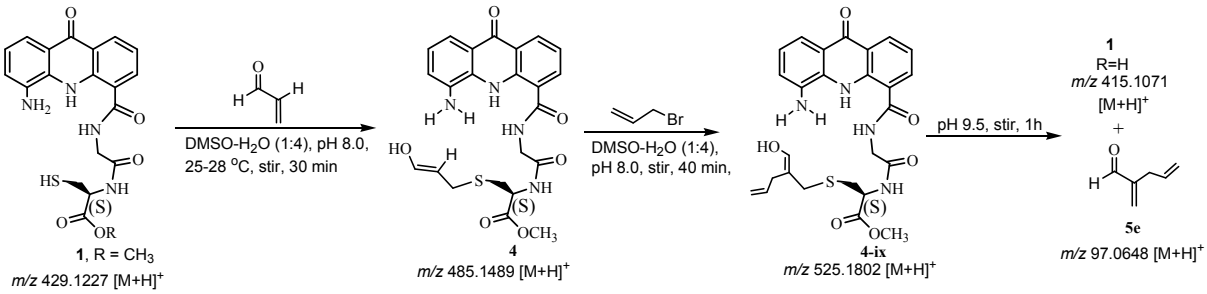


Figure S14. HRMS of the reaction mixture of **4** and 4-nitrobenzyl bromide at pH 9.5, after stirring for 1h. Peak at *m/z* 620.1801 corresponds to **4-viii** (calcd *m/z* 620.1810 $[M+H]^+$). Peak at 192.0647 corresponds to mass of product **5d-vi** (calcd *m/z* 192.0655 $[M+H]^+$).

2-Methylenepent-4-enal (5e).



General procedure was performed on a 1 mmol scale with reagent **1** and acrolein in 20 mL of DMSO-H_2O (1:4, v/v) with stirring at 25 – 28 °C keeping the pH of the reaction mixture 8.0 for 30 min. Then allyl bromide was added and the reaction mixture was further stirred for 40 min. The pH of the reaction mixture was changed to 9.5 and formation of **5e** and **1** (R=H) was detected after 1h of stirring (Figure S15). The reaction mixture was washed with $CHCl_3$ (5x25 mL). Chloroform was removed slowly at 40 – 45 °C. The crude residue was purified by

flash chromatography to furnish the title compound as a transparent oil (78 mg, 0.8 mmol, 82%). ^{1}H NMR[2] (500 MHz, $CDCl_3$): δ 2.58 (m, 2H, CH_2), 4.92-4.93 (m, 1H, CH_2), 4.95 (m, 1H, CH_2), 5.68 (m, 1H, CH), 6.12 (d, *J* =1.1 Hz, 1H, CH_2), 6.14 (d, *J* = 1.1 Hz, 1H, CH_2), 9.83 (s, 1H, CHO). ^{13}C NMR (125 MHz, $CDCl_3$): δ 37.34, 119.06, 129.34, 132.89, 148.01, 191.28. HRMS-ESI (*m/z*) found $[M+H]^+$ 97.0639, C_6H_8O requires 97.0648.

(2). E. Block, S. Ahmad, *J. Am. Chem. Soc*. 1985, **107**, 6731-6732.

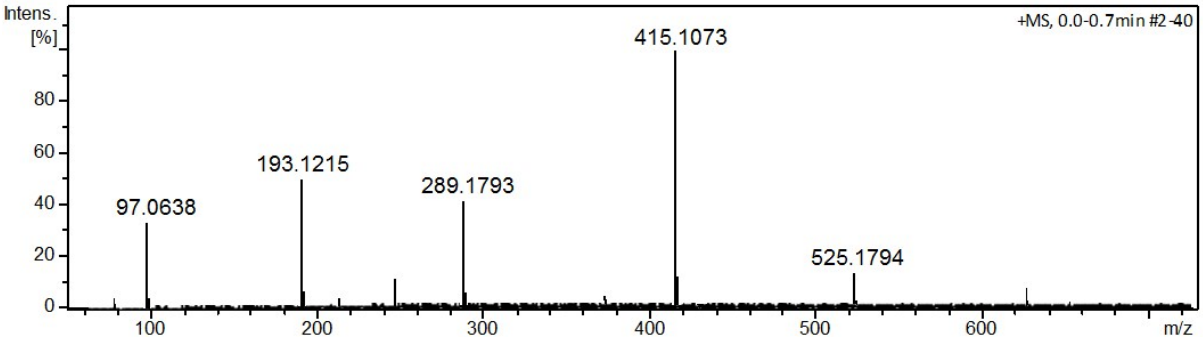
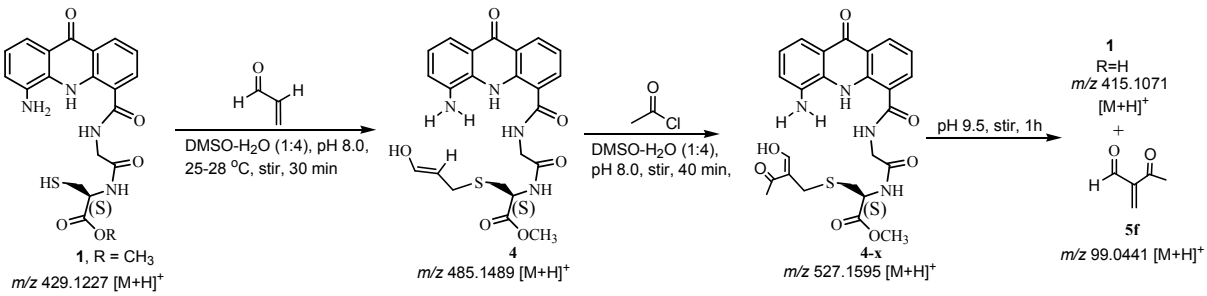


Figure S15. HRMS of the reaction mixture of **4** and allyl bromide at pH 9.5, after stirring for 1h. Peak at *m/z* 525.1794 corresponds to **4-ix** (calcd *m/z* 525.1802 $[M+H]^+$). Peak at 97.0638, 193.1215 and 289.1793 correspond to mass of monomer, dimer and trimer of product **5e** (calcd *m/z* 97.0648, 193.1223 and 289.1798 $[M+H]^+$).

2-Methylene-3-oxobutyraldehyde (5f).



General procedure was performed on a 1 mmol scale with reagent **1** and acrolein in 20 mL of DMSO-H_2O (1:4, v/v) with stirring at 25 – 28 °C keeping the pH of the reaction mixture 8.0 for 30 min. Then acetyl chloride was added and the reaction mixture was further stirred for 40 min. Then the pH of the reaction mixture was changed to 9.5 and formation of **5f** and **1** was observed after 1h of stirring (Figure S16). The reaction mixture was washed with $CHCl_3$ (5x25 mL). Chloroform was removed slowly at 40 – 45 °C. The crude residue was purified by

flash chromatography to furnish the title compound as a transparent oil (107 mg, 0.65 mmol, 67%). ^{1}H NMR (500 MHz, $CDCl_3$): δ 2.35 (s, 3H, CH_3), 6.13 (d, *J* = 1.1 Hz, 1H, CH), 6.14 (d, *J* = 1.1 Hz, 1H, CH), 10.10 (s, 1H, CHO). ^{13}C NMR (125 MHz, $CDCl_3$): δ 30.85, 142.51, 151.86, 190.81, 194.14. HRMS-ESI (*m/z*) found $[M+H]^+$ 99.0438, $C_5H_6O_2$ requires 99.0441.

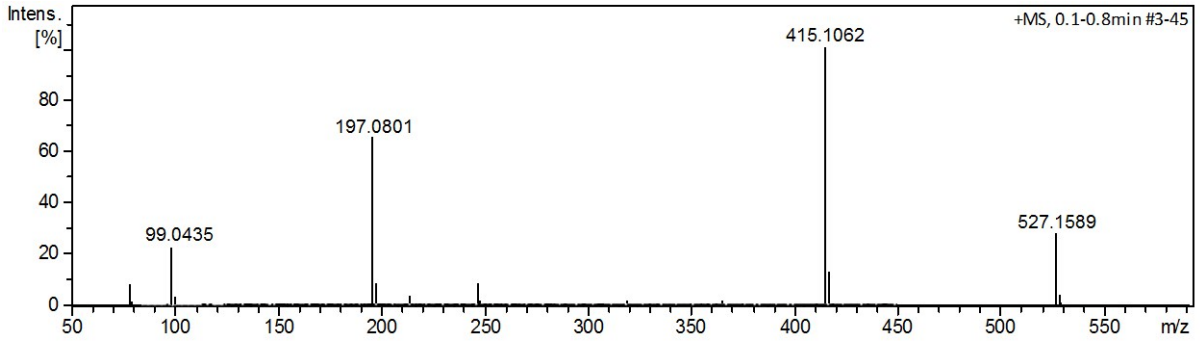
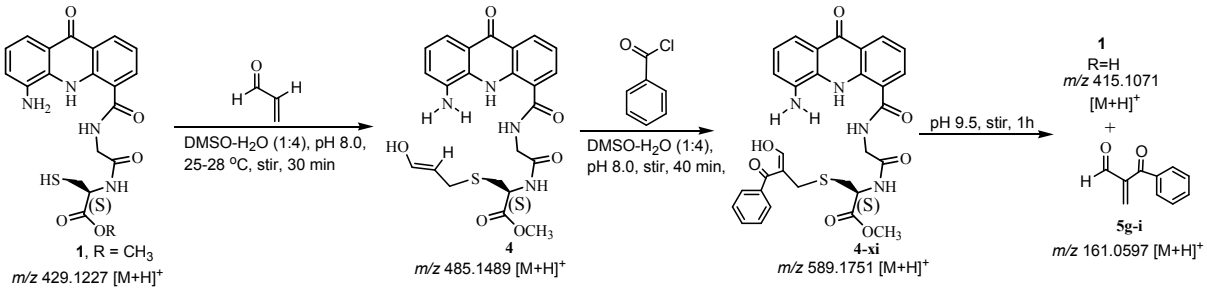


Figure S16. HRMS of the reaction mixture of **4** and acetyl chloride at pH 9.5, after stirring for 1h. Peak at *m/z* 527.1589 corresponds to species **4-x** (calcd *m/z* 527.1595 $[M+H]^+$). Peak at 99.0435 and 197.0801 correspond to mass of monomer and dimer of product **5f** (calcd *m/z* 99.0441 and 197.0808 $[M+H]^+$).

2-Benzoylpropenal (5g-i).



General procedure was performed on a 1 mmol scale with reagent **1** and acrolein in 20 mL of DMSO-H_2O (1:4, v/v) with stirring at 25 – 28 °C keeping the pH of the reaction mixture 8.0 for 30 min. Then benzoyl chloride was added and the reaction mixture was further stirred for 40 min. Then pH of the reaction mixture was changed to 9.5 and after 1h of stirring, formation of **5g-i** and reagent **1** (R=H) was observed (Figure S17). The reaction mixture was washed with $CHCl_3$ (5x25 mL). Chloroform was removed slowly at 40 – 45 °C. The crude residue was purified by flash chromatography to furnish the title compound as a transparent oil (96 mg, 0.6 mmol, 62%). ^{1}H NMR (500 MHz, $CDCl_3$): δ 6.12 (d, *J* = 1.1 Hz, 1H, CH_2),

6.14 (d, J = 1.1 Hz, 1H, CH_2), 7.70-7.73 (m, 2H, ArH), 8.08-8.16 (m, 2H, ArH), 8.57-8.70 (m, 1H, ArH), 10.24 (s, 1H, CHO). ^{13}C NMR (125 MHz, $CDCl_3$): δ 124.30, 124.90, 126.42, 129.14, 132.70, 136.70, 144.32, 147.82, 190.70, 196.61. HRMS-ESI (*m/z*) found $[M+H]^+$ 161.0590, $C_{10}H_8O_2$ requires 161.0597.

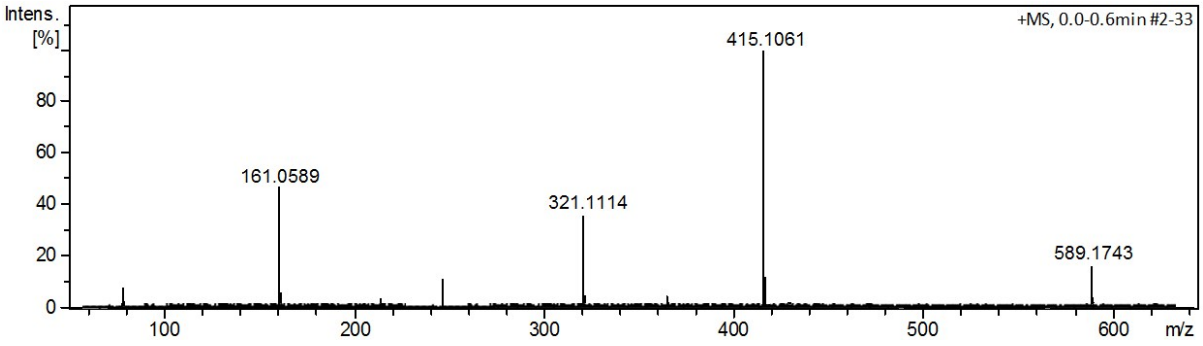
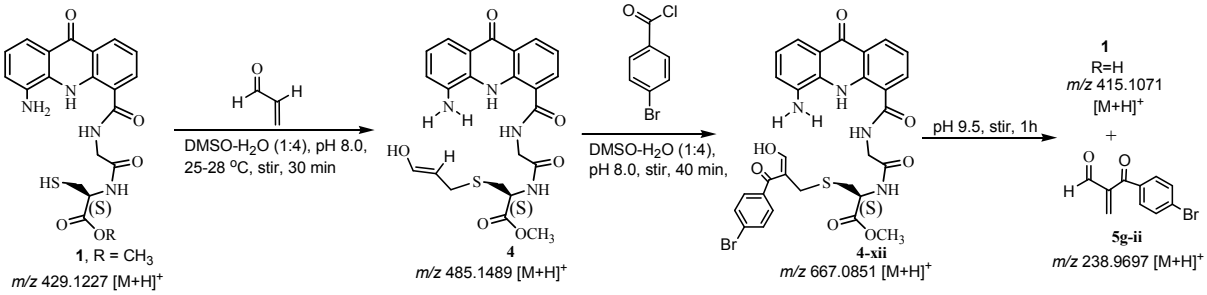


Figure S17. HRMS of the reaction mixture of **4** and benzoyl chloride at pH 9.5, after stirring for 1h. Peak at *m/z* 589.1743 corresponds to m/z of **4-xi** (calcd *m/z* 589.1751 $[M+H]^+$). Peak at 161.0589 and 321.1114 correspond to mass of monomer and dimer of product **5g-i** (calcd *m/z* 161.0597 and 321.1121 $[M+H]^+$).

2-(4-Bromobenzoyl)-propenal (5g-ii).



General procedure was performed on a 1 mmol scale with reagent **1** and acrolein in 20 mL of DMSO-H_2O (1:4, v/v) with stirring at 25 – 28 °C keeping the pH of the reaction mixture 8.0 for 30 min. Then 4-bromobenzoyl chloride was added and the reaction mixture was further stirred for 40 min. Then pH of the reaction mixture was changed to 9.5 and formation of **5g-ii** and **1** (R=H) was detected after 1h of stirring (Figure S18). The reaction mixture was washed with $CHCl_3$ (5x25 mL). Chloroform was removed slowly at 40 – 45 °C. The crude residue was purified by flash chromatography to furnish the title compound as a transparent oil (144

mg, 0.66 mmol, 66%). ^{1}H NMR (500 MHz, $CDCl_3$): δ 6.12 (d, J = 1.2 Hz, 1H, CH_2), 6.14 (d, J = 1.2 Hz, 1H, CH_2), 7.94 (d, J = 8.0 Hz, 2H, ArH), 8.37 (d, J = 8.0 Hz, 2H, ArH), 10.24 (s, 1H, CHO). ^{13}C NMR (125 MHz, $CDCl_3$): δ 126.35, 129.07, 129.90, 130.33, 132.63, 136.63, 147.75, 151.59, 190.75, 192.54. HRMS-ESI (*m/z*) found $[M+H]^+$ 238.9695, $C_{10}H_7O_2Br$ requires 238.9703.

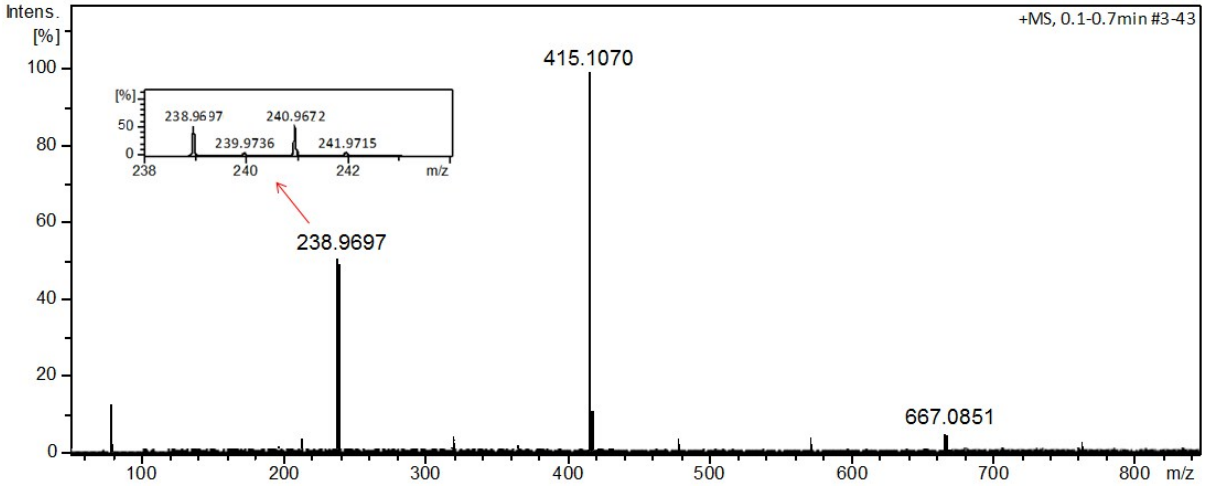
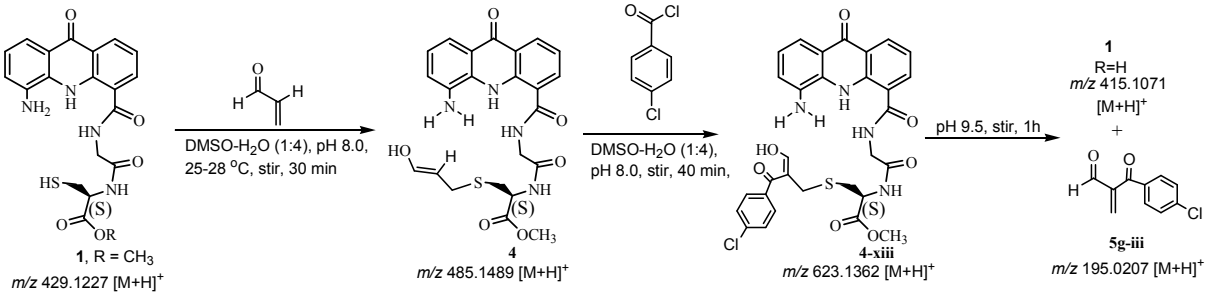


Figure S18. HRMS of the reaction mixture of **4** and 4-bromobenzoyl chloride at pH 9.5, after stirring for 1h. Peak at *m/z* 667.0851 corresponds to m/z of species **4-xii** (calcd *m/z* 667.0851 $[M+H]^+$). Peak at 238.9697 corresponds to mass of product **5g-ii** (calcd *m/z* 238.9702 $[M+H]^+$).

2-(4-Chlorobenzoyl)-propenal (5g-iii).



General procedure was performed on a 1 mmol scale with reagent **1** and acrolein in 20 mL of DMSO-H_2O (1:4, v/v) with stirring at 25 – 28 °C keeping the pH of the reaction mixture 8.0 for 30 min. Then 4-chlorobenzoyl chloride was added and the reaction mixture was further

stirred for 40 min. Then pH of the reaction mixture was changed to 9.5 (using 0.1 N NaOH) and formation of **5g-iii** and **1** (R=H) was detected after 1h of stirring (Figure S19). The reaction mixture was washed with $CHCl_3$ (5x25 mL). Chloroform was removed slowly at 40 – 45 °C. The crude residue was purified by flash chromatography to furnish the title compound as a transparent oil (138 mg, 0.7 mmol, 70%). ^{1}H NMR ($CDCl_3$): δ 6.12 (d, *J* = 0.90 Hz, 1H, CH_2), 6.14 (d, *J* = 0.90 Hz, 1H, CH_2), 7.91 (d, *J* = 7.7 Hz, 2H, ArH), 8.58 (d, *J* = 7.7 Hz, 2H, ArH), 10.24 (s, 1H, CHO). ^{13}C NMR (125 MHz, $CDCl_3$): δ 124.79, 126.31, 129.03, 129.86, 136.59, 142.21, 147.71, 151.55, 190.93, 192.50. HRMS-ESI (*m/z*) found $[M+H]^+$ 195.0201, $C_{10}H_7O_2Cl$ requires 195.0207.

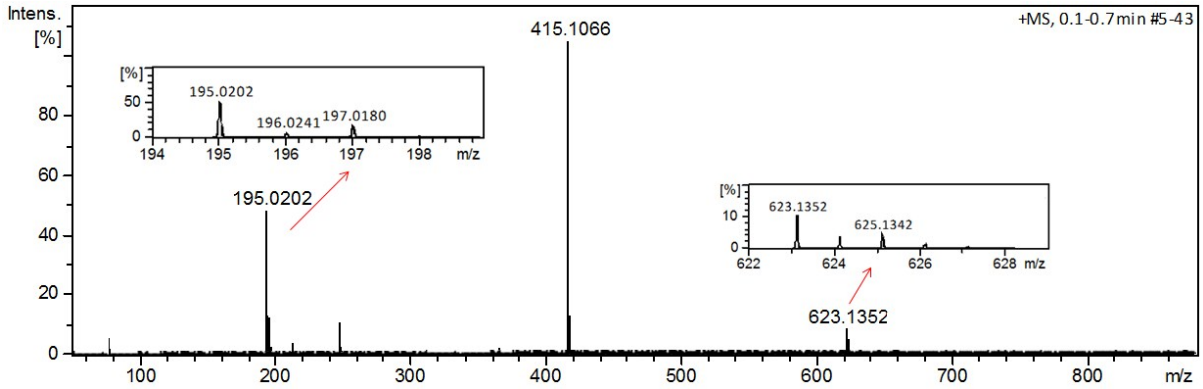
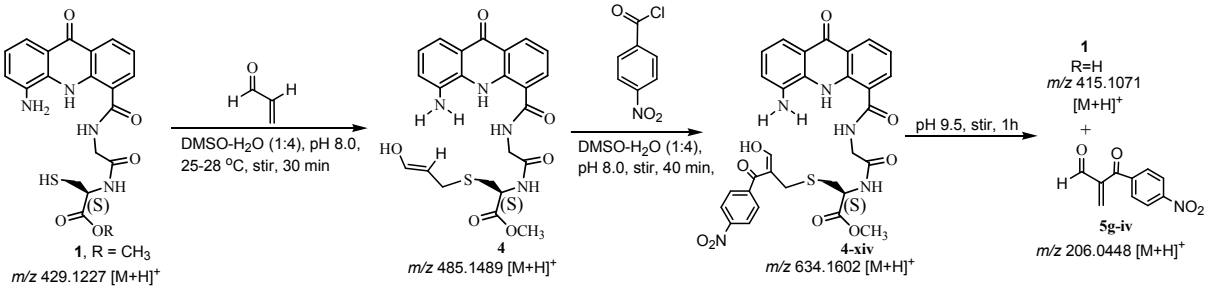


Figure S19. HRMS of the reaction mixture of **4** and 4-chlorobenzoyl chloride at pH 9.5, after stirring for 1h. Peak at *m/z* 623.1352 corresponds to **4-xiii** (calcd *m/z* 623.1362 $[M+H]^+$). Peak at 195.0202 corresponds to mass of product **5g-iii** (calcd *m/z* 195.0207 $[M+H]^+$).

2-(4-Nitrobenzoyl)-propenal (5g-iv).



General procedure was performed on a 1 mmol scale with reagent **1** and acrolein in 20 mL of DMSO-H_2O (1:4, v/v) with stirring at 25 – 28 °C keeping the pH of the reaction mixture 8.0

for 30 min. Then 4-nitrobenzoyl chloride was added and the reaction mixture was further stirred for 40 min. Then pH of the reaction mixture was changed to 9.5 and formation of **5g-iv** and **1** (R=H) was detected after 1h of stirring (Figure S20). The reaction mixture was washed with $CHCl_3$ (5x25 mL). Chloroform was removed slowly at 40 – 45 ^oC. The crude residue was purified by flash chromatography to furnish the title compound as a transparent oil (103 mg, 0.5 mmol, 50%). ^1H NMR (500 MHz, $CDCl_3$): δ 6.37 (d, J = 1.1 Hz, 1H, CH_2), 6.49 (d, J = 1.1 Hz, 1H, CH_2), 7.98 (d, J = 7.8 Hz, 2H, ArH), 8.78 (d, J = 7.8 Hz, 2H, ArH), 10.20 (s, 1H, CHO). ^{13}C NMR (125 MHz, $CDCl_3$): δ 124.52, 125.12, 130.19, 130.61, 144.54, 148.04, 151.88, 186.83, 190.25. HRMS-ESI (*m/z*) found $[M+H]^+$ 206.0438, $C_{10}H_7NO_4$ requires 206.0448.

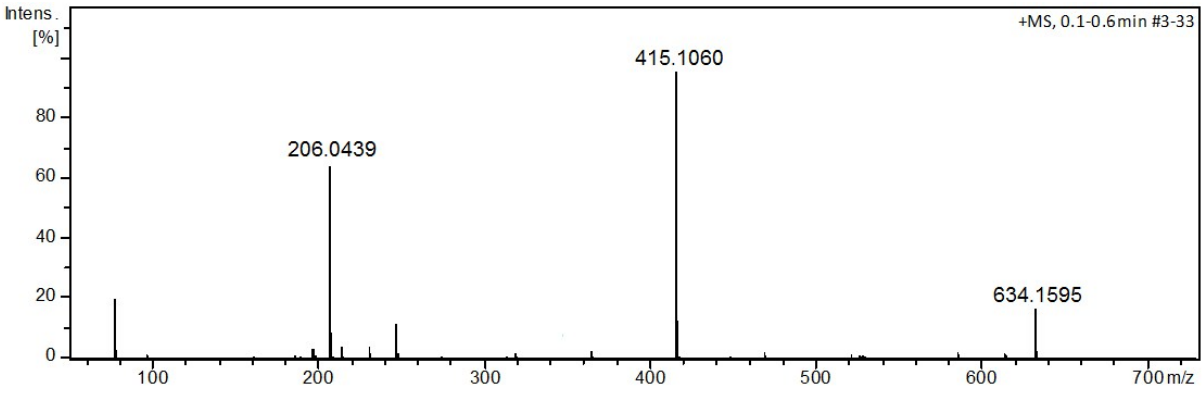
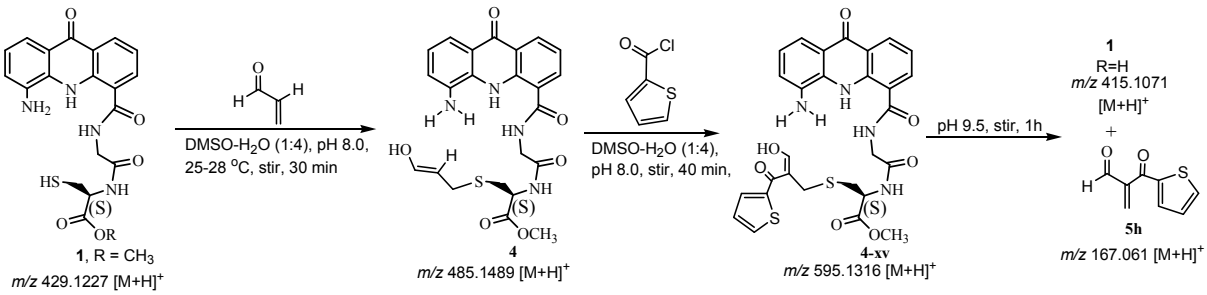


Figure S20. HRMS of the reaction mixture of **4** and 4-nitrobenzoyl chloride at pH 9.5, after stirring for 1h. Peak at *m/z* 634.1595 corresponds to **4-xiv** (calcd *m/z* 634.1602 $[M+H]^+$). Peak at 206.0439 corresponds to mass of product **5g-iv** (calcd *m/z* 206.0448 $[M+H]^+$).

2-(Thiophene-2-carbonyl)-propenal (5h).



General procedure was performed on a 1 mmol scale with reagent **1** and acrolein in 20 mL of DMSO-H_2O (1:4, v/v) with stirring at 25 – 28 ^oC keeping the pH of the reaction mixture 8.0 for 30 min. Then thiophene-2-carboxyl chloride was added and the reaction mixture was further stirred for 40 min. Then pH of the reaction mixture was changed to 9.5 and formation of **5h** and **1** (R=H) was detected after 1h of stirring (Figure S21). The reaction mixture was washed with $CHCl_3$ (5x25 mL). Chloroform was removed slowly at 40 – 45 ^oC. The crude residue was purified by flash chromatography to furnish the title compound as a transparent oil (108 mg, 0.65 mmol, 65%). ^1H NMR ($CDCl_3$): δ 6.12 (d, J = 0.9 Hz, 1H, CH_2), 6.14 (d, J = 0.9 Hz, 1H, CH_2), 7.35 (m, 1H, CH), 7.98 (d, J = 7.0 Hz, 1H, CH), 8.11 (d, J = 7.0 Hz, 1H, CH), 10.26 (s, 1H, CHO). ^{13}C NMR (125 MHz, $CDCl_3$): δ 129.25, 132.81, 136.80, 144.43, 147.92, 151.77, 180.11, 186.14. HRMS-ESI (*m/z*) found $[M+H]^+$ 167.0155, $C_8H_6O_2S$ requires 167.0161.

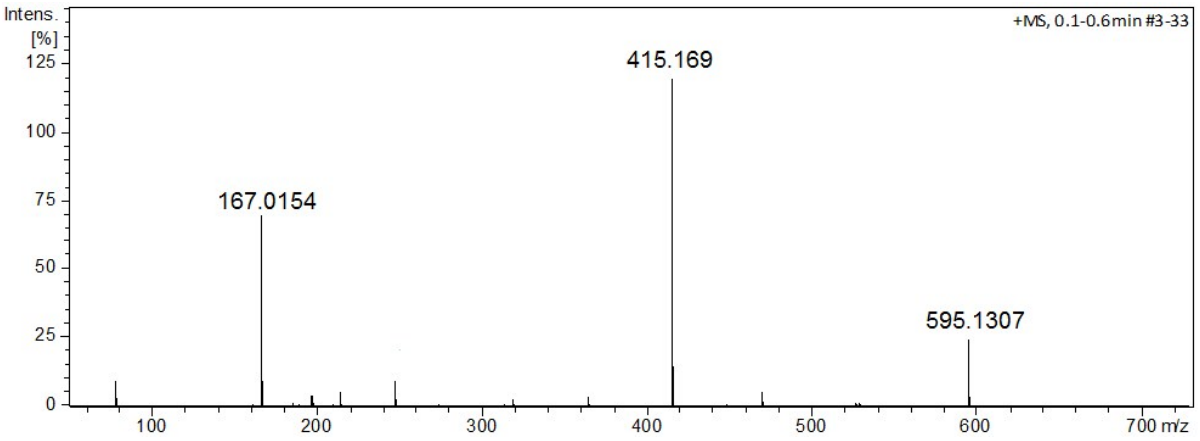
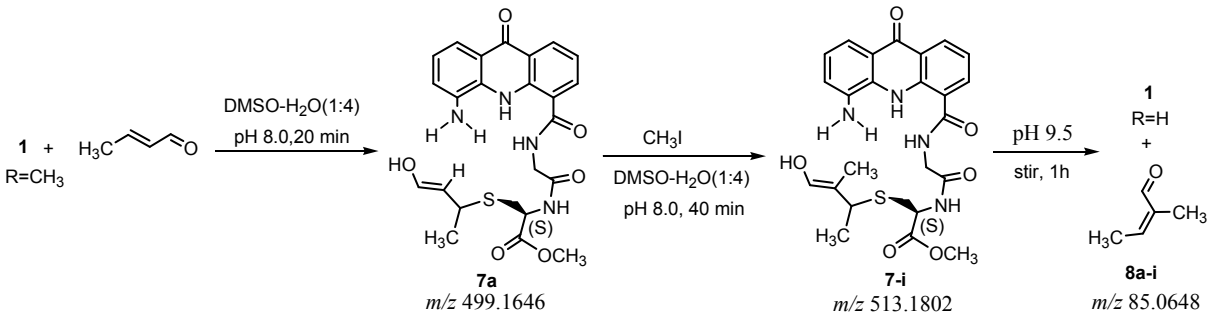


Figure S21. HRMS of the reaction mixture of **4** and thiopehene-2-carboxyl chloride at pH 9.5, after stirring for 1h. Peak at *m/z* 595.1307 corresponds to species **4-xv** (calcd *m/z* 595.1316 $[M+H]^+$). Peak at 167.0154 corresponds to mass of product **5h** (calcd *m/z* 167.0161 $[M+H]^+$).

Similar to the synthesis of compounds **5**, the reaction of compound **1** with crotonaldehyde/cinnamaldehyde/mesityl oxide/4-phenylbut-3-en-2-one provided respective adducts **7**. Further treatment of **7** with the alkylating agents under the same conditions as described above resulted into the formation of compound **8**.

2-Methylbut-2-enal (8a-i).



General procedure was performed on a 1 mmol scale with reagent **1** and crotonaldehyde in 20 mL of DMSO-H_2O (1:4, v/v) with stirring at 25 – 28 ^oC keeping the pH of the reaction mixture 8.0 for 20 min (Figure S22). Then CH_3I was added and the reaction mixture was further stirred for 40 min. The pH of the reaction mixture was changed to 9.5 and formation of **8a-i** and **1** (R=H) was detected after 1h of stirring (Figure S23). The reaction mixture was washed with $CHCl_3$ (5x25 mL). Chloroform was removed slowly at 40 – 45 ^oC. The crude residue was purified by flash chromatography to furnish the title compound as a transparent oil (60 mg, 0.7 mmol, 73%). ^1H NMR (500 MHz, $CDCl_3$): δ 2.01 (d, J = 5.4 Hz, 3H, CH_3), 2.77 (s, 3H, CH_3), 5.92 (q, J = 6.1 Hz, 1H, CH), 9.12 (s, 1H, CHO). ^{13}C NMR (125 MHz, $CDCl_3$): δ 13.87, 15.27, 136.92, 148.03, 194.83. HRMS-ESI (*m/z*) found $[M+H]^+$ 85.0642, C_5H_8O requires 85.0648.

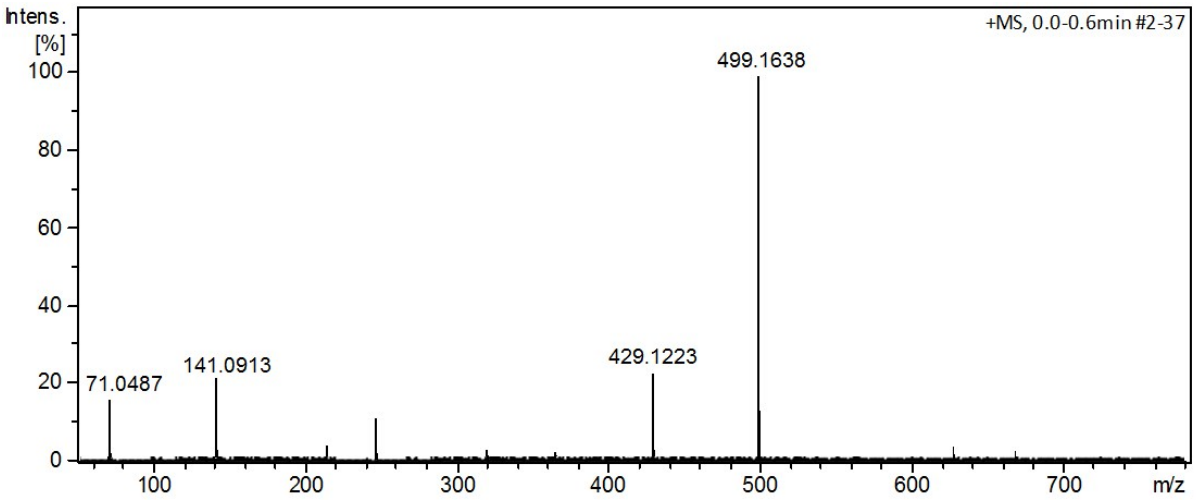


Figure S22. HRMS of the reaction mixture of reagent **1** and crotonaldehyde after 20 min of stirring at pH 8.0. Most intense peak was corresponding to *m/z* of adduct **7a** (calcd *m/z* 499.1646 $[M+H]^+$).

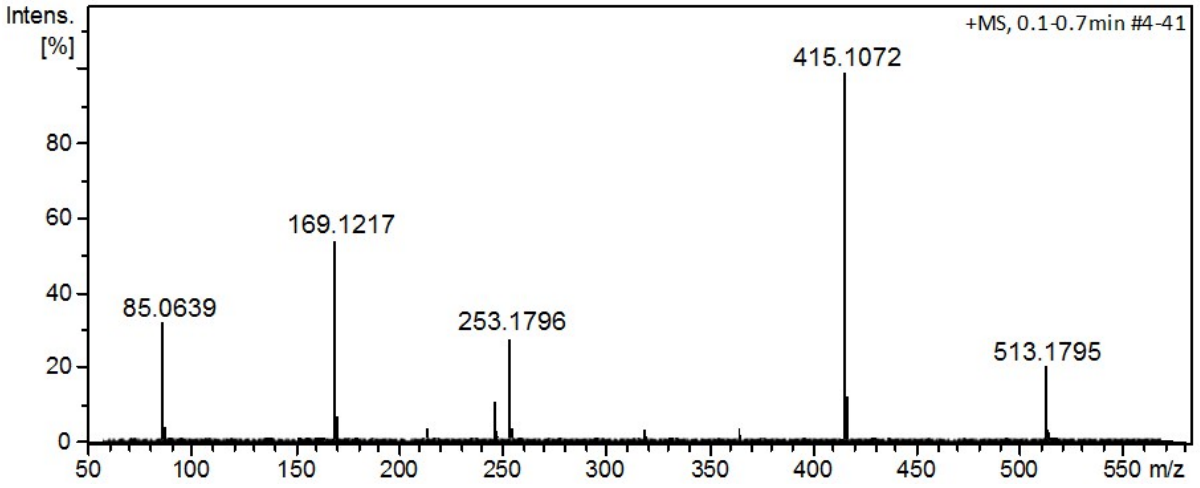


Figure S23. HRMS of the reaction mixture of **1** and crotonaldehyde after the addition of CH_3I and change of pH from 8.0 to 9.5 (1h stirring at room temperature). The peaks at *m/z* 85.0639, 169.1217 and 253.1796 clearly indicate the formation of product **8a-i**, the respective calcd *m/z* is 85.0648, 169.1223 and 253.1798.

Addition of allyl bromide in place of CH_3I in the above reaction led to the formation of product 8a-ii (Figure S24).

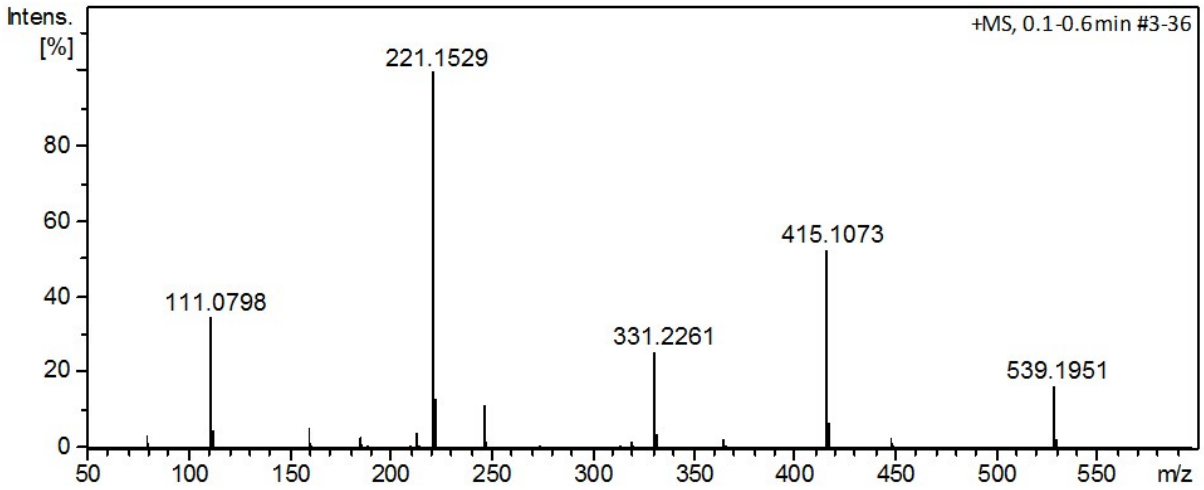
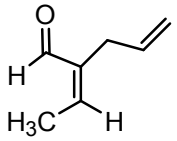


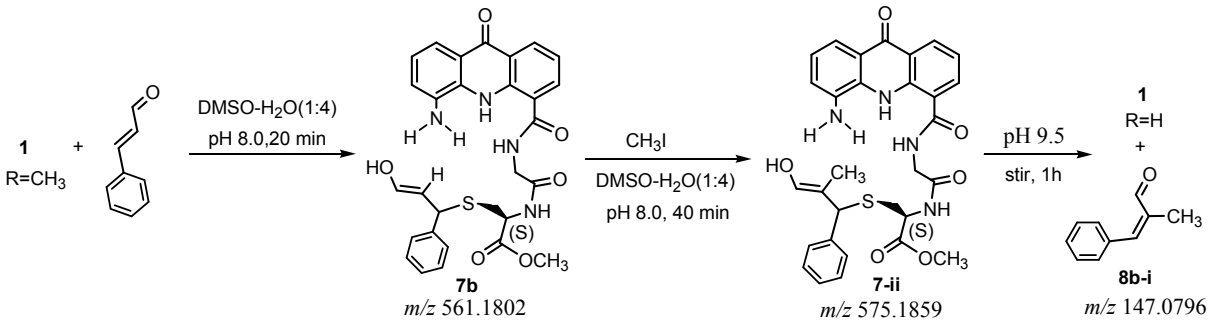
Figure S24. HRMS of the reaction mixture of **1** and crotonaldehyde after the addition of allyl bromide and change of pH from 8.0 to 9.5 (1h stirring at room temperature). The peaks at *m/z* 111.0798, 221.1529 and 331.2261, corresponding to monomer, dimer and trimer of **8a-ii** clearly indicate the formation of product; the respective calcd *m/z* is 111.0804, 221.1536 and 331.2268.

2-Ethylidenepent-4-enal (8a-ii).



Transparent oil (86 mg, 0.78 mmol, 78%). ^{1}H NMR (500 MHz, $CDCl_3$): δ 2.10 (d, *J* = 8.5 Hz, 3H, CH_3), 2.60 (d, *J* = 7.8 Hz, 2H, CH_2), 4.98 (dd, *J* = 1.4 Hz, 7.8 Hz, 1H, CH_2), 5.07 (dd, *J* = 10.0 Hz, 4.0 Hz, 1H, CH_2), 5.68-5.70 (m, 1H, CH), 6.53-6.54 (m, 1H, CH), 9.84 (s, 1H, CHO). ^{13}C NMR (125 MHz, $CDCl_3$): δ 15.77, 36.17, 118.99, 132.82, 136.82, 147.94, 191.10. HRMS-ESI (*m/z*) found $[M+H]^+$ 111.0796, $C_7H_{10}O$ requires 111.0804.

2-Methyl-3-phenylpropenal (8b-i).



General procedure was performed on a 1 mmol scale with reagent **1** and cinnamaldehyde in 20 mL of DMSO-H_2O (1:4, v/v) with stirring at 25 – 28 ^{o}C keeping the pH of the reaction mixture 8.0 for 20 min (Figure S25). Then CH_3I was added and the reaction mixture was further stirred for 40 min. Then pH of the reaction mixture was changed to 9.5 and formation of **8b-i** and **1** (R=H) was detected after 1h of stirring (Figure S26). The reaction mixture was washed with $CHCl_3$ (5x25 mL). Chloroform was removed slowly at 40 – 45 ^{o}C. The crude residue was purified by flash chromatography to furnish the title compound as a thick oil (100 mg, 0.68 mmol, 68%). ^{1}H NMR (500 MHz, $CDCl_3$): δ 2.18 (s, 3H, CH_3), 7.21 (s, 1H, CH), 7.30 (m, 2H, ArH), 7.38 (m, 1H, ArH), 7.56 (m, 2H, ArH), 9.82 (s, 1H, CHO). ^{13}C NMR (125 MHz, $CDCl_3$): δ 12.67, 124.32, 124.92, 126.44, 129.16, 129.99, 132.72, 136.72, 147.84, 193.63. HRMS-ESI (*m/z*) found $[M+H]^+$ 147.0796, $C_{10}H_{10}O$ requires 147.0804.

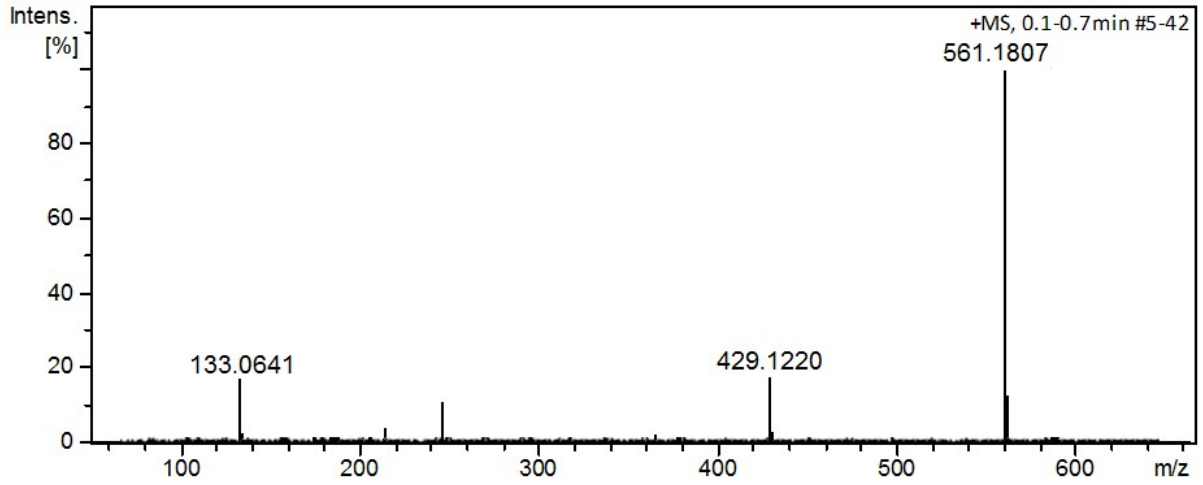


Figure S25. HRMS of the reaction mixture of reagent **1** and cinnamaldehyde after 20 min of stirring at pH 8.0. Most intense peak was corresponding to *m/z* of adduct **7b** (calcd *m/z* 561.1802 $[M+H]^+$).

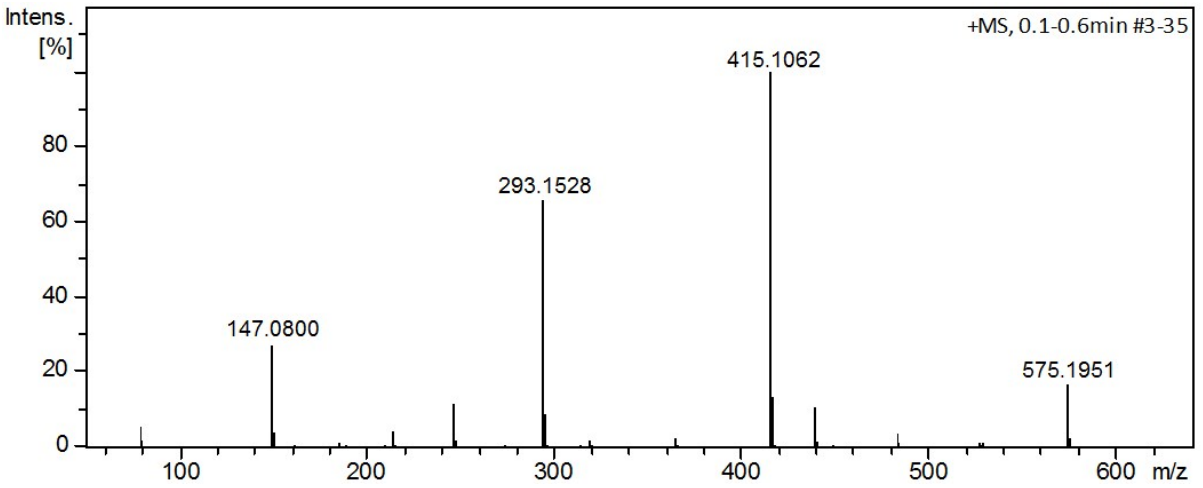


Figure S26. HRMS of the reaction mixture of **1** and cinnamaldehyde after the addition of CH_3I and change of pH from 8.0 to 9.5 (1h stirring at room temperature). The peaks at *m/z* 147.0800, 293.1528 clearly indicate the formation of product **8b-i**, the respective calcd *m/z* is 147.0804, 293.1536 ($[M+H]^+$).

Product 8b-ii was procured by using allyl bromide in place of CH_3I in the above reaction (Figure S27).

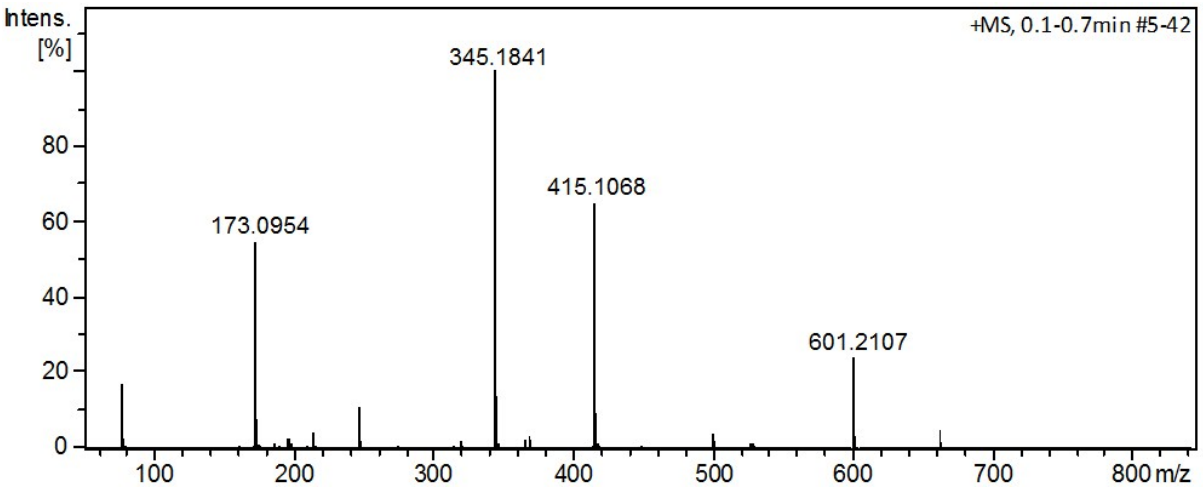
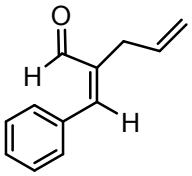


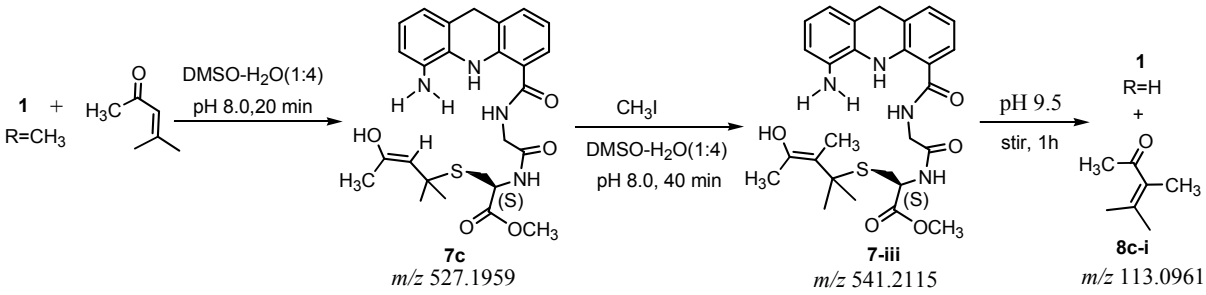
Figure S27. HRMS of the reaction mixture of **1** and cinnamaldehyde after the addition of allyl bromide and change of pH from 8.0 to 9.5 (1h stirring at room temperature). The peaks at *m/z* 173.0954, 345.1841 corresponding to monomer and dimer, respectively clearly indicate the formation of product **8b-ii**, the respective calcd *m/z* is 173.0954, 345.1841.

2-Benzylidenepent-4-enal (8b-ii).



Thick oil (120 mg, 0.7 mmol, 70%). ^{1}H NMR (500 MHz, $CDCl_3$): δ 2.56 (d, J = 7.4 Hz, 2H, CH_2), 4.93 (dd, J = 10.5 Hz, 7.8 Hz, 1H, CH_2), 4.96 (dd, J = 10.5 Hz, 4.5 Hz, 1H, CH_2), 5.67-5.68 (m, 1H, CH), 7.31 (s, 1H, CH), 7.50-7.52 (m, 1H, ArH), 7.82-7.85 (m, 3H, ArH), 8.00 (m, 1H, ArH), 9.85 (s, 1H, CHO). ^{13}C NMR (125 MHz, $CDCl_3$): δ 35.99, 115.74, 124.64, 125.24. 126.76, 129.48, 130.31, 130.73, 133.04, 137.04, 144.66, 191.10. HRMS-ESI (*m/z*) found $[M+H]^+$ 173.0954, $C_{12}H_{12}O$ requires 173.0954.

3,4-Dimethylpent-3-en-2-one (8c-i).



General procedure was performed on a 1 mmol scale with reagent **1** and mesityl oxide in 20 mL of DMSO-H_2O (1:4, v/v) with stirring at 25 – 28 ^oC keeping the pH of the reaction mixture 8.0 for 20 min (Figure S28). Then CH_3I was added and the reaction mixture was further stirred at 25 – 28 ^oC for 40 min. Then pH of the reaction mixture was changed to 9.5 and formation of **8c-i** and **1** (R=H) was detected after 1h of stirring (Figure S29). The reaction mixture was washed with $CHCl_3$ (5x25 mL). Chloroform was removed slowly at 40 – 45 ^oC. The crude residue was purified by flash chromatography to furnish the title compound as a thick oil (73 mg, 0.65 mmol, 65%). ^1H NMR (500 MHz, $CDCl_3$): δ 2.12 (s, 3H, CH_3), 2.15 (s, 3H, CH_3), 2.32 (s, 3H, CH_3), 2.88 (s, 3H, CH_3). ^{13}C NMR (125 MHz, $CDCl_3$): δ 14.68, 21.09, 21.94, 29.63, 129.17, 136.73, 198.64. HRMS-ESI (*m/z*) found $[M+H]^+$ 113.0952, $C_7H_{12}O$ requires 113.0961.

Under the same reaction conditions but using allyl bromide in place of CH_3I provided product **8c-ii** (Figure S30).

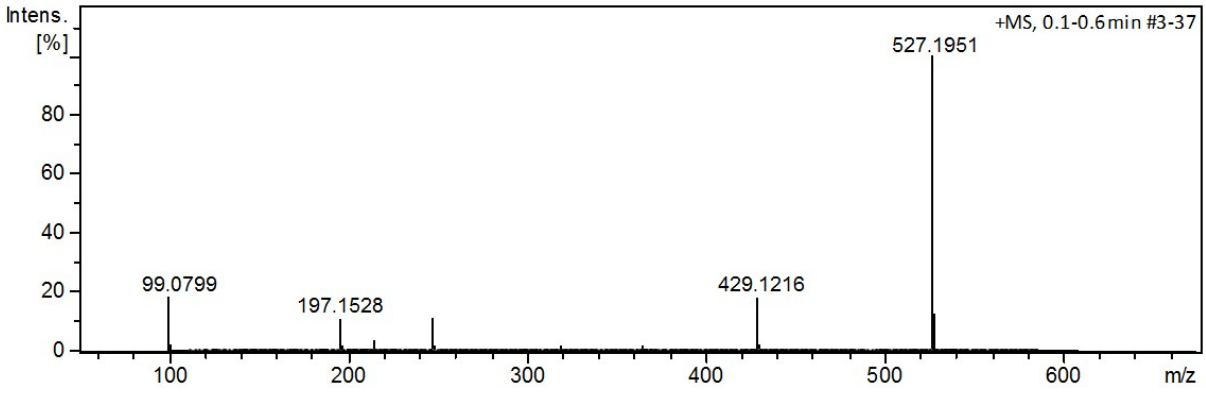


Figure S28. HRMS of the reaction mixture of reagent **1** and mesityl oxide after 20 min of stirring at pH 8.0. Most intense peak was corresponding to *m/z* of adduct **7c** (calcd *m/z* 527.1959 $[M+H]^+$).

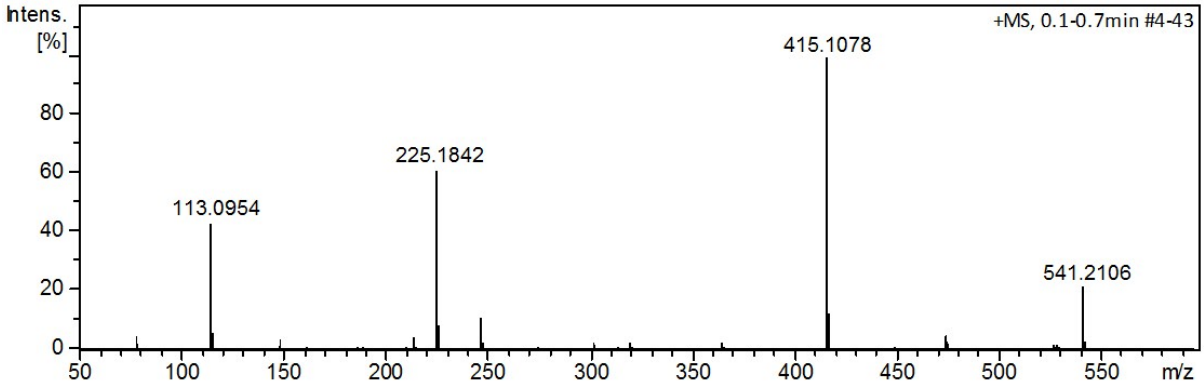


Figure S29. HRMS of the reaction mixture of **1** and mesityl oxide after the addition of CH_3I and change of pH from 8.0 to 9.5 (1h stirring at room temperature). The peaks at *m/z* 113.0954, 225.1842 corresponding to monomer and dimer clearly indicate the formation of product **8c-i**, the respective calcd *m/z* is 113.0961, 225.1849.

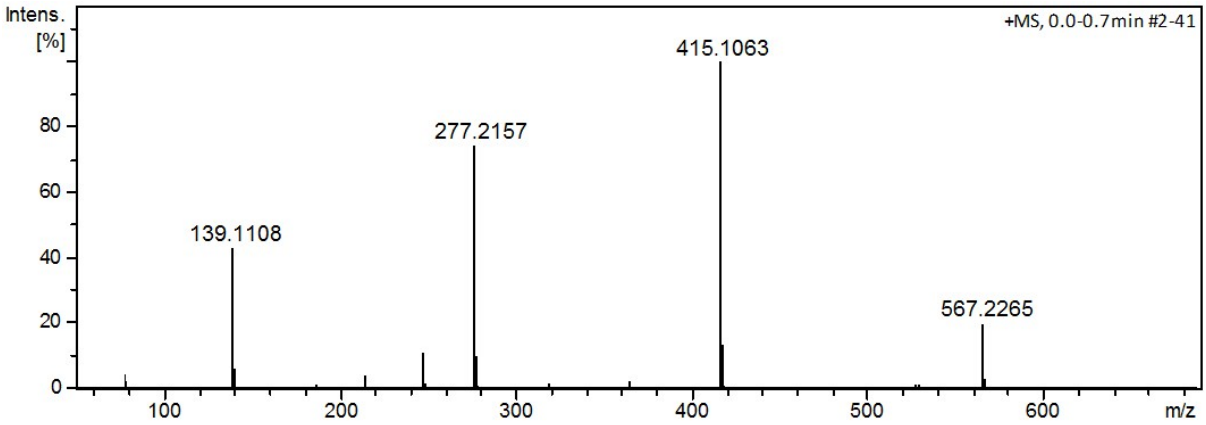
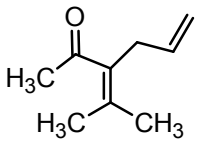


Figure S30. HRMS of the reaction mixture of **1** and mesityl oxide after the addition of allyl bromide and change of pH from 8.0 to 9.5 (1h stirring at room temperature). The peaks at *m/z* 139.1108, 277.2157 corresponding to monomer and dimer, respectively clearly indicate the formation of product **8c-ii**, the respective calcd *m/z* is 139.1117, 277.2162.

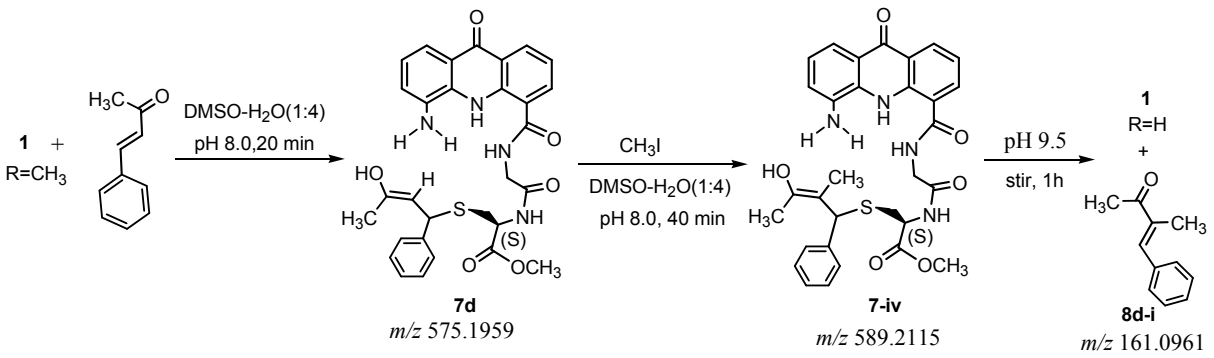
3-Isopropylidenehex-5-en-2-one (8c-ii).



Thick oil (90 mg, 0.66 mmol, 66%). ^{1}H NMR (500 MHz, $CDCl_3$): δ 2.12 (s, 3H, CH_3), 2.15 (s, 3H, CH_3), 2.61 (d, J = 8.7 Hz, 2H, CH_2), 2.88 (s, 3H, CH_3), 4.91-4.94 (m, 1H, CH_2), 4.95-

4.98 (m, 1H, CH_2), 5.65-5.68 (m, 1H, CH). ^{13}C NMR (125 MHz, $CDCl_3$): δ 21.34, 21.74, 28.74, 32.62, 115.37, 130.36, 132.67, 136.67, 194.58. HRMS-ESI (*m/z*) found $[M+H]^+$ 139.1108, $C_9H_{14}O$ requires 139.1117.

3-Methyl-4-phenylbut-3-en-2-one (8d-i).



General procedure was performed on a 1 mmol scale with reagent **1** and 4-phenylbut-3-en-2-one in 30 mL of DMSO-H_2O (1:4, v/v) with stirring at 25 – 28 ^oC keeping the pH of the reaction mixture 8.0 for 20 min (Figure S31). Then CH_3I was added and the reaction mixture was further stirred at 25 – 28 ^oC for 40 min. Then pH of the reaction mixture was changed to 9.5 and formation of **8d-i** and **1** (R=H) was detected after 1h of stirring (Figure S32). The reaction mixture was washed with $CHCl_3$ (5x25 mL). Chloroform was removed slowly at 40 – 45 ^oC. The crude residue was purified by flash chromatography to furnish the title compound as a transparent oil (112 mg, 0.7 mmol, 70%). ^1H NMR (500 MHz, $CDCl_3$): δ 2.25 (s, 3H, CH_3), 2.41 (s, 3H, CH_3), 6.38 (s, 1H, CH), 7.34-7.39 (m, 1H, ArH), 7.41-7.48 (m, 2H, ArH), 7.59-7.66 (m, 2H, ArH). ^{13}C NMR (125 MHz, $CDCl_3$): δ 15.82, 26.23, 126.59, 129.31, 130.14, 130.56, 132.87, 136.87, 144.49, 147.99, 194.78. HRMS-ESI (*m/z*) found $[M+H]^+$ 161.0954, $C_{11}H_{12}O$ requires 161.0961.

Under the same reaction conditions but using allyl bromide in place of CH_3I provided product **8d-ii** (Figure S33).

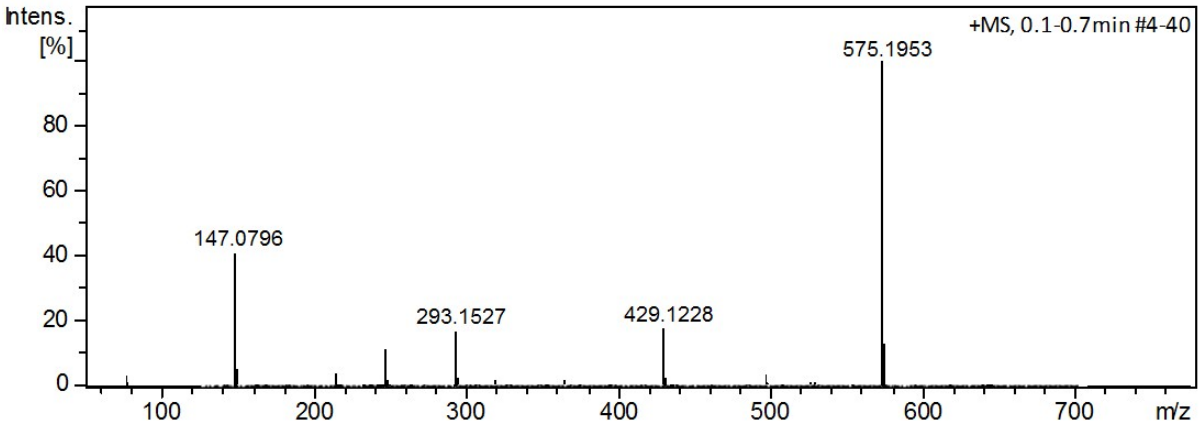


Figure S31. HRMS of the reaction mixture of reagent **1** and 4-phenylbut-3-en-2-one after 20 min of stirring at pH 8.0. Most intense peak was corresponding to *m/z* of adduct **7d** (calcd *m/z* 575.1959 $[M+H]^+$).

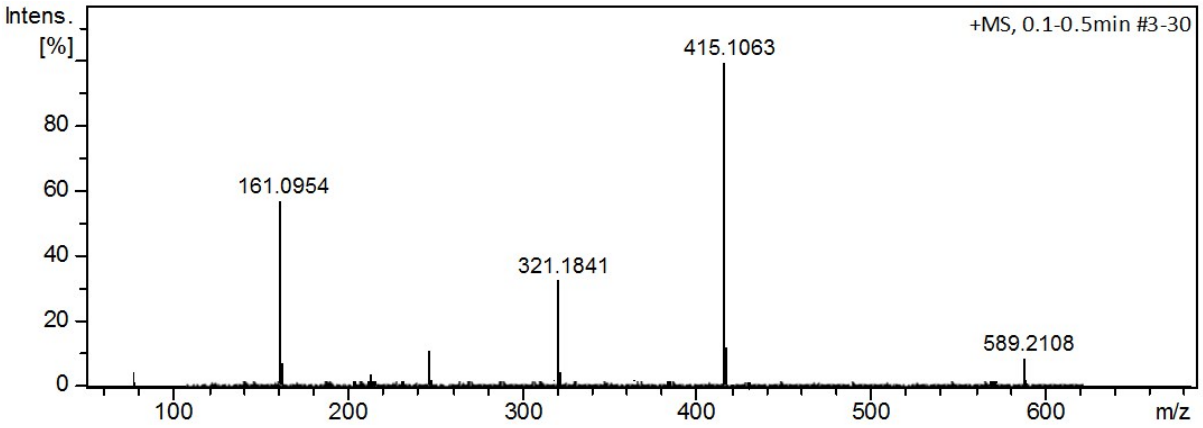


Figure S32. HRMS of the reaction mixture of **1** and 4-phenylbut-3-en-2-one after the addition of CH_3I and change of pH from 8.0 to 9.5 (1h stirring at room temperature). The peaks at *m/z* 161.0954, 321.1841 corresponding to monomer and dimer, respectively clearly indicate the formation of product **8d-i**, the respective calcd *m/z* is 161.0961, 321.1849.

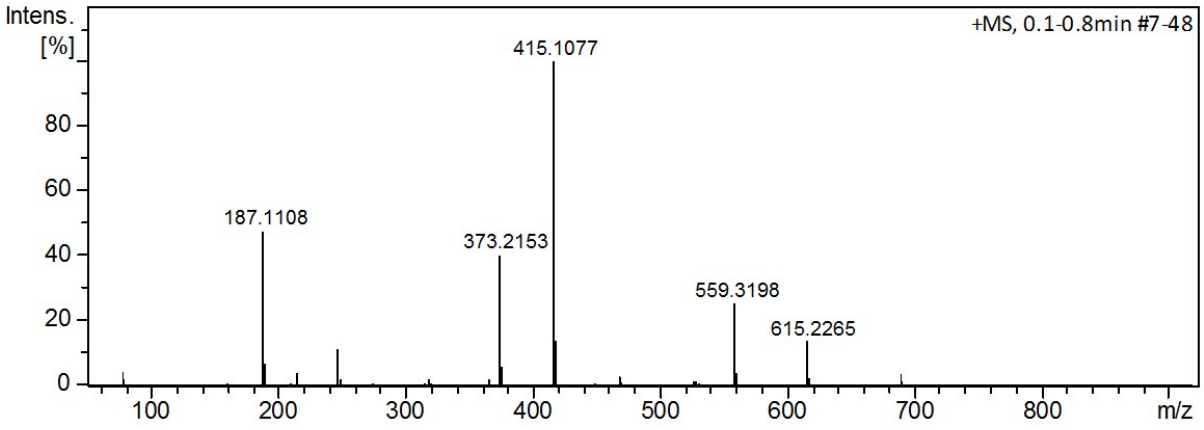
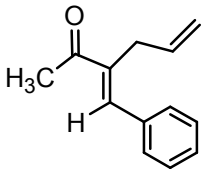


Figure S33. HRMS of the reaction mixture of **1** and 4-phenylbut-3-en-2-one after the addition of allyl bromide and change of pH from 8.0 to 9.5 (1h stirring at room temperature). The peaks at *m/z* 187.1108, 373.2153 and 559.3198 corresponding to monomer, dimer and trimer, respectively clearly indicate the formation of product **8d-ii**, the respective calcd *m/z* is 187.1117, 373.2162 and 559.3207.

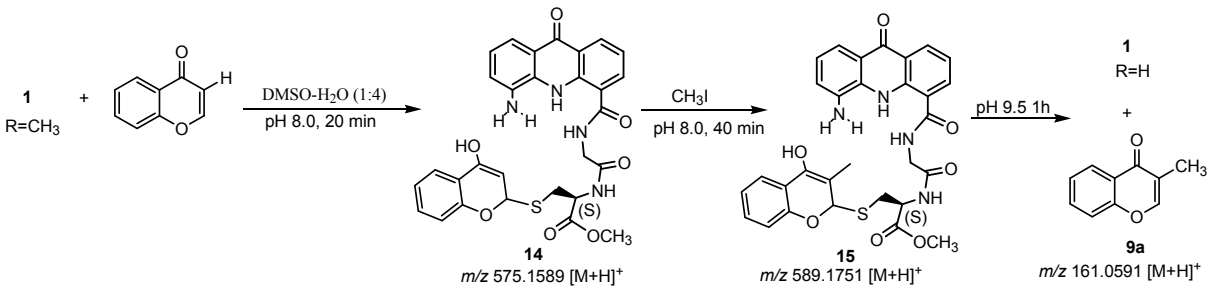
3-Benzylidenehex-5-en-2-one (8d-ii).



Transparent oil (130 mg, 0.7 mmol, 70%). ^{1}H NMR (500 MHz, $CDCl_3$): δ 2.42 (s, 3H, CH_3), 2.62 (d, J = 8.4 Hz, 2H, CH_2), 4.96-4.97 (m, 1H, CH_2), 4.98-4.99 (m, 1H, CH_2), 5.67-5.69 (m, 1H, CH), 7.03 (s, 1H, CH), 7.34-7.39 (m, 1H, ArH), 7.41-7.48 (m, 2H, ArH), 7.59-7.66 (m, 2H, ArH). ^{13}C NMR (125 MHz, $CDCl_3$): δ 26.75, 39.15, 115.50, 124.39, 125.00, 126.52, 129.24, 130.07, 130.49, 132.80, 136.79, 144.42, 195.71. HRMS-ESI (*m/z*) found $[M+H]^+$ 187.1109, $C_{13}H_{14}O$ requires 187.1117.

Under the same reaction conditions as used for procuring compounds **5**, reaction of compound **1** with chromone/2-(5*H*)-furanone and subsequent treatment with alkylating agent provided compound **9** and **10**.

3-Methylchromen-4-one (9a).



General procedure was performed on a 1 mmol scale with reagent **1** and chromone in 20 mL of DMSO-H_2O (1:4, v/v) with stirring at 25 – 28 ^oC keeping the pH of the reaction mixture 8.0 for 20 min (Figure S34). Then CH_3I was added and the reaction mixture was further stirred at 25 – 28 ^oC for 40 min. The pH of the reaction was changed to 9.5 and formation of **9a** and **1** (R=H) was detected after 1h of stirring (Figure S35). The reaction mixture was washed with $CHCl_3$ (5x25 mL). Chloroform was removed slowly at 40 – 45 ^oC. The crude residue was purified by flash chromatography to furnish the title compound as a white solid (112 mg, 0.7 mmol, 70%), mp 95 ^oC. ^1H NMR (500 MHz, $CDCl_3$): δ 2.41 (s, 3H, CH_3), 6.81 (s, 1H, CH), 7.45-7.48 (m, 2H, ArH), 7.54-7.58 (m, 1H, ArH), 7.65-7.68 (m, 1H, ArH). ^{13}C NMR (125 MHz, $CDCl_3$): δ 11.63, 115.37, 118.85, 124.27, 124.88, 126.40, 132.67, 151.64, 157.87, 176.23. HRMS-ESI (*m/z*) found $[M+H]^+$ 161.0591, $C_{10}H_8O_2$ requires 161.0597.

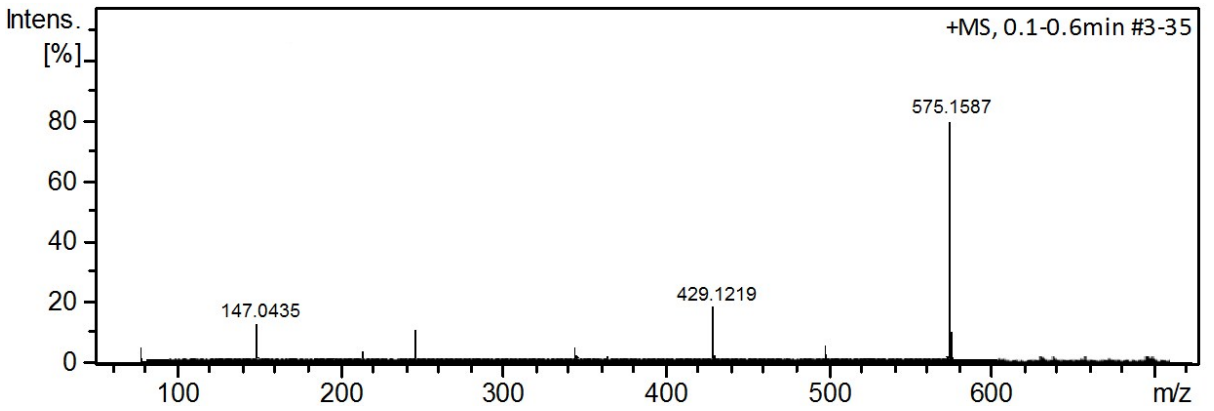


Figure S34. HRMS of the reaction mixture of reagent **1** and chromone after 20 min of stirring at pH 8.0. Most intense peak was corresponding to *m/z* of **14** (calcd *m/z* 575.1595 $[M+H]^+$).

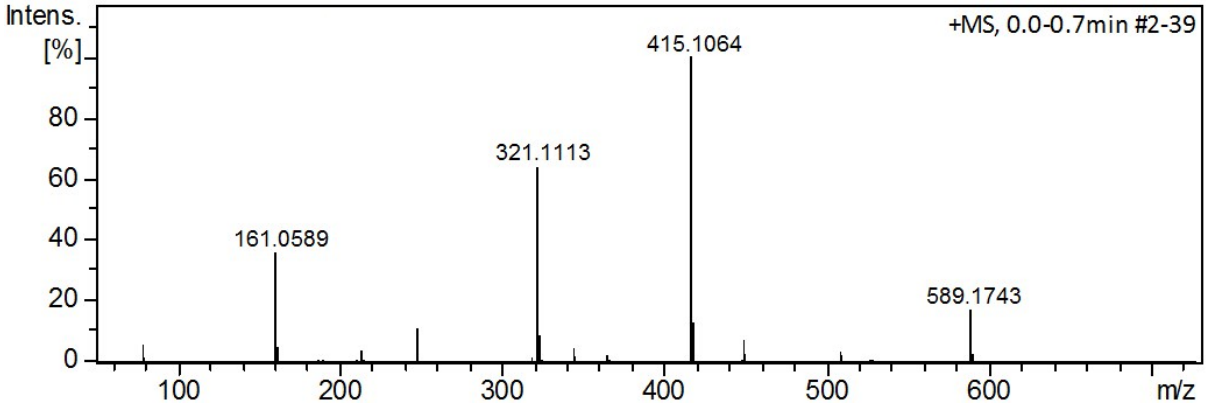
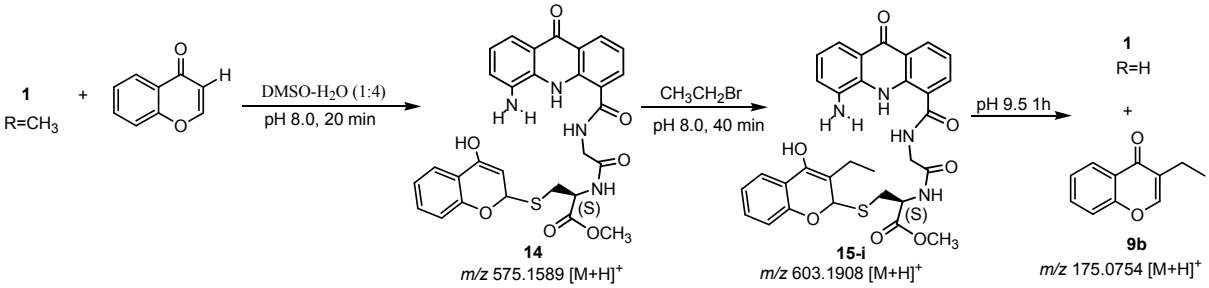


Figure S35. HRMS of the reaction mixture of **1** and chromone after the addition of methyl iodide and change of pH from 8.0 to 9.5 (1h stirring at room temperature). The peaks at *m/z* 161.0589, 321.1113 corresponding to monomer and dimer, respectively clearly indicate the formation of product **9a**, the respective calcd *m/z* is 161.0597 and 321.1121. Peak at *m/z* 589.1743 corresponds to mass of species **15**.

3-Ethylchromen-4-one (9b).



General procedure was performed on a 1 mmol scale with reagent **1** and chromone in 30 mL of DMSO-H_2O (1:4, v/v) with stirring at 25 – 28 ^oC keeping the pH of the reaction mixture 8.0 for 20 min. Then ethyl bromide was added and the reaction mixture was further stirred at 25 – 28 ^oC for 40 min. Then pH of the reaction mixture was changed to 9.5. Formation of **9b** and **1** (R=H) was detected after 1h of stirring (Figure S36). The reaction mixture was washed with $CHCl_3$ (5x25 mL). Chloroform was removed slowly at 40 – 45 ^oC. The crude residue was purified by flash chromatography to furnish the title compound as a white solid (132 mg, 0.75 mmol, 75%), mp 98 ^oC. ^1H NMR (500 MHz, $CDCl_3$): δ 1.27 (t, J = 7.5 Hz, 3H, CH_3), 2.49 (q, J = 7.5 Hz, 2H, CH_2), 6.71 (s, 1H, CH), 6.92 (d, 1H, J = 7.8 Hz, ArH), 7.05 (t, 1H, J = 7.5 Hz, ArH), 7.25-7.29 (m, 2H, ArH). ^{13}C NMR (125 MHz, $CDCl_3$): δ 15.74, 17.86,

115.48, 124.38, 124.98, 126.51, 129.23, 136.78, 147.90, 157.98, 176.12. HRMS-ESI (*m/z*) found $[M+H]^+$ 175.0747, $C_{12}H_{10}O_2$ requires 175.0754.

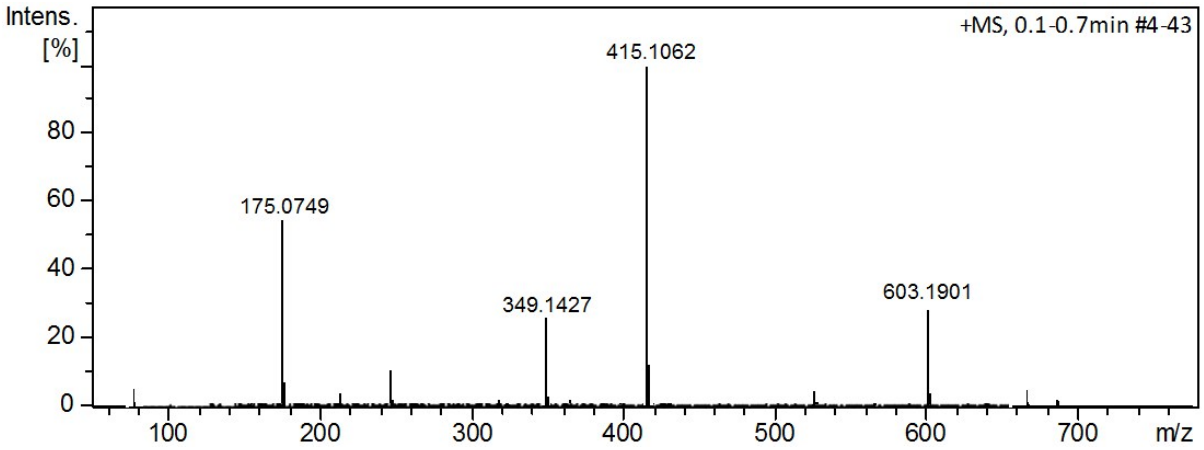
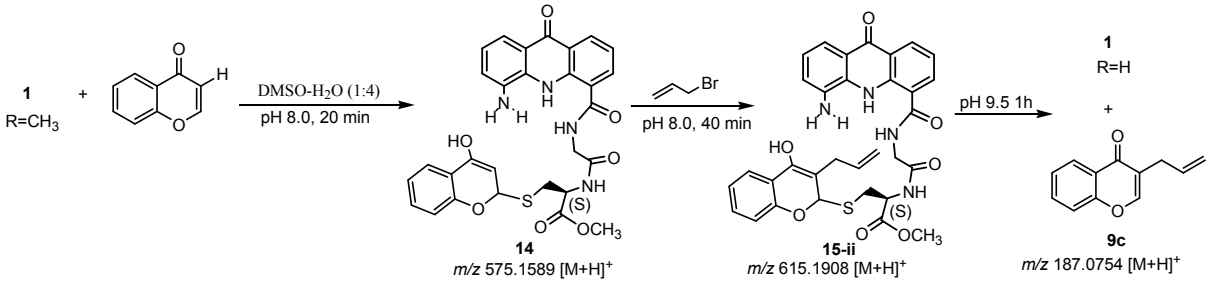


Figure S36. HRMS of the reaction mixture of **1** and chromone after the addition of ethyl bromide and change of pH from 8.0 to 9.5 (1h stirring at room temperature). The peaks at *m/z* 175.0749, 349.1427 corresponding to monomer and dimer, respectively clearly indicate the formation of product **9b**, the respective calcd *m/z* is 175.0754 and 349.1434.

3-Allylchromen-4-one (9c).



General procedure was performed on a 1 mmol scale with reagent **1** and chromone in 30 mL of DMSO-H_2O (1:4, v/v) with stirring at 25 – 28 ^oC keeping the pH of the reaction mixture 8.0 for 20 min. Then allyl bromide was added and the reaction mixture was further stirred at 25 – 28 ^oC for 40 min. Then pH of the reaction mixture was changed to 9.5 and formation of **9c** and **1** (R=H) was detected after 1h of stirring (Figure S37). The reaction mixture was washed with $CHCl_3$ (5x25 mL). Chloroform was removed slowly at 40 – 45 ^oC. The crude residue was purified by flash chromatography to furnish the title compound as a white solid (150 mg, 0.8 mmol, 80%), mp 122 ^oC. ^1H NMR[3] (500 MHz, $CDCl_3$): δ 2.60 (d, J = 5.4 Hz,

2H, CH_2), 4.26-4.28 (m, 1H, CH_2), 4.50-4.53 (m, 1H, CH_2), 5.00-5.02 (m, 1H, CH), 6.51 (s, 1H, CH), 7.35-7.68 (m, 4H, ArH). ^{13}C NMR (125 MHz, $CDCl_3$): δ 36.85, 113.32, 113.49, 115.59, 124.49, 125.09, 126.62, 132.89, 136.89, 158.09, 182.80. HRMS-ESI (*m/z*) found $[M+H]^+$ 187.0748, $C_{12}H_{10}O_2$ requires 187.0754.

3. R. Jana, R. Trivedi, J. A. Tunge, *Org. Lett*. 2009, **11**, 3434-3436.

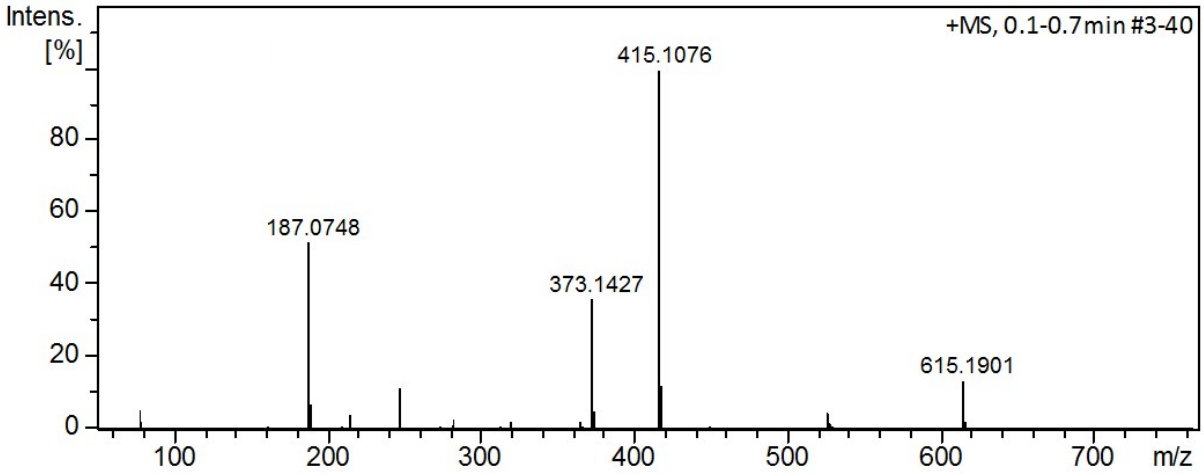
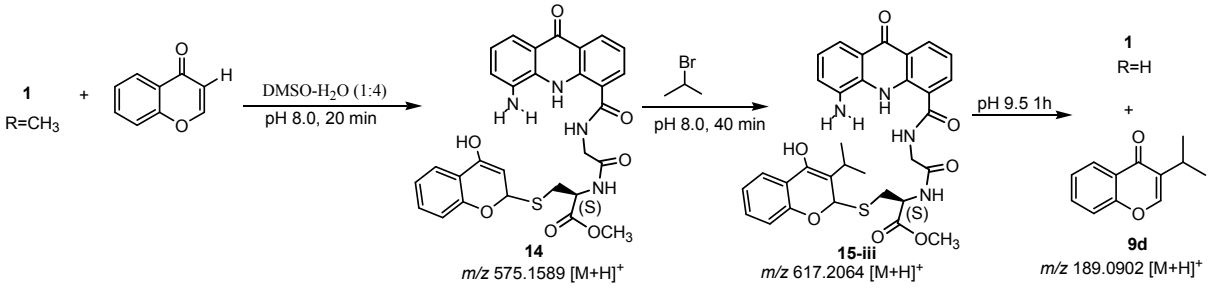


Figure S37. HRMS of the reaction mixture of **1** and chromone after the addition of allyl bromide and change of pH from 8.0 to 9.5 (1h stirring at room temperature). The peaks at *m/z* 187.0748, 373.1427 corresponding to monomer and dimer, respectively clearly indicate the formation of product **9c**, the respective calcd *m/z* is 187.0754 and 373.1434.

3-Isopropylchromen-4-one (9d).



General procedure was performed on a 1 mmol scale with reagent **1** and chromone in 30 mL of DMSO-H_2O (1:4, v/v) with stirring at 25 – 28 ^oC keeping the pH of the reaction mixture 8.0 for 20 min. Then iso-propyl bromide was added and the reaction mixture was further stirred at 25 – 28 ^oC for 40 min. Then pH of the reaction mixture was changed to 9.5 and after 1h of stirring, formation of **9d** and **1** (R=H) was observed (Figure S38). The reaction mixture

was washed with $CHCl_3$ (5x25 mL). Chloroform was removed slowly at 40 – 45 °C. The crude residue was purified by flash chromatography to furnish the title compound as a white solid (150 mg, 0.8 mmol, 80%), mp 125 °C. ^{1}H NMR (500 MHz, $CDCl_3$): δ 1.12 (d, J = 5.5 Hz, 6H, CH_3), 2.48 (m, 1H, CH), 6.74 (s, 1H, CH), 6.94 (d, 1H, J = 7.8 Hz, ArH), 7.05 (t, 1H, J = 7.5 Hz, ArH), 7.24-7.29 (m, 2H, ArH). ^{13}C NMR (125 MHz, $CDCl_3$): δ 21.25, 21.75, 25.71, 115.50, 124.40, 125.00, 126.52, 129.24, 136.79, 151.76, 157.99, 175.71. HRMS-ESI (*m/z*) found $[M+H]^+$ 189.0902, $C_{12}H_{12}O_2$ requires 189.0910.

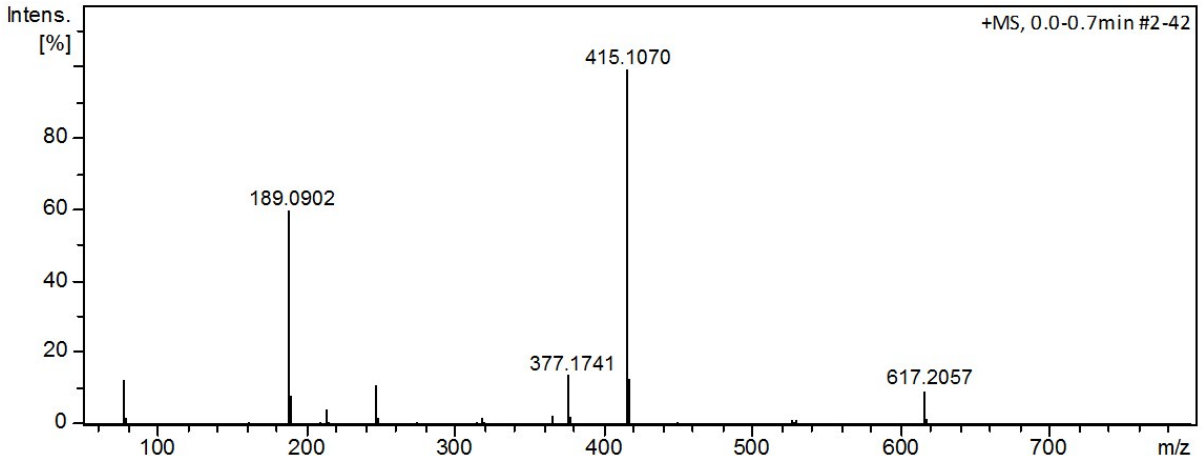
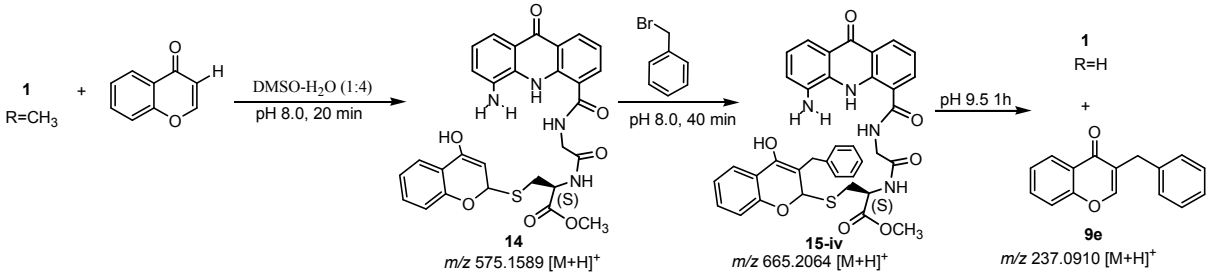


Figure S38. HRMS of the reaction mixture of **1** and chromone after the addition of iso-propyl bromide and change of pH from 8.0 to 9.5 (1h stirring at room temperature). The peaks at *m/z* 189.0902, 377.1741 corresponding to monomer and dimer, respectively clearly indicate the formation of product **9d**, the respective calcd *m/z* is 189.0910 and 377.1747.

3-Benzylchromen-4-one (9e).



General procedure was performed on a 1 mmol scale with reagent **1** and chromone in 30 mL of DMSO-H_2O (1:4, v/v) with stirring at 25 – 28 °C keeping the pH of the reaction mixture 8.0 for 20 min. Then benzyl bromide was added and the reaction mixture was further stirred

at 25 – 28 °C for 40 min. Then pH of the reaction mixture was changed to 9.5 and formation of **9e** and **1** (R=H) was observed after 1h of stirring (Figure S39). The reaction mixture was washed with $CHCl_3$ (5x25 mL). Chloroform was removed slowly at 40 – 45 °C. The crude residue was purified by flash chromatography to furnish the title compound as a white solid (178 mg, 0.75 mmol, 76%), mp 138 °C. ^{1}H NMR (500 MHz, $CDCl_3$): δ 3.93 (s, 2H, CH_2), 6.83 (s, 1H, CH), 6.93-6.97 (m, 2H, ArH), 7.28-7.29 (m, 3H, ArH), 7.49 (d, 1H, *J* = 7.5 Hz, ArH), 7.81-7.93 (m, 3H, ArH). ^{13}C NMR (125 MHz, $CDCl_3$): δ 36.58, 113.23, 115.33, 124.23, 124.83, 126.35, 129.07, 129.90, 130.32, 132.63, 136.63, 144.25, 157.82, 182.15. HRMS-ESI (*m/z*) found $[M+H]^+$ 237.0914, $C_{16}H_{12}O_2$ requires 237.0910.

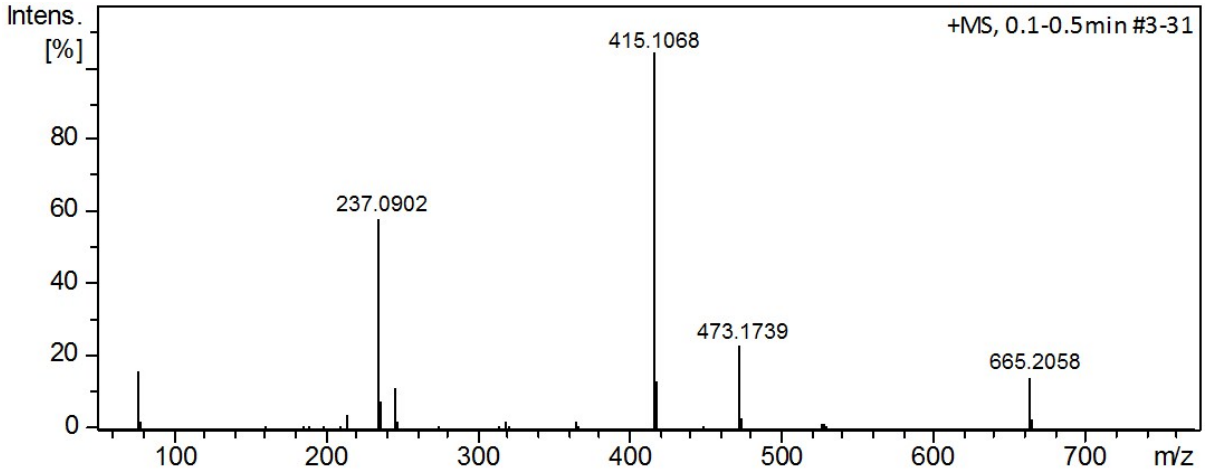
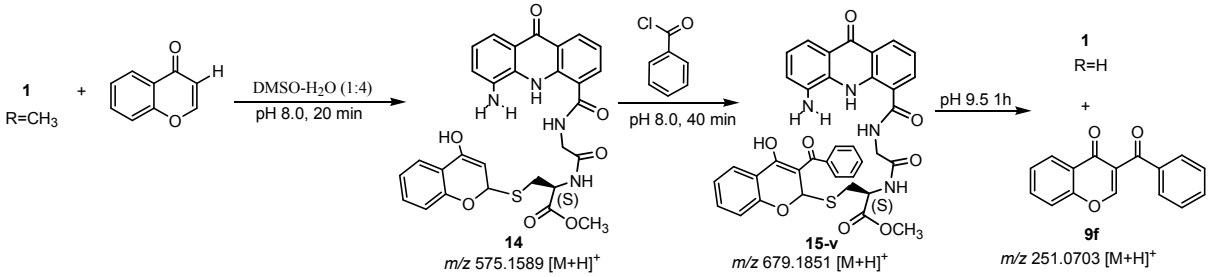


Figure S39. HRMS of the reaction mixture of **1** and chromone after the addition of benzyl chloride and change of pH from 8.0 to 9.5 (1h stirring at room temperature). The peaks at *m/z* 237.0902, 473.1739 corresponding to monomer and dimer, respectively clearly indicate the formation of product **9e**, the respective calcd *m/z* is 237.0910 and 473.1747.

3-Benzoylchromen-4-one (9f).



General procedure was performed on a 1 mmol scale with reagent **1** and chromone in 50 mL of DMSO-H_2O (1:4, v/v) with stirring at 25 – 28 °C keeping the pH of the reaction mixture

8.0 for 20 min. Then benzoyl chloride was added and the reaction mixture was further stirred at 25 – 28 °C for 40 min. Then pH of the reaction mixture was changed to 9.5 and formation of **9f** and **1** (R=H) was observed after 1h of stirring (Figure S40). The reaction mixture was washed with $CHCl_3$ (5x25 mL). Chloroform was removed slowly at 40 – 45 °C. The crude residue was purified by flash chromatography to furnish the title compound as a white solid (175 mg, 0.7 mmol, 70%), mp 136 °C. ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.06-7.09 (m, 2H, CH+ArH), 7.40-7.42 (m, 3H, ArH), 7.61 (m, 1H, ArH), 7.93 (m, 1H, ArH), 7.98-8.00 (m, 2H, ArH), 8.50 (d, *J* = 7.2 Hz, 1H, ArH). ^{13}C NMR (125 MHz, $CDCl_3$): δ 115.73, 119.20, 124.63, 125.23, 126.75, 129.47, 130.30, 130.72, 133.03, 137.03, 144.65, 151.99, 158.22, 177.36, 190.94. HRMS-ESI (*m/z*) found $[M+H]^+$ 251.0695, $C_{16}H_{10}O_3$ requires 251.0703.

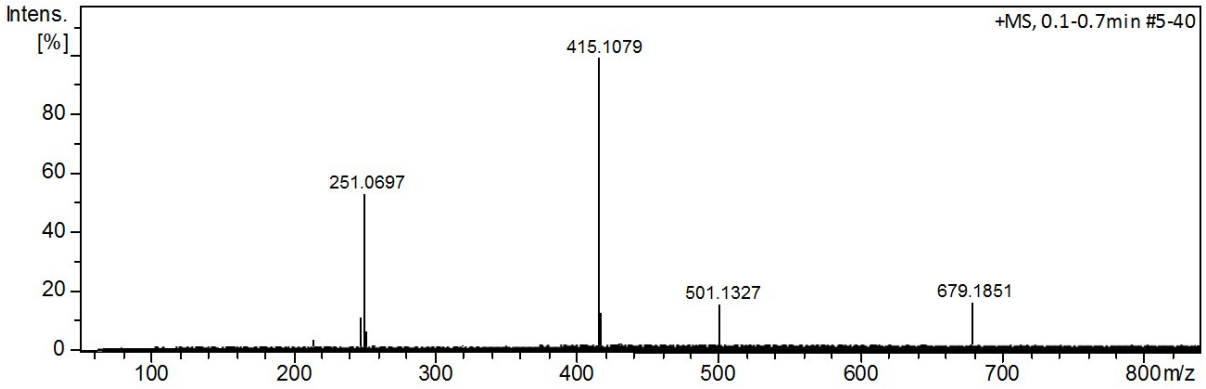
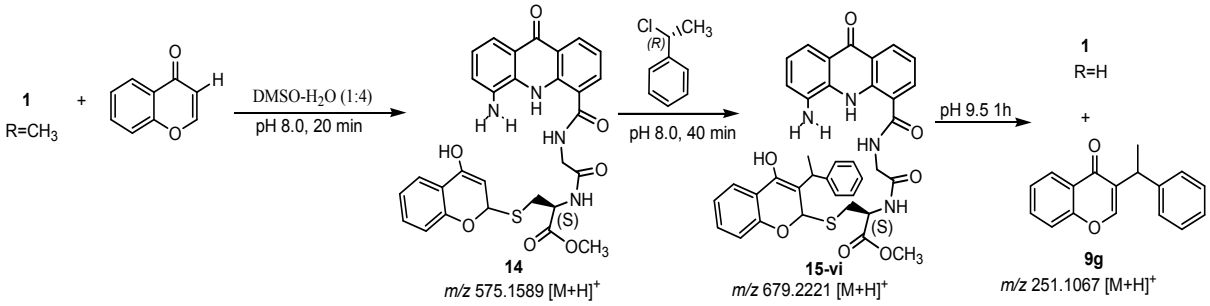


Figure S40. HRMS of the reaction mixture of **1** and chromone after the addition of benzoyl chloride and change of pH from 8.0 to 9.5 (1h stirring at room temperature). The peaks at *m/z* 251.0697, 501.1327 corresponding to monomer and dimer, respectively clearly indicate the formation of product **9f**, the respective calcd *m/z* is 251.0703 and 501.1333.

(*S*)- 3-(1-Phenylethyl)-chromen-4-one (9g).



General procedure was performed on a 1 mmol scale with reagent **1** and chromone in 30 mL of DMSO-H_2O (1:4, v/v) with stirring at 25 – 28 °C keeping the pH of the reaction mixture

8.0 for 20 min. Then (*R*)-1-bromoethyl benzene was added and the reaction mixture was further stirred at 25 – 28 ^{o}C for 40 min. Then pH of the reaction mixture was changed to 9.5 and formation of **9g** and **1** (R=H) was detected after 1h of stirring (Figure S41). The reaction mixture was washed with $CHCl_3$ (5x25 mL). Chloroform was removed slowly at 40 – 45 ^{o}C. The crude residue was purified by flash chromatography to furnish the title compound as a creamish solid (176 mg, 0.7 mmol, 73%), mp 148 ^{o}C. $[\alpha]_D$ = -22^{o} (1, $CHCl_3$), ^{1}H NMR (500 MHz, $CDCl_3$): δ 1.58 (d, *J* = 6.5 Hz, 3H, CH_3), 3.57-3.59 (m, 1H, CH), 6.71 (s, 1H, CH), 6.90-6.93 (m, 2H, ArH), 7.24-7.27 (m, 3H, ArH), 7.45 (m, 1H, ArH), 7.77 (d, *J* = 7.2 Hz, 1H, ArH), 7.83-7.84 (m, 1H, ArH), 7.90 (m, 1H, ArH). ^{13}C NMR (125 MHz, $CDCl_3$): δ 19.22, 44.81, 115.56, 119.03, 124.46, 125.06, 126.58, 129.30, 130.13, 130.55, 132.86, 136.86, 144.48, 147.98, 158.05, 182.77. HRMS-ESI (*m/z*) found $[M+H]^+$ 251.1059, $C_{17}H_{14}O_2$ requires 251.1067.

Similar to the above reaction, use of (*S*)- 1-bromoethyl benzene provided product **9h**. The reaction mixture exhibited similar HRMS as given in figure S41.

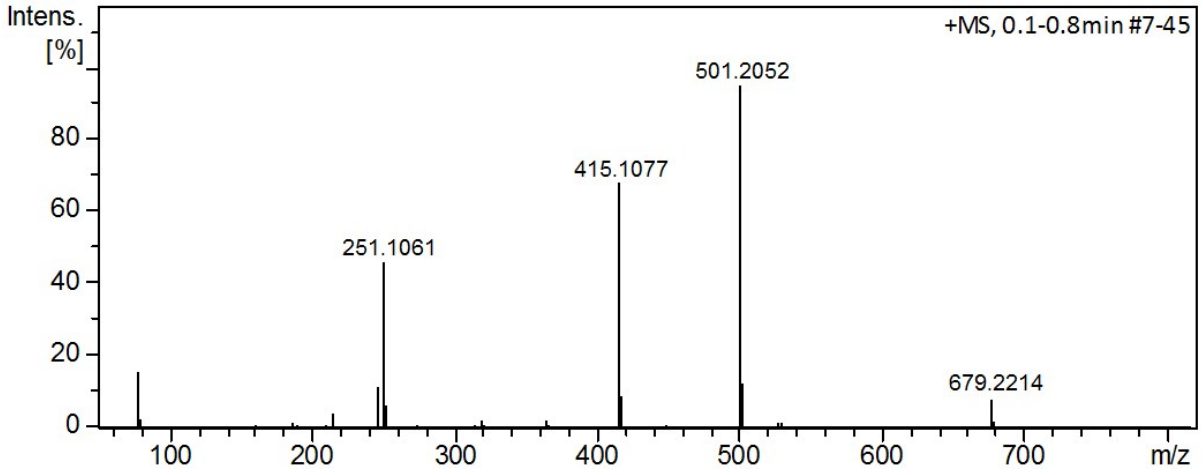
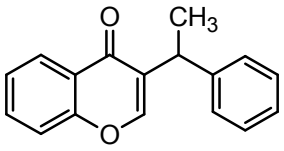


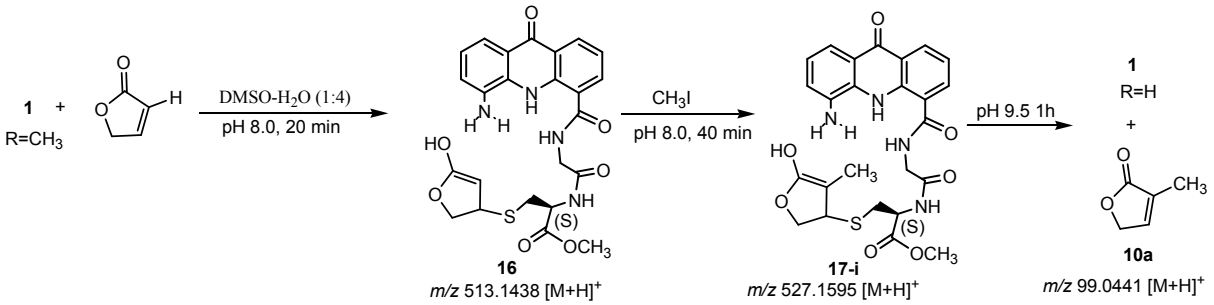
Figure S41. HRMS of the reaction mixture of **1** and chromone after the addition of (*R*)-1-phenylethyl bromide and change of pH from 8.0 to 9.5 (1h stirring at room temperature). The peaks at *m/z* 251.1061, 501.2052 corresponding to monomer and dimer, respectively clearly indicate the formation of product **9g**, the respective calcd *m/z* is 251.1067 and 501.2060. Reagent **1** was also regenerated.

(*R*)- 3-(1-Phenylethyl)-chromen-4-one (9h).



General procedure was performed on a 1 mmol scale with reagent **1** and chromone in 30 mL of DMSO-H_2O (1:4, v/v) with stirring at 25 – 28 ^oC keeping the pH of the reaction mixture 8.0 for 20 min. Then (*S*)-1-bromoethyl benzene was added and the reaction mixture was further stirred at 25 – 28 ^oC for 40 min. Then pH of the reaction mixture was changed to 9.5 and formation of **9h** and **1** (R=H) was observed after 1h of stirring. The reaction mixture was washed with $CHCl_3$ (5x25 mL). Chloroform was removed slowly at 40 – 45 ^oC. The crude residue was purified by flash chromatography to furnish the title compound as a creamish solid (175 mg, 0.7 mmol, 70%), mp 148 ^oC. $[\alpha]_D$ = 24^o (1, $CHCl_3$), ^1H NMR (500 MHz, $CDCl_3$): δ 1.54 (d, *J* = 6.5 Hz, 3H, CH_3), 3.64 (m, 1H, CH), 6.88 (s, 1H, CH), 7.26 (m, 1H, ArH), 7.28 (m, 2H, ArH), 7.36 (m, 2H, ArH), 7.45 (m, 1H, ArH), 7.53 (d, *J* = 7.4 Hz, 1H, ArH), 7.56 (m, 1H, ArH), 8.11 (d, *J* = 7.8 Hz, 1H, ArH). ^{13}C NMR (125 MHz, $CDCl_3$): δ 19.63, 46.89, 116.06, 119.22, 123.34, 123.74, 125.69, 125.73, 127.59, 127.67, 128.55, 128.58, 135.13, 140.49, 150.54, 157.08, 182.81. HRMS-ESI (*m/z*) found $[M+H]^+$ 251.1059, $C_{17}H_{14}O_2$ requires 251.1067.

3-Methyl-5*H*-furan-2-one (10a).



General procedure was performed on a 1 mmol scale with reagent **1** and 2(5*H*)-furanone in 30 mL of DMSO-H_2O (1:4, v/v) with stirring at 25 – 28 ^oC keeping the pH of the reaction mixture 8.0 for 20 min (Figure S42). Then CH_3I was added and the reaction mixture was further stirred at 25 – 28 ^oC for 40 min. Then pH of the reaction mixture was changed to 9.5 and formation of **10a** and **1** (R=H) was observed after 1h of stirring (Figure S43). The reaction mixture was washed with $CHCl_3$ (5x25 mL). Chloroform was removed slowly at 40

– 45 °C. The crude residue was purified by flash chromatography to furnish the title compound as a thick oil (70 mg, 0.7 mmol, 72%). ^{1}H NMR[4,5] (500 MHz, $CDCl_3$): δ 1.94 (s, 3H, CH_3), 4.09 (d, *J* = 7.5 Hz, 2H, CH_2), 7.44 (dd, *J* = 6.6 Hz, 7.0 Hz, 1H, CH). ^{13}C NMR (125 MHz, $CDCl_3$): δ 18.77, 65.17, 132.82, 144.44, 166.07. HRMS-ESI (*m/z*) found $[M+H]^+$ 99.0433, $C_5H_6O_2$ requires 99.0441.

(4) E. Yoneda, S.-W. Zhang, D.-Y. Zhou, K. Onitsuka, S. Takashashi, *J. Org. Chem*. 2003, **68**, 8571-8576.

(5) J. Boukouvalas, R. P. Loach, *J. Org. Chem*. 2008, **73**, 8109-8112.

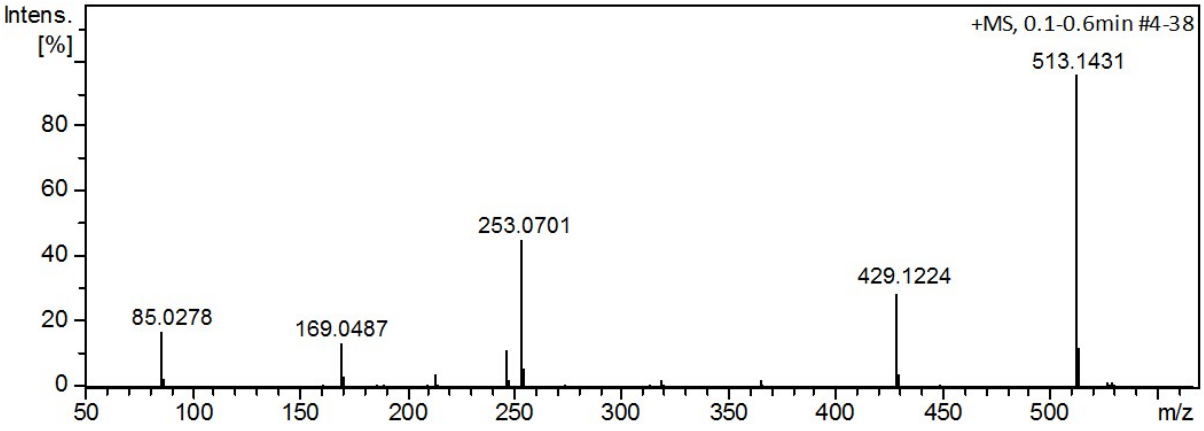


Figure S42. HRMS of the reaction mixture of reagent **1** and 2-(5*H*)-furanone after 20 min of stirring at pH 8.0. Most intense peak was corresponding to *m/z* of **16** (calcd *m/z* 513.1438 $[M+H]^+$).

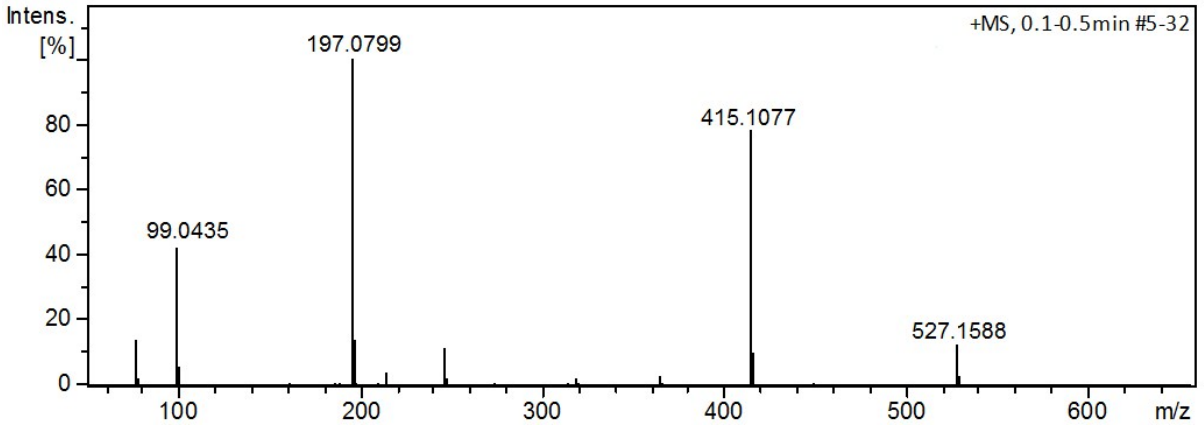
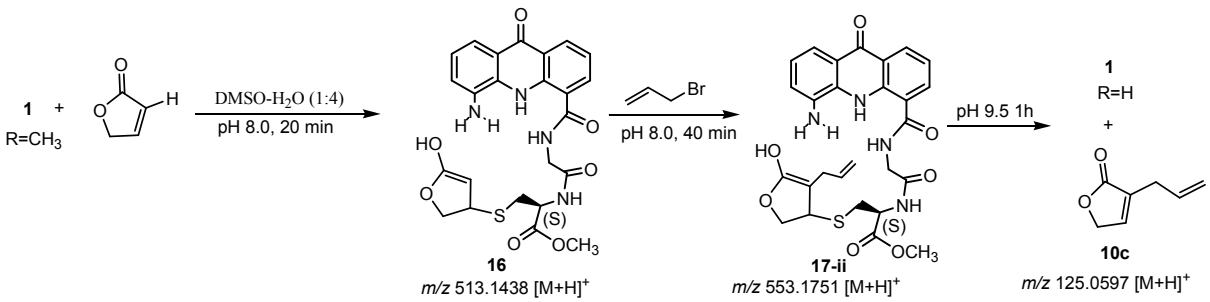


Figure S43. HRMS of the reaction mixture of **1** and 2(5*H*)-furanone after the addition of methyl iodide and change of pH from 8.0 to 9.5 (1h stirring at room temperature). The peaks at *m/z* 99.0435, 197.0799 corresponding to monomer and dimer, respectively clearly indicate the formation of product **10a**, the respective calcd *m/z* is 99.0441 and 197.0808.

3-Allyl-5*H*-furan-2-one (10c).



General procedure was performed on a 1 mmol scale with reagent **1** and 2(5*H*)-furanone in 30 mL of DMSO-H_2O (1:4, v/v) with stirring at 25 – 28 ^oC keeping the pH of the reaction mixture 8.0 for 20 min. Then allyl bromide was added and the reaction mixture was further stirred at 25 – 28 ^oC for 40 min. Then pH of the reaction mixture was changed to 9.5 and formation of the product **10c** and **1** (R=H) was observed after 1h of stirring (Figure S44). The reaction mixture was washed with $CHCl_3$ (5x25 mL). Chloroform was removed slowly at 40 – 45 ^oC. The crude residue was purified by flash chromatography to furnish the title compound as a thick oil (87 mg, 0.7 mmol, 73%). ^1H NMR[5] (500 MHz, $CDCl_3$): δ 2.60 (d, *J* = 5.5 Hz, 2H, CH_2), 4.09 (d, *J*=7.5 Hz, 2H, CH_2), 4.26-4.28 (m, 1H, CH_2), 4.50-4.53 (m, 1H, CH_2), 5.20-5.22 (m, 1H, CH), 7.44 (dd, *J* = 8.0 Hz, 4.5 Hz, 1H, CH). ^{13}C NMR (125 MHz, $CDCl_3$): δ 35.13, 66.73, 118.95, 130.08, 132.78, 144.40, 166.03. HRMS-ESI (*m/z*) found $[M+H]^+$ 125.0591, $C_7H_8O_2$ requires 125.0597.

(5) J. Boukouvalas, R. P. Loach, *J. Org. Chem*. 2008, **73**, 8109-8112.

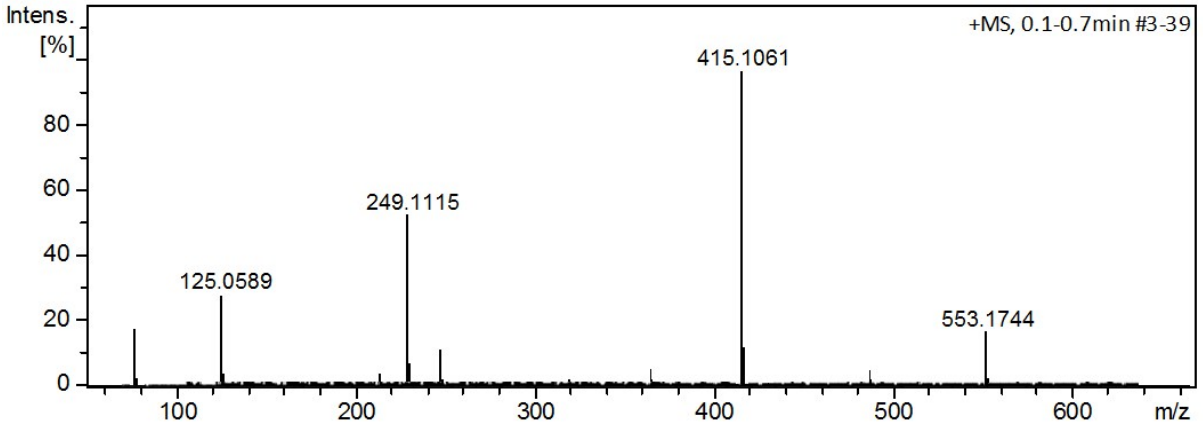
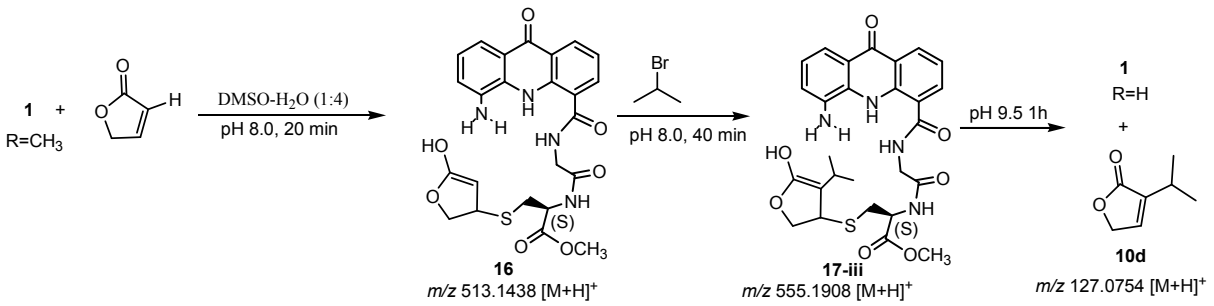


Figure S44. HRMS of the reaction mixture of **1** and 2(5*H*)-furanone after the addition of allyl bromide and change of pH from 8.0 to 9.5 (1h stirring at room temperature). The peaks at *m/z* 125.0589, 249.1115 corresponding to monomer and dimer, respectively clearly indicate the formation of product **10c**, the respective calcd *m/z* is 125.0597 and 249.1121.

3-Isopropyl-5*H*-furan-2-one (10d).



General procedure was performed on a 1 mmol scale with reagent **1** and 2(5*H*)-furanone in 30 mL of DMSO-H_2O (1:4, v/v) with stirring at 25 – 28 ^oC keeping the pH of the reaction mixture 8.0 for 20 min. Then iso-propyl bromide was added and the reaction mixture was further stirred at 25 – 28 ^oC for 40 min. Then pH of the reaction mixture was changed to 9.5 after 1h of stirring, formation of **10d** and **1** (R=H) was observed (Figure S45). The reaction mixture was washed with $CHCl_3$ (5x25 mL). Chloroform was removed slowly at 40 – 45 ^oC. The crude residue was purified by flash chromatography to furnish the title compound as a thick oil (90 mg, 0.7 mmol, 70%). ^1H NMR (500 MHz, $CDCl_3$): δ 1.12 (d, J = 6.9 Hz, 6H, CH_3), 1.87-1.92 (m, 1H, CH), 4.64 (d, J = 7.2 Hz, 2H, CH_2), 7.57-7.59 (m, 1H, CH). ^{13}C NMR (125 MHz, $CDCl_3$): δ 21.04, 21.81, 32.07, 69.09, 132.73, 144.36, 173.07. HRMS-ESI (*m/z*) found $[M+H]^+$ 127.0744, $C_7H_{10}O_2$ requires 127.0754.

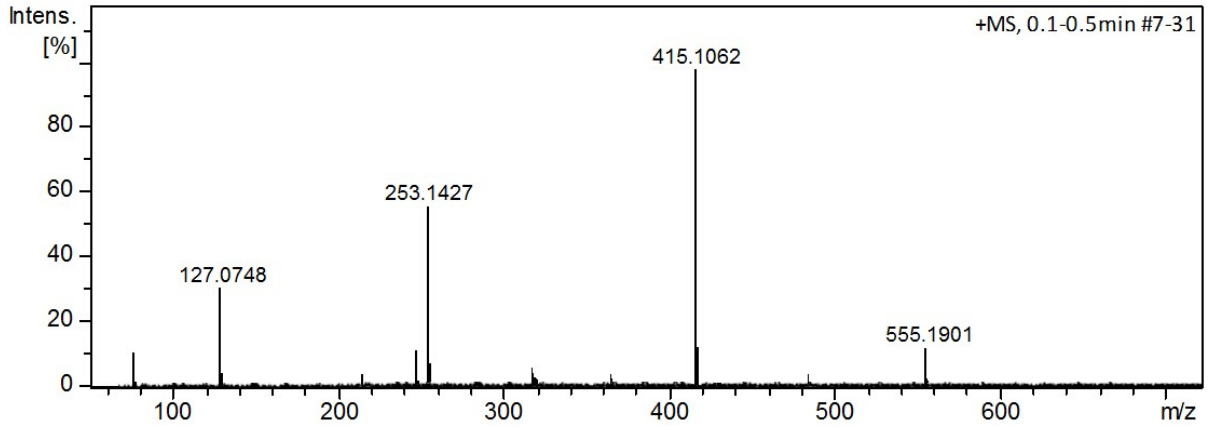
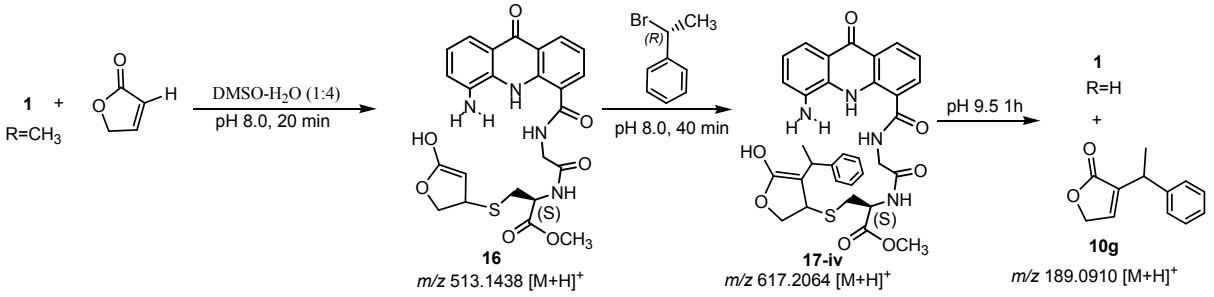


Figure S45. HRMS of the reaction mixture of **1** and 2(5*H*)-furanone after the addition of iso-propyl bromide and change of pH from 8.0 to 9.5 (1h stirring at room temperature). The peaks at *m/z* 127.0748, 253.1427 corresponding to monomer and dimer, respectively clearly indicate the formation of product **10d**, the respective calcd *m/z* is 127.0754 and 253.1434.

(*S*)-3-(1-Phenylethyl)-5*H*-furan-2-one (10g).



General procedure was performed on a 1 mmol scale with reagent **1** and 2(5*H*)-furanone in 30 mL of DMSO-H_2O (1:4, v/v) with stirring at 25 – 28 ^oC keeping the pH of the reaction mixture 8.0 for 20 min. Then (*R*)-1-bromoethyl benzene was added and the reaction mixture was further stirred at 25 – 28 ^oC for 40 min. Then pH of the reaction mixture was changed to 9.5 and formation of **10g** and **1** (R=H) was observed after 1h of stirring (Figure S46). The reaction mixture was washed with $CHCl_3$ (5x25 mL). Chloroform was removed slowly at 40 – 45 ^oC. The crude residue was purified by flash chromatography to furnish the title compound as a white amorphous solid (thick liquid solidified at low temperature) (123 mg, 0.65 mmol, 65%), mp 102-5 ^oC. $[\alpha]_D$ = -20^o (1, $CHCl_3$), ^1H NMR (500 MHz, $CDCl_3$): δ 1.70 (d, *J* = 6.5 Hz, 3H, CH_3), 3.64 (q, *J* = 6.5 Hz, 1H, CH), 4.88 (d, *J* = 7.4 Hz, 2H, CH_2), 6.92-6.99 (m, 3H, ArH), 7.30-7.31 (m, 2H, ArH), 7.88-7.89 (dd, *J* = 7.4 Hz, 4.5 Hz, 1H, CH). ^{13}C NMR (125 MHz, $CDCl_3$): δ 19.75, 50.15, 71.15, 124.39, 125.00, 126.52, 129.24, 130.06, 136.79, 140.12, 144.42, 166.04. HRMS-ESI (*m/z*) found $[M+H]^+$ 189.0901, $C_{12}H_{12}O_2$ requires 189.0910.

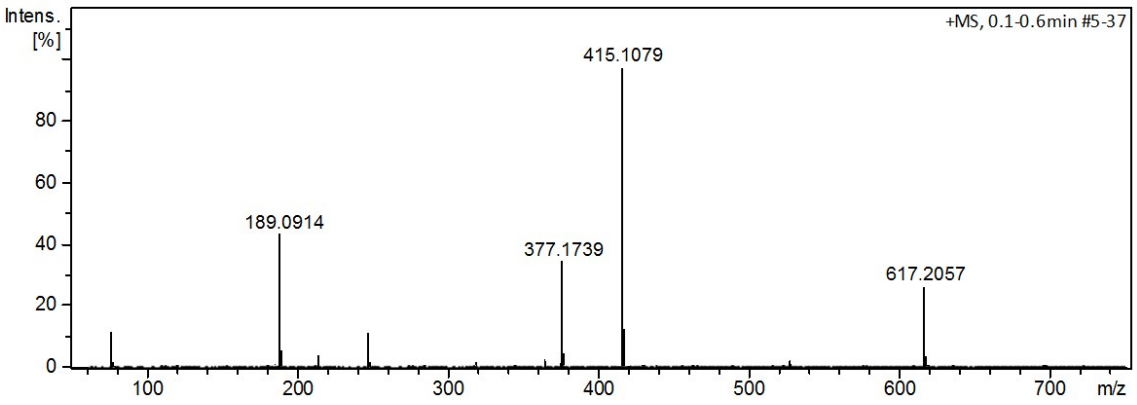
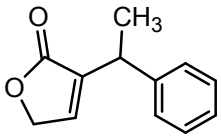


Figure S46. HRMS of the reaction mixture of **1** and 2(5*H*)-furanone after the addition of (*R*)/(*S*)-1-bromoethyl benzene and change of pH from 8.0 to 9.5 (1h stirring at room temperature). The peaks at *m/z* 189.0914, 377.1739 corresponding to monomer and dimer, respectively clearly indicate the formation of product **10g/10h**, the respective calcd *m/z* is 189.0910 and 377.1747.

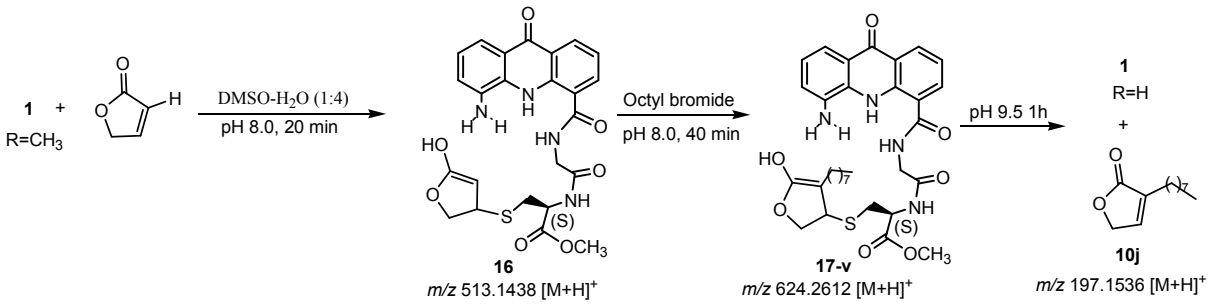
(*R*)-(1-Phenylethyl)-5*H*-furan-2-one (10h).



General procedure was performed on a 1 mmol scale with reagent **1** and 2(5*H*)-furanone in 30 mL of DMSO-H_2O (1:4, v/v) with stirring at 25 – 28 ^oC keeping the pH of the reaction mixture 8.0 for 20 min. Then (*S*)-1-bromoethyl benzene was added and the reaction mixture was further stirred at 25 – 28 ^oC for 40 min. Then pH of the reaction mixture was changed to 9.5 and formation of the product and **1** (R=H) was observed after 1h of stirring (similar mass spectrum was recorded as shown in figure S46). The reaction mixture was washed with $CHCl_3$ (5x25 mL). Chloroform was removed slowly at 40 – 45 ^oC. The crude residue was purified by flash chromatography to furnish the title compound as a white amorphous solid (108 mg, 0.6 mmol, 62%), mp 105 ^oC. $[\alpha]_D = 24^o$ (1, $CHCl_3$), ^1H NMR (500 MHz, $CDCl_3$): δ 1.71 (d, *J* = 6.5 Hz, 3H, CH_3), 3.63 (q, J = 6.5 Hz, 1H, CH), 4.89 (d, *J* = 7.6 Hz, 2H, CH_2), 6.92-6.99 (m, 3H, ArH), 7.30-7.31 (m, 2H, ArH), 7.88-7.90 (dd, *J* = 7.4 Hz, 4.5 Hz, 1H, CH). ^{13}C NMR (125 MHz, $CDCl_3$): δ 19.52, 50.72, 71.21, 124.50, 125.86, 126.52, 129.26, 130.36, 136.23, 140.10, 144.60, 166.39. HRMS-ESI (*m/z*) found $[M+H]^+$ 189.0908, $C_{12}H_{12}O_2$ requires 189.0910.

10i. With the same experimental procedure as used for the synthesis of compounds 10g, 10h but using (*R*,*S*)-1-phenylethyl bromide, compound 10i was obtained which has same ^1H NMR spectrum as for compounds 10g,h. $[\alpha]_D$ of compound 10i was zero and certainly, as expected, it was a mixture of 10g and 10h.

3-Octyl-5*H*-furan-2-one (10j).



General procedure was performed on a 1 mmol scale with reagent **1** and 2(5*H*)-furanone in 30 mL of DMSO-H_2O (1:4, v/v) with stirring at 25 – 28 ^oC keeping the pH of the reaction mixture 8.0 for 20 min. Then octyl bromide was added and the reaction mixture was further

stirred at 25 – 28 °C for 40 min. Then pH of the reaction mixture was changed to 9.5 and formation of **10j** and **1** (R=H) was observed after 1h of stirring (Figure S47). The reaction mixture was washed with $CHCl_3$ (5x25 mL). Chloroform was removed slowly at 40 – 45 °C. The crude residue was purified by flash chromatography to furnish the title compound as a white solid (108 mg, 0.6 mmol, 60%), mp 112 °C. ^{1}H NMR[6] (500 MHz, $CDCl_3$): δ 0.85 (t, *J* = 6.3 Hz, 3H, CH_3), 1.49-1.64 (m, 12H, 6xCH_2), 1.74-1.78 (m, 2H, CH_2), 4.57 (d, *J* = 7.8 Hz, 2H, CH_2), 7.17-7.20 (m, 1H, CH). ^{13}C NMR (125 MHz, $CDCl_3$): δ 11.74, 18.45, 18.86, 19.22, 22.74, 34.74, 70.14, 132.79, 136.78, 166.04. HRMS-ESI (*m/z*) found $[M+H]^+$ 197.1530, $C_{12}H_{20}O_2$ requires 197.1536.

(6) M. Tsubuki, K. Takashashi, T. Honda, *J. Org. Chem*. 2009, **74**, 1422-1425.

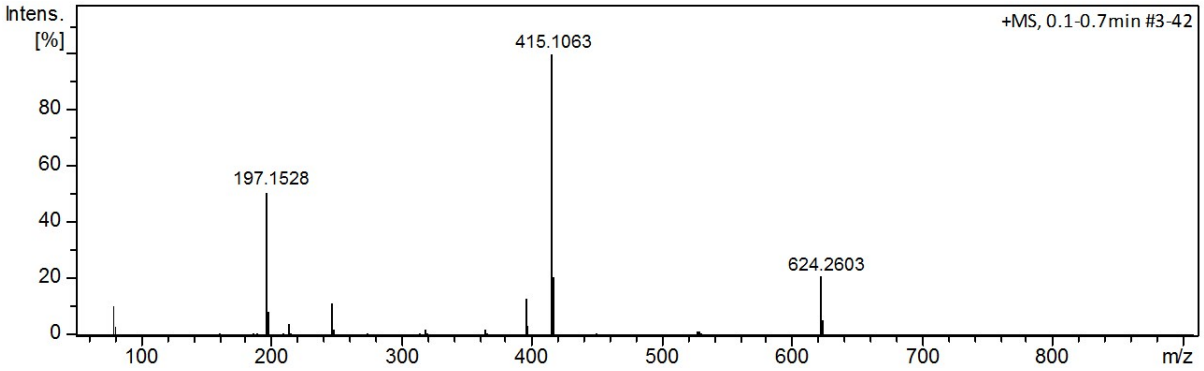


Figure S47. HRMS of the reaction mixture of **1** and 2(5*H*)-furanone after the addition of 1-octyl bromide and change of pH from 8.0 to 9.5 (1h stirring at room temperature). The peaks at *m/z* 197.1528 was corresponding to product **10j**, the respective calcd *m/z* is 197.1536.

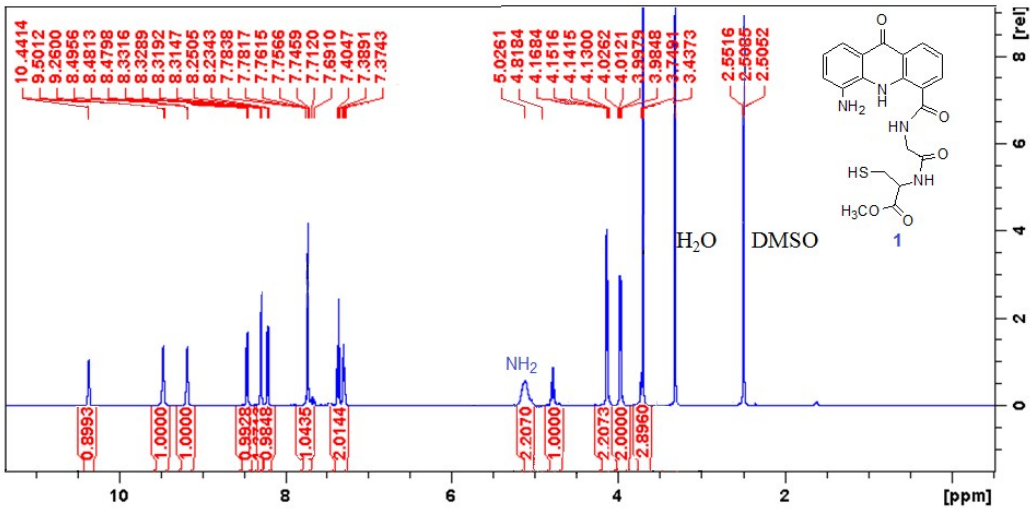


Figure S48a. ^{1}H NMR spectrum of compound **1** (R=OCH_3).

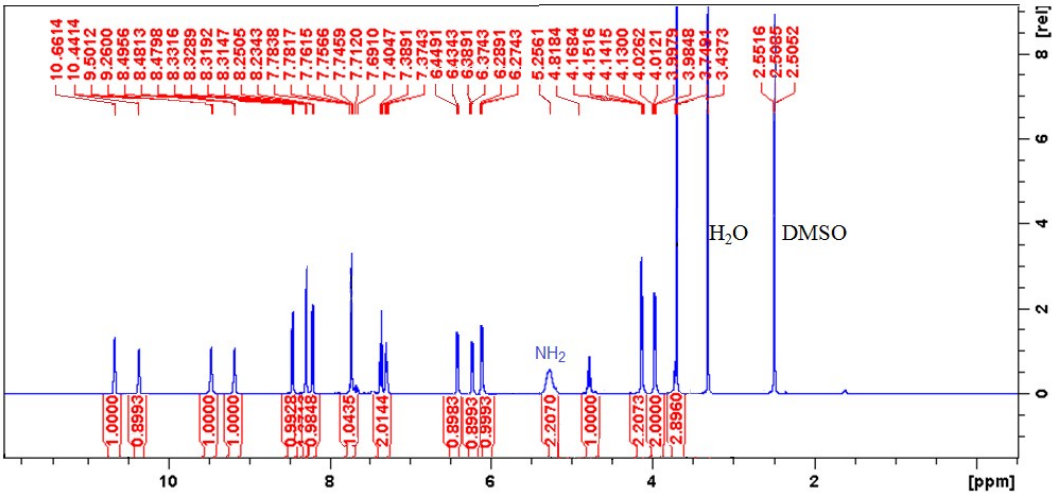


Figure S48b. ^{1}H NMR spectrum of reaction mixture of compound **1** and acrolein. NH_2 signal is shifted downfield.

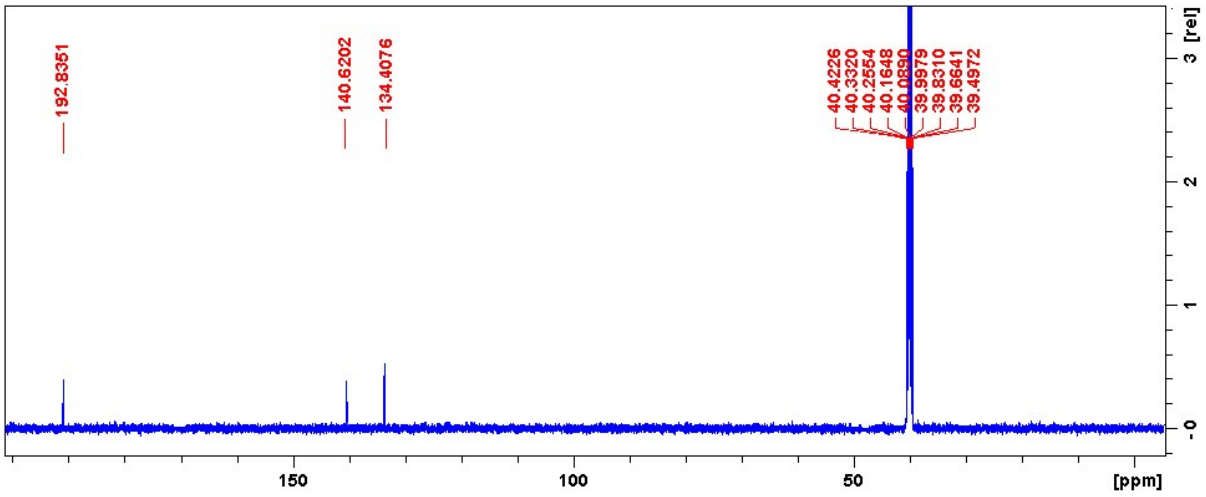


Figure 48c. ^{13}C NMR spectrum of acrolein in DMSO-d_6.

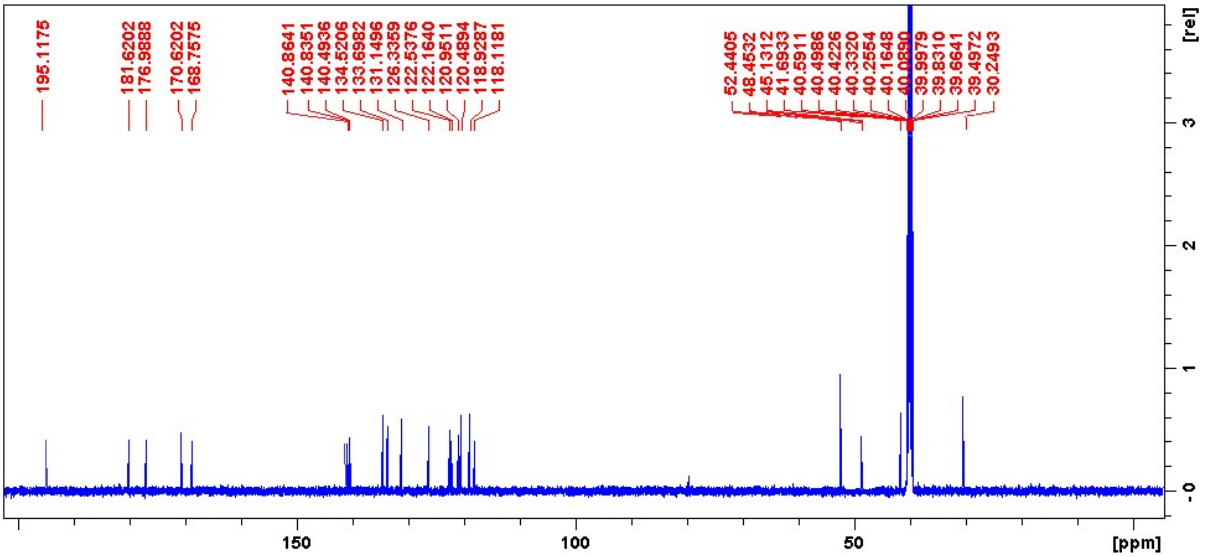


Figure S48d. ^{13}C NMR spectrum of reaction mixture of compound **1** and acrolein. Carbonyl C of acrolein is shifted downfield.

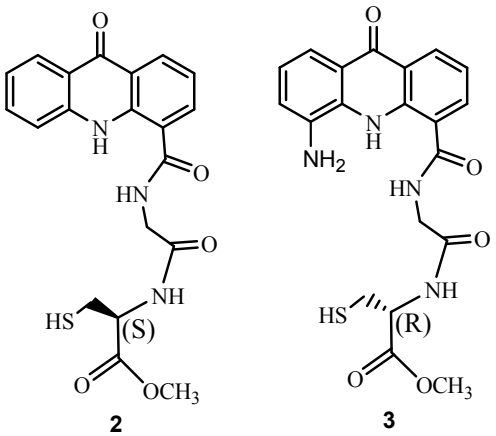


Figure S49. These compounds did not react with α, β-unsaturated carbonyl system under the present reaction conditions

Reaction of reagent 1 with acrolein and subsequent methylation in DMSO-D_2O. Solution of compound **1** (1 mmol) and acrolein (1.2 equiv) in 40 ml DMSO-D_2O (1:4, v/v) having pH 8.0 was stirred at 25-28 ^oC. Development of a new spot on TLC plate and the peak corresponding to *m/z* of **1** – acrolein (compared with D_2O exchanged adduct **4**) was observed after 1.5 h of stirring the reaction mixture. Then CH_3I (1.5 equiv) was added to the reaction mixture and pH was changed to 9.5. It took 4h for the formation of the new product and reagent **1** (R=H). Therefore, in comparison to the reaction in DMSO-H_2O, it took longer time in DMSO-D_2O (Figure S49).

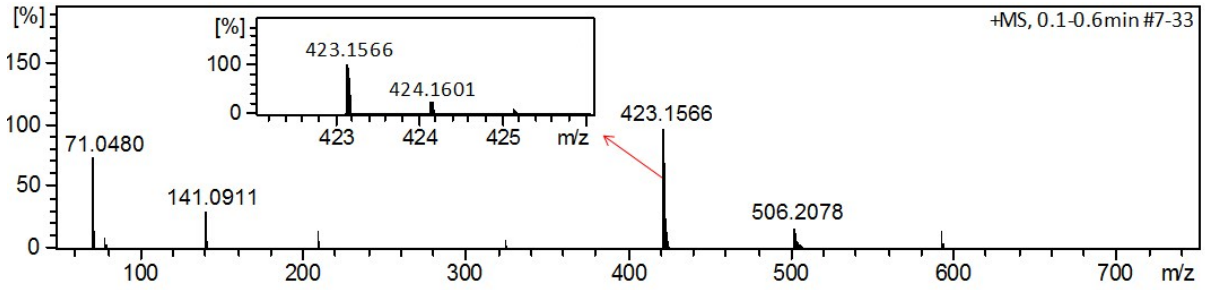


Figure S50. HRMS of the reaction mixture of **1** and acrolein in DMSO-D_2O after the addition of CH_3I and change of pH from 8.0 to 9.5 (6h stirring at room temperature). The peaks at *m/z* 506.2078 corresponds to 1 – acrolein adduct after methylation (deuteriated) (calcd *m/z* 506.2085 $[M+D]^+$). Peak at *m/z* 423.1566 corresponds to deuteriated reagent **1** (R = H) (calcd *m/z* 423.1573 $[M+D]^+$).

^{1}H NMR, ^{13}C NMR and high resolution mass spectra of the compounds

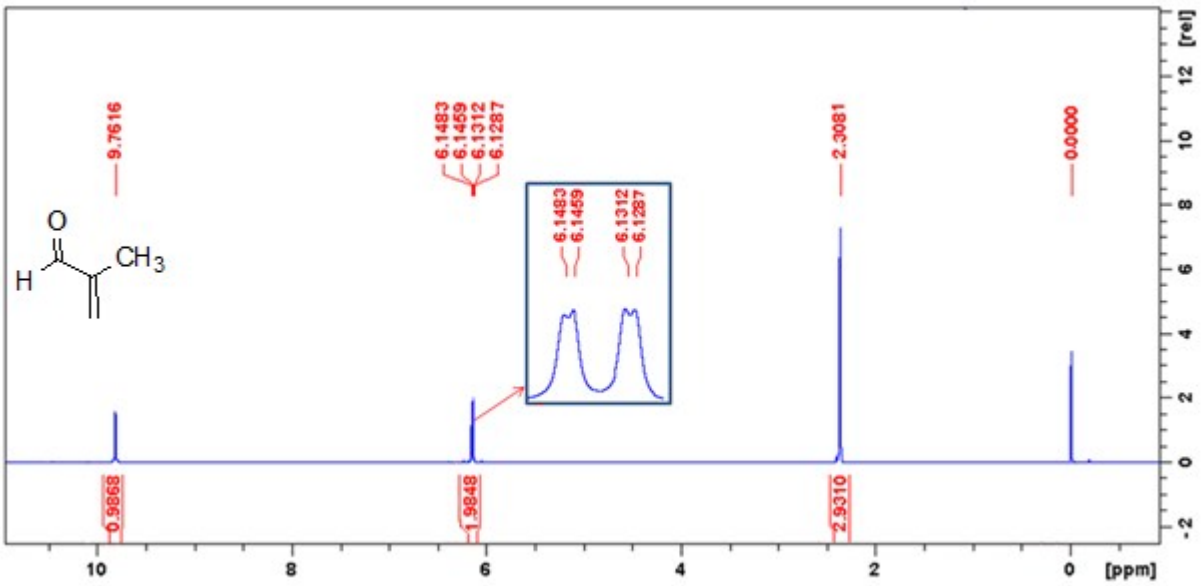


Figure S51a. ^{1}H NMR spectrum of compound **5a**.

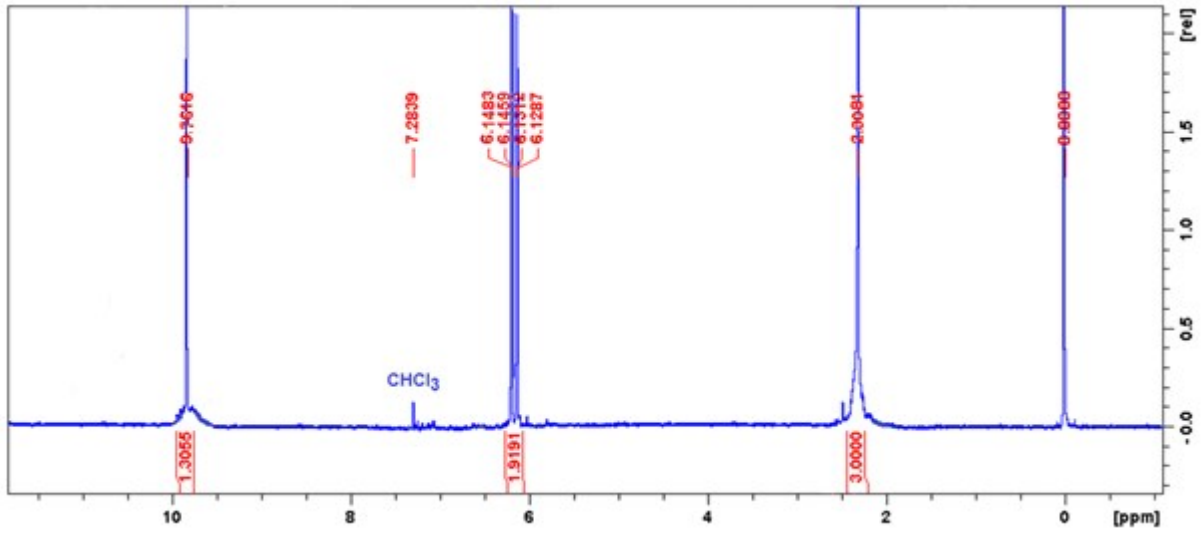


Figure S51b. Vertical expansion of ^{1}H NMR spectrum of compound **5a**.

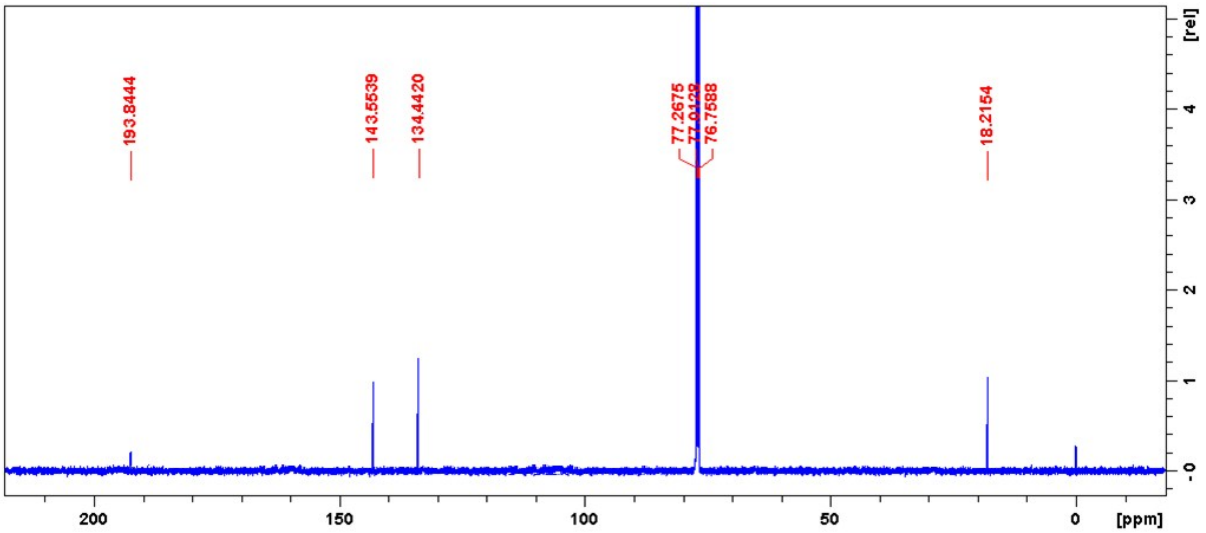


Figure S52. ^{13}C NMR spectrum of compound **5a**.

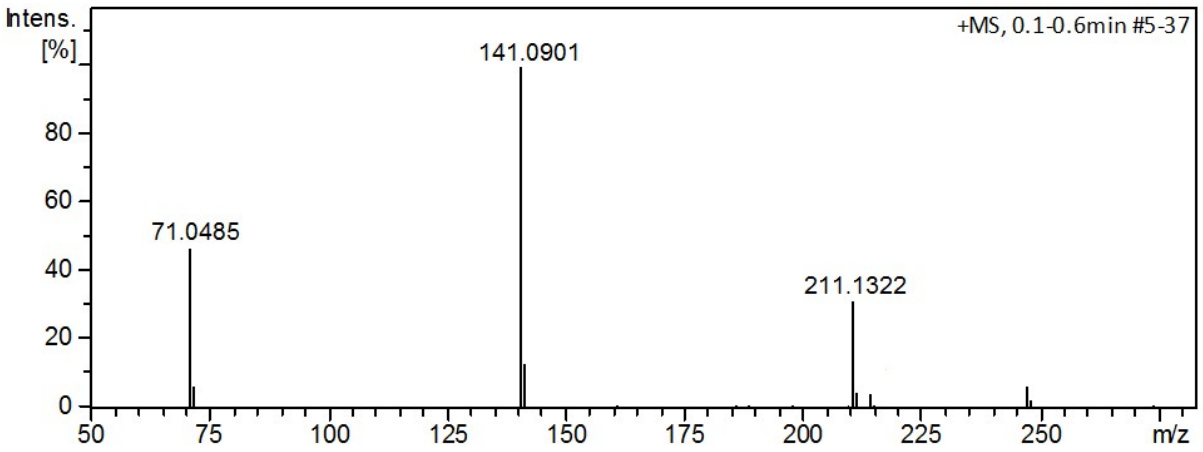


Figure S53. HRMS of **5a** showing peaks due to monomer (71.0485), dimer (141.0901) and trimer (211.1322) of the product.

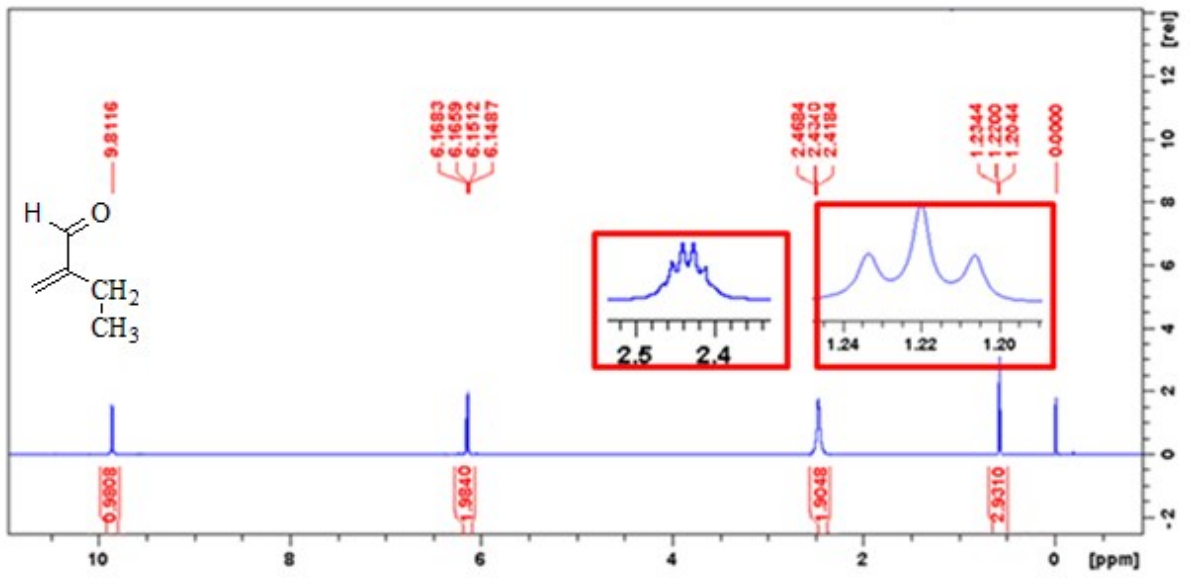


Figure S54. ^{1}H NMR spectrum of compound **5b**.

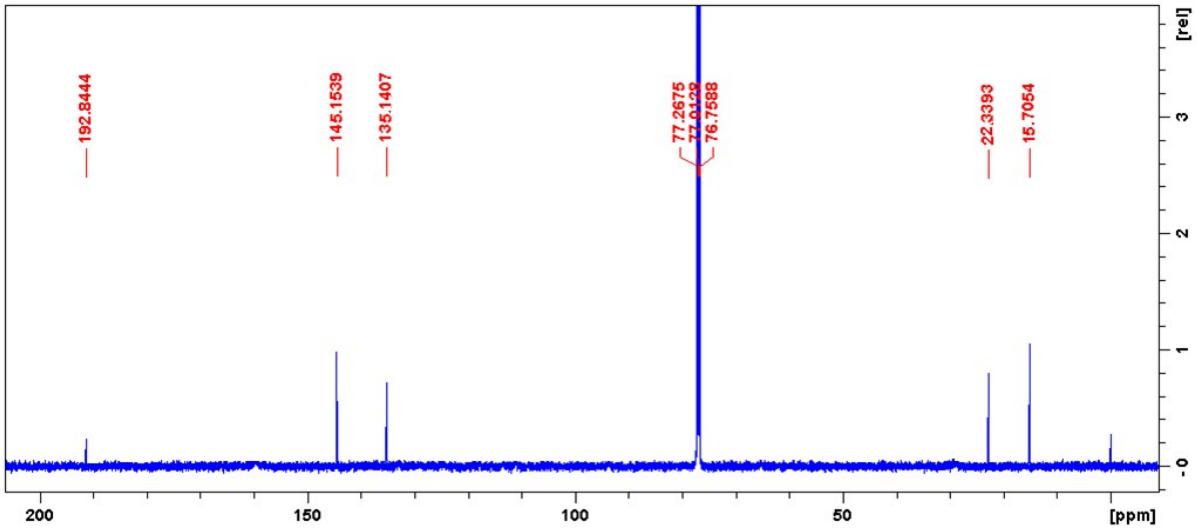


Figure S55. ^{13}C NMR spectrum of compound **5b**.

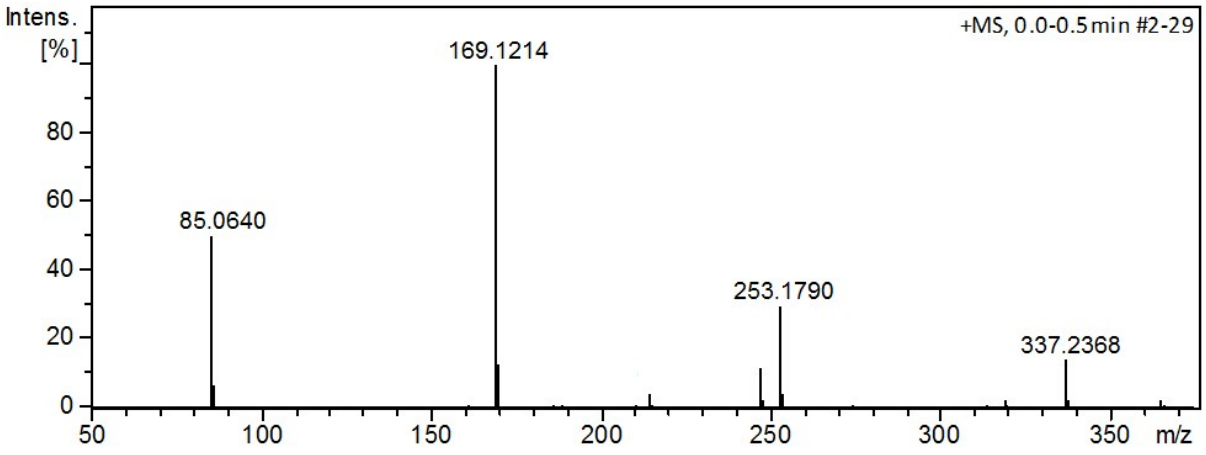


Figure S56. HRMS of **5b**. Peaks at *m/z* 85.0640, 169.1214, 253.1790 and 337.2368 correspond to monomer, dimer, trimer and tetramer of the product, respectively.

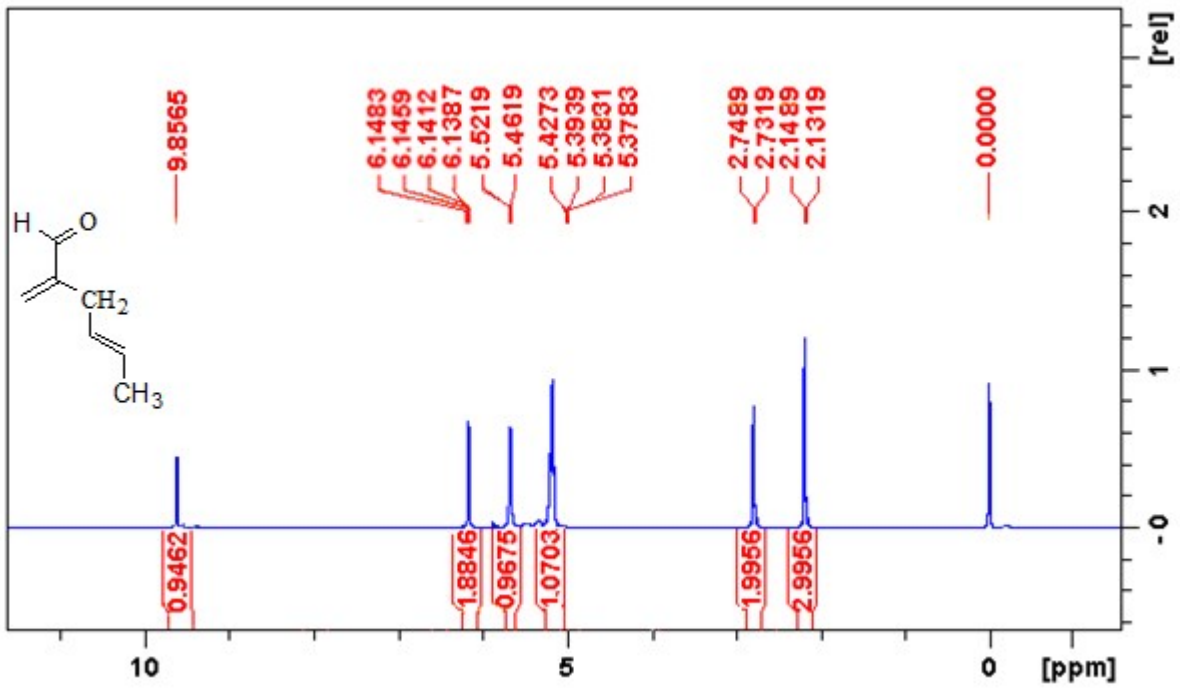


Figure S57. ^{1}H NMR spectrum of compound **5c**.

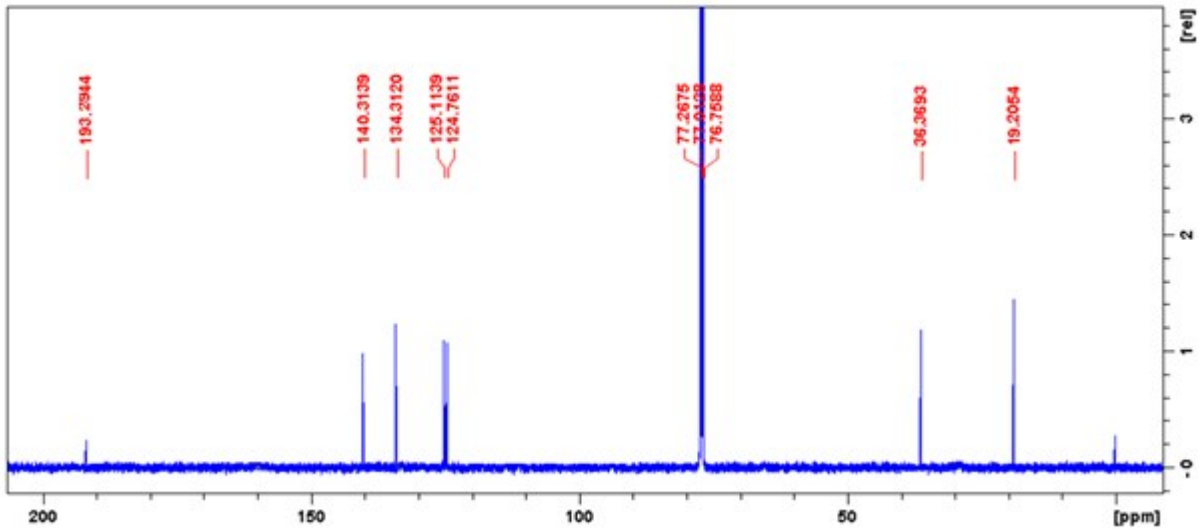


Figure S58. ^{13}C NMR spectrum of compound **5c**.

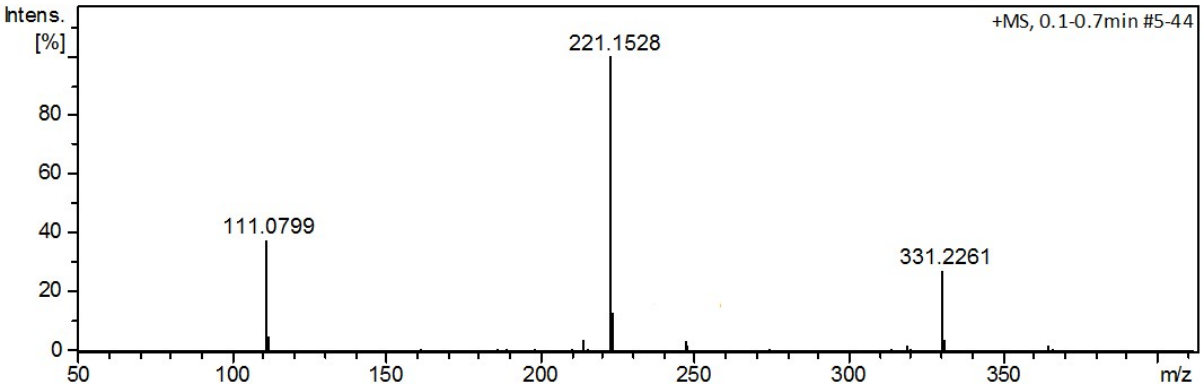


Figure S59. HRMS of **5c**.

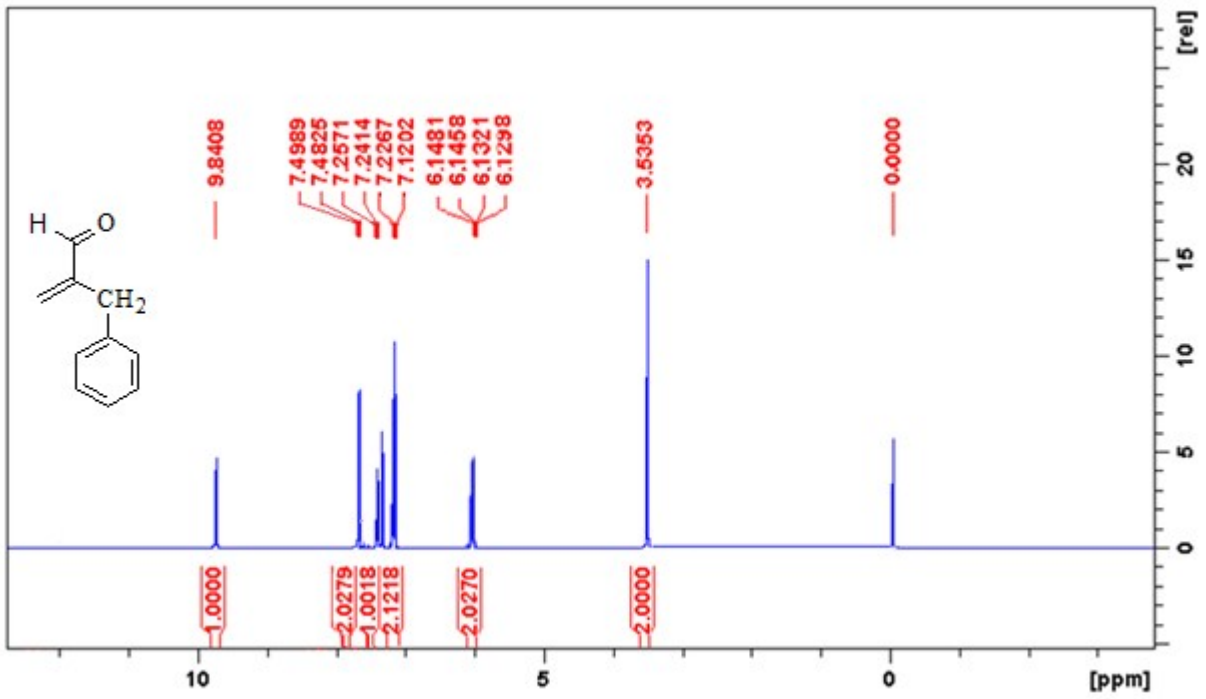


Figure S60. [1]H NMR spectrum of compound **5d-i**.

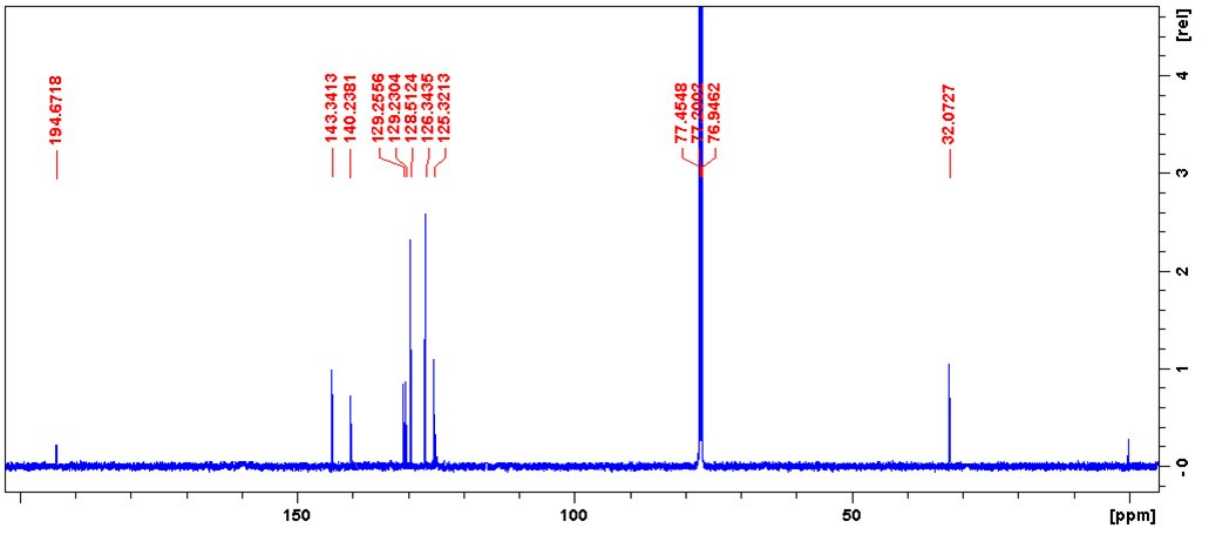


Figure S61. [13]C NMR spectrum of compound **5d-i**.

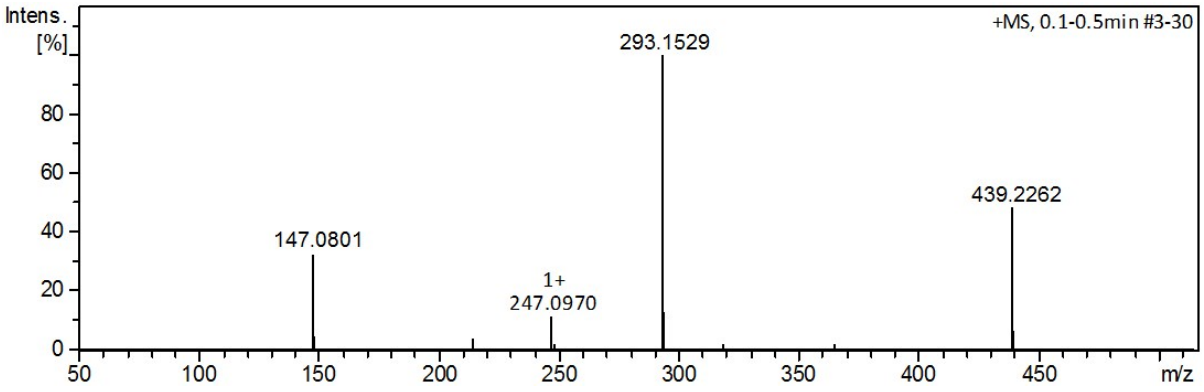


Figure S62. HRMS of **5d-i**.

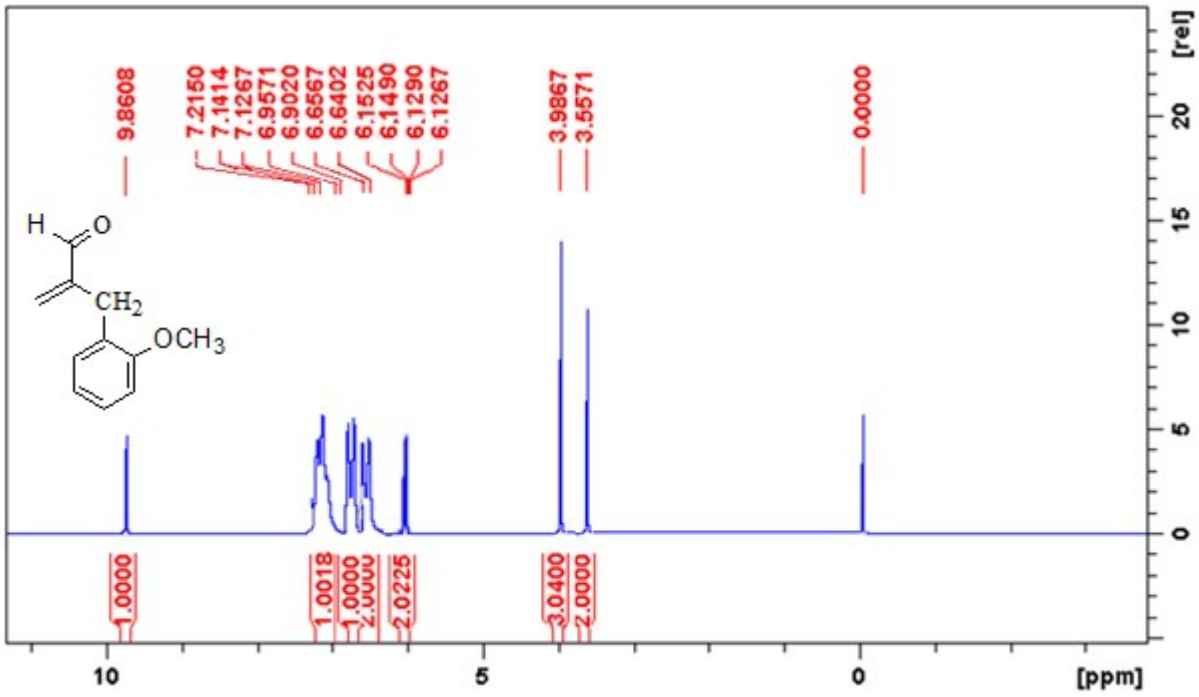


Figure S63. ^{1}H NMR spectrum of compound **5d-ii**.

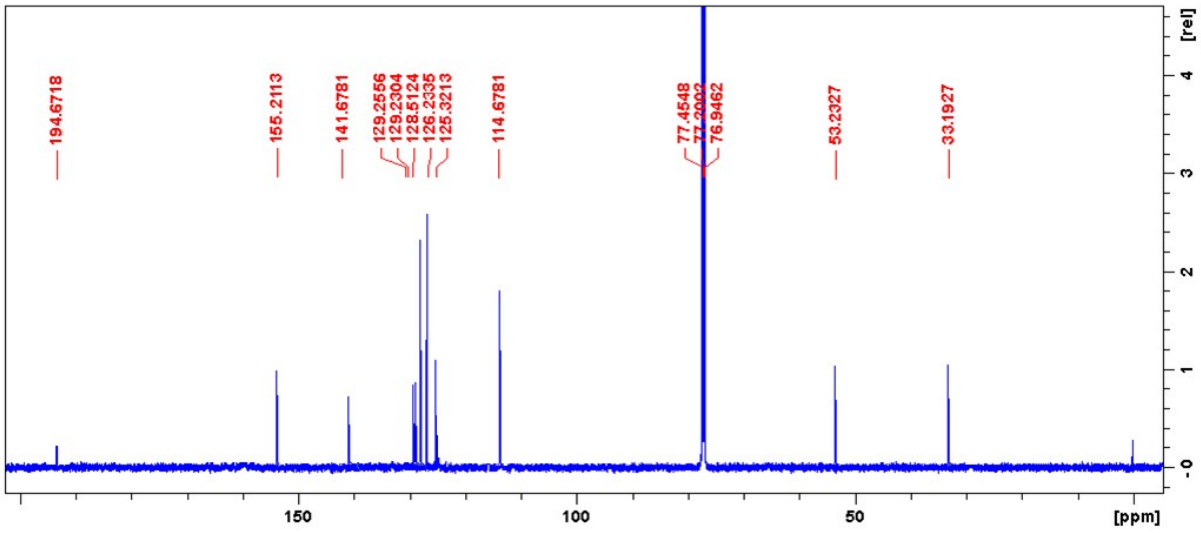


Figure S64. ^{13}C NMR spectrum of compound **5d-ii**.

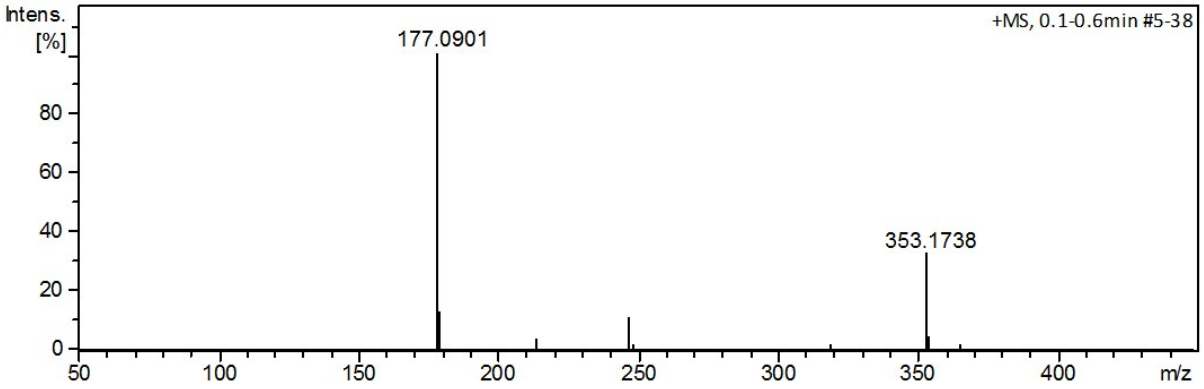


Figure S65. HRMS of **5d-ii**.

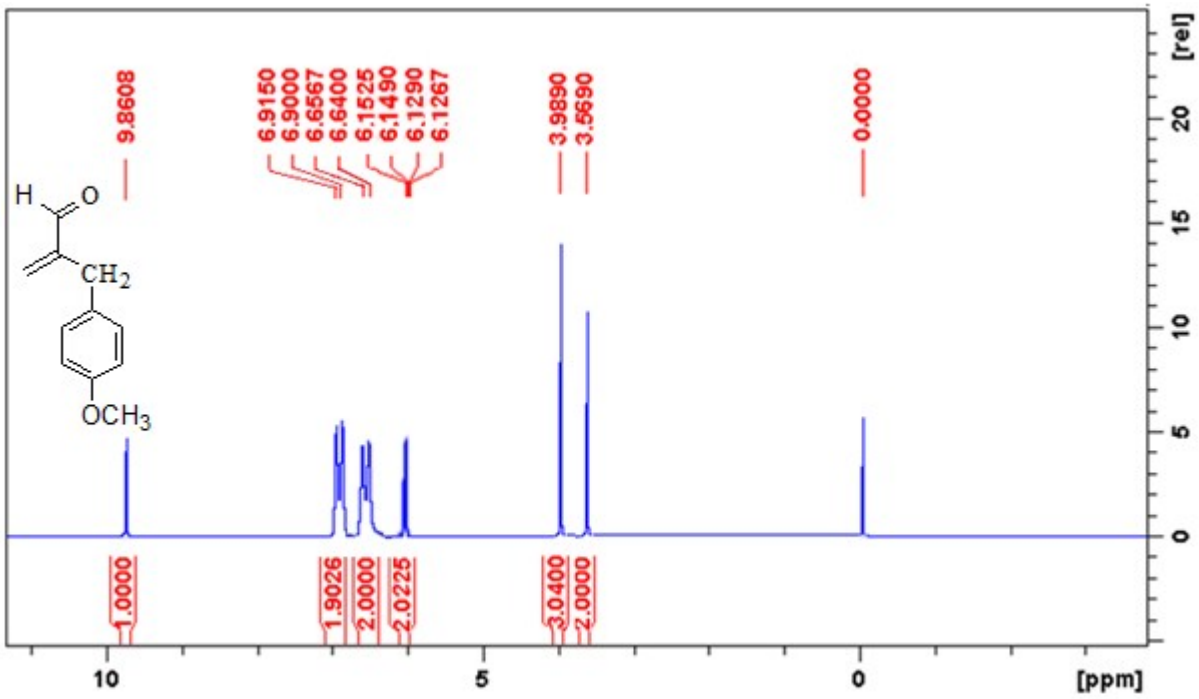


Figure S66. ^{1}H NMR spectrum of compound **5d-iii**.

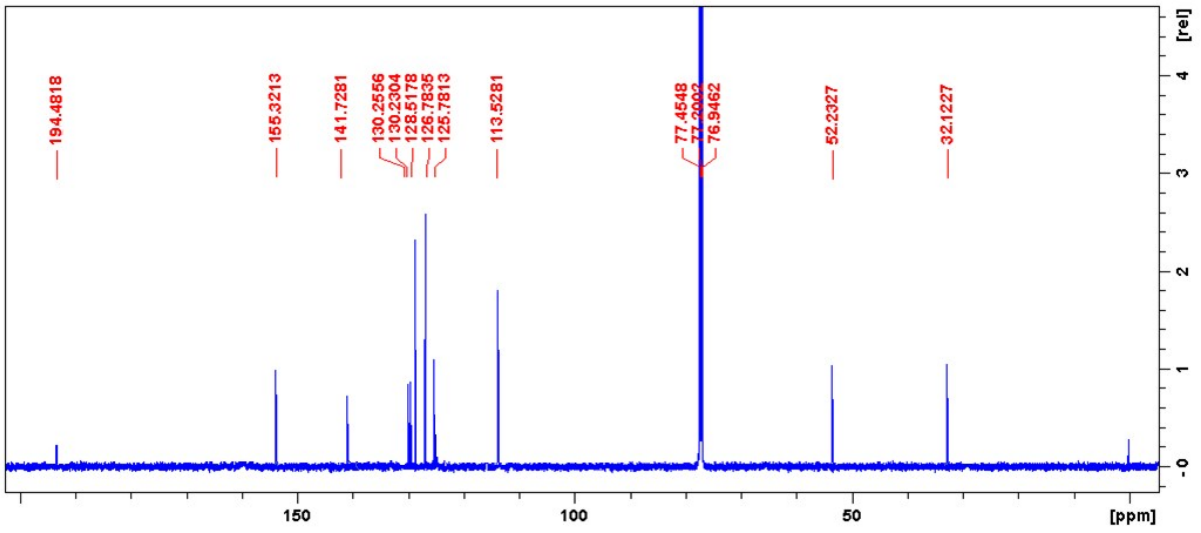


Figure S67. ^{13}C NMR spectrum of compound **5d-iii**.

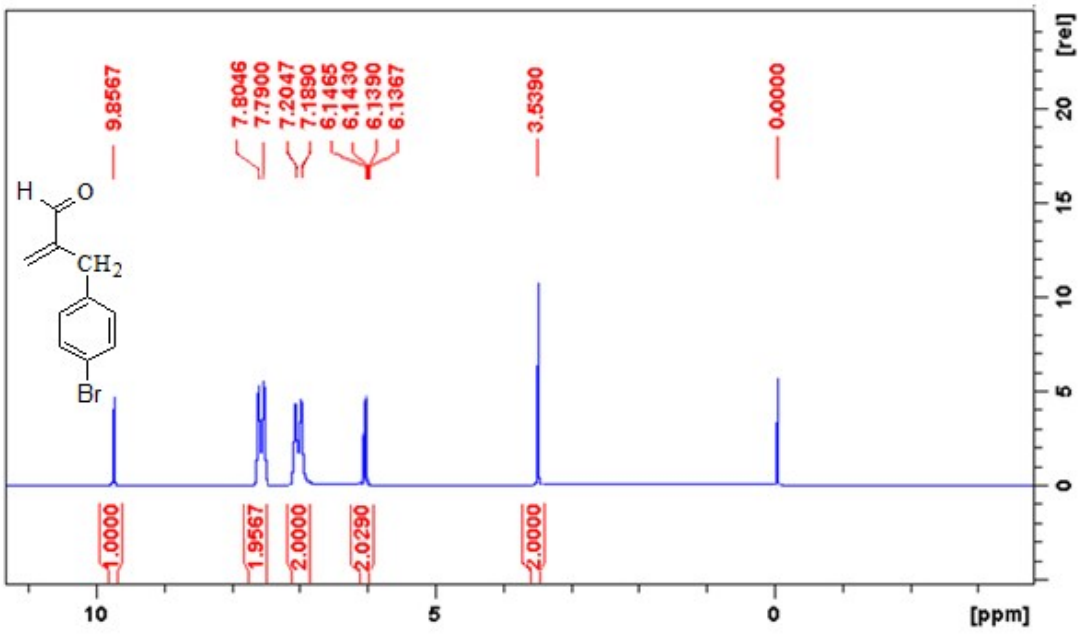


Figure S68. ^{1}H NMR spectrum of compound **5d-iv**.

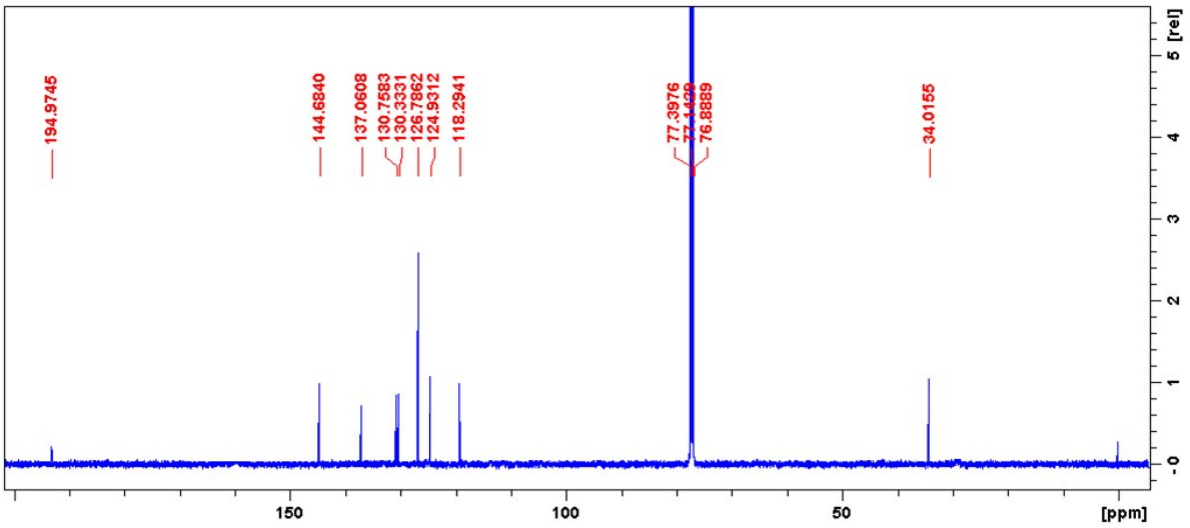


Figure S69. ^{13}C NMR spectrum of compound **5d-iv**.

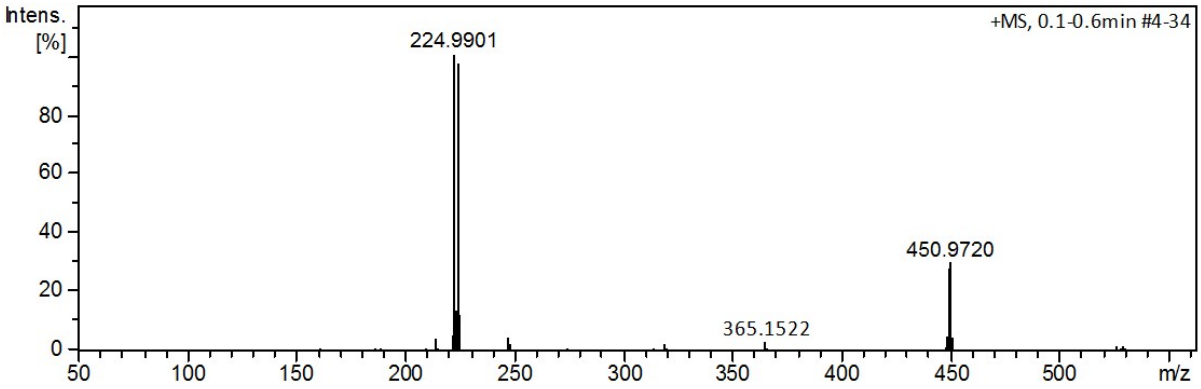


Figure S70. HRMS of **5d-iv**.

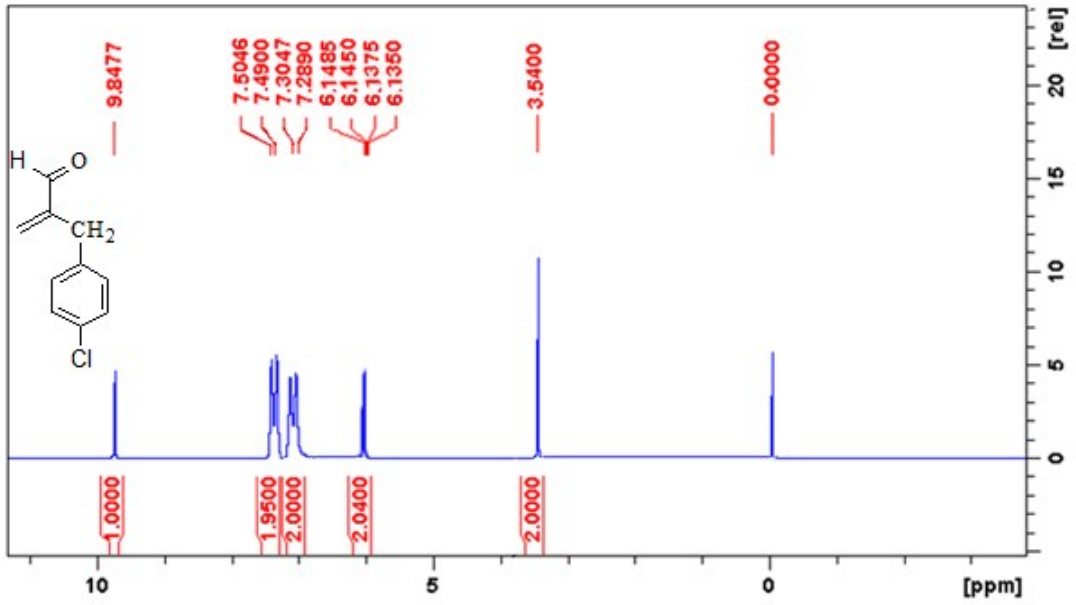


Figure S71. ^{1}H NMR spectrum of compound **5d-v**.

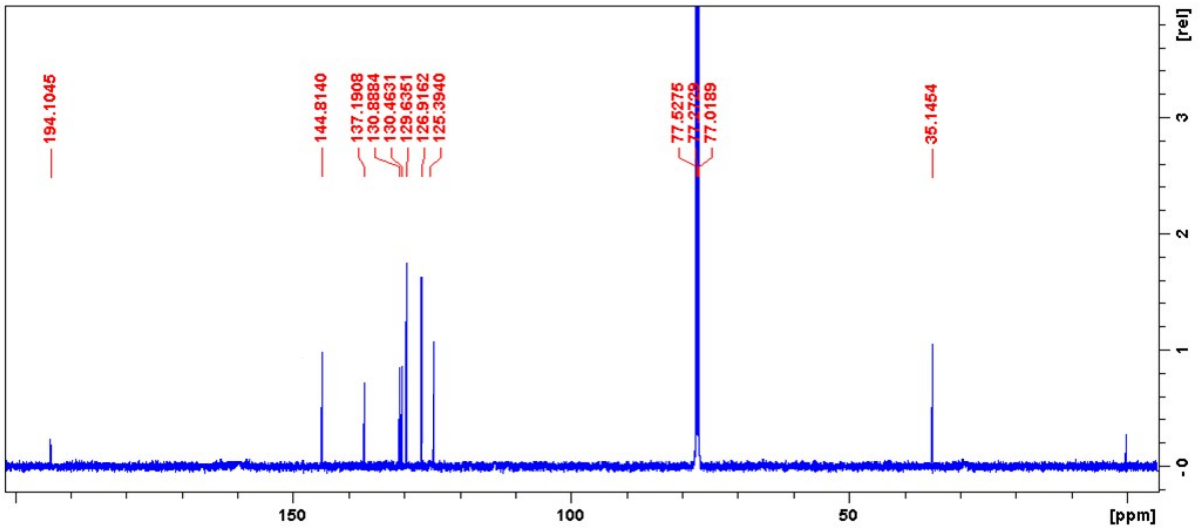


Figure S72. ^{13}C NMR spectrum of compound **5d-v**.

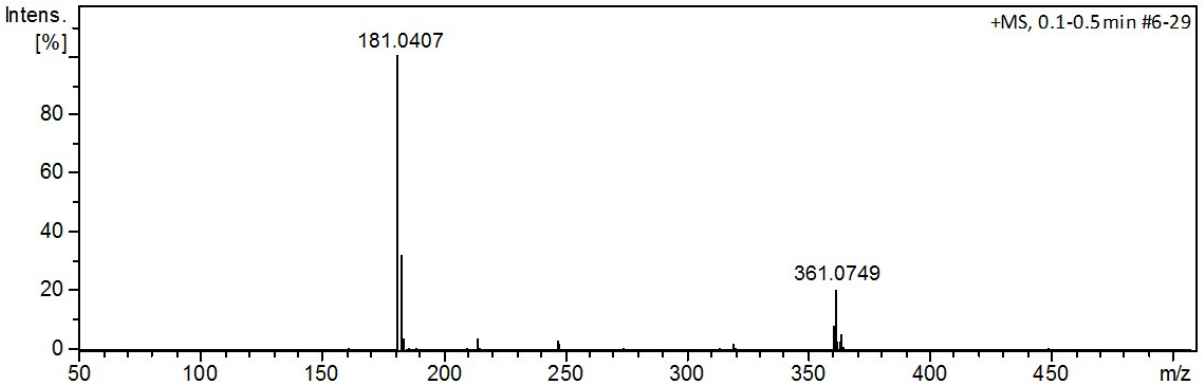


Figure S73. HRMS of **5d-v**.

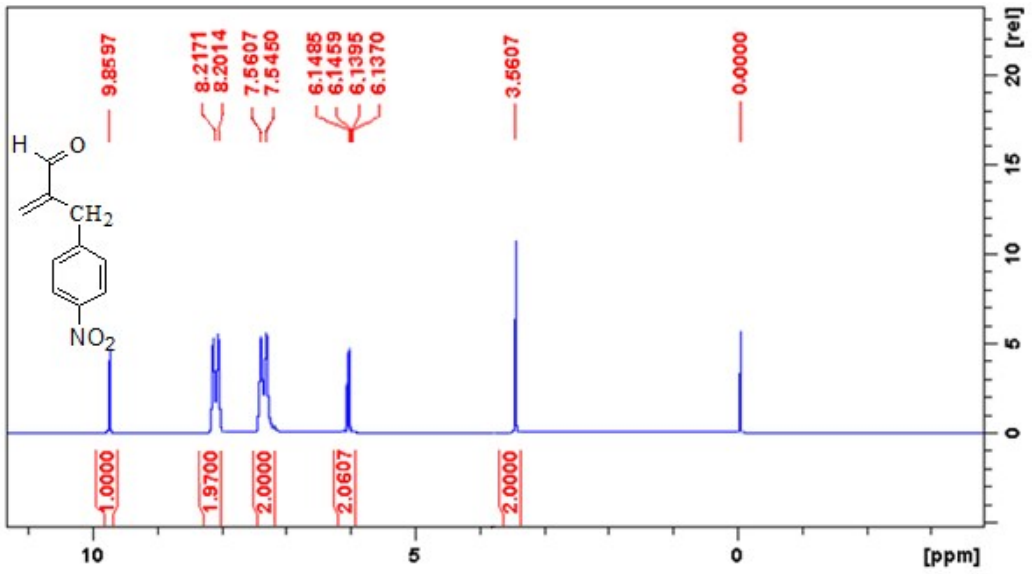


Figure S74. ^{1}H NMR spectrum of compound **5d-vi**.

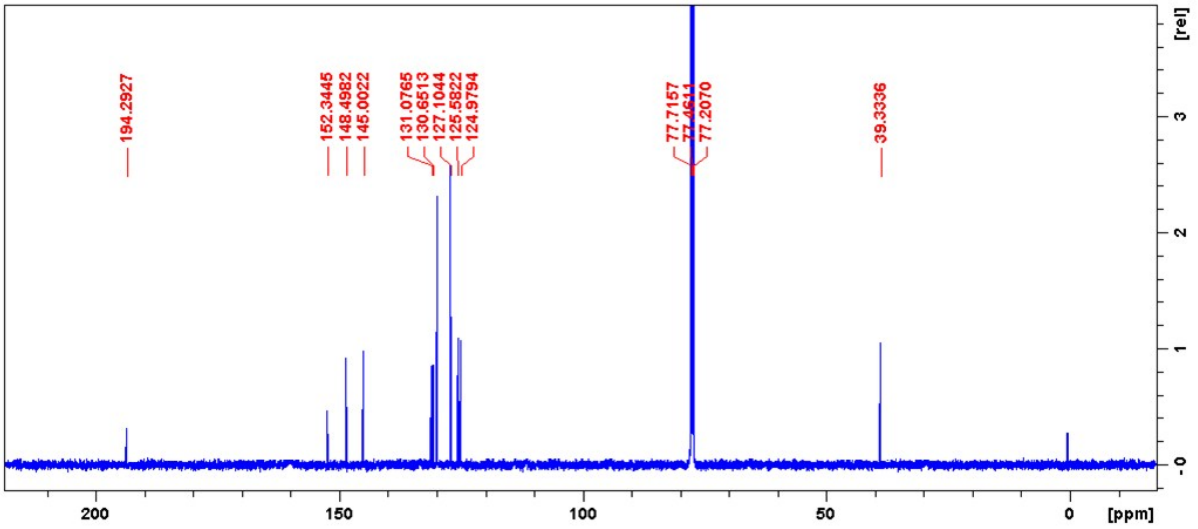


Figure S75. ^{13}C NMR spectrum of compound **5d-vi**.

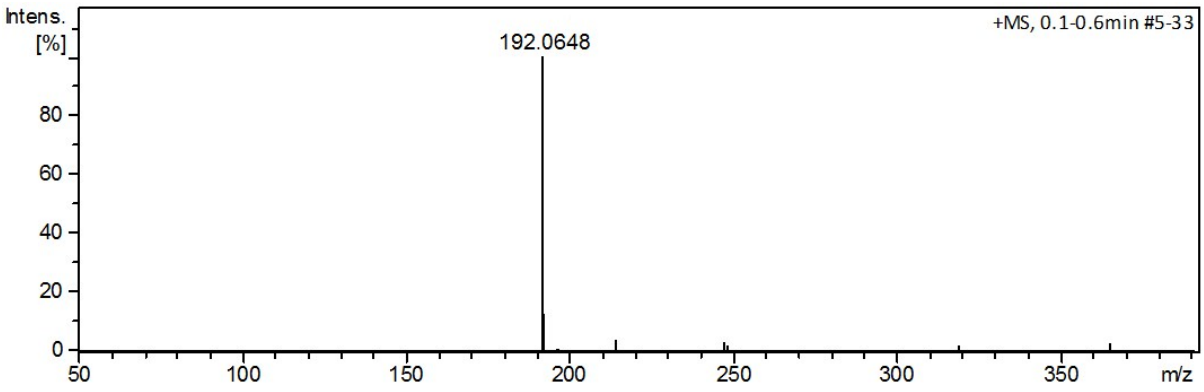


Figure S76. HRMS of **5d-vi**.

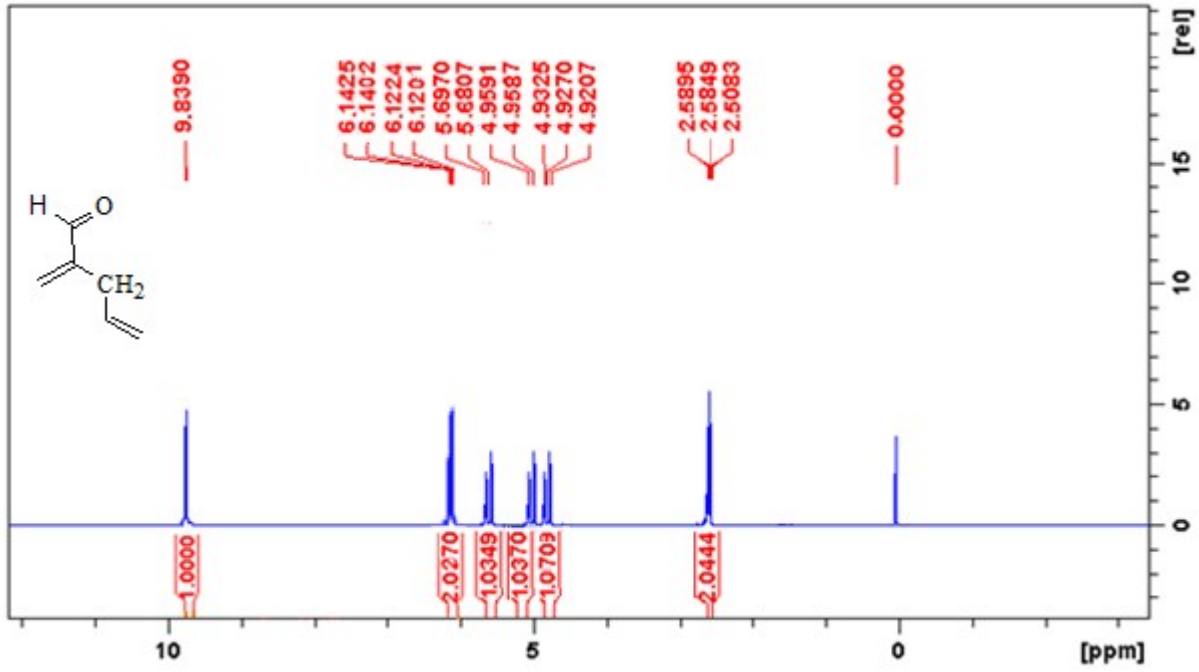


Figure S77. ^{1}H NMR spectrum of compound **5e**.

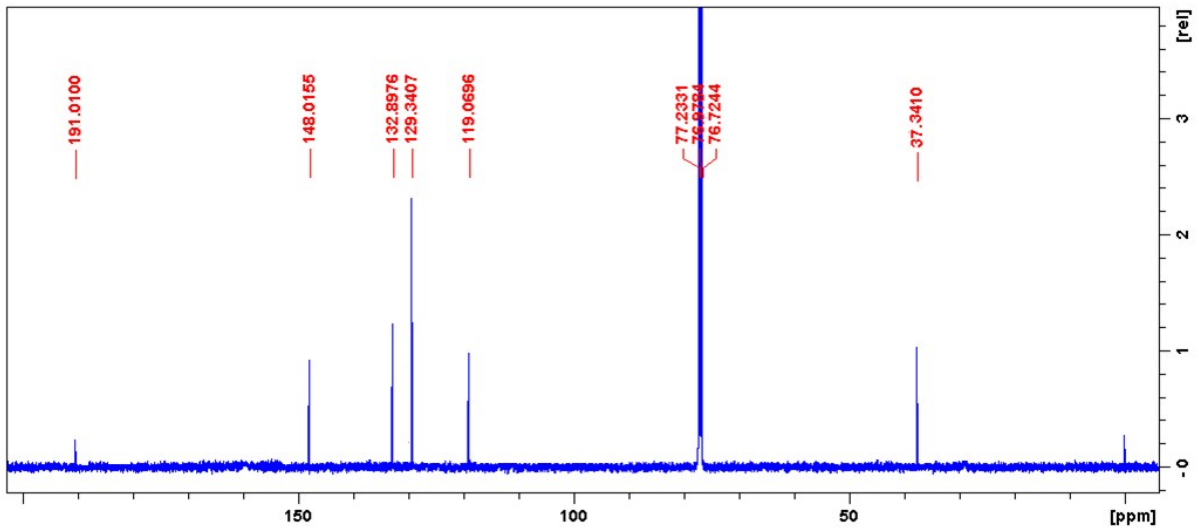


Figure S78. ^{13}C NMR spectrum of compound **5e**.

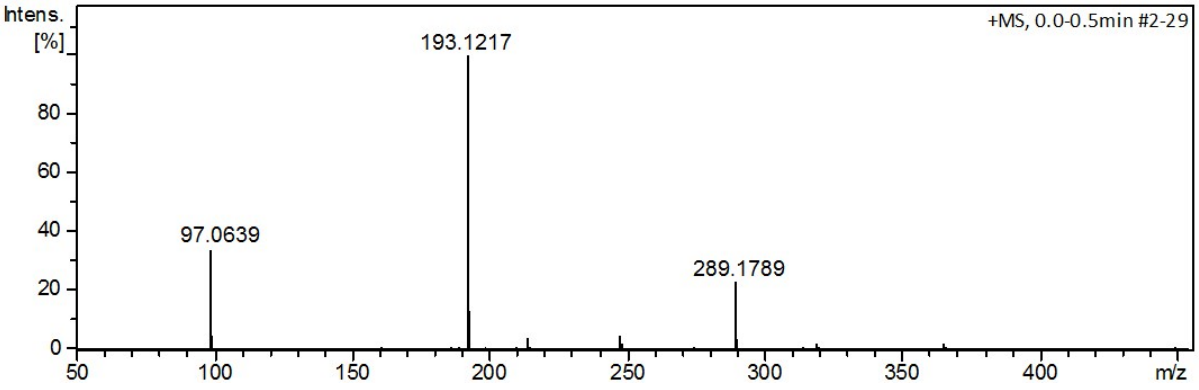


Figure S79. HRMS of **5e**.

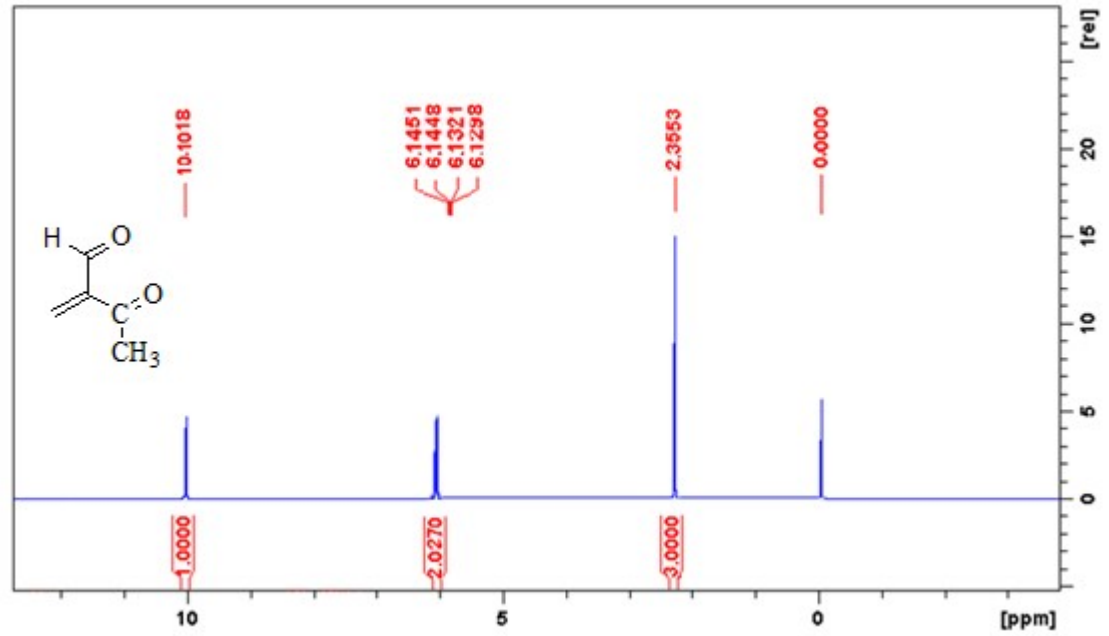


Figure S80. ^{1}H NMR spectrum of compound **5f**.

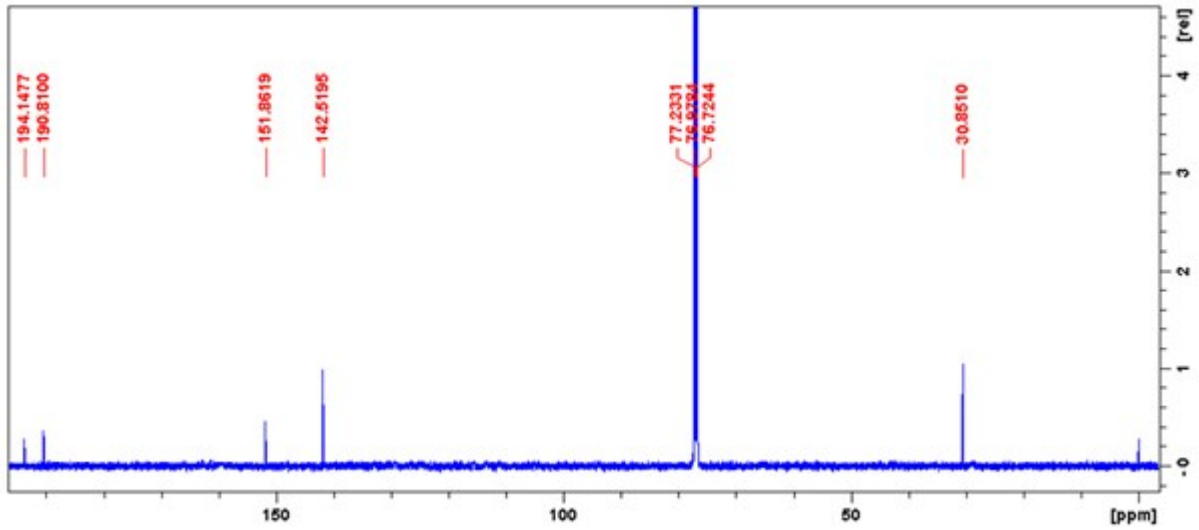


Figure S81. ^{13}C NMR spectrum of compound **5f**.

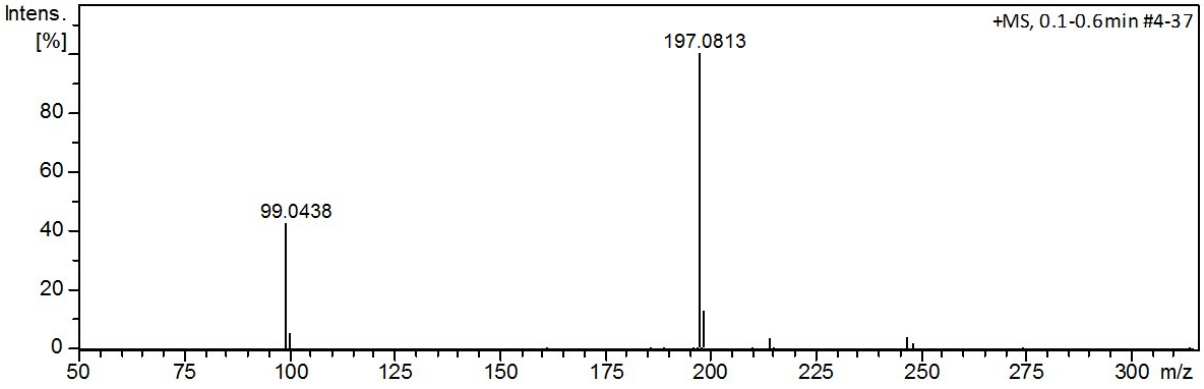


Figure S82. HRMS of **5f**.

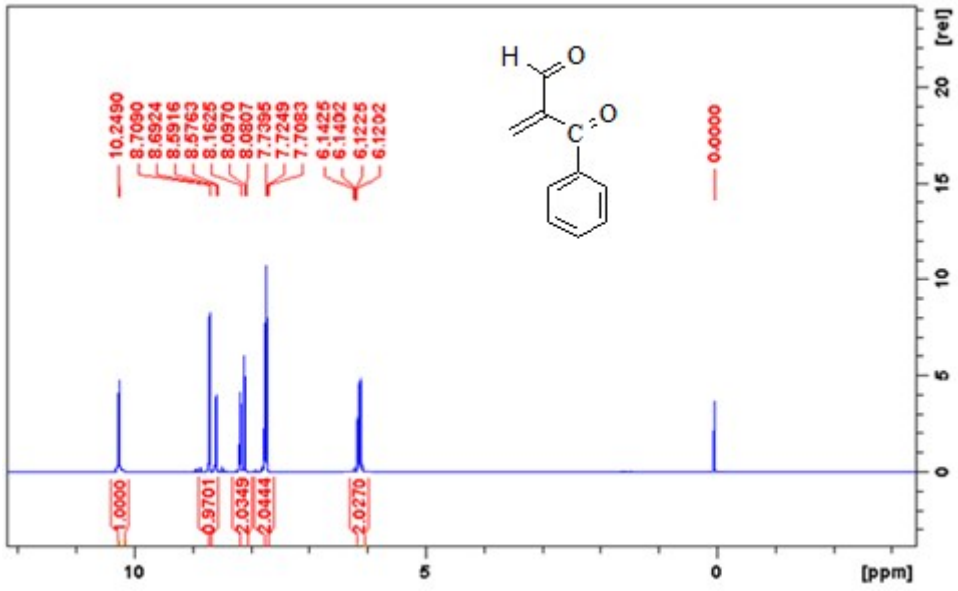


Figure S83. ^{1}H NMR spectrum of compound **5g-i**.

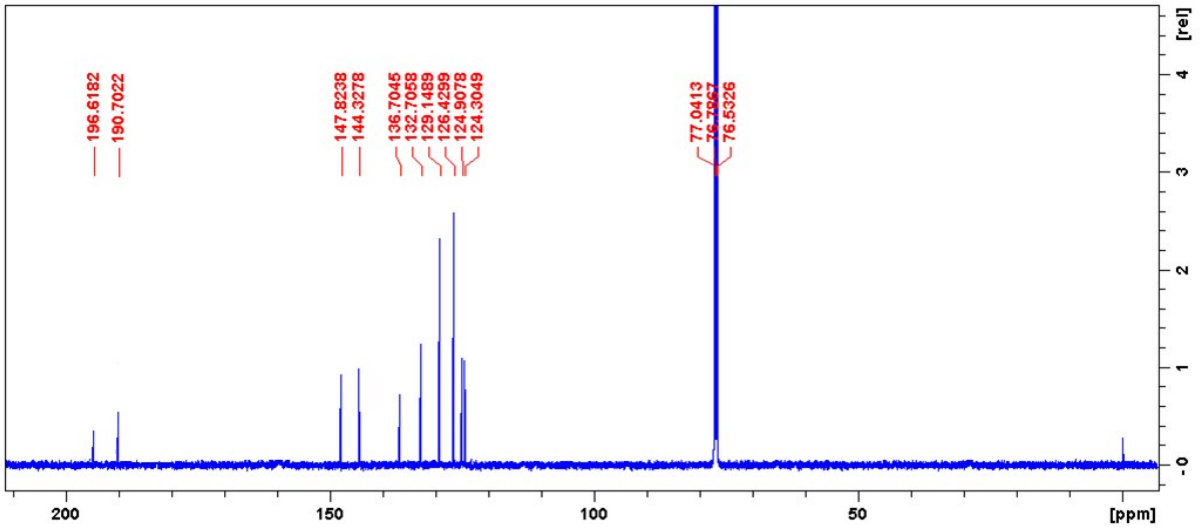


Figure S84. ^{13}C NMR spectrum of compound **5g-i**.

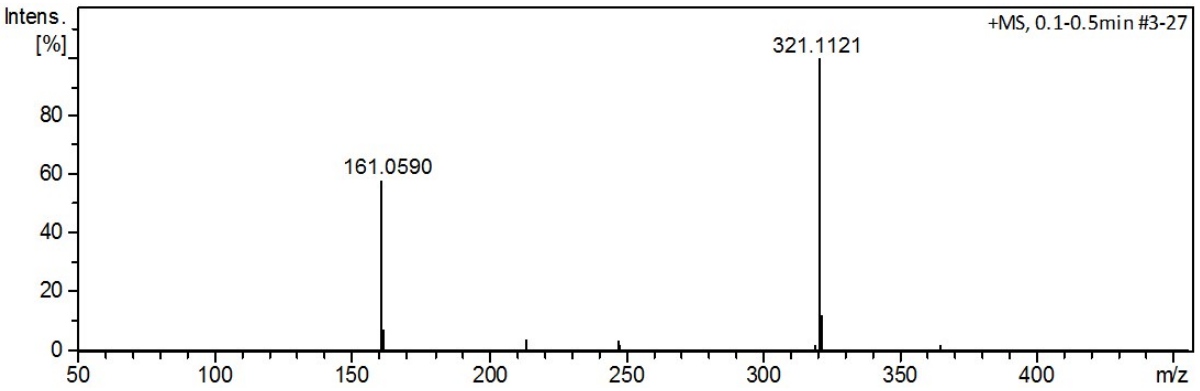


Figure S85. HRMS of **5g-i**.

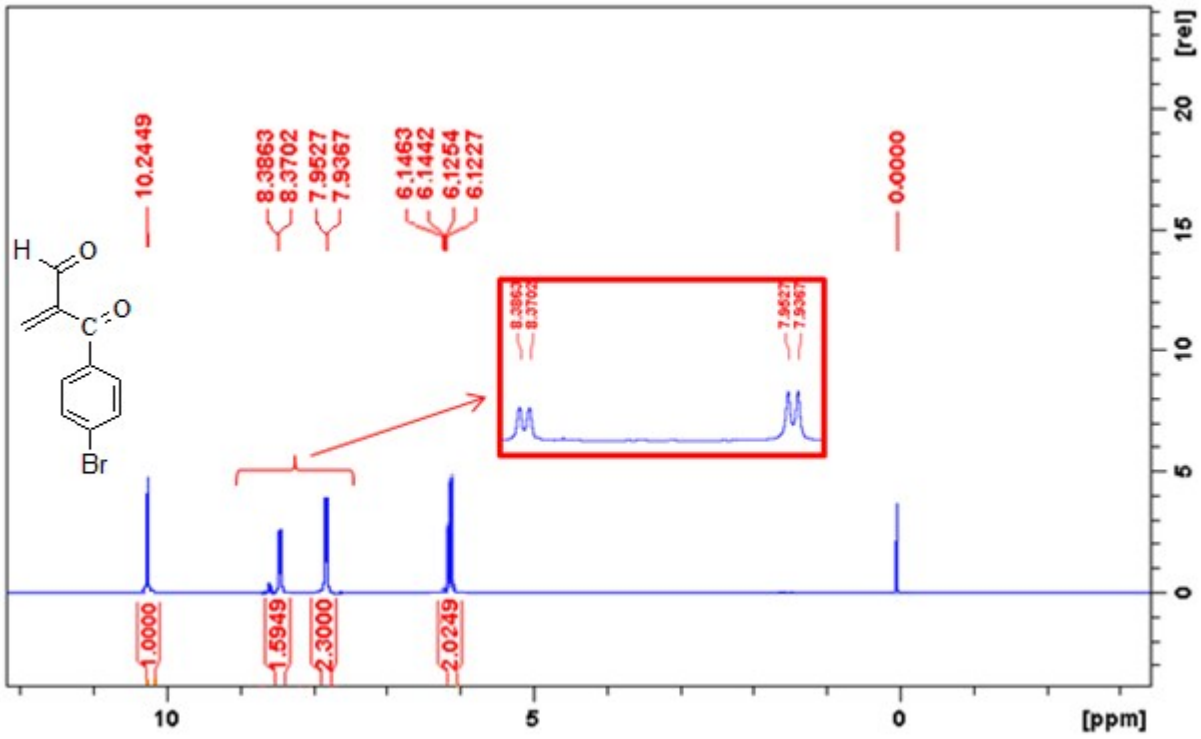


Figure S86. ^{1}H NMR spectrum of compound **5g-ii.**

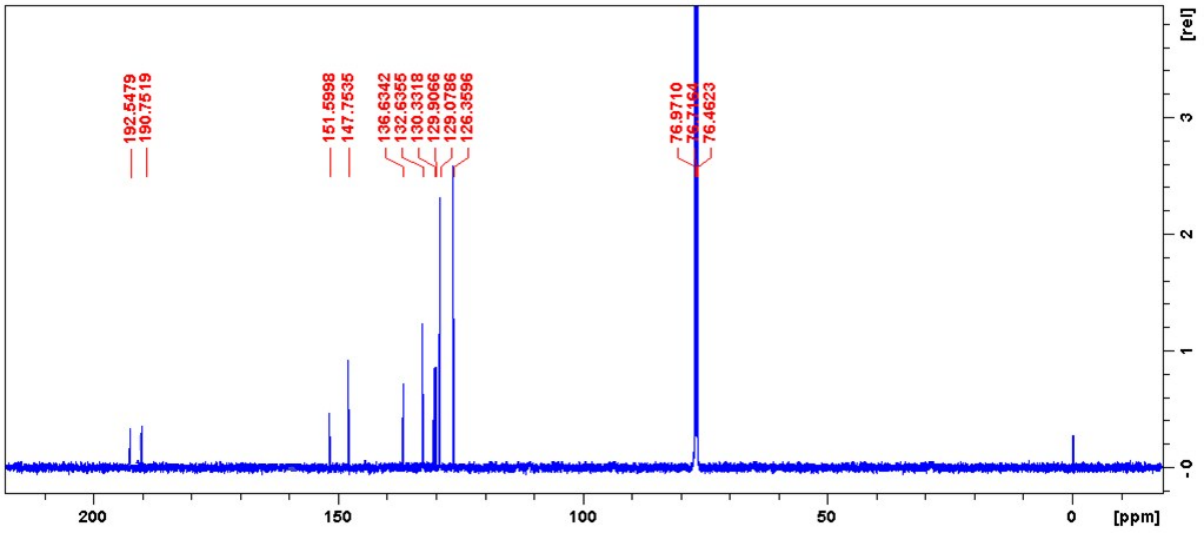


Figure S87. ^{13}C NMR spectrum of compound **5g-ii.**

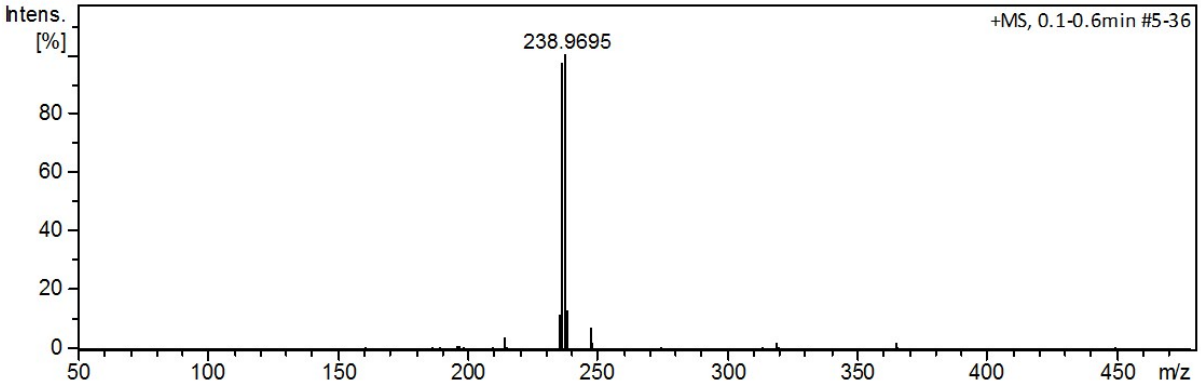


Figure S88. HRMS of **5g-ii**.

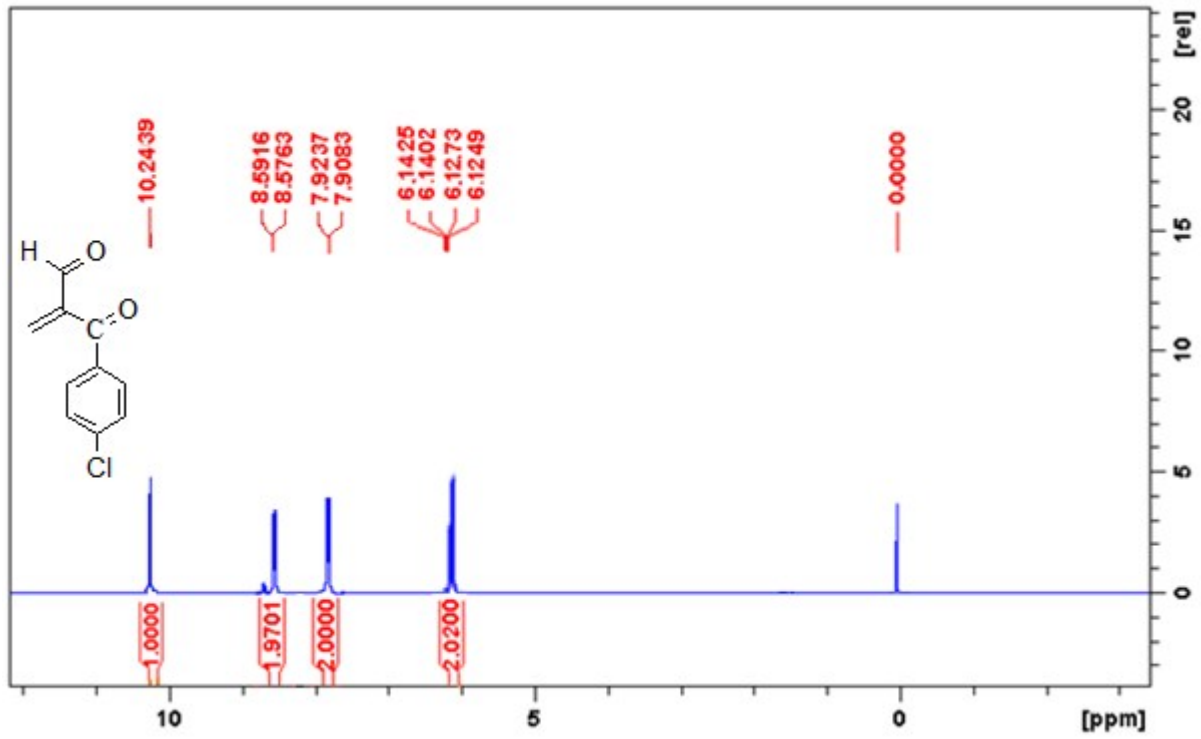


Figure S89. ^{1}H NMR spectrum of compound **5g-iii.**

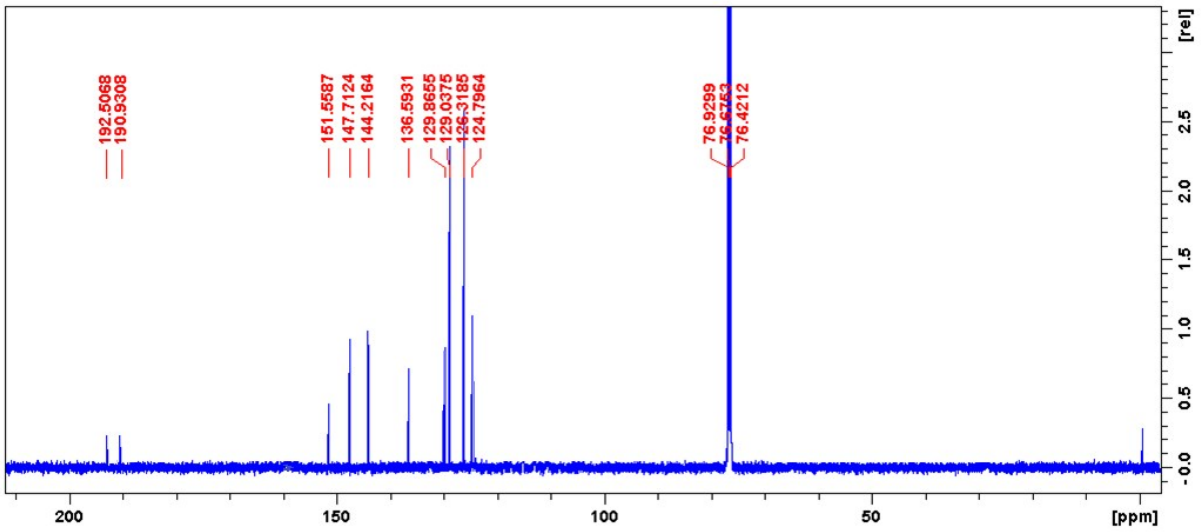


Figure S90. ^{13}C NMR spectrum of compound **5g-iii.**

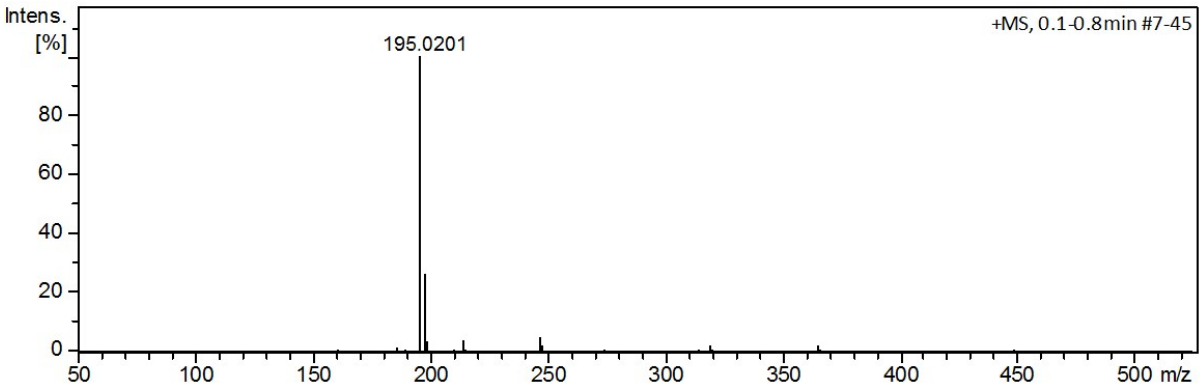


Figure S91. HRMS of **5g-iii**.

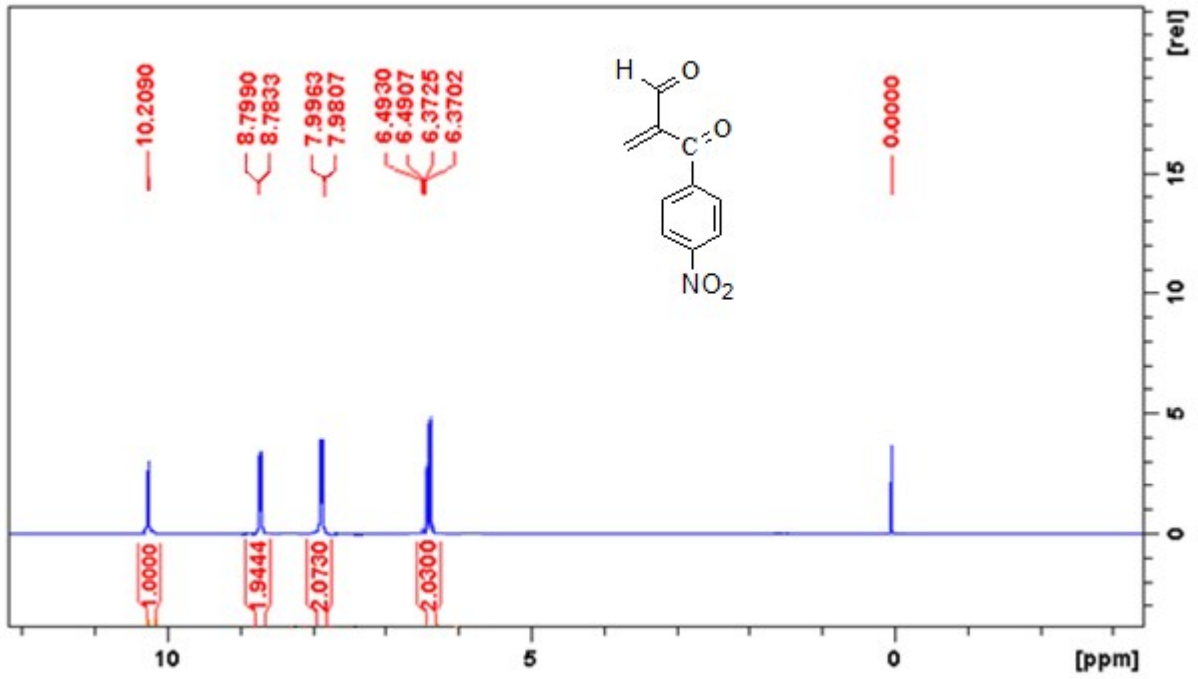


Figure S92. [1]H NMR spectrum of compound **5g-iv**.

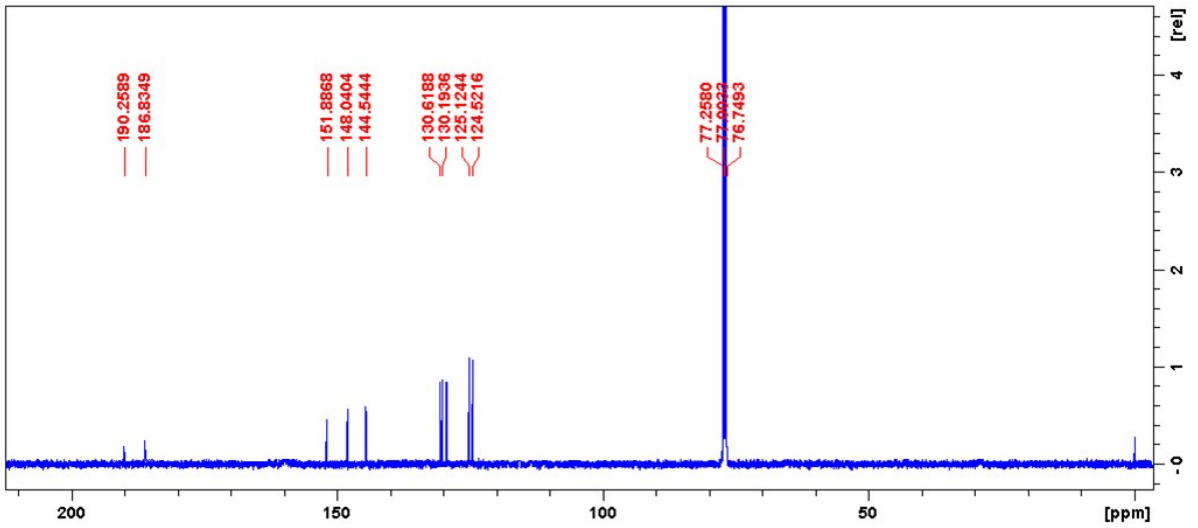


Figure S93. [13]C NMR spectrum of compound **5g-iv**.

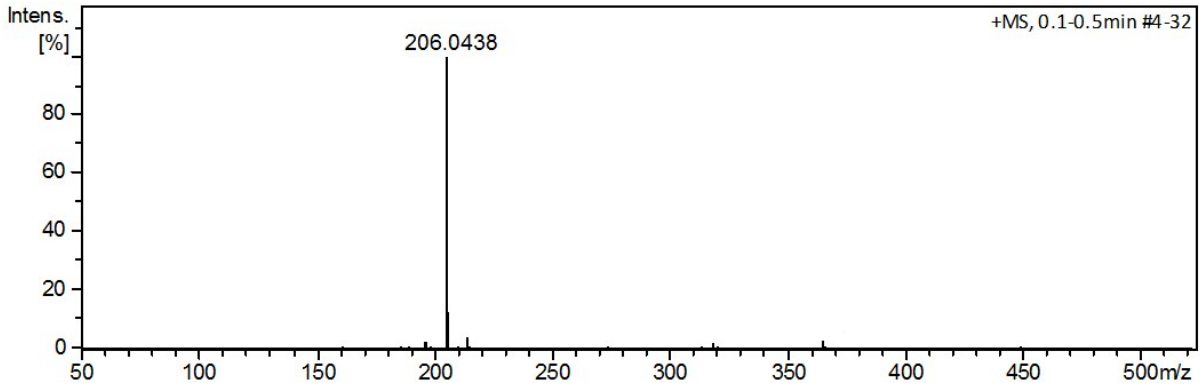


Figure S94. HRMS of **5g-iv**.

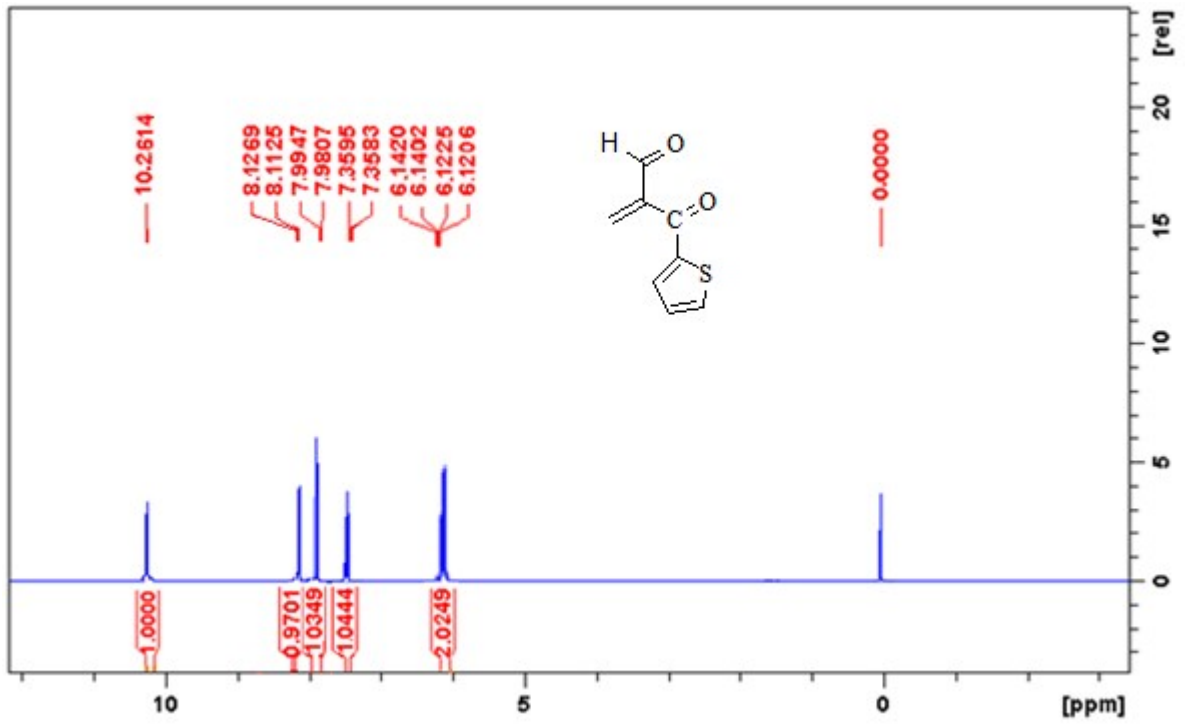


Figure S95. ^{1}H NMR spectrum of compound **5h**.

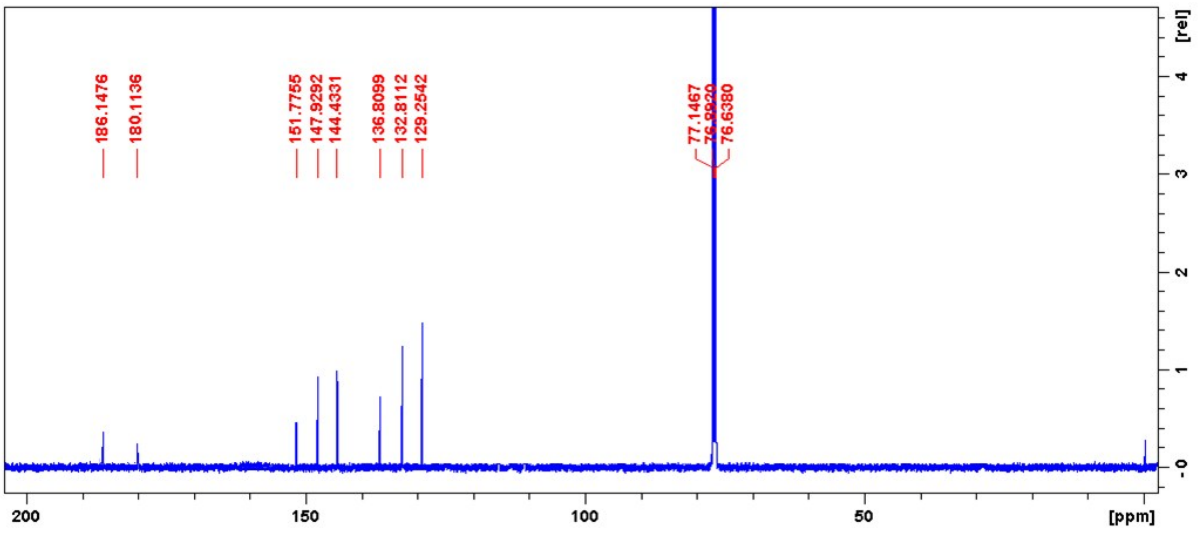


Figure S96. ^{13}C NMR spectrum of compound **5h**.

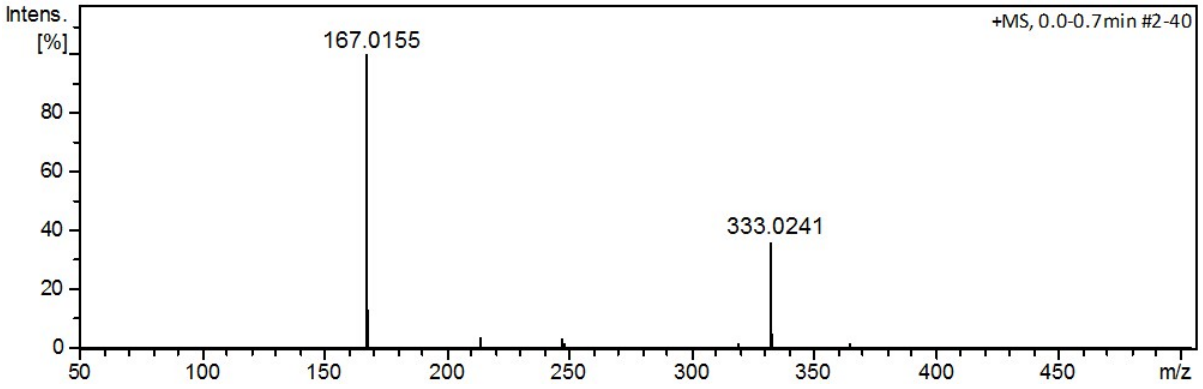


Figure S97. HRMS of **5h**.

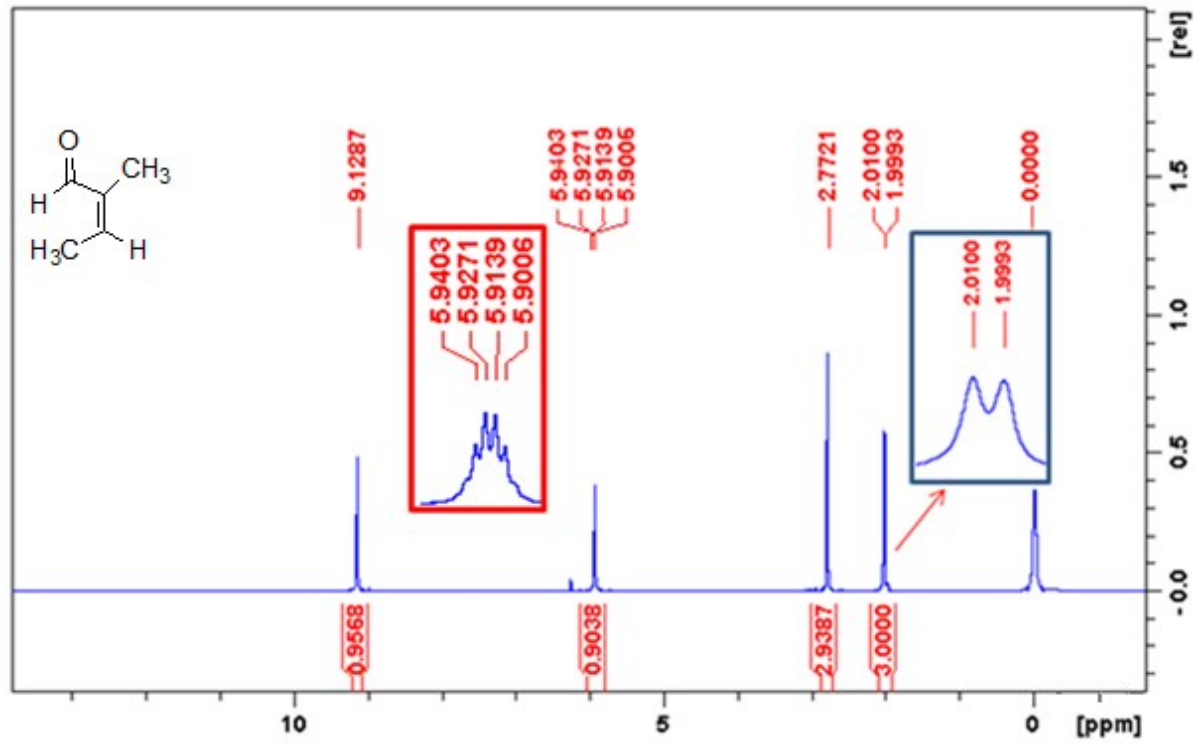


Figure S98. ^{1}H NMR spectrum of compound **8a-i**.

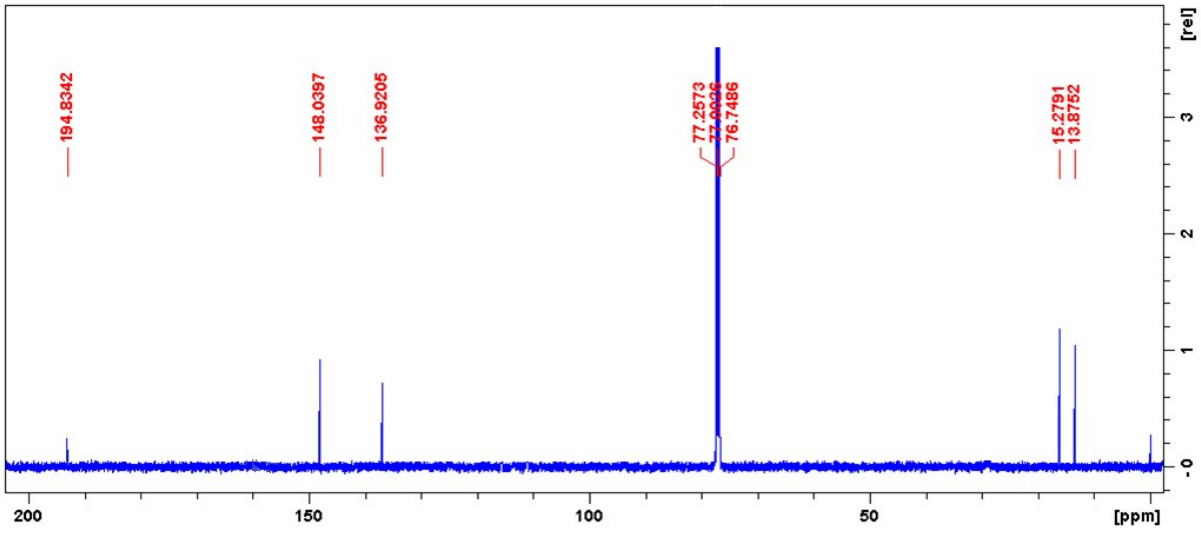


Figure S99. ^{13}C NMR spectrum of compound **8a-i**.

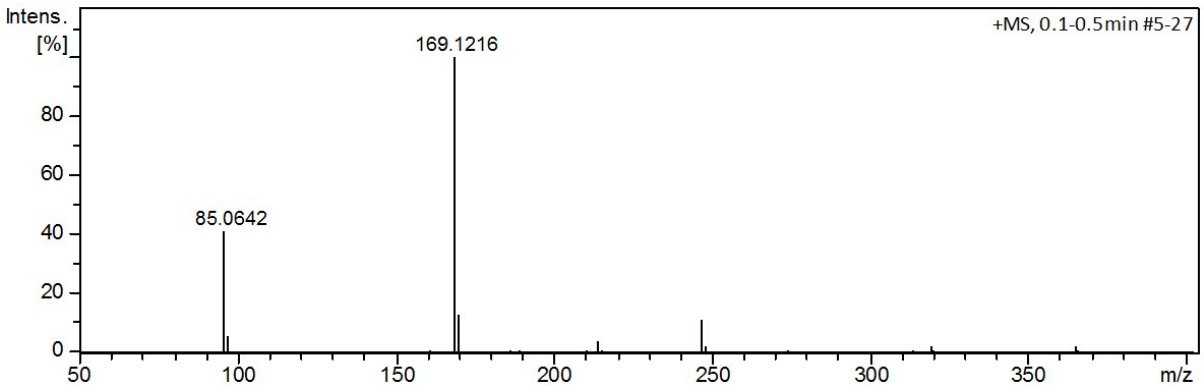


Figure S100. HRMS of **8a-i**.

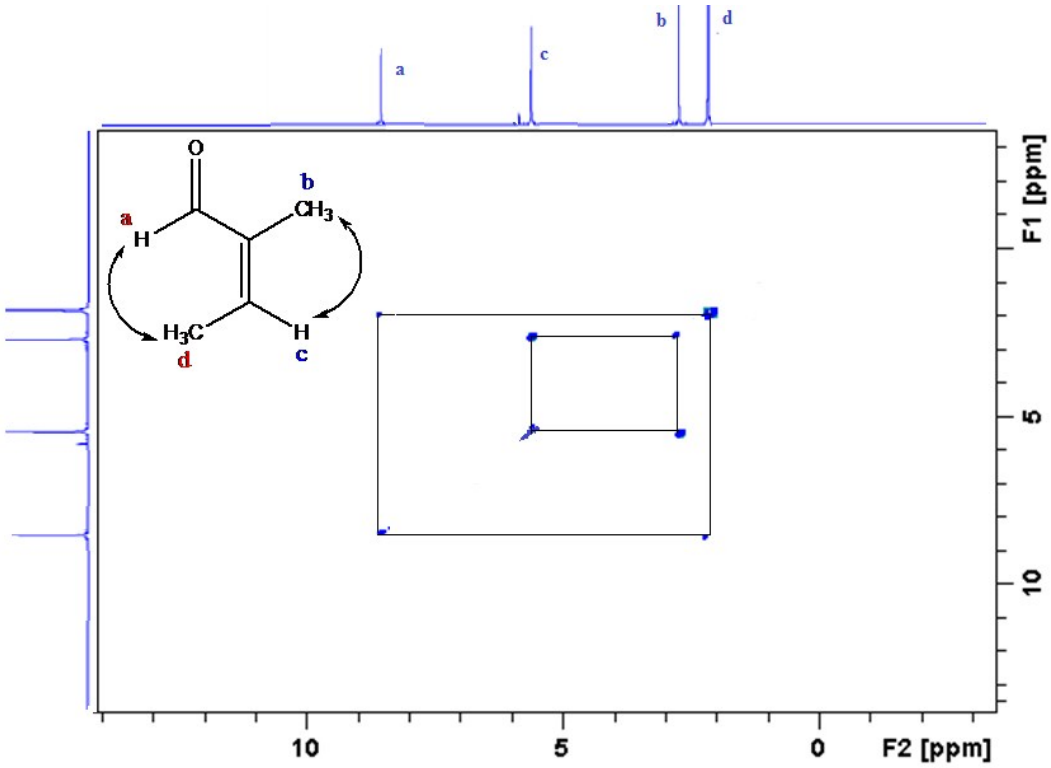


Figure S101. ROESY spectrum of compound **8a-i** (mixing time was 300 ms, ns = 8, NE = 128) indicating the geometry of the molecule as shown in the inset. Same spectrum was seen when mixing time was changed to 500 ms, ns 32 and NE 512.

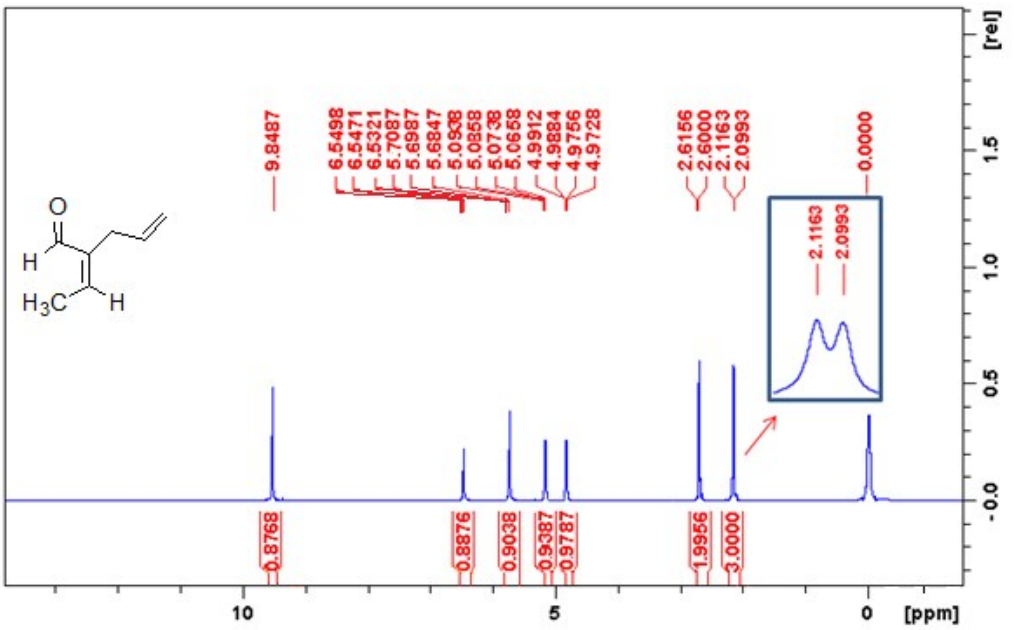


Figure S102. ^{1}H NMR spectrum of compound **8a-ii**.

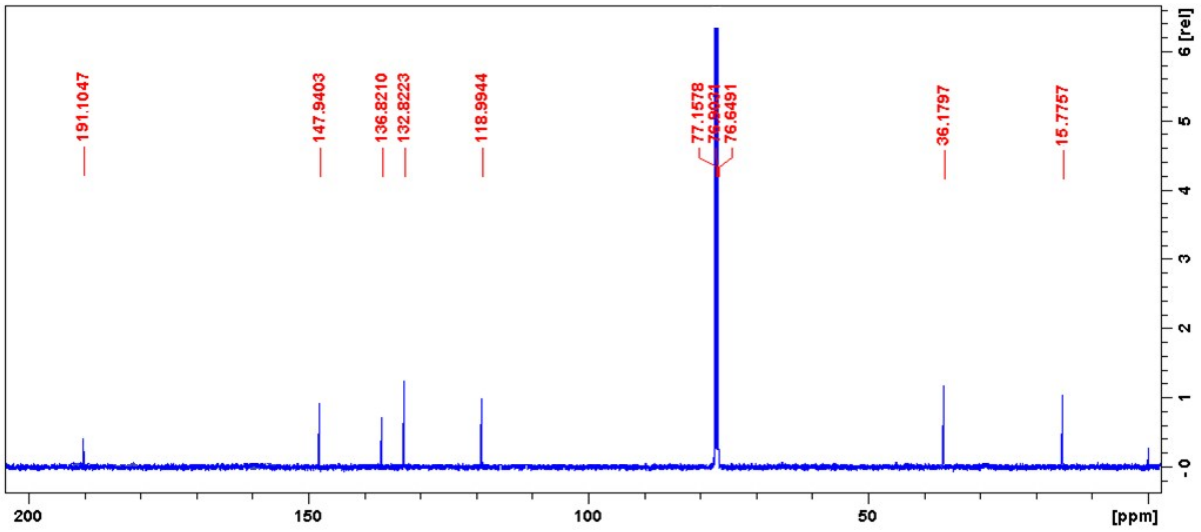


Figure S103. ^{13}C NMR spectrum of compound **8a-ii**.

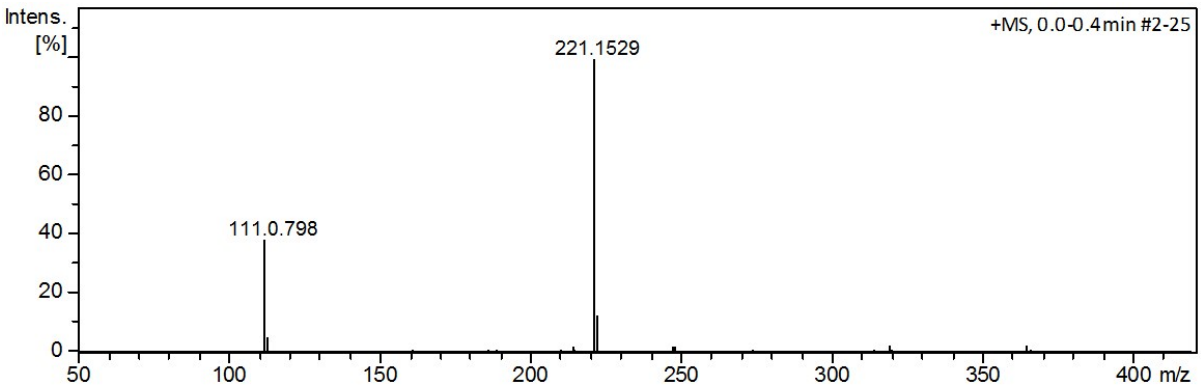


Figure S104. HRMS of **8a-ii**.

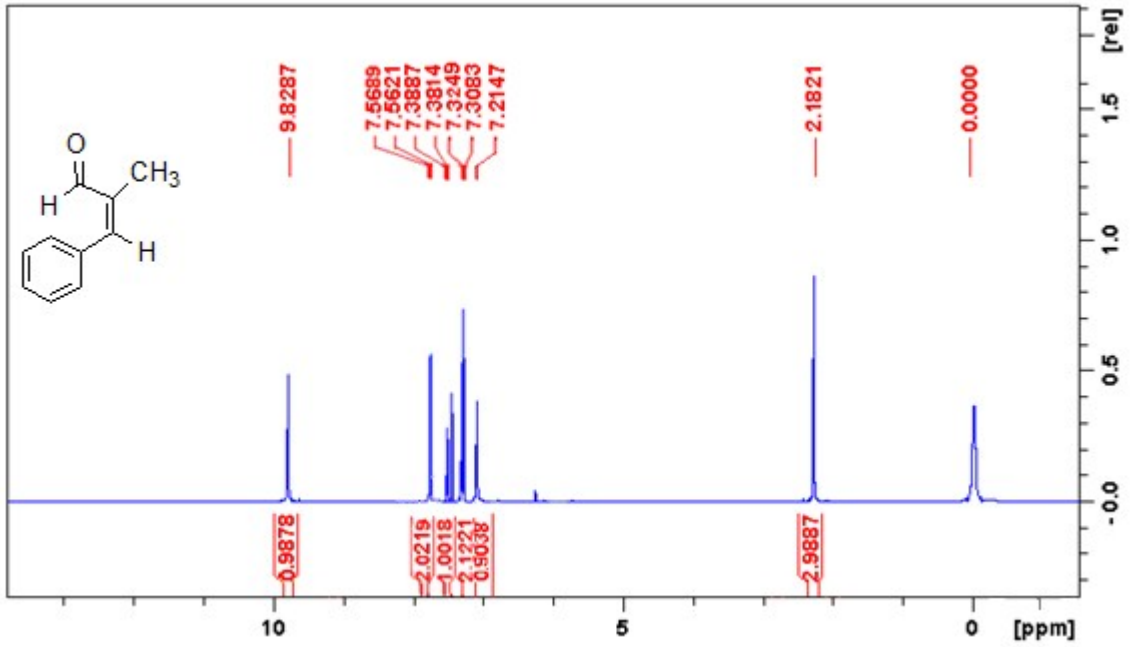


Figure S105. ^{1}H NMR spectrum of compound **8b-i**.

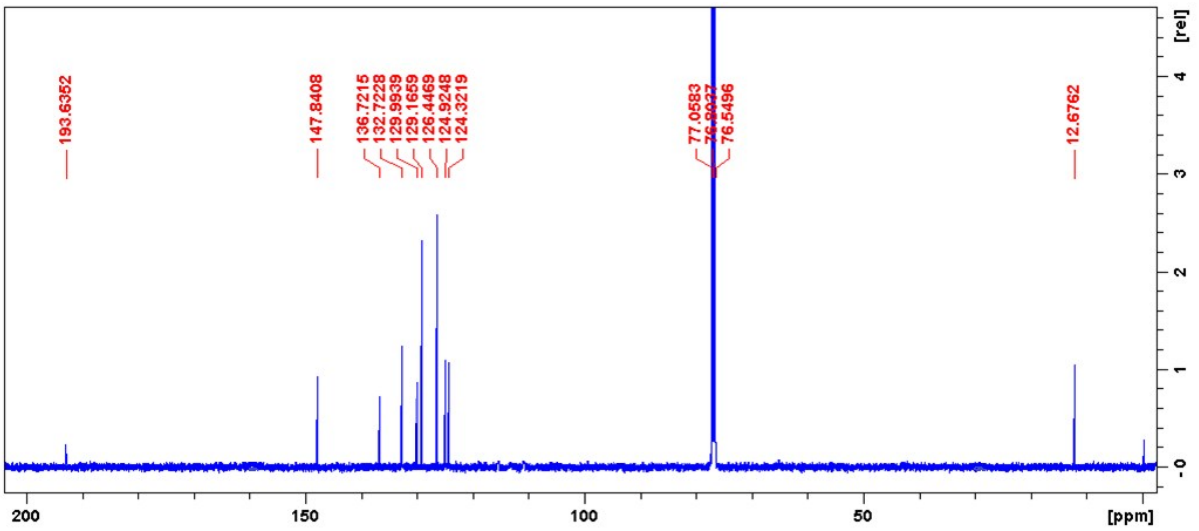


Figure S106. ^{13}C NMR spectrum of compound **8b-i**.

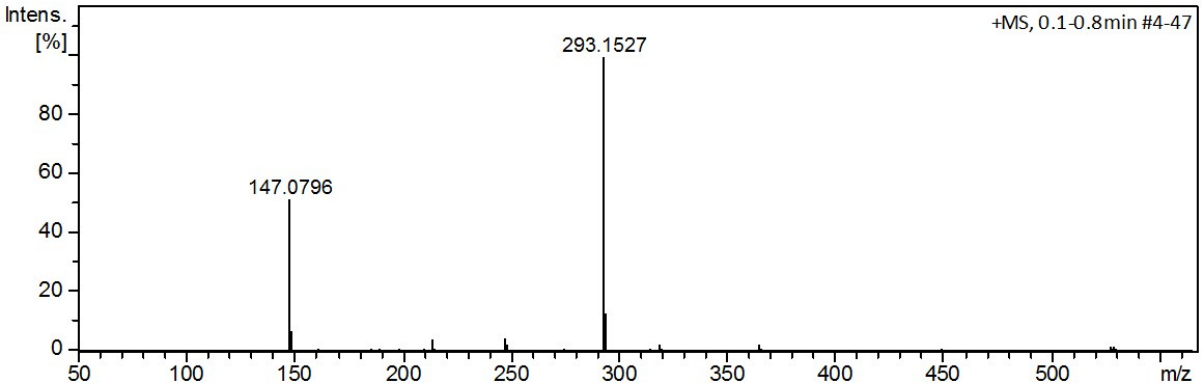


Figure S107. HRMS of **8b-i**.

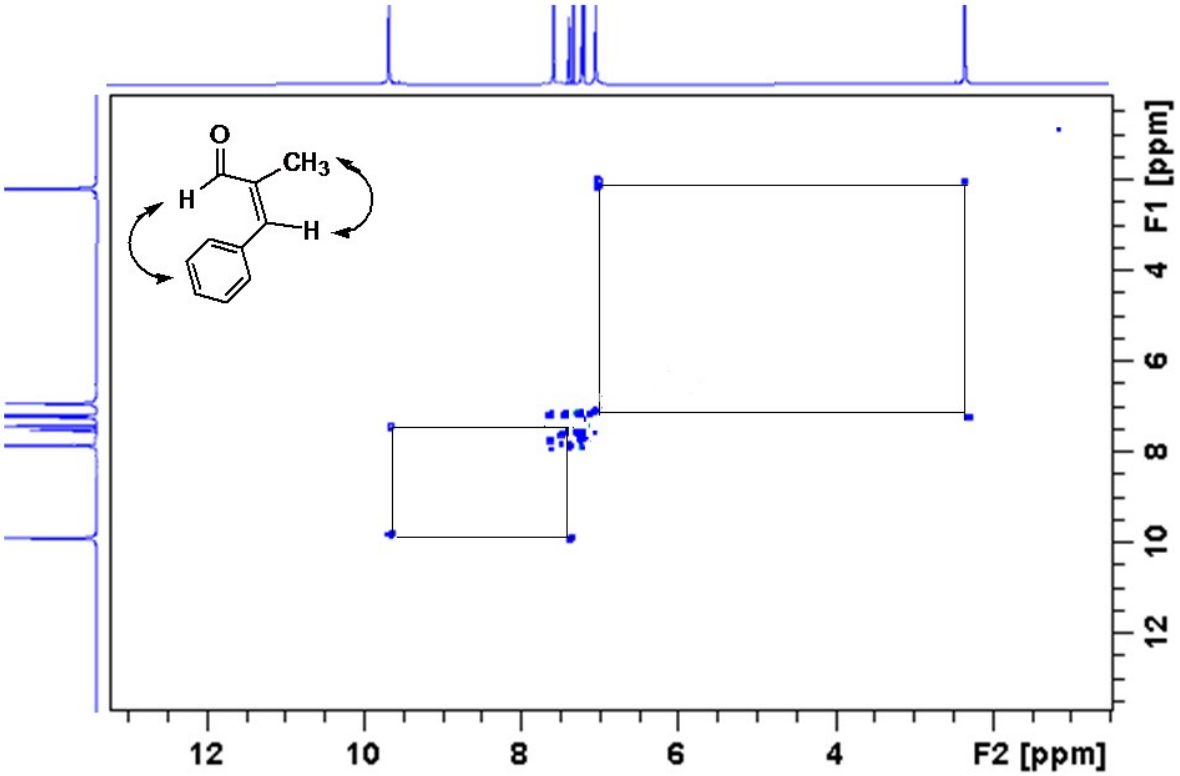


Figure S108. ROESY spectrum of compound **8b-i** indicating the geometry of the molecule across C=C bond. Same spectrum was seen when the experiment was run with mixing time 500 ms, ns 32 and NE 512.

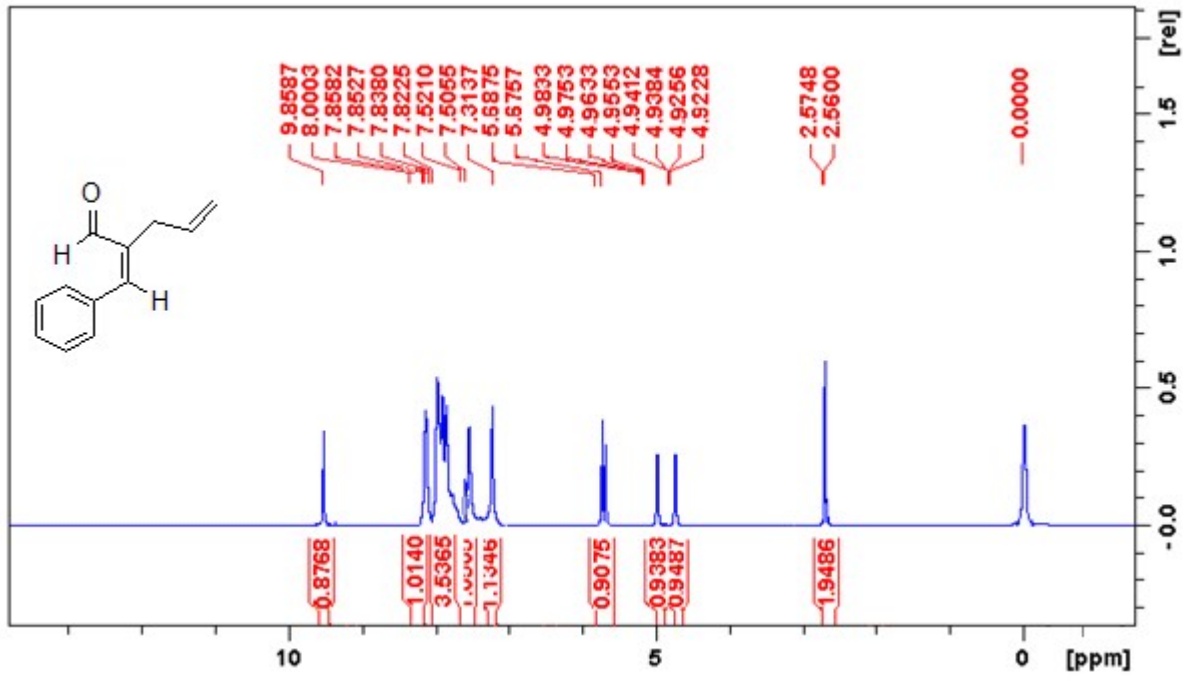


Figure S109. ^{1}H NMR spectrum of compound **8b-ii**.

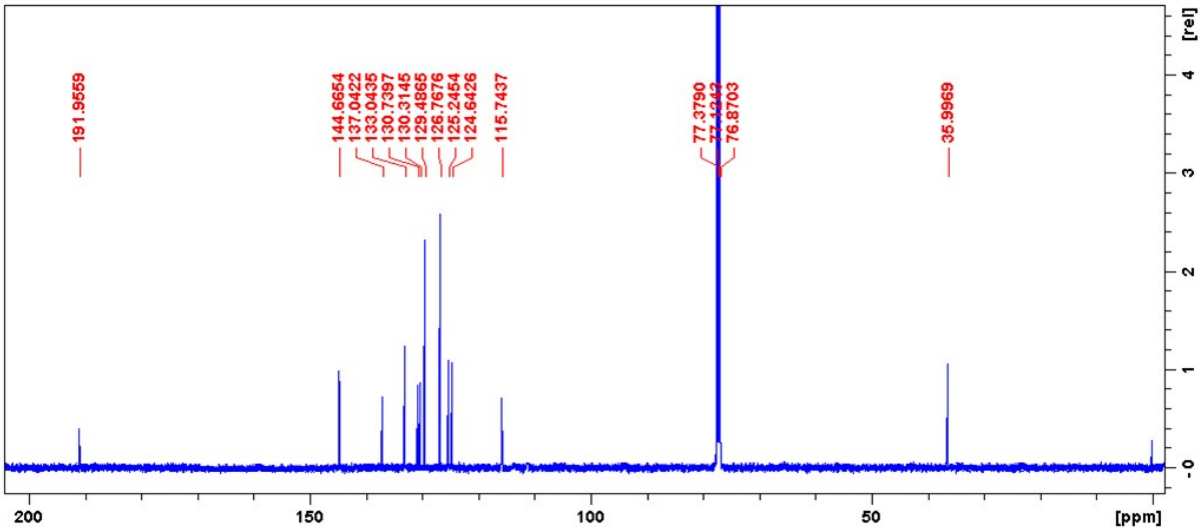


Figure S110. ^{13}C NMR spectrum of compound **8b-ii**.

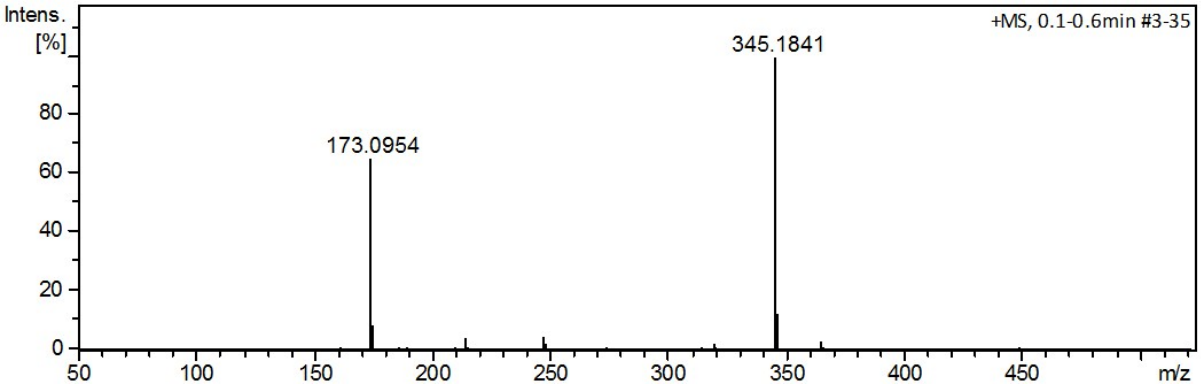


Figure S111. HRMS of **8b-ii**.

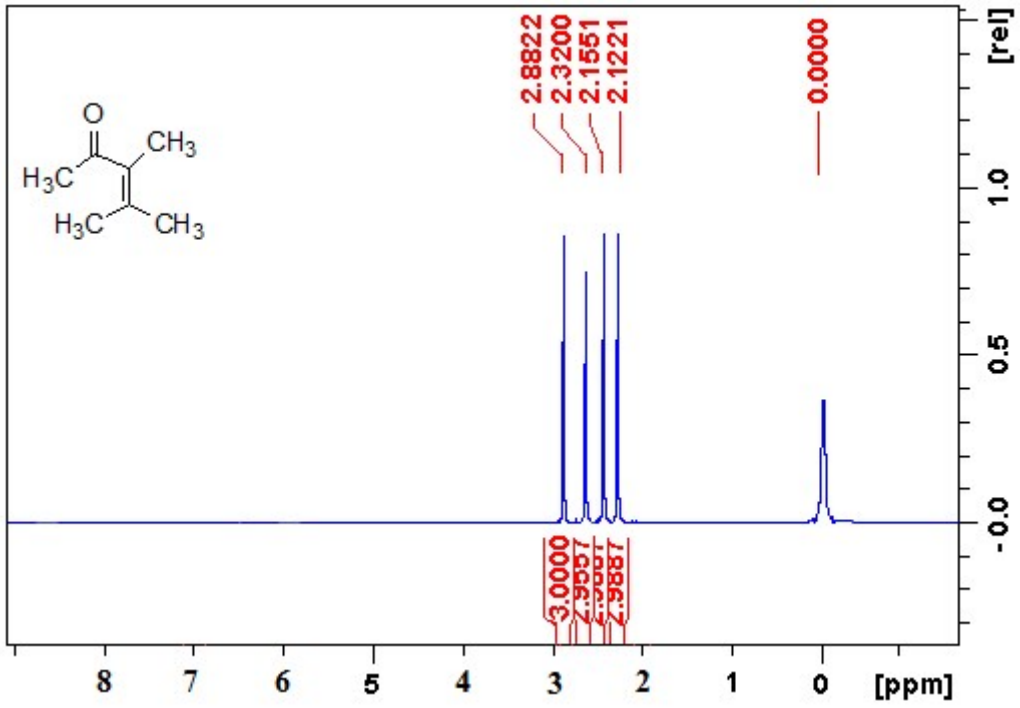


Figure S112. ^{1}H NMR spectrum of compound **8c-i**.

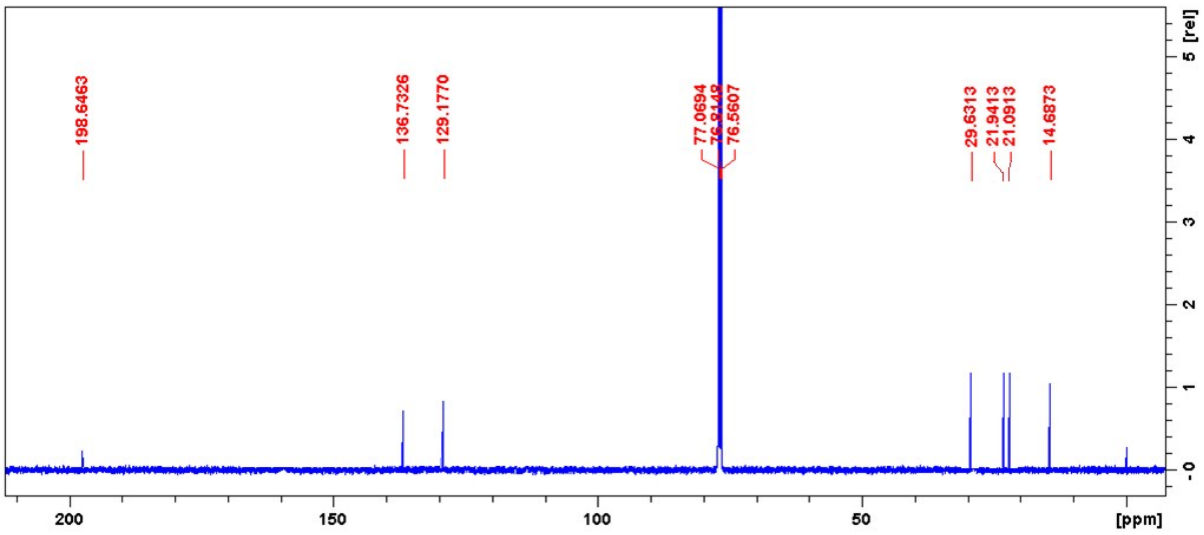


Figure S113. ^{13}C NMR spectrum of compound **8c-i**.

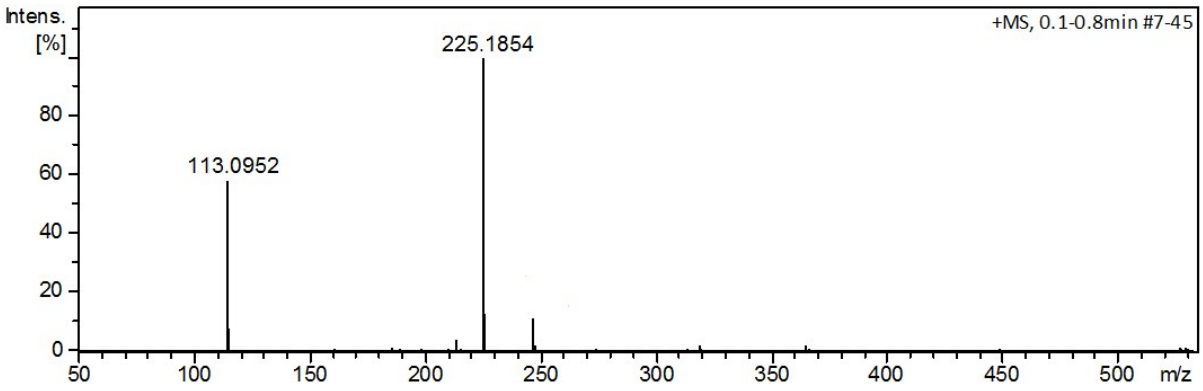


Figure S114. HRMS of **8c-i**.

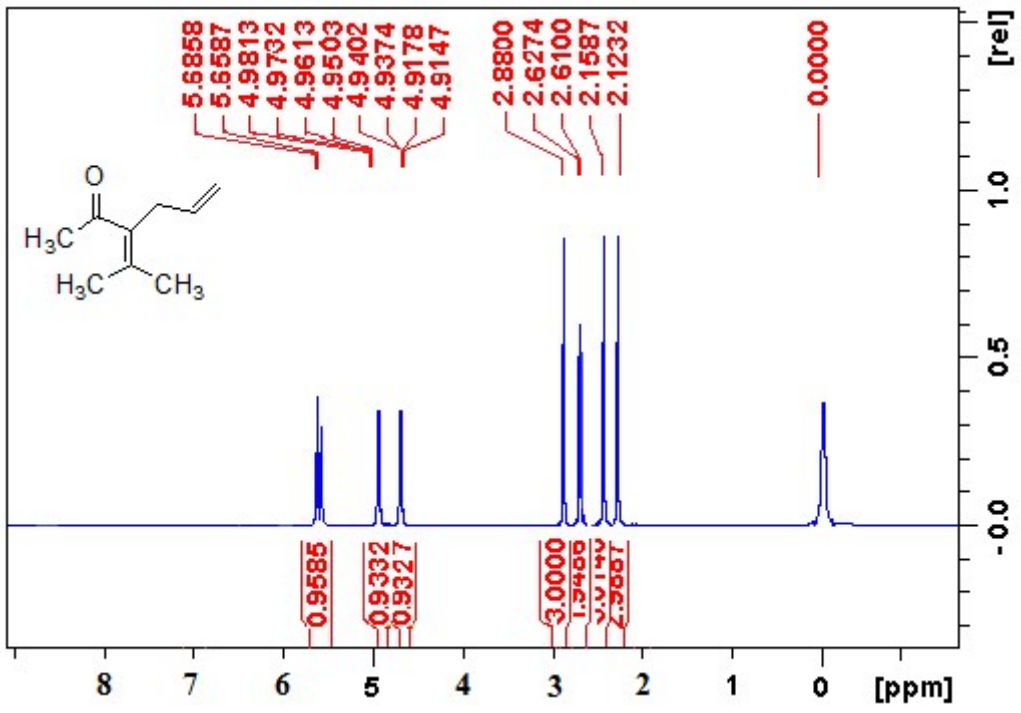


Figure S115. ^{1}H NMR spectrum of compound **8c-ii**.

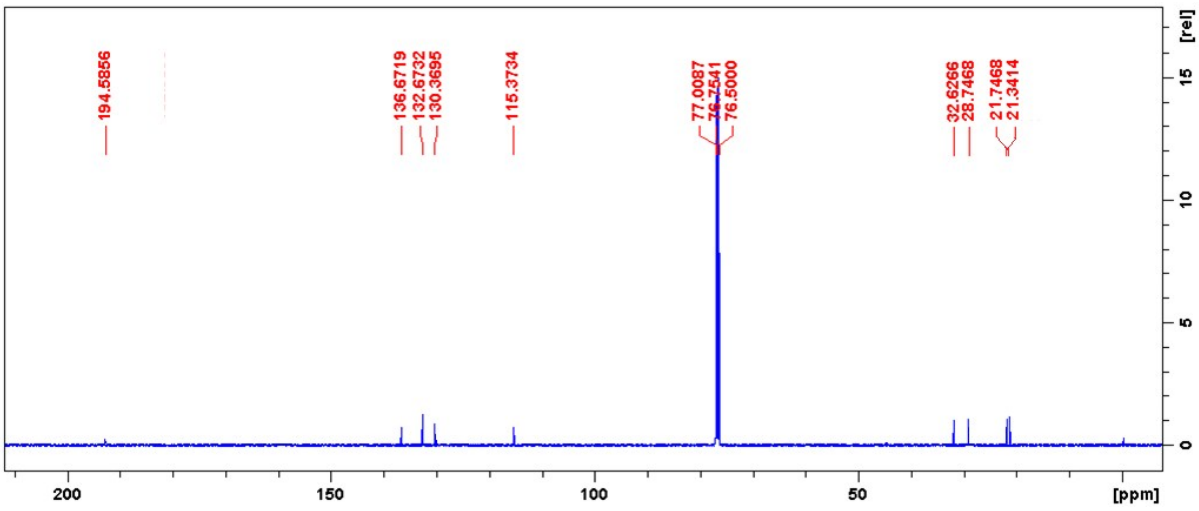


Figure S116. ^{13}C NMR spectrum of compound **8c-ii**.

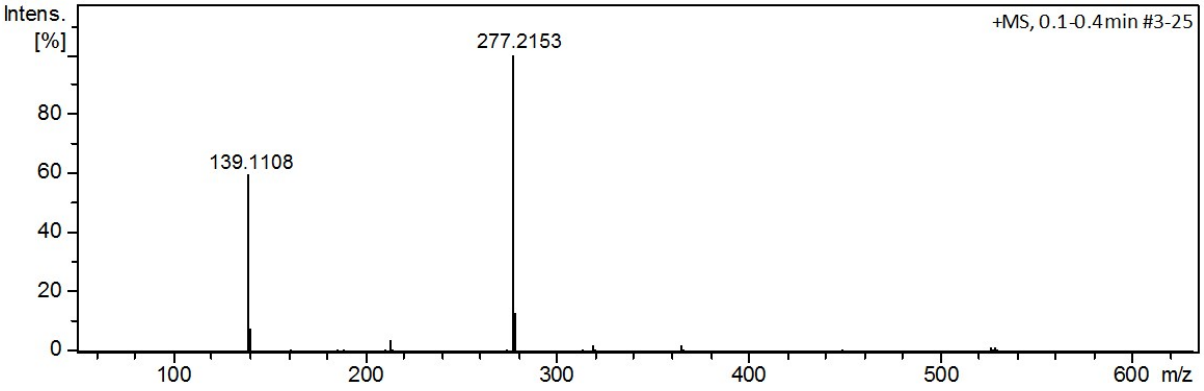


Figure S117. HRMS of **8c-ii**.

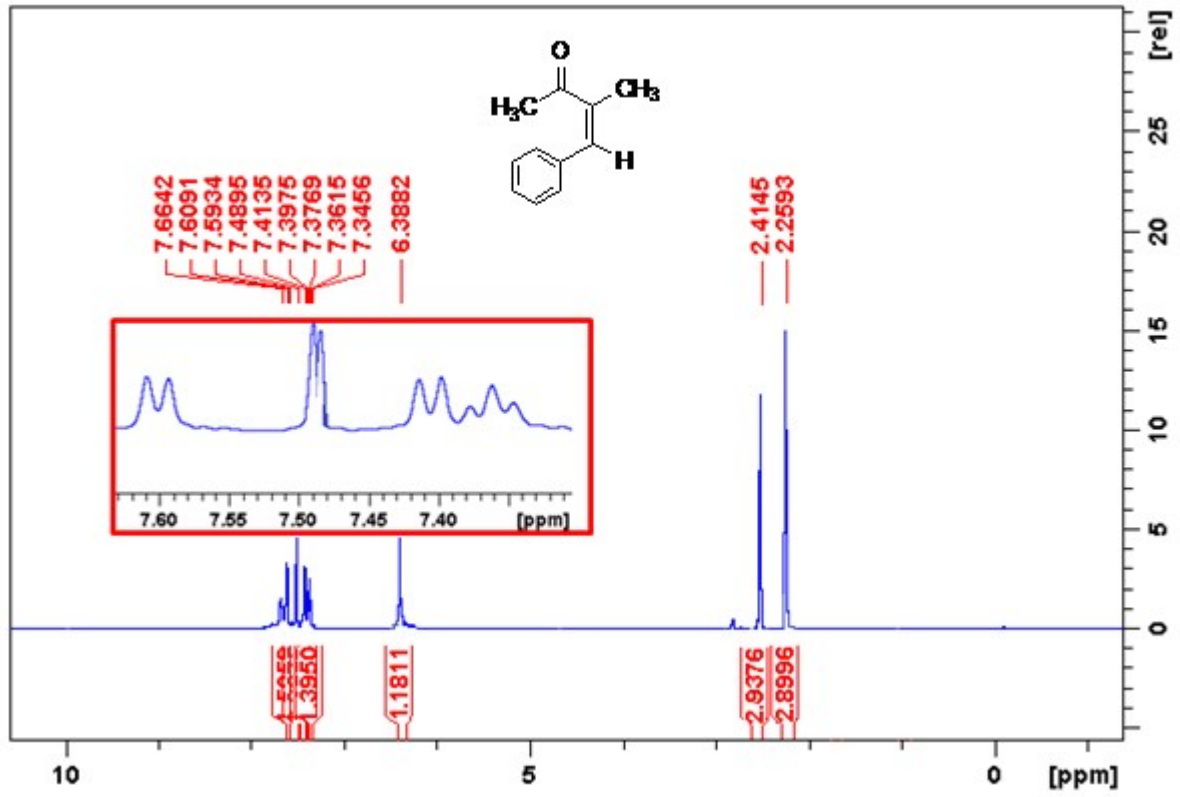


Figure S118. ^{1}H NMR spectrum of compound **8d-i**.

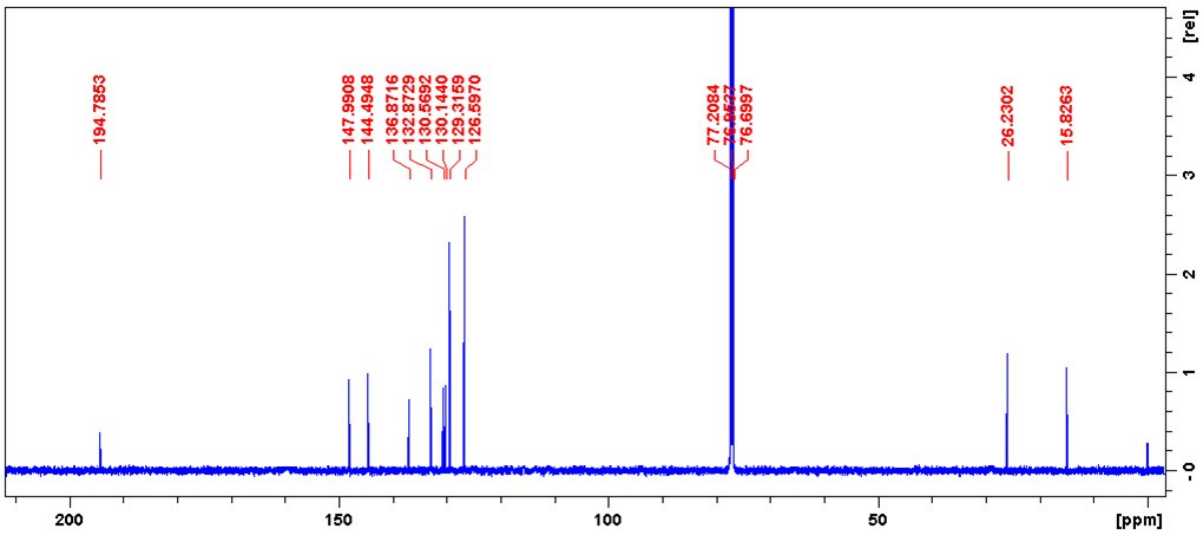


Figure S119. ^{13}C NMR spectrum of compound **8d-i**.

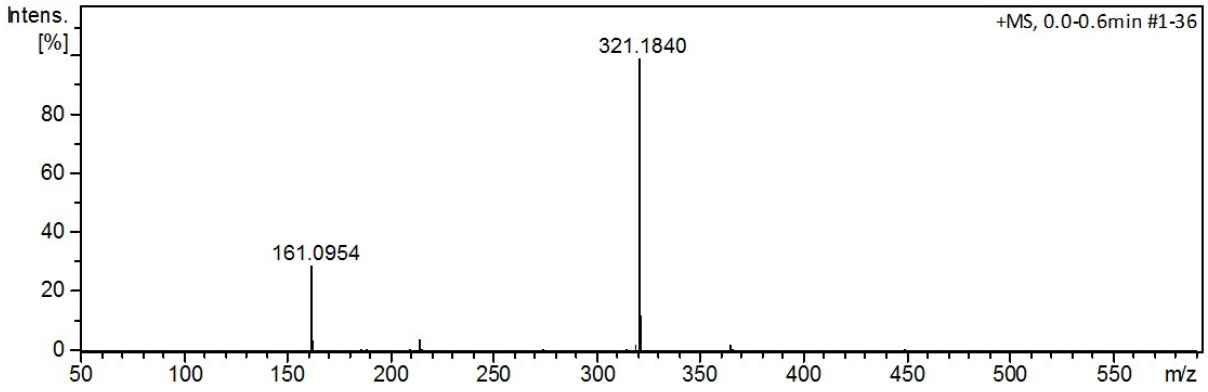


Figure S120. HRMS of **8d-i**.

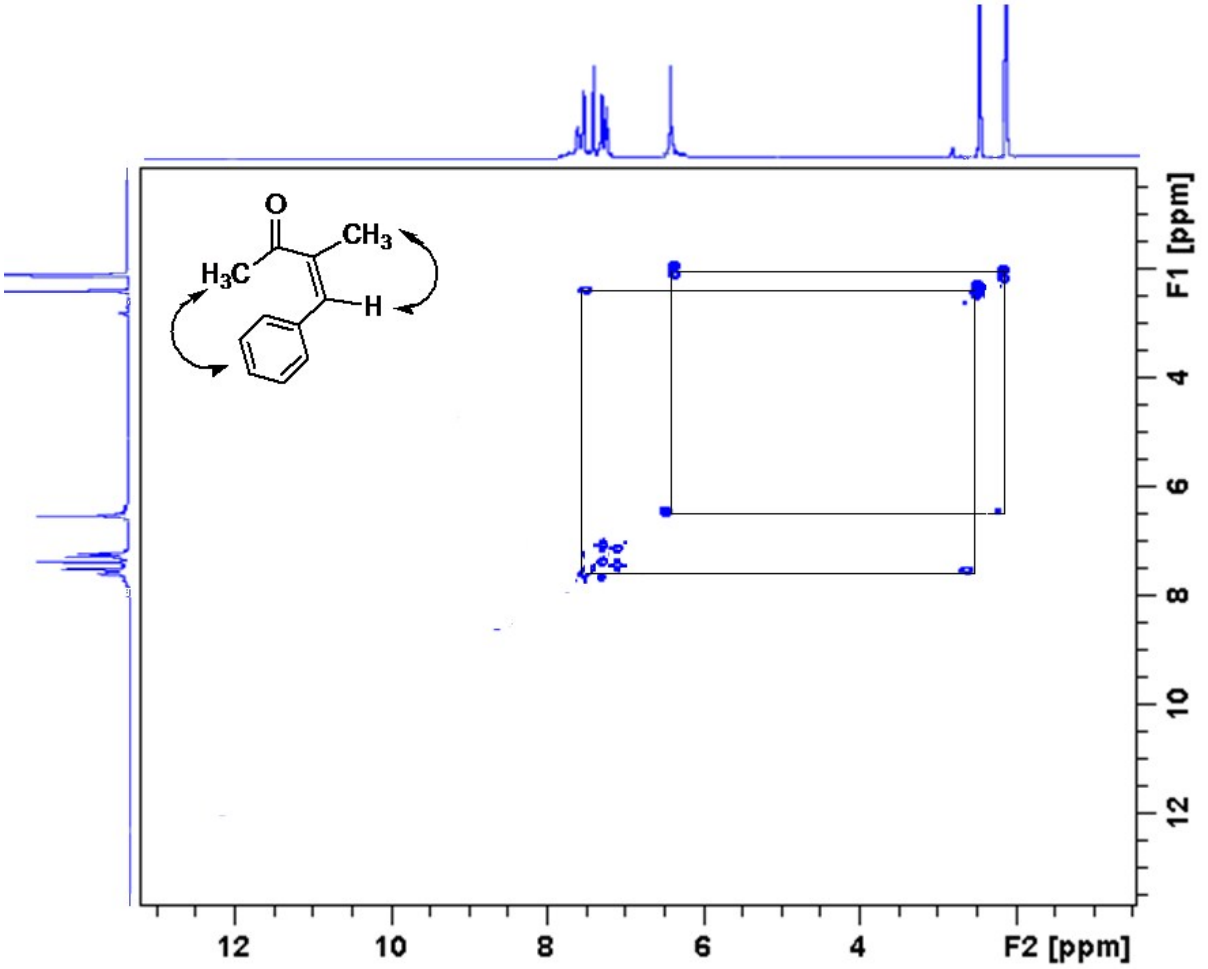


Figure S121. ROESY spectrum of compound **8d-i** indicating the geometry of the molecule across C = C bond. Mixing time was 500 ms, ns 32 and NE 512.

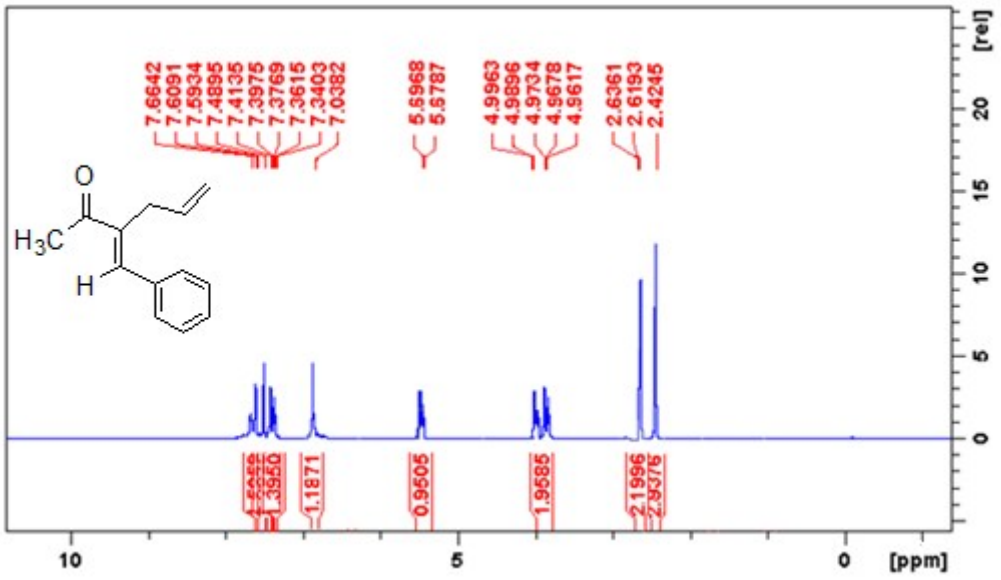


Figure S122. [1]H NMR spectrum of compound **8d-ii**.

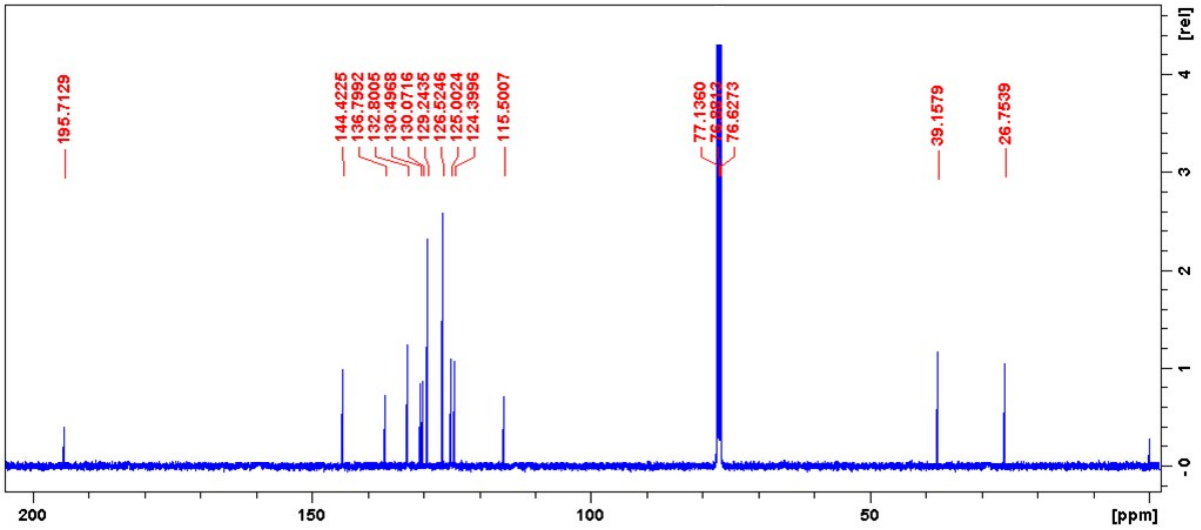


Figure S123. [13]C NMR spectrum of compound **8d-ii**.

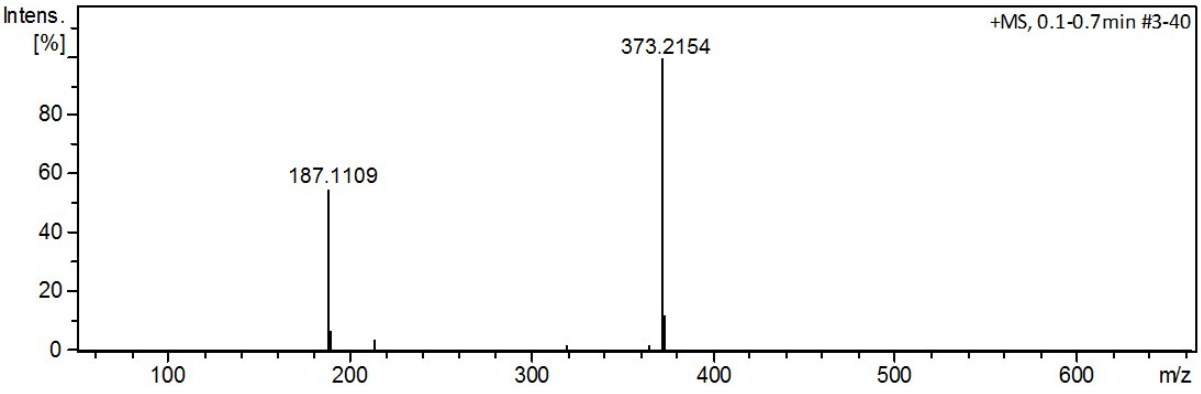


Figure S124. HRMS of **8d-ii**.

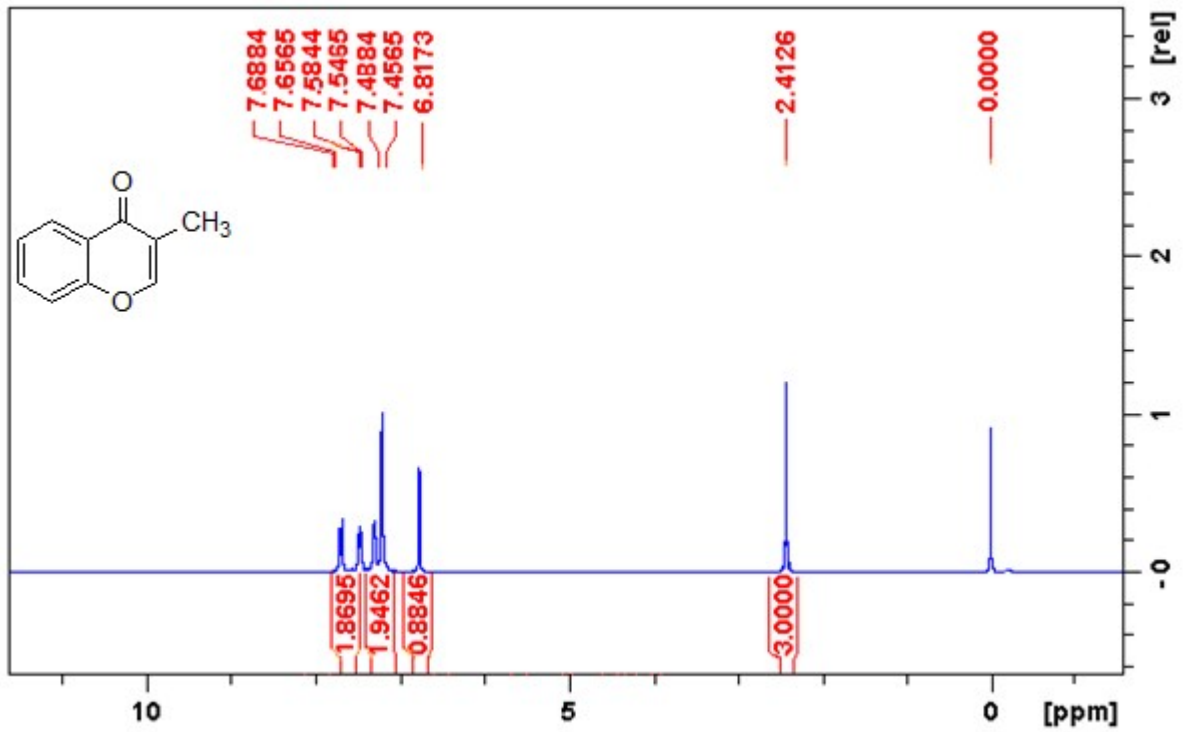


Figure S125. ^{1}H NMR spectrum of compound **9a**.

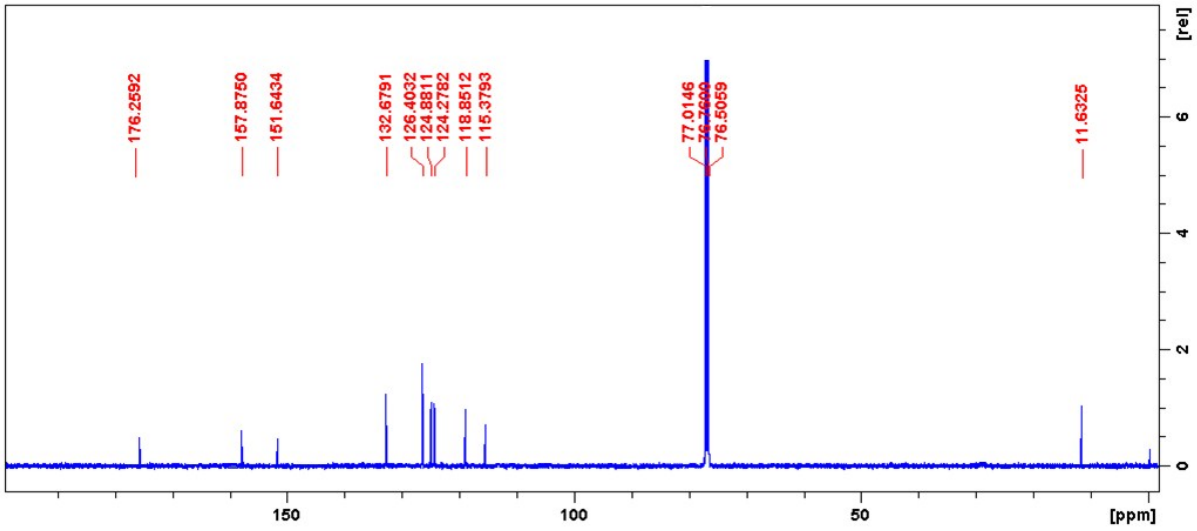


Figure S126. ^{13}C NMR spectrum of compound **9a**.

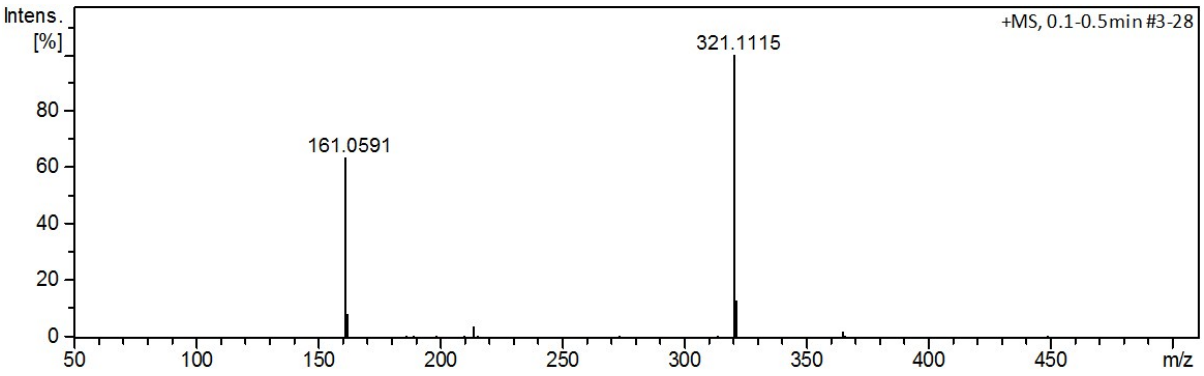


Figure S127. HRMS of **9a**.

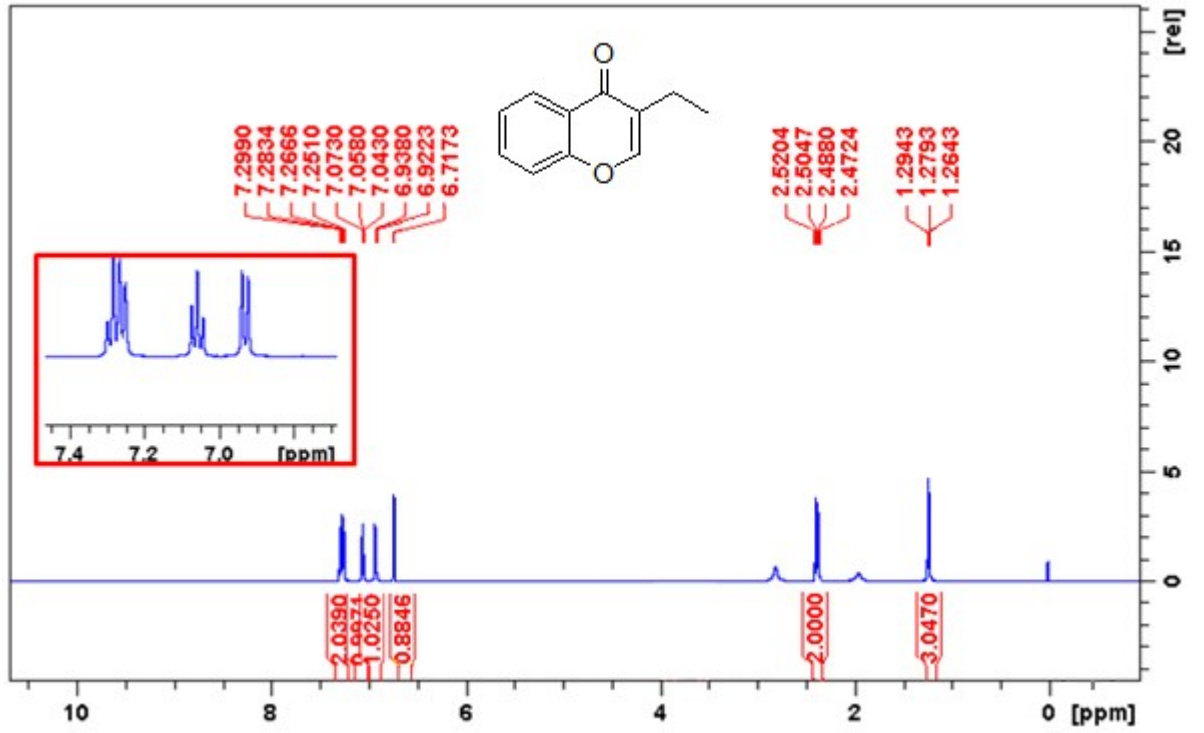


Figure S128. ^{1}H NMR spectrum of compound **9b**.

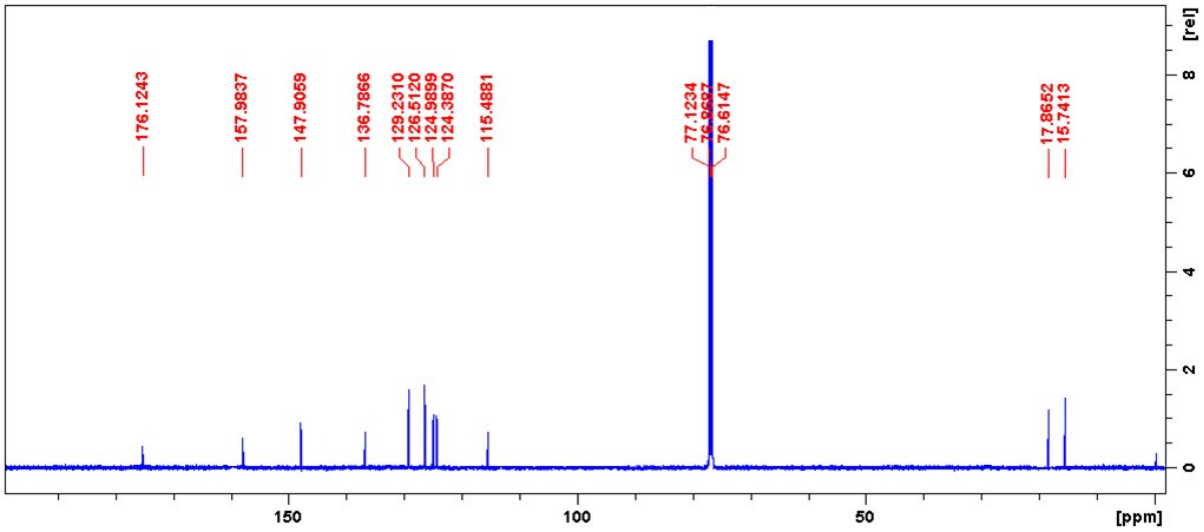


Figure S129. ^{13}C NMR spectrum of compound **9b**.

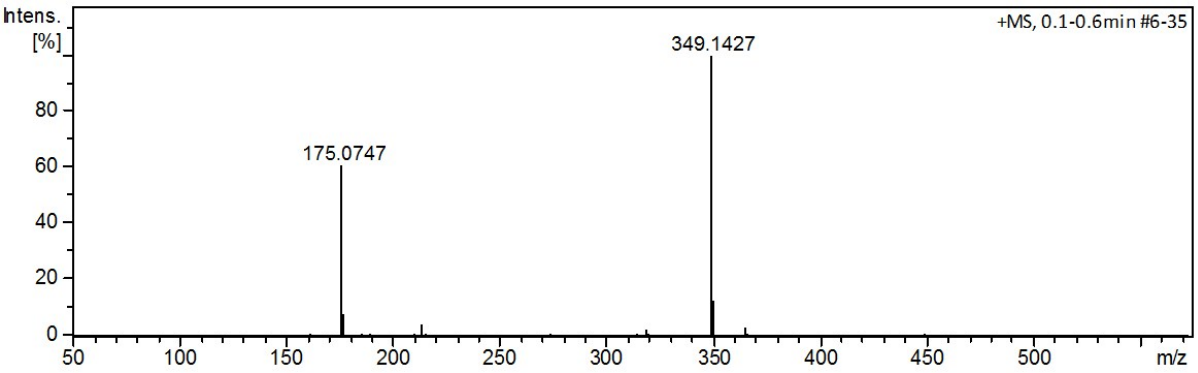


Figure S130. HRMS of **9b**.

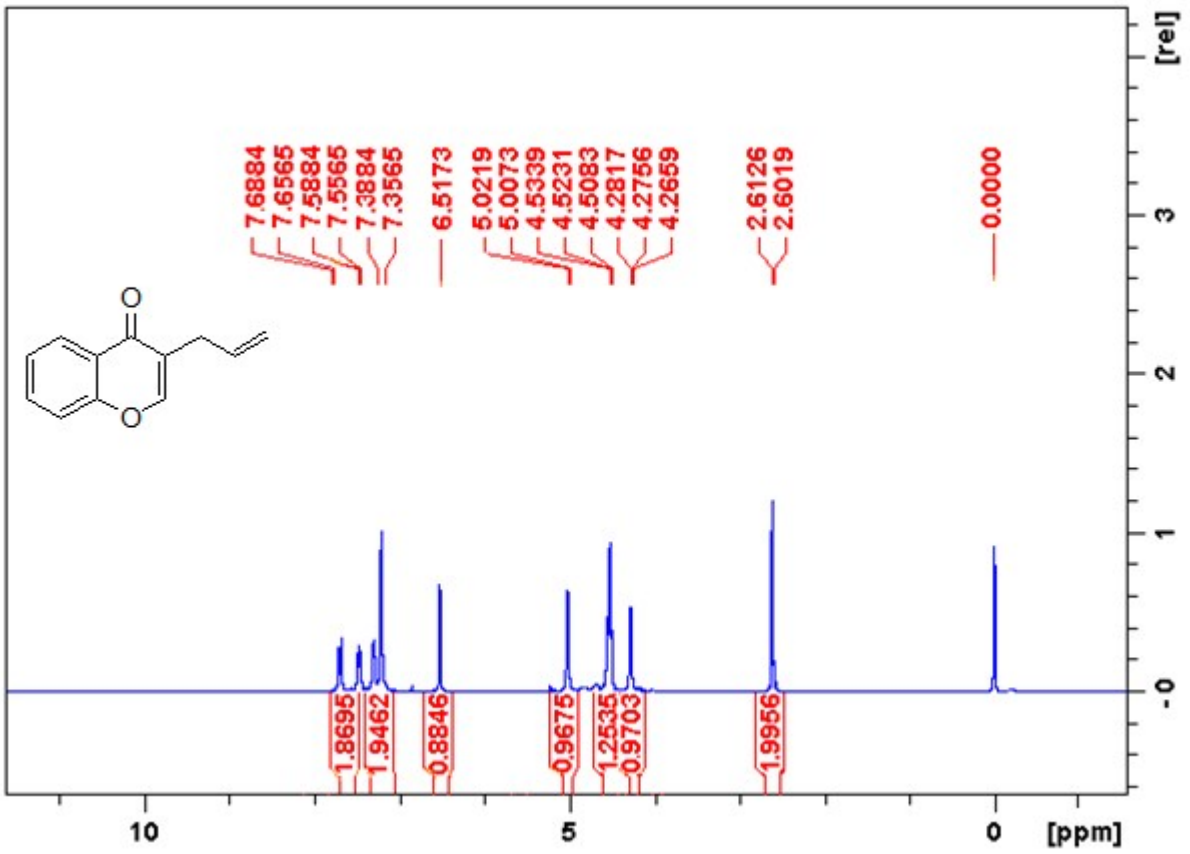


Figure S131. ^{1}H NMR spectrum of compound **9c**.

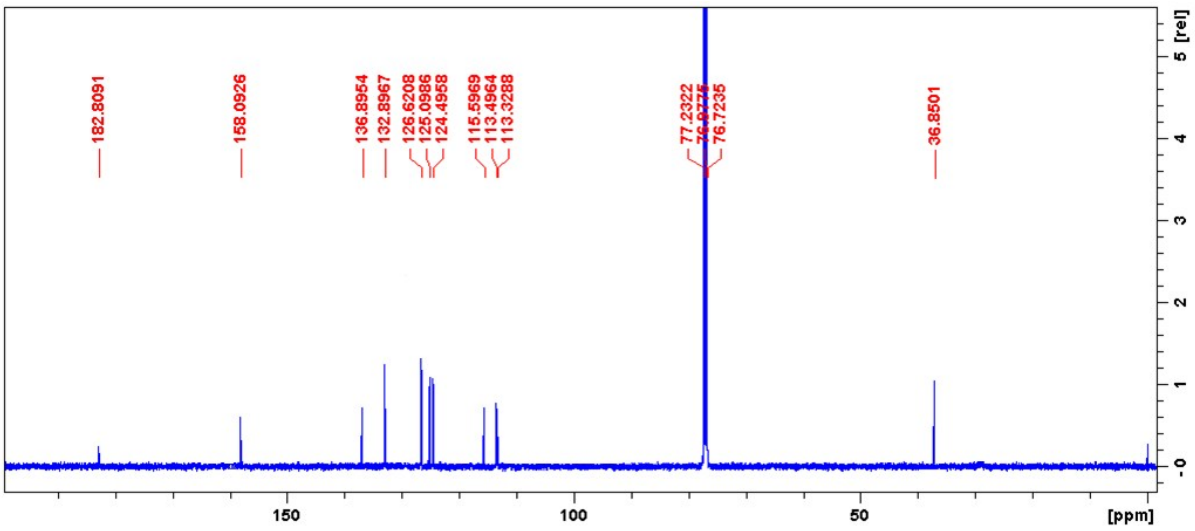


Figure S132. ^{13}C NMR spectrum of compound **9c**.

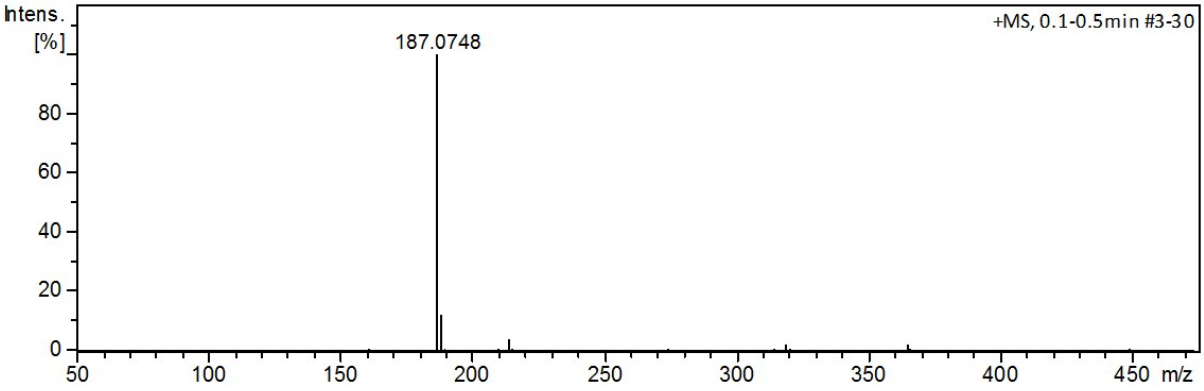


Figure S133. HRMS of **9c**.

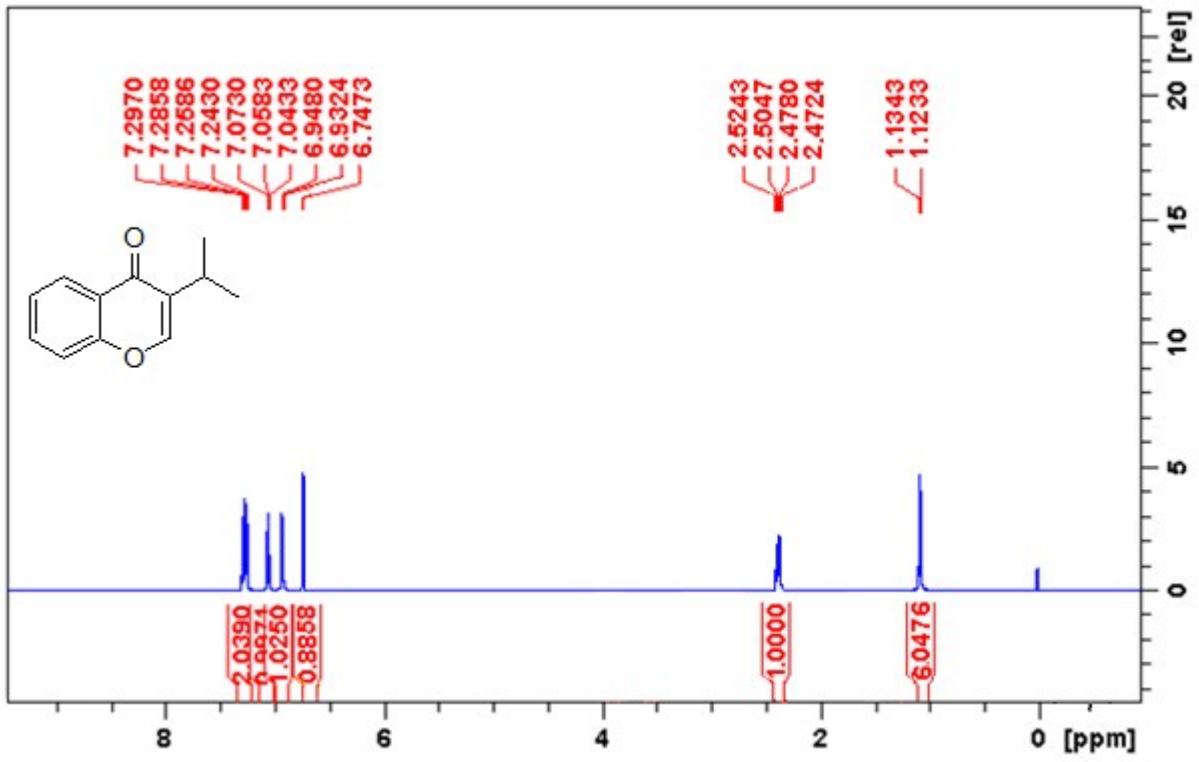


Figure S134. [1]H NMR spectrum of compound **9d**.

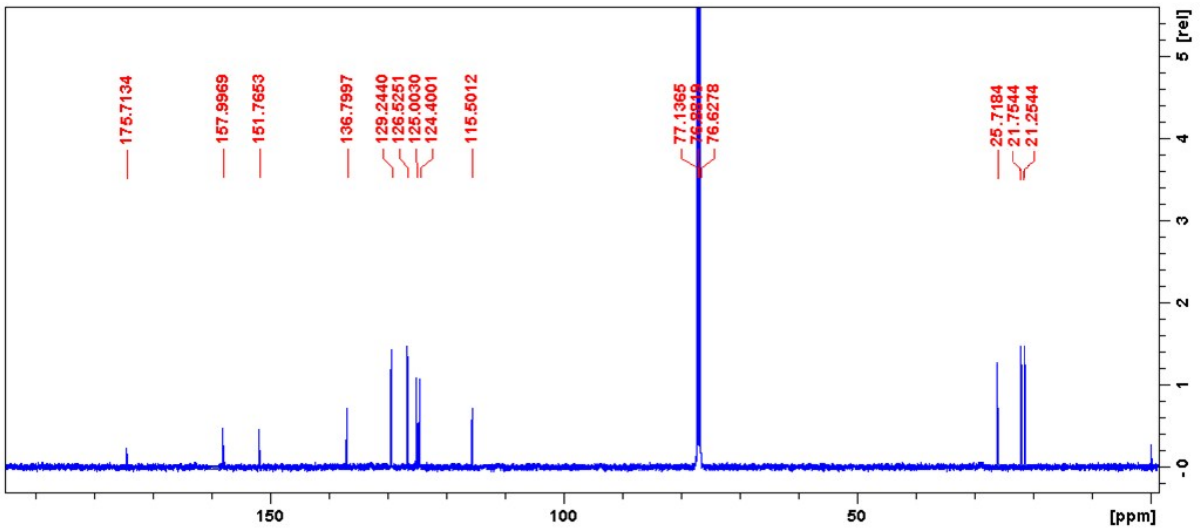


Figure S135. ^{13}C NMR spectrum of compound **9d**.

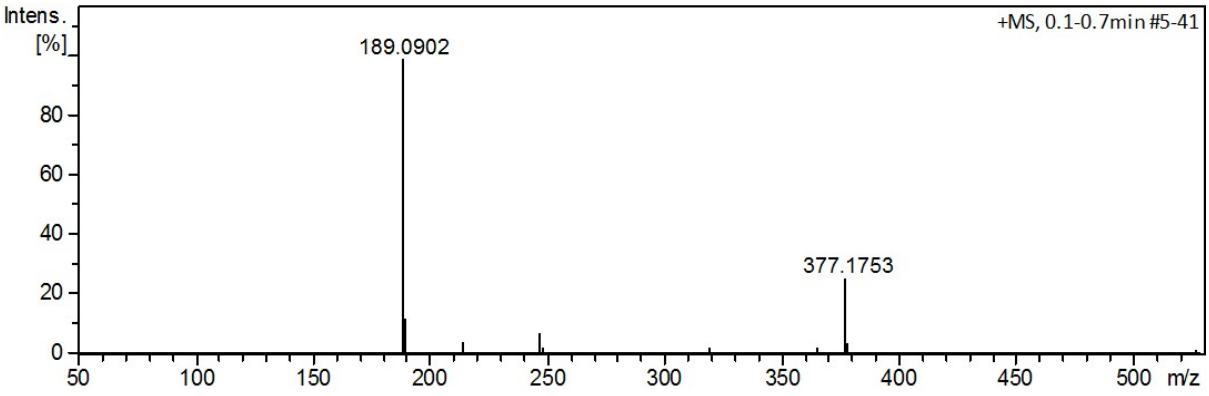


Figure S136. HRMS of **9d**.

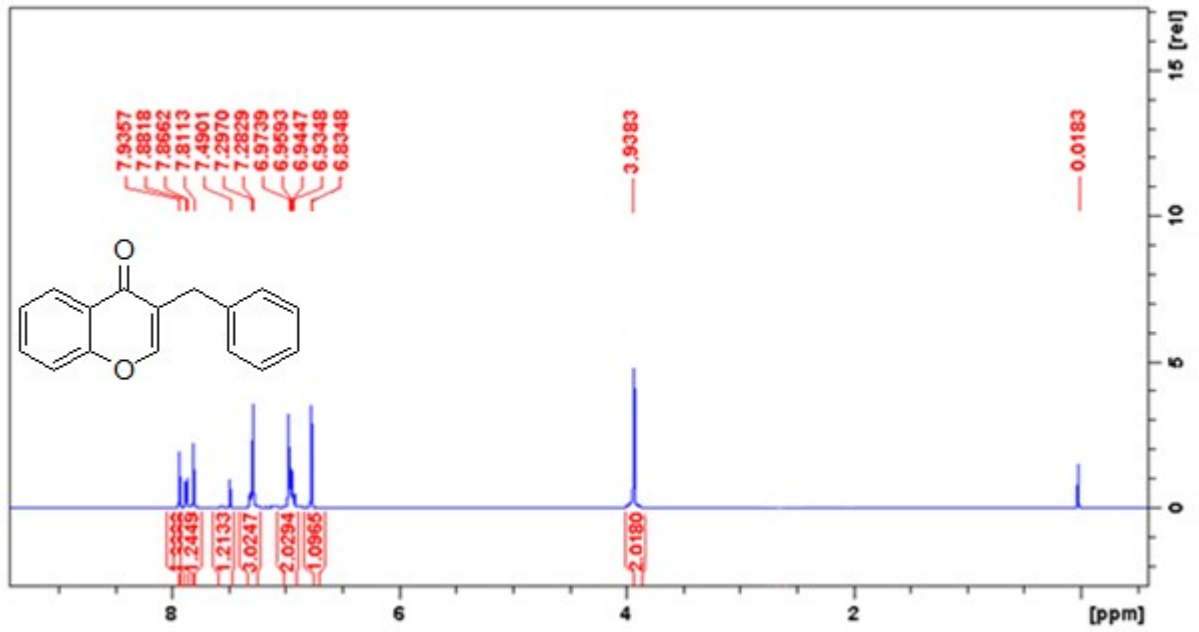


Figure S137. [1]H NMR spectrum of compound **9e**.

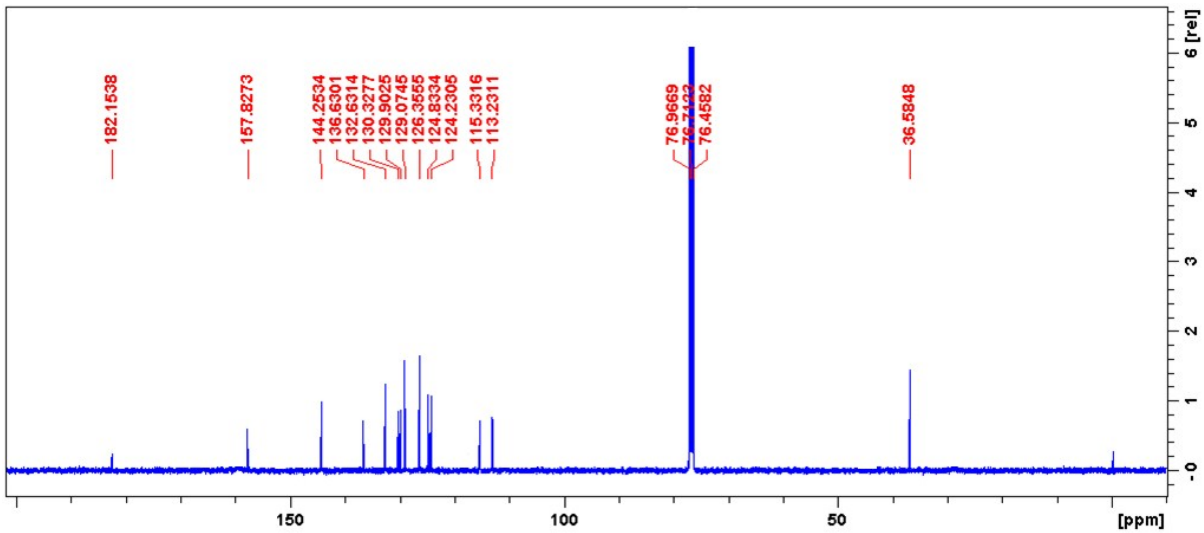


Figure S138. [13]C NMR spectrum of compound **9e**.

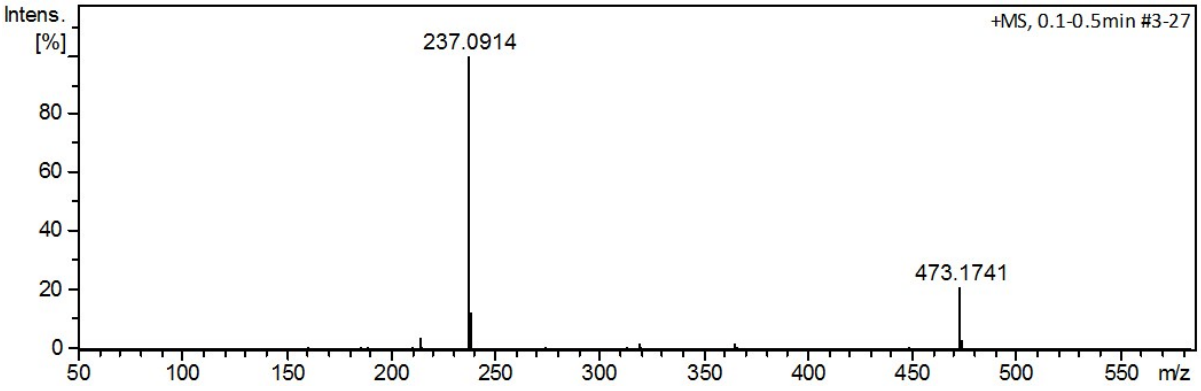


Figure S139. HRMS of **9e**.

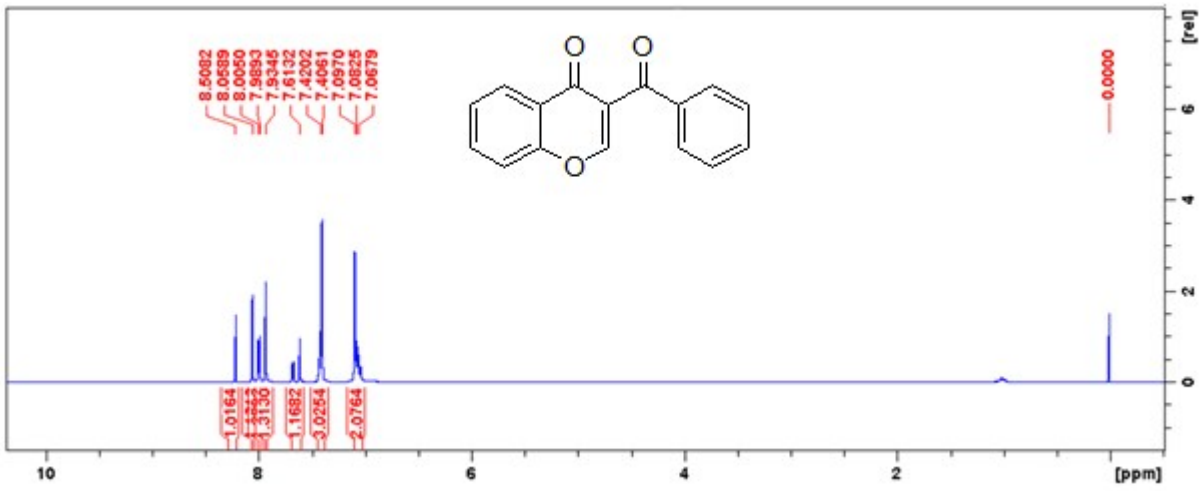


Figure S140. [1]H NMR spectrum of compound **9f**.

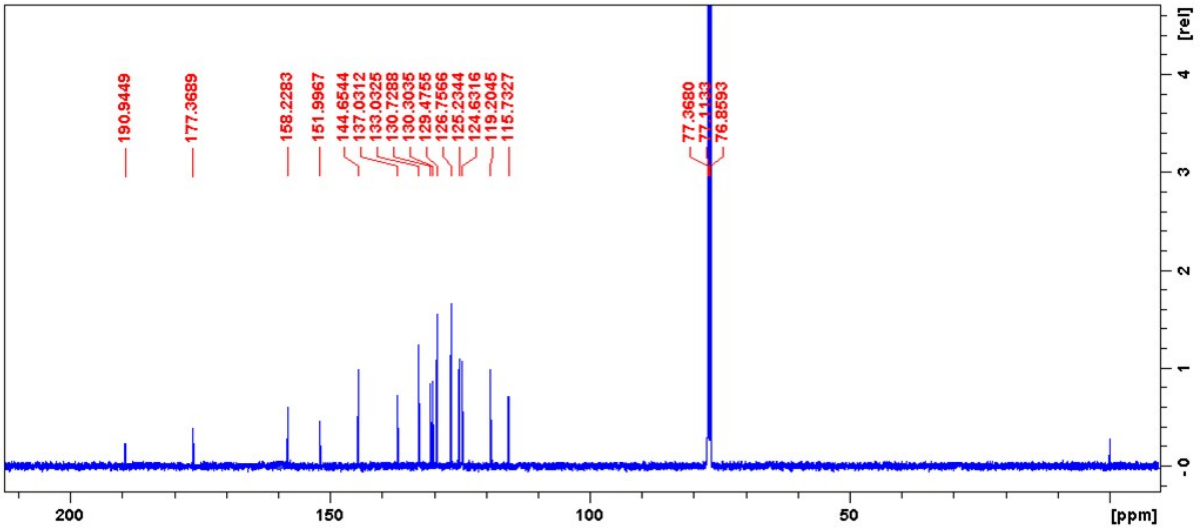


Figure S141. [13]C NMR spectrum of compound **9f**.

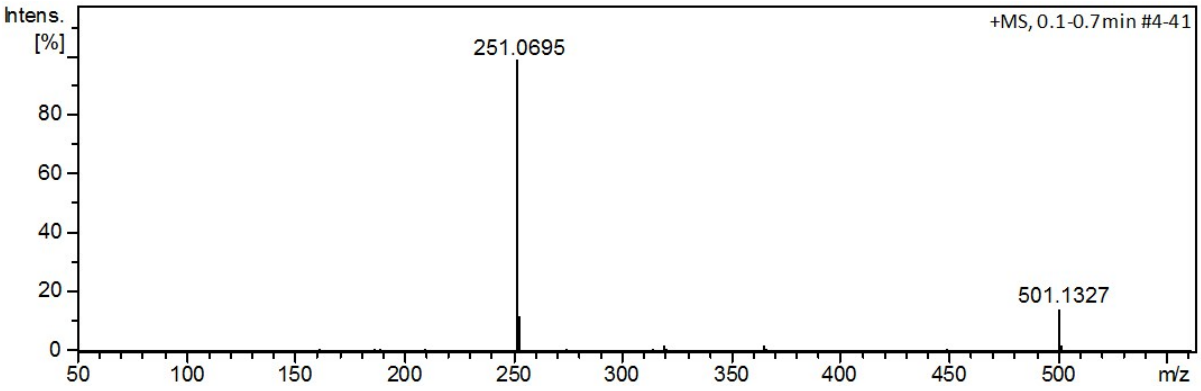


Figure S142. HRMS of **9f**.

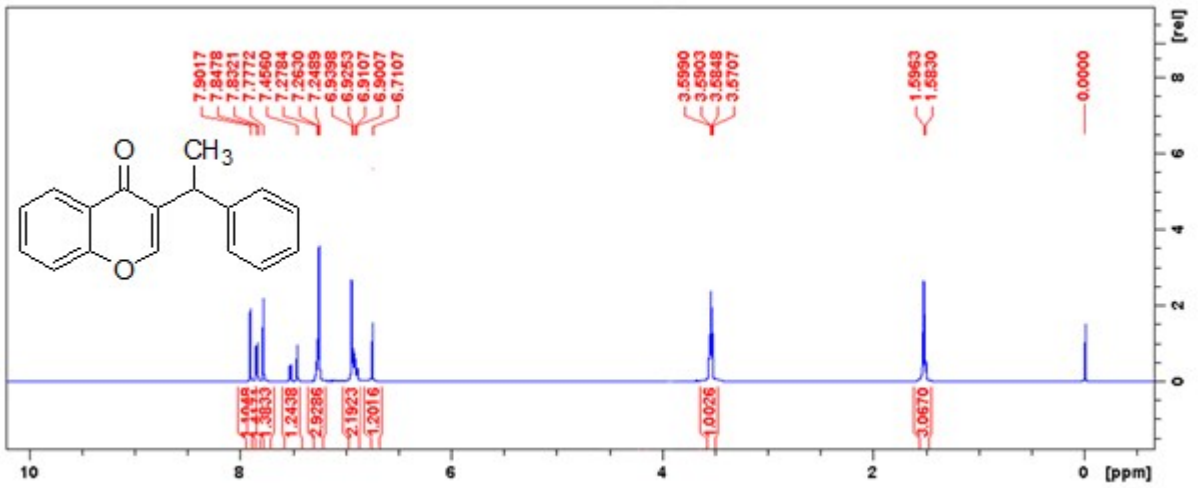


Figure S143. ^{1}H NMR spectrum of compound **9g**.

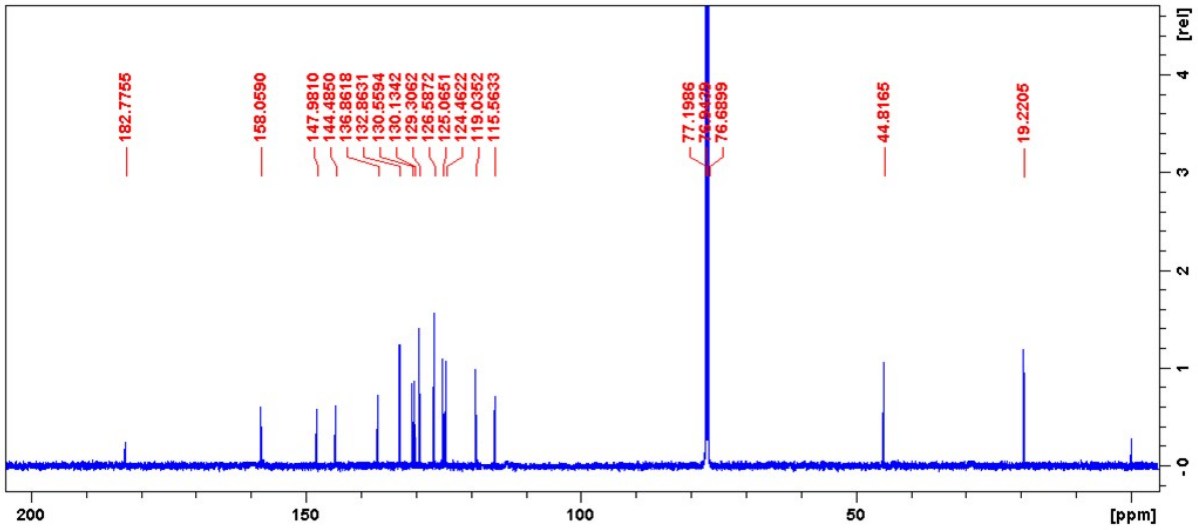


Figure S144. ^{13}C NMR spectrum of compound **9g**.

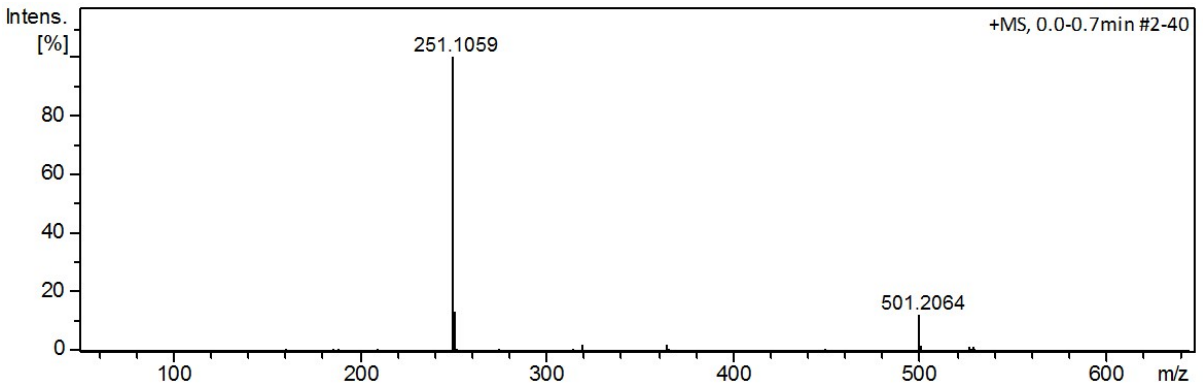


Figure S145. HRMS of **9g**.

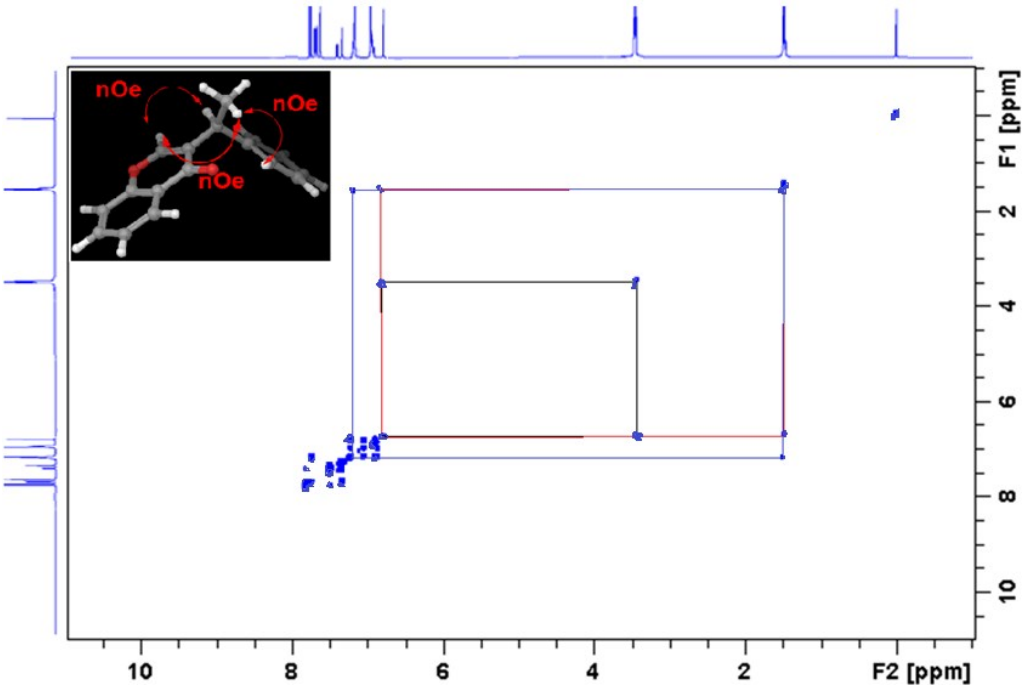


Figure S146. ROESY spectrum of compound **9g** (mixing time was 300 ms, ns = 32, NE = 512) Inset: Energy minimized geometry of compound **9g** at the B3LYP/6-31G* level, nOe observed between the different atoms/groups is represented by double head arrows.

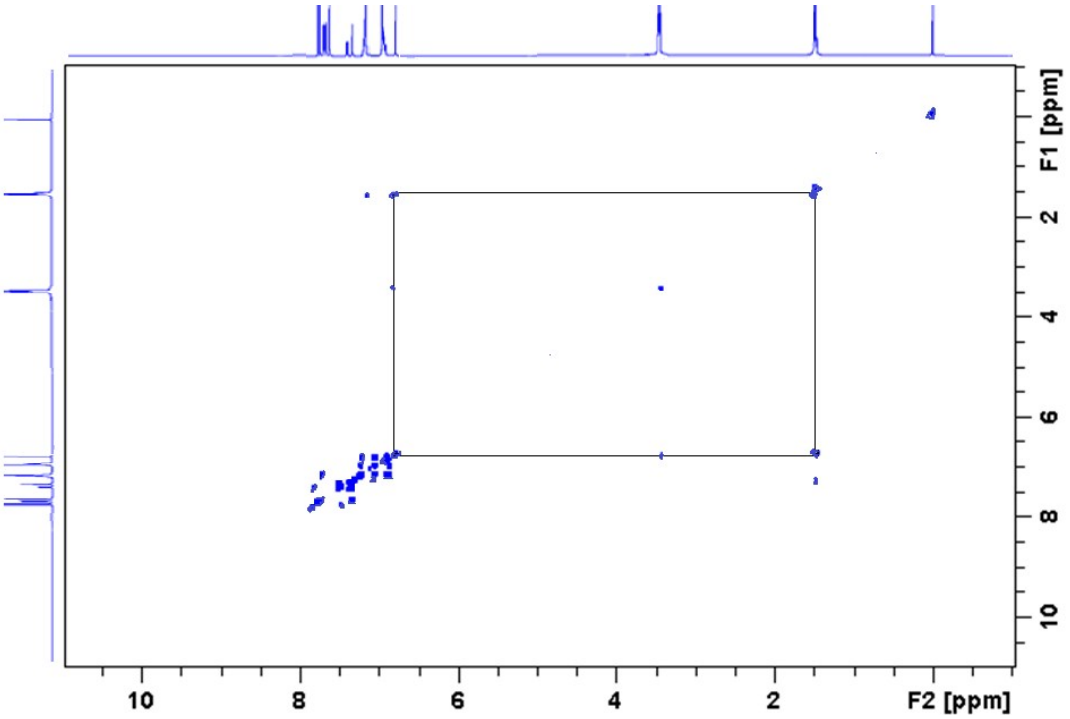


Figure S147. ROESY spectrum of compound **9h** (mixing time was 300 ms, ns = 32, NE = 512). Similar to the observations for compound **9g**, nOe was also observed in compound **9h**.

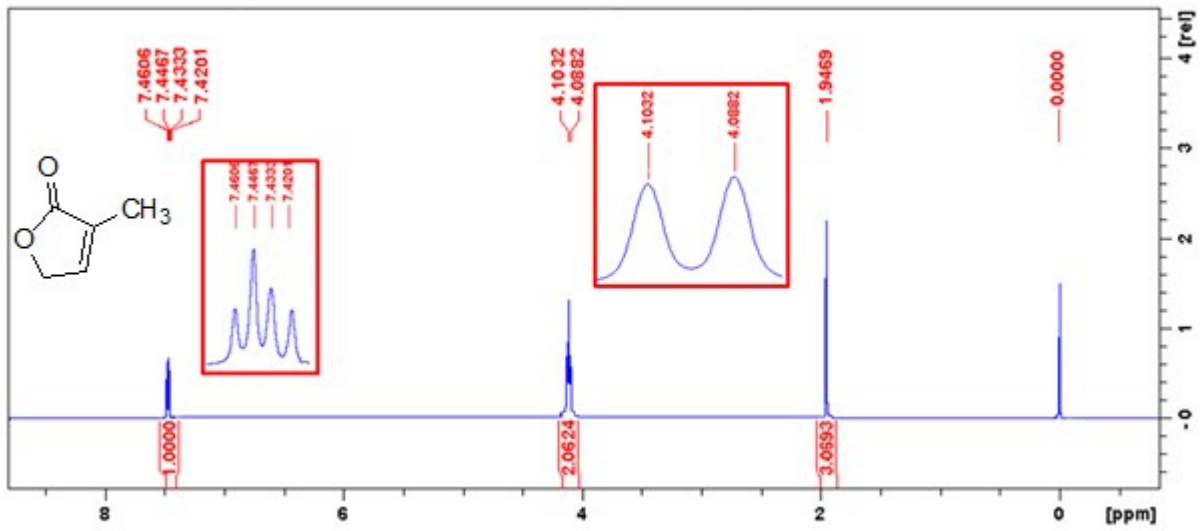


Figure S148. [1]H NMR spectrum of compound **10a**.

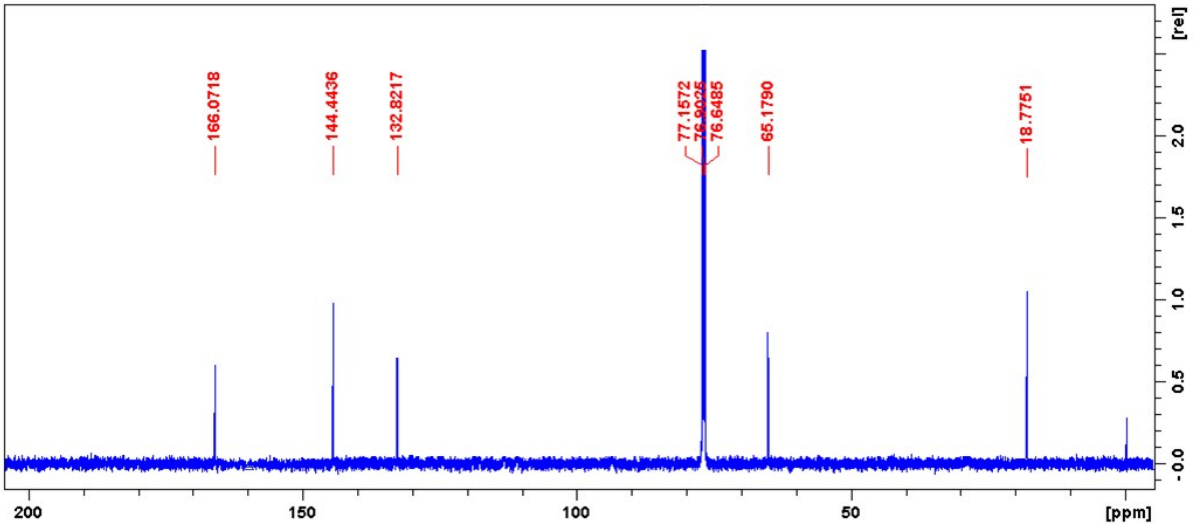


Figure S149. [13]C NMR spectrum of compound **10a**.

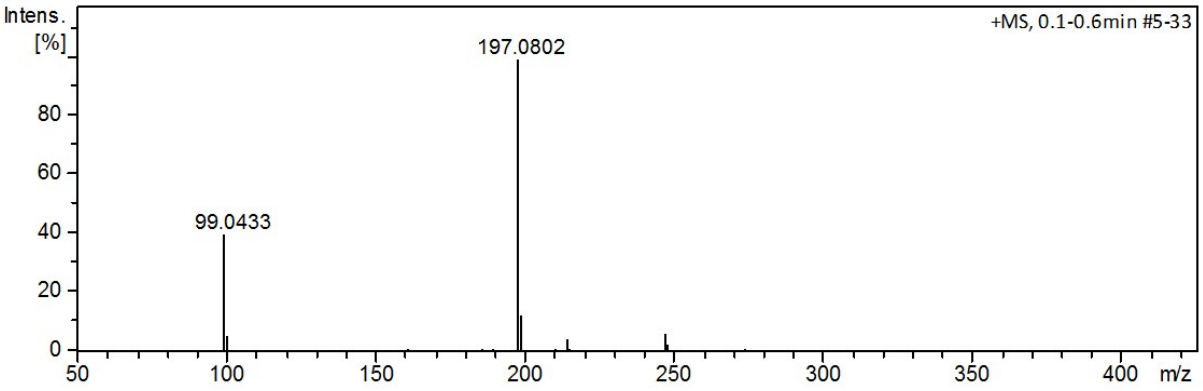


Figure S150. HRMS of **10a**.

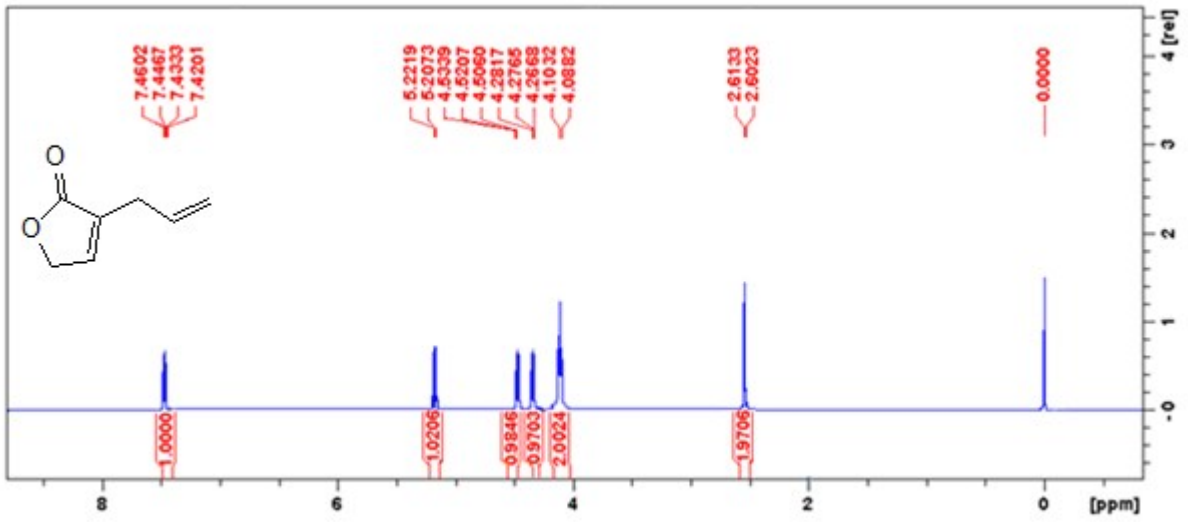


Figure S151. [1]H NMR spectrum of compound **10c**.

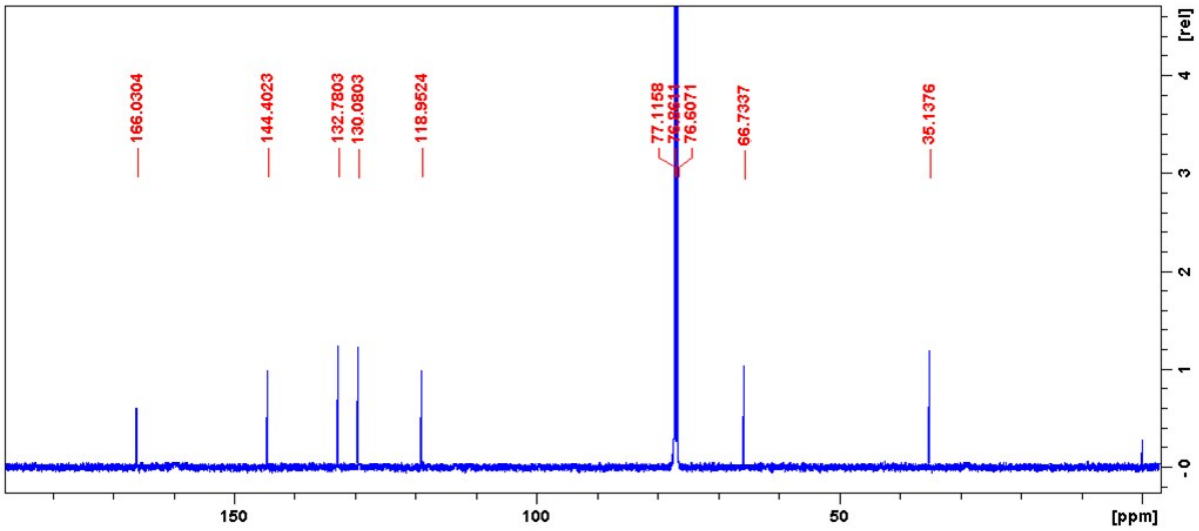


Figure S152. [13]C NMR spectrum of compound **10c**.

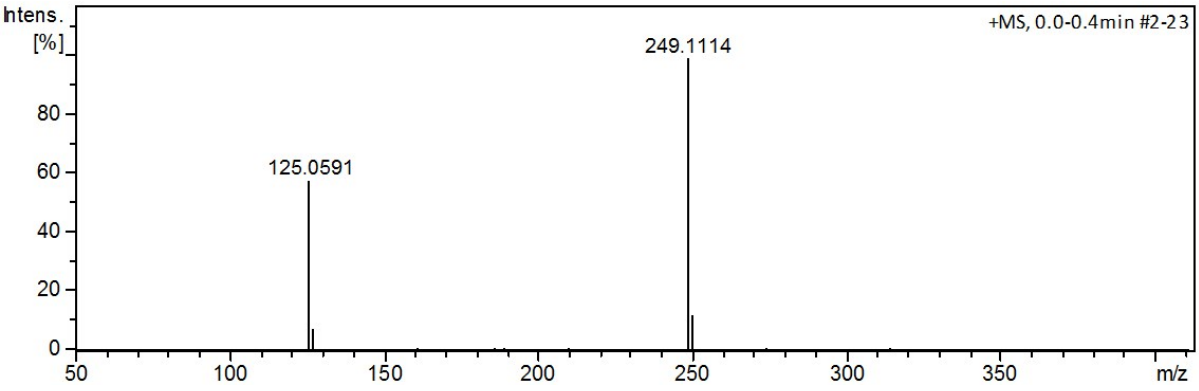


Figure S153. HRMS of **10c**.

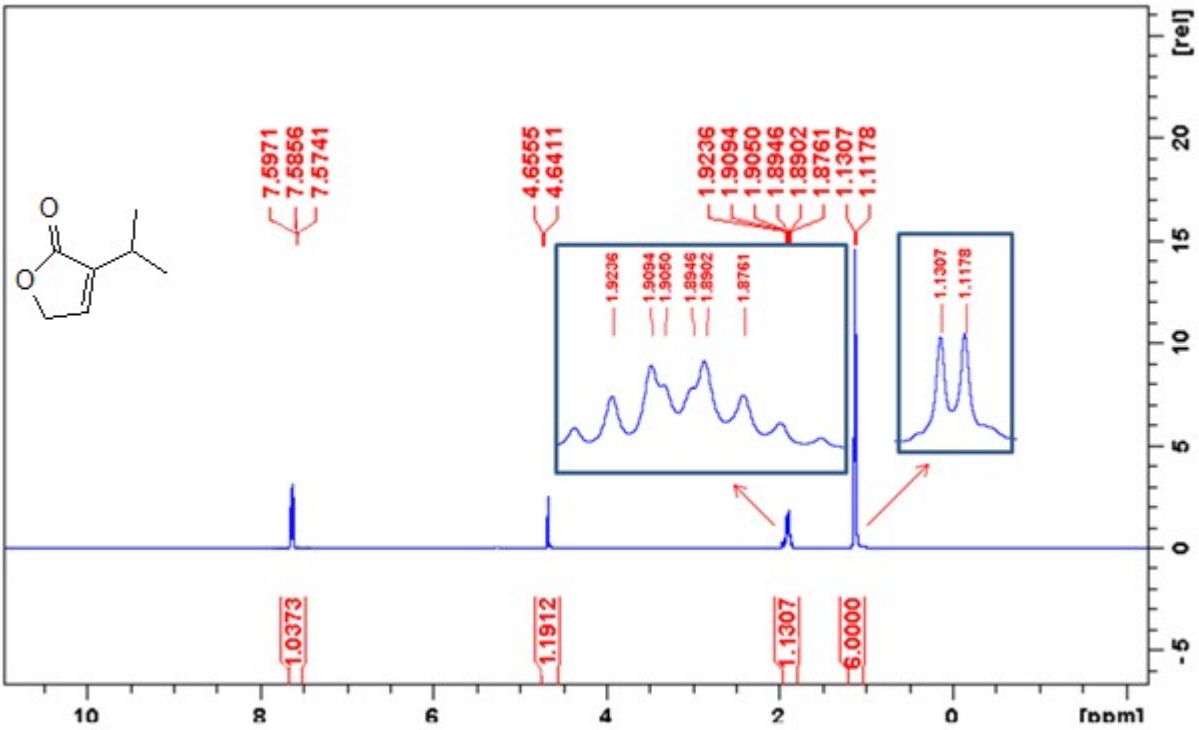


Figure S154. ^{1}H NMR spectrum of compound **10d**.

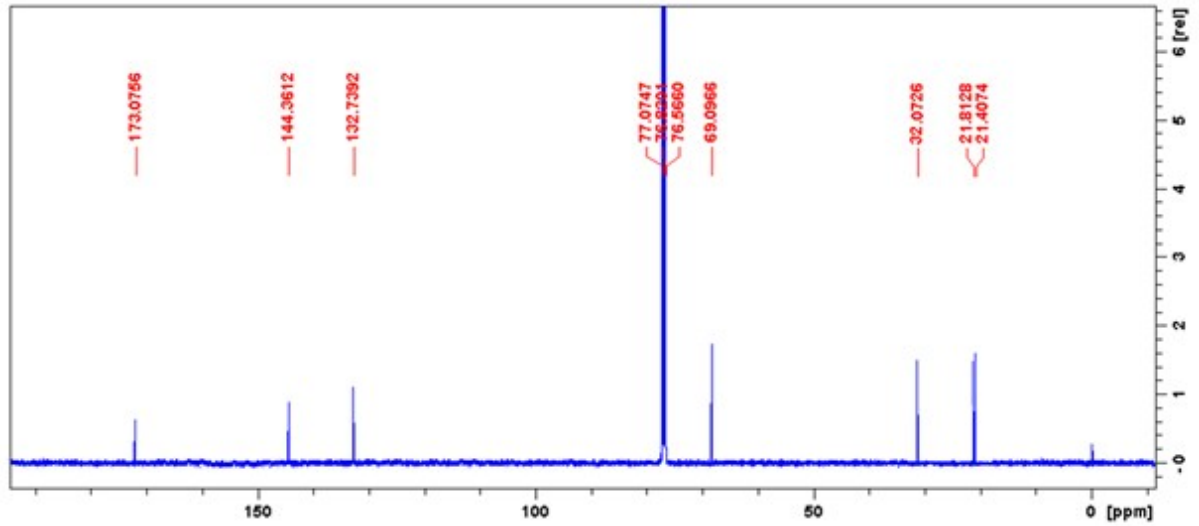


Figure S155. ^{13}C NMR spectrum of compound **10d**.

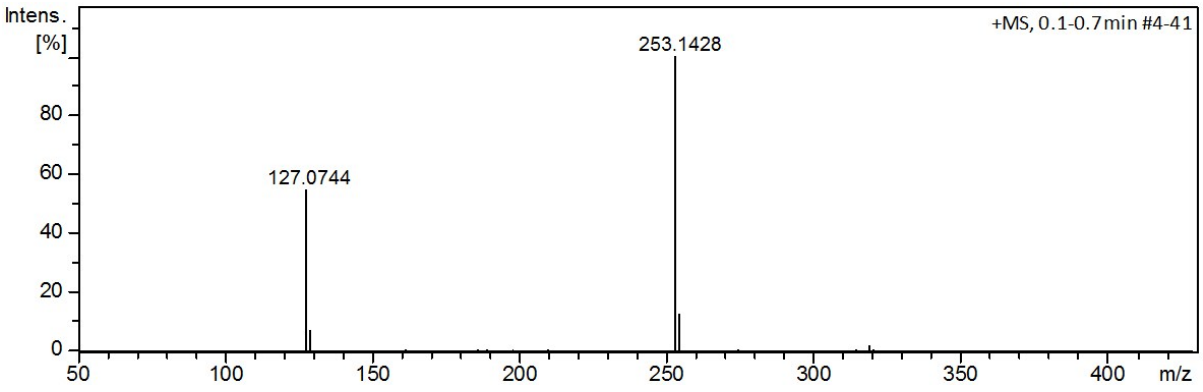


Figure S156. HRMS of **10d**.

Figure S157. ^{1}H NMR spectrum of compound **10g**.

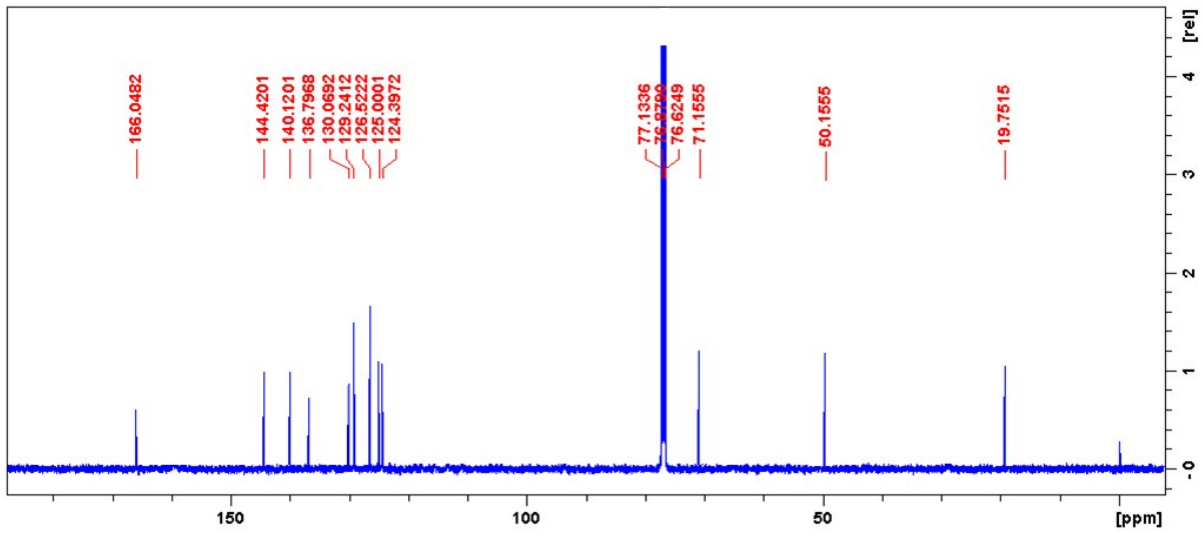


Figure S158. ^{13}C NMR spectrum of compound **10g**.

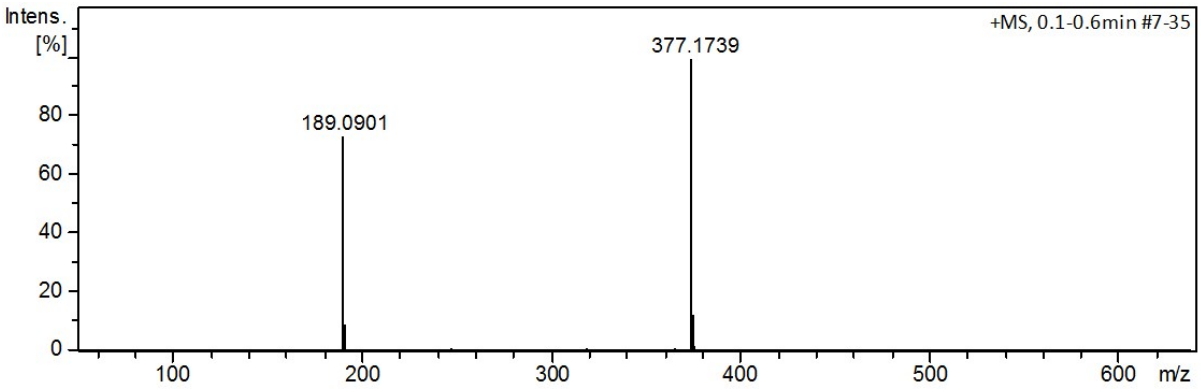


Figure S159. HRMS of **10g**.

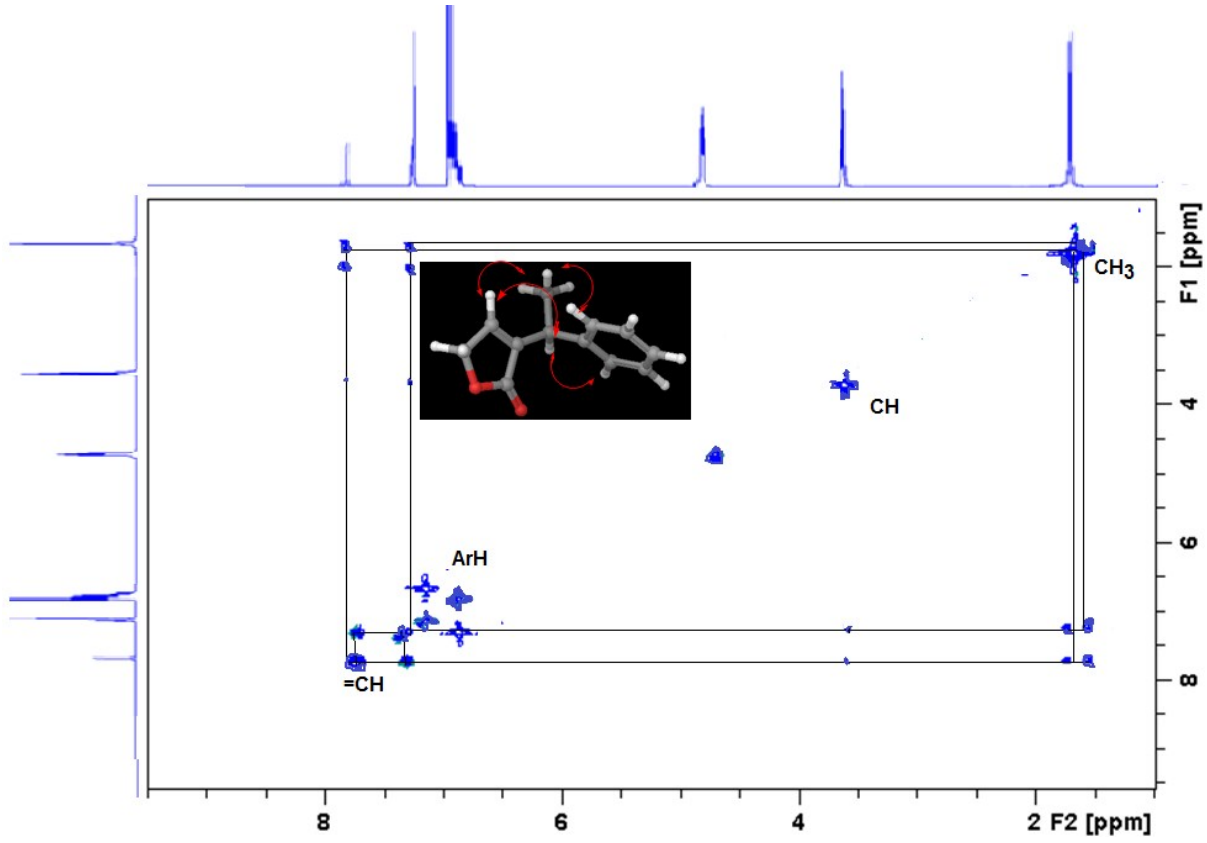


Figure S160. ROESY spectrum of compound **10g** (mixing time was 300 ms, ns = 32, NE = 1024). Inset: nOe, as observed from the NMR experiment is represented by double head arrows.

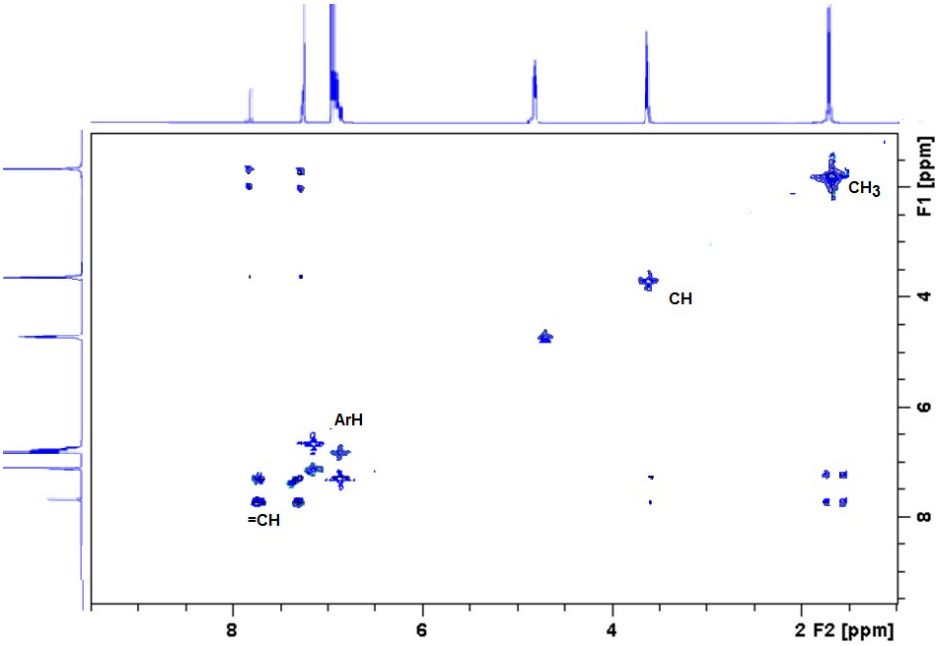


Figure S161. ROESY spectrum of compound **10h** (mixing time was 300 ms, ns = 32, NE = 1024).

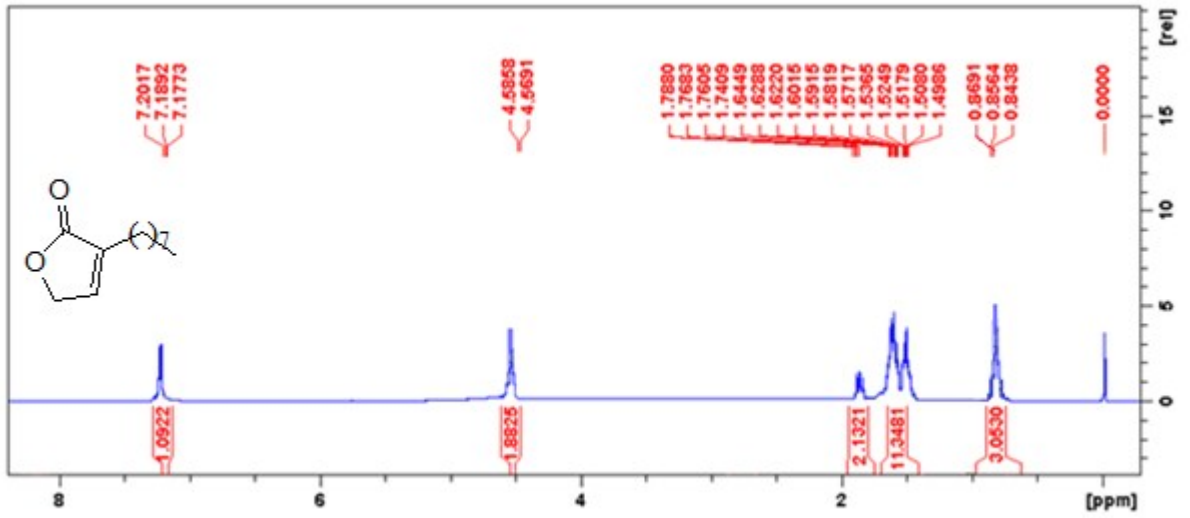


Figure S162. ^{1}H NMR spectrum of compound **10j**.

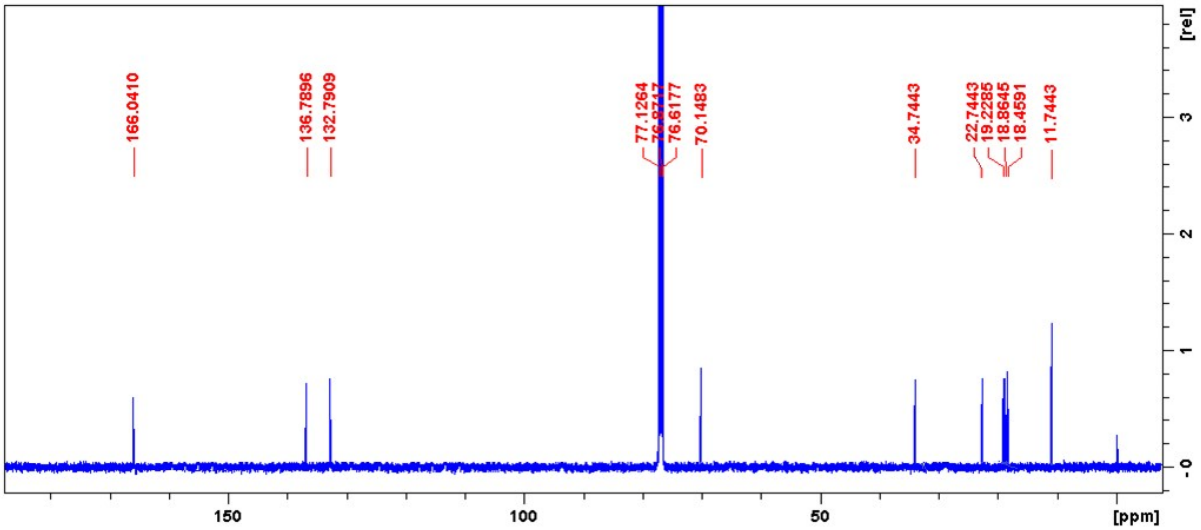


Figure S163. ^{13}C NMR spectrum of compound **10j**.

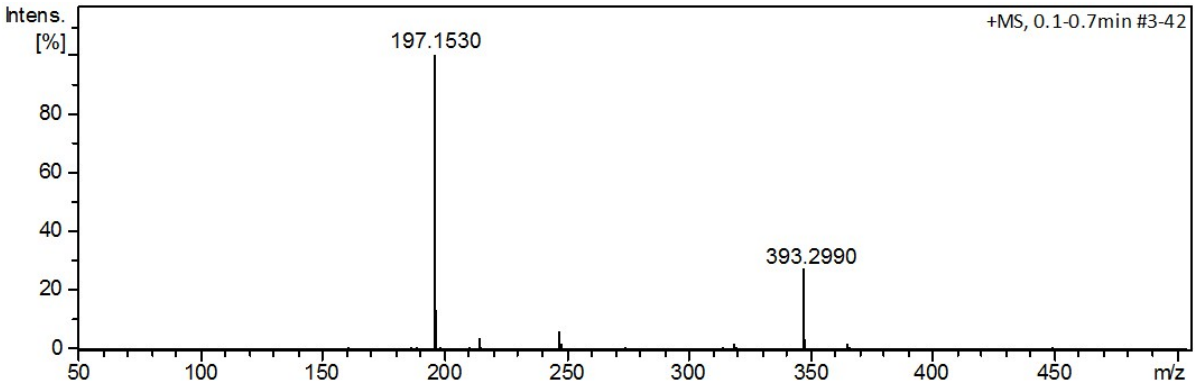
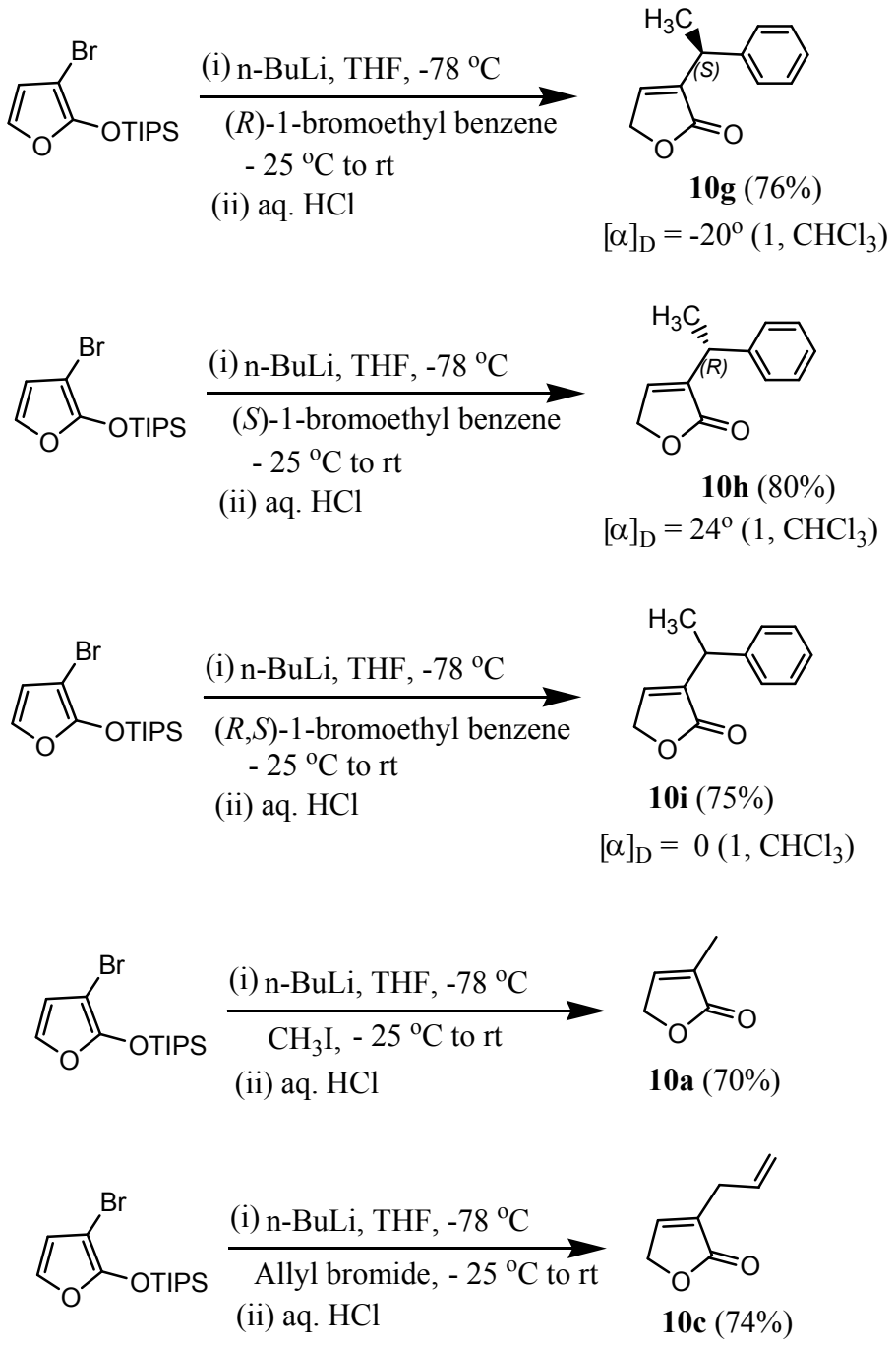


Figure S164. HRMS of **10j**.

Probable mode of action of enolate 11 (Scheme 3) with the electrophile

The stereochemistry at the asymmetric centre of compounds **9g,h** and **10g,h** throws light on the mode of reaction of enolate 11 and the electrophile. The synthesis of enantiomerically pure compounds **10g** and **10h** and their racemic mixture (**10i**) by the literature method (Scheme S2) was performed. The comparison of these compounds with those prepared in the present MS (Figure S168) indicates the possibility of S_N2 mechanism for the reaction of enolate 11 and the electrophile.



Scheme S2. Synthesis of compounds **10a**, **10c**, **10g**, **10h** and **10i** according to the reported procedure (*J. Org. Chem*. **2006**, *71*, 6670 – 6673; *J. Org. Chem.* **2008**, *73*, 8109–8112).

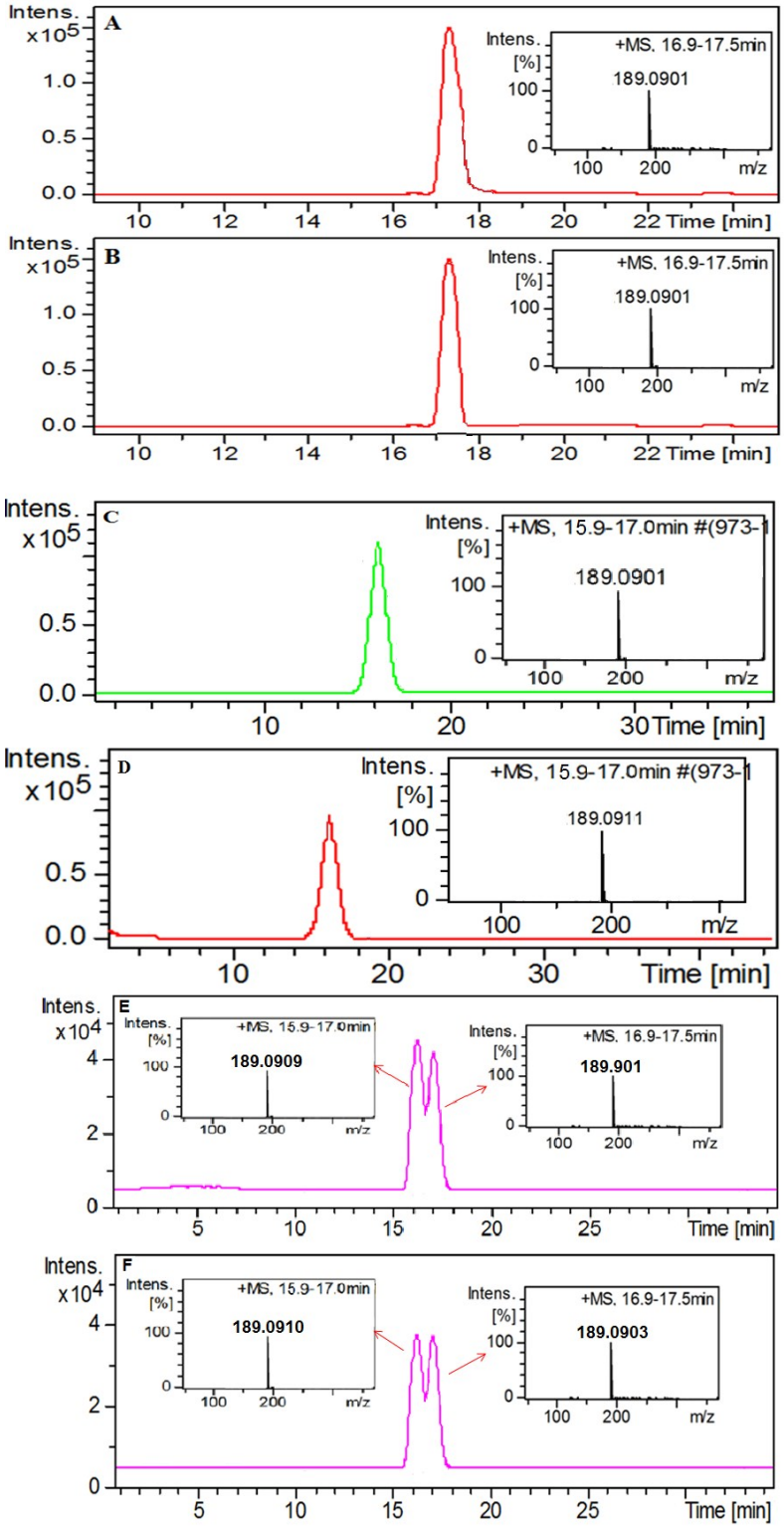


Figure S165. (A) LC-MS of **10g** prepared through the present procedure, (B) LC-MS of **10g** prepared through reported procedure (Scheme S2), (C) LC-MS of **10h** prepared through the present procedure, (D) LC-MS of **10h** prepared through reported procedure (Scheme S2), (E) LC-MS of **10i** prepared through the present procedure, (F) LC-MS of **10i** prepared through the reported procedure (Scheme S2).

Percentage Purity of the compounds

The purity of the compounds was checked by qHNMR (quantitative ^{1}H NMR).[7] Dimethylsulfone was used as internal calibrant (IC) and the purity of the compound was calculated by using the following formula:

$$P\ [\%] = n_{IC}.Int_t.MW_t.m_{IC.}\ P_{IC}/n_t.Int_{IC}.MW_{IC}.m_s$$

Where:

Int is the integral,

MW is the molecular weight,

m is the mass,

n is the number of protons,

P is the purity (in %),

IC is the internal calibrant,

s is the sample and

t is the target molecule.

For these experiments, ^{1}H NMR spectra were recorded under the following conditions:

Pulse Program: zg with 90^o pulse (Bruker) *Spinning status*: Non-spinning

Sample temperature: 25 ^{o}C *Acquired Data points*: 64000, *Dummy Scans*: 4, *Acquisition time*: 4s *Spectral window*: 20 ppm, *O1P*: 6 ppm, *Number of Scans*: 64

All the compounds were having purity >99%.

(7) Pauli, G. F.; Chen, S. –N.; Simmler, C.; Lankin, D. C.; Godecke, T.; Jaki, B. U.; Friesen, J. B.; McAlpine, J. B.; Napolitano, J. G. *J. Med. Chem*. **2014**, *57*, 9220-9231.