Supplementary Information
For
Thymidylate Synthase Inspired Biomodel Reagent for the Conversion of Uracil to Thymine

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General note: ^{1}H and ^{13}C NMR spectra were recorded on Bruker 500 MHz NMR spectrometer using 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 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 and NMR spectra. For LC-MS, Dionex Ultimate 3000 system was linked to mass spectrometer. Chirobiotic® T 10 μm chiral HPLC column (25 cm x 4.6 mm) was used for ensuring the chiral purity of the peptides. Acetonitrile-water (1:1), each charged with 0.1% formic acid, 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. Reactions were monitored by thin layer chromatography (TLC), mass spectrometery and NMR spectroscopy. 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. IR spectral data were recorded on FTIR (VARIAN 660 IR) instruments. Optical rotation was recorded on AT-100 Atago automatic polarimeter.

Although the ^{1}H NMR spectra of the compounds did not exhibit extra peaks but still to ascertain the quantitative purity, the quantitative HNMR (qNMR) were checked in accordance with the procedure given in ref 27 (main text). For this purpose ^{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

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.

Experimental Procedure:

5-Amino-9-oxo-9,10-dihydroacridine-4-carboxylic acid ethyl ester.

A mixture of 2-chloro-3-nitrobenzoic acid (5 g, 25 mmol), anthranillic acid (4 g, 30 mmol), K_2CO_3 (6 g, 45 mmol), CuO (150 mg, 2 mmol) in 50 ml amyl alcohol was heated at 160 ^oC for 36 h. After the completion of reaction, amyl alcohol was evaporated under reduced pressure and reaction mixture was washed with hot water. The precipitates were filtered and further treated with 10 ml conc H_2SO_4 at 90-100 ^oC for 2 h to obtain 5-nitro-9-oxo-9,10-dihydroacridine-4-carboxylic acid (5g, 66%) which was esterified on treatment with $NaOC_2H_5$ (Na in ethanol).

For reduction of the nitro group, H_2 gas was passed through the mixture of 5-nitro-9-oxo-9,10-dihydroacridine-4-carboxylic acid ethyl ester (5 g, 16 mmol) and Pd-C (200 mg, 2 mmol) taken in 30 ml CH_3OH, 200 µL glacial acetic acid and 30 ml H_2O. After 5h of the reaction, the reaction mixture was filtered through sintered glass funnel. The filtrate was concentrated under vacuum. The residue was washed with diethyl ether to obtain 5-amino-9-oxo-9,10-dihydroacridine-4-carboxylic acid ethyl ester (2 g, 44 %), mp 250 ^oC. HRMS-ESI (*m/z*): $[M+H]^+$ calculated for $C_{16}H_{14}N_2O_3$, 282.0990; found 282.0999.

5-Amino-10-oxiranmethyl-9-oxo-9,10-dihydroacridine-4-carboxylic acid (21) (Scheme S1).

5-Amino-9-oxo-9,10-dihydroacridine-4-carboxylic acid ethyl ester (2g, 7 mmol), 1 ml (13 mmol) epichlorohydrin and K_2CO_3 (2.5 g, 18 mmol) were taken in DMF (15 ml) and stirred for 8 h. After the completion of reaction (TLC monitoring), the reaction mixture was extracted with ethyl acetate. The organic phase was washed with water, dried over anhydrous Na_2SO_4 and concentrated under vacuum. The residue was solidified with diethyl ether and treated with LiOH in acetone-water (2:1, v/v) (pH 9.0) followed by extraction with ethyl

acetate (5 x 25 ml) to isolate pure 5-amino-10-oxiranmethyl-9-oxo-9,10-dihydroacridine-4-carboxylic acid (1.72g, 65%), mp 160 ^{o}C, $[\alpha]_D$ +26^{o} (c 1.00, MeOH). HRMS-ESI (*m/z*): $[M+H]^+$ calculated for $C_{17}H_{14}N_2O_4$, 311.1026; found 311.1025. Alternatively, compound **21** was also prepared by the reaction of 5-nitro-9-oxo-9,10-dihydroacridine-4-carboxylic acid ethyl ester with epichlorohydrin using K_2CO_3 in DMF (using same procedure as stated above) followed by reduction of nitro group with Pd-C/H_2 and hydrolysis of ester with LiOH (taken in acetone-H_2O).

[(5-Amino-10-oxiranmethyl-9-oxo-9,10-dihydroacridine-4-carbonyl)-amino]-acetic acid (22) (Scheme S1).

Mixture of 5-amino-10-oxiranmethyl-9-oxo-9,10-dihydroacridine-4-carboxylic acid (1.5 g, 5 mmol), glycine methyl ester hydrochloride (1g, 8 mmol), triethyl amine (3 ml, 20 mmol) and ethyl chloroformate (2 ml, 20 mmol) in DMF (15 ml) was stirred at 0 ^{o}C for 1 h. After completion of reaction (TLC monitoring) the reaction mixture was extracted with chloroform. The organic phase was washed with water and dried over anhydrous Na_2SO_4. The solvent was evaporated under vacuum and the residue was column chromatographed using ethyl acetate and hexane as eluents to isolate pure compound. It was further taken in 20 ml acetone – water (2:1, v/v) containing 0.05 N LiOH to procure [(5-amino-10-oxiranmethyl-9-oxo-9,10-dihydroacridine-4-carbonyl)-amino]-acetic acid **(22)**, (1g, 48%) mp 175 ^{o}C, $[\alpha]_D$ +23^{o} (c 1.00, MeOH). HRMS-ESI (*m/z*): $[M+H]^+$ calculated for $C_{19}H_{17}N_3O_5$, 368.1240; found 368.1225.

{2-[(5-Amino-10-oxiranmethyl-9-oxo-9,10-dihydro-acridine-4-carbonyl)-amino]-acetylamino}-acetic acid (23) (Scheme S1).

Compound **22** (1 g, 2.7 mmol) was taken in DMF (15 ml) and treated with glycine methyl ester hydrochloride (800 mg, 6.3 mmol) in the presence of 800 µl (5.7 mmol) triethyl amine and 600 µl (6.27 mmol) ethyl chloroformate at 0 ^{o}C for 1 h. After completion of reaction (TLC monitoring), the reaction mixture was extracted with chloroform. The organic phase was washed with water, dried over anhydrous Na_2SO_4 and evaporated under vacuum. The residue was column chromatographed using ethyl acetate and hexane as eluents to isolate pure compound. This compound was further taken in 20 ml acetone – water (2:1, v/v) containing 0.05 N LiOH for procuring compound **23** (850 mg, 55%), mp 182 ^{o}C, $[\alpha]_D$ +24^{o} (c 1.00, MeOH). HRMS-ESI (*m/z*): $[M+H]^+$ calculated for $C_{21}H_{20}N_4O_6$, 425.1455; found 425.1452.

(2-{2-[(5-Amino-10-oxiranmethyl-9-oxo-9,10-dihydro-acridine-4-carbonyl)-amino]-acetylamino}-acetylamino)-acetic acid (24) (Scheme S1).

Using the same procedure as for the formation of compound **23** from compound **22**, compound **24** was obtained by the coupling of another glycine with compound **23** (50%), mp 190 ^{o}C, $[\alpha]_D$ +24^{o} (c 1.00, MeOH). HRMS-ESI (*m/z*): $[M+H]^+$ calculated for $C_{23}H_{23}N_5O_7$, 482.1670; found 482.1673.

2-{2-[(5-Amino-10-oxiranmethyl-9-oxo-9,10-dihydroacridine-4-carbonyl)-amino]-acetylamino}-3-mercapto-propionic acid methyl ester (1) (Scheme S1).

Compound **22** (1 g, 2.7 mmol) was taken in DMF (15 ml) and treated with D/L-cysteine methyl ester hydrochloride (1.2 g, 7 mmol) in the presence of 1.0 ml (7 mmol) triethyl amine and 800 µl (8.3 mmol) ethyl chloroformate at 0 ^{o}C for 1 h. After completion of reaction (TLC monitoring) the reaction mixture was extracted with chloroform (5 x 25 ml). The organic phase was washed with water (5 x 25 ml) and dried over anhydrous Na_2SO_4. After removing the solvent under vacuum, the residue was column chromatographed using ethyl acetate and hexane as eluents to isolate pure compound **1** (1.4 g, 72%), mp 166 ^{o}C, $[\alpha]_D$ +20^{o} (c 1.00, MeOH). ^{1}H NMR (500 MHz, DMSO-d_6, δ): 2.73 (dd, *J* =10.0 Hz, 5.5 Hz, -CH_2, 1H), 2.89 (t, *J* =10.0 Hz, -CH_2, 1H), 3.63-3.73 (m, -CH, 1H), 3.74 (s, -OCH_3, 3H), 3.98-4.02 (m, -CH_2, 2H), 4.13-4.16 (m, -CH_2, 2H), 4.49-4.52 (dd, *J* = 9.2 Hz, 5.5 Hz, -OCH_2, 1H), 4.73-4.75 (m, -CH, 1H), 4.85-4.88 (dd, *J* =9.4 Hz, 2.8 Hz, -OCH_2, 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), 9.50-9.51 (br, NH, 1H). ^{13}C NMR (125 MHz, DMSO-d_6, δ): 181.75, 176.98, 170.62, 168.75, 140.83, 134.52, 133.69, 131.14, 126.33, 122.53, 122.16, 120.95, 120.48, 118.92, 56.11, 52.44, 50.24, 48.45, 45.13, 41.69, 30.15. IR (KBr, thin film) ν_{max} (cm^{-1}): 3648 (NH_2), 3628 (NH), 3603 (NH), 1747 (CO), 1616 (CO), 1578 (CO), 1515 (CO). HRMS-ESI (*m/z*): $[M+H]^+$ calculated for $C_{23}H_{24}N_4O_6S$, 485.1489; found 485.1485.

2-(2-{2-[(5-Amino-10-oxiranmethyl-9-oxo-9,10-dihydroacridine-4-carbonyl)-amino]-acetylamino}-acetylamino)-3-mercapto-propionic acid methyl ester (2) (Scheme S1).

Compound **23** (500 mg, 1.2 mmol) was taken in DMF (15 ml) and treated with D/L-cysteine methyl ester hydrochloride (450 mg, 2.6 mmol) in the presence of 300 µl (2 mmol) triethyl amine and 200 µl (2 mmol) ethyl chloroformate at 0 ^{o}C for 1 h. After completion of reaction (TLC monitoring), the reaction mixture was extracted with chloroform (5 x 25 ml). The organic phase was washed with water (5 x 25 ml) and dried over anhydrous Na_2SO_4 and the residue was column chromatographed using ethyl acetate and hexane as eluents to isolate pure compound **2** (610 mg, 68%), mp 161 ^{o}C, $[\alpha]_D$ +18^{o} (c 1.00, MeOH). ^{1}H NMR (500 MHz, DMSO-d_6) δ: 2.87-2.95 (dd, *J* =9.0 Hz, 2.2 Hz, -CH_2, 1H), 3.13-3.16 (dd, *J* =3.5 Hz, 3.0 Hz, -CH_2, 1H), 3.38-3.66 (m, -CH, 1H), 3.69 (s, -OCH_3, 3H), 3.92-3.93 (m, -CH_2, 2H),

3.95-4.0 (m, CH_2, 4H), 4.48-4.49 (d, *J* = 2.0, CH_2, 1H), 4.78-4.80 (dd, *J* = 8.0, 2.0, CH_2, 1H), 4.81-4.82 (m, CH, 1H), 5.04-5.06 (br, NH_2, 2H), 7.13-7.20 (m, ArH, 1H), 7.29-7.46 (m, ArH, 2H), 7.68-7.95 (m, 1ArH+SH, 2H), 8.21-8.32 (m, ArH, 2H), 8.43 (br, NH, 1H), 8.73 (br, NH, 1H), 9.09-9.11 (br, NH, 1H); ^{13}C NMR (125 MHz, DMSO-d_6) δ: 181.69, 176.11, 170.62, 168.40, 168.11, 140.86, 134.52, 133.69, 131.14, 126.33, 122.53, 122.16, 120.95, 120.48, 118.92, 56.14, 52.44, 50.24, 48.45, 45.13, 41.83, 41.53, 30.24. IR (KBr, thin film) ν_{max} (cm^{-1}): 3645 (NH_2), 3627 (NH), 3610 (NH), 3471 (NH), 1748 (CO), 1680 (CO), 1620 (CO), 1577 (CO), 1560 (CO). HRMS-ESI (*m/z*): $[M+H]^+$ calculated for $C_{25}H_{27}N_5O_7S$, 542.1703; found 542.1708.

2-[2-(2-{2-[(5-Amino-10-oxiranmethyl-9-oxo-9,10-dihydroacridine-4-carbonyl)-amino]-acetylamino}-acetylamino)-acetylamino]-3-mercapto-propionic acid methyl ester (3) (Scheme S1).

Compound **24** (300 mg, 0.62 mmol) was taken in DMF (10 ml) and treated with D/L-cysteine methyl ester hydrochloride (250 mg, 1.5 mmol) in the presence of 200 µl (1.4 mmol) triethyl amine and 100 µl (1 mmol) ethyl chloroformate at 0 ^oC for 1 h. After completion of reaction (TLC monitoring) the reaction mixture was extracted with chloroform (5 x 25 ml). The organic phase was washed with water (5 x 25 ml), dried over anhydrous Na_2SO_4 and concentrated under vacuum. The residue was column chromatographed using ethyl acetate and hexane as eluents to isolate pure compound **3** (310 mg, 63%), mp 153 ^oC, $[\alpha]_D$ +20^o (c 1.00, MeOH). ^{1}H NMR (500 MHz, DMSO-d_6, δ): 2.81-2.85 (dd, *J* =8.0 Hz, 4.5 Hz, -CH_2, 1H), 2.96-2.97 (t, *J* =4.5 Hz, -CH_2,1H), 2.99-3.00 (m, -CH, 1H), 3.51 (s, -OCH_3, 3H), 3.97-3.99 (m, -CH_2, 2H), 4.00-4.08 (m, -CH_2, 6H), 4.24-4.25 (dd, *J* =5.3 Hz, 5.3 Hz, -CH_2, 1H), 4.46-4.47 (m, -CH, 1H), 4.54-4.56 (dd, *J* = 10.0 Hz, 2.2 Hz, -CH_2, 1H), 5.03-5.05 (b, NH_2, 2H), 7.04-7.06 (m, ArH, 2H), 7.30-7.38 (m, ArH, 1H), 7.71-7.78 (m, ArH, 1H), 8.16-8.18 (m, ArH, 1H), 8.23-8.25 (br, NH, 1H), 8.41-8.45 (m, ArH+SH, 2H), 8.56 (br, NH, 1H), 9.19-9.21 (br, NH, 2H). ^{13}C NMR (125 MHz, DMSO-d_6, δ): 180.16, 176.98, 170.62, 168.75, 168.11, 168.06, 140.83, 134.52, 133.67, 131.14, 126.33, 122.53, 122.16, 120.95, 120.48, 118.92, 55.13, 51.84, 50.24, 48.45, 45.13, 41.73, 41.53, 29.14. IR (KBr, thin film) ν_{max} (cm^{-1}): 3646 (NH_2), 3628 (NH), 3610 (NH), 3471 (NH), 3276 (NH), 1749 (CO), 1680 (CO), 1622 (CO), 1580 (CO), 1551 (CO), 1560 (CO). HRMS- ESI (*m/z*): $[M+H]^+$ calculated for $C_{27}H_{30}N_6O_8S$, 599.1918; found 599.1920.

Reaction of compound 1d with uracil (General procedure for reaction of compounds 1 – 3 with uracil).

The reaction mixture containing compound **1d** (500 mg, 1 mmol) and uracil (150 mg, 1.3 mmol) in 20 ml DMSO:H_2O (1:4) at pH 8.0 (using 0.01 N NaOH) was stirred at 25 – 30 ^oC for 2 h. The reaction was monitored by TLC, by recording the HRMS and NMR of the reaction mixture. After 2h of stirring, the pH of the reaction mixture was changed to 6.5 (using 0.01 N HCl). When no further change was observed in the reaction mixture (after 2.5h of stirring), it was extracted with ethyl acetate (4 x 25 ml). The organic phase was dried over anhydrous Na_2SO_4 and concentrated under vacuum. The residue was column chromatographed using ethyl acetate and hexane as eluents to isolate pure compound **11**. **Reactions of other compounds with uracil were also checked through the above said procedure.**

Compound 11 (Scheme 1b). (85%), mp 143 ^oC, $[\alpha]_D$ -10^o (c 1.00, MeOH). ^1H NMR (500 MHz, DMSO-d_6, δ): 3.59 (s, -OCH_3, 3H), 3.87-3.89 (d, J =9.3 Hz, -SCH_2, 2H), 4.13-4.16 (m, -CH_2, 2H), 4.49-4.51 (m, -CH, 1H), 5.06 (br, NH_2, 2H), 5.29 (s, -SCH, 1H), 5.50-5.51 (dd, J =3.2 Hz, 3.2 Hz, -CH_2, 2H), 5.71-5.73 (dd, J =6.0 Hz, 3.2 Hz, -CH_2, 1H), 6.09-6.12 (dd, J =10.0 Hz, 2.3 Hz, -CH_2, 1H), 6.48-6.49 (m, -CH, 1H), 7.40-7.49 (m, ArH, 2H), 7.70-7.72 (m, ArH, 1H), 8.23-8.25 (m, ArH, 1H), 8.31 (m, ArH, 1H), 8.49-8.50 (m, ArH, 1H), 8.78 (br, NH, 1H), 9.19 (br, NH, 1H), 9.39 (br, NH, 1H), 9.50-9.51 (br, NH, 1H). ^{13}C NMR (125 MHz, DMSO-d_6, δ): 176.98, 170.61, 168.76, 167.76, 165.76, 153.76, 141.27, 140.84, 134.51, 133.69, 131.14, 126.33, 122.53, 120.95, 120.48, 118.92, 118.11, 115.05, 96.27, 60.48, 54.44, 52.13, 42.46, 28.83. IR (KBr, thin film) ν_{max} (cm^{-1}): 3647 (NH_2), 3620 (NH), 3612 (NH), 3471 (NH), 3275 (NH), 1749 (CO), 1681 (CO), 1620 (CO), 1581 (CO), 1560 (CO), 1550 (CO). HRMS-ESI (*m/z*): $[M+H]^+$ calculated for $C_{27}H_{26}N_6O_7S$, 579.1656; found 579.1650.

Compound 16. As described above for other compounds, similar procedure was used to couple Gly and *S*-Cys on acridine and hence to obtain compound **16** (Scheme S2) (81%), mp 175 ^oC, $[\alpha]_D$ -8^o (c 1.00, MeOH). ^1H 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.

Compound 17. Compounds *S*-**17** and *R*-**17** were obtained by the usual coupling reactions of glycine with 5-amino-9-oxo-9,10-duhydroacridine-4-carboxylic acid followed by the coupling with *S*-cysteine and *R*-cysteine, respectively (Scheme S3) (75%), mp 170 ^{o}C, $[\alpha]_D$ -8^{o} for *S*-**17** and +11^{o} for *R*-**17** (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 18. By using the same procedure as for reaction of model compounds with uracil, compound **18** was obtained by the reaction of compound *S*-**17** with uracil (68%), mp 156 ^{o}C, $[\alpha]_D$ -10^{o} (c 1.00, MeOH) . ^{1}H NMR (500 MHz, DMSO-d_6, δ): 3.60 (s, -OCH_3, 3H), 3.88 (d, *J* =9.3 Hz, -SCH_2, 2H), 4.13-4.16 (m, -CH_2, 2H), 4.49-4.51 (m, -CH, 1H), 5.06 (br, NH_2, 2H), 5.26 (m, -SCH, 1H), 5.51 (m, -CH, 1H), 7.40-7.49 (m, ArH, 2H), 7.70-7.72 (m, ArH, 3H), 8.23-8.31 (m, ArH, 1H), 8.42-8.43 (br, NH, 1H), 8.78 (br, NH, 1H), 9.19 (br, NH, 1H), 9.39 (br, NH, 1H), 9.50-9.51 (br, NH, 1H). ^{13}C NMR (125 MHz, DMSO-d_6, δ): 176.97, 170.61, 168.77, 165.74, 160.76, 141.32, 140.83, 134.51, 133.67, 131.11, 126.34, 122.54, 120.94, 118.91, 115.15, 96.25, 60.43, 54.44, 52.13, 42.43, 28.82. IR (KBr, thin film) ν_{max} (cm^{-1}): 3642 (NH_2), 3625 (NH), 3632 (NH), 3423 (NH), 3473 (NH), 3273 (NH), 3228 (OH), 1751 (CO), 1680 (CO), 1622 (CO), 1570 (CO), 1550 (CO). HRMS-ESI (*m/z*): $[M+H]^+$ calculated for $C_{24}H_{24}N_6O_7S$, 541.1499; found 541.1478.

It is worth to mention that compound ***R*-17** did not react with uracil under the current reaction conditions which indicates the role of stereochemistry at C_α of Cys.

Uracil-d_3. We followed the reported procedure for C5-deuteration of uracil.[2,3] However, we got uracil-d_3 (Figure S54) and it was used for reaction with compound **1d**.

Compound 1d-$^{13}C_{epox}$. This compound was prepared through same procedure as used for the preparation of compound **1d** but epichlorohydrin-^{13}C was used in place of normal epichlorohydrin (Figure S48).

Conversion of compound 11 to 13 and subsequent treatment with NADH. The reaction mixture containing compound **11** (600 mg, 1 mmol) in 15 ml DMSO:water (1:4) was treated with 0.05 N LiOH (pH 9.5). The reaction mixture was stirred at 25 – 26 ^{o}C. After the

completion of reaction (TLC monitoring, 30 min), the reaction mixture was neutralized with 0.1 M HCl. The resulting solid was filtered and washed with water to isolate pure compound **13** (380 mg, 65%), mp 170 ^{o}C, $[\alpha]_D$ -8^{o} (c 1.00, MeOH). ^{1}H NMR (500 MHz, DMSO-d_6, δ): 3.87-3.89 (d, J =9.3 Hz, -SCH_2, 2H), 4.13-4.16 (m, -CH_2, 2H), 4.48-4.51 (m, -CH, 1H), 5.04 (br, NH_2, 2H), 5.30 (s, -SCH, 1H), 5.50-5.51 (dd, J =3.2 Hz, 3.2 Hz, -CH_2, 2H), 5.72-5.75 (dd, J =6.0 Hz, 3.2 Hz, -CH_2, 1H), 6.08-6.11 (dd, J =10.0 Hz, 2.3 Hz, -CH_2, 1H), 6.48-6.49 (m, -CH, 1H), 7.41-7.49 (m, ArH, 2H), 7.70-7.74 (m, ArH, 1H), 8.23-8.25 (m, ArH, 1H), 8.31 (m, ArH, 1H), 8.49-8.50 (m, ArH, 1H), 8.76 (br, NH, 1H), 9.20 (br, NH, 1H), 9.40 (br, NH, 1H), 9.50-9.52 (br, NH, 1H), 12.11 (br, OH, 1H). ^{13}C NMR (125 MHz, DMSO-d_6, δ): 177.12, 170.60, 168.66, 165.78, 161.09, 141.25, 140.84, 134.52, 133.68, 131.14, 126.30, 122.53, 121.11, 118.93, 115.05, 96.27, 60.46, 54.38, 42.44, 28.83. IR (KBr, thin film) ν_{max} (cm^{-1}): 3646 (NH_2), 3625 (NH), 3612 (NH), 3467 (NH), 3295 (NH), 3175 (OH), 1744 (CO), 1682 (CO), 1619 (CO), 1581 (CO), 1563 (CO), 1560 (CO). HRMS-ESI (*m/z*): $[M+H]^+$ calculated for $C_{26}H_{24}N_6O_7S$, 565.1499; found 565.1487.

Without isolation of comopund **13**; after the conversion of **11** to **13** (HRMS), the reaction mixture was treated with NADH (β-nicotinamide adenine dinucleotide, reduced disodium salt hydrate) (536 mg, 1.2 equiv of **13**) at pH 7.0 and stirred at 25 – 30 ^{o}C (TLC and HRMS monitoring). After removal of the solvent, the crude residue was purified by flash chromatography using ethyl acetate – hexane/ethyl acetate - metahnol as eluents. Thymine (82%) (LC-MS comparison with commercial sample) and compound **15** (80%) were isolated. For **15**: mp 164 ^{o}C, $[\alpha]_D$ -12^{o} (c 1.00, MeOH). ^{1}H NMR (500 MHz, DMSO-d_6, δ): 3.78-3.89 (d, J =9 Hz, 5.7 Hz, -SCH_2, 2H), 4.13-4.16 (m, -CH_2, 2H), 4.49-4.51 (m, -CH, 1H), 5.09 (br, NH_2, 2H), 5.58-5.63 (dd, J =10.05 Hz, J =13.45 Hz, -CH_2, 1H), 6.09-6.14 (dd, J =4.75 Hz, J =20.7 Hz, -CH_2, 1H), 6.46-6.50 (dd, J = 4.3 Hz, 15.7 Hz, -CH, 1H), 7.40-7.49 (m, ArH, 2H), 7.70-7.72 (m, ArH+SH, 2H), 8.23-8.25 (m, ArH, 1H), 8.31 (m, ArH, 1H), 8.49 (m, ArH, 1H), 8.71 (br, NH, 1H), 9.19 (br, NH, 1H), 9.89 (br, OH, 1H). IR (KBr, thin film) ν_{max} (cm^{-1}): 3645 (NH_2), 3620 (NH), 3618 (NH), 3180 (OH),1723 (CO), 1625 (CO), 1583 (CO), 1562 (CO). HRMS-ESI (*m/z*): $[M+H]^+$ calculated for $C_{21}H_{20}N_4O_5S$, 441.1227; found 441.1220.

Compound 20. Same steps of experimental procedure were followed as for the reaction of compound **1d** and uracil (for obtaining compound **15**). The reaction mixture containing compound **1d**-$^{13}C_{epox}$ (500 mg, 1 mmol) and uracil (150 mg, 1.3 mmol) in 20 ml DMSO:H_2O (1:4) at pH 8.0 (using 0.01 N NaOH) was stirred at 25 – 30 ^{o}C for 2 h. The reaction was monitored by TLC as well as by recording the HRMS and NMR of the reaction mixture.

After 2 h of stirring, the pH of the reaction mixture was changed to 6.5 (using 0.01 N HCl). When no further change was observed in the reaction mixture (after 2.5h of stirring), its pH was shifted to 9.5 (using 0.01 N NaOH) by which the ester group was hydrolyzed (HRMS). Further, the reaction mixture was treated with 0.01 M NADH (1.2 equiv of **1d**-$^{13}C_{epox}$) at pH 7.0. After removal of the solvent, the crude residue was purified with flash chromatography using ethyl acetate – hexane/ethyl acetate - methanol as eluents to obtain uracil-$^{13}CH_3$ (73%) and compound **20** (330 mg, 70%), mp 164 ^{o}C, $[\alpha]_D$ -13^{o} (c 1.00, MeOH). ^{1}H NMR (500 MHz, DMSO-d_6, δ): 3.79-3.88 (d, J =8.5 Hz, 5.0 Hz, -SCH_2, 2H), 4.11-4.14 (m, -CH_2, 2H), 4.47-4.51 (m, -CH, 1H), 5.02 (br, NH_2, 2H), 5.55-5.66 (8 lines, J_{HH} =4.6 Hz, J_{HH} =15.6 Hz, J_{CH} =55.22 Hz, -CH_2, 1H), 5.84-5.98 (12 lines, J_{HH} =5.60 Hz, J_{HH} =16.8 Hz, J_{CH} =64.07 Hz, -CH_2, 1H), 6.38-6.43 (16 lines, J_{HH} = 10.35 Hz, J_{HH} = 4.50 Hz, $^2J_{CH}$ = 50.5 Hz, $^1J_{CH}$ =101.20 Hz, -CH, 1H), 7.40-7.50 (m, ArH, 2H), 7.73-7.76 (m, ArH+SH, 2H), 8.23-8.26 (m, ArH, 1H), 8.37 (m, ArH, 1H), 8.52-8.53 (m, AH, 1H), 8.67 (br, NH, 1H), 8.80 (br, NH, 1H), 9.79 (br, OH, 1H). IR (KBr, thin film) ν_{max} (cm^{-1}): 3640 (NH_2), 3616 (NH), 3612 (NH), 3185 (OH),1720 (CO), 1627 (CO), 1585 (CO), 1561 (CO). HRMS-ESI (*m/z*): $[M+H]^+$ calculated for $C_{21}H_{20}N_4O_5S$, 443.1227; found 443.1380.

Reaction of compound 1d with uracil/uracil-d_3 in DMSO

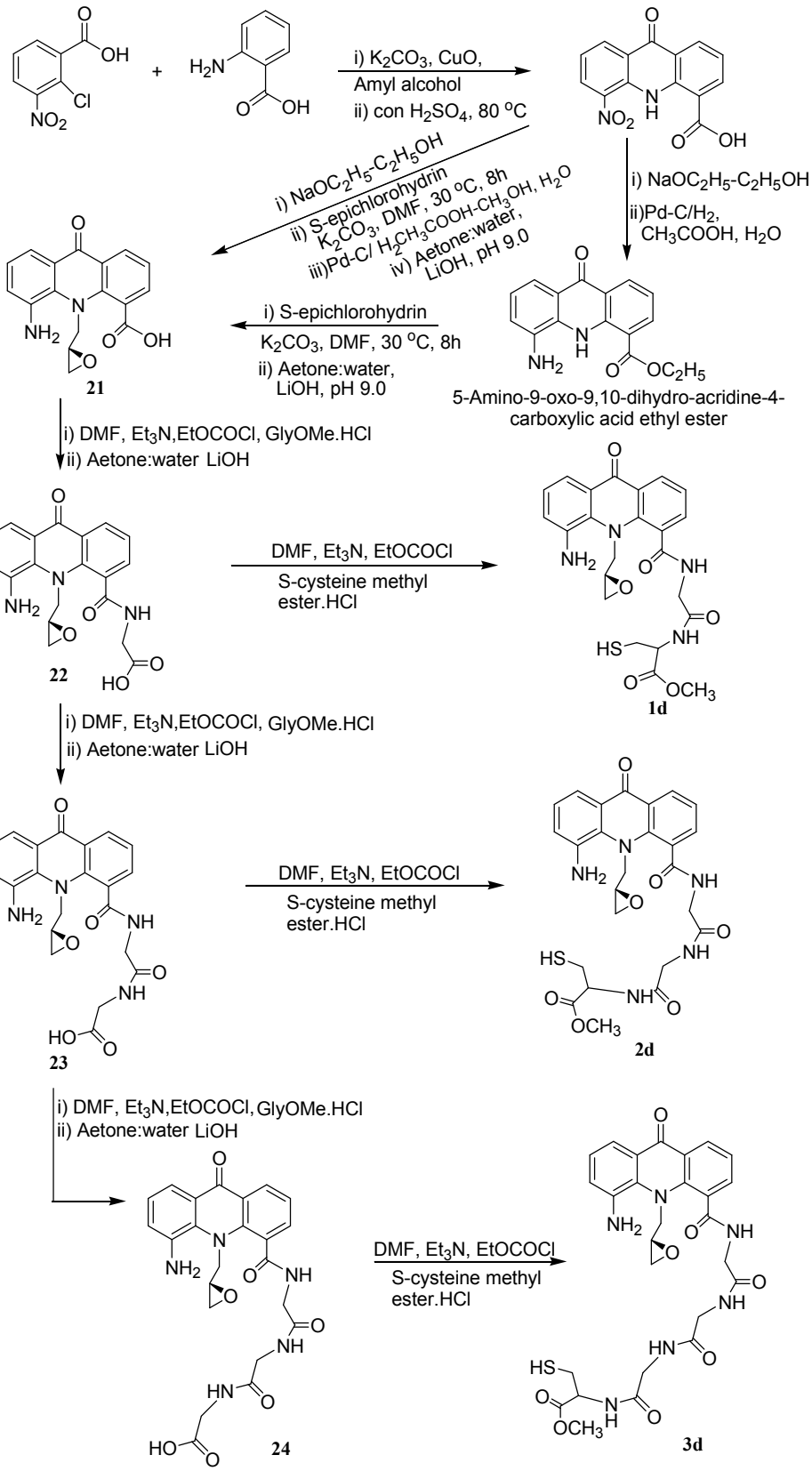
A mixture of compound **1d** (100 mg, 0.20 mmol), uracil (30 mg, 0.25 mmol) and K_2CO_3 (40 mg, 0.26 mmol) in DMSO (10 ml, HPLC grade, min assay 99.9%) was stirred at 25 – 30 ^{o}C. The reaction was monitored by thin layer chromatography and by recording the HRMS of the reaction mixture by taking out the aliquots at 20 min intervals. It took 3.5h till the formation of product **11**. The reaction was quenched with water and extracted with ethyl acetate (4 x 25 ml). The combined organic part was washed with cold water and dried over anhydrous Na_2SO_4. The organic solvent was evaporated under vacuum and purified by flash chromatography using ethyl acetate–hexane as eluent to obtain pure product **11** (70 mg, 55%).

Similarly, the reaction of **1d** with uracil-d_3 was perfromed in DMSO (HPLC grade, min assay 99.9%) which took 6h for the formation of compound **19** (detection with HRMS and NMR spectra). The reaction mixture was subjected to flash chromatography and compound **19** was isolated by using ethyl acetate and hexane as eluents. Throughout the reaction, we used dry conditions that enabled us to catch deuterium in the product **19**. In order to avoid moisture contact, flash chromatography was performed quickly and we were able to isolate only 35% of **19**.

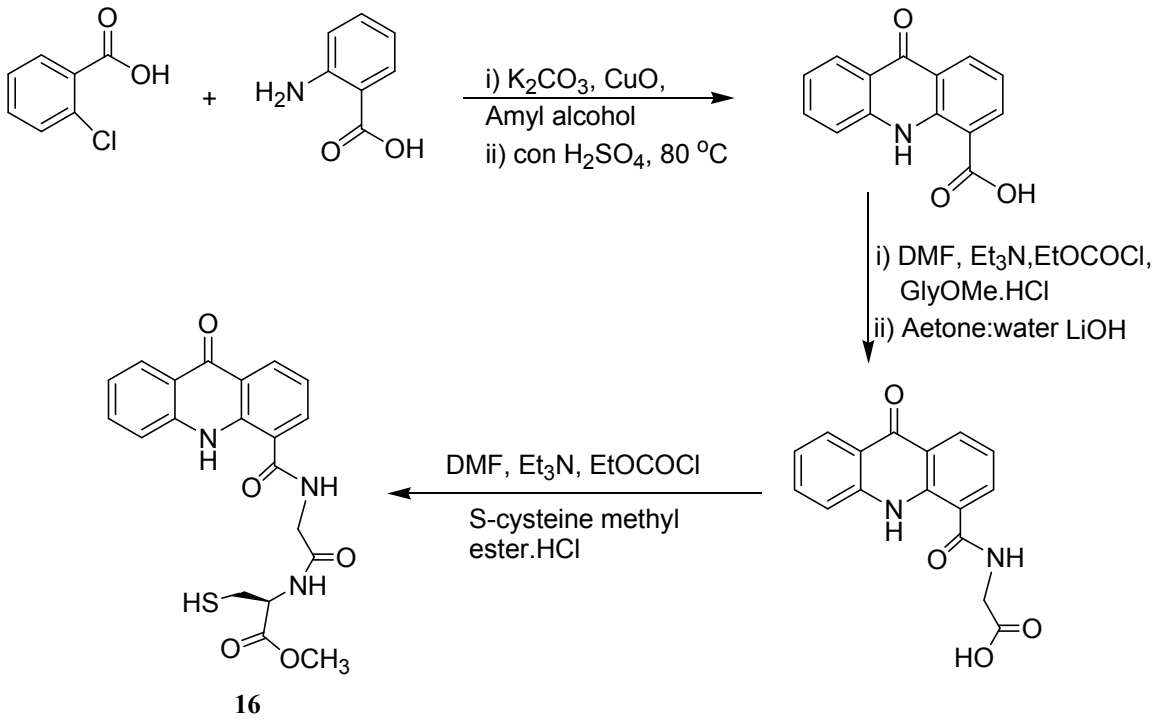
Reaction of compound 13 and NaH. Solution of compound **13** (550 mg, 1 mmol) and NaH (25 mg, 1 mmol) in DMSO (10 ml) was stirred at 25 – 28 ^{o}C. The reaction was monitored with TLC and high resolution mass spectrometry. After 1h of stirring, mass spectrum of the reaction mixture showed two peaks corresponding to *m/z* of thymine and compound **15**. Reaction was quenched with ice cold water and extracted with ethyl acetate. The crude product was purified by flash chromatography for isolating thymine (93 mg, 77%) and compound **15** (290 mg, 70%).

Reaction of compound 13 and LiCl. Solution of compound **13** (550 mg, 1 mmol) and LiCl (50 mg, 1 mmol) in DMSO (10 ml) was stirred at 100 ^{o}C (no reaction takes place at lower temperature). The reaction was monitored with TLC and high resolution mass spectrometry. After 2h of stirring, mass spectrum of the reaction mixture showed two peaks corresponding to *m/z* of 5-chloromethyl-1*H*-pyrimidine-2,4-dione and compound **15**. Reaction was quenched with ice cold water and extracted with ethyl acetate. The crude product was purified by flash chromatography to get 5-chloromethyl-1*H*-pyrimidine-2,4-dione (120 mg, 78%) and compound **15** (320 mg, 74%).

Energy minimization. Not shown in the MS, the test compounds were energy minimized for getting an idea about the stable conformation. Compound was built in the builder tool kit of the software Argus Lab 4.0.1. Energy minimizations were performed using semi-empirical method PM3. About 20,000 iterations were recorded until the geometry optimization was attained which was indicated by the software ‘convergence attained’.

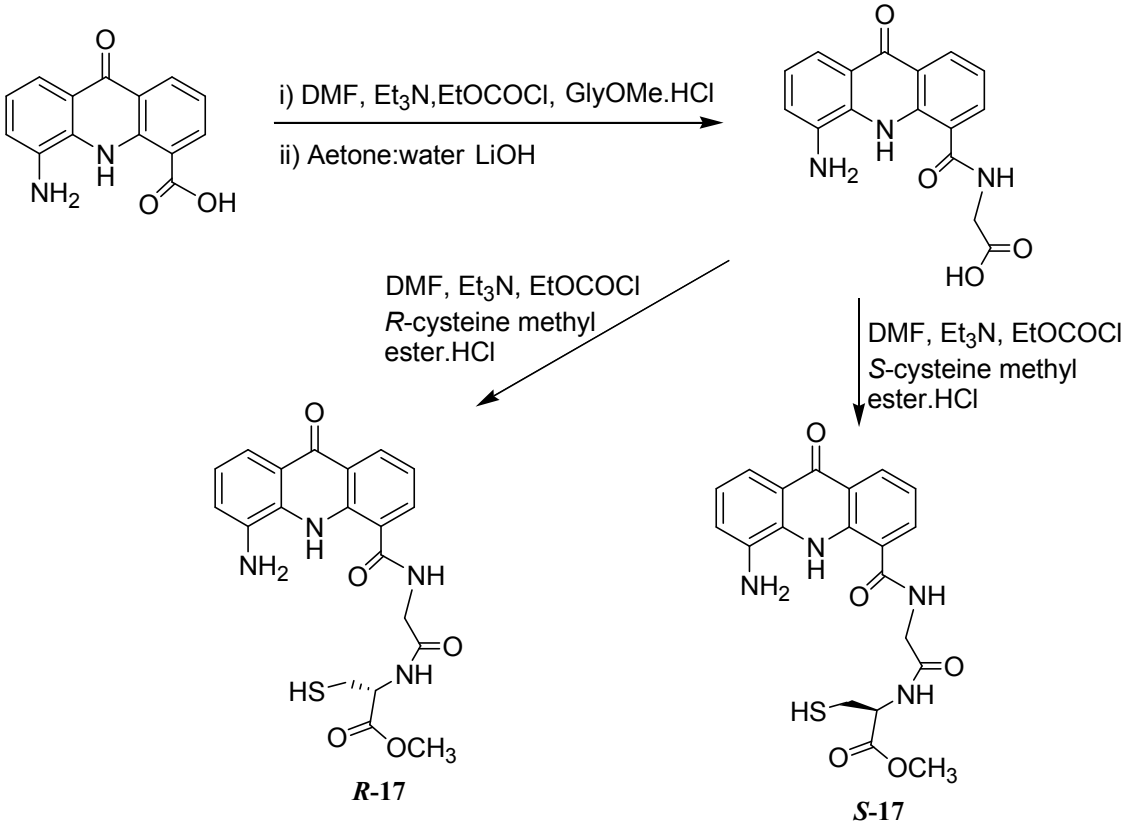


Scheme S1. Synthesis of compounds **1d**–**3d**. Isomers of compounds **1d – 3d** were synthesized through the same procedure but using other stereoisomers of epichlorohydrin and cysteine.



16

Scheme S2. Synthetic protocol for compound **16**.



***R*-17** ***S*-17**

Scheme S3. Synthetic protocol for compound **17**.

LC-MS of compounds 1–3. Procedure for recording LC-MS is mentioned in the General note.

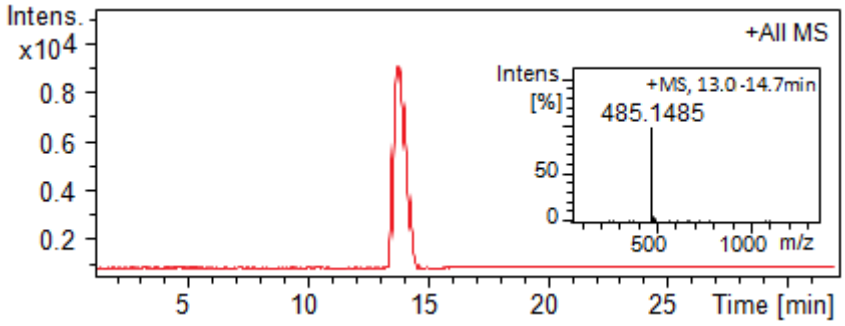


Figure S1. LC-MS of compound **1a**.

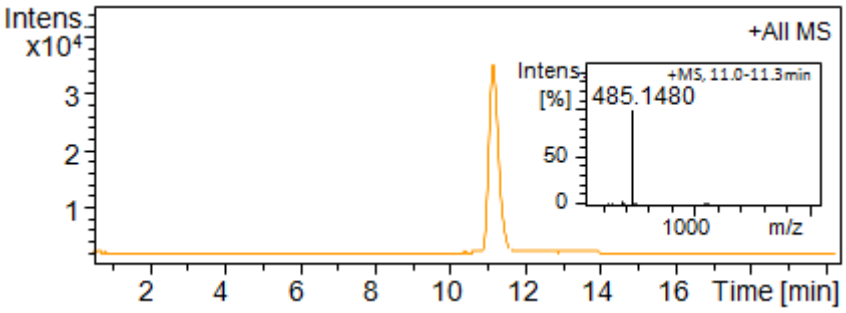


Figure S2. LC-MS of compound **1b**.

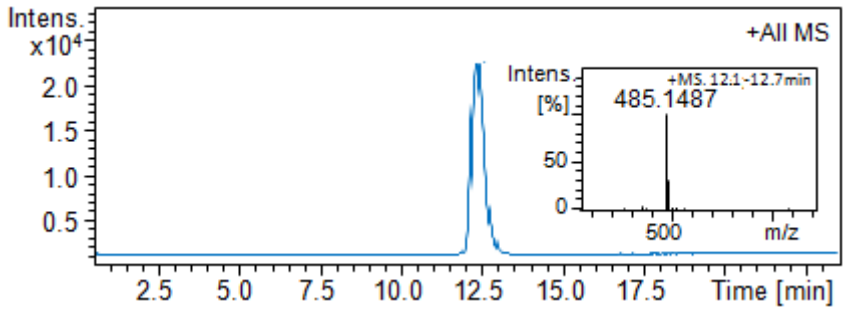


Figure S3. LC-MS of compound **1c**.

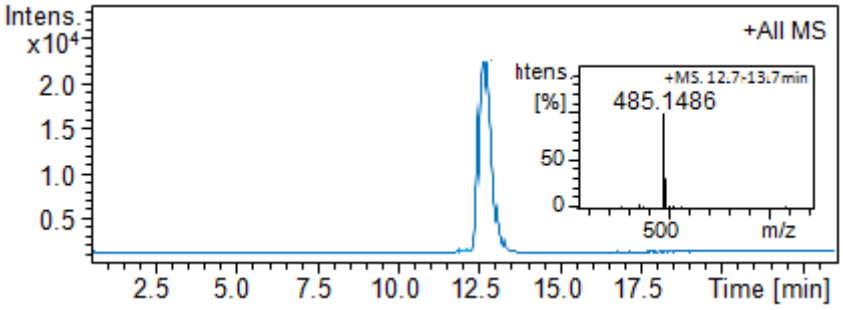


Figure S4. LC-MS of compound **1d**.

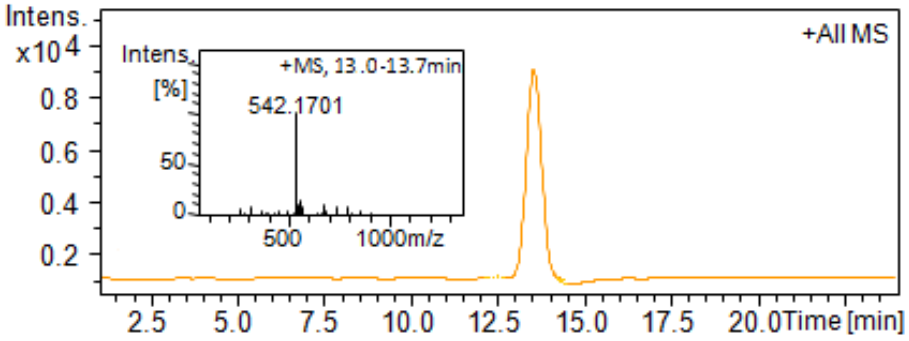


Figure S5. LC-MS of compound **2a**.

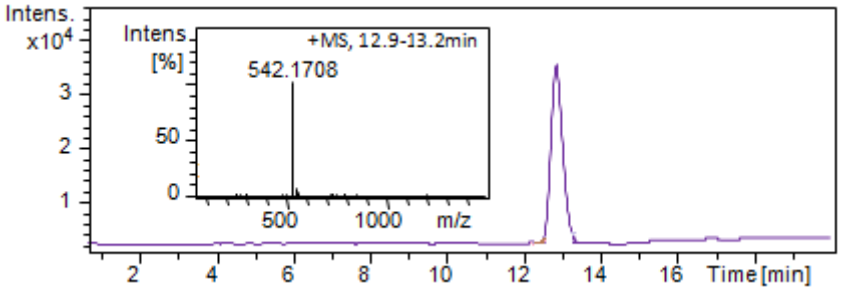


Figure S6. LC-MS of compound **2b**.

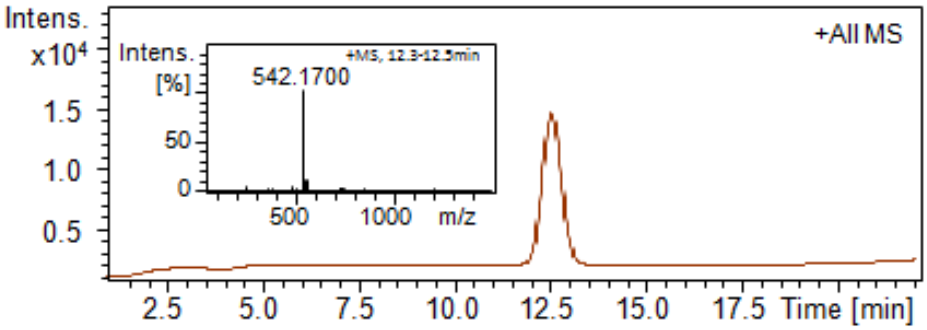


Figure S7. LC-MS of compound **2c**.

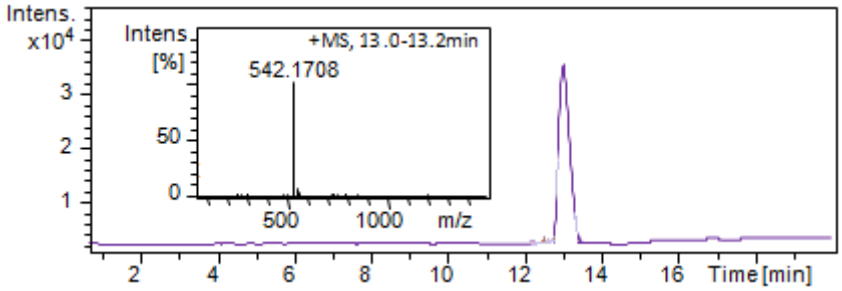


Figure S8. LC-MS of compound **2d**.

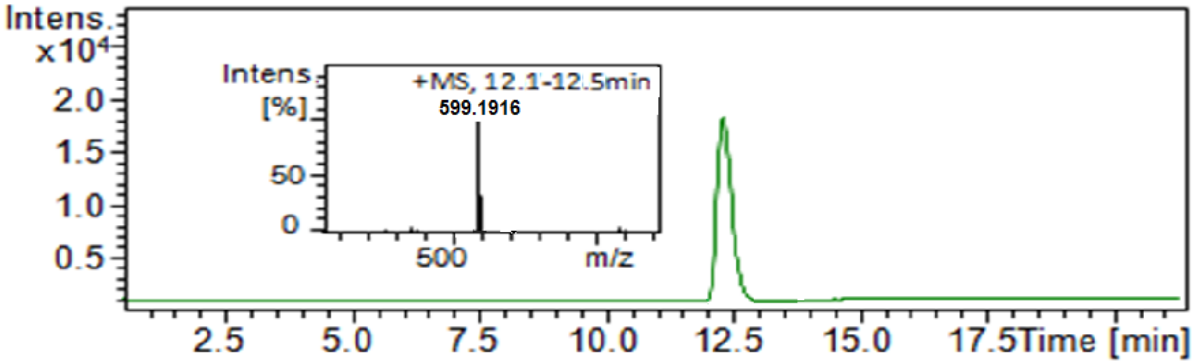


Figure S9. LC-MS of compound **3a**.

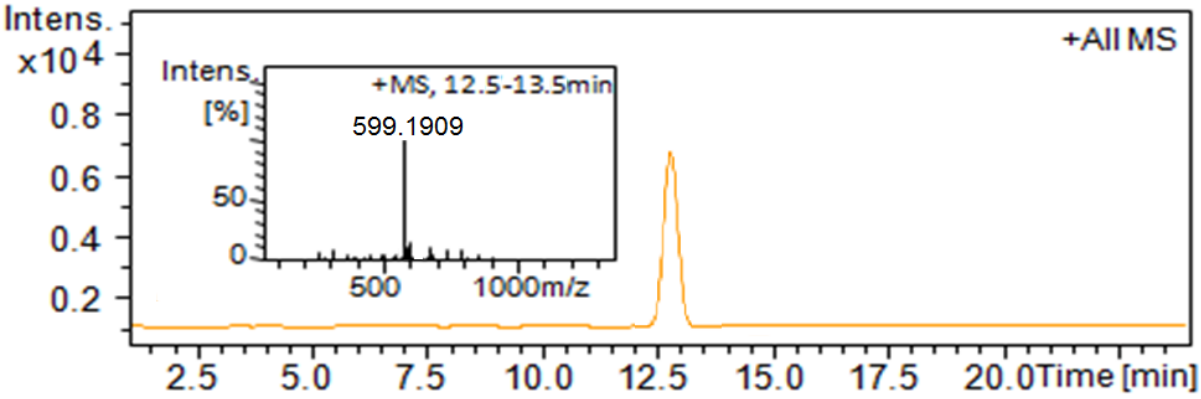


Figure S10. LC-MS of compound **3b**.

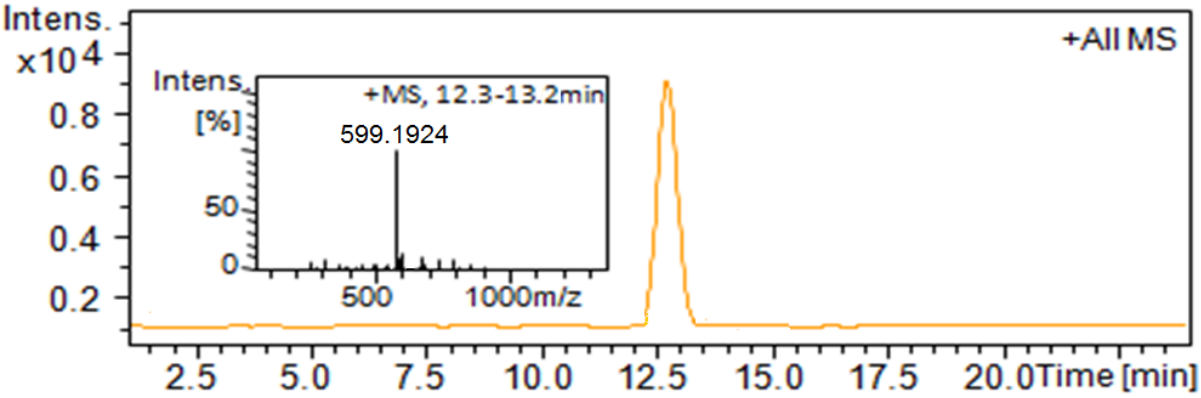


Figure S11. LC-MS of compound **3c**.

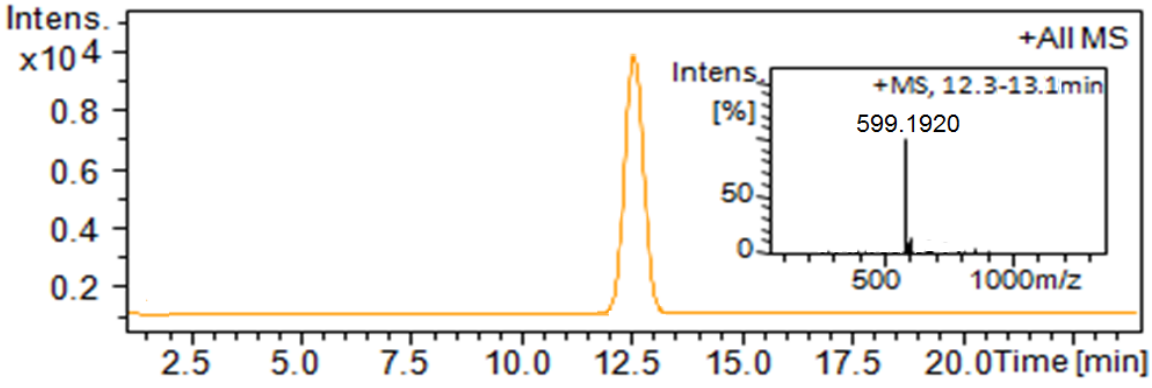


Figure S12. LC-MS of compound **3d**.

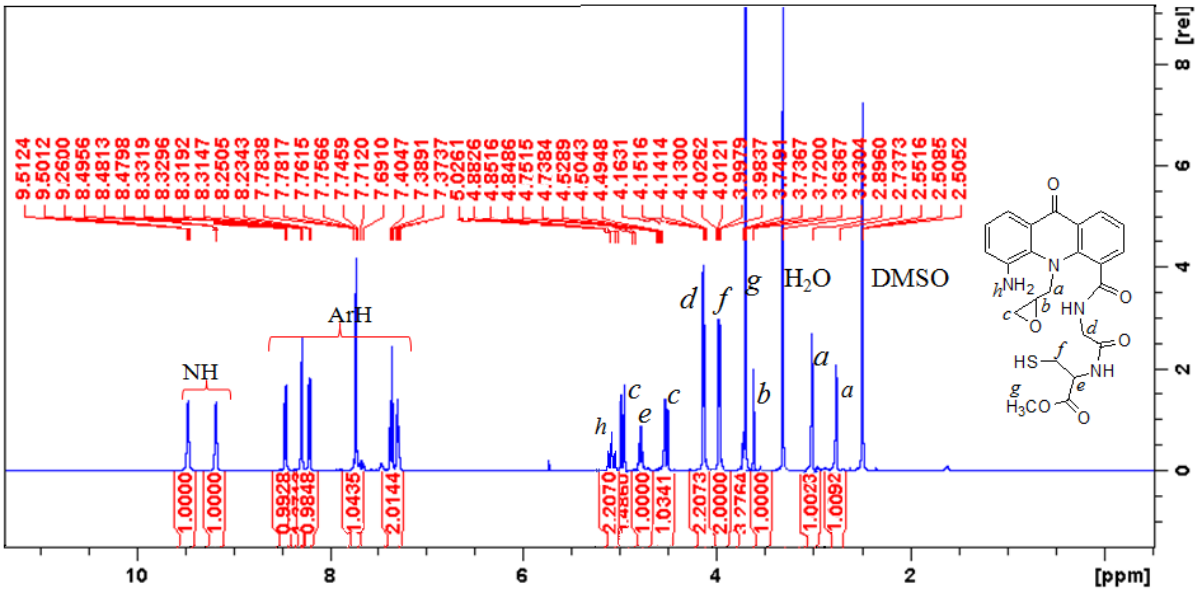


Figure S13. ^{1}H NMR spectrum of compound **1d** (DMSO-d_6).

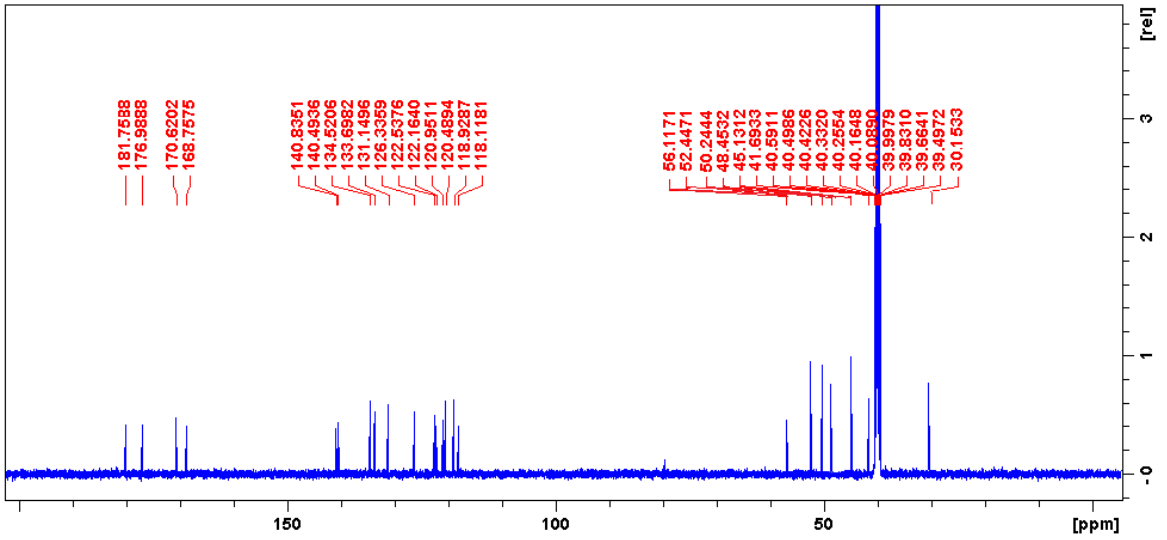


Figure S14. ^{13}C NMR spectrum of compound **1d**.

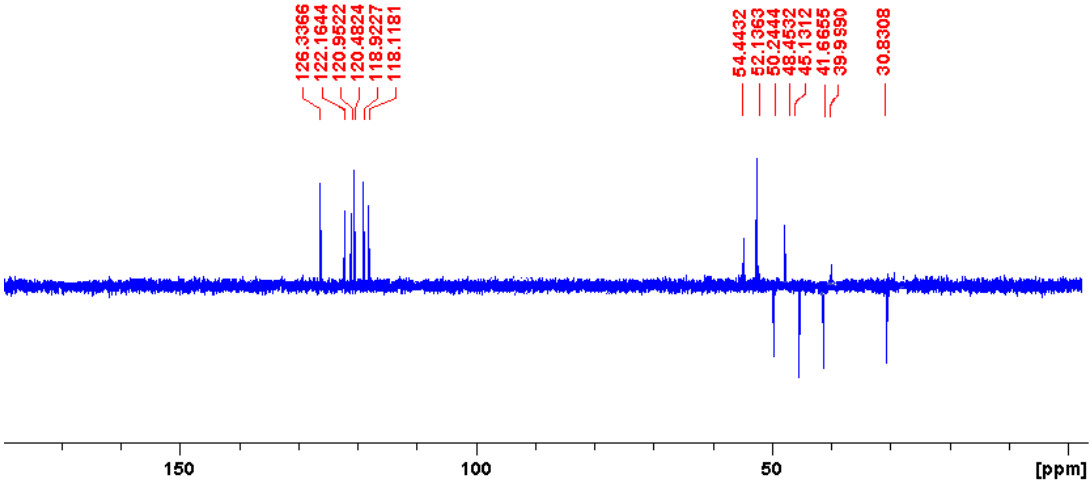


Figure S15. DEPT-135 NMR spectrum of compound **1d**.

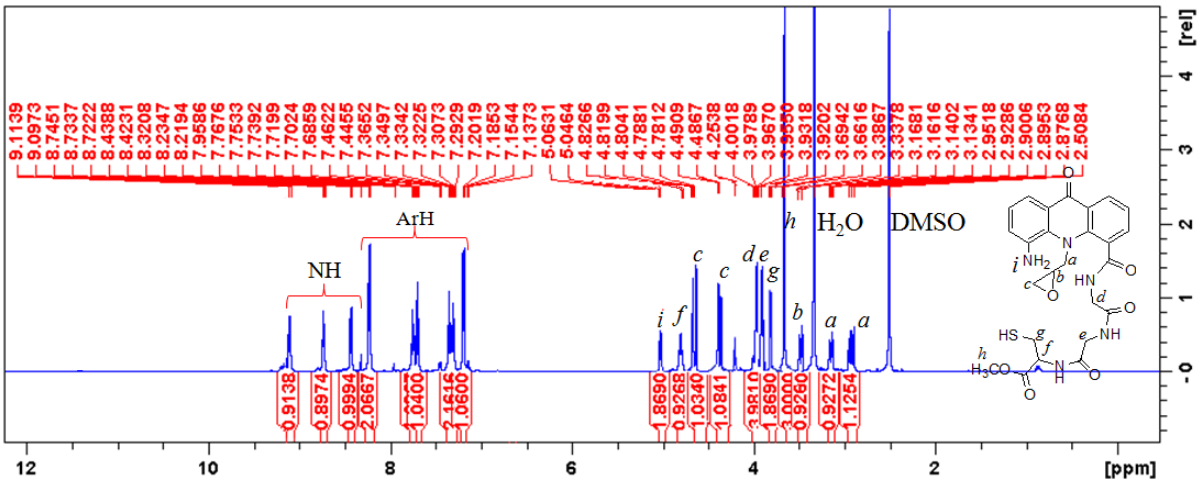


Figure S16. ^{1}H NMR spectrum of compound **2d** (DMSO-d_6).

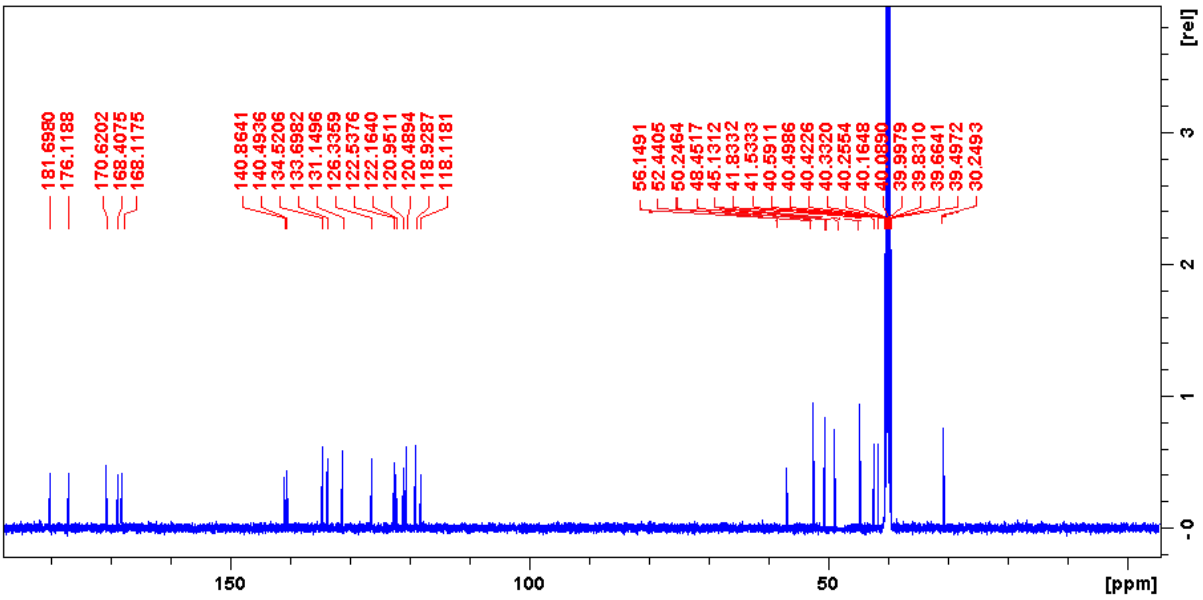


Figure S17. ^{13}C NMR spectrum of compound **2d**.

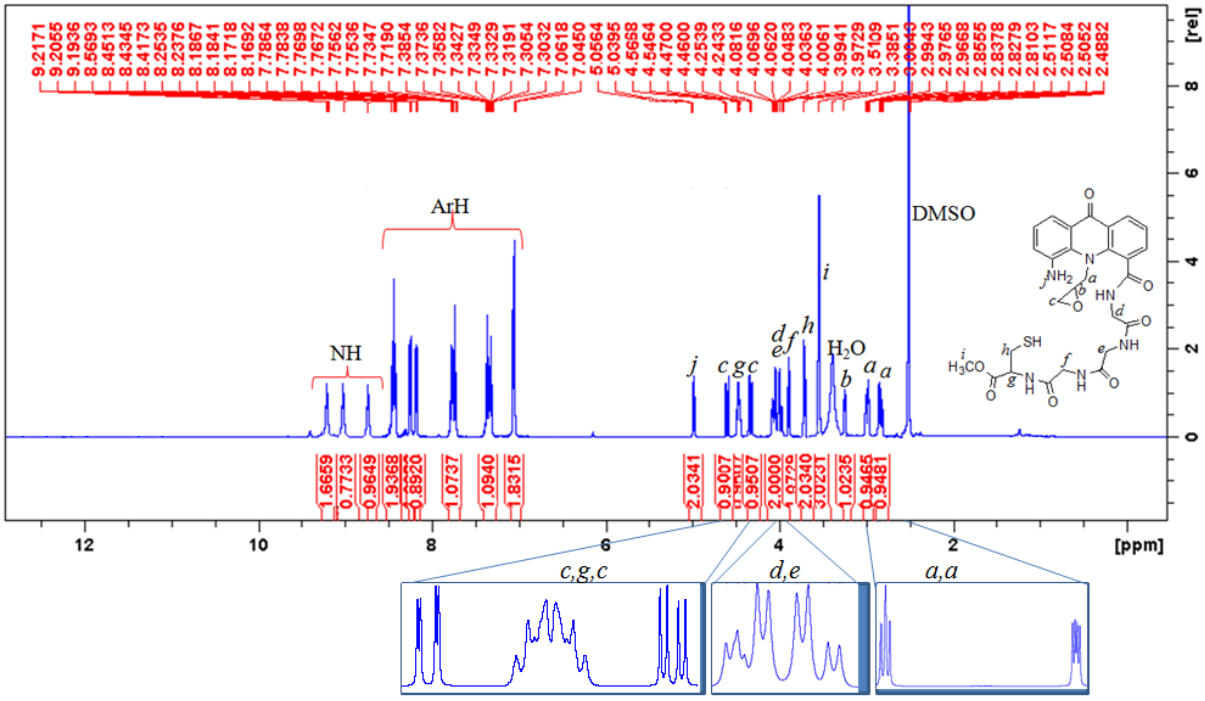


Figure S18. ^{1}H NMR spectrum of compound **3d** (DMSO-d_6)

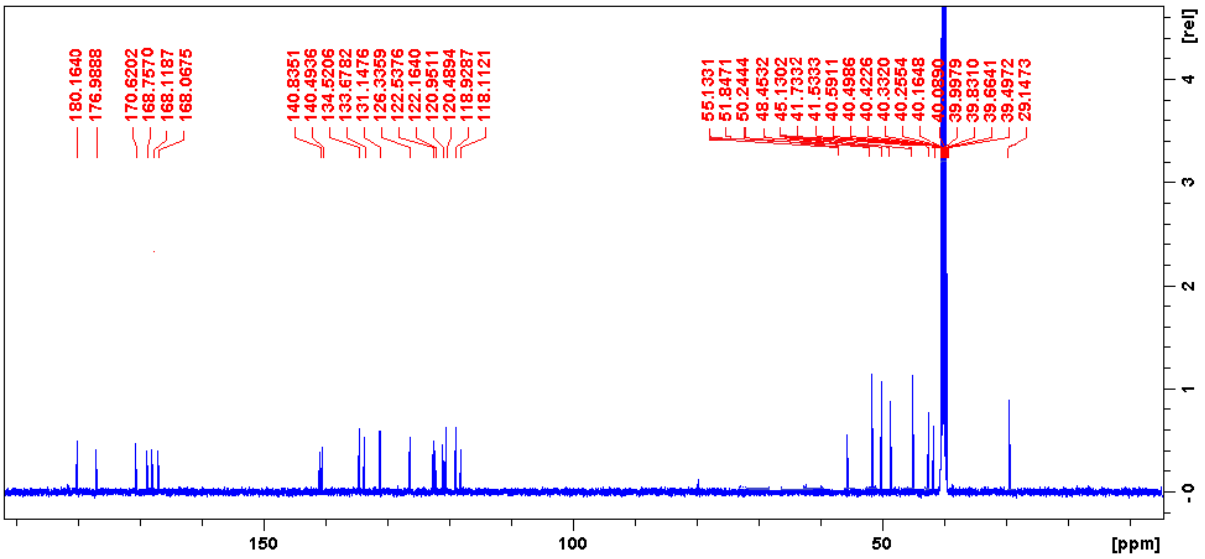


Figure S19. ^{13}C NMR spectrum of compound **3d**.

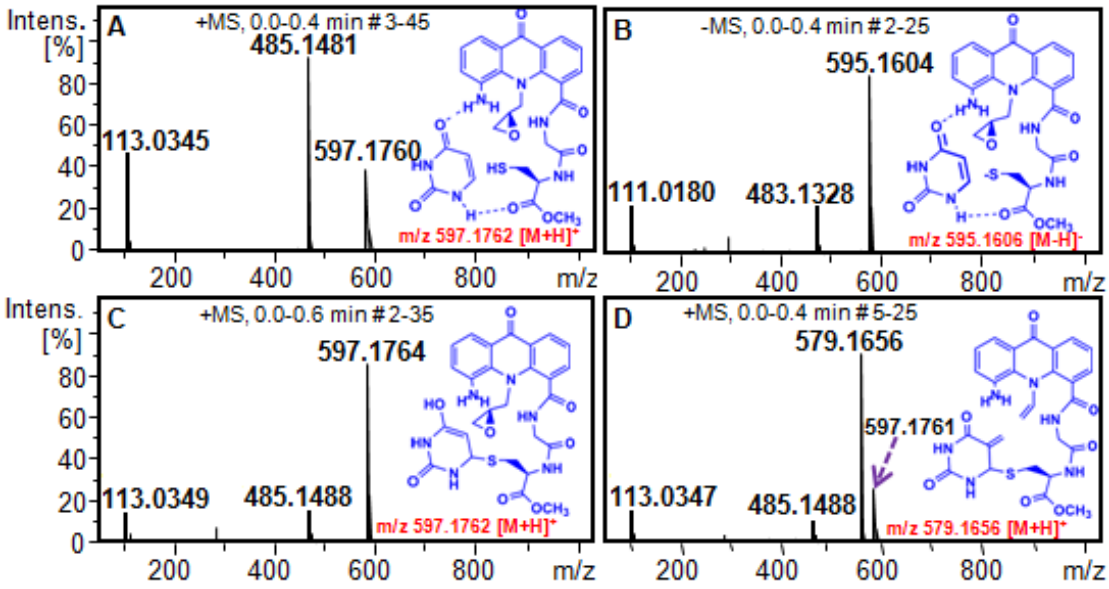


Figure S20. HRMS of the reaction mixture of compound **1d** and uracil: (A) 10 min after attaining pH 8.0 (+ve ESI mode), (B) 10 min after attaining pH of the reaction 8.0 (-ve ESI mode), (C) after 2h at pH 8.0, (D) after 30 min of stirring at pH 6.5.

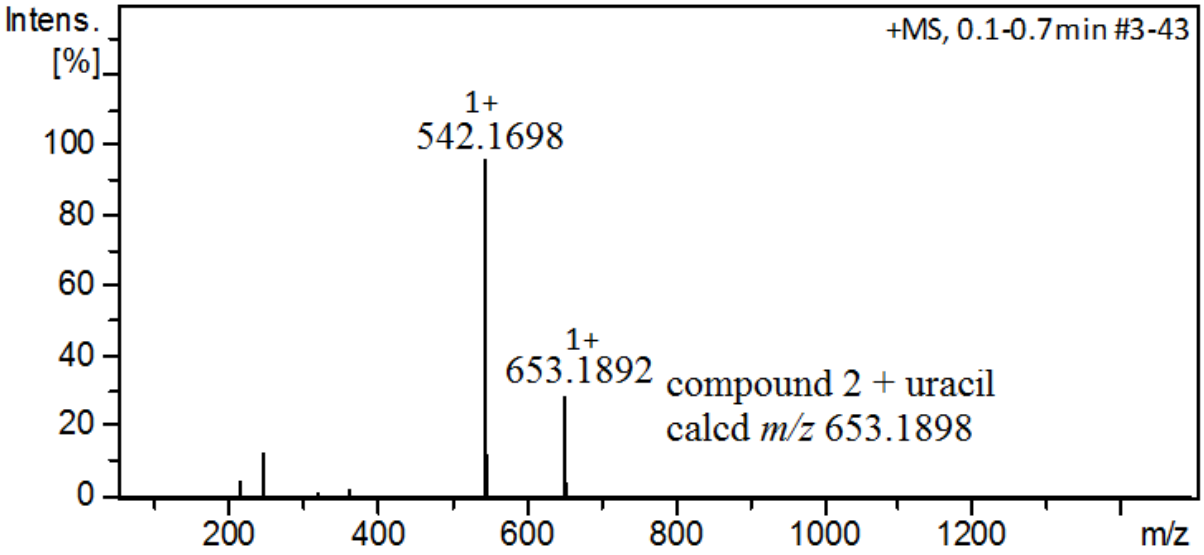


Figure S21. HRMS of the reaction mixture of compound **2a** and uracil after 2h stirring at pH 8.0. Similar spectra were recorded for the reaction mixtures of other isomers of compound **2** and uracil.

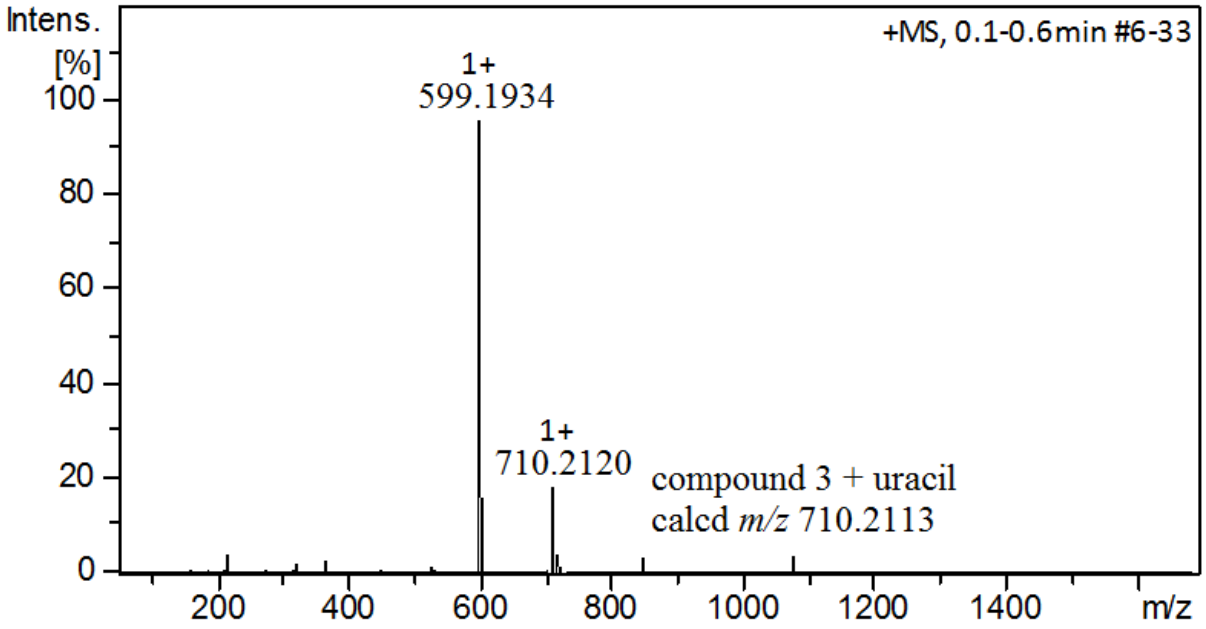


Figure S22. HRMS of the reaction mixture of compound **3a** and uracil after 2h of stirring at pH 8.0. Similar spectra were recorded for the reaction mixtures of other isomers of compound **3** and uracil.

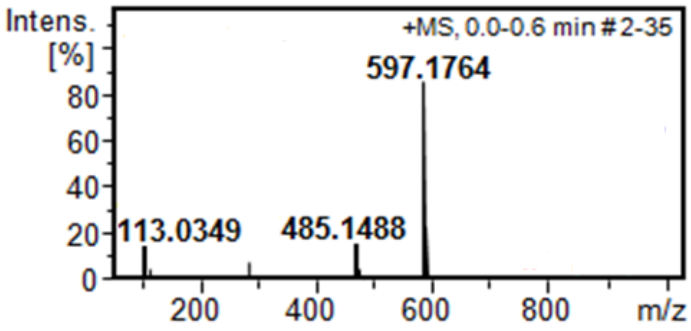


Figure S23a. HRMS of compound **7** (calcd *m/z* 597.1764, $[M+H]^+$).

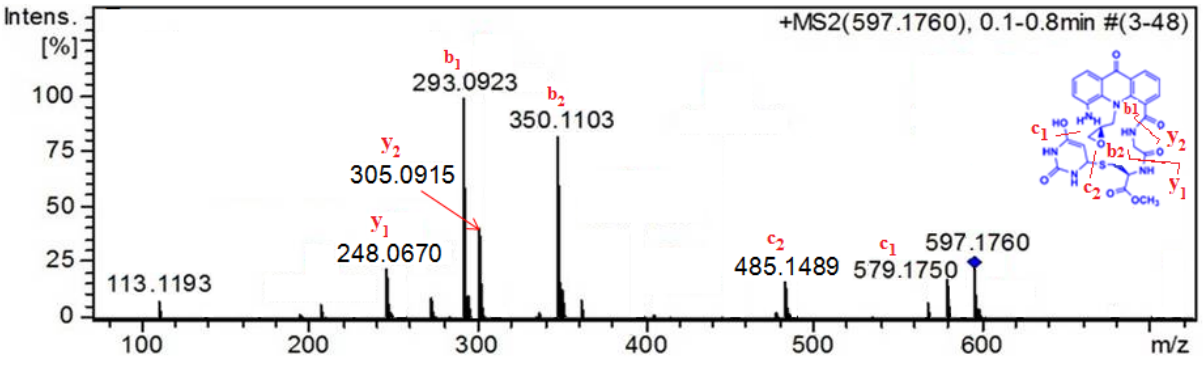


Figure S23b. MS2 spectrum of compound **7.** Notation C_1, C_2 is used arbitrarily while y_1, y_2 and b_1, b_2 correspond to the fragmentation of peptide.

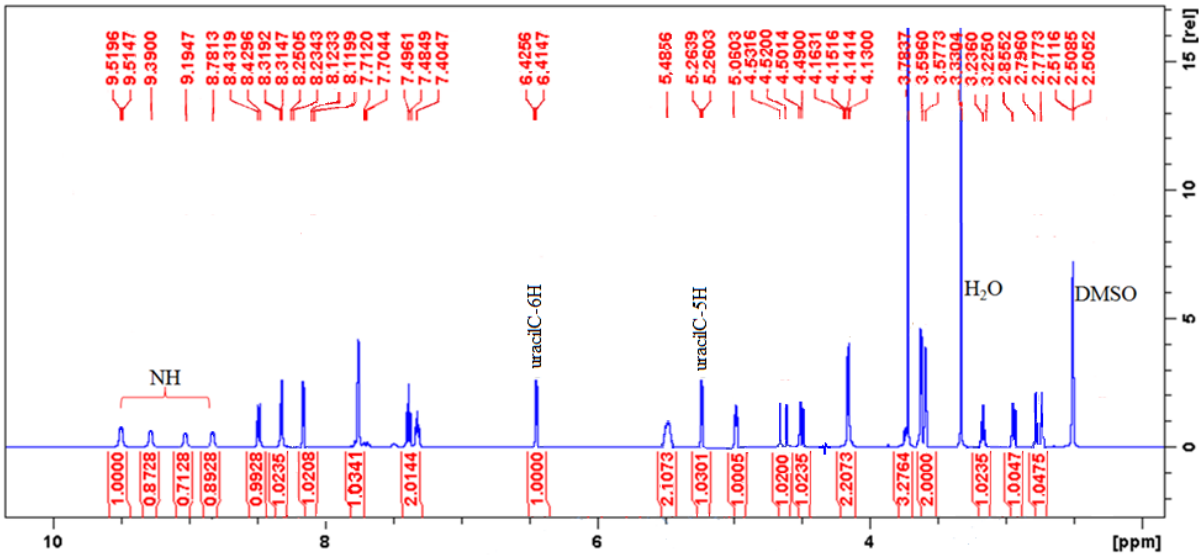


Figure S23c. ^{1}H NMR spectrum of the reaction mixture of compound **1d** and uracil after 2 h of the reaction at pH 8.0. Since there was no further change in the reaction mixture, it was worked up and the spectrum probably corresponds to species **7** (Scheme 1b). The solvent was DMSO-H_2O (1:4, v/v) and DMSO-d_6 was used for lock purpose. H_2O peak was suppressed.

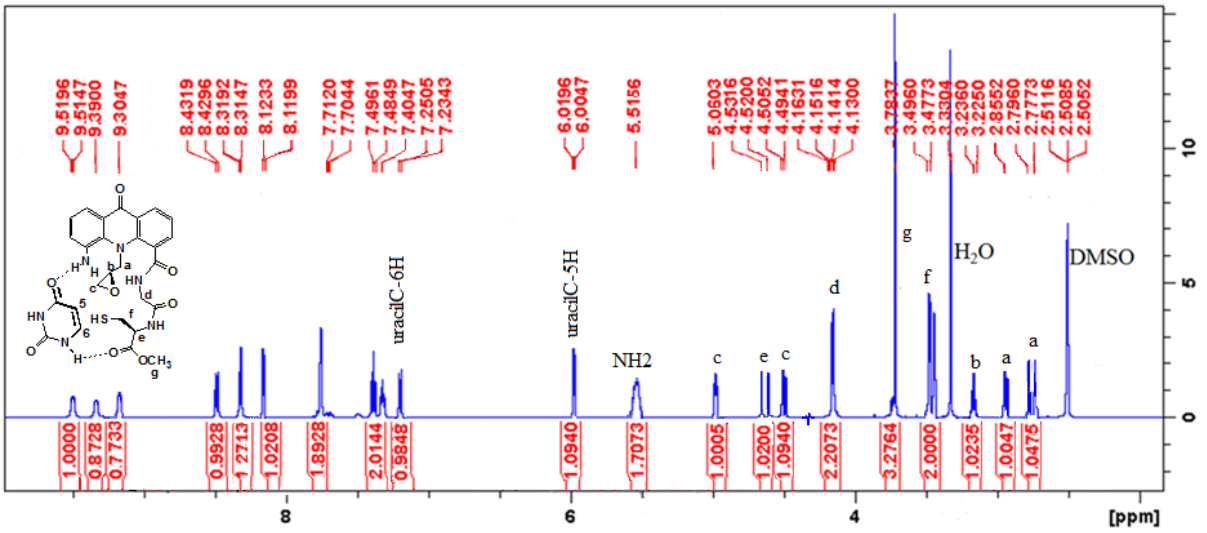


Figure S24a. ^{1}H NMR spectrum of the reaction mixture of compound **1d** and uracil after 30 min of their mixing (pH 8.0) (formation of species **5**/**6**, Scheme 1b). In comparison to the NH_2 signal of **1d** (Figure S13), here it was shifted by 0.5 ppm.

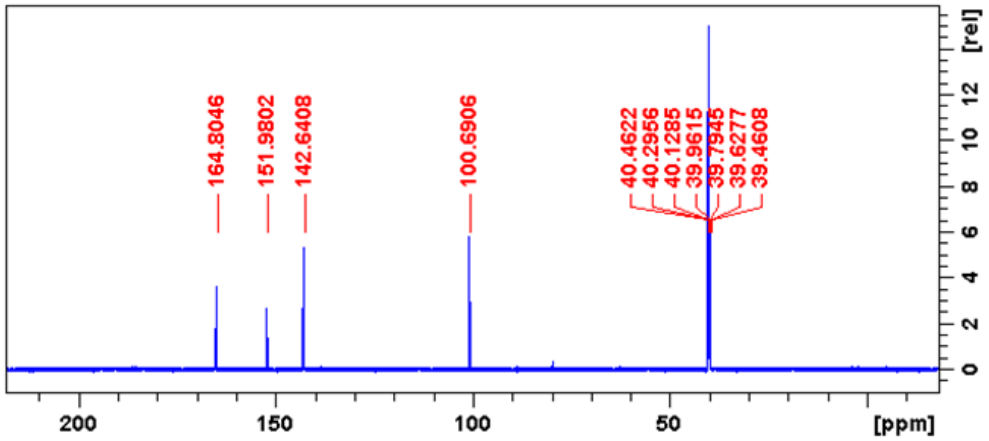


Figure S24b. ^{13}C NMR spectrum of uracil (recorded for making comparison). DMSO – H_2O (1:4, v/v) was the solvent.

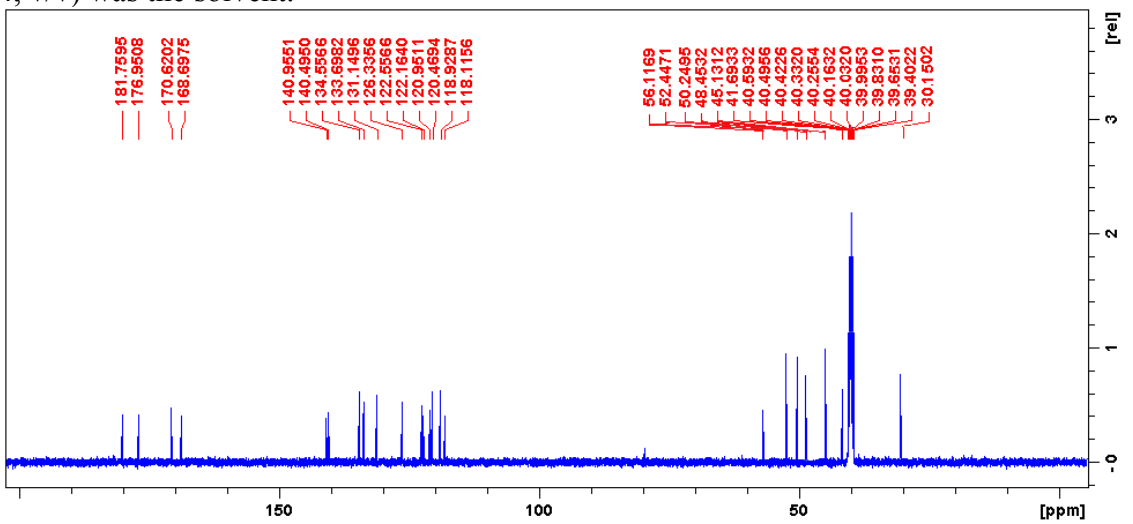


Figure S24c. ^{13}C NMR spectrum of compound **1d** recorded in DMSO – H_2O (1:4, v/v).

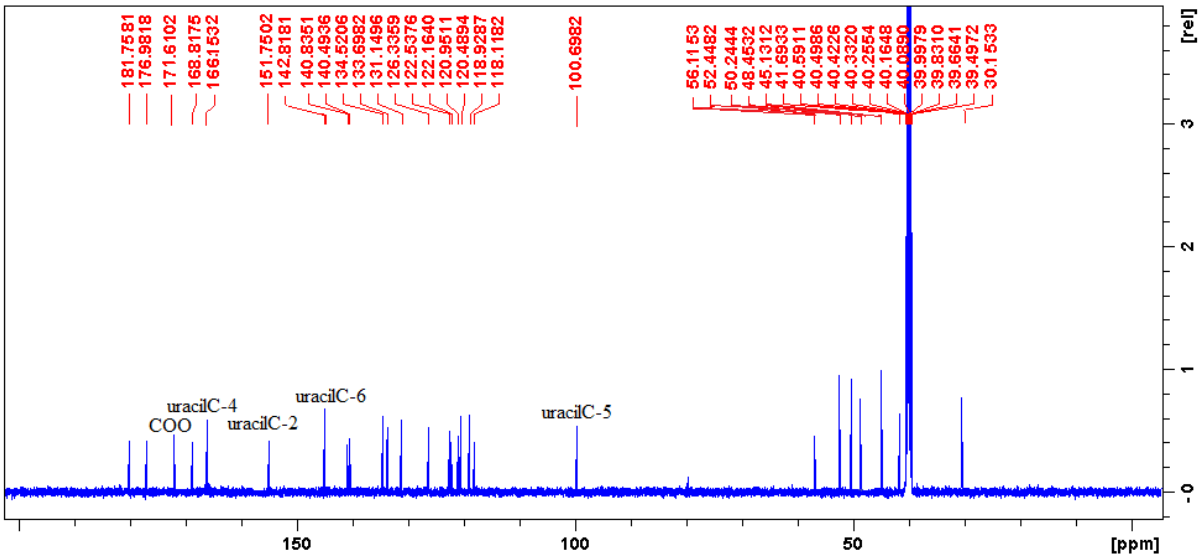
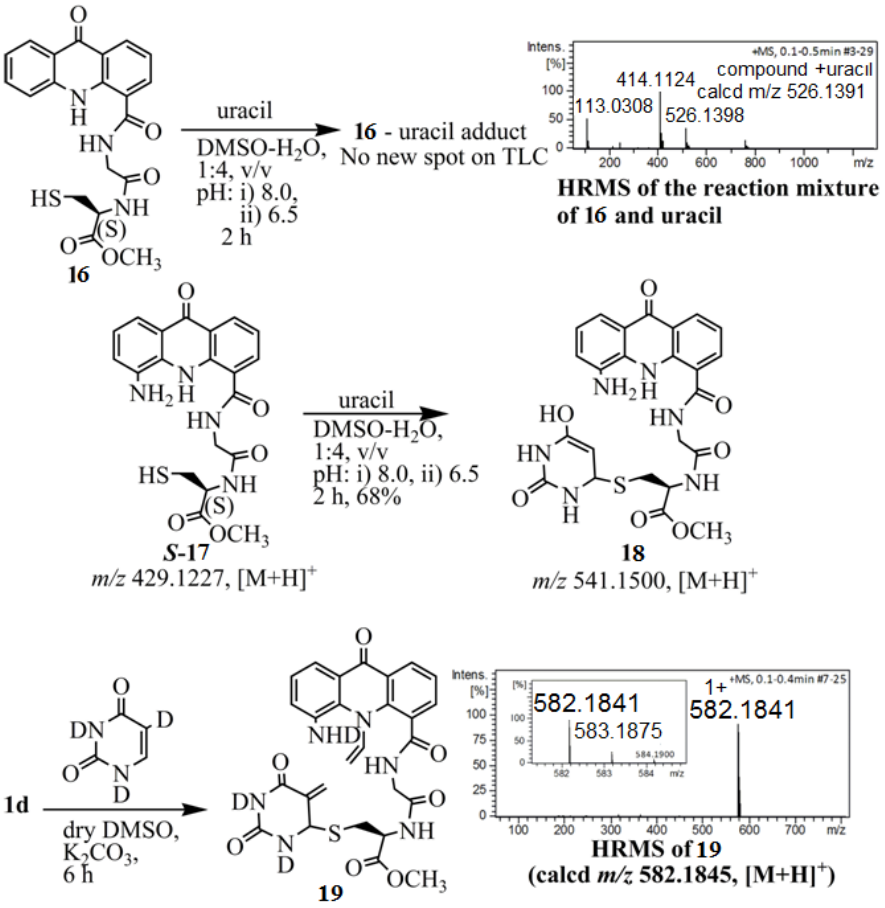


Figure S24d. ^{13}C NMR spectrum of the reaction mixture of compound **1d** and uracil after 30 min of their mixing (pH 8.0). Characteristic shift in uracilC-4 and ester carbonyl of **1d** is visible. DMSO – H_2O (1:4, v/v) was the solvent.



Scheme S4. Experiments supporting the role of NH_2 in the reaction of **1d** and uracil.

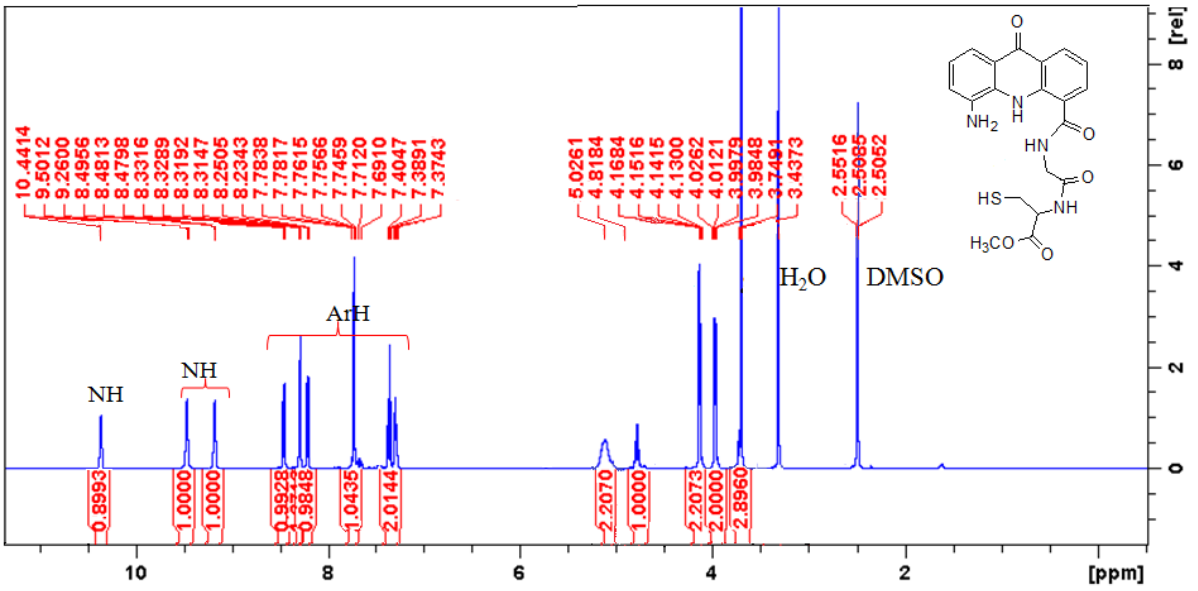


Figure S25. ^{1}H NMR spectrum of compound **17**.

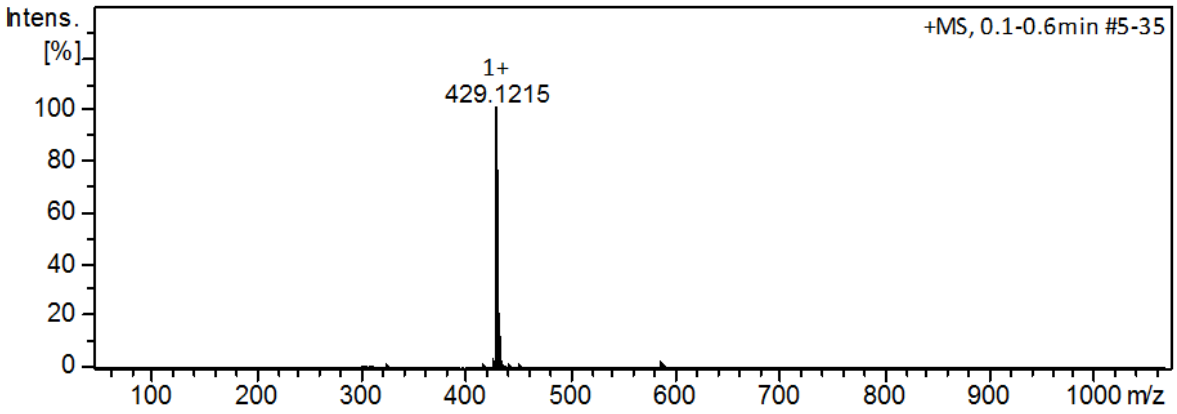


Figure S26. HRMS of compound **17**.

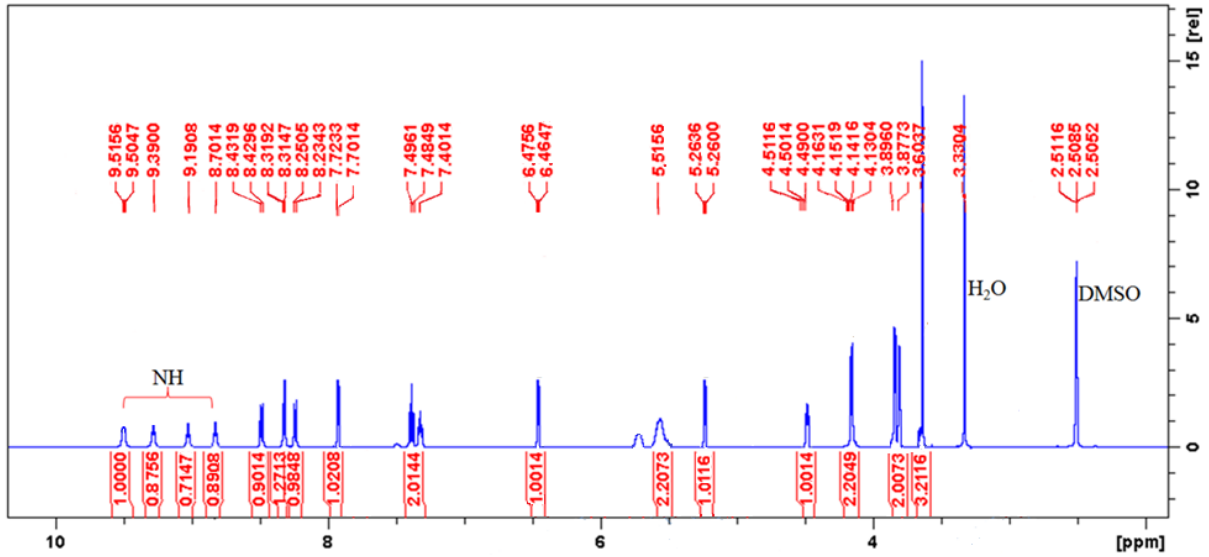


Figure S27. ^{1}H NMR spectrum of compound **18**.

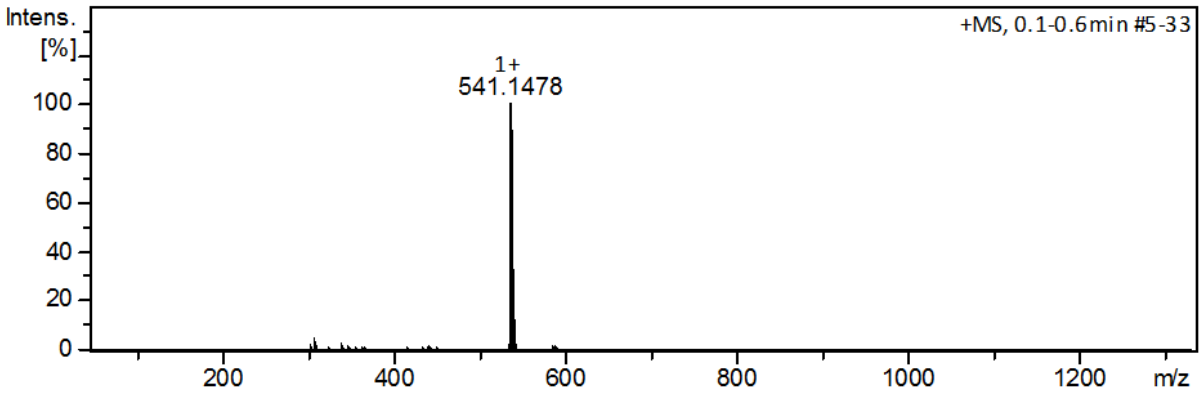


Figure S28. HRMS of compound **18**.

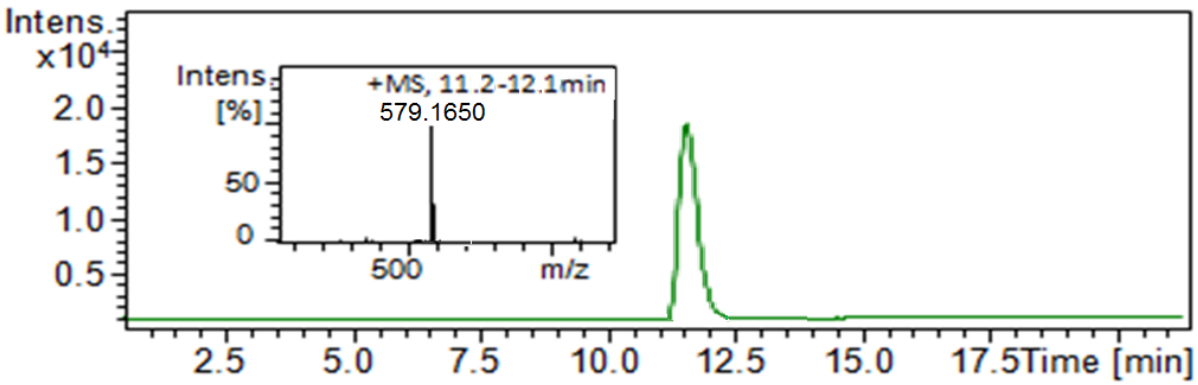


Figure S29a. LC-MS of compound **11**.

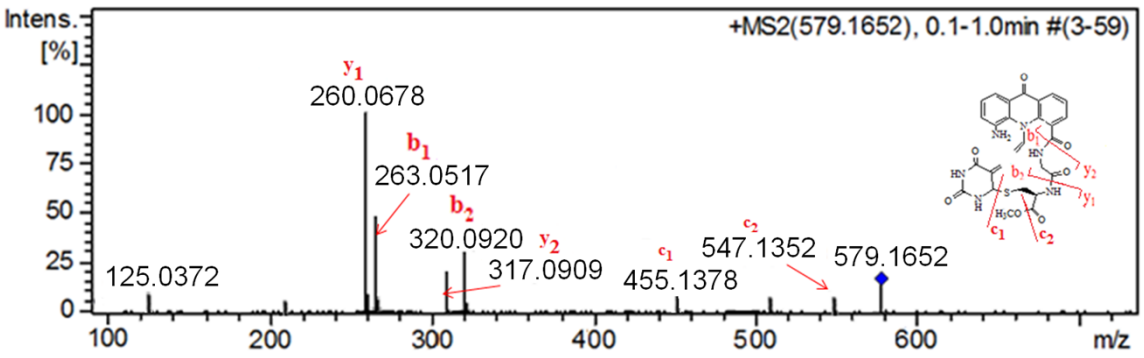


Figure 29b. MS2 spectrum of compound **11**. Notation C_1, C_2 is used arbitrarily whereas y_1, y_2 and b_1, b_2 correspond to fragmentation of peptide.

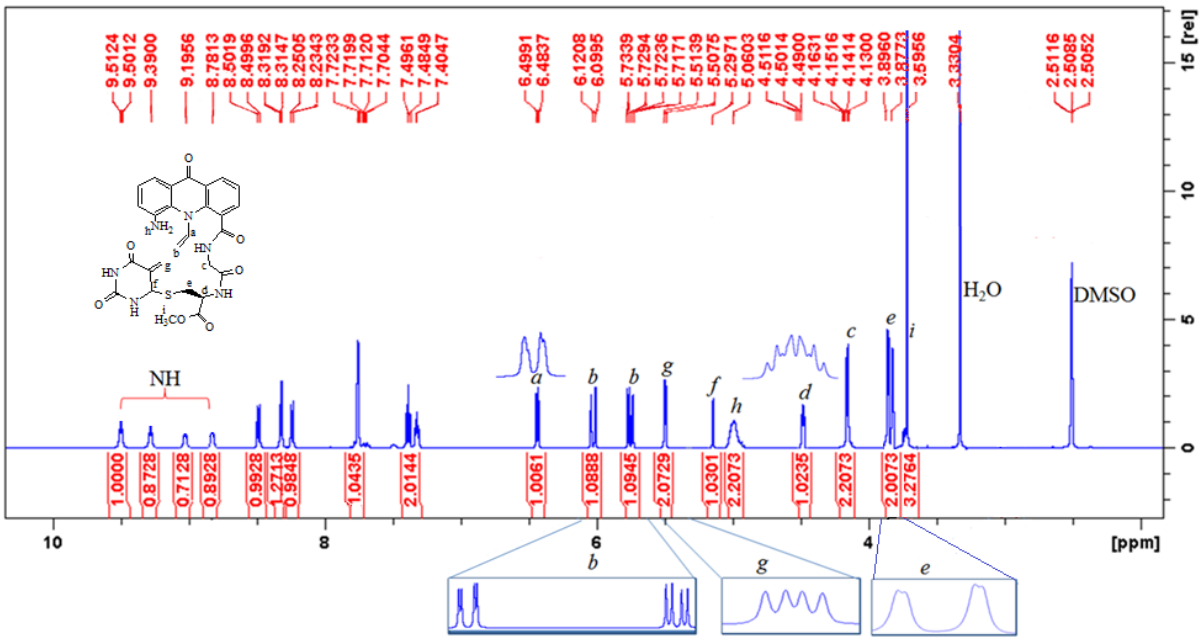


Figure S30. ^{1}H NMR spectrum of compound **11** (DMSO-d_6).

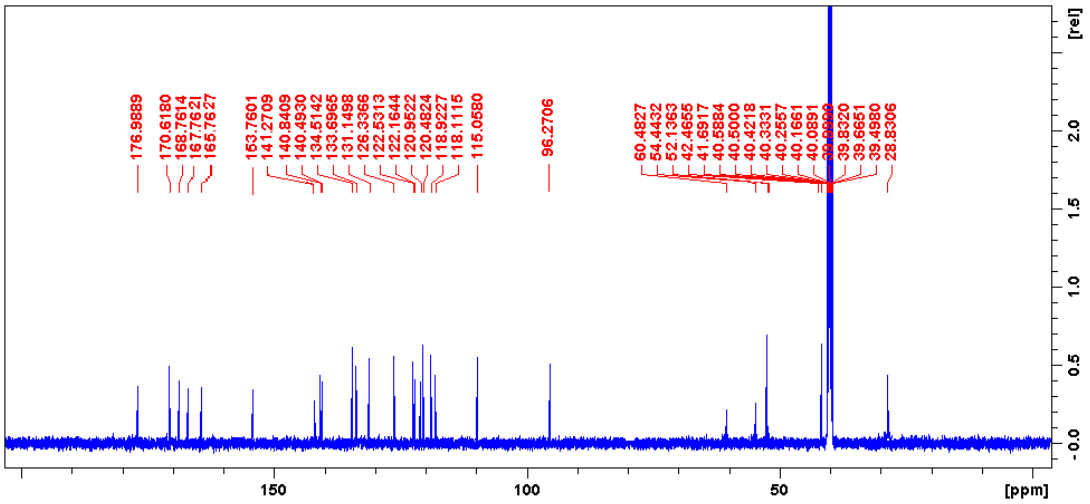


Figure S31. ^{13}C NMR spectrum of compound **11**.

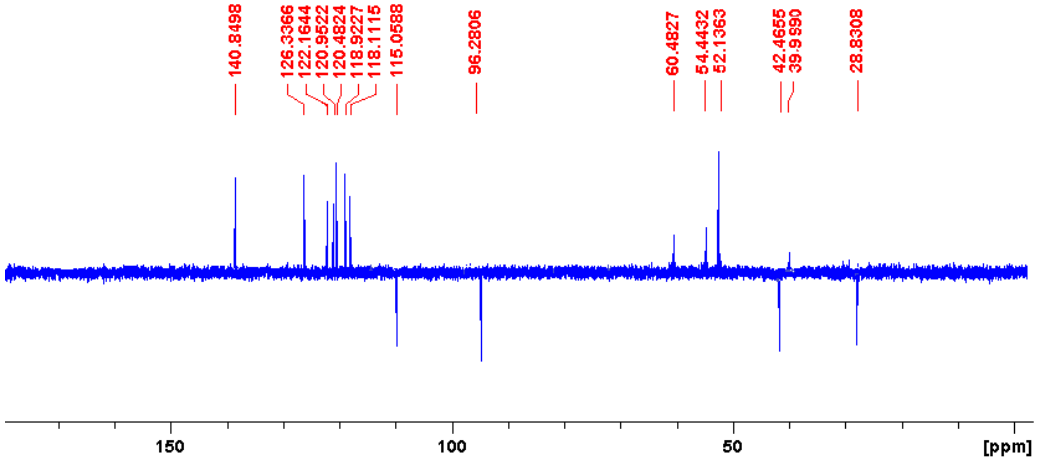


Figure S32a. DEPT-135 NMR spectrum of compound **11**.

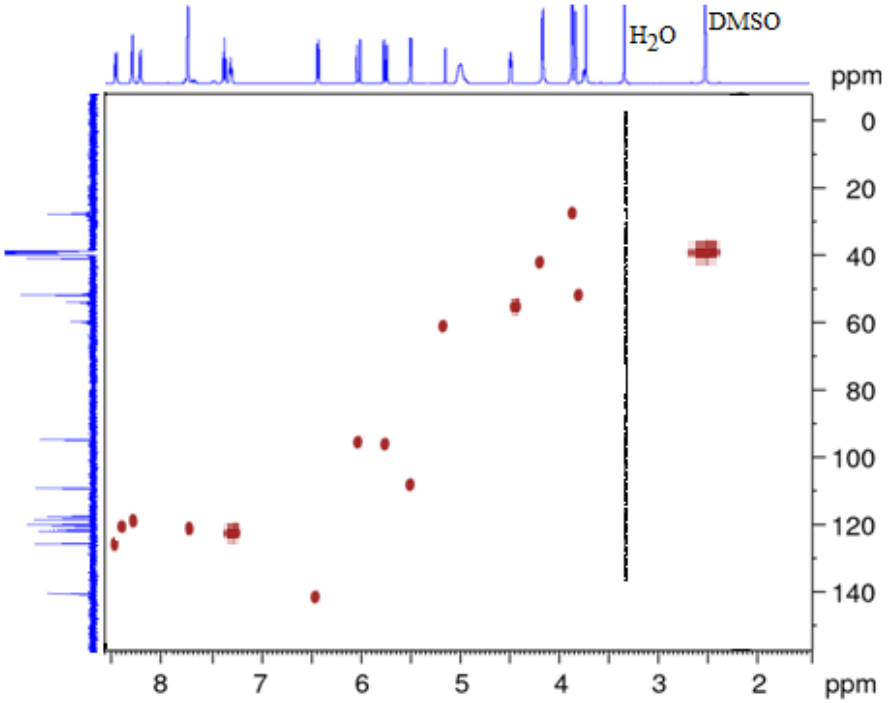


Figure S32b. HSQC NMR spectrum of compound **11**.

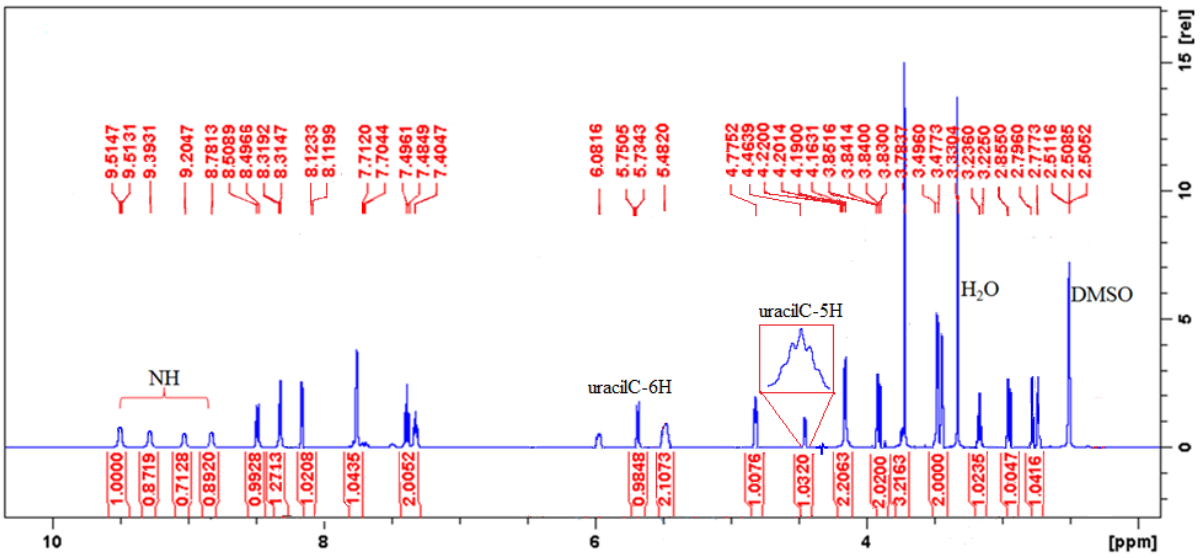


Figure S33. ^{1}H NMR spectrum of the reaction mixture of compound **1d** and uracil after 15 min of changing the pH to 6.5. The spectrum corresponds to species **8** (Scheme 1b). UracilC-5H and uracilC-6H are shifted upfield. Multiplicity of uracilC-5H also changed from doublet to multiplet. The solvent was DMSO-H_2O (1:4, v/v) and DMSO-d_6 was used for lock purpose. The H_2O peak was suppressed.

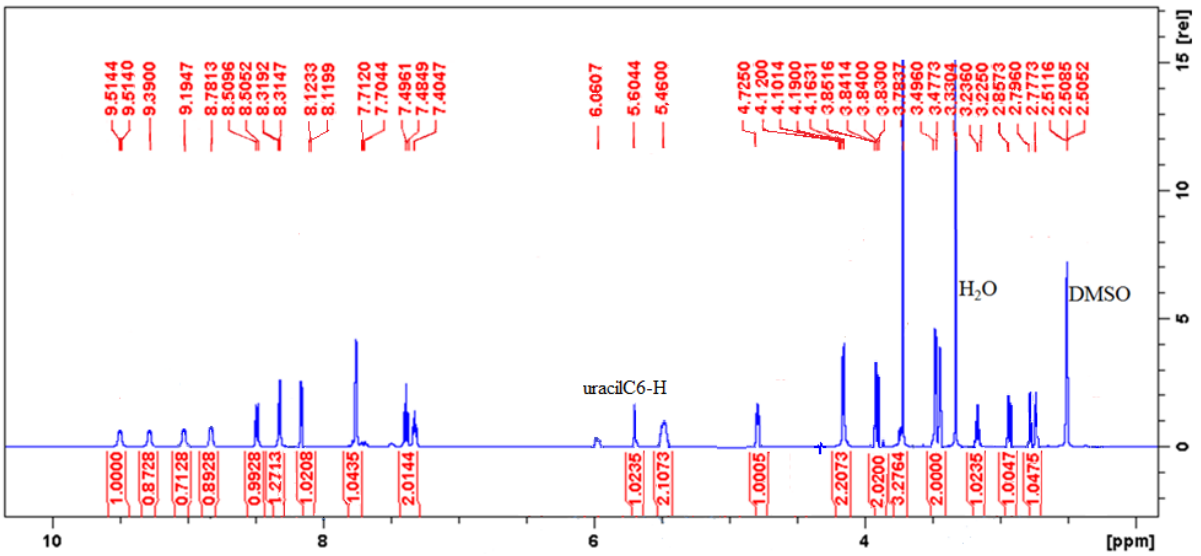


Figure S34. ^{1}H NMR spectrum of the reaction mixture of compound **1d** and uracil after 25 min of changing the pH to 6.5. The spectrum probably corresponds to species **9** (Scheme 1b). Signal due to uracilC-5H is finished and uracilC-6H converted to a singlet. The solvent was DMSO-H_2O (1:4, v/v) and DMSO-d_6 was used for lock purpose. The H_2O peak was suppressed.

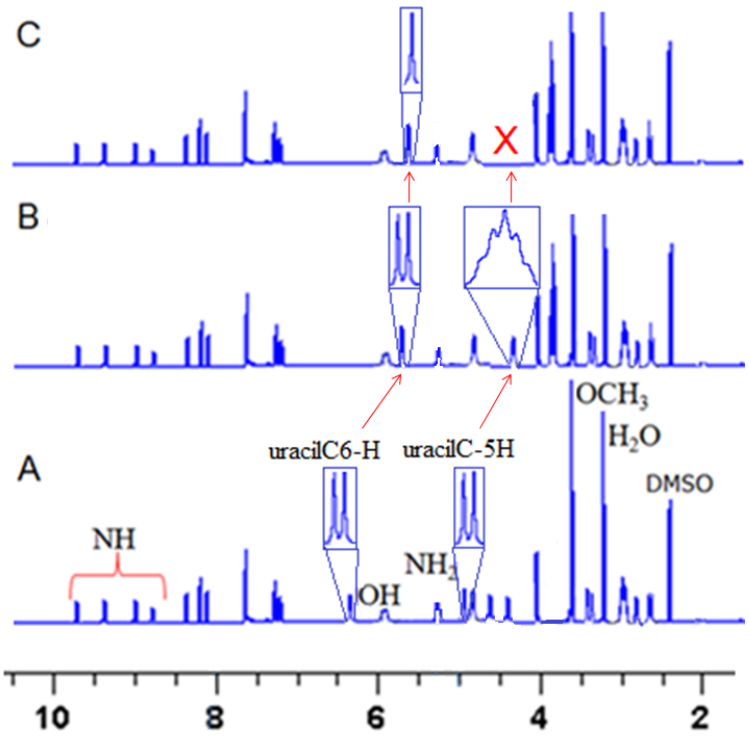


Figure S35. ^{1}H NMR spectrum of the reaction mixture of compound **1d** and uracil: (A) after 2h of the reaction at pH 8.0, isolated and purified, probably corresponds to species 7, (B) 15 min after changing the pH of the reaction mixture to 6.5, the NMR spectrum corresponds to species 8, (C) 25 min after changing the pH to 6.5 and probably species 9 was formed. All the NMR spectra were recorded at 500 MHz spectrometer using H_2O – DMSO (4:1, v/v) as the solvent (locked with DMSO-d_6). H_2O signal was suppressed. The peak marked as H_2O is due to the water of DMSO.

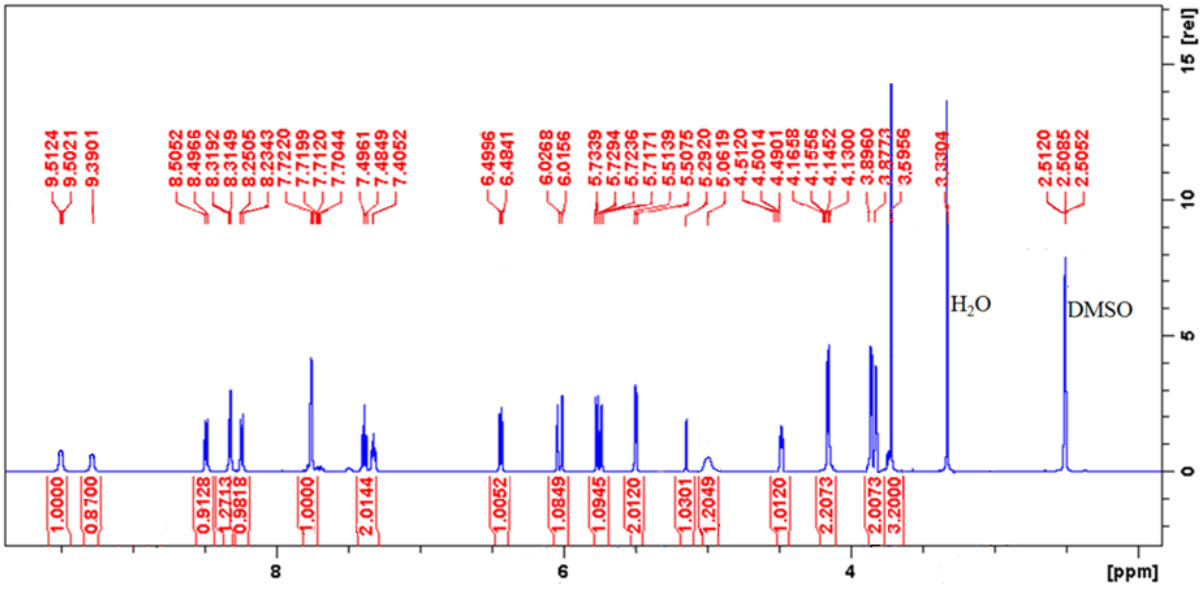


Figure S36a. ^{1}H NMR spectrum of compound **19** (DMSO-d_6 was used for lock purpose).

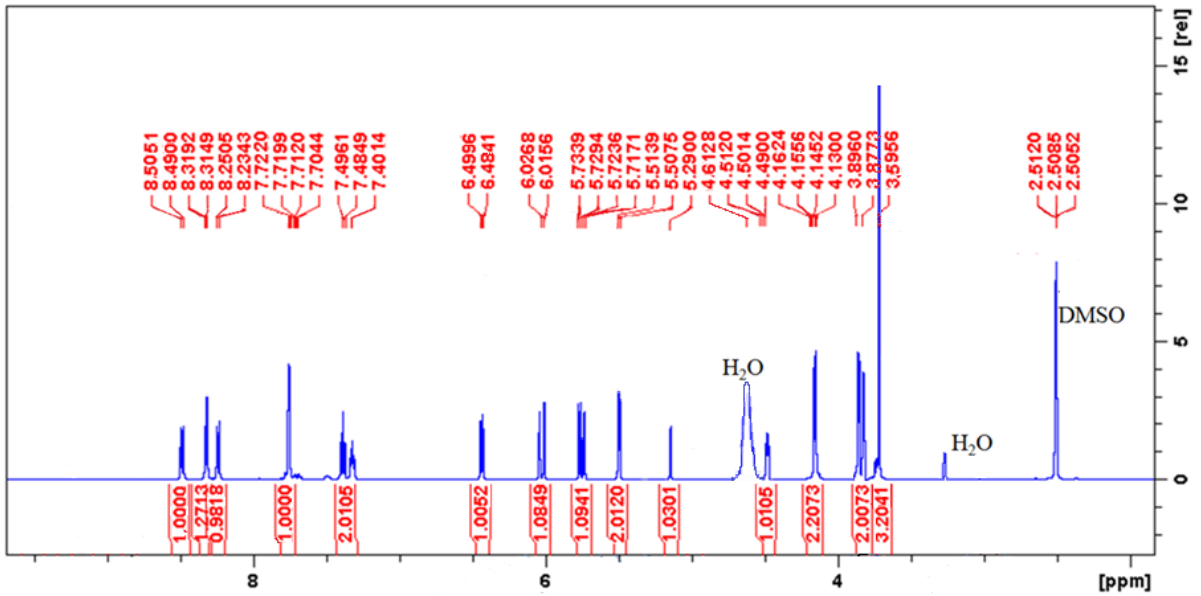


Figure S36b. ^{1}H NMR spectrum of compound **19** in DMSO-d_6 after addition of D_2O.

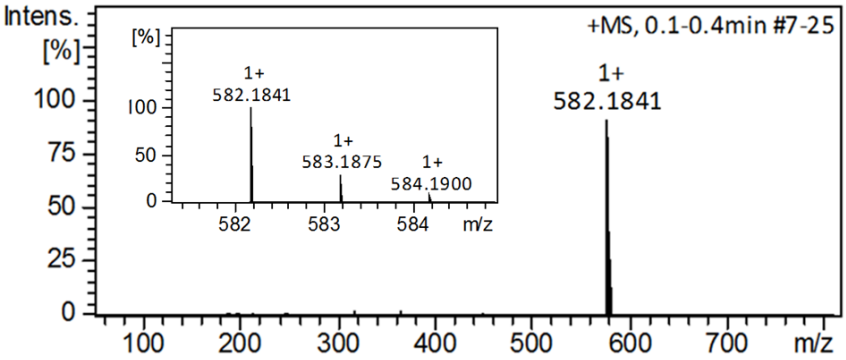


Figure S37. HRMS of compound **19**. Inset: expansion to show isotopic pattern.

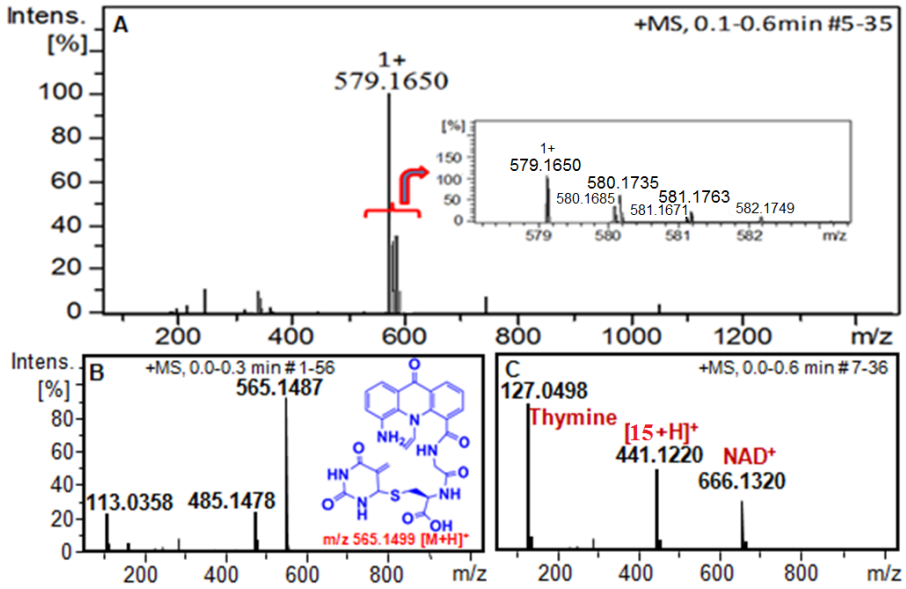


Figure S38. HRMS of the reaction mixture containing: (A) compound **11** and NADH, (B) reaction mixture of compound **11** at pH 9.5 showing formation of **13**, (C) compound **13** and NADH showing formation of thymine and **15**.

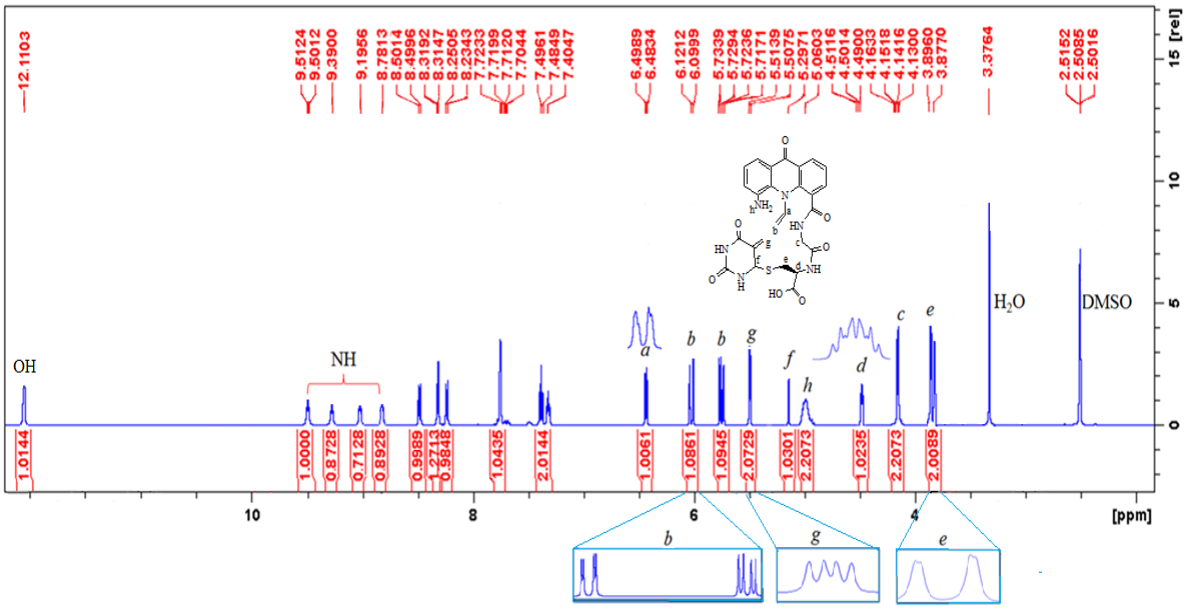


Figure S39. ^{1}H NMR spectrum of compound **13**. DMSO-d_6 was used as the solvent.

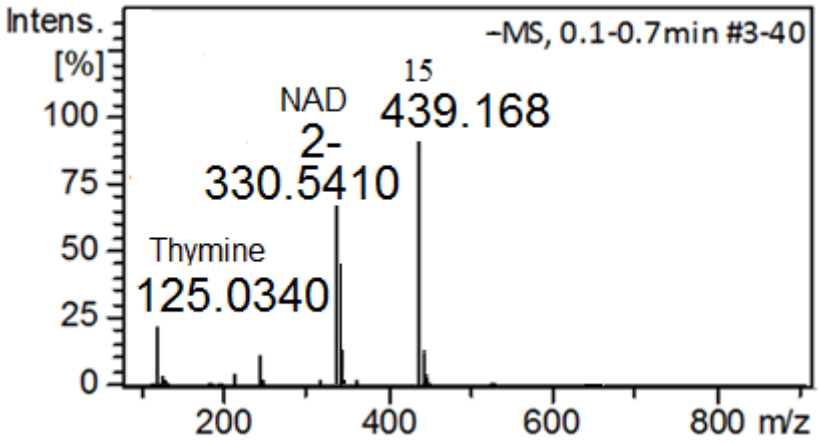


Figure S40. HRMS of the reaction mixture containing compound **13** and NADH recorded in the –ve ESI mode showing thymine ion peak at *m/z* 125 $[M-H]^-$ (low intensity in –ve ESI mode), doubly charged NAD ion at *m/z* 330 $[M-2H]^{2-}$ and **15** ion at *m/z* 439 $[M-H]^-$.

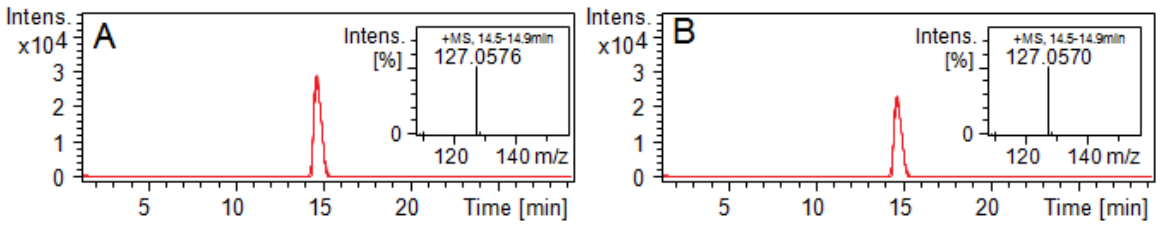


Figure S41. (A) LC-MS of one of the products obtained after treatment of compound **13** with NADH, (B) LC-MS of commercial sample of thymine.

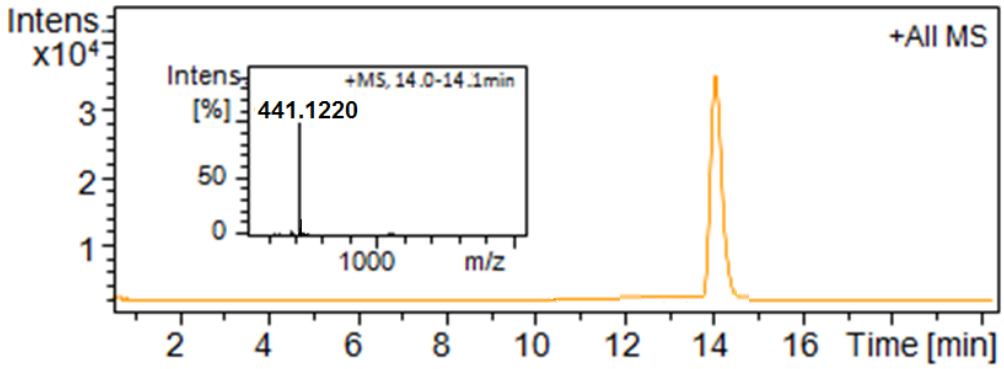


Figure S42a. LC-MS of compound **15**.

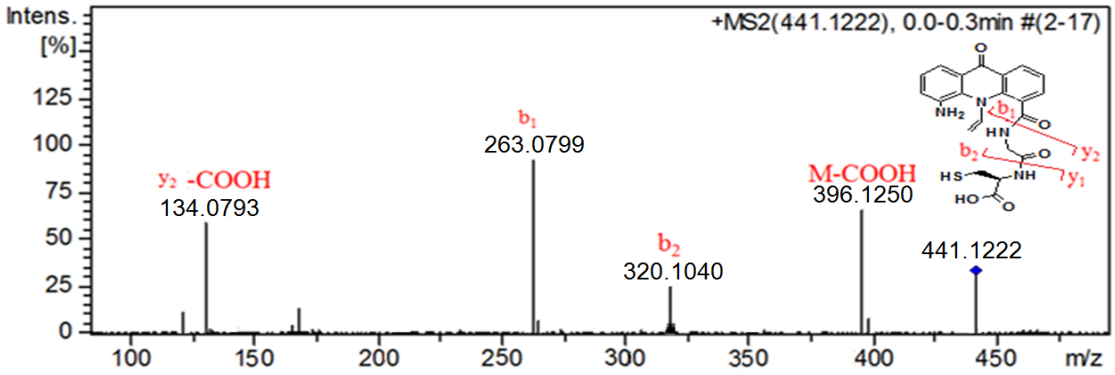


Figure S42b. MS2 spectrum of compound **15**.

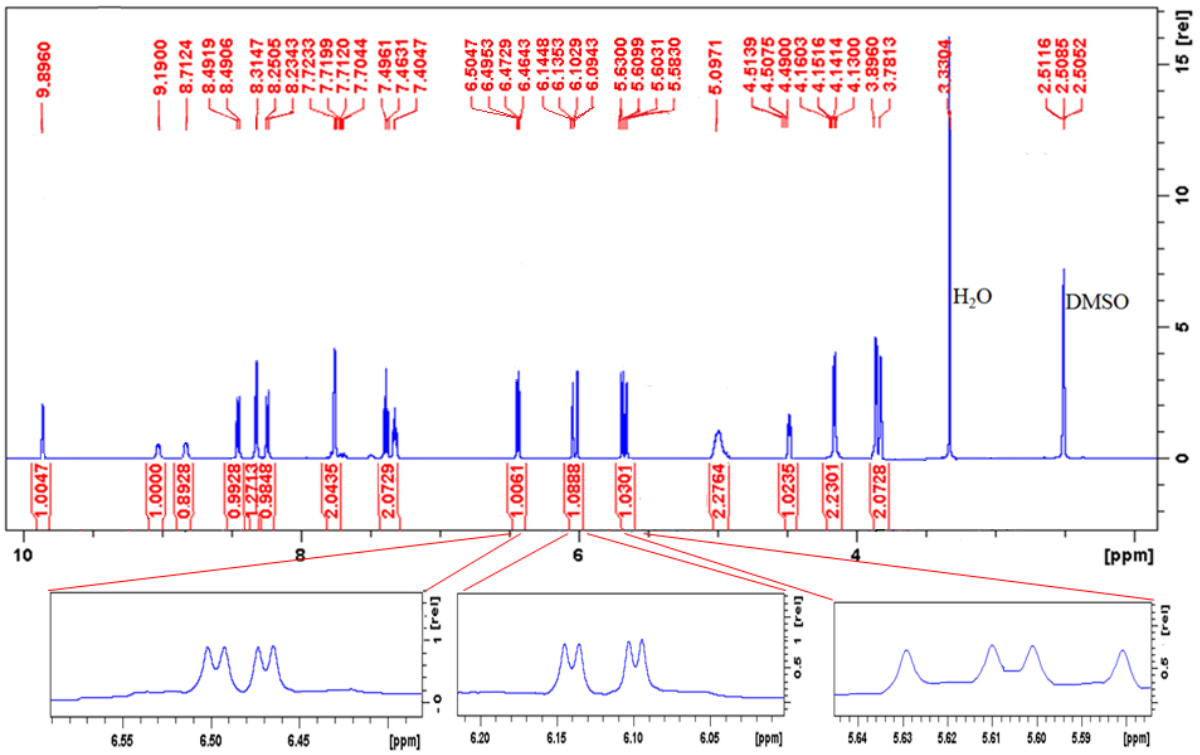


Figure S42c. ^{1}H NMR spectrum of compound **15** (DMSO-d_6).

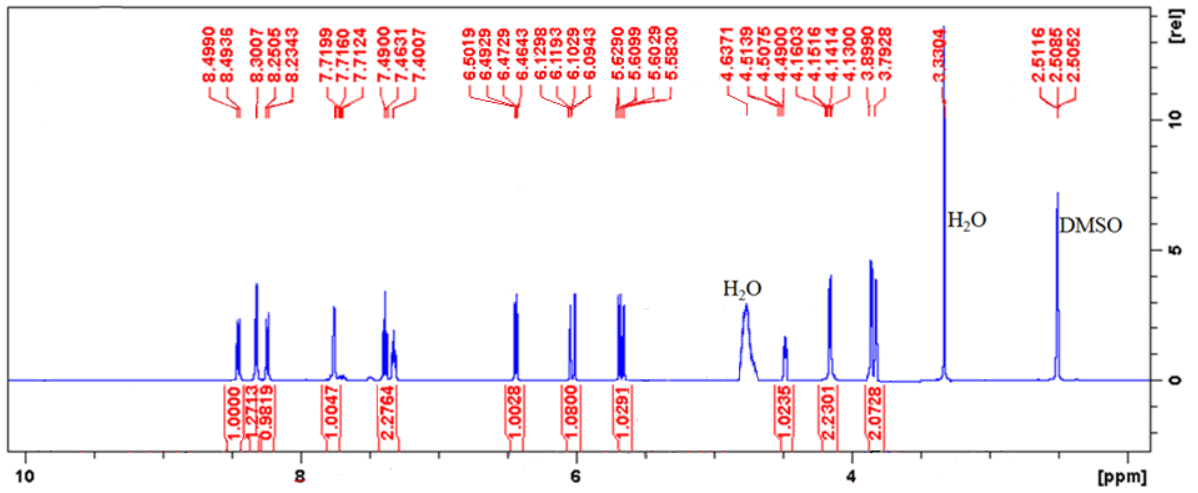


Figure S42d. ^{1}H NMR spectrum of compound **15** in DMSO-d_6 after addition of one drop of D_2O.

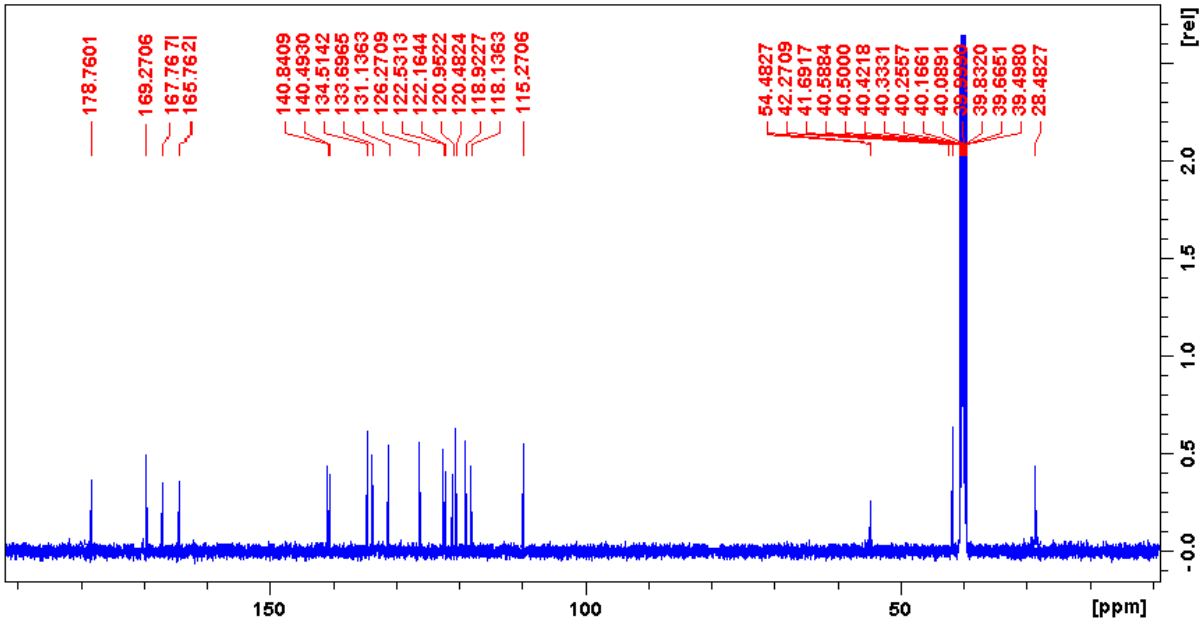


Figure S42e. ^{13}C NMR spectrum of compound **15**.

UV-vis monitoring of this part of the reaction showed decrease in intensity of the NADH band at 340 nm (Figure S43) and emergence of an absorption peak at 270 nm indicating the conversion of NADH to NAD^+. The H^- transfer step was also confirmed by treating compound 13 with NaH and LiCl and isolation of thymine and 5-chloromethyluracil,[4] respectively (Scheme S5, Figure S44) along with compound 15.

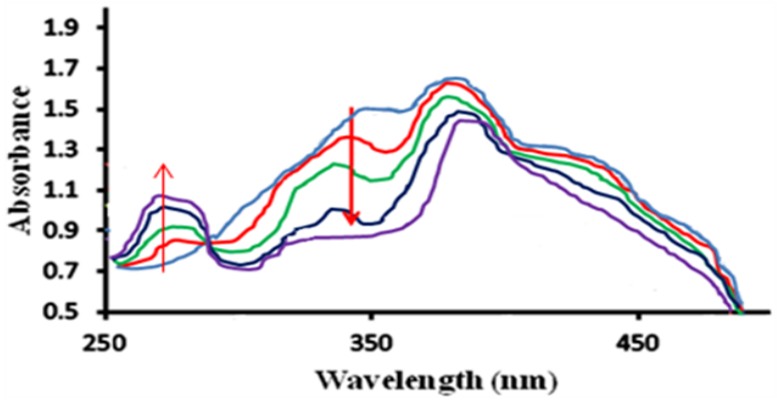


Figure S43. UV-vis spectra of the reaction mixture (recorded after every 5 min) showing decrease in intensity of 340 nm band and indicating conversion of NADH to NAD^+.

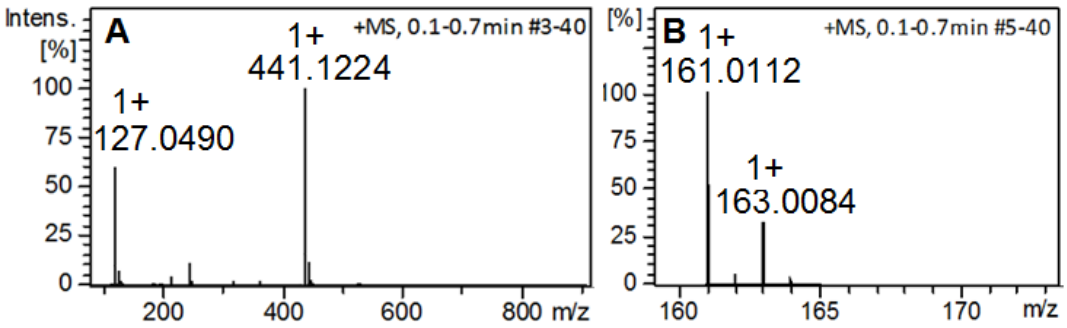
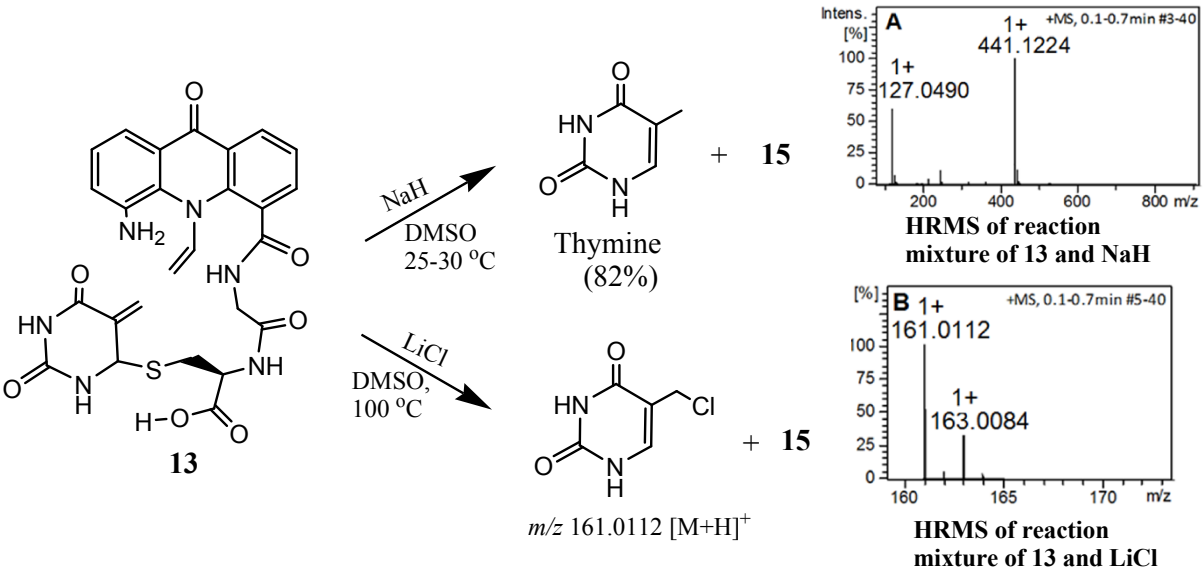
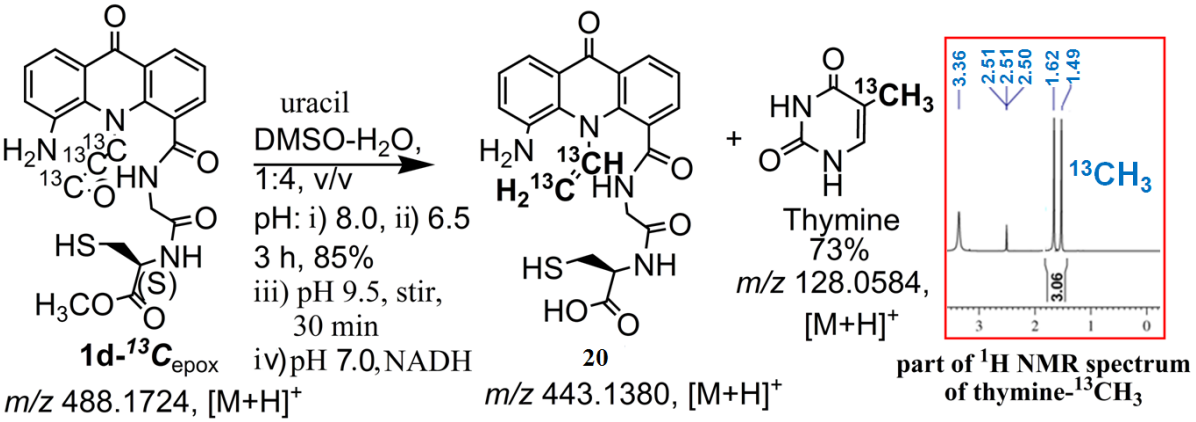


Figure S44. HRMS of the reaction mixture of (A) compound **13** and NaH after 1h of stirring at 25–28 °C, (B) compound **13** and LiCl after stirring for 2h at 100 °C. A part of the spectrum is expanded for showing isotopic pattern due to the presence of Cl (calcd *m/z* 161.0112, $[M+H]^+$).



Scheme S5. Reaction of compound **13** with NaH and LiCl.



Scheme S6. Reaction in support of the products of Scheme 1b.

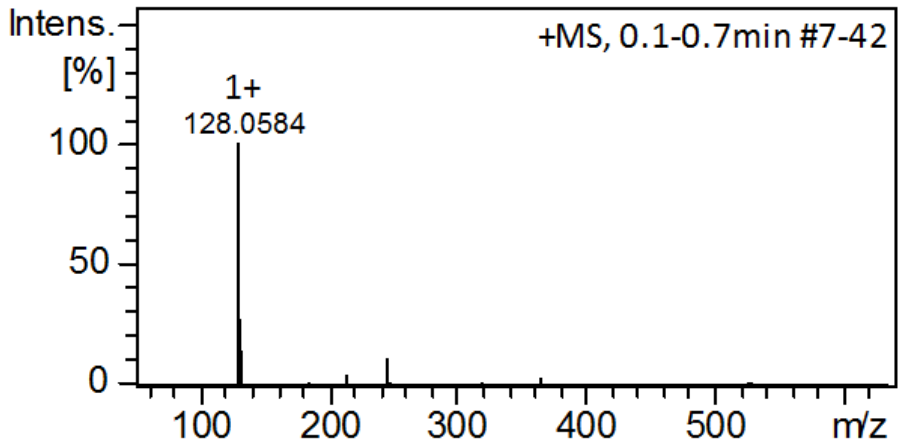


Figure S45a. HRMS of thymine-$^{13}CH_3$ (calcd *m/z* 128.0580, $[M+H]^+$).

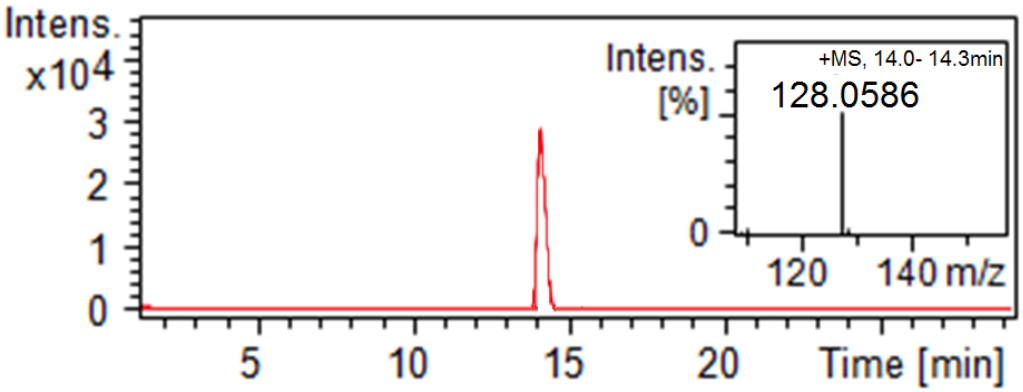


Figure 45b. LC-MS of thymine-$^{13}CH_3$.

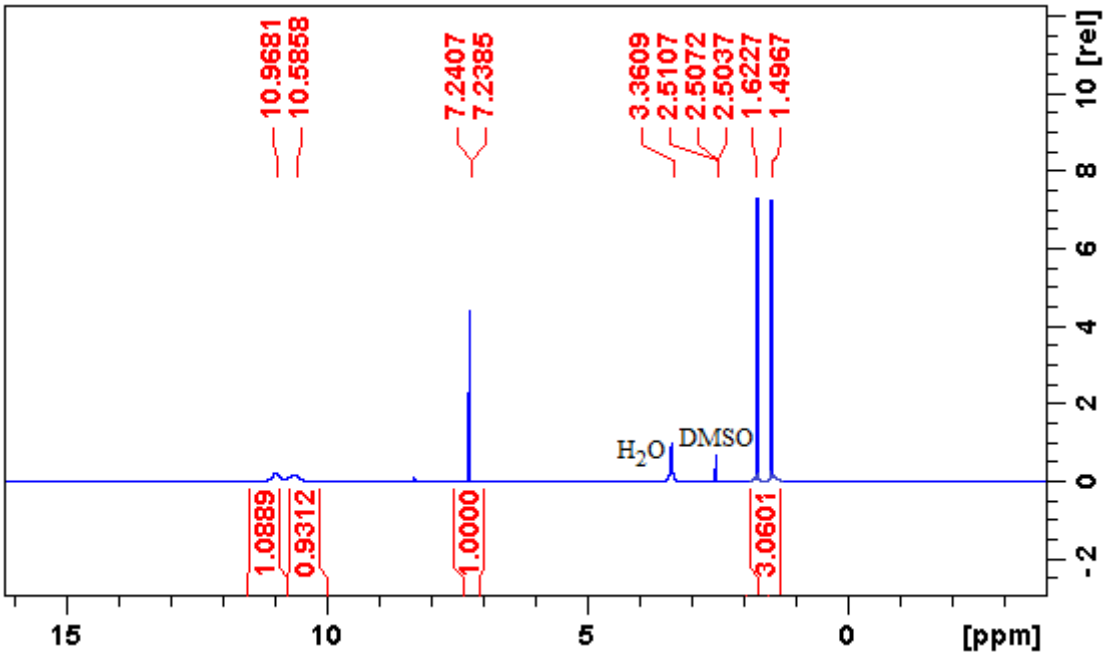


Figure S45c. ^{1}H NMR spectrum of thymine having $^{13}CH_3$ at C-5. $J_{1H\text{-}13C}$ is 65 Hz.

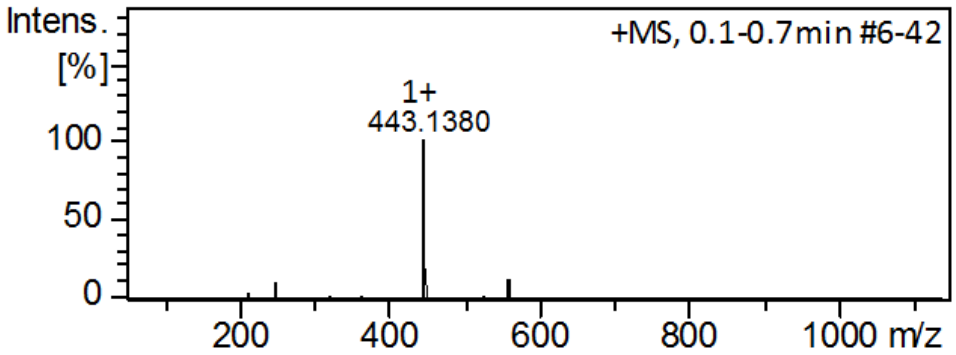


Figure S46a. HRMS of compound **20** (calcd *m/z* 443.1384, $[M+H]^+$).

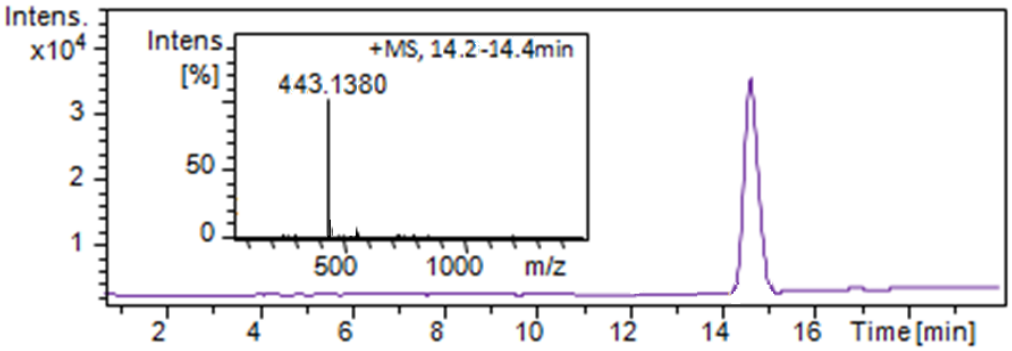


Figure S46b. LC-MS of compound **20**.

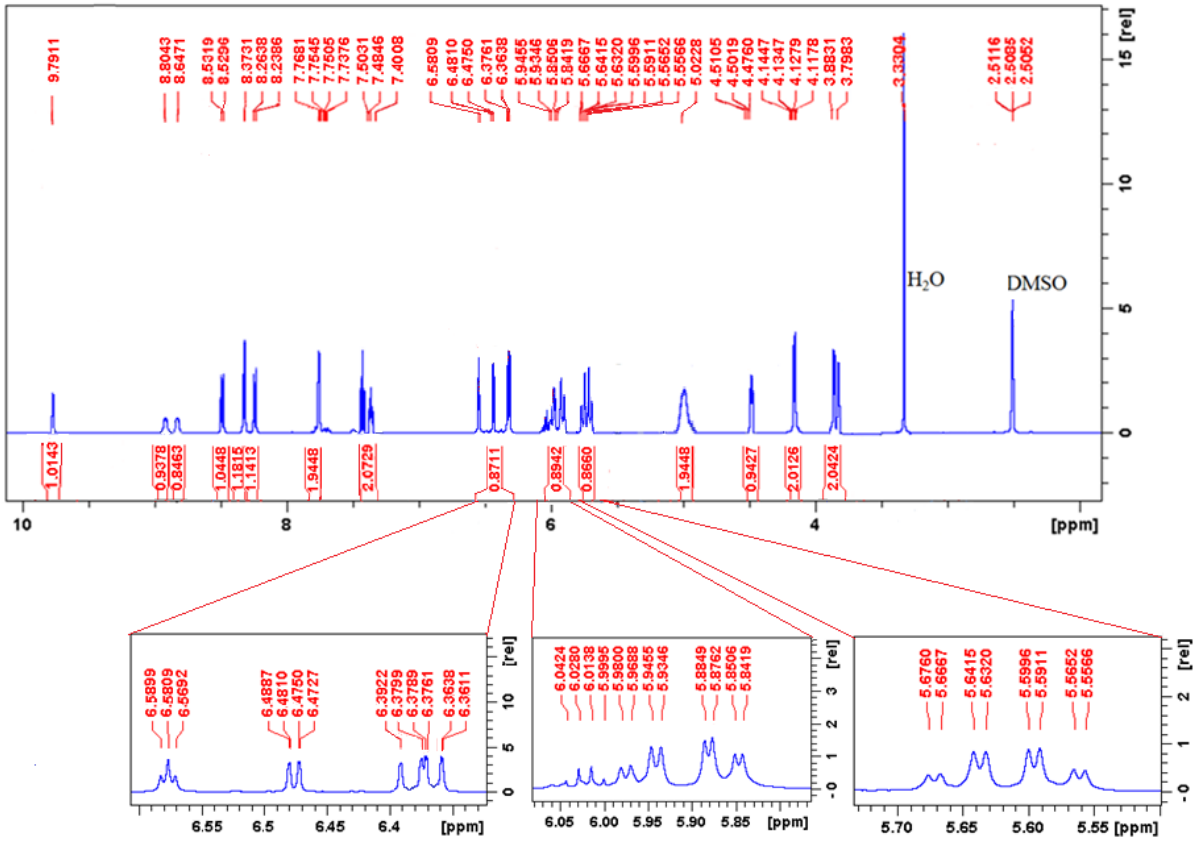


Figure S46c. ^{1}H NMR spectrum of compound **20**. Coupling constants were caculated with the help of decoupling experiments.

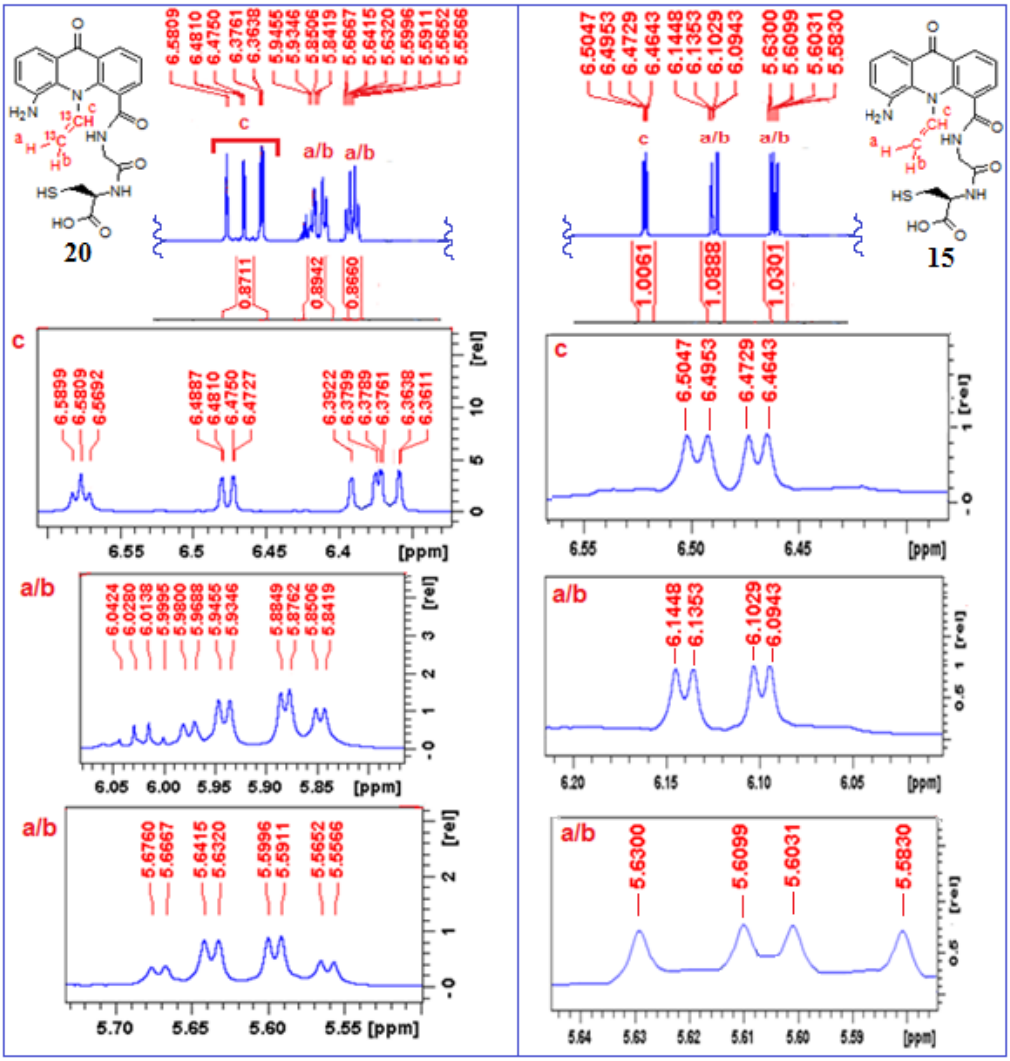


Figure 46d. Comparison of olefininc part of the ^{1}H NMR spectrum of compound **15** and **20**.

Table S1. Comparison of the working of model reactions for various steps of TSase catalysis with the biomodel reagent reported here.

S. No.	Model reaction	Reaction conditions	Lit.
1	Dehalogenation of 5-bromo-2-deoxyuridine.	37 ^{o}C, 10 mM [2-^{14}C, 6-^{3}H] BrdUrd (^{14}C, 0.61 μ Ci, ^{3}H, 1.89 μ Ci), 0.25 M L-Cysteine, pH 7.3	ref 19
2	Interaction of TSase with 5-Fduridylate	20 μl [3H] FAH_4, 46 nM TSase, 3.1 μM FdUMP, Tris buffer, 1 hr	ref 20
3	Isolation of intermediate in glutamate 60 mutants of TSase.	25 ^{o}C, 4.5 μM E60A or E60L Ts, 6.7 μM [6-^{3}H] dUMP (15 Ci/mmol), 400 μM C_2H_4 folate, TES buffer	ref 21
4	Trapping of C5 Methylene intermediate.	25 ^{o}C, 500 μg Trp82Tyr, 300 μM CH_2H_4 folate, 13 mM formalin, 50 mM $MgCl_2$, 2 mM EDTA, 150 mM β-mercaptoethanol, 10 μM dUMP, 50 mM TES, pH 7.4	ref 22
5	Reduction of 5-Uracilylmethylenepyridinium salts with thiols to thymine derivative.	Toluene, reflux, 2 days	ref 25
6	Mimic of overall TSase reaction using 6-methylamino-1,3-dimethyluracil	F_3CCOOH in CAN, reflux under argon	ref 28
7	(i) Reaction of cysteine unit at C6 of uracil, (ii) capturing of CH_2 by C5 of uracil (iii) hydride transfer (iv) formation of thymine	DMSO-H_2O (1:4), pH 8.0, 6.5, 9.5, 7.0; 3h	Present contribu-tion

High Resolution Mass Spectra

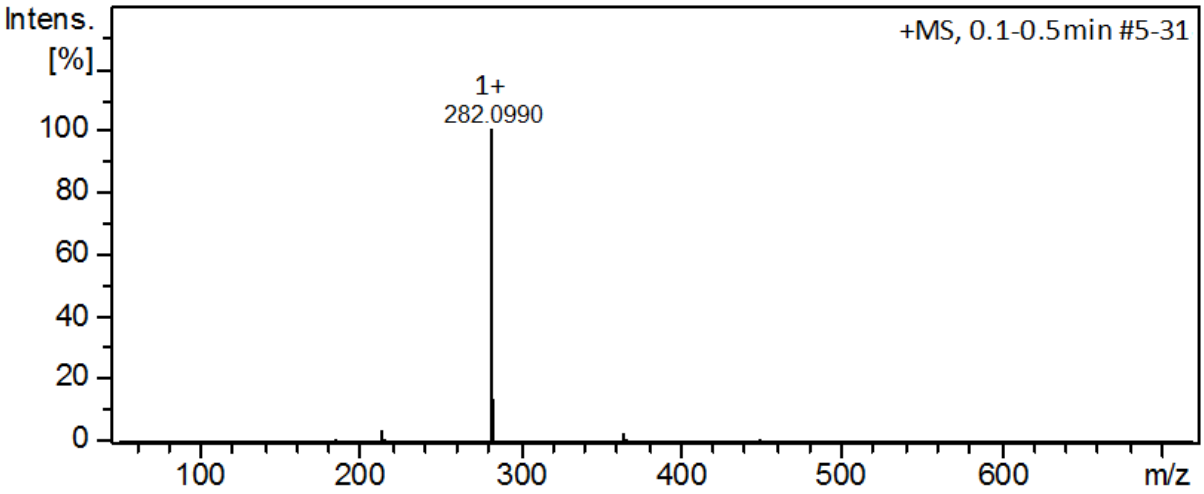


Figure S47. HRMS of 5-amino-9-oxo-9,10-dihydroacridine-4-carboxylic acid ethyl ester.

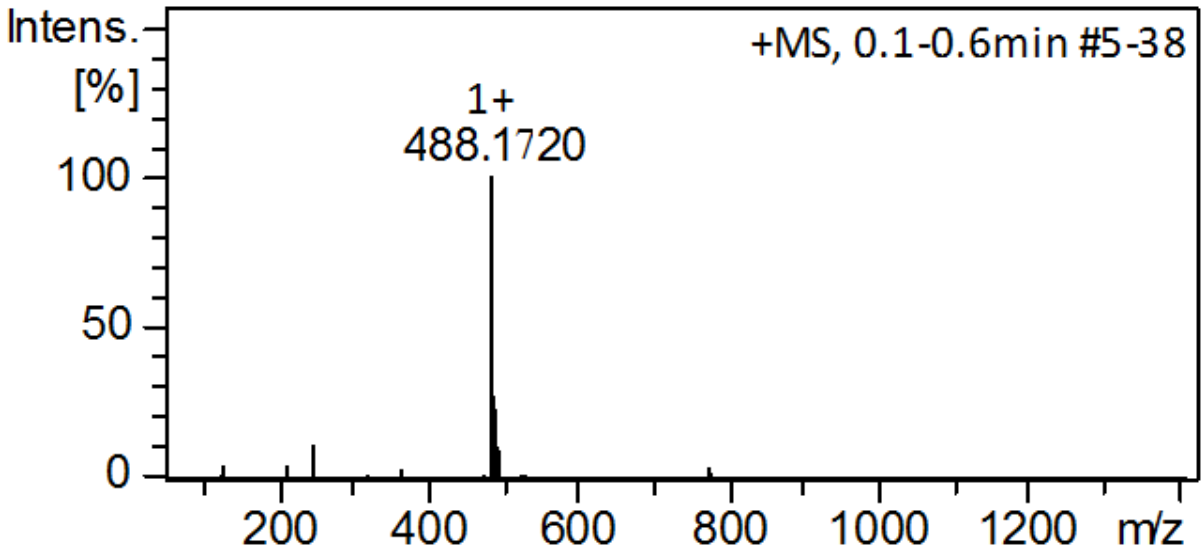


Figure S48. HRMS of compound **1d**-$^{13}C_{epox}$ (calcd *m/z* 488.1724, $[M+H]^+$).

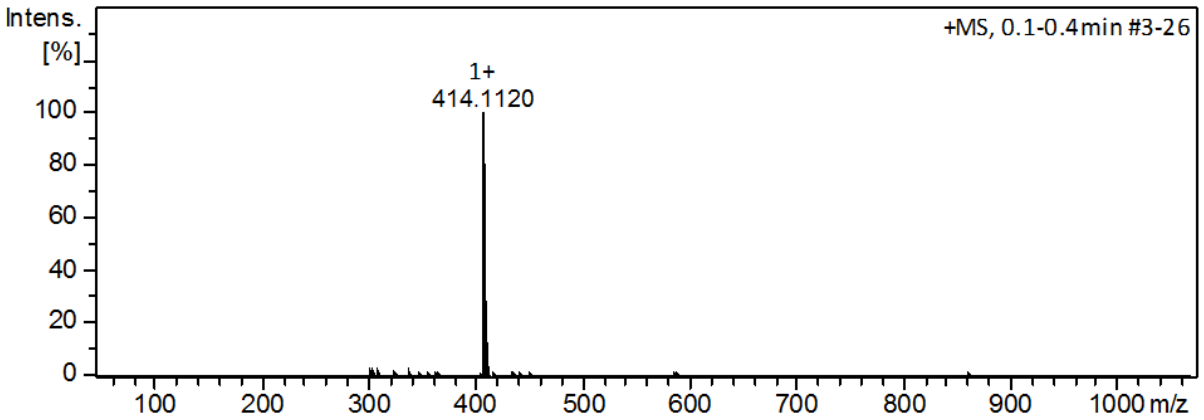


Figure S49. HRMS of compound **16**.

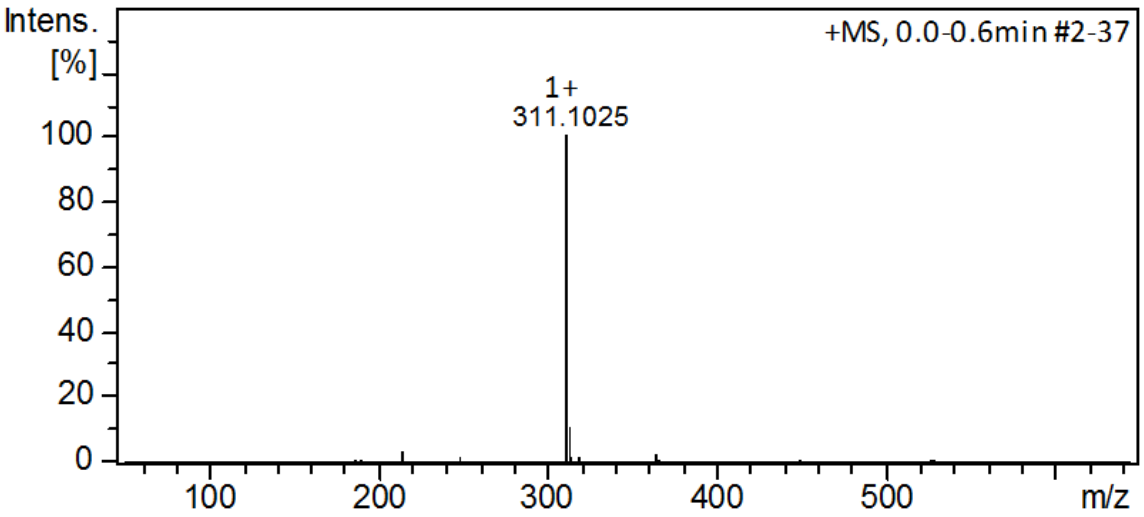


Figure S50. HRMS of compound **21**.

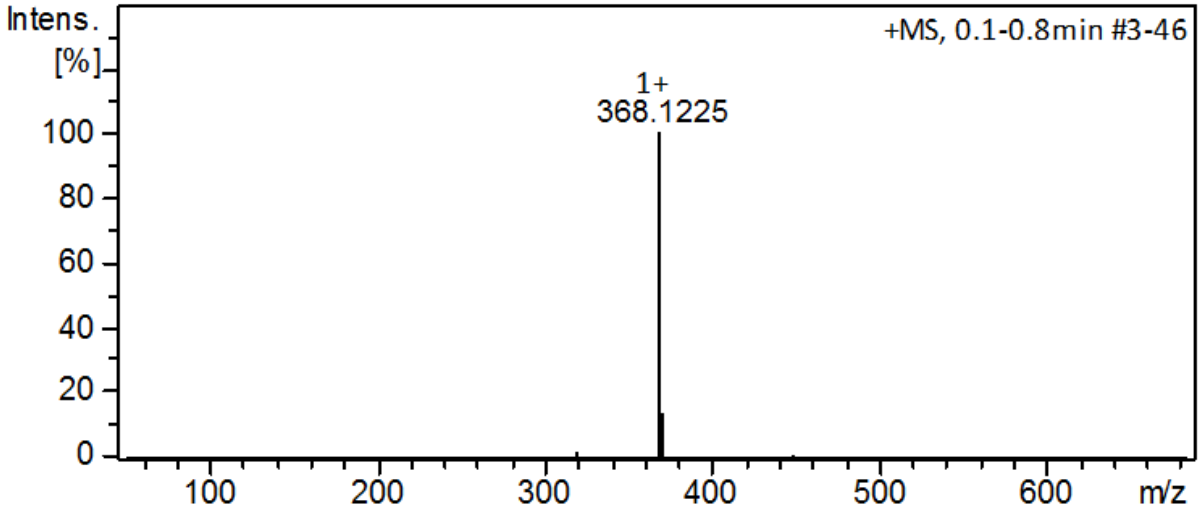


Figure S51. HRMS of compound **22**.

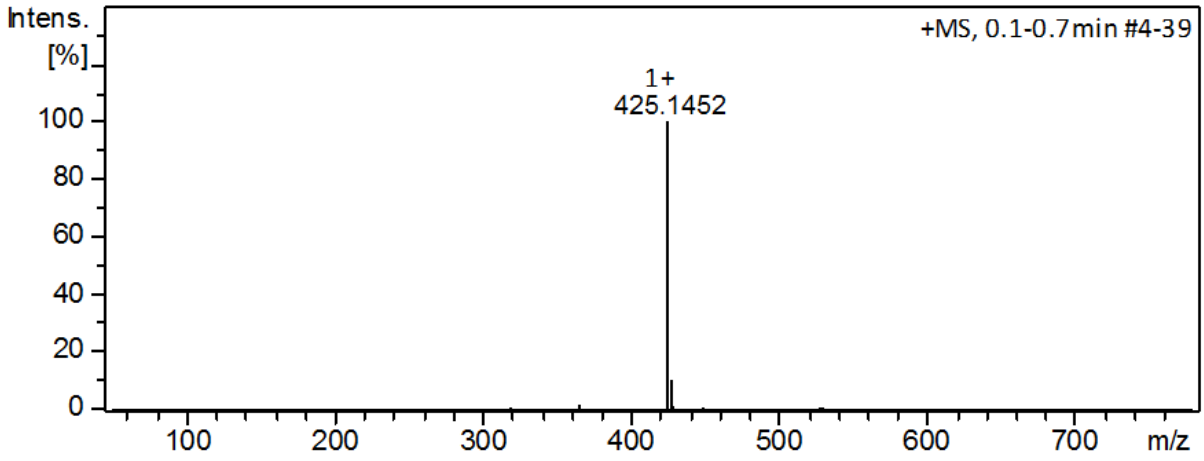


Figure S52. HRMS of compound **23.**

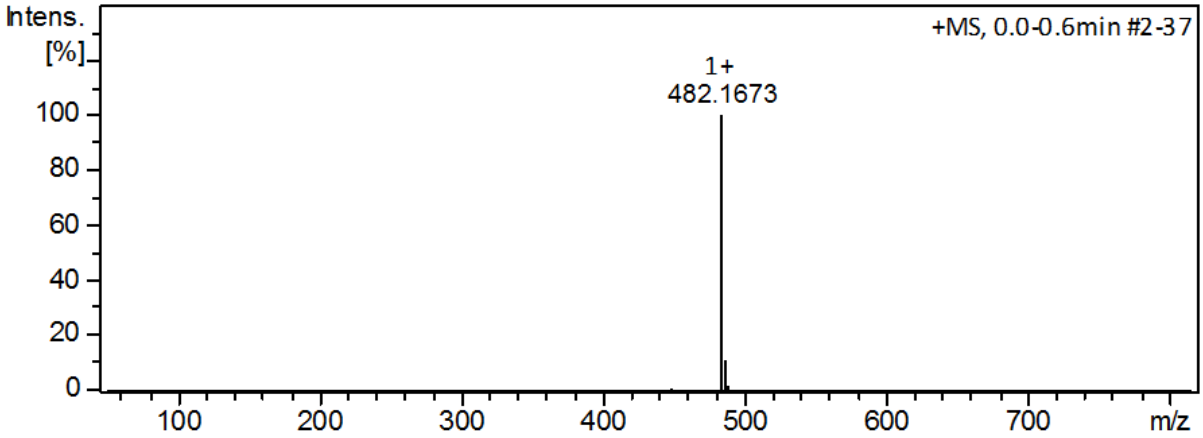


Figure S53. HRMS of compound **24.**

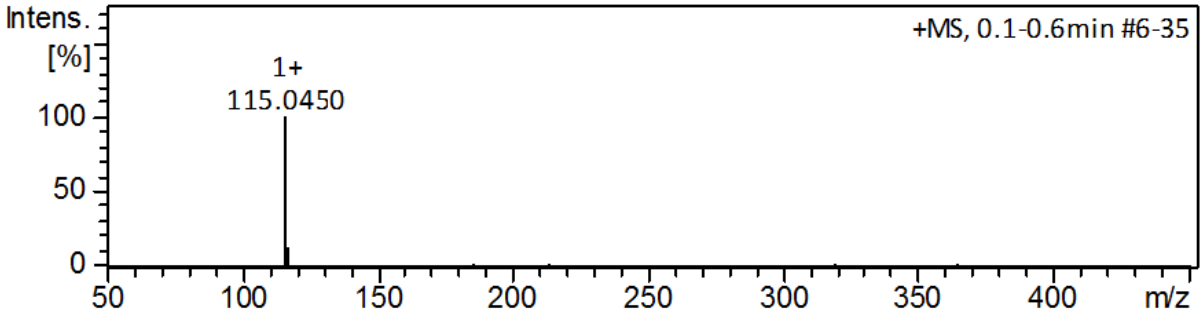


Figure S54. HRMS of deuterated uracil showing formation of uracil-d_3 (calcd *m/z* 115.0455, $[M+H]^+$).

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