Electronic supplementary materials *Mendeleev Commun*., 2018, **28**, 439–441

Chlorotrimethylsilane-promoted synthesis of 1,2,4-triazolopyrimidines from 3,5-diamino-1,2,4-triazoles and pentane-2,4-diones

Alexander V. Astakhov, Kyrill Yu. Suponitsky and Victor M. Chernyshev

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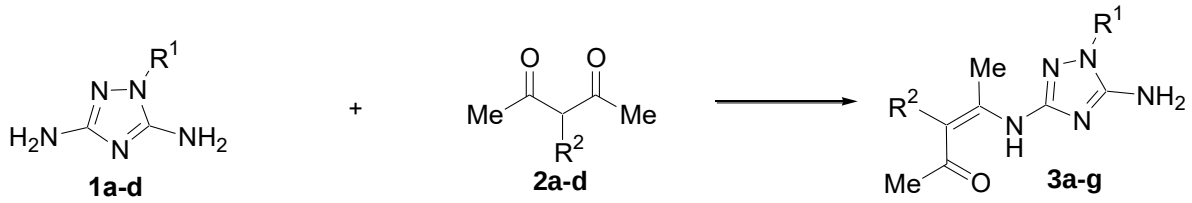
Table S1. Synthesis of enamino ketones **3a-g**

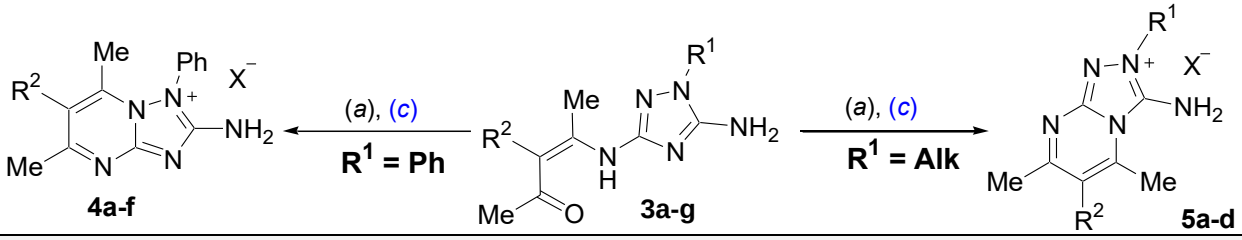


1a - R^1 = Ph; **1b** - R^1 = Bn;
1c - R^1 = 4-$ClC_6H_4CH_2$; **1d** - R^1 = *n*-Pr

2a - R^2 = H; **2b** - R^2 = Cl;
2c - R^2 = Me; **2d** - R^2 = *n*-Bu

Compounds **3**	R^1	R^2	Isolated yield, %
3a	Ph	H	84
3b	Ph	Cl	76
3c	Ph	Me	46
3d	Bn	H	71
3e	Bn	Cl	53
3f	4-$ClC_6H_4CH_2$	H	62
3g	4-$ClC_6H_4CH_2$	Cl	47

Table S2. Synthesis of compounds **4-5** by heterocyclization of enamino ketones **3a-g**



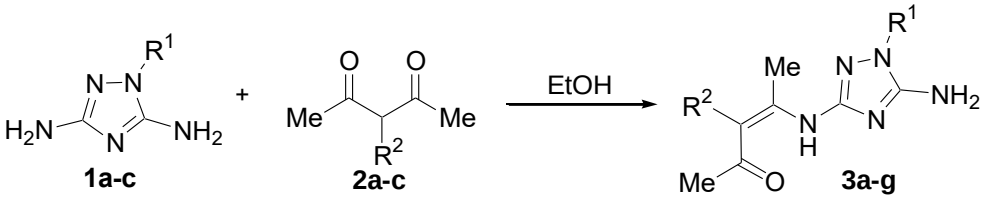
Compounds **4-5**	R^1	R^2	X^-	Isolated yield *(Method)*, %
4a	Ph	H	Br	64 (*a*)
4b	Ph	H	Cl	34 (*a*), 98 (*c*)
4c	Ph	Cl	Br	62 (*a*)
4d	Ph	Cl	Cl	36 (*a*), 93 (*c*)
4e	Ph	Me	Br	58 (*a*)
4f	Ph	Me	Cl	48 (*a*), 94 (*c*)
5a	Bn	H	Cl	32 (*a*), 87 (*c*)
5b	Bn	Cl	Cl	46 (*a*), 95 (*c*)
5c	4-$ClC_6H_4CH_2$	H	Cl	42 (*a*), 86 (*c*)
5d	4-$ClC_6H_4CH_2$	Cl	Cl	36 (*a*), 84 (*c*)

Synthetic procedures and characterization of isolated compounds

General Information

Melting points were determined in open capillary tubes in a Thiele apparatus and are uncorrected. ^{1}H and ^{13}C NMR spectra were recorded on a Bruker DRX 500 instrument at 500 MHz and 125 MHz in DMSO-d_6. ^{1}H and ^{13}C{1H} chemical shifts are given in ppm using TMS as an internal standard or relative to the residual peak of the solvent (δ 2.50 for DMSO-d_6) for the proton spectra and the ^{13}C{^{1}H} DMSO-d_6 signal (δ 39.52) for the carbon spectra. Mass spectra were recorded in the form of *m/z* (intensity relative to base 100) using electron impact ionization (70 eV). High resolution mass spectra (HRMS) were obtained on a TOF MS instrument using electrospray ionization (ESI) in positive ion mode (interface capillary voltage – 4500 V).

General procedure for the synthesis of compounds 3a-g.



A solution of the corresponding diaminotriazole **1a-c** (6 mmol) and 1,3-diketone **2a-c** (7.8 mmol) was refluxed in EtOH (3 ml) for 5 h, then water (1 ml) was added. After cooling, the resulting precipitate was collected by filtration and recrystallized from ethanol.

(3*Z*)-4-[(5-Amino-1-phenyl-1*H*-1,2,4-triazol-3-yl)amino]pent-3-en-2-one (3a). Yield 1.29 g (84%), colourless needles, mp 160-160.5 °C, R_f = 0.45. ^{1}H NMR *δ*, ppm (*J*, Hz): 2.02 (s., 3H, CH_3), 2.32 (s., 3H, CH_3), 5.29 (s., 1H, 3-C<u>H</u>), 6.62 (s., 2H, NH_2), 7.32-7.36 (m., 1H, Ph), 7.47-7.55 (m., 4H, Ph), 12.51 (s., 1H, NH). ^{13}C NMR *δ*, ppm: 21.2 (<u>C</u>H_3), 29.3 (<u>C</u>H_3), 99.3 (C-3 of penten-2-one), 122.4, 126.7, 129.4, 137.1 (carbons of Ph), 153.9, 155.4 (carbons of triazole), 157.5 (C-4 of penten-2-one), 196.4 (CO). HRMS (ESI) calcd for $C_{13}H_{16}N_5O$ $[M+H]^+$ 258.1349, found 258.1351.

(3*E*)-4-[(5-Amino-1-phenyl-1*H*-1,2,4-triazol-3-yl)amino]-3-chloropent-3-en-2-one (3b). Yield 1.33 g (76%), yellow-greenish needles, mp 164-165 °C, R_f = 0.47. ^{1}H NMR *δ*, ppm (*J*, Hz): 2.31 (s., 3H, CH_3), 2.60 (s., 3H, CH_3), 6.69 (s., 2H, NH_2), 7.34-7.37 (m., 1H, Ph), 7.48-7.55 (m., 4H, Ph), 12.83 (s., 1H, NH). ^{13}C NMR *δ*, ppm: 18.4 (<u>C</u>H_3), 28.9 (<u>C</u>H_3), 105.3 (C-3 of penten-2-one), 122.5, 126.9, 129.4, 136.9 (carbons of Ph), 154.0, 154.9, 155.6 (carbons of triazole and C-4 of penten-2-one), 194.8 (CO). HRMS (ESI) calcd for $C_{13}H_{15}ClN_5O$ $[M+H]^+$ 292.0960, found 292.0963.

(3*Z*)-4-[(5-Amino-1-phenyl-1*H*-1,2,4-triazol-3-yl)amino]-3-methylpent-3-en-2-one (3c). Yield 0.75 g (46%), colourless plates, mp 163-164 °C, R_f = 0.47. ^{1}H NMR *δ*, ppm (*J*, Hz): 1.88 (s., 3H, CH_3), 2.15 (s., 3H, CH_3), 2.40 (s., 3H, CH_3), 6.57 (s., 2H, NH_2), 7.31-7.35 (m., 1H, Ph), 7.47-7.54 (m., 4H, Ph), 13.43 (s., 1H, NH). ^{13}C NMR *δ*, ppm: 14.3 (<u>C</u>H_3), 17.1 (<u>C</u>H_3), 29.1 (<u>C</u>H_3), 102.7 (C-3 of penten-2-one), 122.3, 126.5, 129.4, 137.1 (carbons of Ph), 153.7, 154.9, 155.7 (carbons of triazole and C-4 of penten-2-one), 197.8 (CO). HRMS (ESI) calcd for $C_{14}H_{18}N_5O$ $[M+H]^+$ 272.1506, found 272.1504.

(3*Z*)-4-[(5-Amino-1-benzyl-1*H*-1,2,4-triazol-3-yl)amino]pent-3-en-2-one (3d). Yield 1.16 g (71%), colourless prisms, mp 140-141 °C, R_f = 0.44. NMR ^{1}H *δ*, ppm (*J*, Hz): 1.98 (s., 3H, CH_3), 2.24 (s., 3H, CH_3), 5.04 (s., 2H, CH_2), 5.21 (s., 1H, 3-CH), 6.49 (s., 2H, NH_2), 7.23-7.34 (m., 5H, Ph), 12.43 (s., 1H, NH). NMR ^{13}C *δ*, ppm: 20.9 (<u>C</u>H_3), 29.1 (<u>C</u>H_3), 48.8 (<u>C</u>H_2), 98.6 (C-3 of penten-2-one), 127.26, 127.31, 128.4, 136.9 (carbons of Ph), 154.5 (C-3′ of triazole), 154.8 (C-5′ of triazole), 157.6 (C-4 of penten-2-one), 195.9 (CO). HRMS (ESI) calcd for $C_{14}H_{18}N_5O$ $[M+H]^+$ 272.1506, found 272.1504.

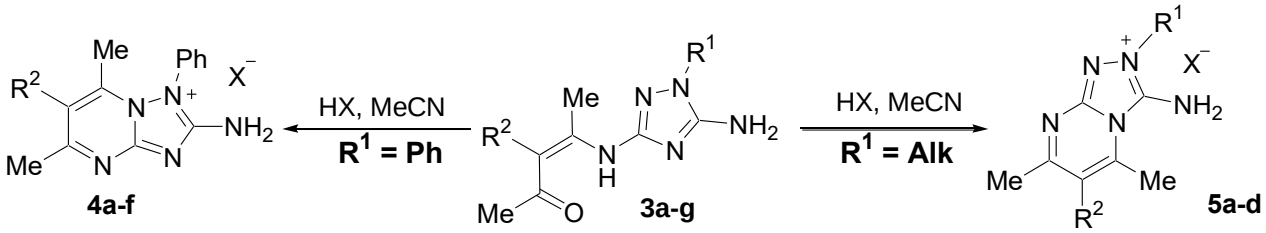
(3*E*)-4-[(5-Amino-1-benzyl-1*H*-1,2,4-triazol-3-yl)amino]-3-chloropent-3-en-2-one (3e). Yield 0.97 g (53%), yellow-greenish needles, mp 175-175.5 °C, R_f = 0.46. NMR ^{1}H *δ*, ppm (*J*, Hz): 2.27 (s., 3H, CH_3), 2.52 (s., 3H, CH_3), 5.06 (s., 2H, CH_2), 6.61 (s., 2H, NH_2), 7.21-7.36 (m., 5H, Ph), 12.85 (s., 1H, NH). NMR ^{13}C *δ*, ppm: 18.3 (<u>C</u>H_3), 28.8 (<u>C</u>H_3), 48.9 (<u>C</u>H_2), 104.8 (C-3 of penten-2-one), 127.3, 127.3, 128.5, 136.8 (carbons of Ph), 154.0 (C-3′ of triazole), 154.9 (C-5′ of triazole), 155.9 (C-4 of penten-2-one), 194.3 (CO). HRMS (ESI) calcd for $C_{14}H_{17}ClN_5O$ $[M+H]^+$ 306.1116, found 306.1118.

(3*Z*)-4-{[5-Amino-1-(4-chlorobenzyl)-1*H*-1,2,4-triazol-3-yl]amino}pent-3-en-2-one (3f). Yield 1.13 g (62%), colorless prisms, mp 162-164 °C, R_f = 0.44. NMR ^{1}H δ, ppm (*J*, Hz): 1.98 (s., 3H, CH_3), 2.23 (s., 3H, CH_3), 5.03 (s., 2H, CH_2), 5.22 (s., 1H, 3-CH), 6.55 (s., 2H, NH_2), 7.23-7.25 (m., 2H, Ar), 7.40-7.42 (m., 2H, Ar), 12.44 (s., 1H, NH). NMR ^{13}C δ, ppm: 21.0 ($\underline{C}H_3$), 29.2 ($\underline{C}H_3$), 48.2 ($\underline{C}H_2$), 98.7 (C-3 of penten-2-one), 128.5, 129.2, 132.1, 136.0 (carbons of Ph), 154.7 (C-3′ of triazole), 154.9 (C-5′ of triazole), 157.6 (C-4 of penten-2-one), 196.0 (CO). HRMS (ESI) calcd for $C_{14}H_{17}ClN_5O$ $[M+H]^+$ 306.1116, found 306.1118.

(3*E*)-4-{[5-Amino-1-(4-chlorobenzyl)-1*H*-1,2,4-triazol-3-yl]amino}-3-chloropent-3-en-2-one (3g). Yield 0.96 g (47%), colorless prisms, mp 183-184°C, R_f = 0.43. NMR ^{1}H δ, ppm (*J*, Hz): 2.28 (s., 3H, CH_3), 2.52 (s., 3H, CH_3), 5.06 (s., 2H, CH_2), 6.64 (s., 2H, NH_2), 7.25 (d., *J*=8.2, 2H, Ar), 7.42 (d., *J*=8.2, 2H, Ar), 12.85 (s., 1H, NH). NMR ^{13}C δ, ppm: 18.3 ($\underline{C}H_3$), 28.8 ($\underline{C}H_3$), 48.2 ($\underline{C}H_2$), 104.8 (C-3 of penten-2-one), 128.5, 129.2, 132.1, 135.8 (carbons of Ph), 154.2 (C-3′ of triazole), 154.9 (C-5′ of triazole), 155.8 (C-4 of penten-2-one), 194.4 (CO). HRMS (ESI) calcd for $C_{14}H_{16}Cl_2N_5O$ $[M+H]^+$ 340.0726, found 340.0726.

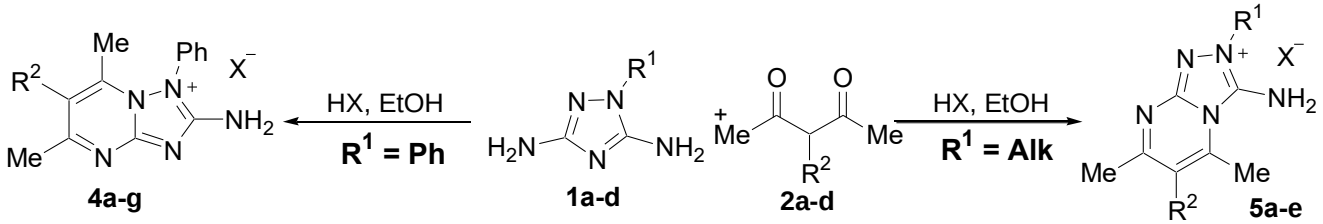
General procedure for the synthesis of compounds 4a-g and 5a-e.

Method (a)



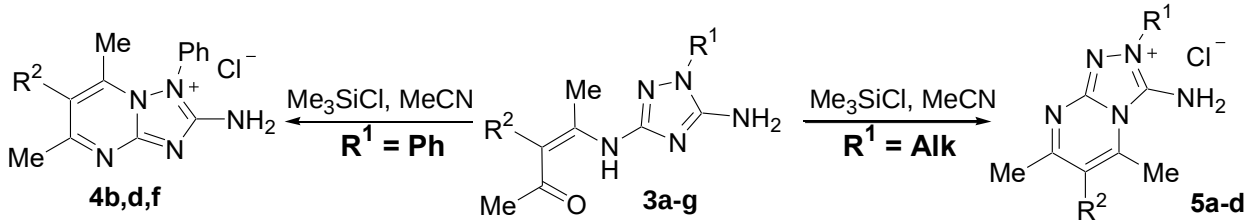
A mixture of compound **3a-g** (1.17 mmol) and 36% HCl (0.154 g, 1.521 mmol) or 40% HBr (0.308 g, 1.521 mmol) in MeCN (4 ml) was refluxed for 2 min, then evaporated to a small volume (1-2 ml), diluted with Et_2O (4 ml) and cooled to 0-5 °C. The product precipitated was collected by filtration and recrystallized from MeCN.

Method (b)



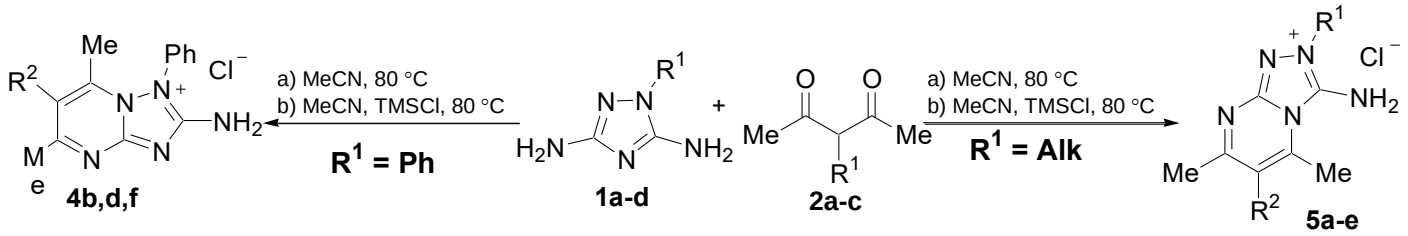
A solution of diaminotriazole **1a-d** (2.85 mmol), diketone **2a-c** (3.71 mmol), and 36% HCl (0.376 g, 3.71 mmol) or 40% HBr (0.750 g, 3.71 mmol) in EtOH (4 ml) was refluxed for 30 min, then evaporated to a small volume (1-2 ml), diluted with Et_2O (4 ml) and cooled to 0-5 °C. The product precipitated was collected by filtration and recrystallized from MeCN.

Method (c)



A mixture of compound **3a-g** (1.17 mmol), MeCN (2.5 ml) and TMSCl (0.255 g, 2.34 mmol) was refluxed for 2 min, then evaporated to a small volume (~1 ml), diluted with Et_2O (2 ml) and cooled to 0-5 °C. The product precipitated was collected by filtration and recrystallized from MeCN.

Method (d)



A mixture of diaminotriazole **1a-d** (2.85 mmol), diketone **2a-c** (3.71 mmol), and MeCN (4 ml) was refluxed for 5 h, then volatiles were evaporated in *vacuo*. Dry MeCN (4 ml) was added to the residue, the mixture was heated to dissolution, then TMSCl (0.621 g, 5.7 mmol) was added and the mixture was refluxed for 2-3 min. The mixture was evaporated to a small volume (~2 ml), diluted with Et_2O (4 ml) and cooled to 0-5 °C. The product precipitated was collected by filtration and recrystallized from MeCN.

2-Amino-5,7-dimethyl-1-phenyl[1,2,4]triazolo[1,5-*a*]pyrimidin-1-ium bromide (4a). Yield 240 mg (64%, *method (a)*), 582 mg (64%, *method (b)*), colorless prisms, mp 223-224 °C. NMR ^{1}H δ, ppm (*J*, Hz): 1.98 (s., 3H, CH_3), 2.59 (s., 3H, CH_3), 7.29 (s., 1H, CH), 7.69-7.87 (m., 5H, Ph), 8.36 (s., 2H, NH_2). NMR ^{13}C δ, ppm: 17.7 (7-$\underline{C}H_3$), 24.4 (5-$\underline{C}H_3$), 113.6 (C-6), 130.1, 130.3, 132.2, 132.7 (carbons of Ph), 147.9 (C-7), 153.9, 159.8 (carbons of triazole), 170.5 (C-5). HRMS (ESI) calcd for $C_{13}H_{14}N_5$ $[M\text{-}Br^-]^+$ 240.1244, found 240.1250.

2-Amino-5,7-dimethyl-1-phenyl[1,2,4]triazolo[1,5-*a*]pyrimidin-1-ium chloride (4b). Yield 109 mg (34%, *method (a)*), 250 mg (32%, *method (b)*), 317 mg (98%, *method (c)*), 725 mg (92%, *method (d)*), colourless prisms, mp 214-216 °C. NMR ^{1}H δ, ppm (*J*, Hz): 1.96 (s., 3H, CH_3), 2.60 (s., 3H, CH_3), 7.26 (CH), 7.68-7.85 (m., 5H, Ph), 8.45 (s., 2H, NH_2). NMR ^{13}C δ, ppm: 17.7 (7-$\underline{C}H_3$), 24.4 (5-$\underline{C}H_3$), 113.6 (C-6), 130.2, 130.4, 132.3, 132.7 (carbons of Ph), 147.9 (C-7), 154.0, 159.9 (carbons of triazole), 170.5 (C-5). HRMS (ESI) calcd for $C_{13}H_{14}N_5$ $[M\text{-}Cl^-]^+$ 240.1244, found 240.1241.

2-Amino-6-chloro-5,7-dimethyl-1-phenyl[1,2,4]triazolo[1,5-*a*]pyrimidin-1-ium bromide (4c). Yield 256 mg (62%, *method (a)*), 378 mg (37%, *method (b)*), yellowish prisms, mp 145-146 °C. NMR ^{1}H δ, ppm (*J*, Hz): 2.12 (s., 3H, CH_3), 2.73 (s., 3H, CH_3), 7.70-7.82 (m., 5H, Ph), 8.59 (s., 2H, NH_2). NMR ^{13}C δ, ppm: 16.0 (7-$\underline{C}H_3$), 24.5 (5-$\underline{C}H_3$), 119.6 (C-6), 129.6, 130.7, 132.5, 132.7 (carbons of Ph), 146.5 (C-7), 152.4, 160.7 (carbons of triazole), 168.2 (C-5). HRMS (ESI) calcd for $C_{13}H_{13}ClN_5$ $[M\text{-}Br^-]^+$ 274.0854, found 274.0851.

2-Amino-6-chloro-5,7-dimethyl-1-phenyl[1,2,4]triazolo[1,5-*a*]pyrimidin-1-ium chloride (4d). Yield 130 mg (36%, *method (a)*), 284 mg (32%, *method (b)*), 337 mg (93%, *method (c)*), 804 mg (91%, *method (d)*), yellowish prisms, mp 127-128 °C. NMR ^{1}H δ, ppm (*J*, Hz): 2.11 (s., 3H, CH_3), 2.73 (s., 3H, CH_3), 7.68-7.81 (m., 5H, Ph), 8.64 (s., 2H, NH_2). NMR ^{13}C δ, ppm: 16.0 (7-$\underline{C}H_3$), 24.5 (5-$\underline{C}H_3$), 119.5 (C-6), 129.5, 130.6, 132.6, 132.7 (carbons of Ph), 146.5 (C-7), 152.5, 160.8 (carbons of triazole), 168.2 (C-5). HRMS (ESI) calcd for $C_{13}H_{13}ClN_5$ $[M\text{-}Cl^-]^+$ 274.0854, found 274.0847.

2-Amino-5,6,7-trimethyl-1-phenyl[1,2,4]triazolo[1,5-*a*]pyrimidin-1-ium bromide (4e). Yield 226 mg (58%, *method (a)*), 572 mg (60%, *method (b)*), colourless prisms, mp 148-150 °C. NMR ^{1}H δ, ppm (*J*, Hz): 2.01 (s., 3H, CH_3), 2.22 (s., 3H, CH_3), 2.64 (s., 3H, CH_3), 7.66-7.78 (m., 5H, Ph), 8.38 (s., 2H, NH_2). NMR ^{13}C δ, ppm: 13.6 ($\underline{C}H_3$), 15.4 ($\underline{C}H_3$), 24.5 ($\underline{C}H_3$), 120.1 (C-6), 129.0, 130.5, 132.2, 133.8 (carbons of Ph), 146.2 (C-7), 152.9, 160.9 (carbons of triazole), 170.6 (C-5). HRMS (ESI) calcd for $C_{14}H_{16}N_5$ $[M\text{-}Br^-]^+$ 254.1400, found 254.1400.

2-Amino-5,6,7-trimethyl-1-phenyl[1,2,4]triazolo[1,5-*a*]pyrimidin-1-ium chloride (4f). Yield 162 mg (48%, *method (a)*), 447 mg (54%, *method (b)*), 318 mg (94%, *method (c)*), 720 mg (87%, *method (d)*), colorless prisms, mp 133-134 °C. NMR ^{1}H δ, ppm (*J*, Hz): 2.01 (s., 3H, CH_3), 2.22 (s., 3H, CH_3), 2.64 (s., 3H, CH_3), 7.66-7.78 (m., 5H, Ph), 8.38 (s., 2H, NH_2). NMR ^{13}C δ, ppm: 13.5 ($\underline{C}H_3$), 15.3 ($\underline{C}H_3$), 24.5 ($\underline{C}H_3$), 121.0 (C-6), 129.0, 130.5, 132.1, 133.9 (carbons of Ph), 146.2 (C-7), 153.0, 160.9 (carbons of triazole), 170.6 (C-5). HRMS (ESI) calcd for $C_{14}H_{16}N_5$ $[M\text{-}Cl^-]^+$ 254.1400, found 254.1403.

2-Amino-6-butyl-5,7-dimethyl-1-phenyl[1,2,4]triazolo[1,5-*a*]pyrimidin-1-ium bromide (4g). Yield 524 mg (49%, *method (b)*), colourless prisms, mp 143-144 °C. NMR ^{1}H δ, ppm (*J*, Hz): 0.87-0.91 (m., 3H, $C\underline{H}_3$ of Bu), 1.35-1.37 (m., 4H, $2C\underline{H}_2$), 2.01 (s., 3H, CH_3), 2.60-2.65 (m., 2H, CH_2), 2.67 (s., 3H, CH_3), 7.66-7.80 (m., 5H, Ph), 8.36 (s., 2H, NH_2). NMR ^{13}C δ, ppm: 13.7 ($\underline{C}H_3$ of Bu), 15.0 (7-$\underline{C}H_3$), 22.0 ($\underline{C}H_2$), 23.8

(5-$\underline{C}H_3$), 26.7 ($\underline{C}H_2$), 30.6 ($\underline{C}H_2$), 124.0 (C-6), 129.3, 130.5, 132.2, 133.7 (carbons of Ph), 146.5 (C-7), 152.8, 160.7 (carbons of triazole), 170.2 (C-5). HRMS (ESI) calcd for $C_{17}H_{22}N_5$ $[M\text{-}Br^-]^+$ 296.1870, found 296.1863.

3-Amino-2-benzyl-5,7-dimethyl[1,2,4]triazolo[4,3-*a*]pyrimidin-2-ium chloride (5a). Yield 109 mg (32%, *method (a)*), 312 mg (38%, *method (b)*), 295 mg (87%, *method (c)*), 678 mg (82%, *method (d)*), colourless prisms, mp 215-217 °C. HRMS (ESI) calcd for $C_{14}H_{16}N_5$ $[M\text{-}Cl^-]^+$ 254.1400, found 254.1404. ^1H and ^{13}C NMR spectra are identical to the described in the literature.[1]

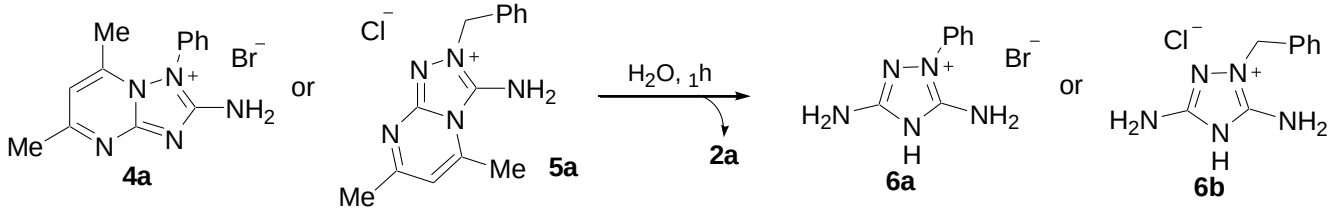
3-Amino-2-benzyl-6-chloro-5,7-dimethyl[1,2,4]triazolo[4,3-*a*]pyrimidin-2-ium chloride (5b). Yield 175 mg (46%, *method (a)*), 387 mg (42%, *method (b)*), 360 mg (95%, *method (c)*), 850 mg (92%, *method (d)*), colourless prisms, mp 211-214 °C. HRMS (ESI) calcd for $C_{14}H_{15}ClN_5$ $[M\text{-}Cl^-]^+$ 288.1010, found 288.1010. ^1H and ^{13}C NMR spectra are identical to the described in the literature.[1]

3-Amino-2-(4-chlorobenzyl)-5,7-dimethyl[1,2,4]triazolo[4,3-*a*]pyrimidin-2-ium chloride (5c). Yield 158 mg (42%, *method (a)*), 334 mg (36%, *method (b)*), 325 mg (86%, *method (c)*), 720 mg (78%, *method (d)*), colourless prisms, mp 233-234 °C. NMR ^1H δ, ppm (*J*, Hz): 2.44 (s., 3H, CH_3), 2.84 (s., 3H, CH_3), 5.73 (s., 2 H, CH_2), 6.82 (s., 1H, CH), 7.45 (d., *J*=8.5, 2H, Ar), 7.51 (d., *J*=8.5, 2H, Ar), 9.05 (s., 2H, NH_2). NMR ^{13}C δ, ppm: 18.1 (5-$\underline{C}H_3$), 25.0 (7-$\underline{C}H_3$), 50.3 ($\underline{C}H_2$), 111.7 (C-6), 128.5, 130.3, 133.0, 133.3 (carbons of Ar), 144.3 (C-3), 146.1 (C-5), 147.9 (C-8a), 169.9 (C-7). HRMS (ESI) calcd for $C_{14}H_{15}ClN_5$ $[M\text{-}Cl^-]^+$ 288.1010, found 288.1016.

3-Amino-6-chloro-2-(4-chlorobenzyl)-5,7-dimethyl[1,2,4]triazolo[4,3-*a*]pyrimidin-2-ium chloride (5d). Yield 150 mg (36%, *method (a)*), 350 mg (34%, *method (b)*), 351 mg (84%, *method (c)*), 770 mg (75%, *method (d)*), colourless prisms, mp 223-224 °C. NMR ^1H δ, ppm (*J*, Hz): 2.58 (s., 3H, CH_3), 2.97 (s., 3H, CH_3), 5.75 (s., 2H, CH_2), 7.45-7.51 (m., 5H, Ar), 9.23 (s., 2H, NH_2). NMR ^{13}C δ, ppm: 15.8 (5-$\underline{C}H_3$), 24.9 (7-$\underline{C}H_3$), 50.5 ($\underline{C}H_2$), 118.2 (C-6), 128.6, 130.3, 133.0, 133.1 (carbons of Ar), 143.2 (C-5), 144.5 (C-3), 145.6 (C-8a), 167.0 (C-7). HRMS (ESI) calcd for $C_{14}H_{14}Cl_2N_5$ $[M\text{-}Cl^-]^+$ 322.0621, found 322.0628.

3-Amino-5,7-dimethyl-2-propyl[1,2,4]triazolo[4,3-*a*]pyrimidin-2-ium chloride (5e). Yield 318 mg (46%, *method (b)*), 496 mg (72%, *method (d)*), colourless plates, mp 208-210 °C. NMR ^1H δ, ppm (*J*, Hz): 0.94 (t., *J*=7.4, 3H, $C\underline{H}_3$ of Pr), 1.76-1.84 (m., 2H, $C\underline{H}_2$), 2.45 (s., 3H, CH_3), 2.84 (s., 3H, CH_3), 4.30 (t., *J*=7.1, 2H, 2-$C\underline{H}_2$), 6.82 (s., 1H, 6-CH), 8.69 (s., 2H, NH_2). NMR ^{13}C δ, ppm: 10.5 ($\underline{C}H_3$ of Pr), 18.1 (5-$\underline{C}H_3$), 21.3 ($\underline{C}H_2$), 24.9 (7-$\underline{C}H_3$), 49.5 (2-$\underline{C}H_2$), 111.7 (C-6), 143.9 (C-3), 145.9 (C-5), 147.6 (C-8a), 169.5 (C-7). HRMS (ESI) calcd for $C_{10}H_{16}N_5$ $[M\text{-}Cl^-]^+$ 206.1400, found 206.1399.

Procedure for the hydrolysis of compound 4a and 5a



A suspension of compound **4a** (320 mg, 1 mmol) or **5a** (290 mg, 1 mmol) in water (5 ml) was refluxed for 1 h. The solvent was evaporated *in vacuo* and the residue was recrystallized from propan-2-ol (0.5 ml) to give compounds **6a** or **6b**.

3,5-Diamino-1-phenyl-1*H*-1,2,4-triazol-4-ium bromide (6a). Yield 223 mg (87%), colourless prisms, mp 248-249 °C. ^1H and ^{13}C NMR spectra are identical to the described in the literature.[2]

3,5-Diamino-1-benzyl-1*H*-1,2,4-triazol-4-ium chloride (6b). Yield 190 mg (84%), colourless prisms, mp 229-230 °C. NMR ^1H δ, ppm (*J*, Hz): 5.12 (s., 2H, CH_2), 6.60 (br. s., 2H, 3-NH_2), 7.28-7.36 (m., 5H, Ph), 8.43 (s., 2H, 5-NH_2). NMR ^{13}C δ, ppm: 49.4 ($\underline{C}H_2$) 127.91, 127.9, 128.6, 135.3 (carbons of Ph), 147.9 (C-5), 150.5 (C-3). MS, *m/z* (*I*, %): 189 ($[M\text{-}Cl]^+$, 69), 98 (13), 91 (100), 70 (34), 65 (15), 43 (32), 38 (14).

References

1. A. V. Astakhov and V. M. Chernyshev, *Chem. Heterocycl. Compd.*, 2012, **48**, 1417

2. V. M. Chernyshev; A. V. Astakhov; V. V. Ivanov; Z. A. Starikova. *Acta Crystallographica Sec. E*, 2010, **66**, o1644.

Detailed results of quantum chemical calculations

Computational details

Quantum chemical calculations were performed using the Gaussian'09 suite of computational programs[1] at the DFT B3LYP/6-311++G(2d,2p) level of theory with the options Opt = Tight and Int=(Grid=199974).[2] The solvent effects were modeled by the integral equation formalism version of the polarizable continuum model (IEF-PCM) developed by Tomasi.[3] The character of the stationary points on the potential energy surface (local minimum) was confirmed by calculation of the Hessian matrix at the same level of theory within the harmonic approximation. All optimized geometries had only real frequencies.

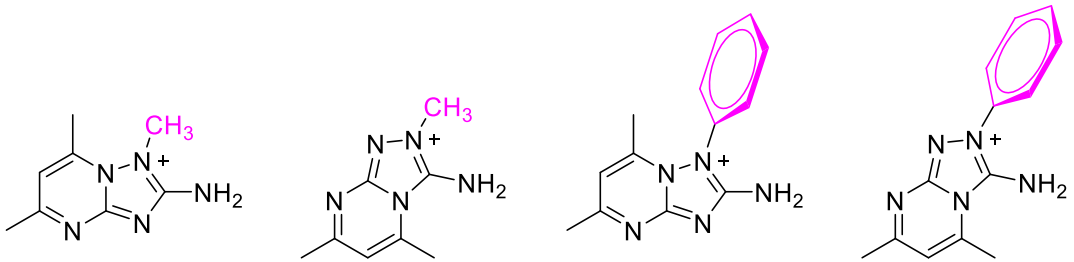
References

[1] M. J. Frisch, G. W. Trucks, H. B. Schlegel, G. E. Scuseria, M. A. Robb, J. R. Cheeseman, G. Scalmani, V. Barone, B. Mennucci, G. A. Petersson, H. Nakatsuji, M. Caricato, X. Li, H. P. Hratchian, A. F. Izmaylov, J. Bloino, G. Zheng, J. L. Sonnenberg, M. Hada, M. Ehara, K. Toyota, R. Fukuda, J. Hasegawa, M. Ishida, T. Nakajima, Y. Honda, O. Kitao, H. Nakai, T. Vreven, J. A. Montgomery Jr., J. E. Peralta, F. Ogliaro, M. J. Bearpark, J. Heyd, E. N. Brothers, K. N. Kudin, V. N. Staroverov, R. Kobayashi, J. Normand, K. Raghavachari, A. P. Rendell, J. C. Burant, S. S. Iyengar, J. Tomasi, M. Cossi, N. Rega, N. J. Millam, M. Klene, J. E. Knox, J. B. Cross, V. Bakken, C. Adamo, J. Jaramillo, R. Gomperts, R. E. Stratmann, O. Yazyev, A. J. Austin, R. Cammi, C. Pomelli, J. W. Ochterski, R. L. Martin, K. Morokuma, V. G. Zakrzewski, G. A. Voth, P. Salvador, J. J. Dannenberg, S. Dapprich, A. D. Daniels, Ö. Farkas, J. B. Foresman, J. V. Ortiz, J. Cioslowski, D. J. Fox, *Gaussian 09, Revision D.01* Gaussian, Inc., Wallingford, CT, USA (2009).

[2] a) A. D. Becke, *The Journal of Chemical Physics* **1993**, *98*, 5648-5652; b) C. Lee, W. Yang, R. G. Parr, *Phys. Rev. B* **1988**, *37*, 785-789.

[3] a) S. M. Bachrach, John Wiley & Sons, Inc., **2014**, p. 632 p; b) G. Scalmani, M. J. Frisch, *J. Chem. Phys.* **2010**, *132*, 114110; c) J. Tomasi, B. Mennucci, R. Cammi, *Chem. Rev.* **2005**, *105*, 2999-3094.

Table S3. Total energies (*E*), zero point energies (*ZPE*), thermal corrections to Gibbs free energies (G_T^{298}) and relative energies[a] (ΔG^0 and ΔG^{298}), equilibrium constants (*K*), relative populations (*x*)[b] and dipole moments (μ) of the isomers 4-A and 5-A or 4-B and 5-B at 0 and 298 K calculated at the B3LYP 6-311++G(2d,2p)



Tautomer	*E*, a.u	*ZPE*, kcal/mol	G_T^{298}, kcal/mol	ΔE, kcal/mol	ΔG^0, kcal/mol	ΔG^{298}, kcal/mol	ΔG^0, kJ/mol	ΔG^{298}, kJ/mol	*K*(eq)	*x*, %	μ, D
				Gas phase (ε = 1)							
4-A	-585.783268	129.55	105.26	0.00	0.00	0.00	0.00	0.00	1.0	97.2	5.84
5-A	-585.779645	129.21	105.08	2.27	1.93	2.10	8.09	8.76	$2.9\cdot10^{-2}$	2.8	6.74
4-B	-777.579748	161.93	135.23	0.00	0.00	0.00	0.00	0.00	1.0	100.0	3.71
5-B	-777.572013	162.29	135.30	4.85	5.22	4.93	21.85	20.62	$2.4\cdot10^{-4}$	$2.4\cdot10^{-2}$	6.77
				Aqueous solution (IEF-PCM, ε = 78.4)							
4-A	-585.861811	129.44	104.94	0.00	0.00	0.00	0.00	0.00	1.00	97.2	8.55
5-A	-585.859640	129.54	105.67	1.36	1.46	2.10	6.14	8.77	$2.9\cdot10^{-2}$	2.8	9.55
4-B	-777.651320	162.10	134.41	0.00	0.00	0.00	0.00	0.00	1.00	99.8	5.30
5-B	-777.646246	162.25	134.94	3.18	3.34	3.71	13.98	15.54	$1.9\cdot10^{-3}$	0.19	10.11

[a] Relative Gibbs Free Energies ΔG^0 and ΔG^{298} were computed from the relationships $\Delta G^0 = \Delta E + ZPE$ and $\Delta G^{298} = \Delta E + G_T^{298}$

[b] The values of *x* were calculated by means of equation: $x = \frac{K_i}{\sum_{i=1}^{n} K_i}$, where $K_i = e^{-\Delta G^{298}/RT}$ is constant of equilibrium between the tautomer *i* and that of the lowest energy, ΔG^{298} is the difference between the Gibbs free energies of these tautomers at 298 K (*T* = 298 K), and *R* is the universal gas constant.

Cartesian coordinates for computed structures

B3LYP 6-311++G(2d,2p) fully optimized geometries, given in standard XYZ format: coordinates are Cartesian coordinates in the usual order, units are ångströms, first line indicates total number of atoms, second line is structure number and calculation options.

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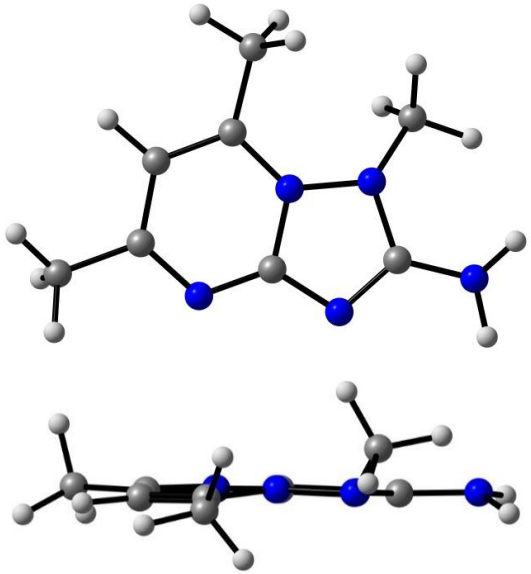

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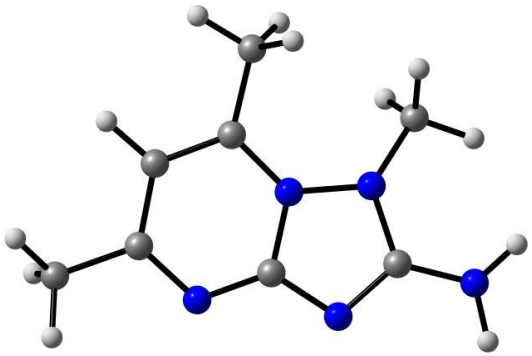

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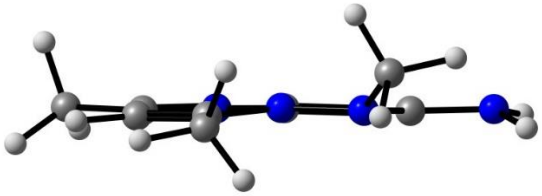

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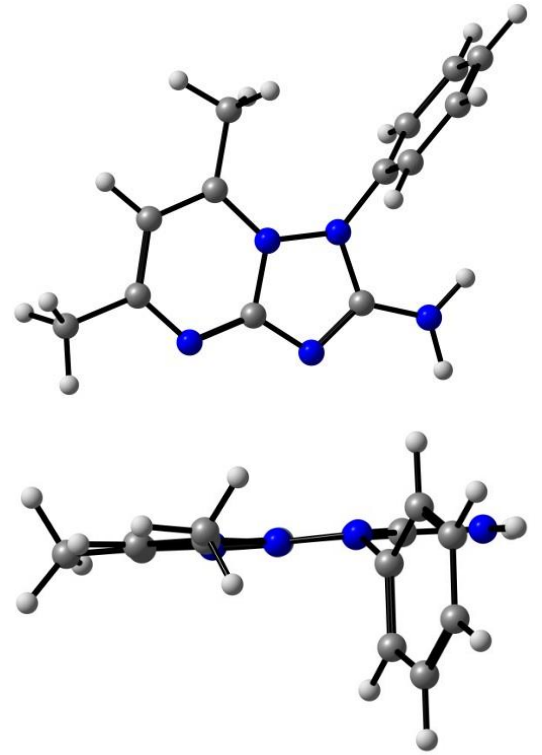

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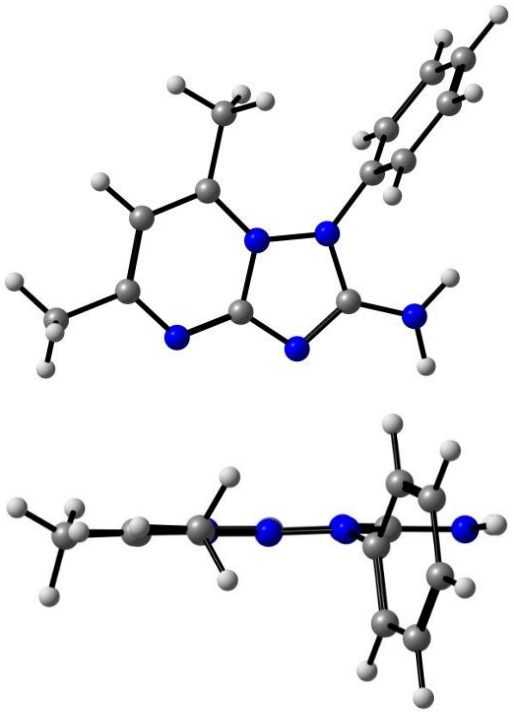

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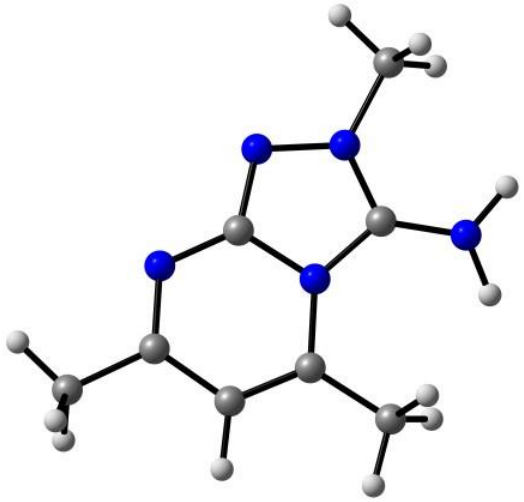

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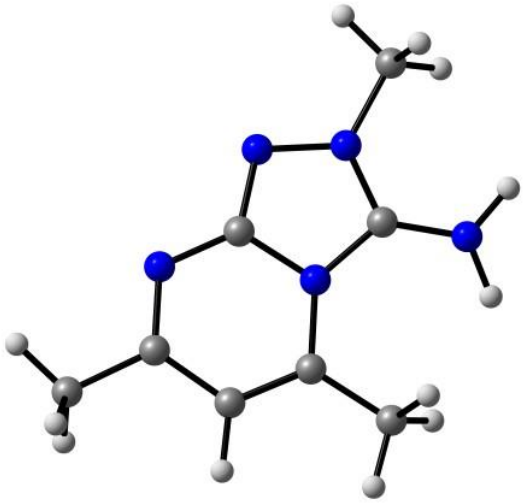

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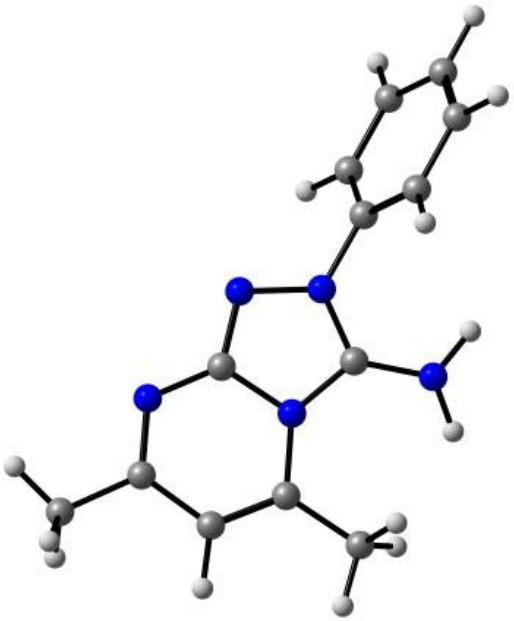

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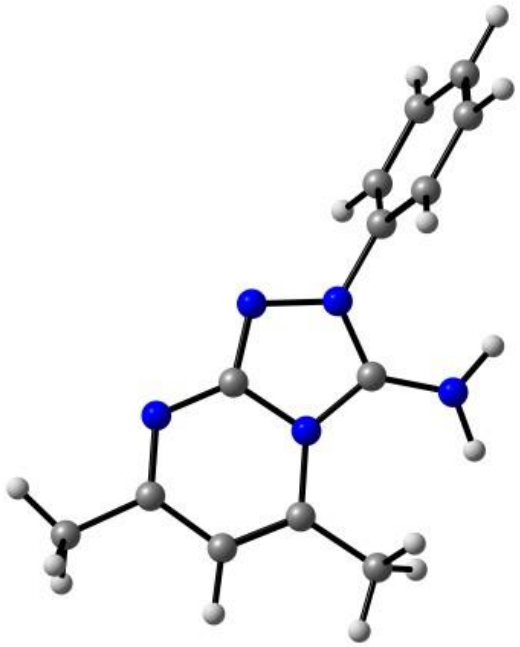


X-Ray investigations

X-ray single-crystal diffraction data for compounds 3a and 4g

Experimental

Single crystals of compounds **3a** and **4g** were obtained by slow evaporation of their solutions in C_2H_5OH and CH_3CN, respectively. X-ray experiments were carried out using SMART APEX2 CCD (λ(Mo-Kα)=0.71073 Å, graphite monochromator, *ω*-scans). Collected data were analyzed by the SAINT и SADABS programs incorporated into the APEX2 program package.[1] All structures were solved by the direct methods and refined by the full-matrix least-squares procedure against F^2 in anisotropic approximation. The refinement was carried out with the SHELXTL program.[2] The details of data collection and crystal structures refinement are summarized in Table S4. CCDC (numbers 1519403 and 1519405 for compounds **3a** and **4g**, respectively) contains the supplementary crystallographic data for this paper. These data can be obtained free of charge via www.ccdc.cam.ac.uk/data_request/cif.

In molecule **3a** (Fig. S1), due probably to sterical reasons, the phenyl ring is rotated relative to the central triazole ring so that torsion angle C7-N1-C1-C2 is equal to -37.3(2)°. At the same time, fragment of penten-2-one (N5-C10-C11-C12-O1) is nearly coplanar to the triazole. However length of the N5-C8 bond (1.382(2)Å) indicates almost no conjugation between those moieties due probably to formation of peudoaromatic six-membered H-bonded cycle. Mean *X*-ray lengths for corresponding C-N bond are 1.394 and 1.355Å for pyramidal and planar configuration of the nitrogen atom, correspondingly.[3] Conjugation between the amino group and triazole ring is more pronounced (N4-C7 bond length is 1.350(2)Å) in spite of pyramidal configuration of the N4 atom.

Upon a transition to bromide **4g** (Fig. S2), the acceptor ability of the central bicycle increases relative to that of triazole in **3a**, and, as consequence, the amino group becomes planar and its conjugation with the bicycle becomes stronger (N5-C1 bond length is 1.320(2)Å). As in the case of compound **3a**, the phenyl ring in **4g** are also not coplanar to the central bicycle (torsion angle C1-N1-C7-C12 is 74.1(2)°).

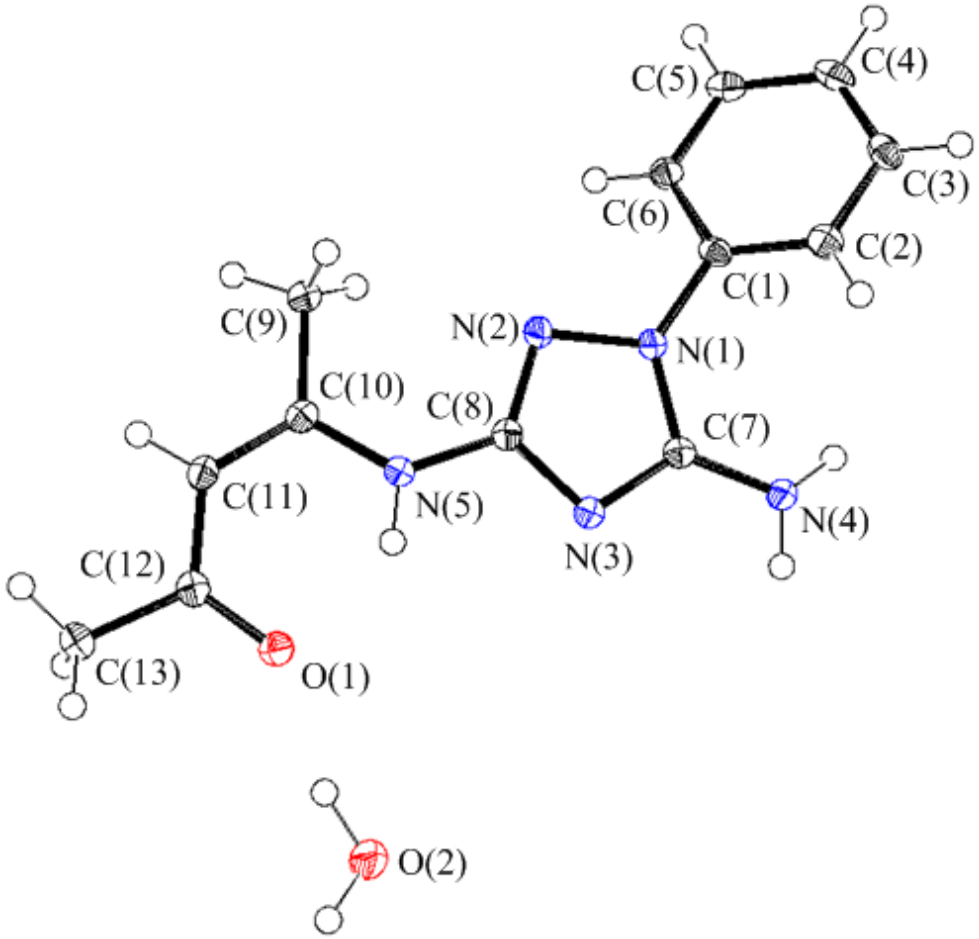


Figure S1. General view of the molecular structure of compound **3a**. Thermal ellipsoids are drawn at the 50% probability level.

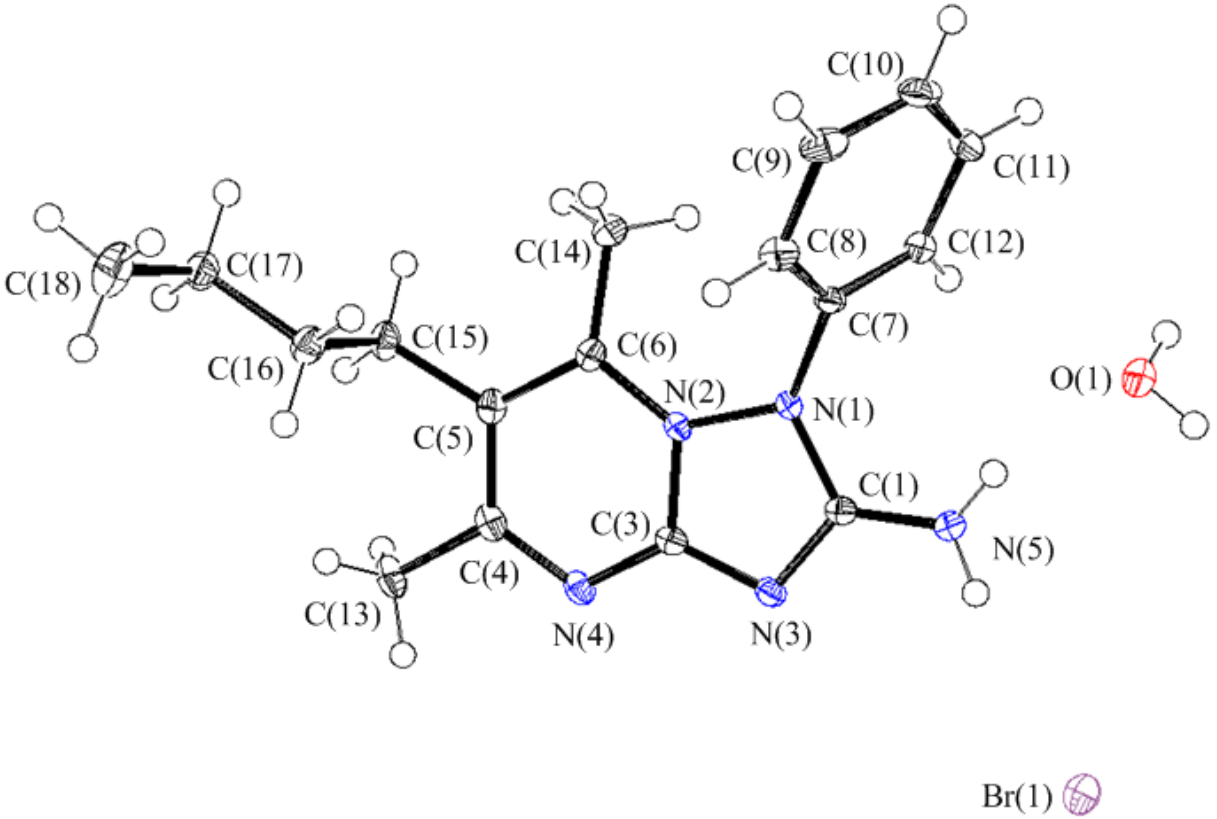


Figure S2. General view of the cation of compound **4g**. Thermal ellipsoids are drawn at the 50% probability level.

Table S4. Crystallographic data for compounds **3a** and **4g**.

	3a	**4g**
Empirical formula	$C_{13}H_{15}N_5O\ H_2O$	$C_{17}H_{22}N_5^+\ Br^-\ H_2O$
Fw	275.32	394.32
Temperature, K	100	100
Crystal system	Monoclinic	Monoclinic
Space group	$P2_1/n$	$P2_1/c$
a, Å	7.3708(14)	11.6895(7)
b, Å	21.614(4)	9.5654(6)
c, Å	8.4421(16)	16.1360(9)
β, deg	97.968(3)	95.7650(10)
V, Å^3	1331.9(4)	1795.12(19)
Z	4	4
ρ_{calc}, g·cm^{-3}	1.373	1.459
F(000)	584	816
μ, mm^{-1}	0.097	2.304
θ range, deg.	1.88 – 27.00	2.48 – 30.00
Reflections collected	13364	22369
Independent reflections / R_{int}	2872/ 0.0227	5242/0.0267
Completeness to theta θ, %	98.6	99.9
GOF (F^2)	1.018	1.023
Reflections with $I>2\sigma(I)$	2576	4603
$R_1(F)$ ($I>2\sigma(I)$)[a]	0.0352	0.0231
$wR_2(F^2)$ (all data)[b]	0.0949	0.0602
Largest dif. peak/hole, *e*·Å^{-3}	0.260 / -0.294	0.431 / -0.438

[a] $R_1 = \sum||F_o| - |F_c||/\sum(F_o)$; [b] $wR_2 = (\sum[w(F_o^2 - F_c^2)^2]/\sum[w(F_o^2)^2]^{½}$

References

1. *APEX2*, Bruker AXS Inc., Madison, Wisconsin, USA, **2009**.
2. Sheldrick, G.M. *Acta Cryst*, **2008**, *A64*, 112.
3. Allen, F. H.; Kennard, O.; Watson, D. G.; Brammer, L.; Orpen, A. G.; Taylor, R. *J. Chem. Soc., Perkin Trans. 2*, **1987**, S1.

HRMS and NMR spectra

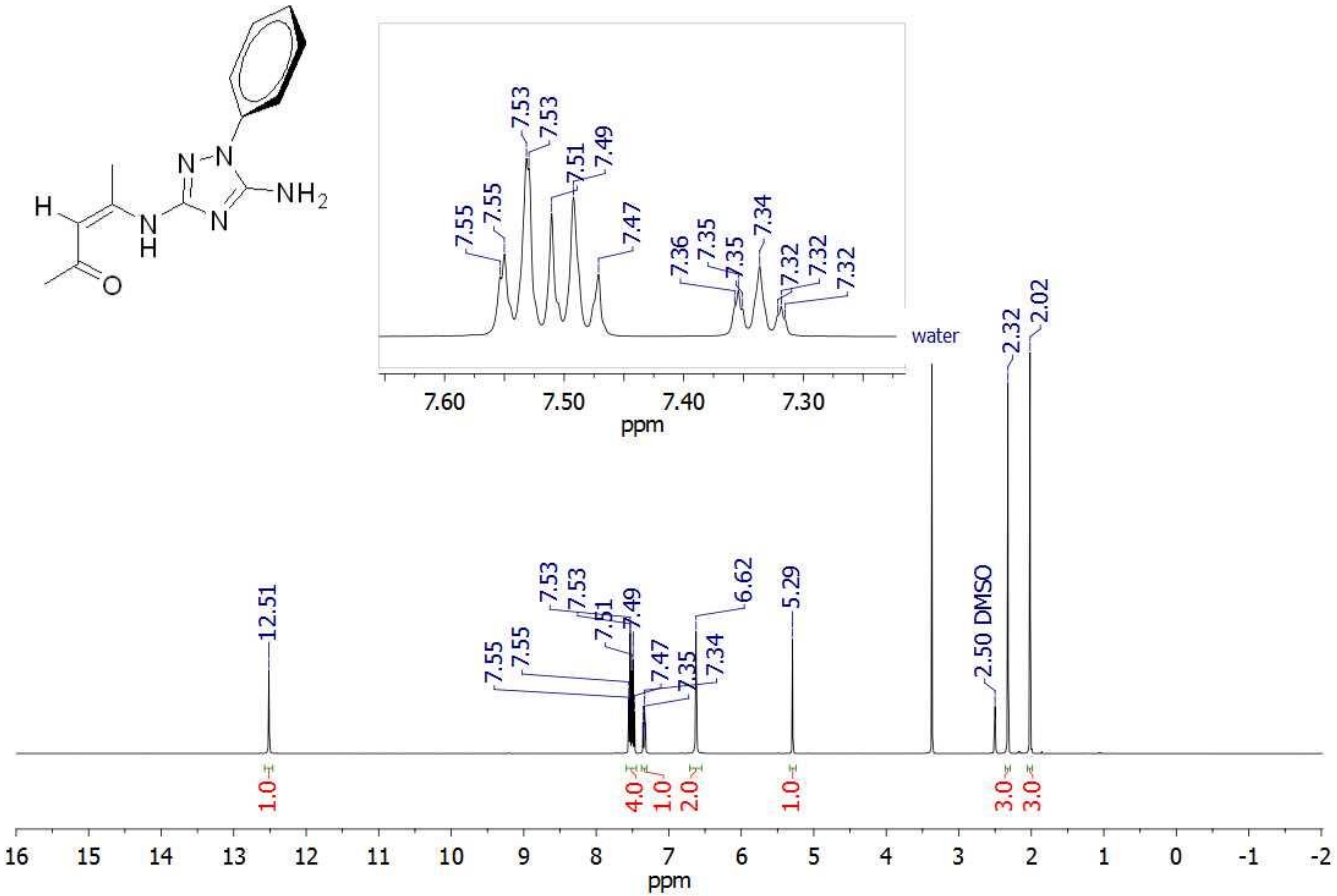


Figure S3. ^{1}H NMR spectrum of compound **3a** (DMSO-d_6)

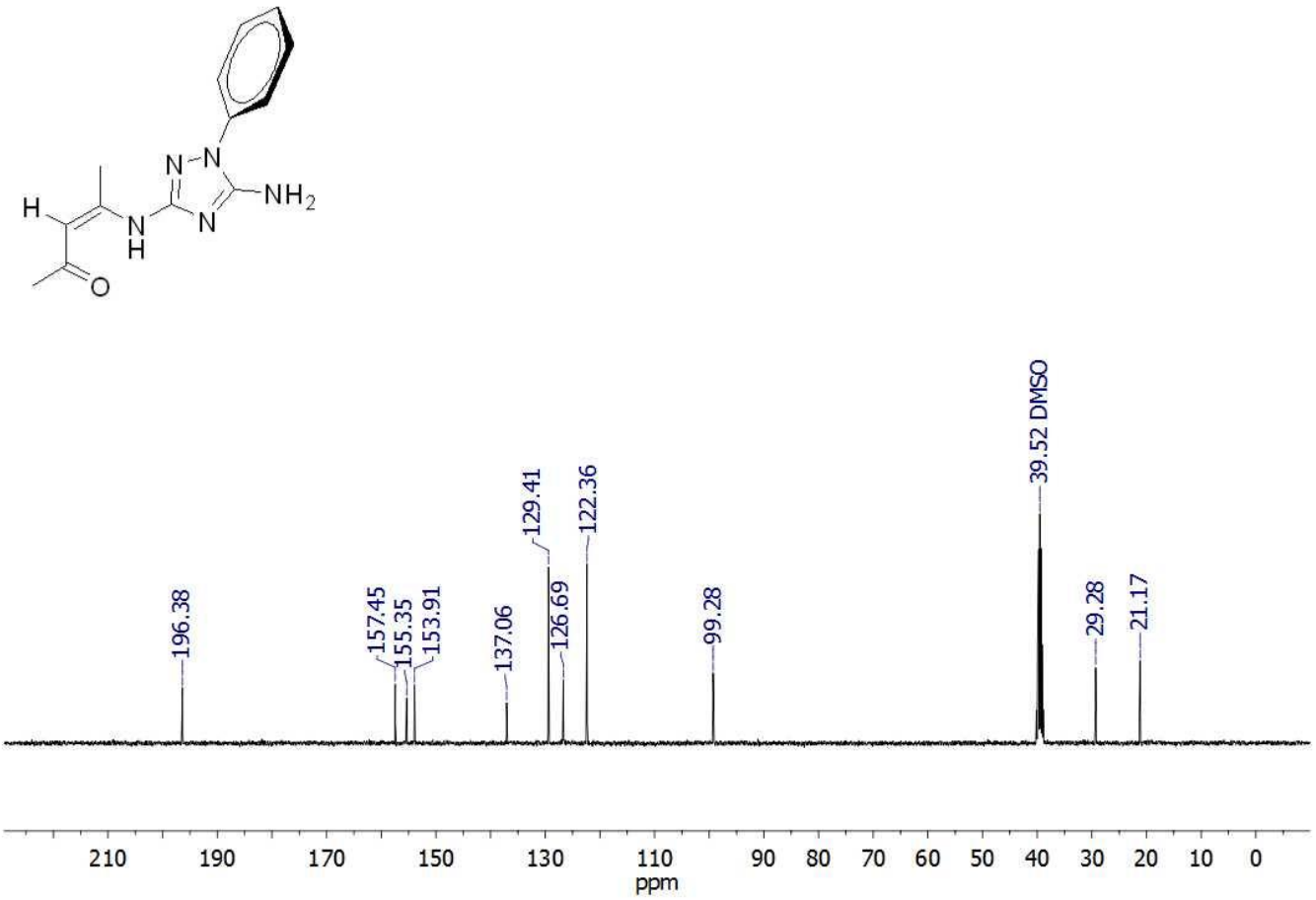


Figure S4. ^{13}C NMR spectrum of compound **3a** (DMSO-d_6)

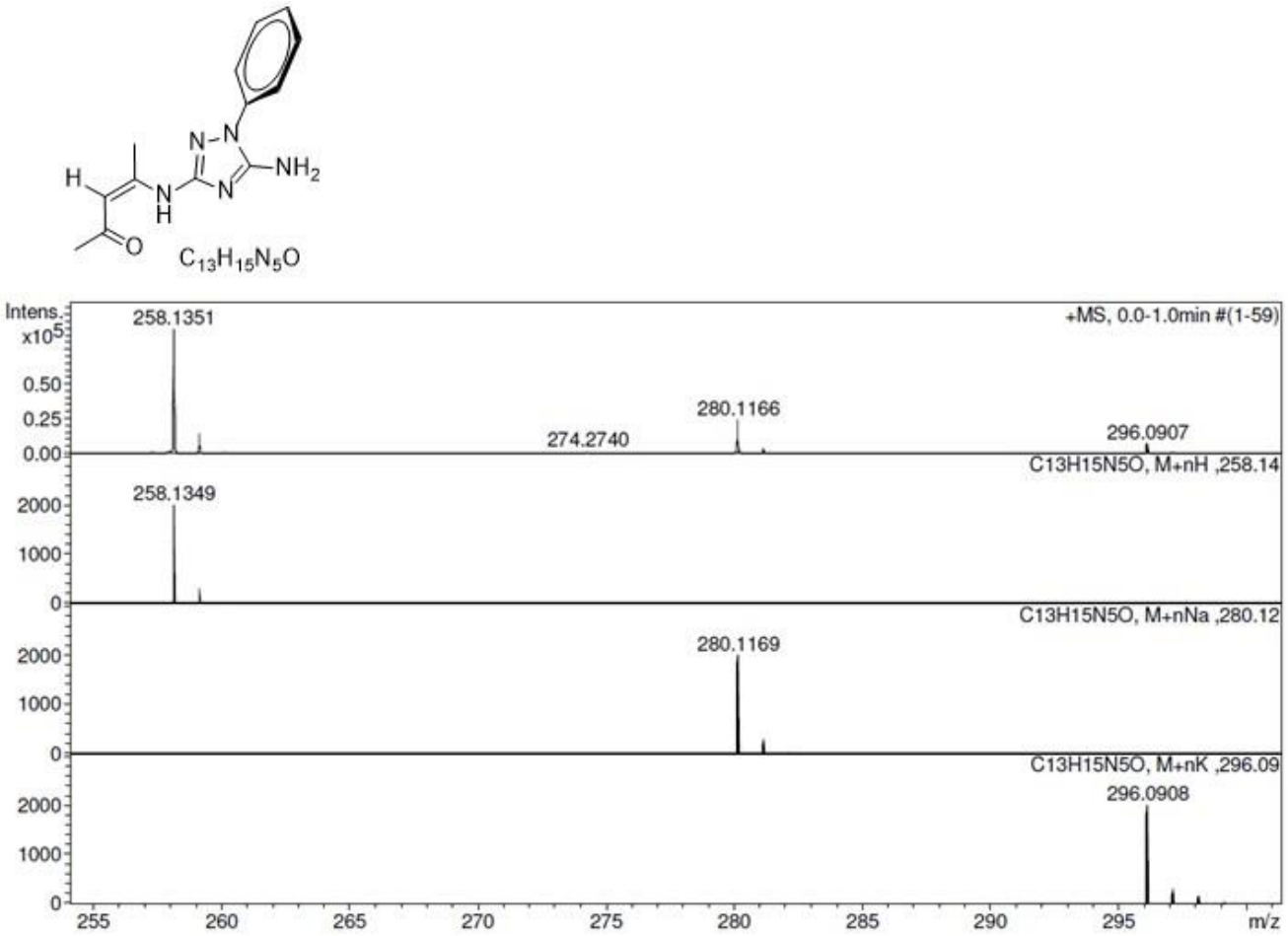


Figure S5. HRMS (ESI^+) of compound **3a**

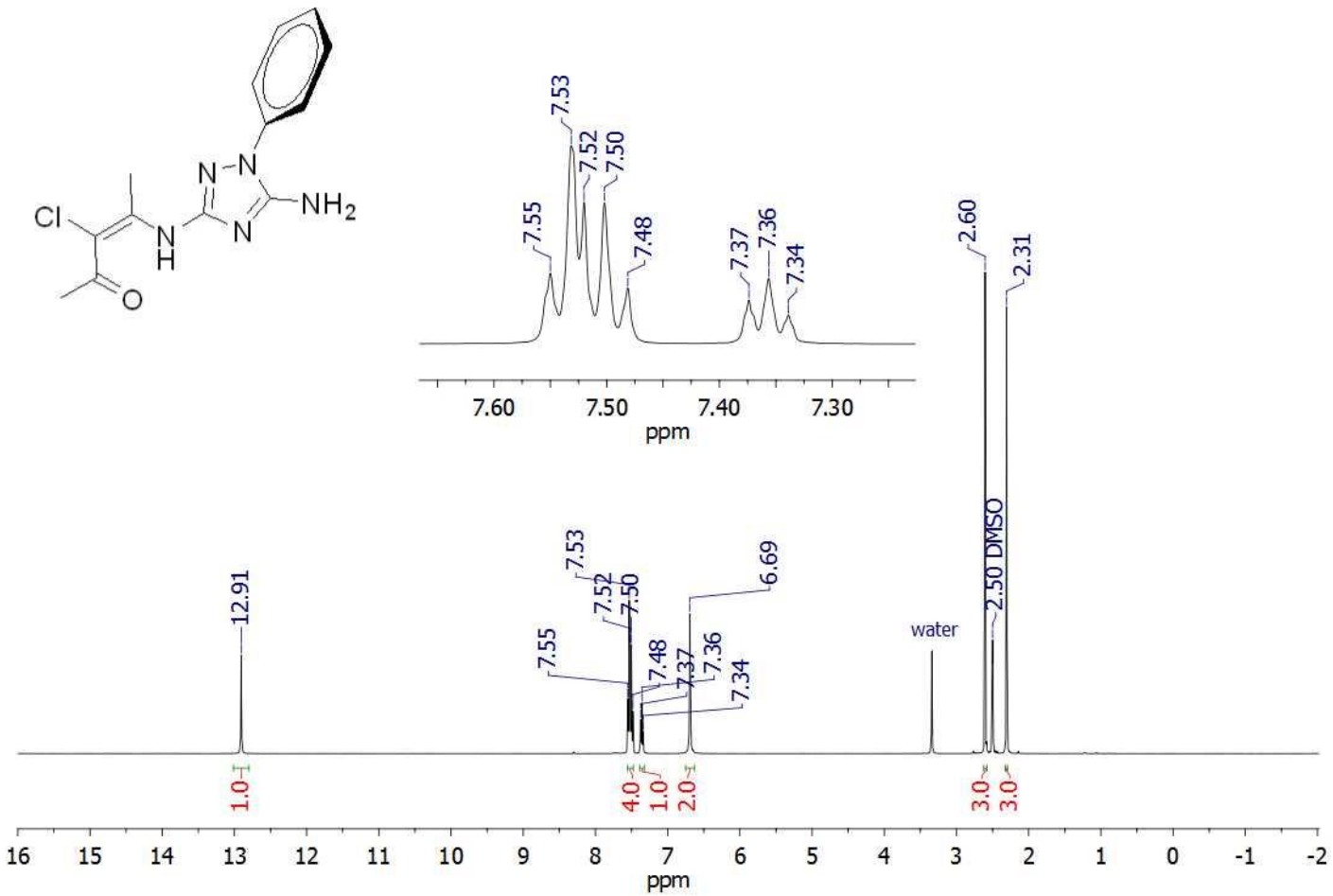


Figure S6. ^{1}H NMR spectrum of compound **3b** (DMSO-d_6)

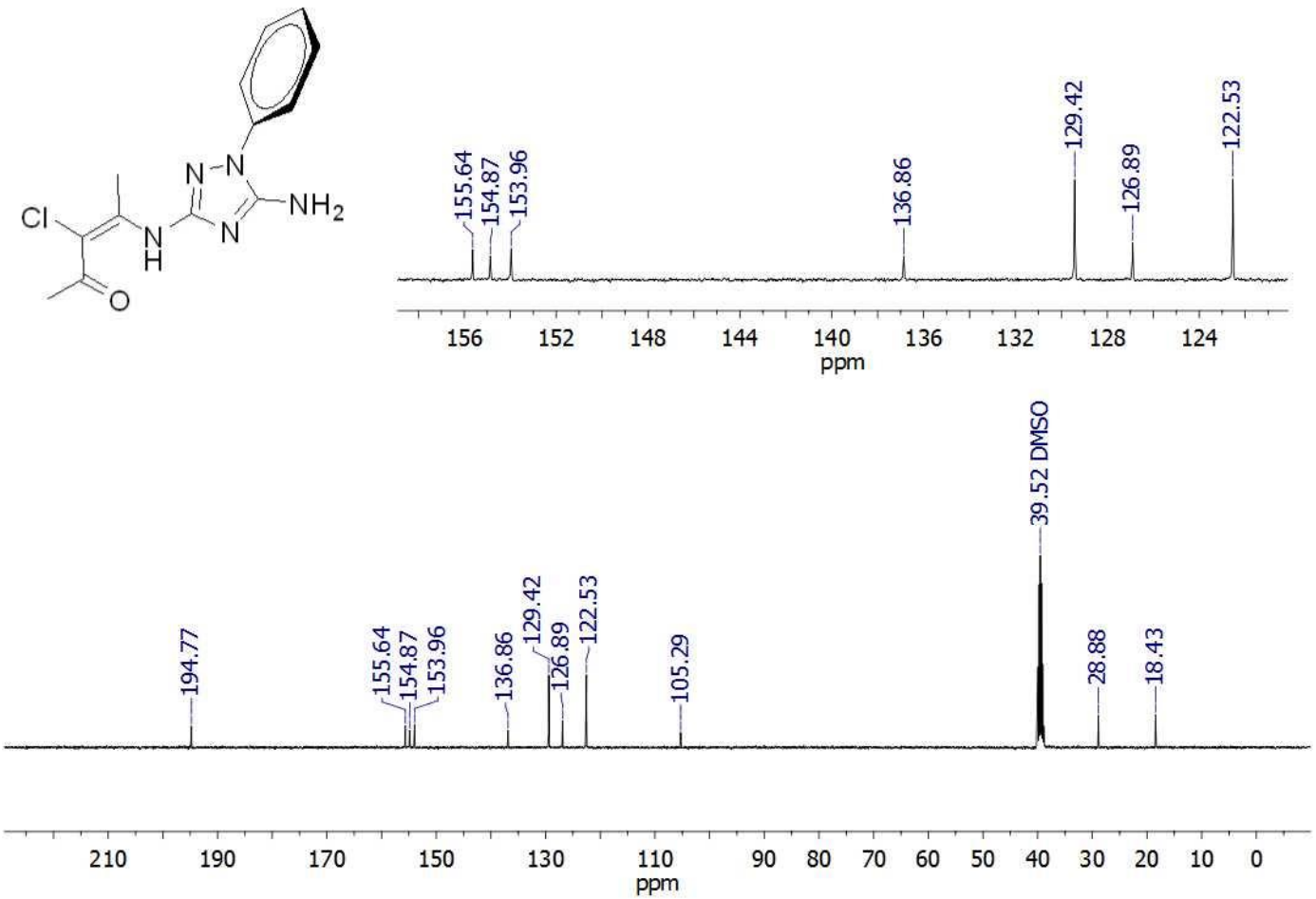
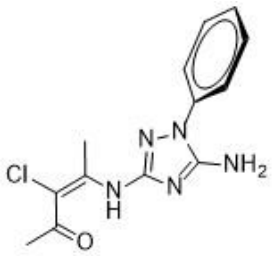


Figure S7. ^{13}C NMR spectrum of compound **3b** (DMSO-d_6)



Chemical Formula: $C_{13}H_{14}ClN_5O$

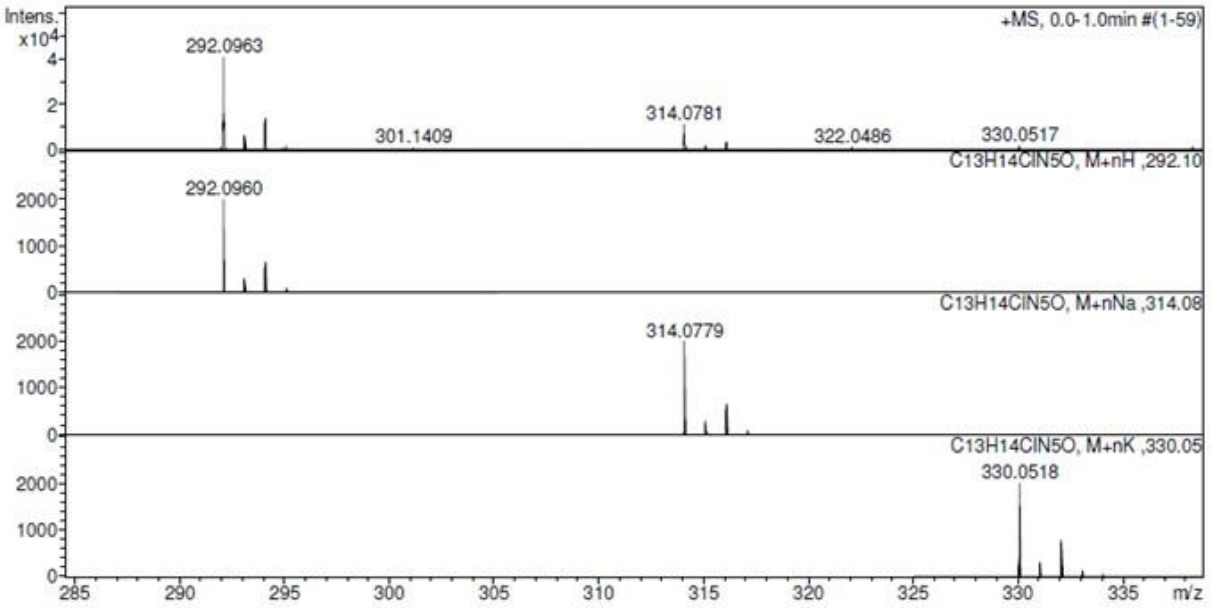


Figure S8. HRMS (ESI^+) of compound **3b**

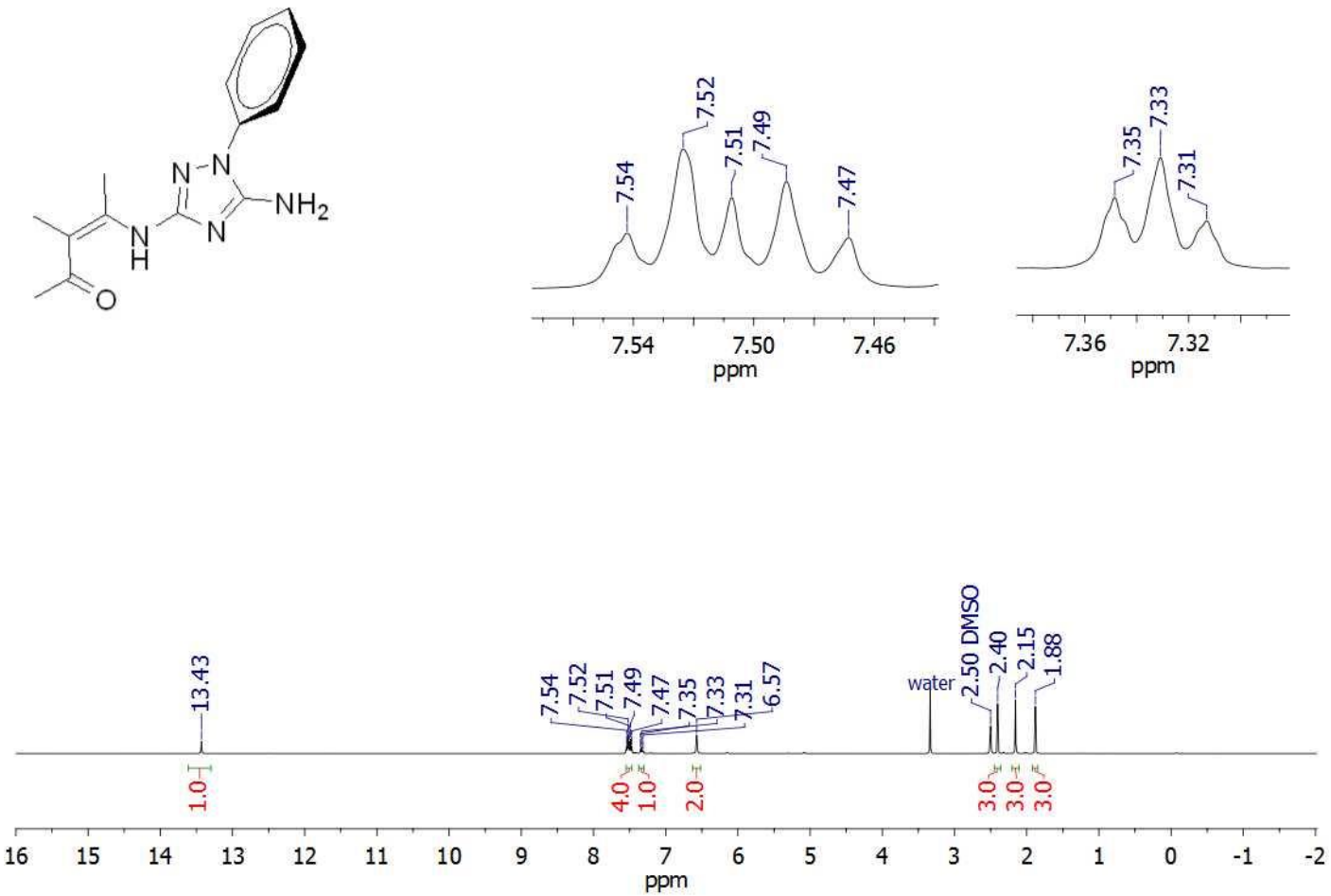


Figure S9. ^{1}H NMR spectrum of compound **3c** (DMSO-d_6)

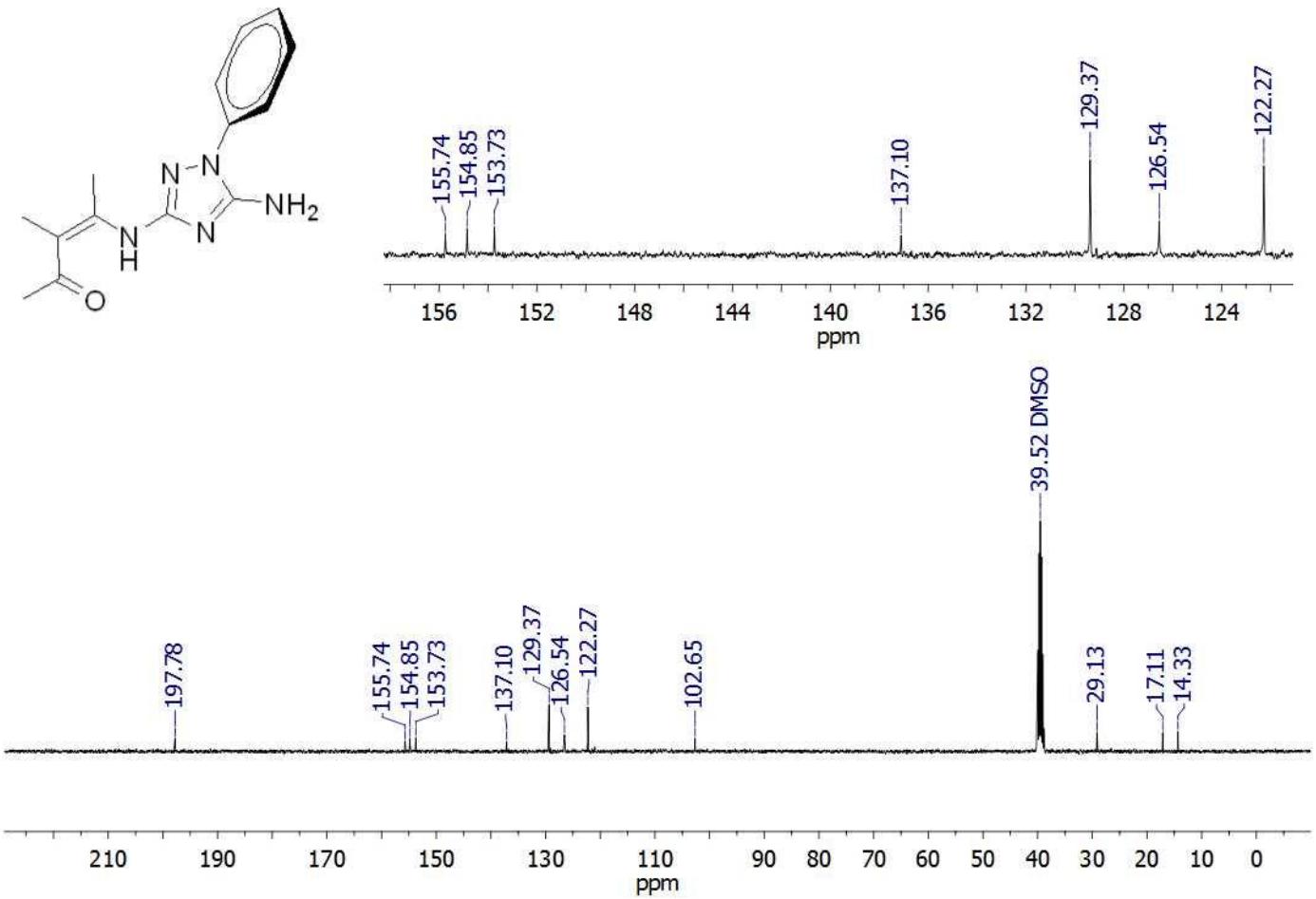


Figure S10. ^{13}C NMR spectrum of compound **3c** (DMSO-d_6)

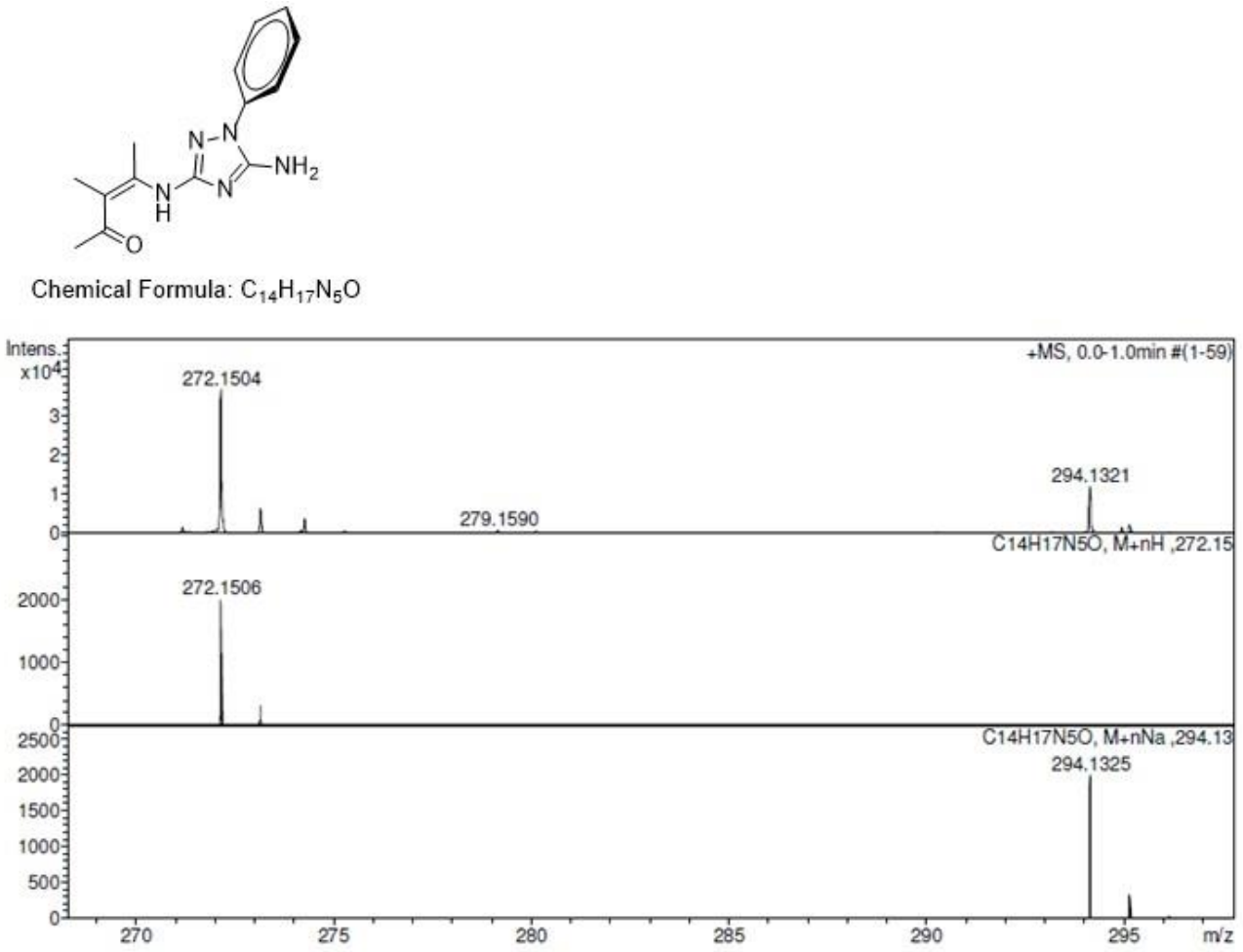


Figure S11. HRMS (ESI^+) of compound **3c**

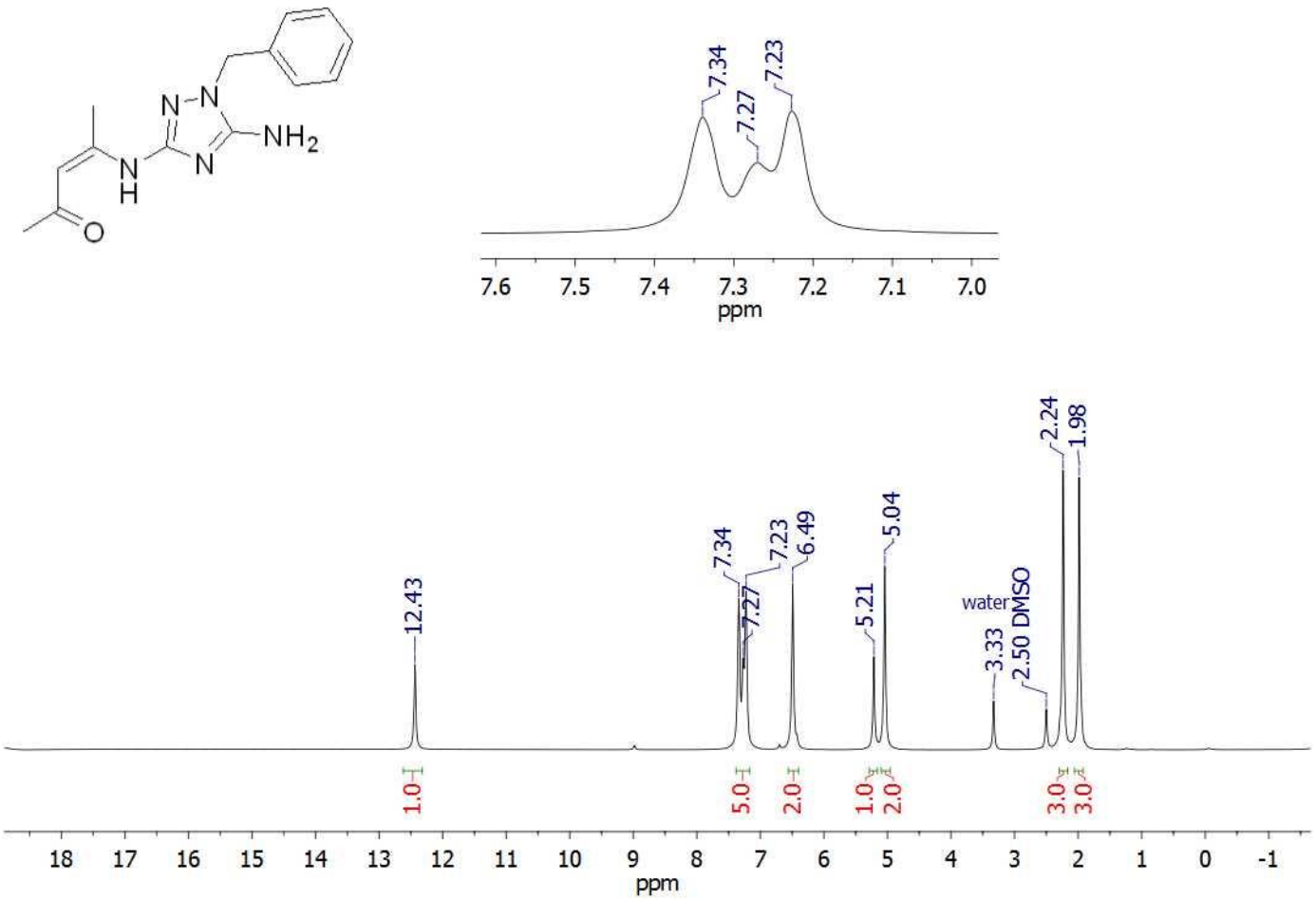


Figure S12. ^{1}H NMR spectrum of compound **3d** (DMSO-d_6)

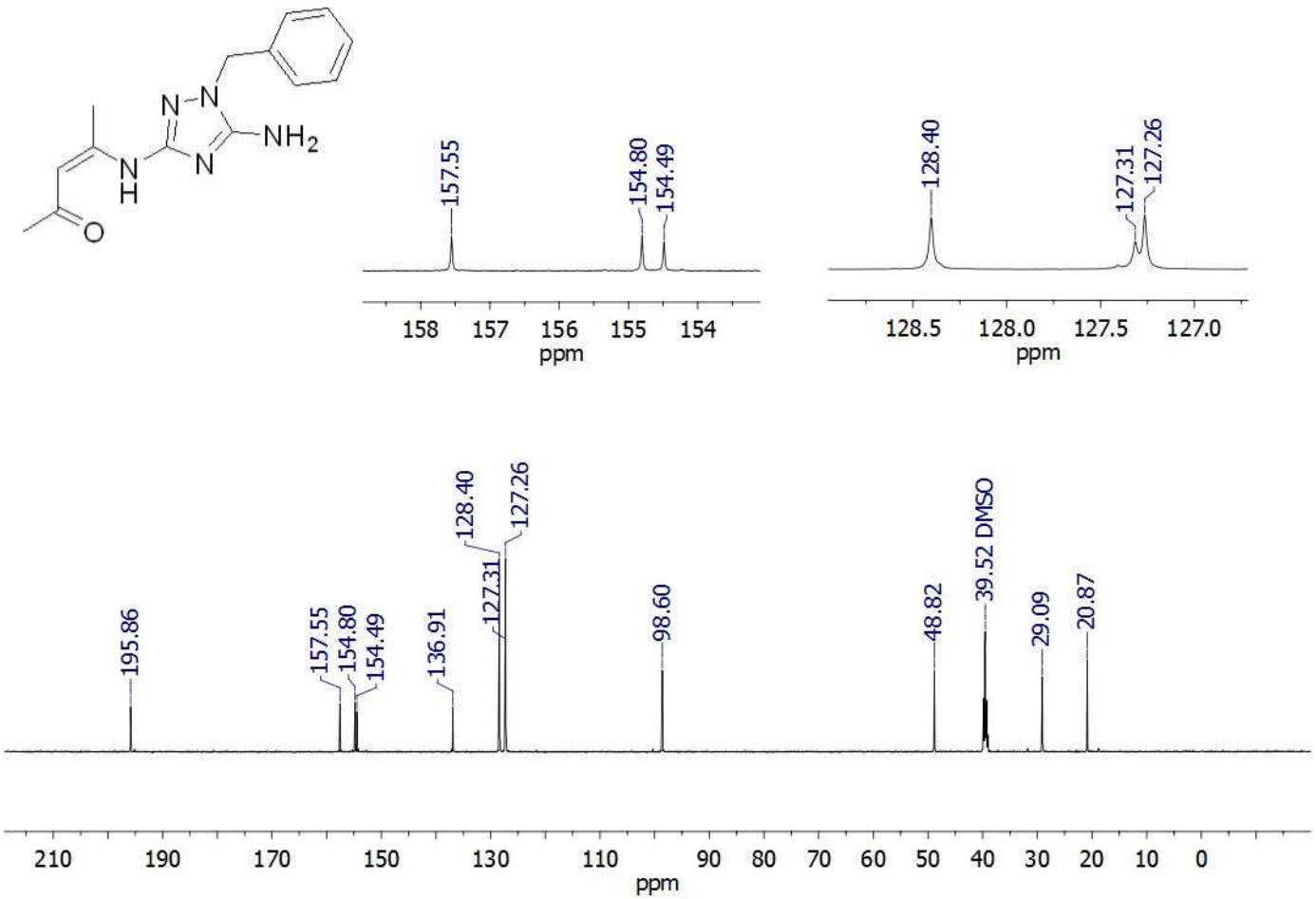


Figure S13. ^{13}C NMR spectrum of compound **3d** (DMSO-d_6)

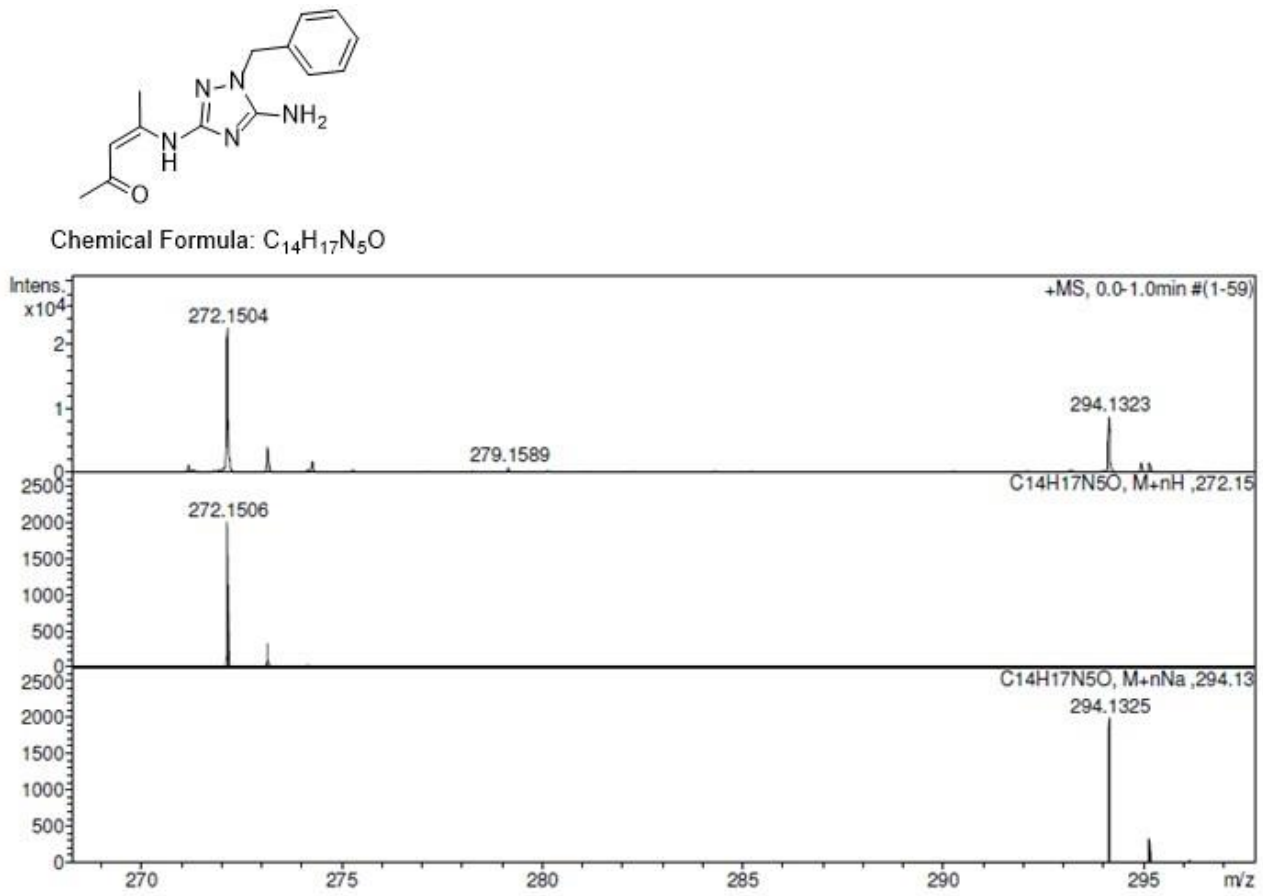


Figure S14. HRMS (ESI^+) of compound **3d**

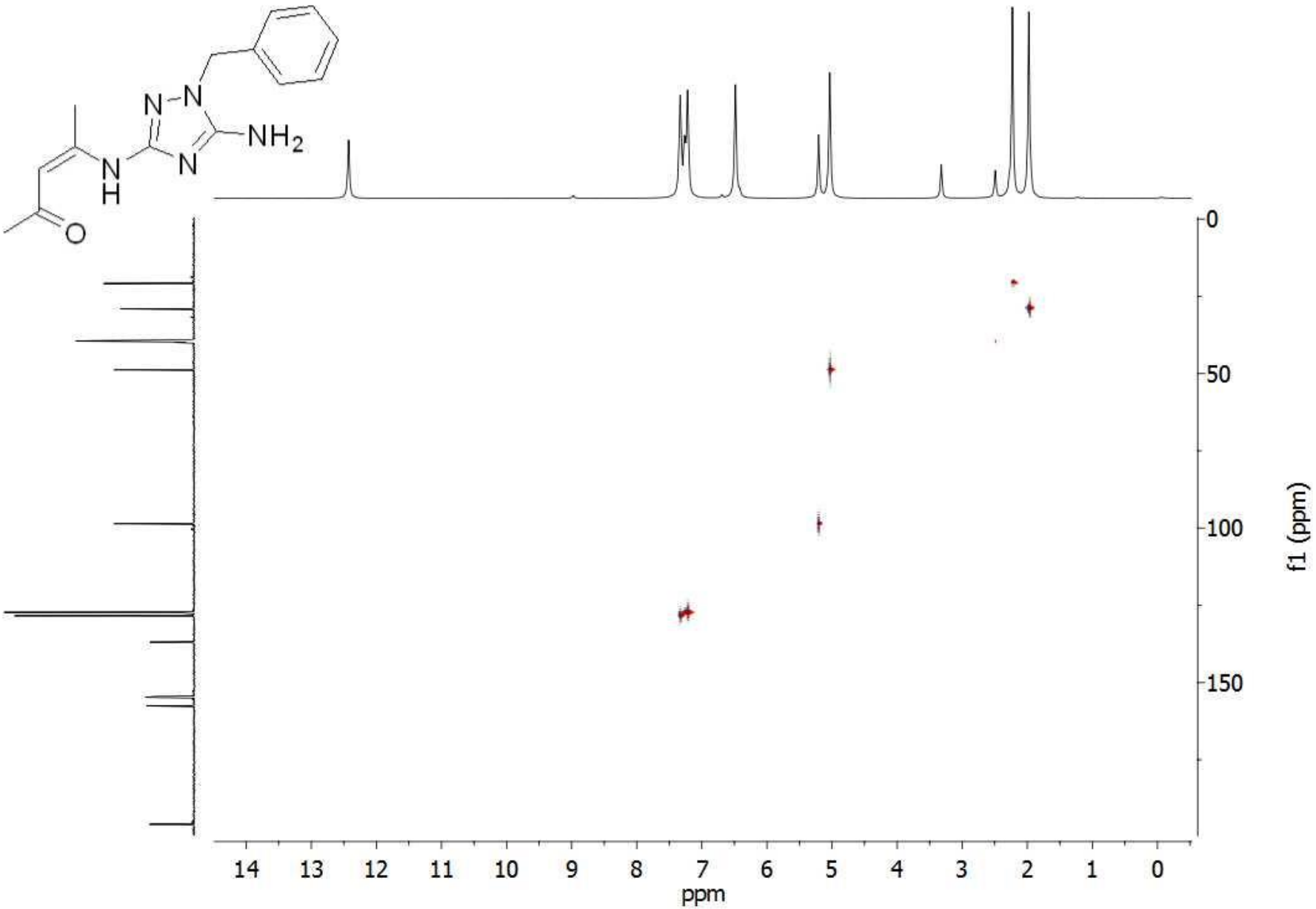


Figure S15. ^{1}H-^{13}C HSQC spectrum of compound **3d** (DMSO-d_6)

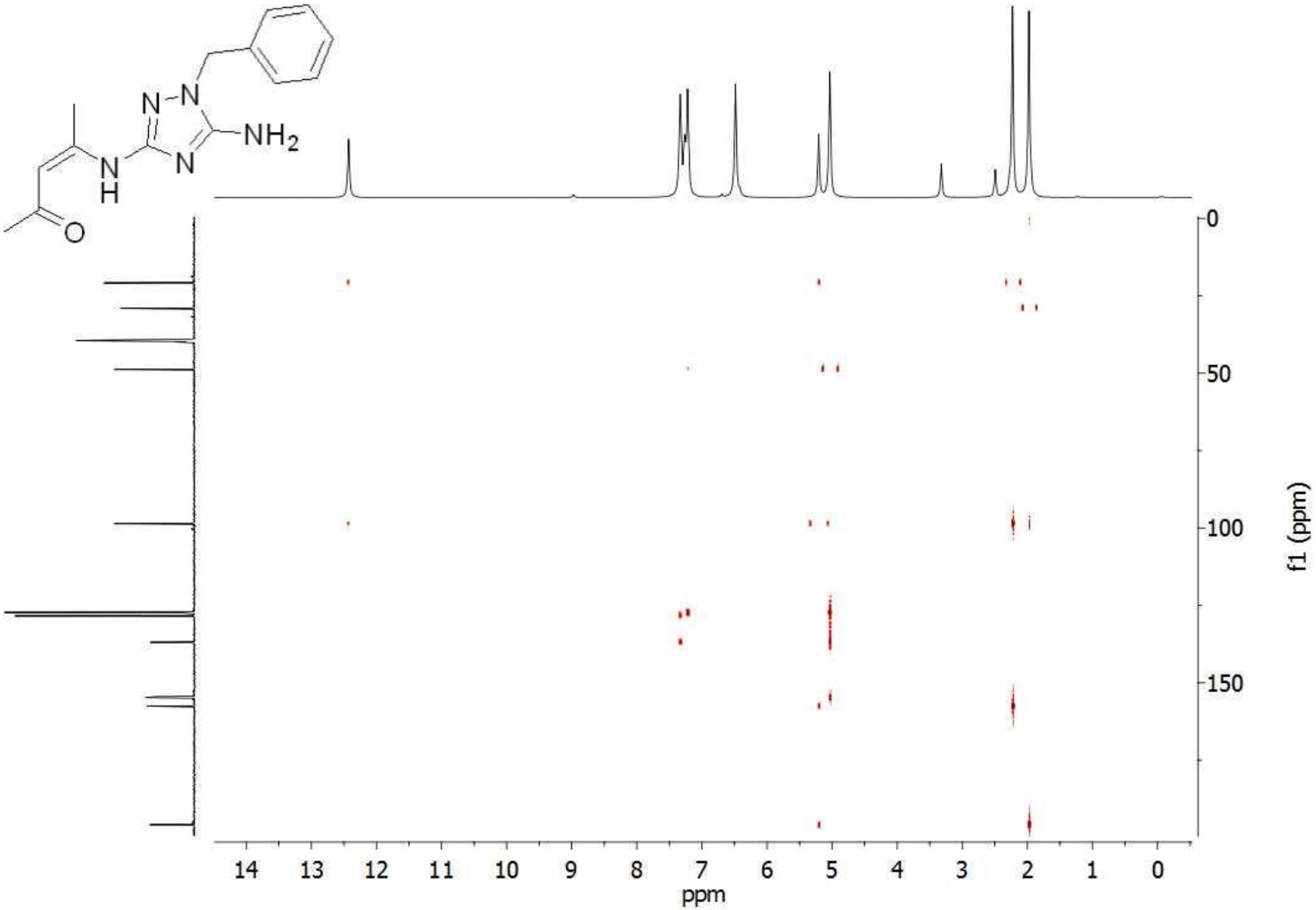


Figure S16. ^{1}H-^{13}C HMBC spectrum of compound **3d** (DMSO-d_6)

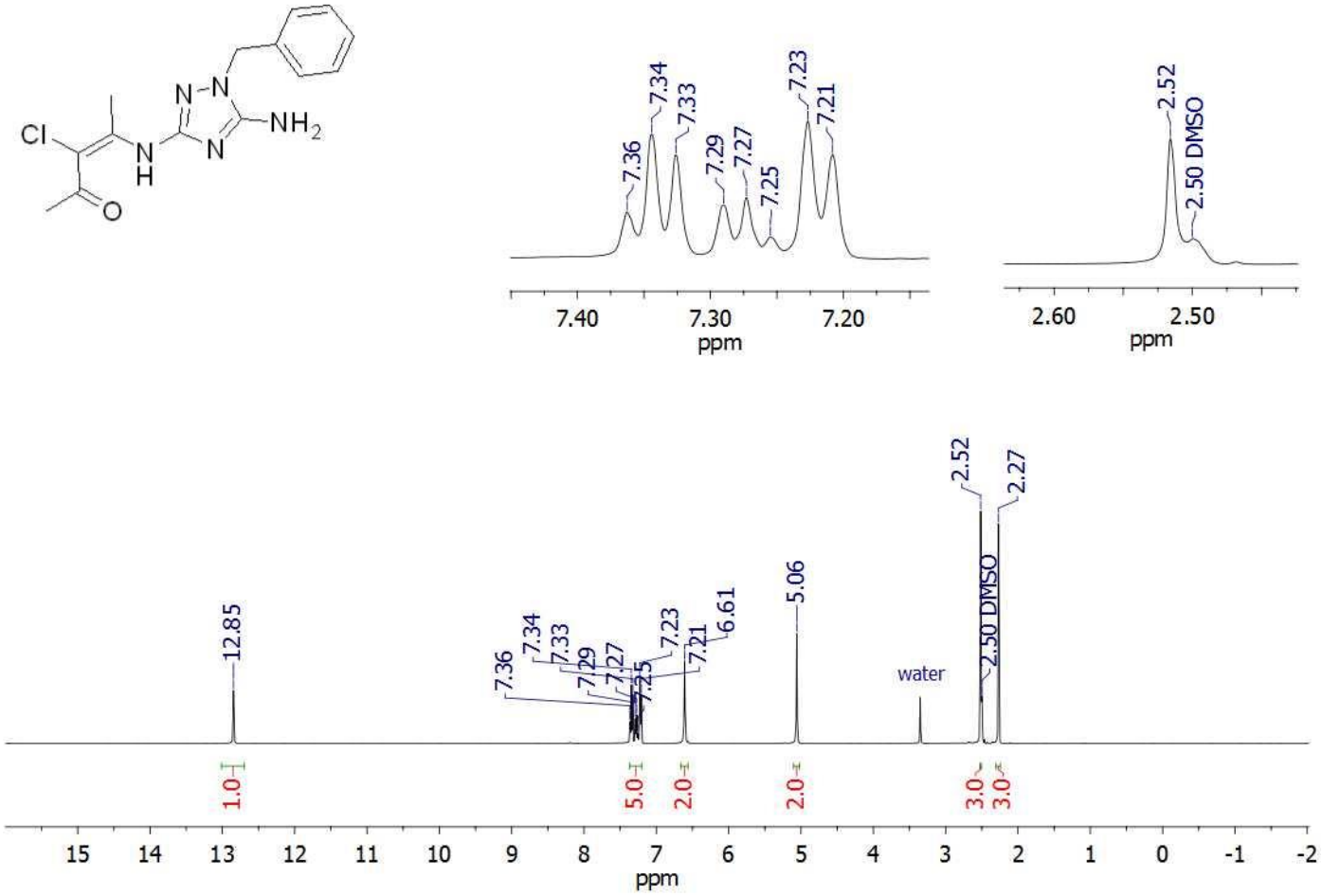


Figure S17. [1]H NMR spectrum of compound **3e** (DMSO-d_6)

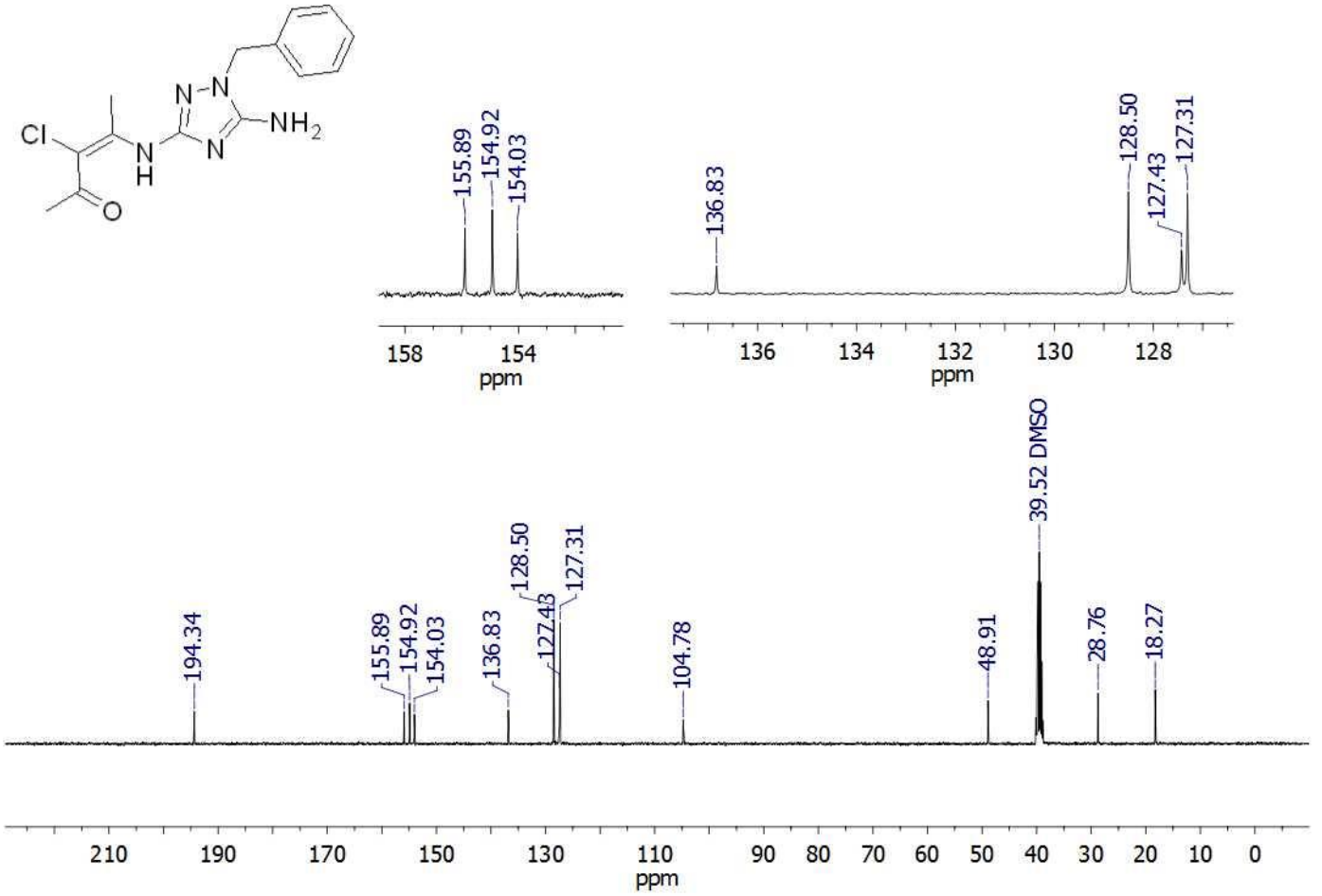


Figure S18. [13]C NMR spectrum of compound **3e** (DMSO-d_6)

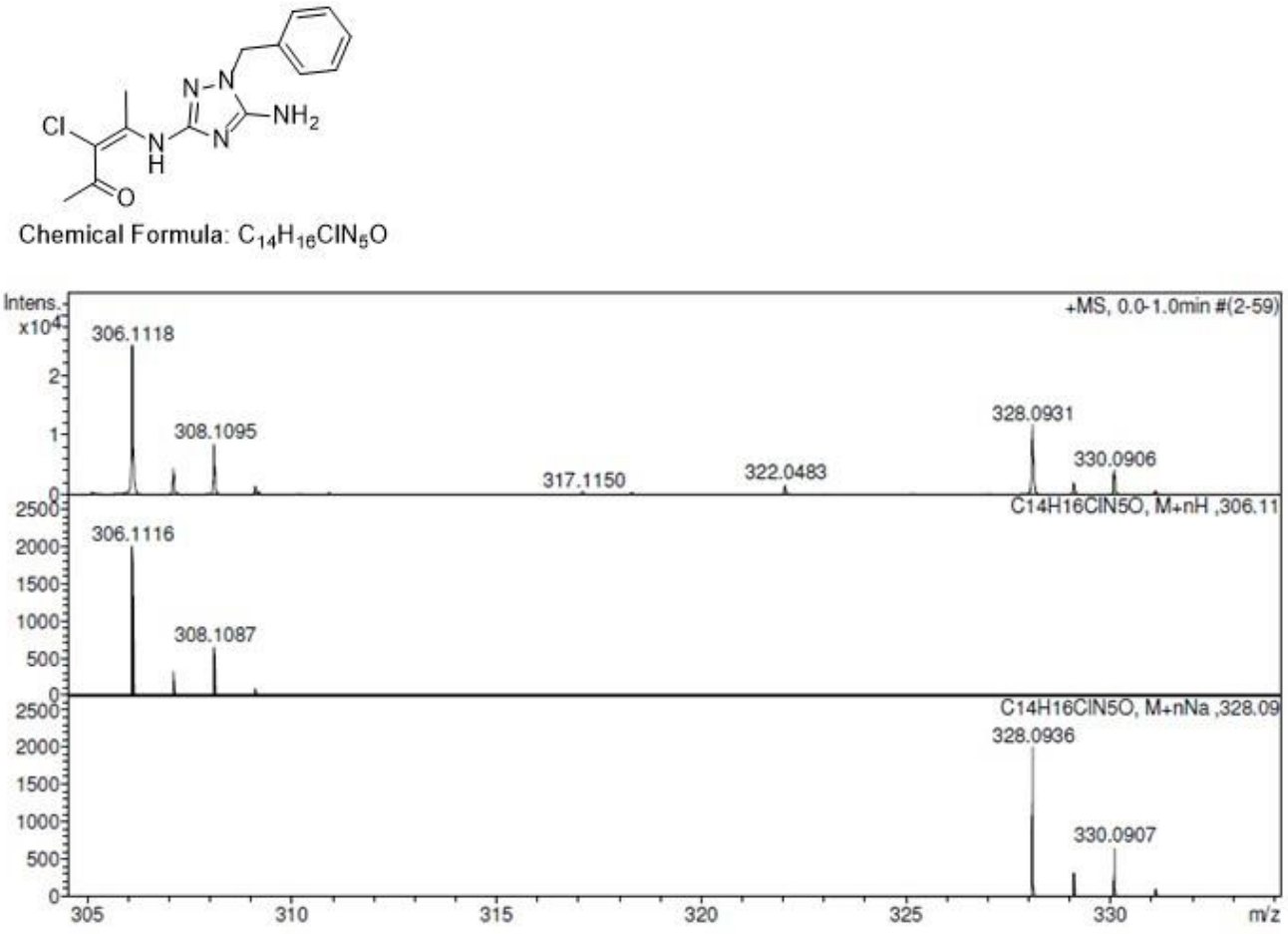


Figure S19. HRMS (ESI^+) of compound **3e**

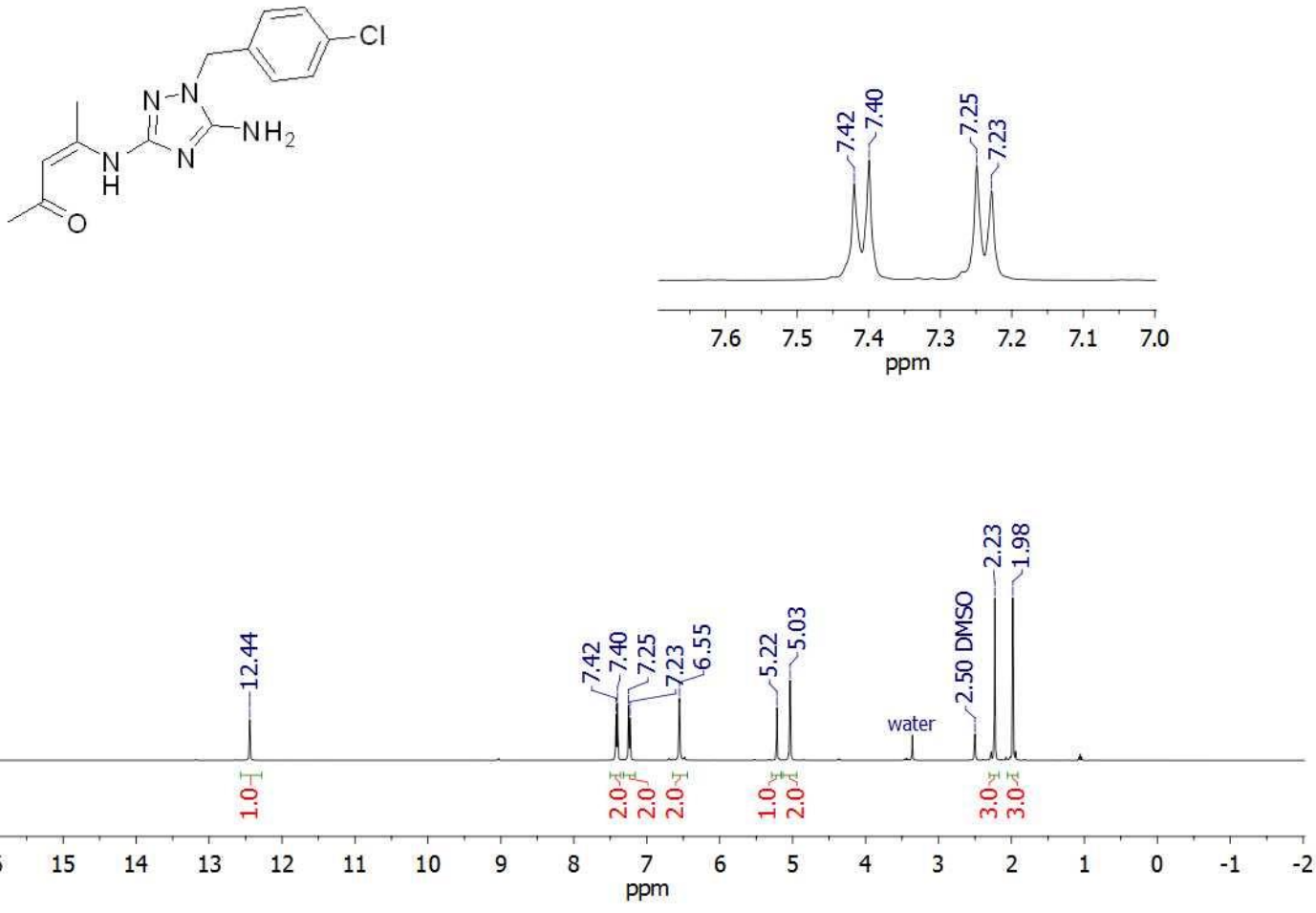


Figure S20. ^1H NMR spectrum of compound **3f** (DMSO-d_6)

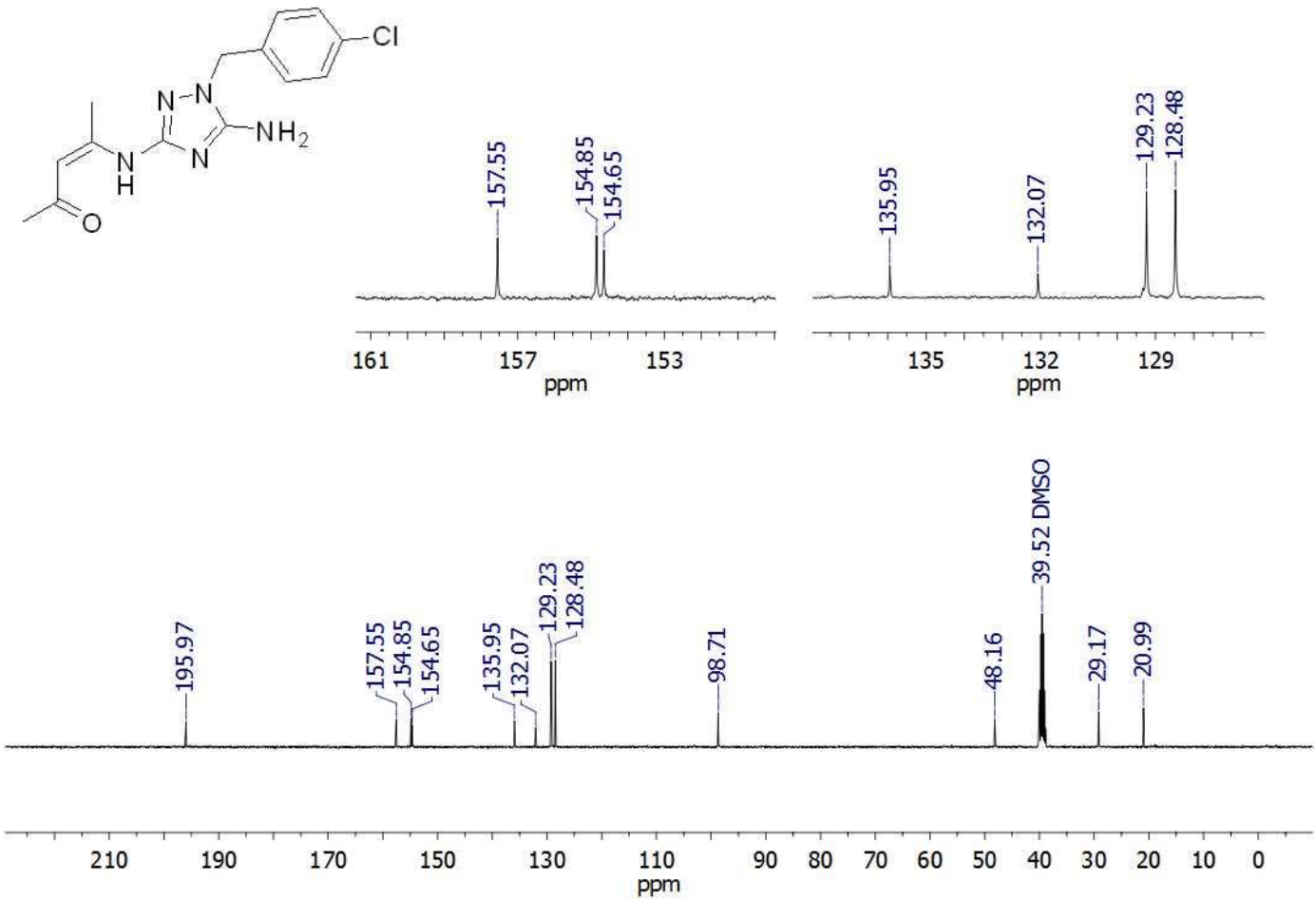


Figure S21. ^{13}C NMR spectrum of compound **3f** (DMSO-d_6)

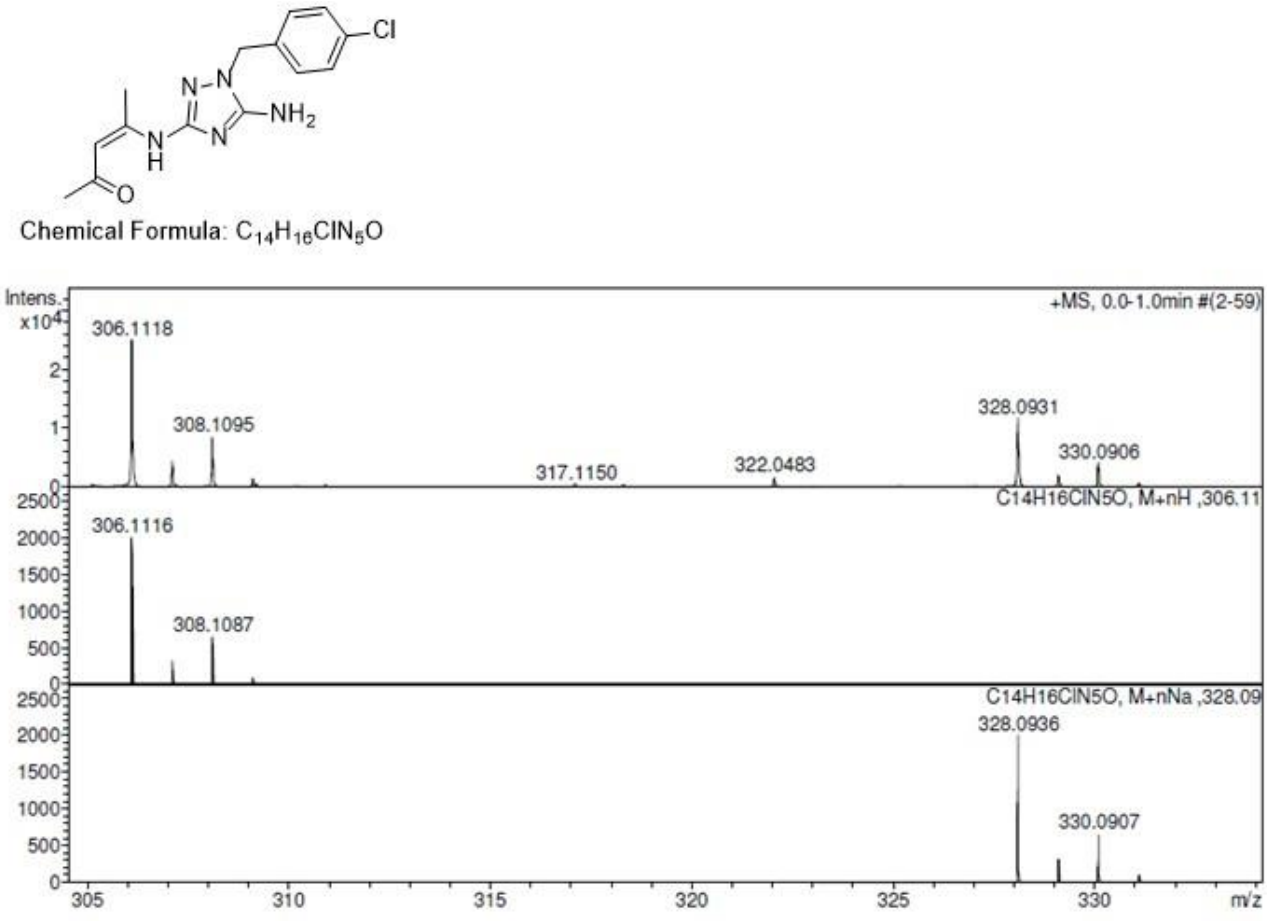


Figure S22. HRMS (ESI$^+$) of compound **3f**

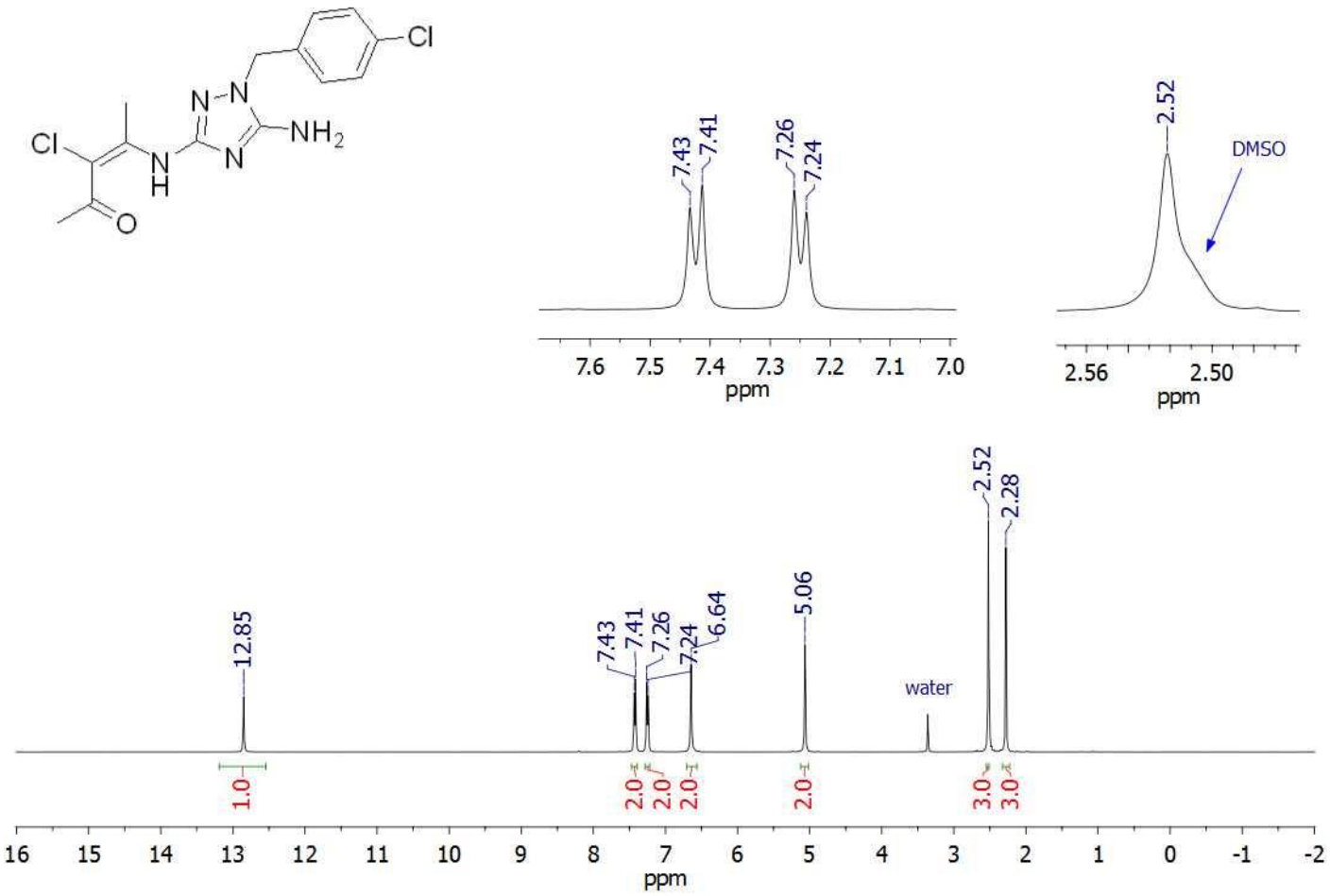


Figure S23. [1]H NMR spectrum of compound **3g** (DMSO-d_6)

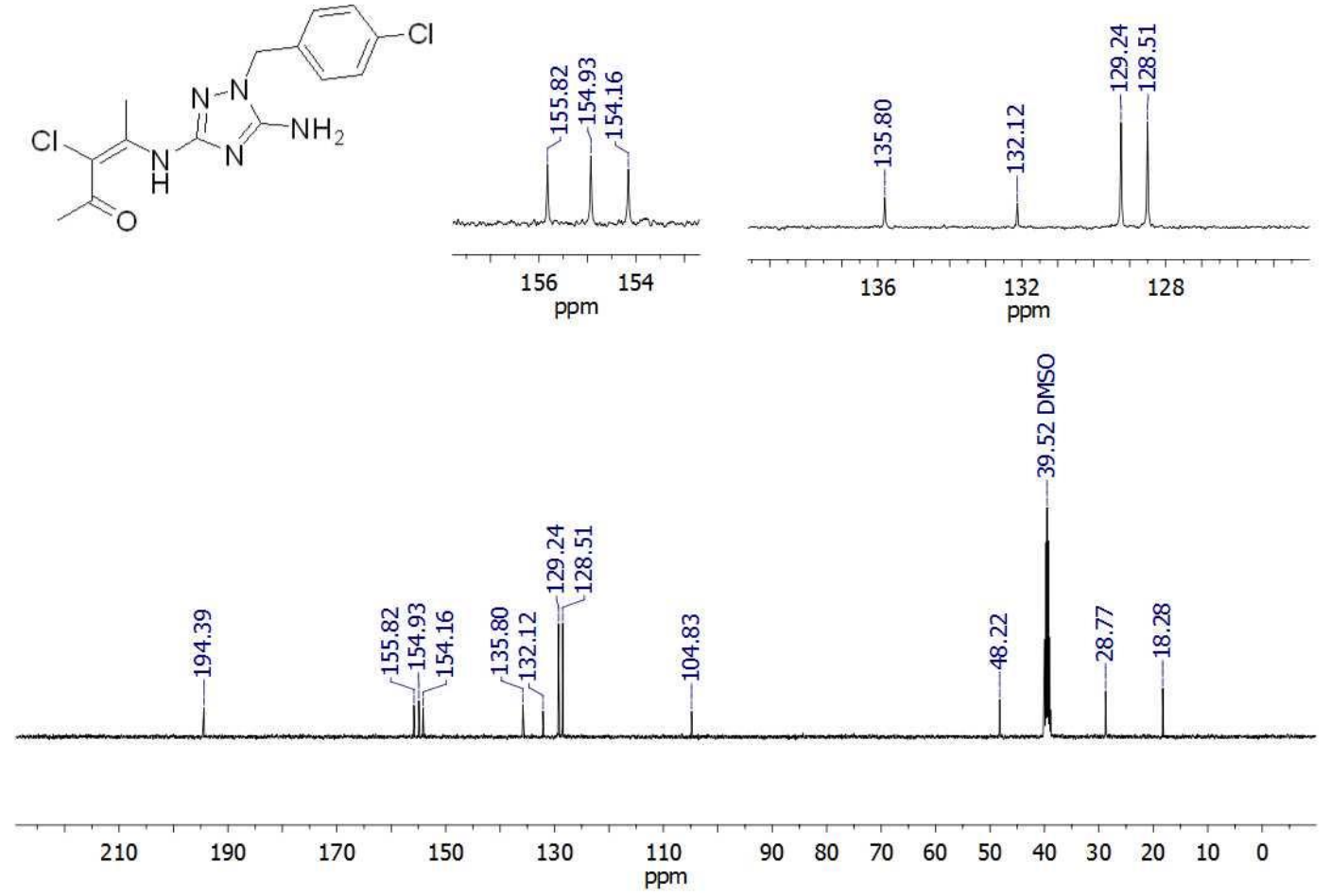


Figure S24. [13]C NMR spectrum of compound **3g** (DMSO-d_6)

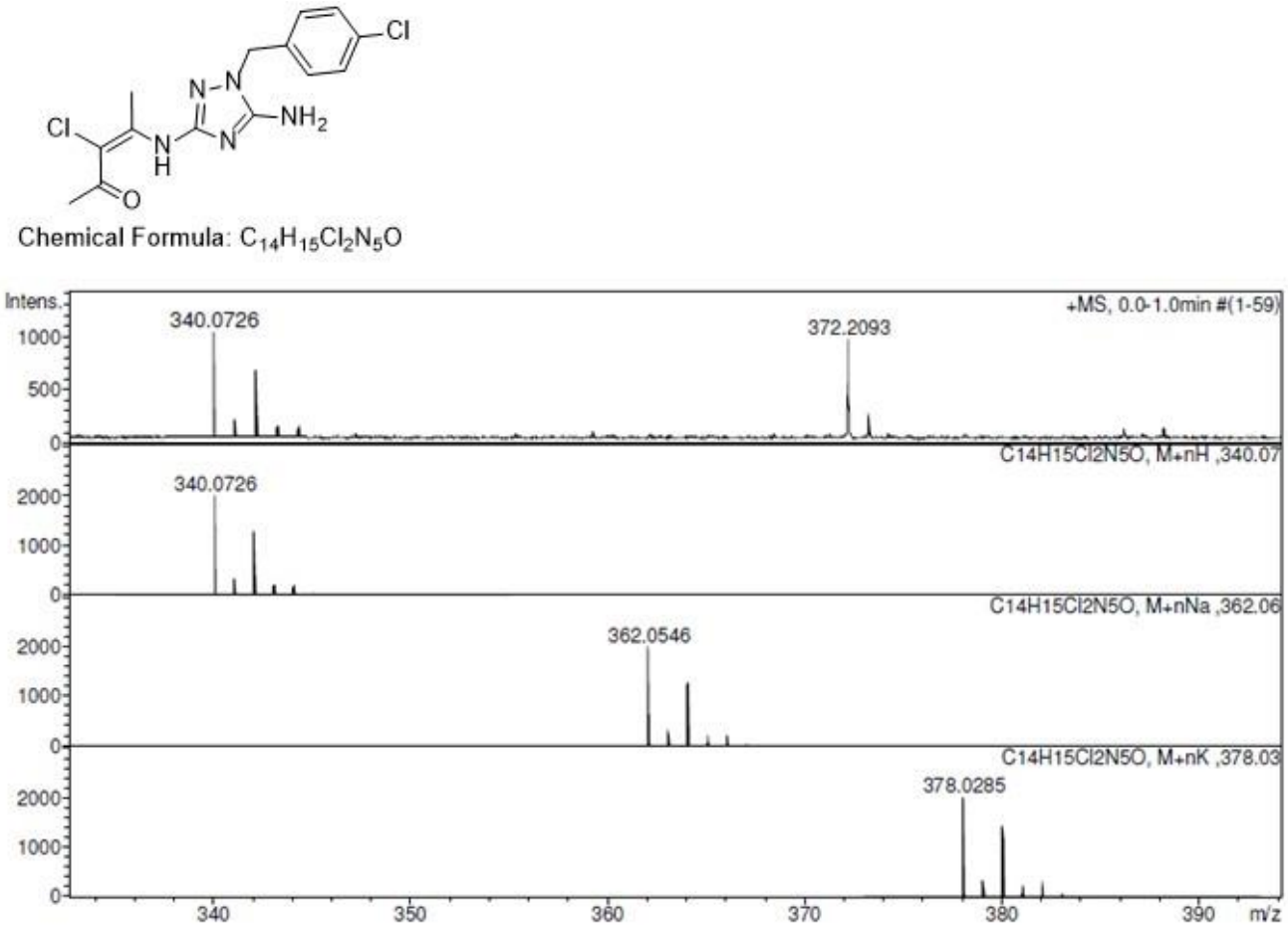


Figure S25. HRMS (ESI$^+$) of compound **3g**

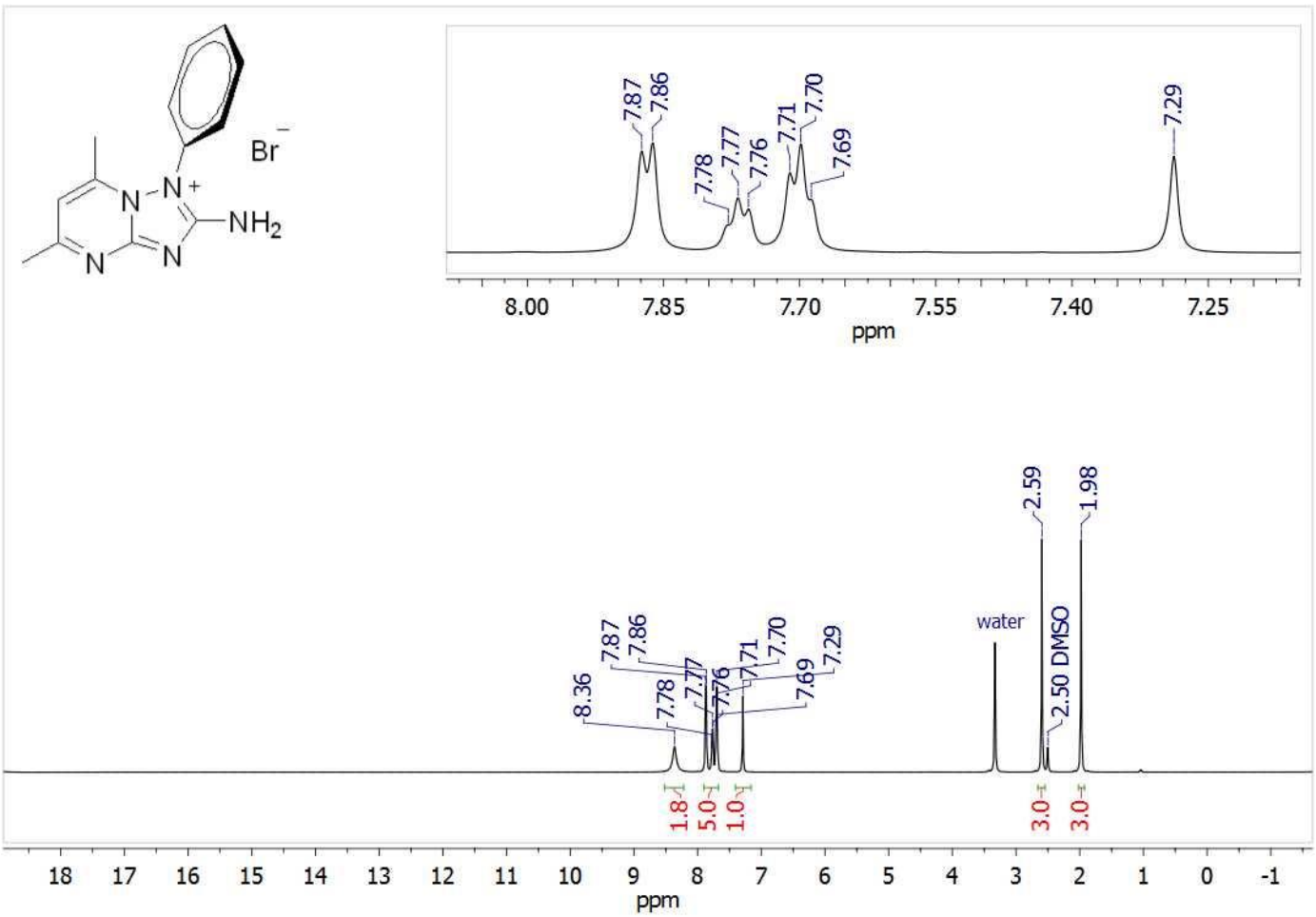


Figure S26. ^{1}H NMR spectrum of compound **4a** (DMSO-d_6)

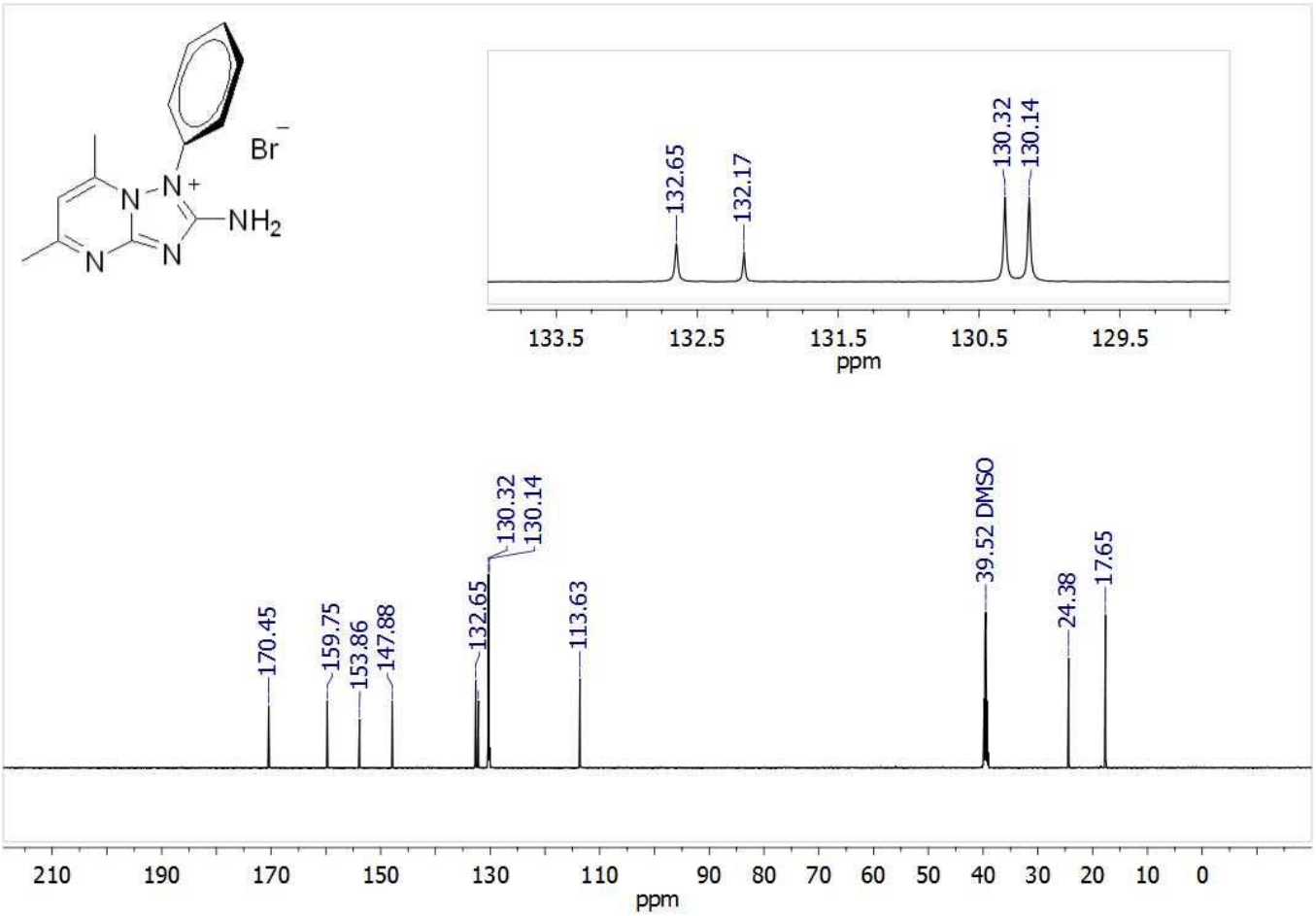
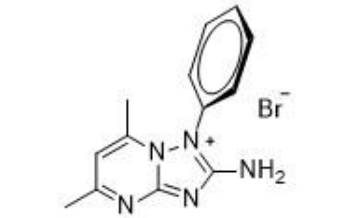


Figure S27. ^{13}C NMR spectrum of compound **4a** (DMSO-d_6)



Chemical Formula: $C_{13}H_{14}BrN_5$

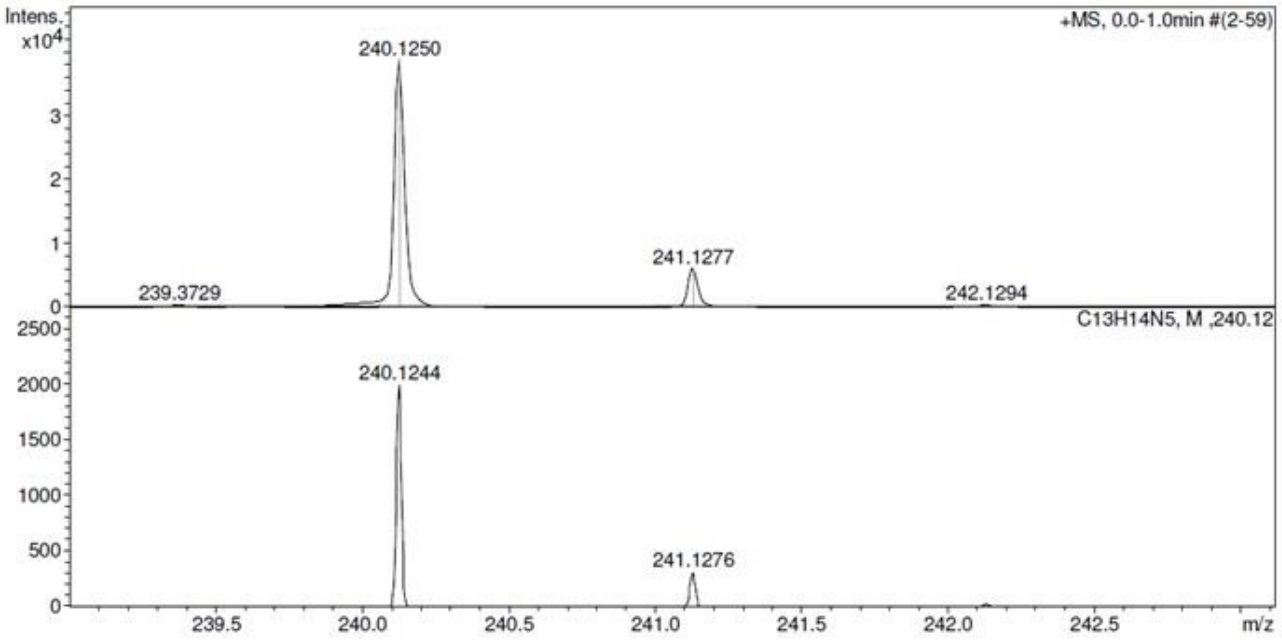


Figure S28. HRMS (ESI$^+$) of compound **4a**

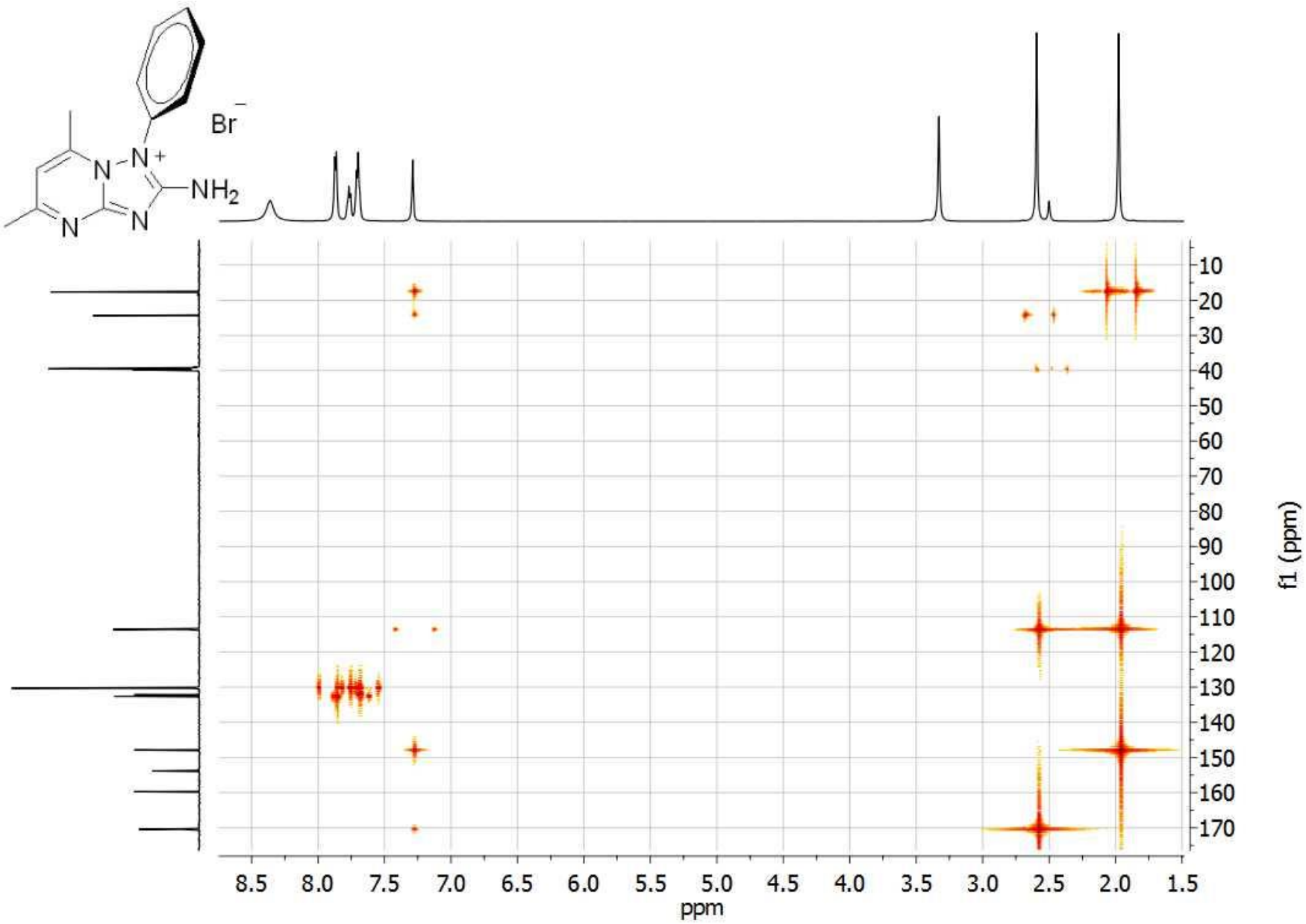


Figure S29. ^{1}H-^{13}C HMBC spectrum of compound **4a** (DMSO-d_6)

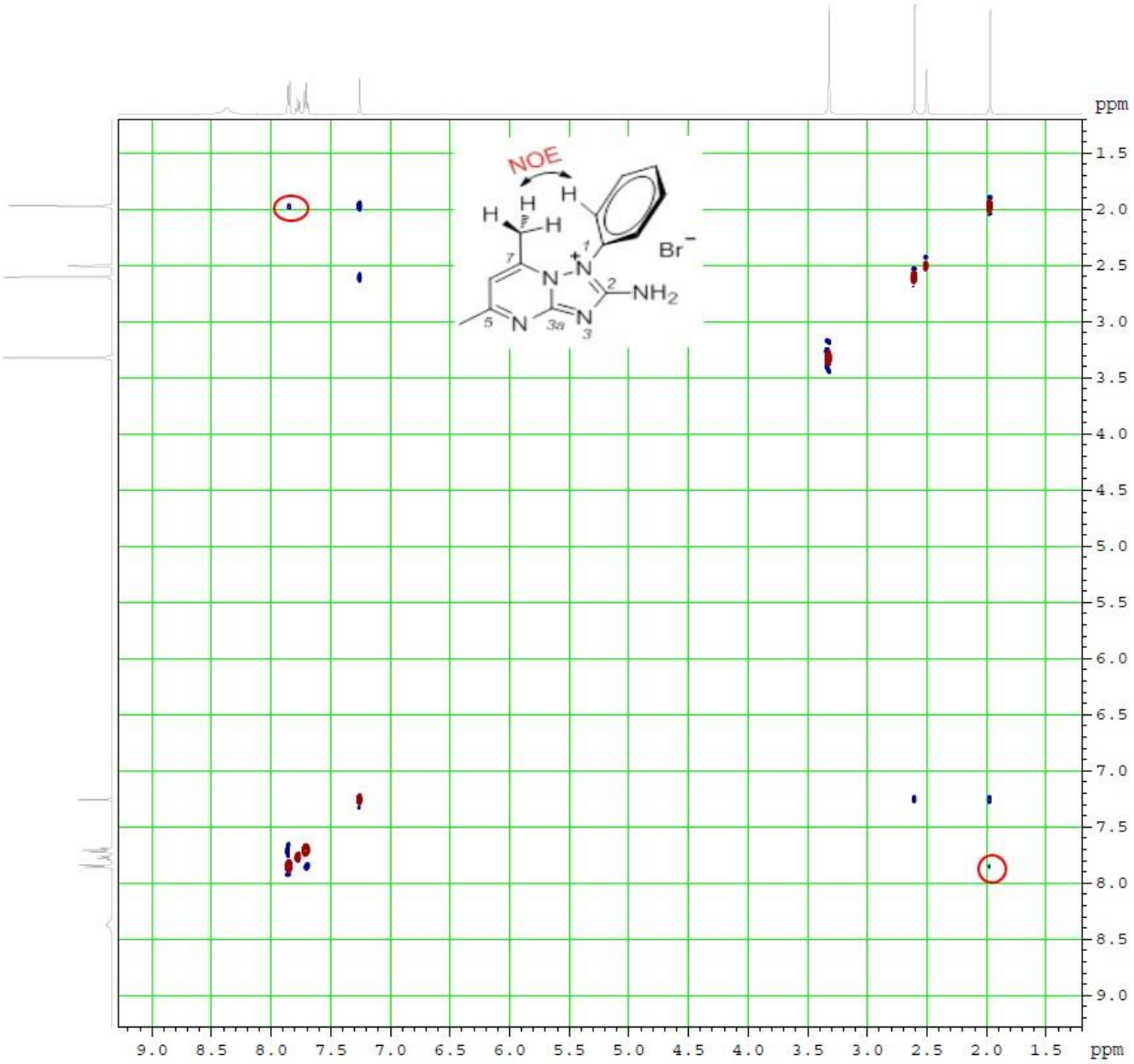


Figure S30. NOESY spectrum of compound **4a** (DMSO-d_6)

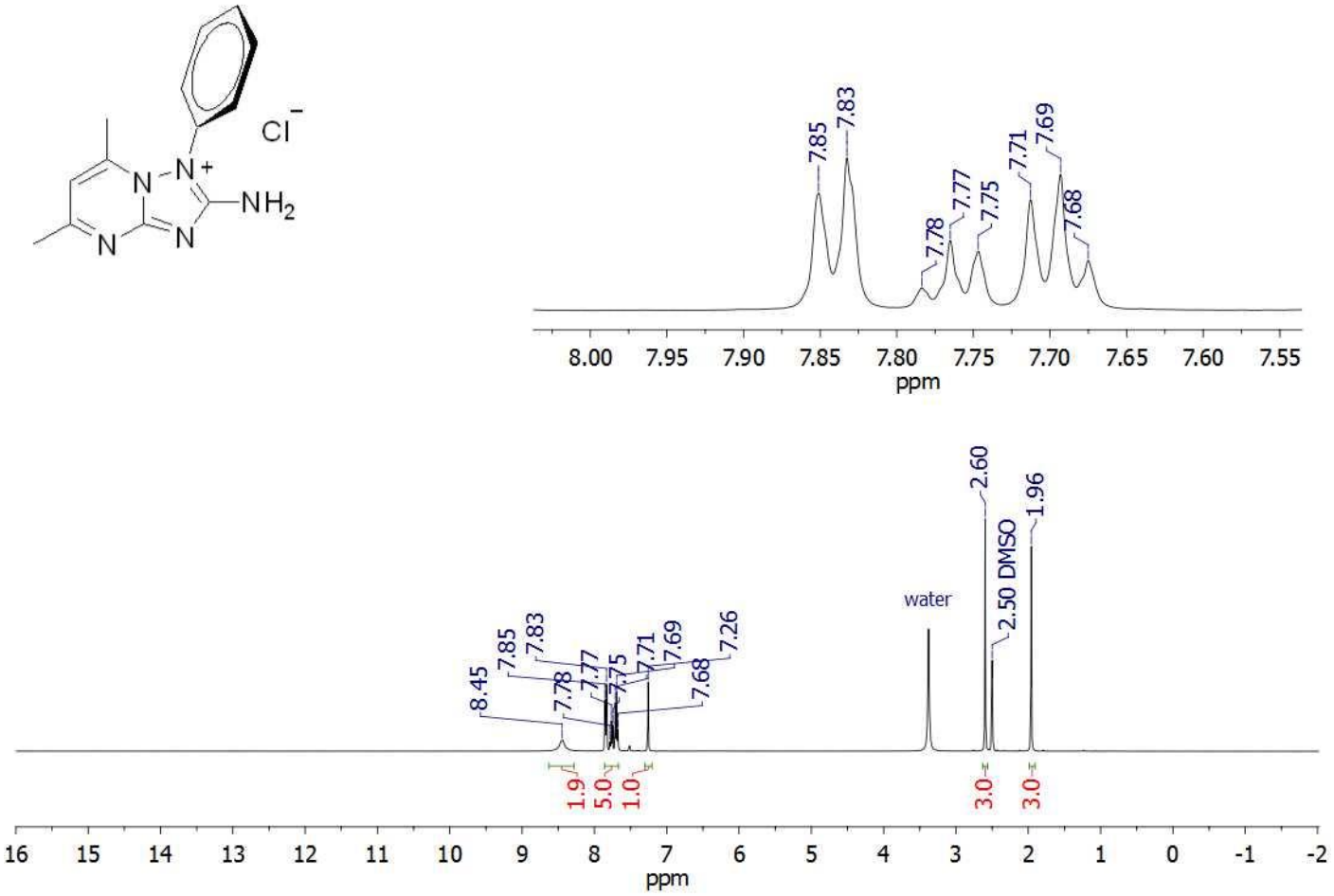


Figure S31. [1]H NMR spectrum of compound **4b** (DMSO-d_6)

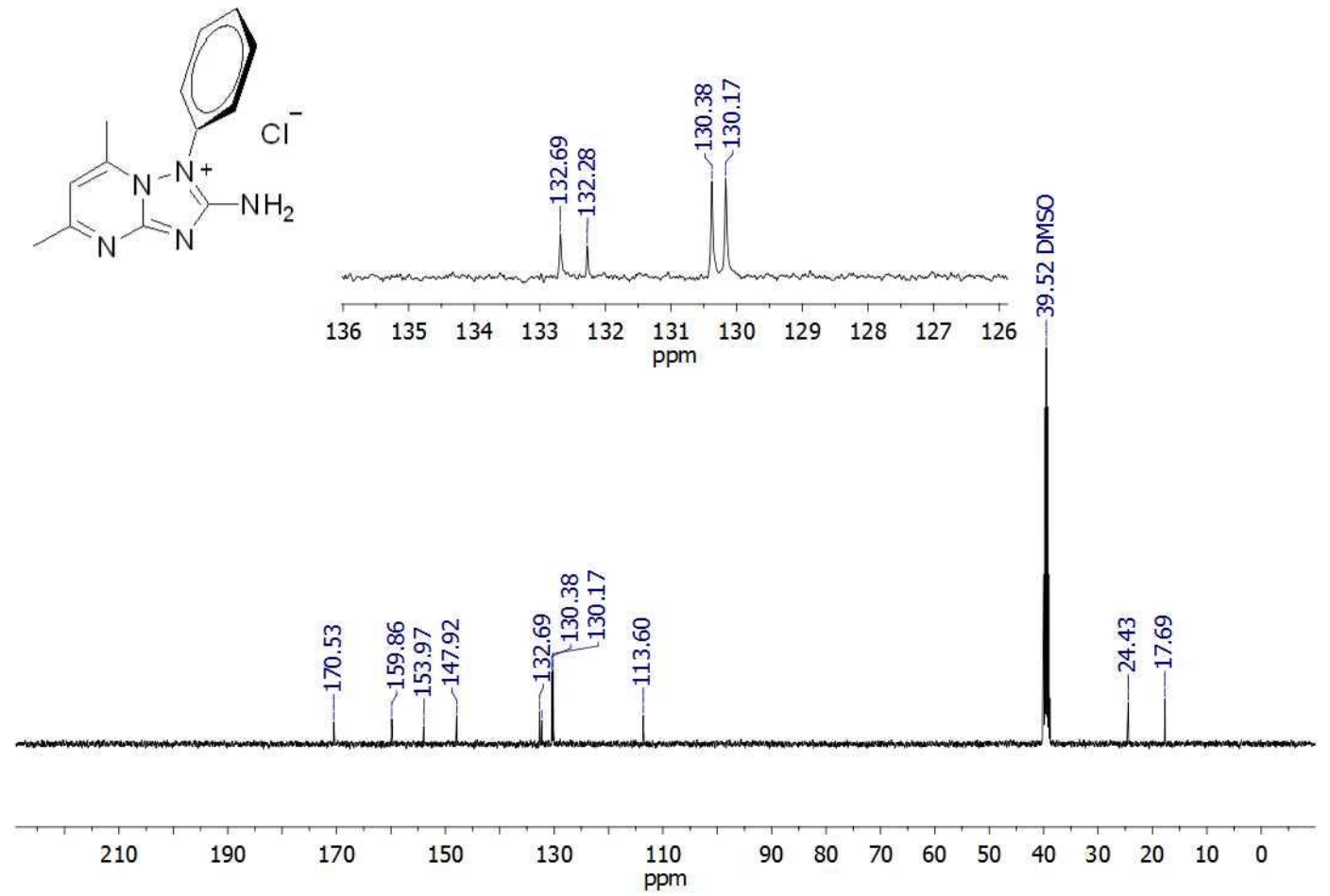


Figure S32. [13]C NMR spectrum of compound **4b** (DMSO-d_6)

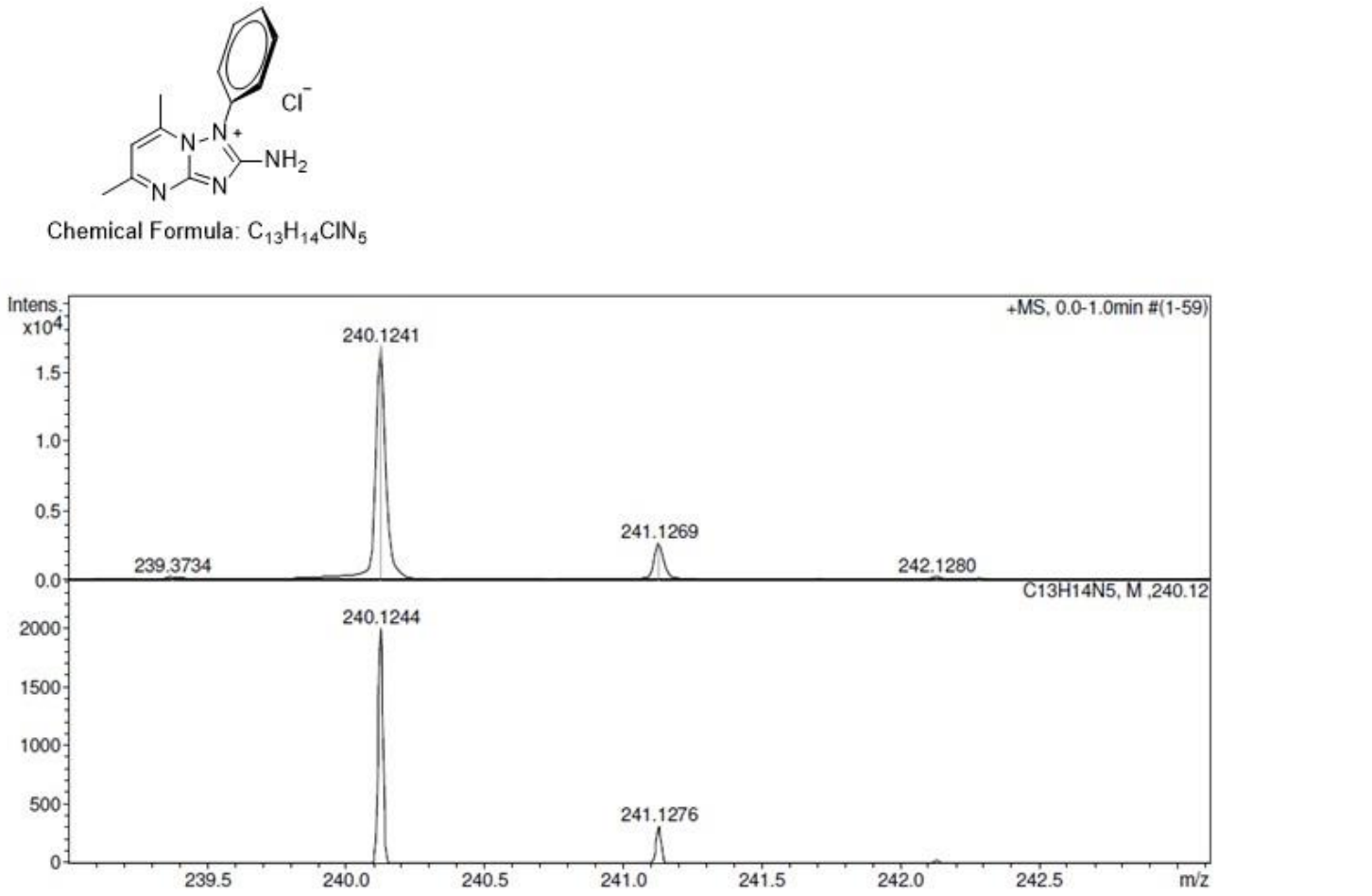


Figure S33. HRMS (ESI$^+$) of compound **4b**

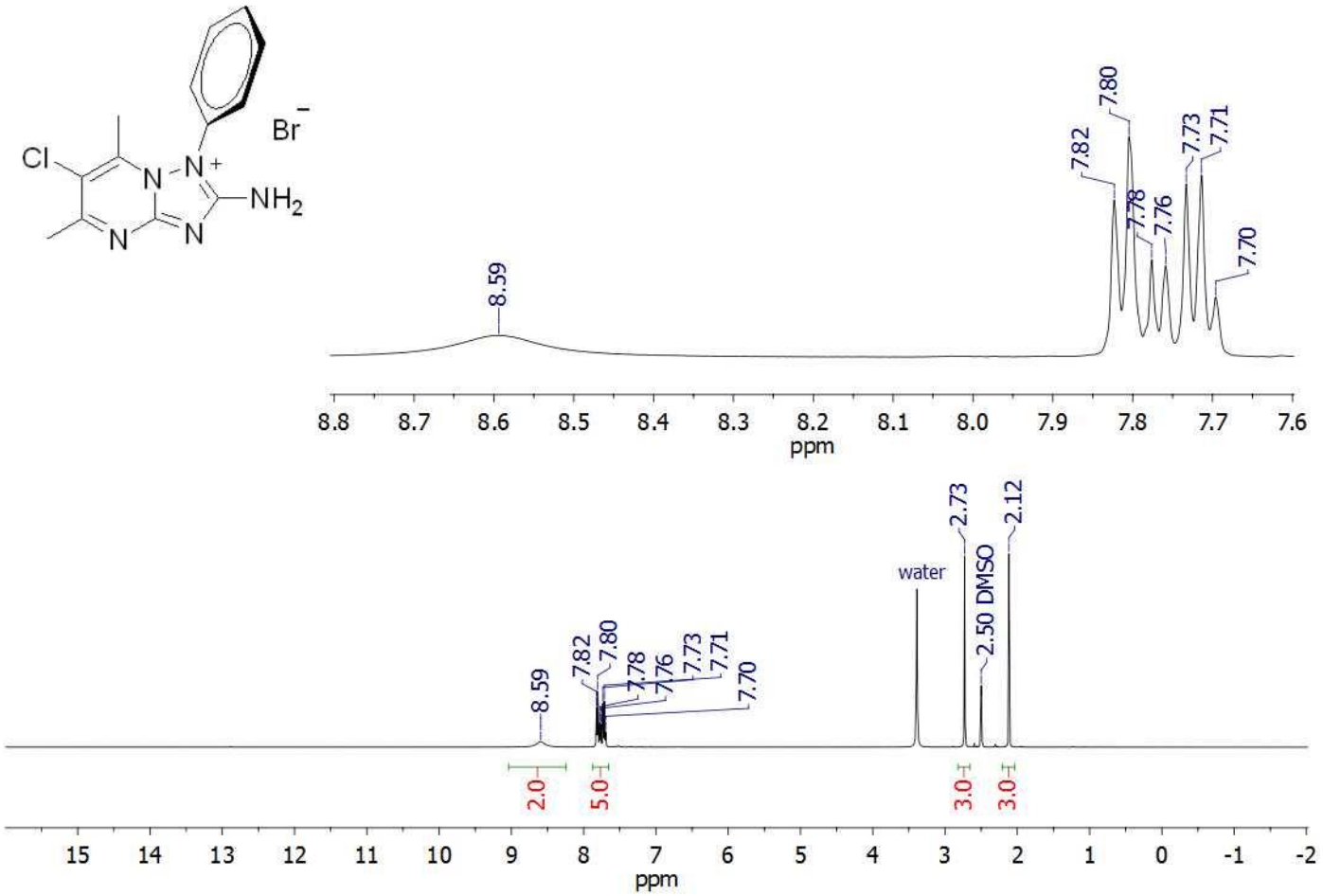


Figure S34. ^{1}H NMR spectrum of compound **4c** (DMSO-d_6)

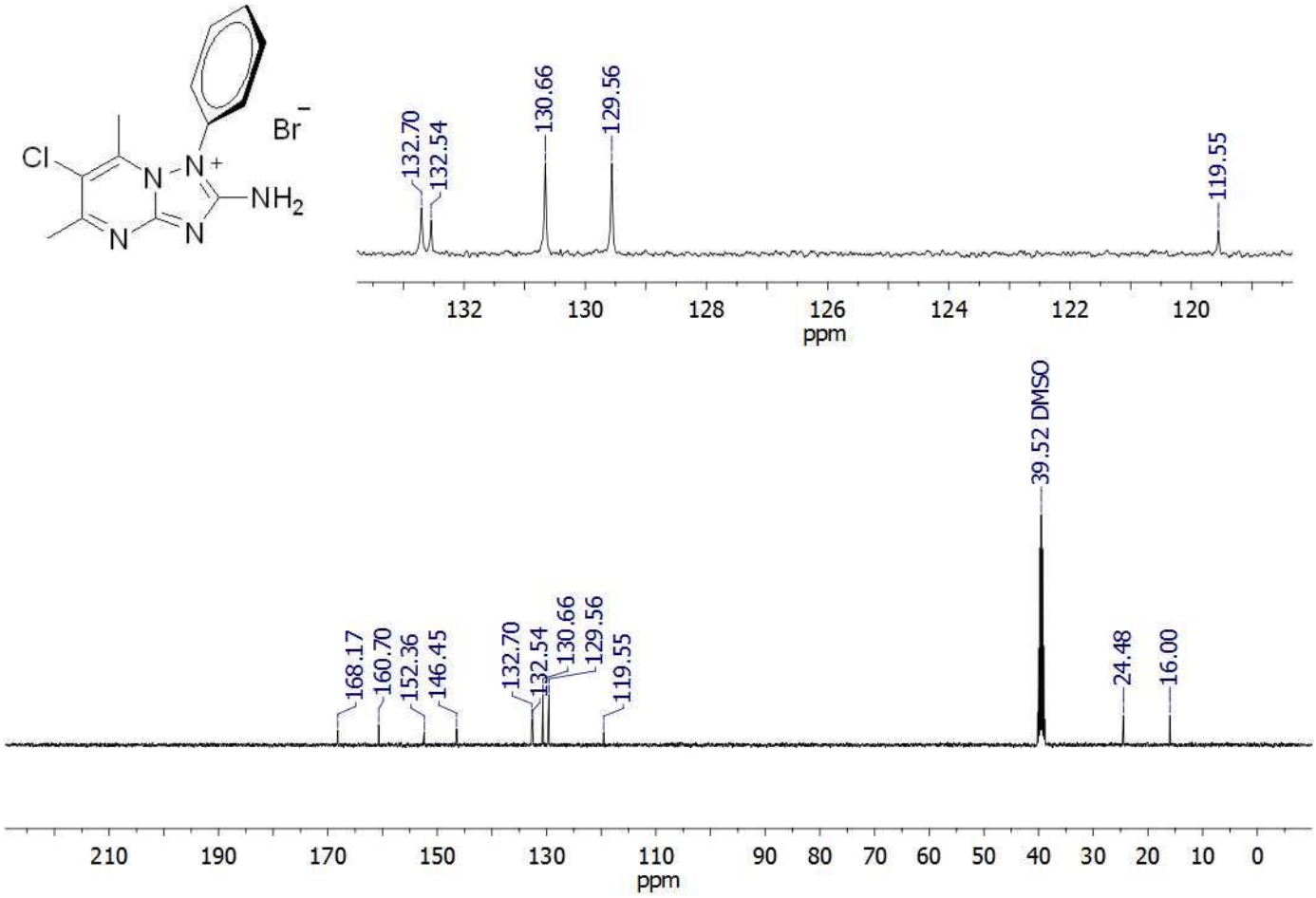


Figure S35. ^{13}C NMR spectrum of compound **4c** (DMSO-d_6)

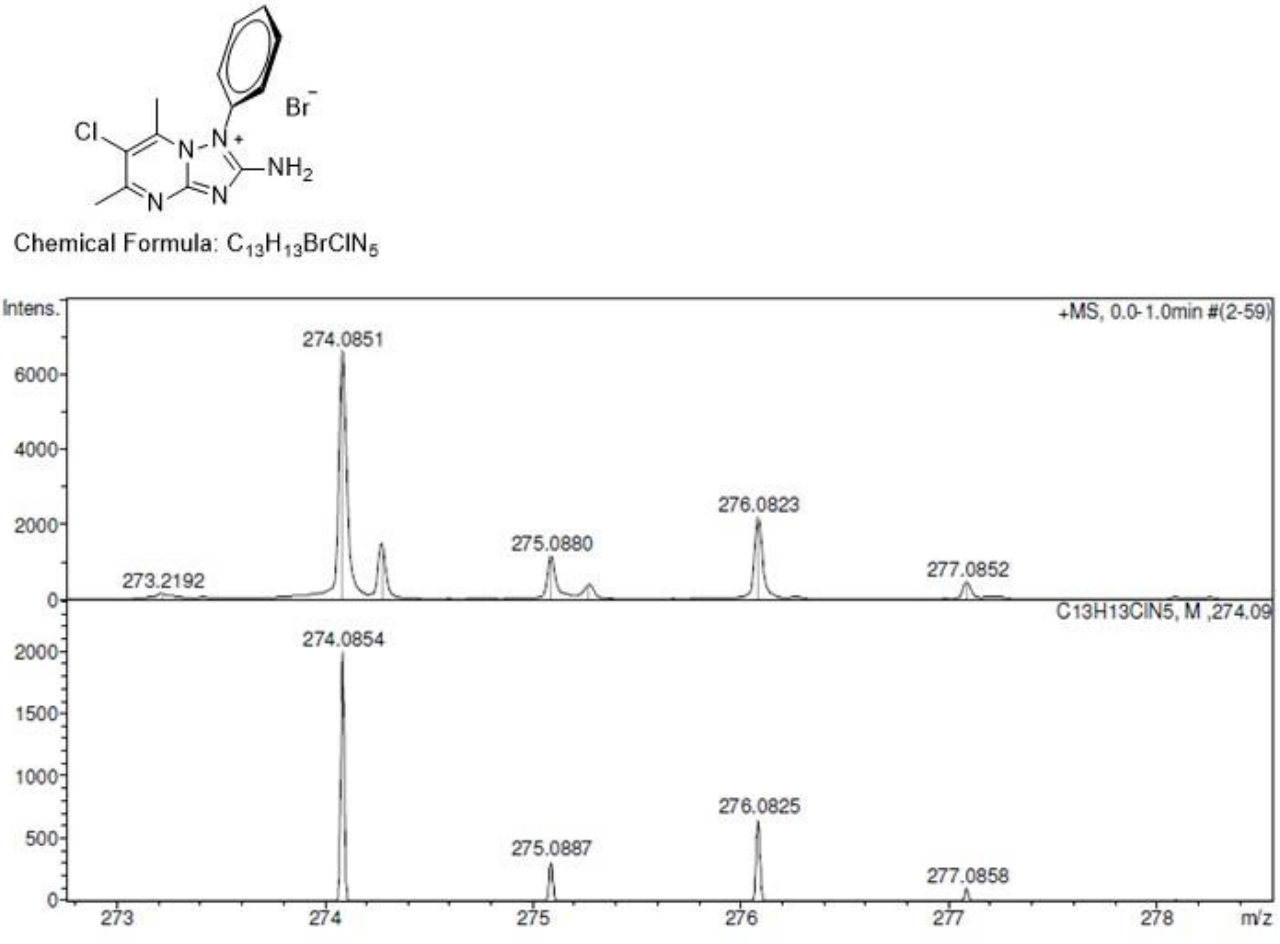


Figure S36. HRMS (ESI$^+$) of compound **4c**

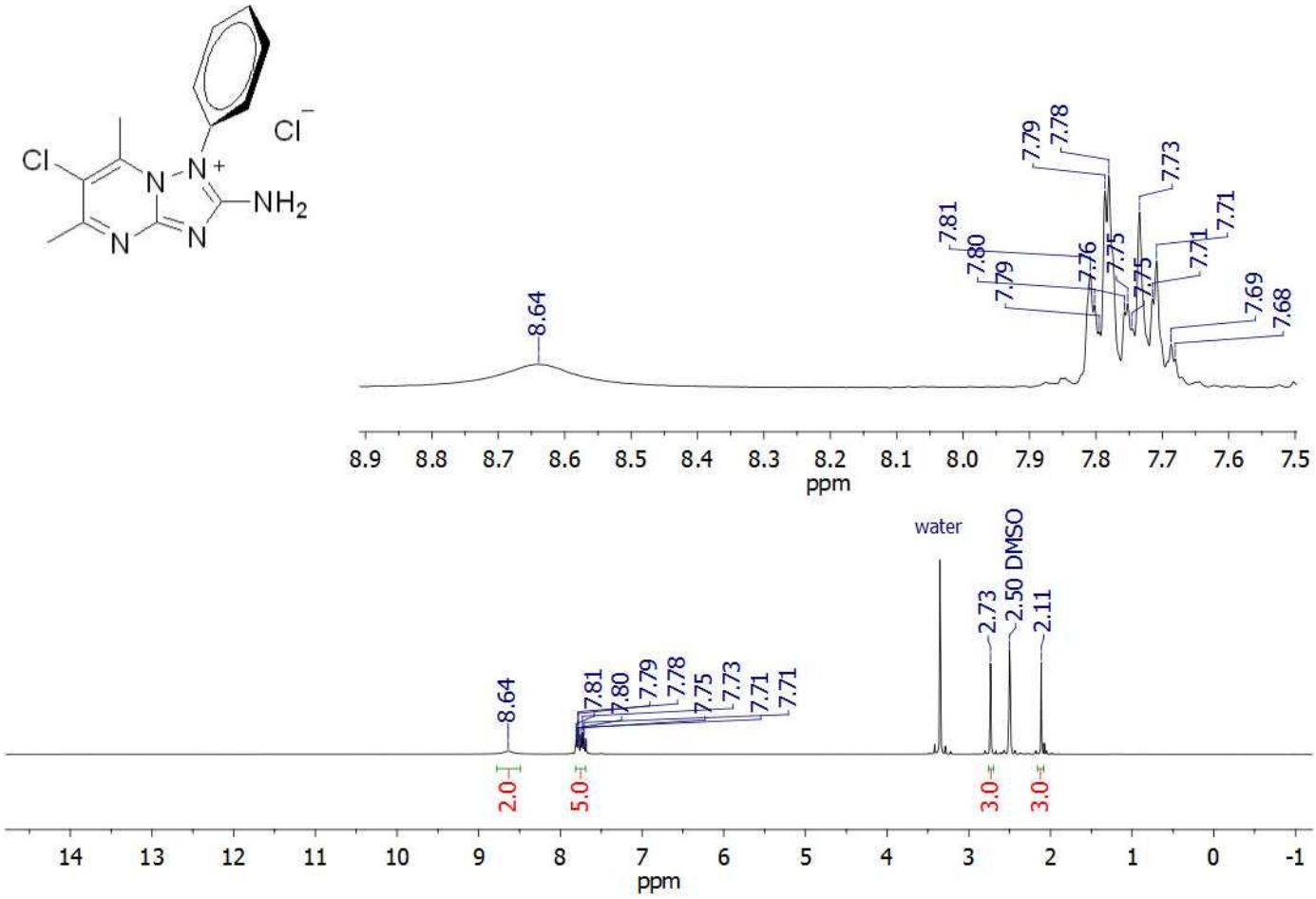


Figure S37. [1]H NMR spectrum of compound **4d** (DMSO-d_6)

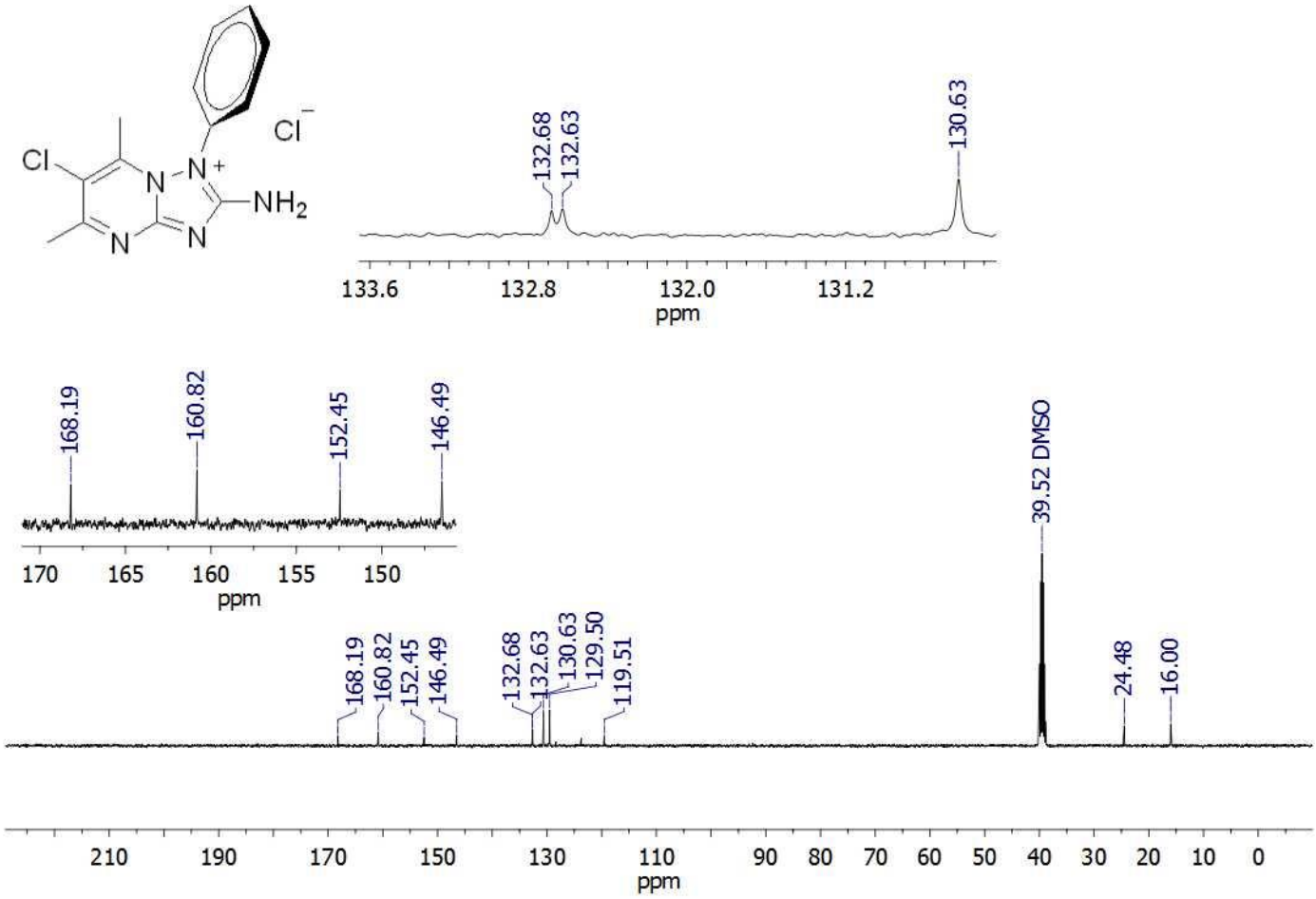


Figure S38. [13]C NMR spectrum of compound **4d** (DMSO-d_6)

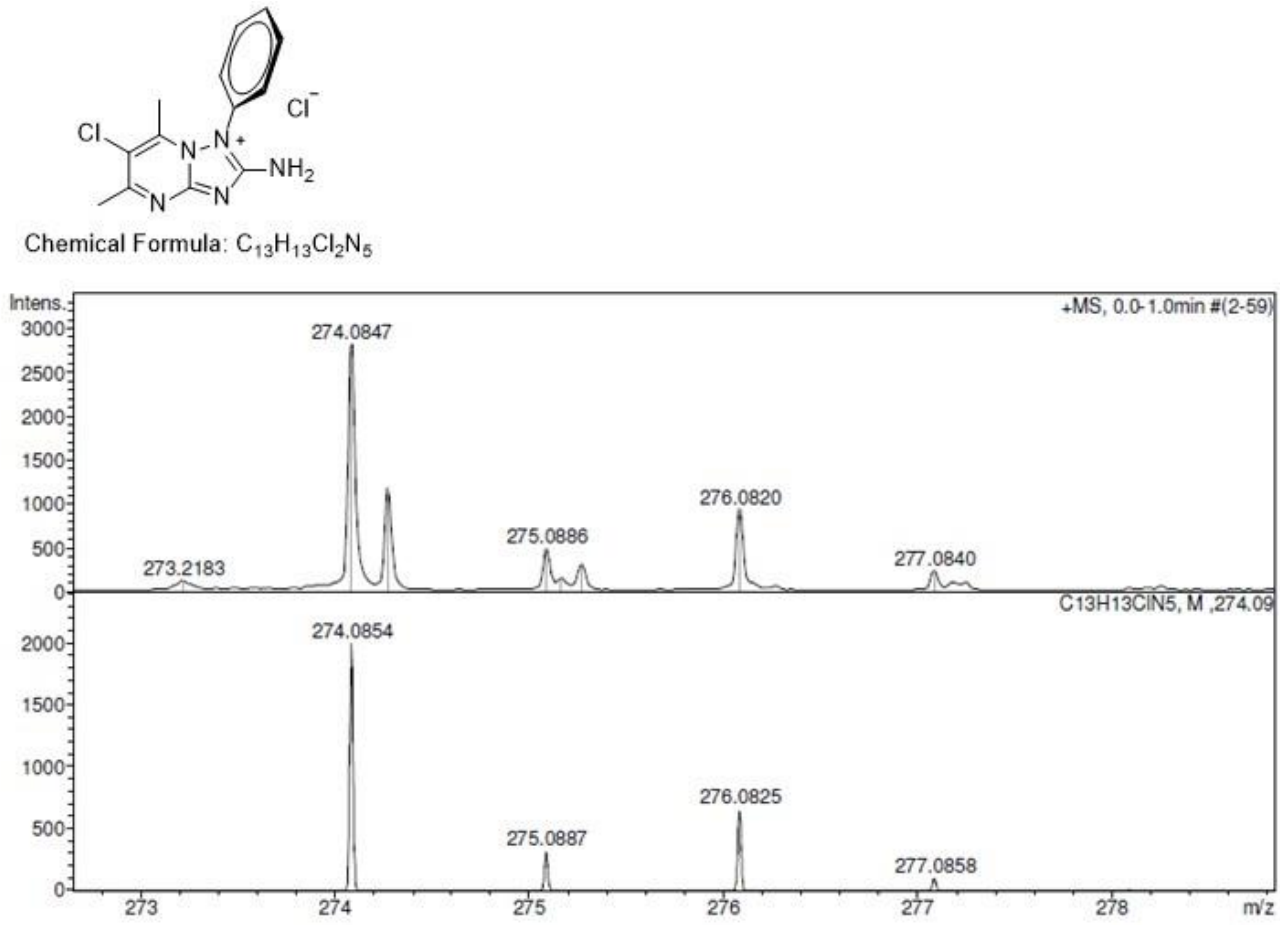


Figure S39. HRMS (ESI$^+$) of compound **4d**

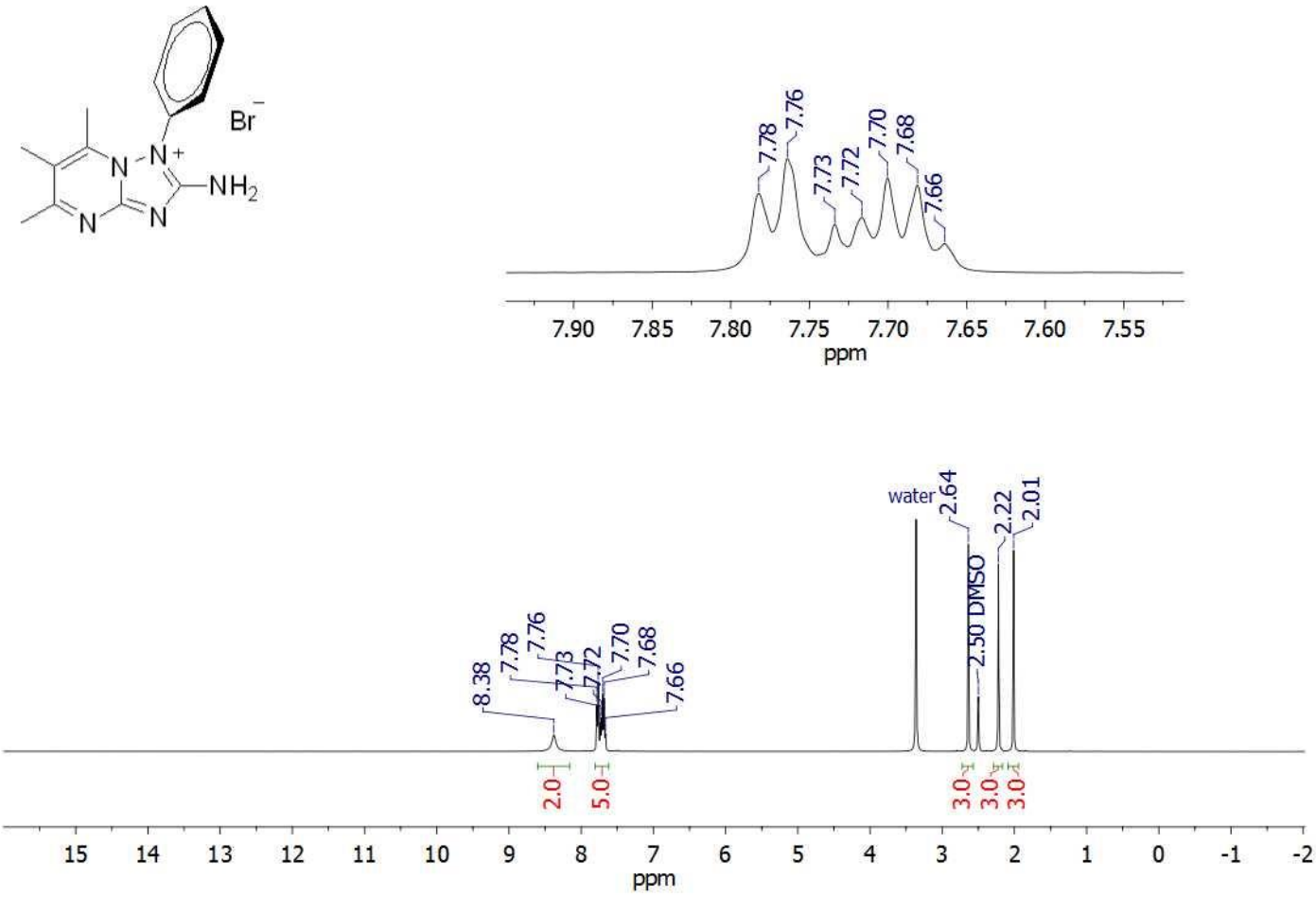


Figure S40. ^{1}H NMR spectrum of compound **4e** (DMSO-d_6)

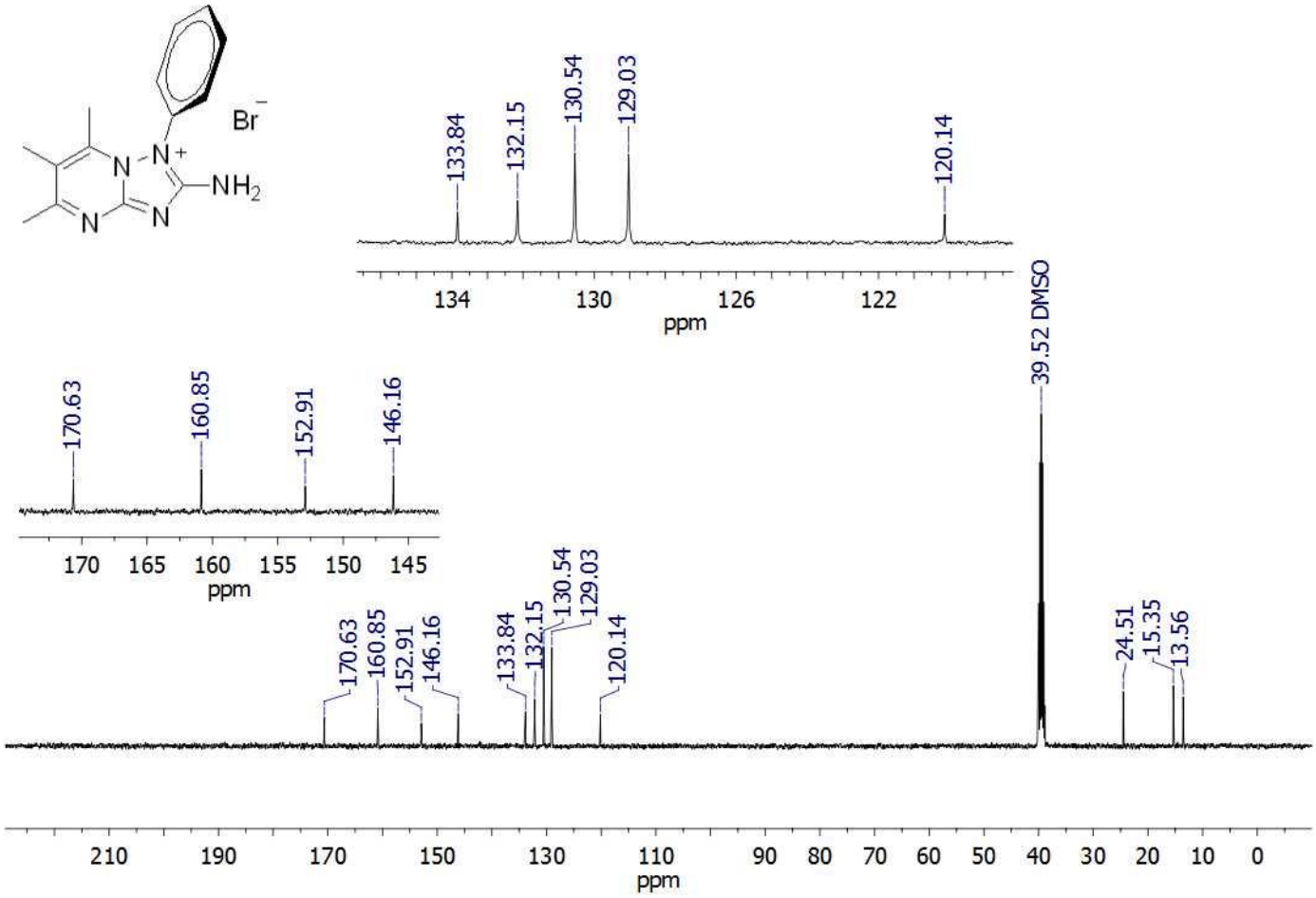


Figure S41. ^{13}C NMR spectrum of compound **4e** (DMSO-d_6)

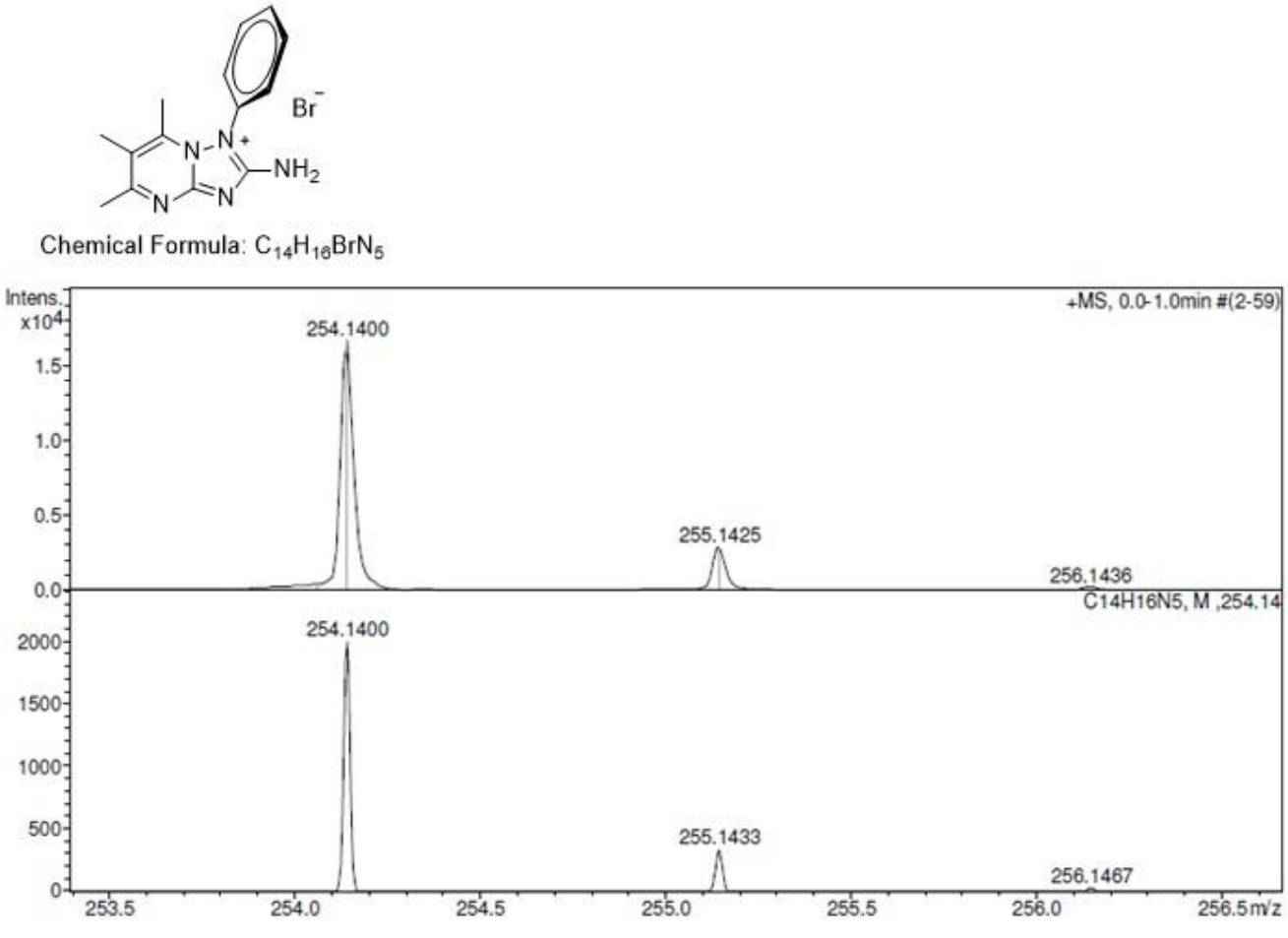


Figure S42. HRMS (ESI$^+$) of compound **4e**

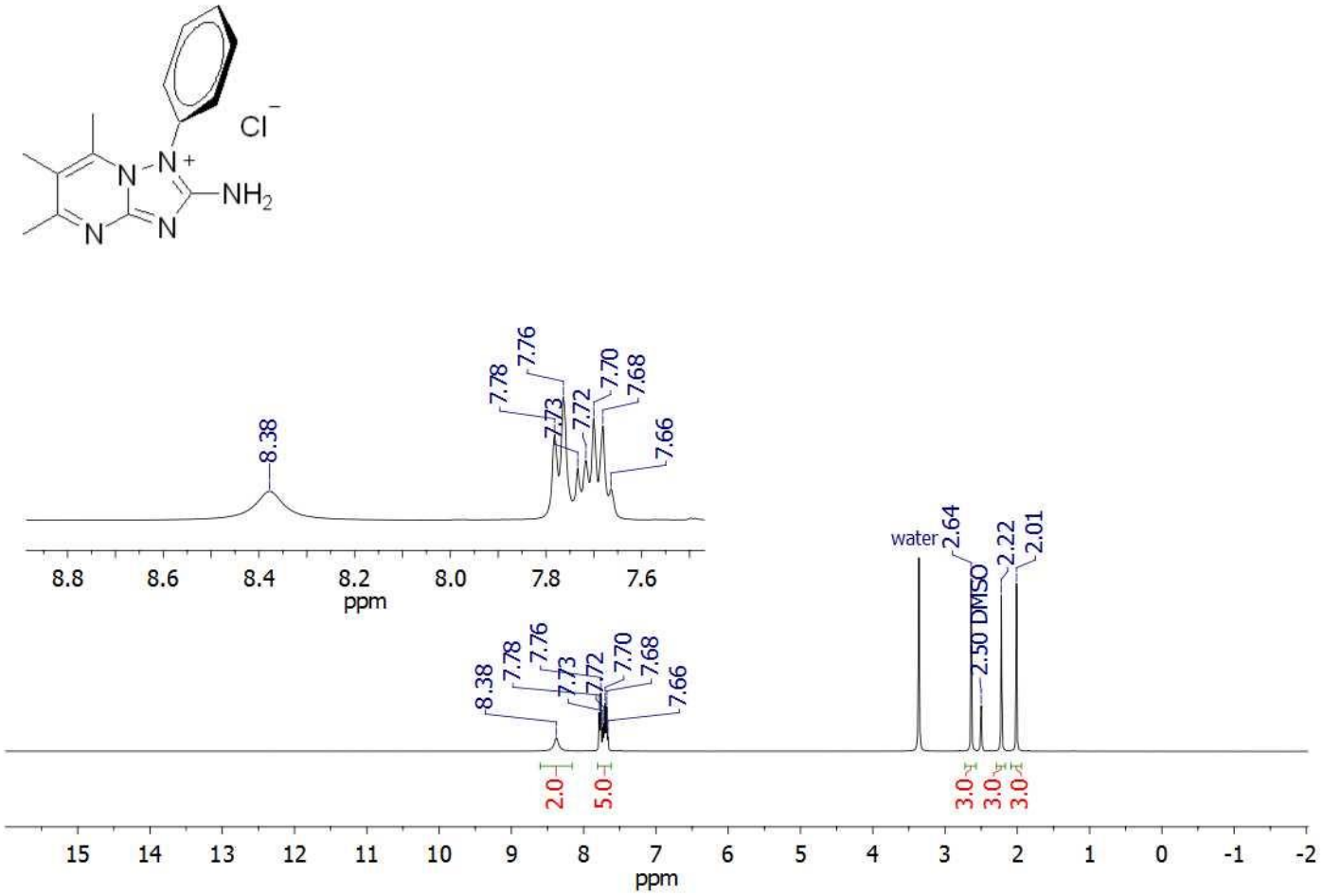


Figure S43. [1]H NMR spectrum of compound **4f** (DMSO-d_6)

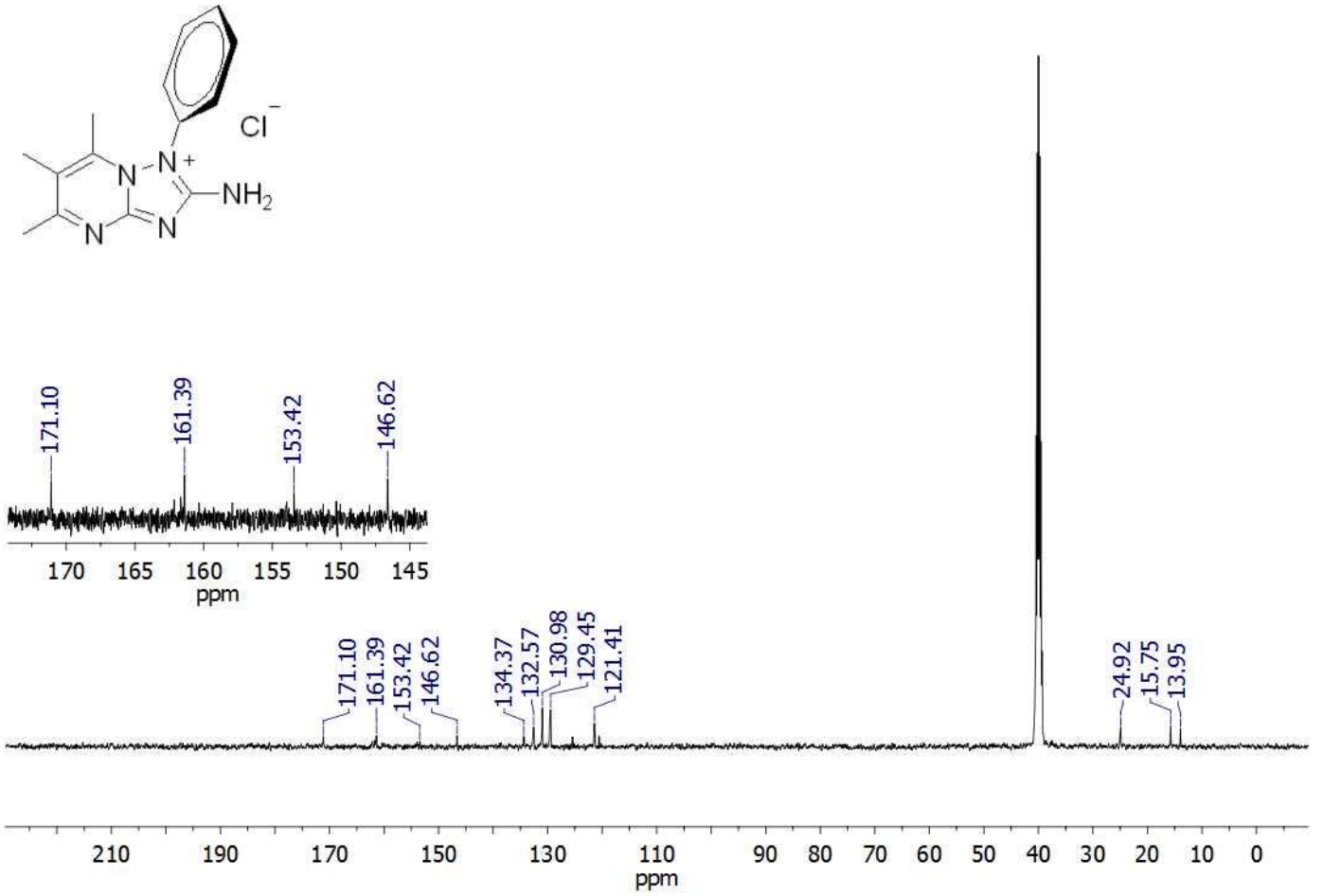


Figure S44. [13]C NMR spectrum of compound **4f** (DMSO-d_6)

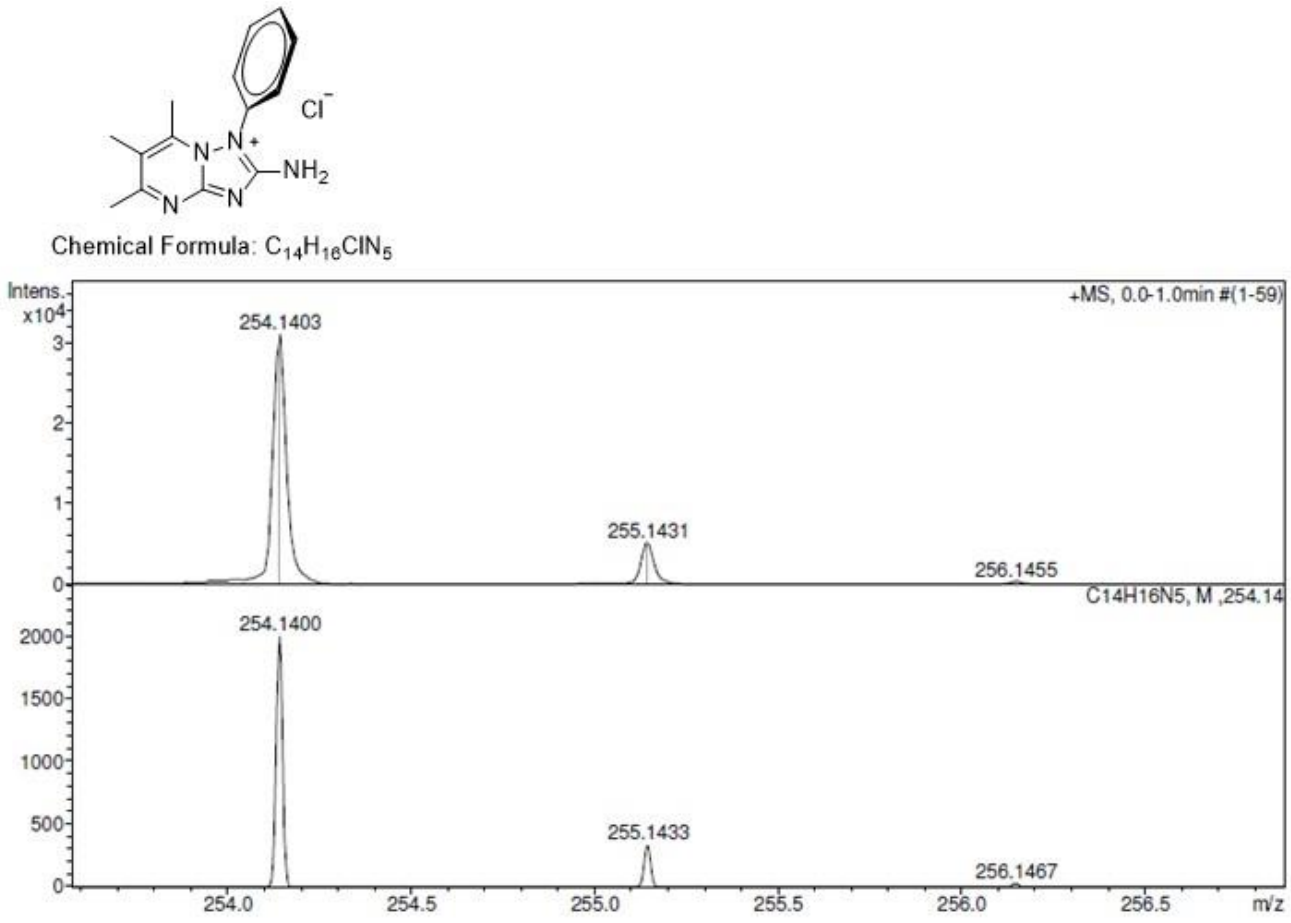


Figure S45. HRMS (ESI$^+$) of compound **4f**

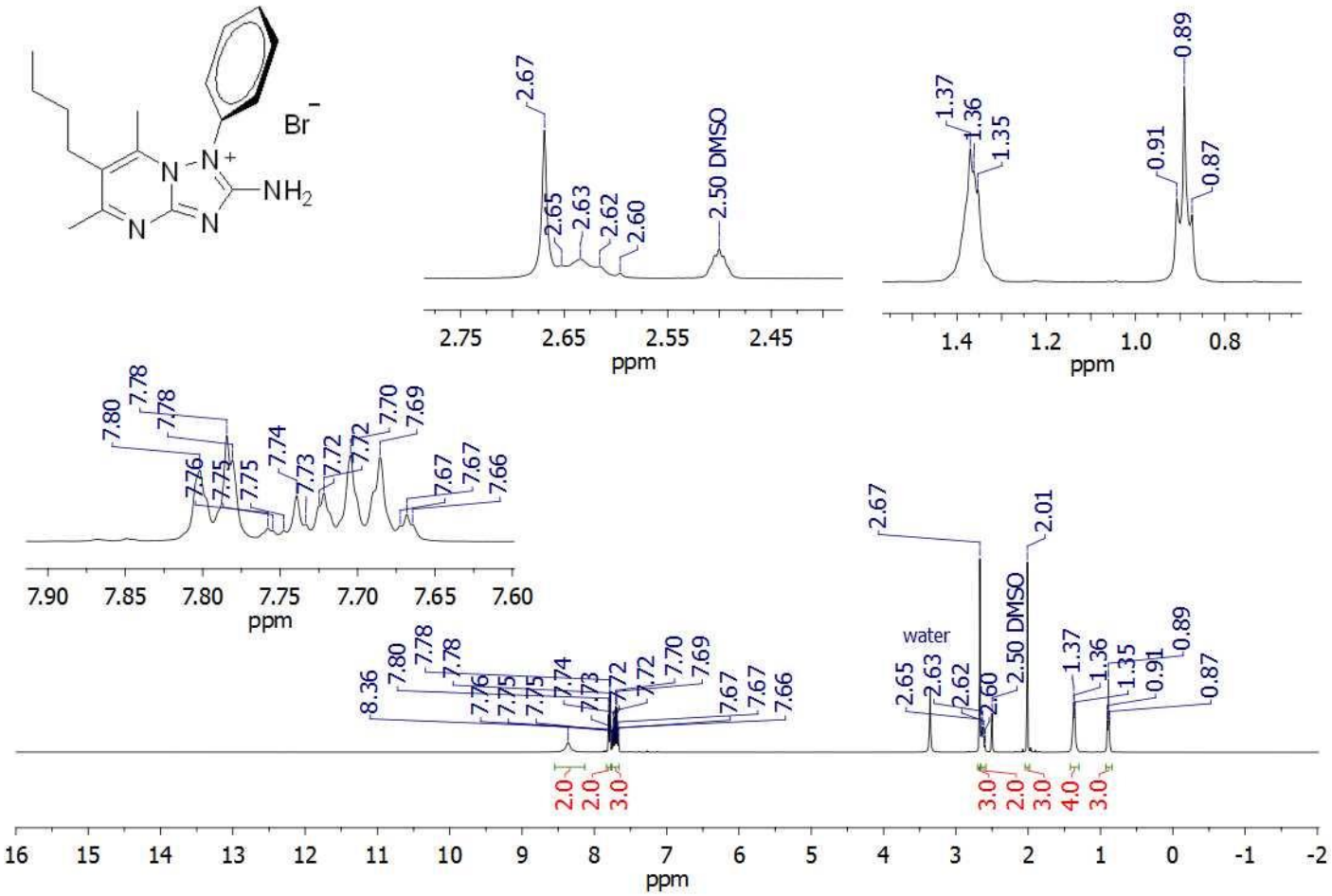


Figure S46. ^{1}H NMR spectrum of compound **4g** (DMSO-d_6)

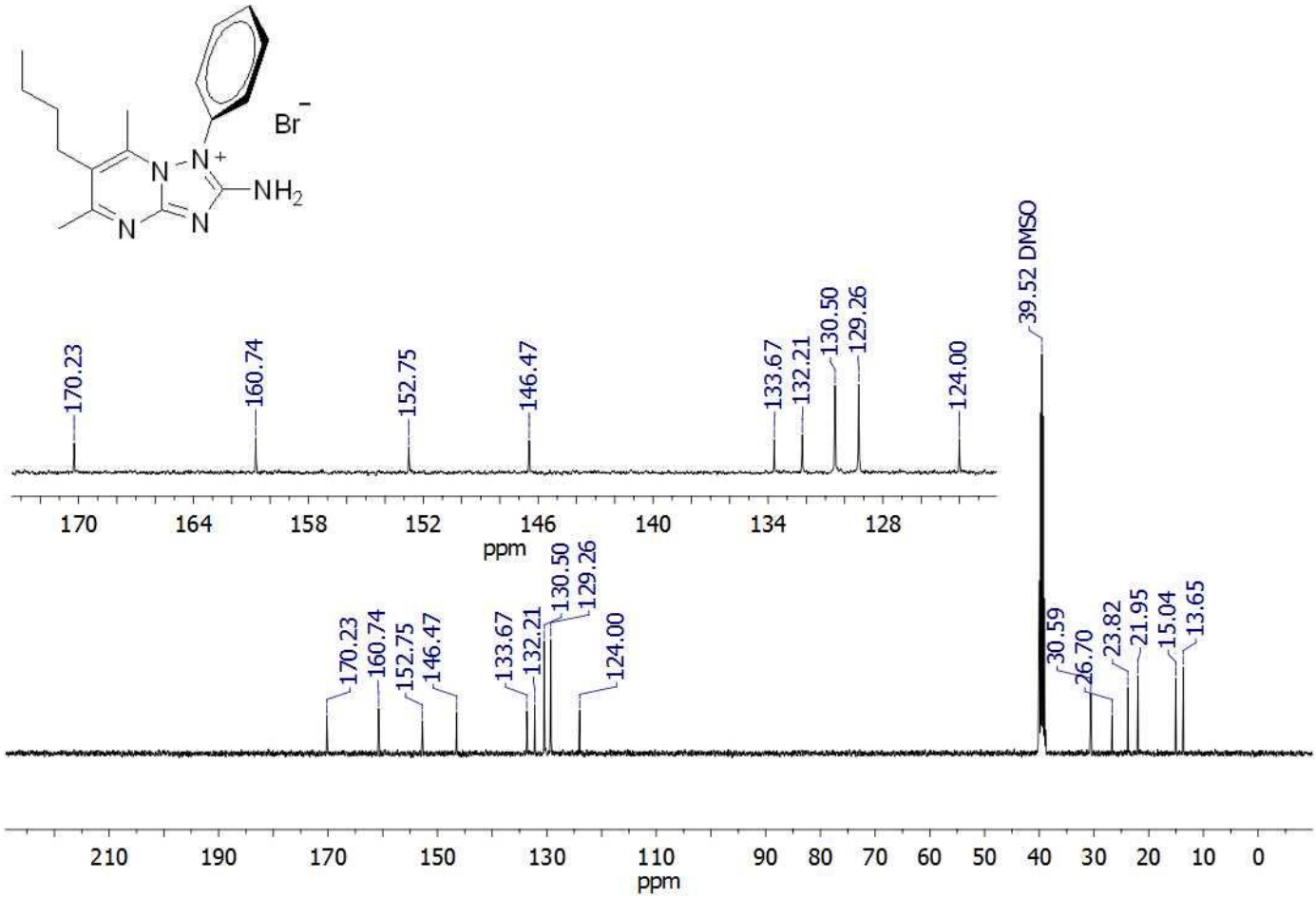


Figure S47. ^{13}C NMR spectrum of compound **4g** (DMSO-d_6)

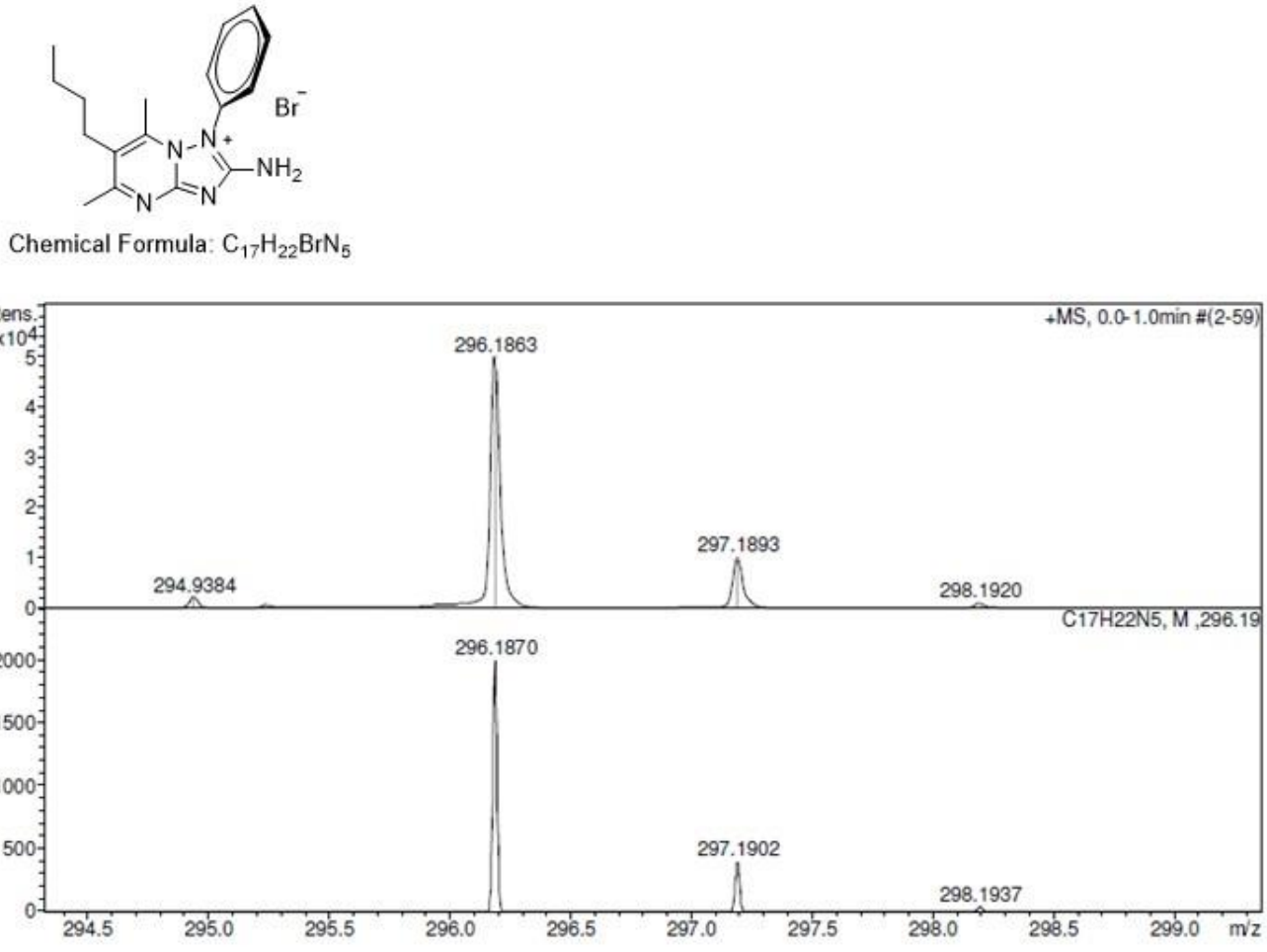


Figure S48. HRMS (ESI$^+$) of compound **4g**

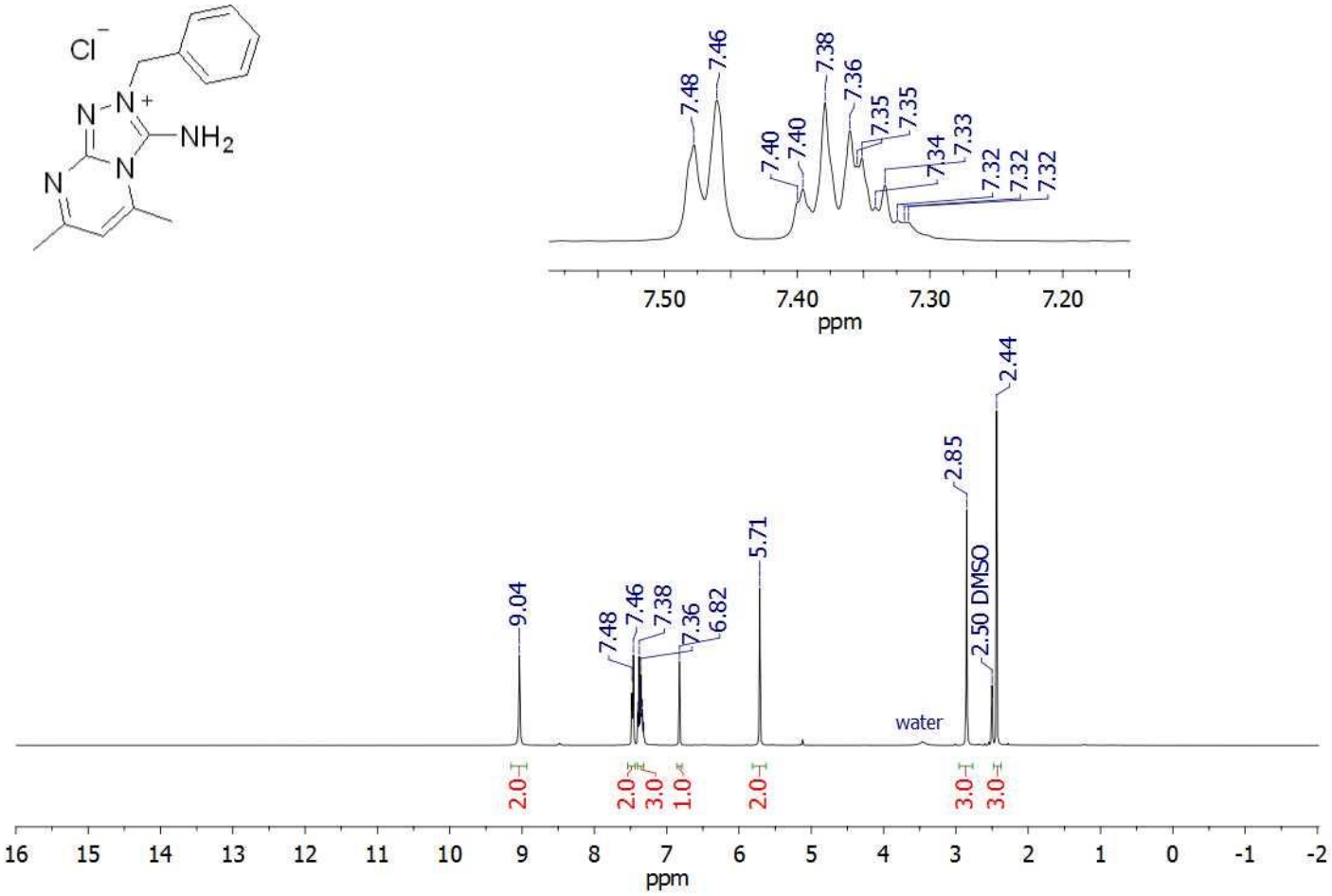


Figure S49. [1]H NMR spectrum of compound **5a** (DMSO-d_6)

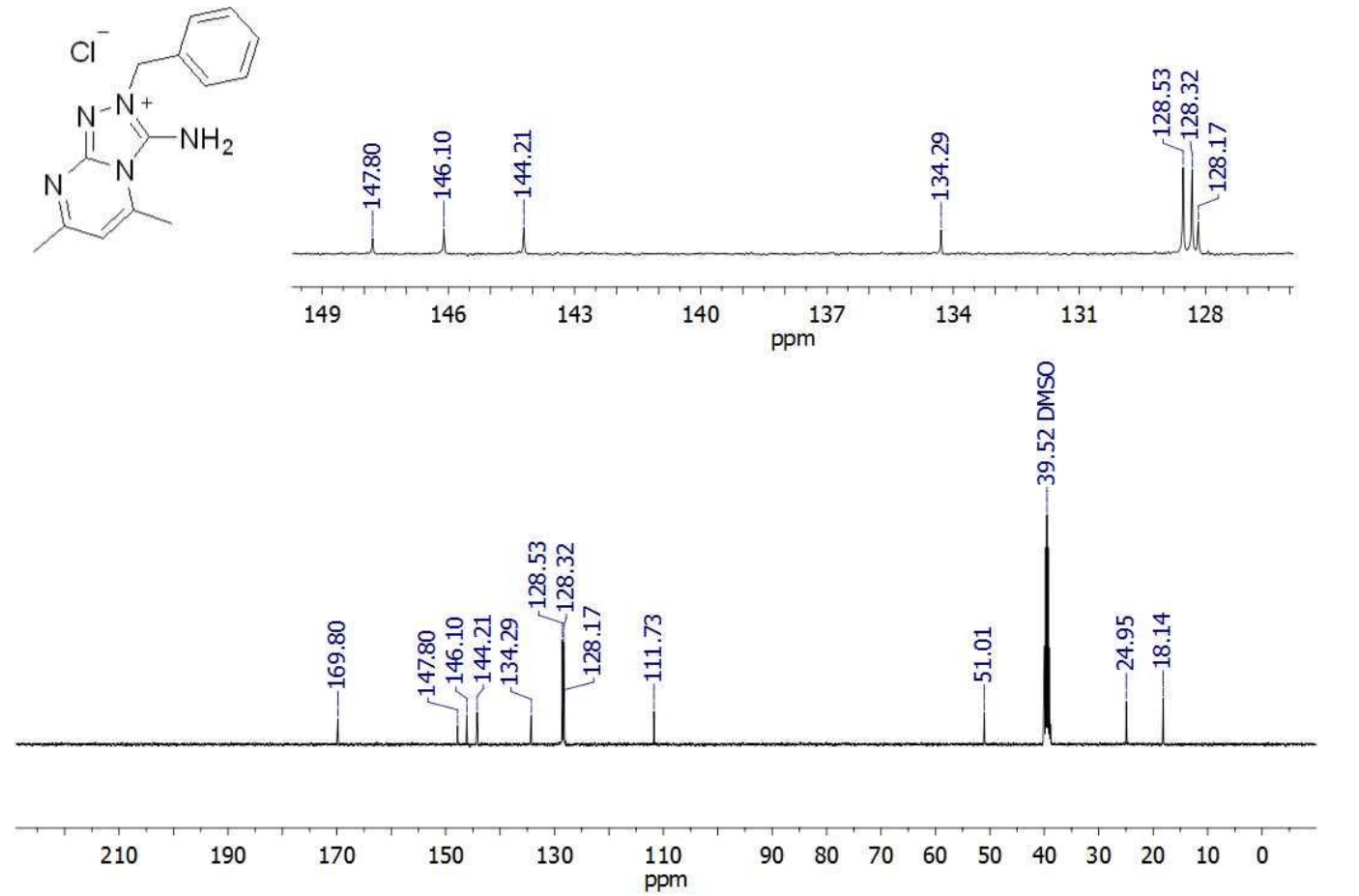


Figure S50. [13]C NMR spectrum of compound **5a** (DMSO-d_6)

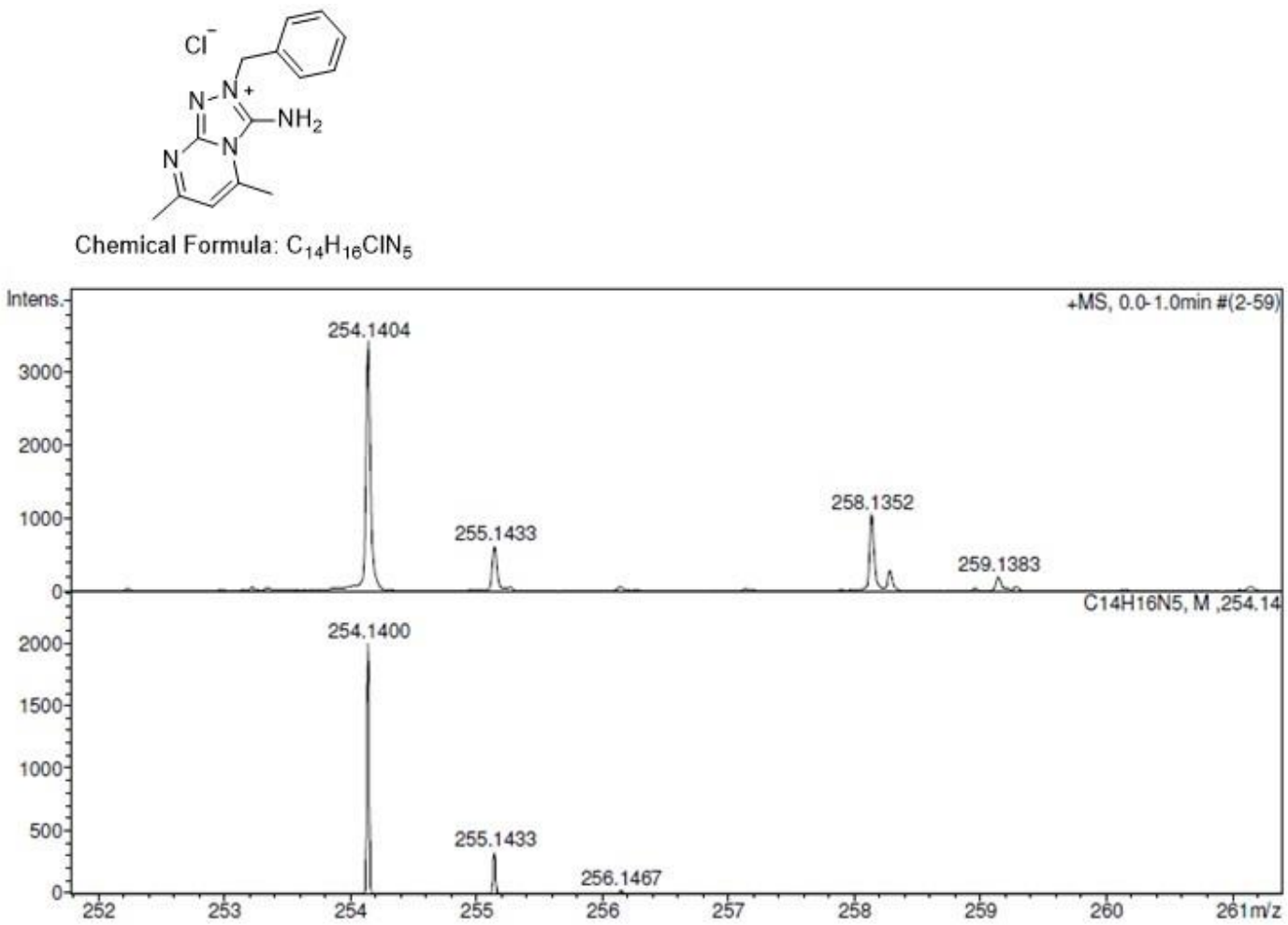


Figure S51. HRMS (ESI^+) of compound **5a**

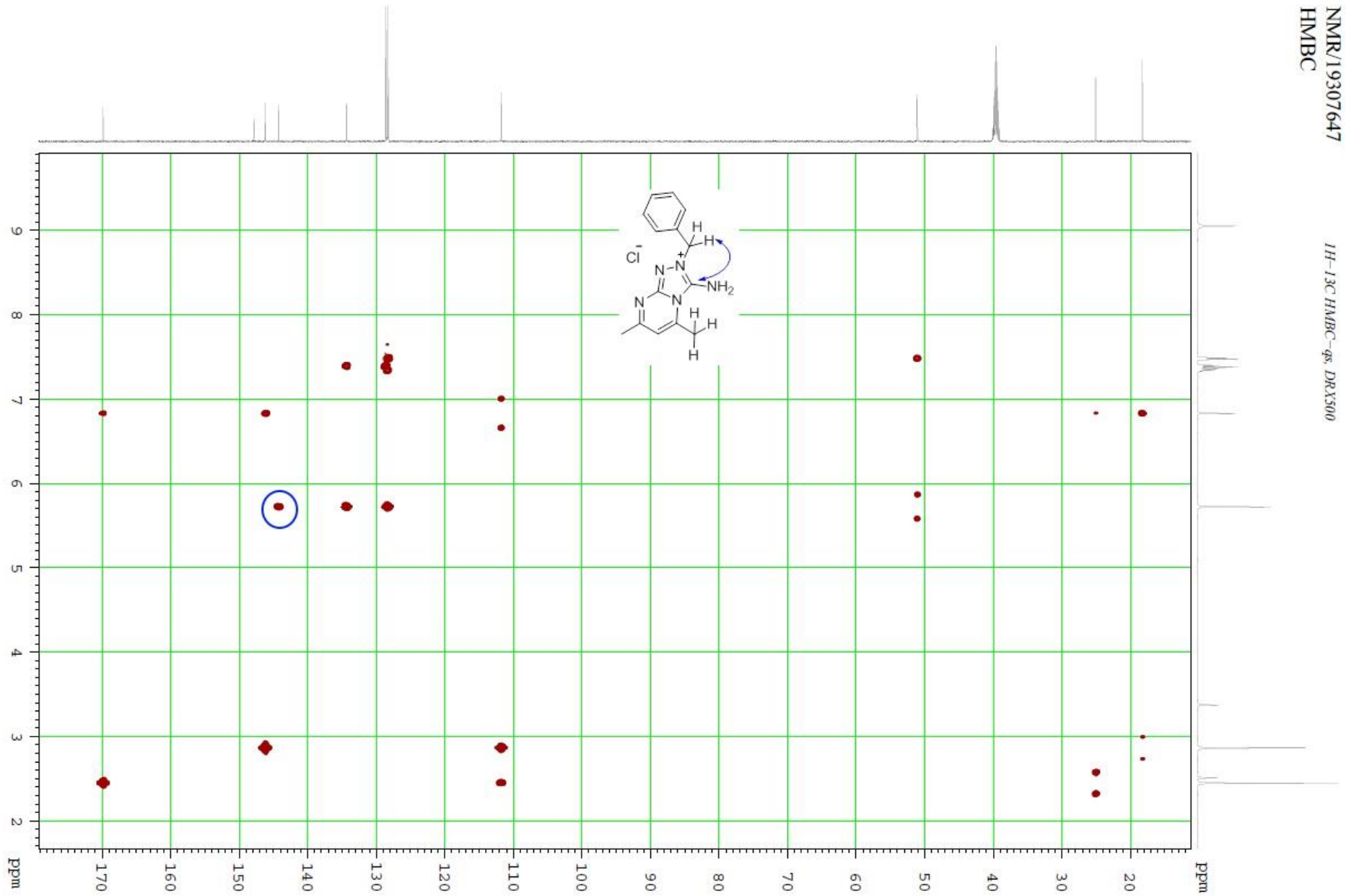


Figure S52. ^{1}H-^{13}C HMBC spectrum of compound **5a** (DMSO-d_6)

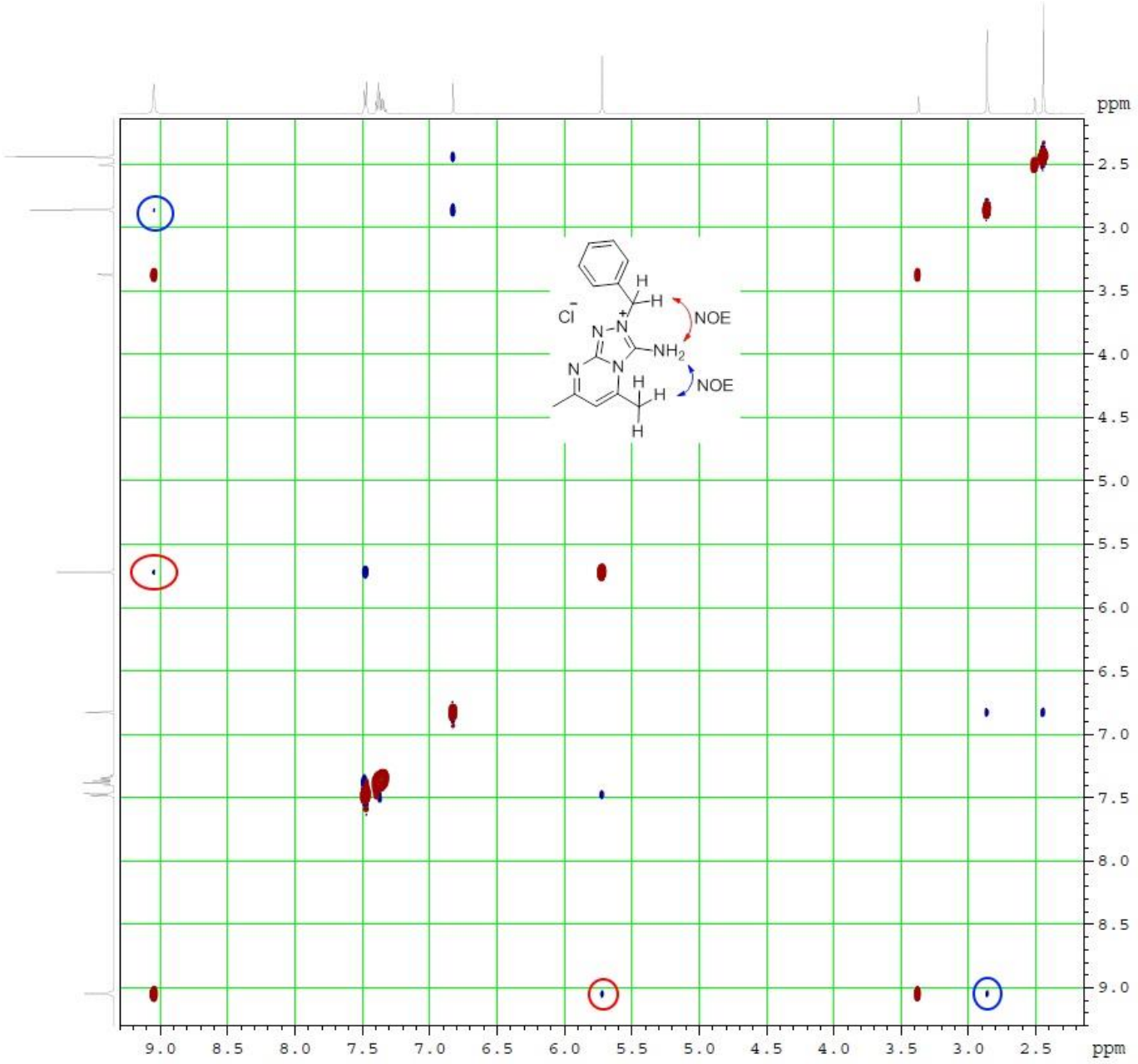


Figure S53. NOESY spectrum of compound **5a** (DMSO-d_6)

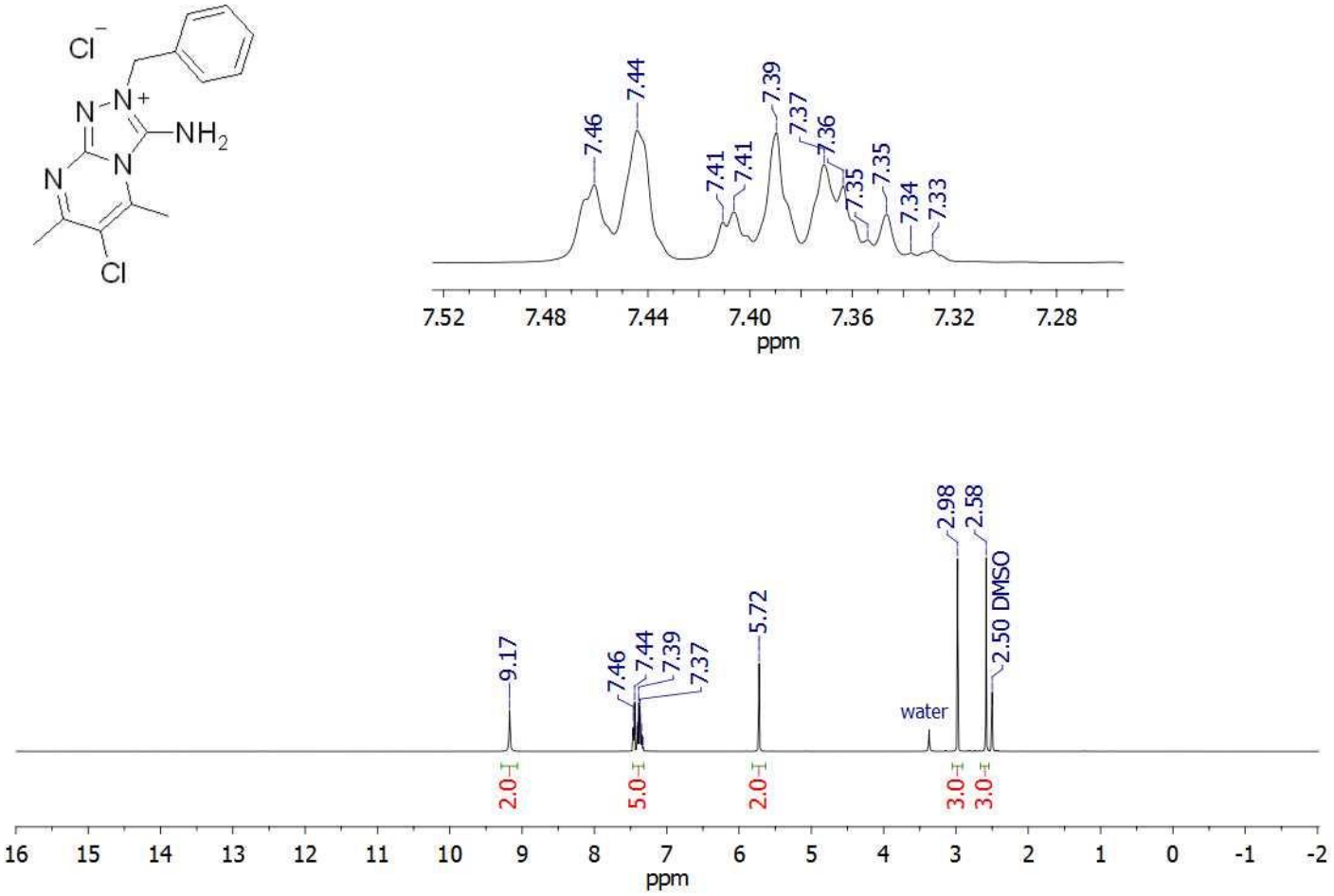


Figure S54. [1]H NMR spectrum of compound **5b** (DMSO-d_6)

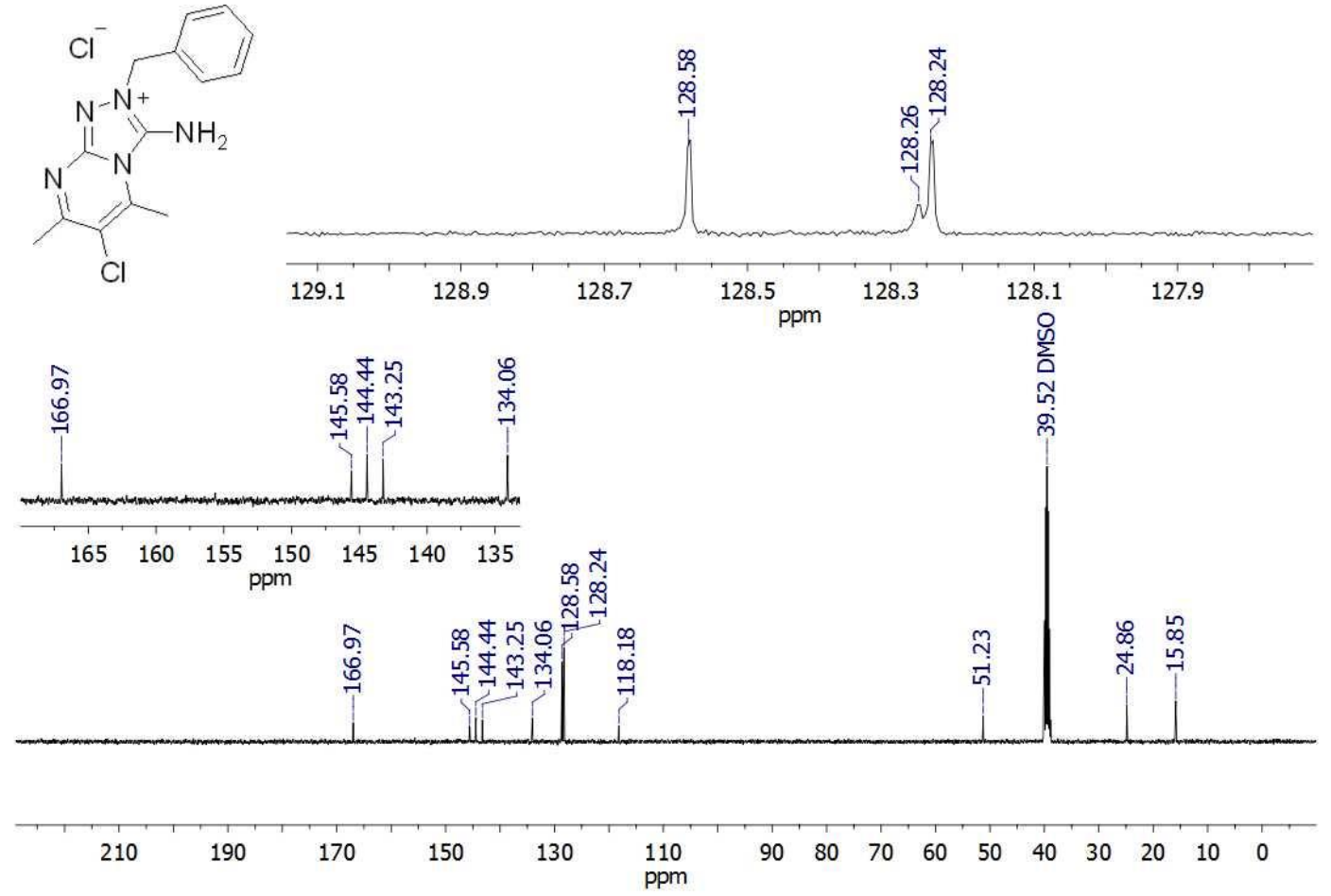


Figure S55. [13]C NMR spectrum of compound **5b** (DMSO-d_6)

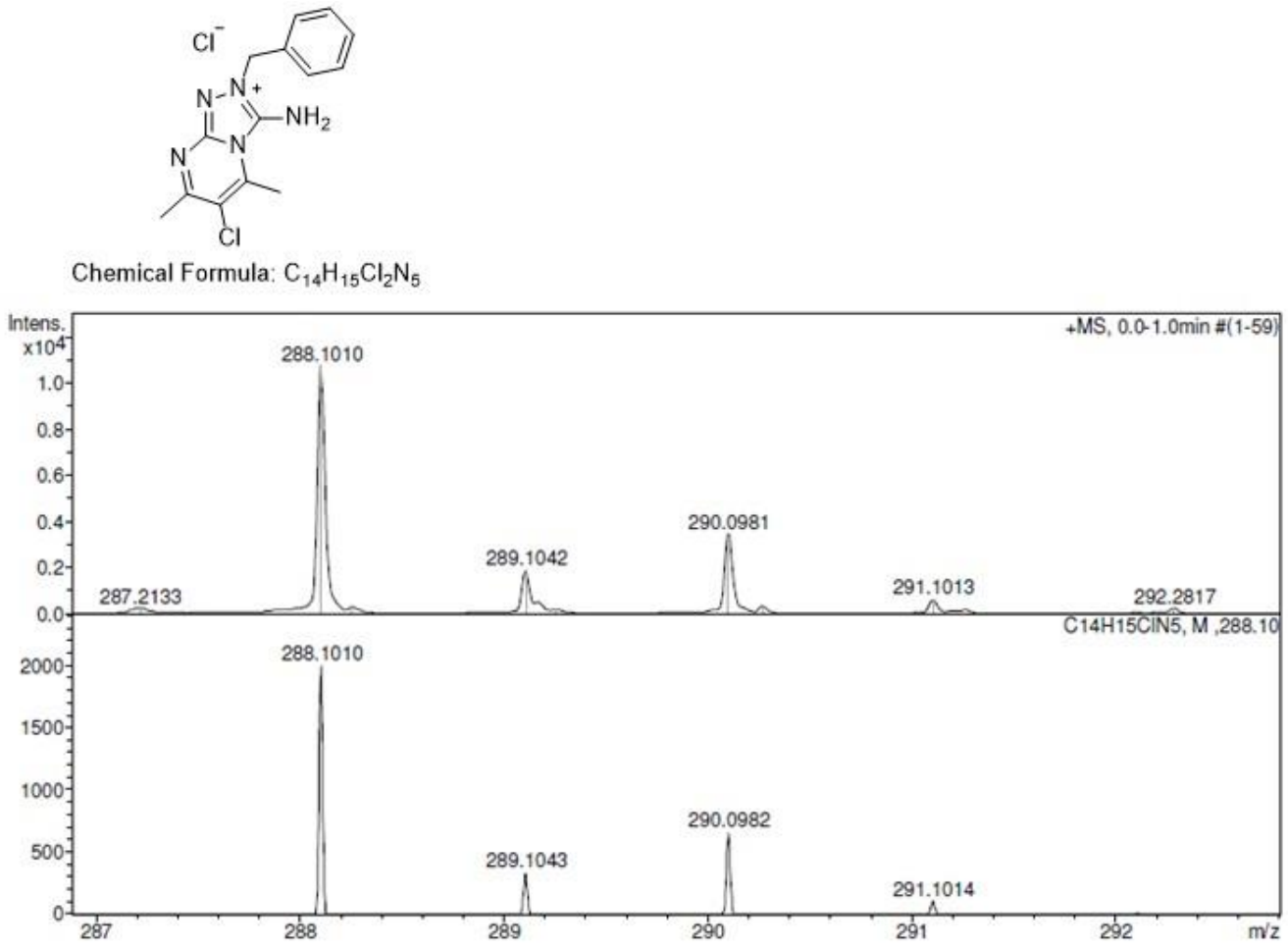


Figure S56. HRMS (ESI$^+$) of compound **5b**

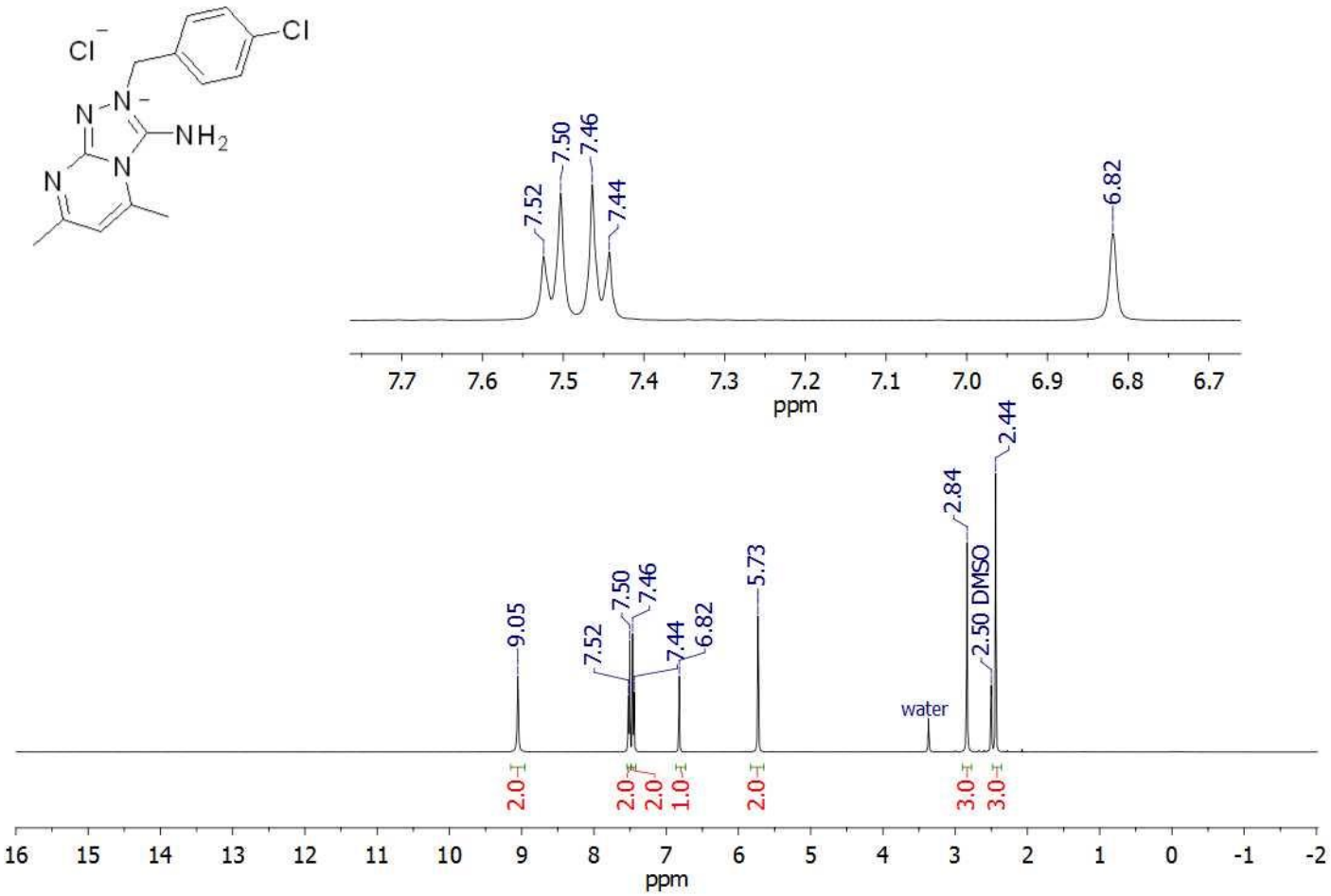


Figure S57. ^{1}H NMR spectrum of compound **5c** (DMSO-d_6)

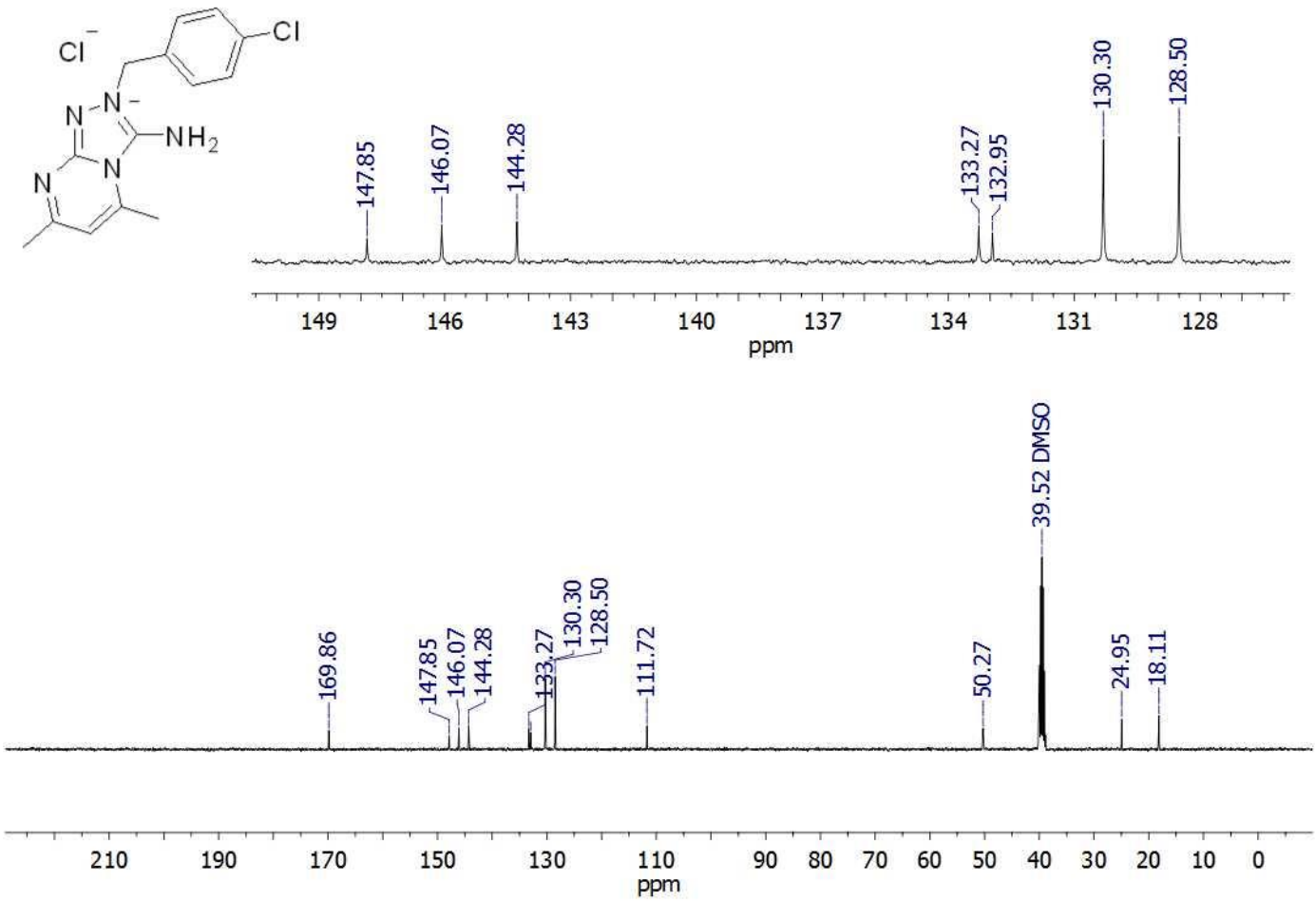


Figure S58. ^{13}C NMR spectrum of compound **5c** (DMSO-d_6)

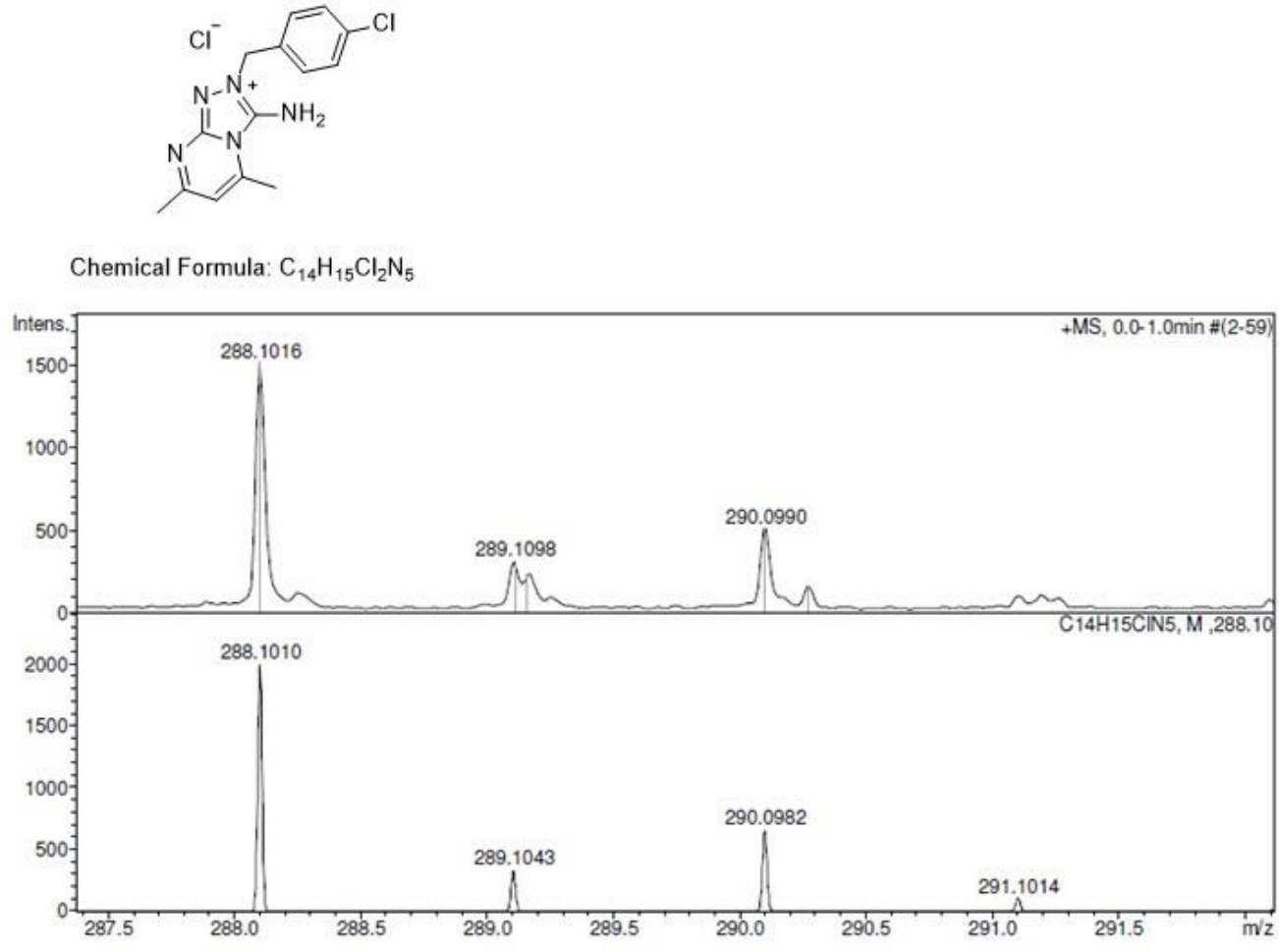


Figure S59. HRMS (ESI$^+$) of compound **5c**

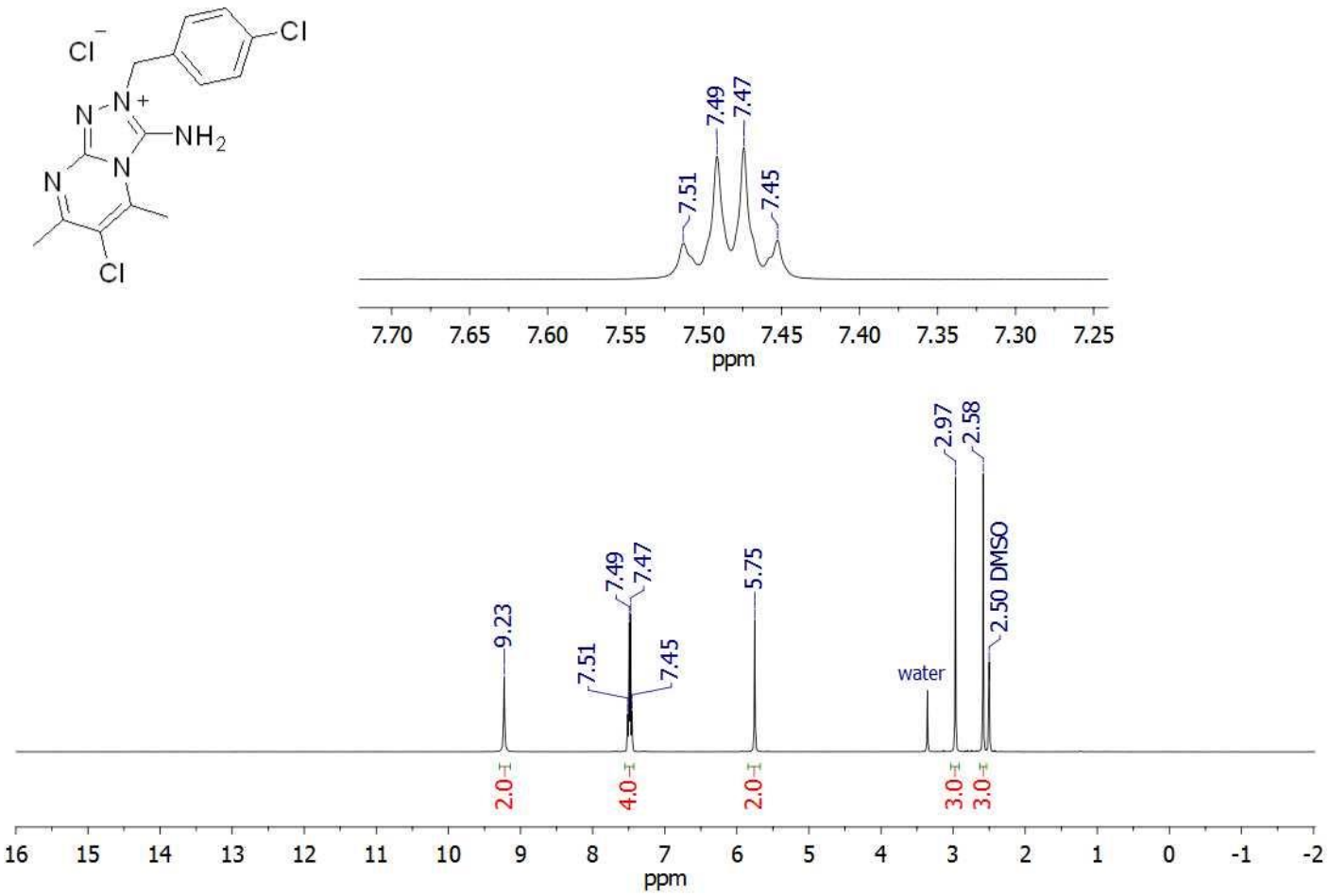


Figure S60. [1]H NMR spectrum of compound **5d** (DMSO-d_6)

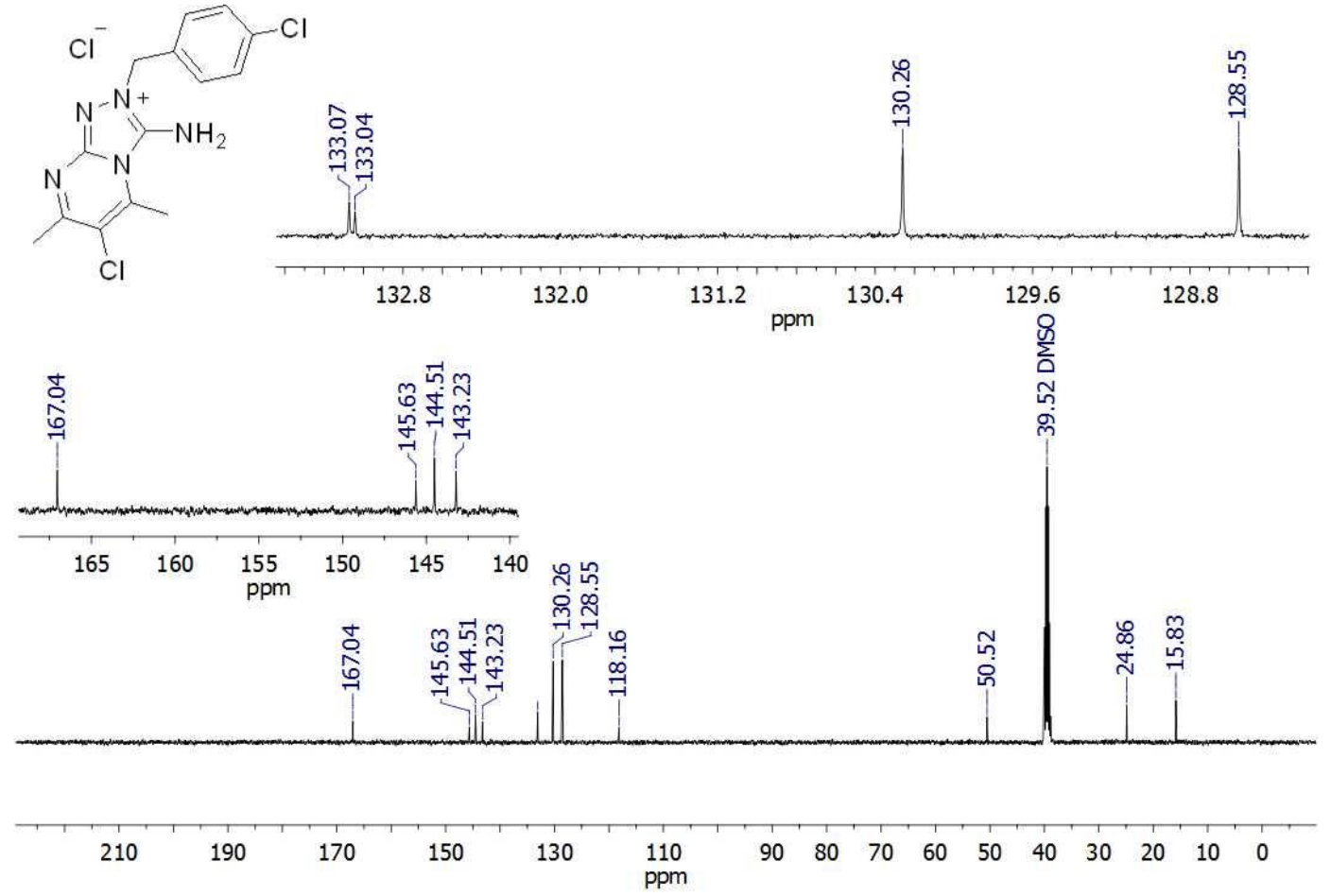


Figure S61. [13]C NMR spectrum of compound **5d** (DMSO-d_6)

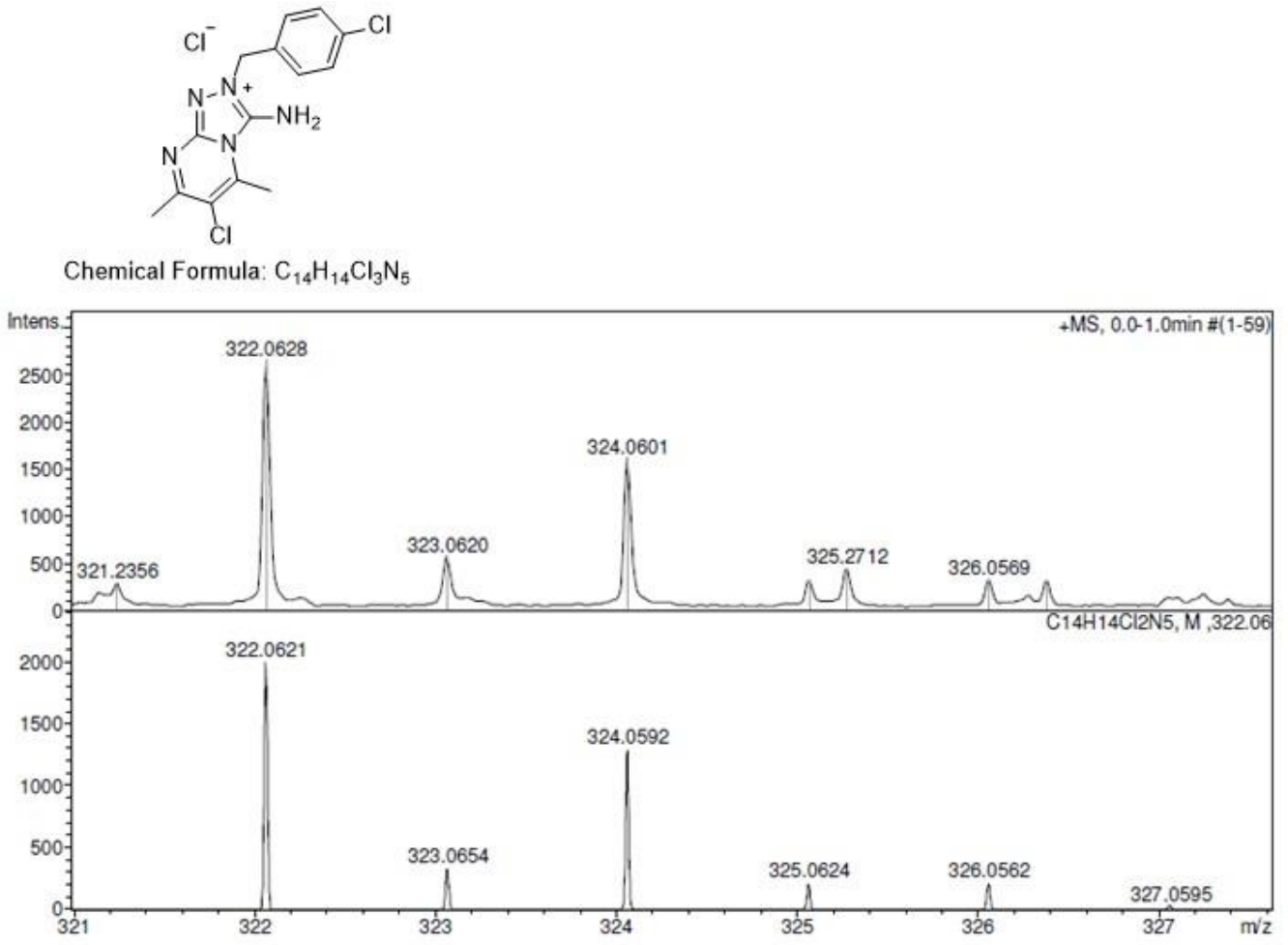


Figure S62. HRMS (ESI$^+$) of compound **5d**

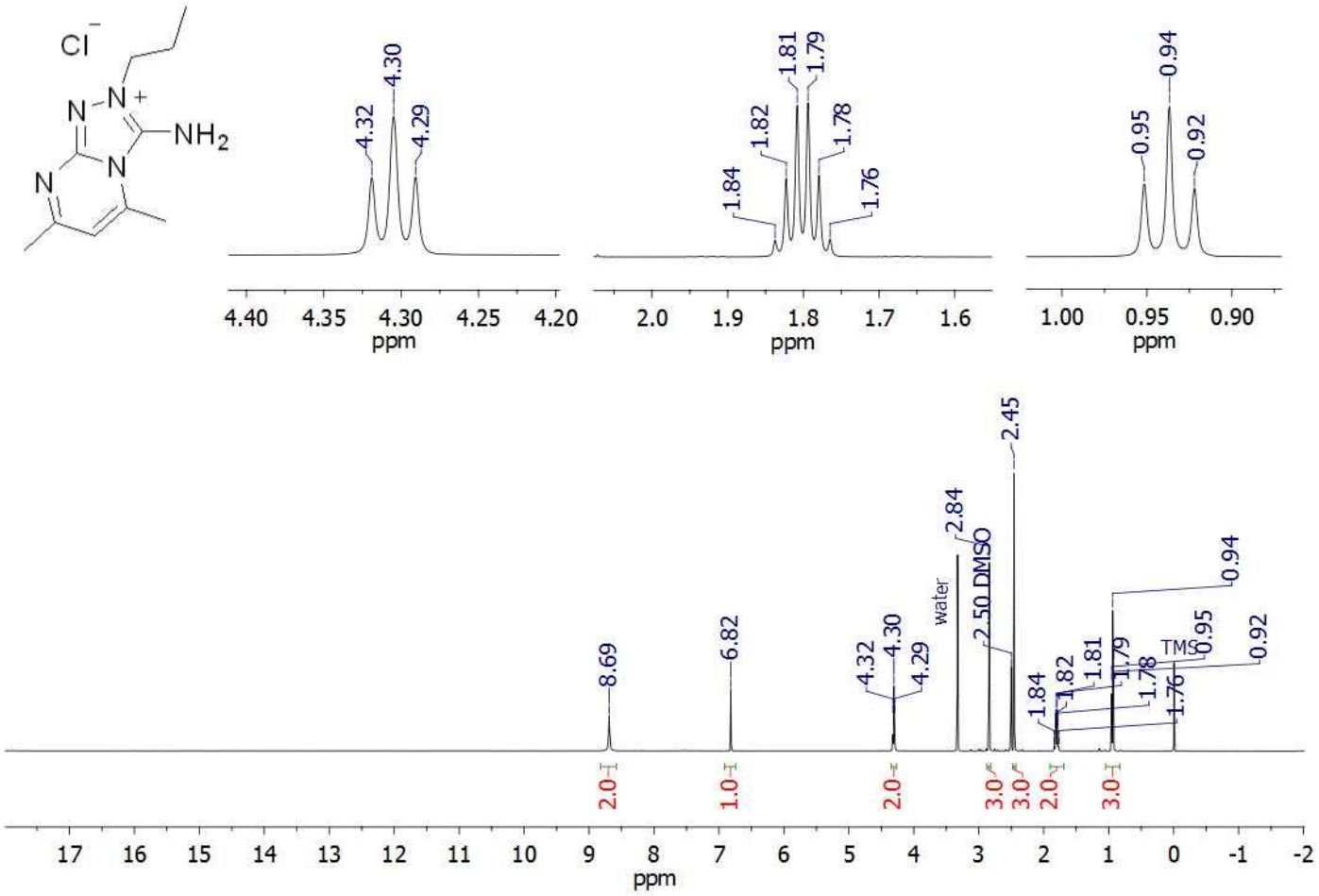


Figure S63. ^{1}H NMR spectrum of compound **5e** (DMSO-d_6)

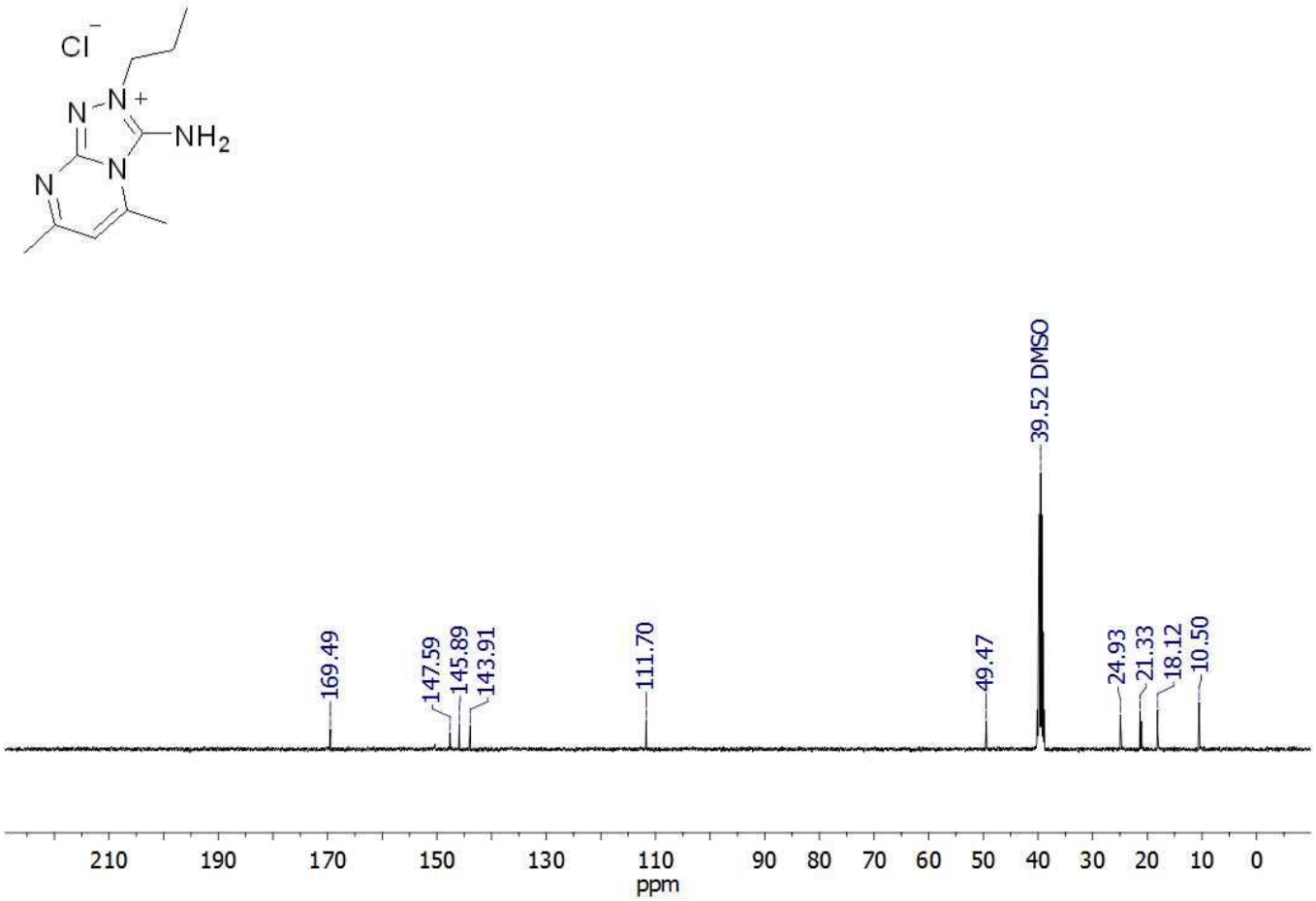


Figure S64. ^{13}C NMR spectrum of compound **5e** (DMSO-d_6)

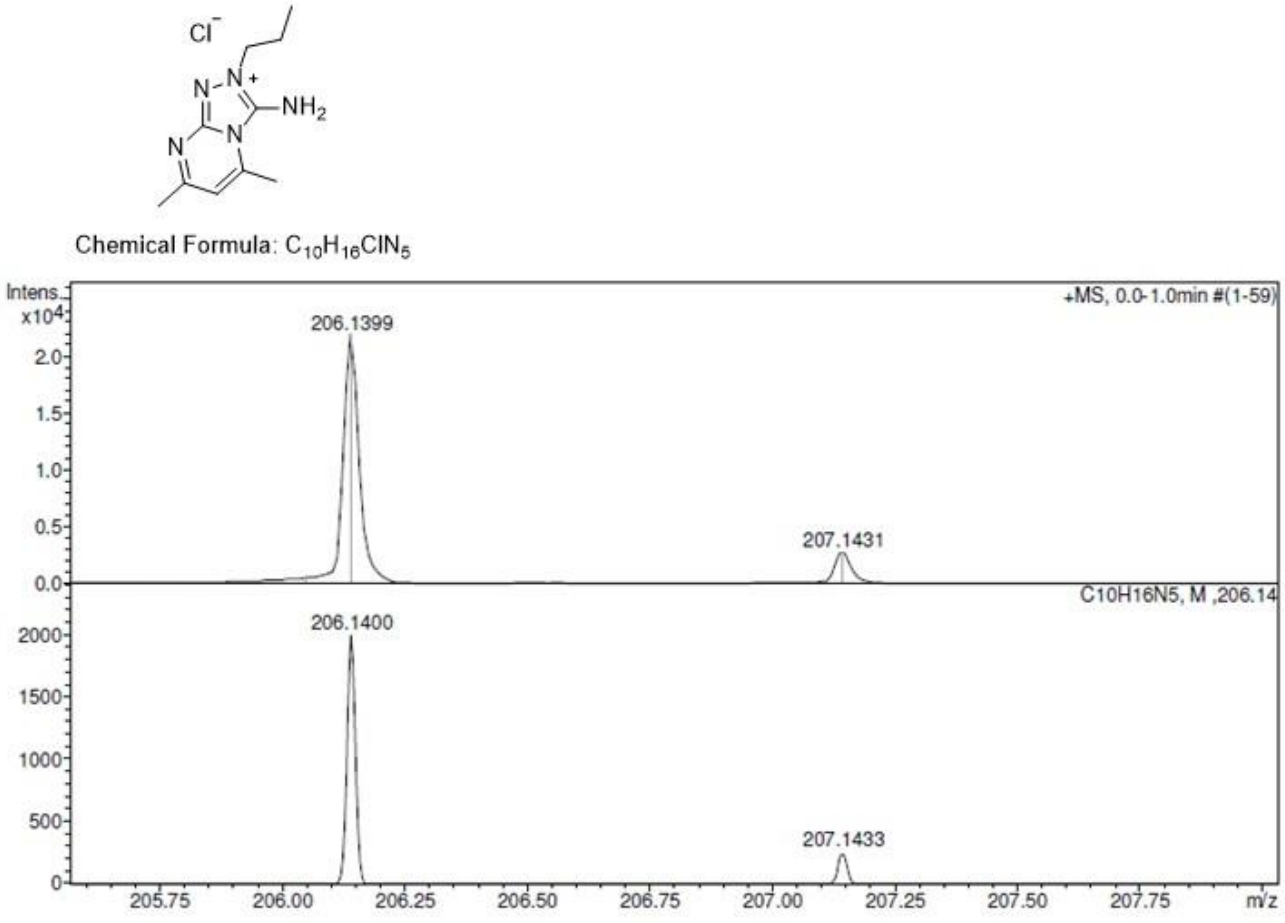


Figure S65. HRMS (ESI$^+$) of compound **5e**

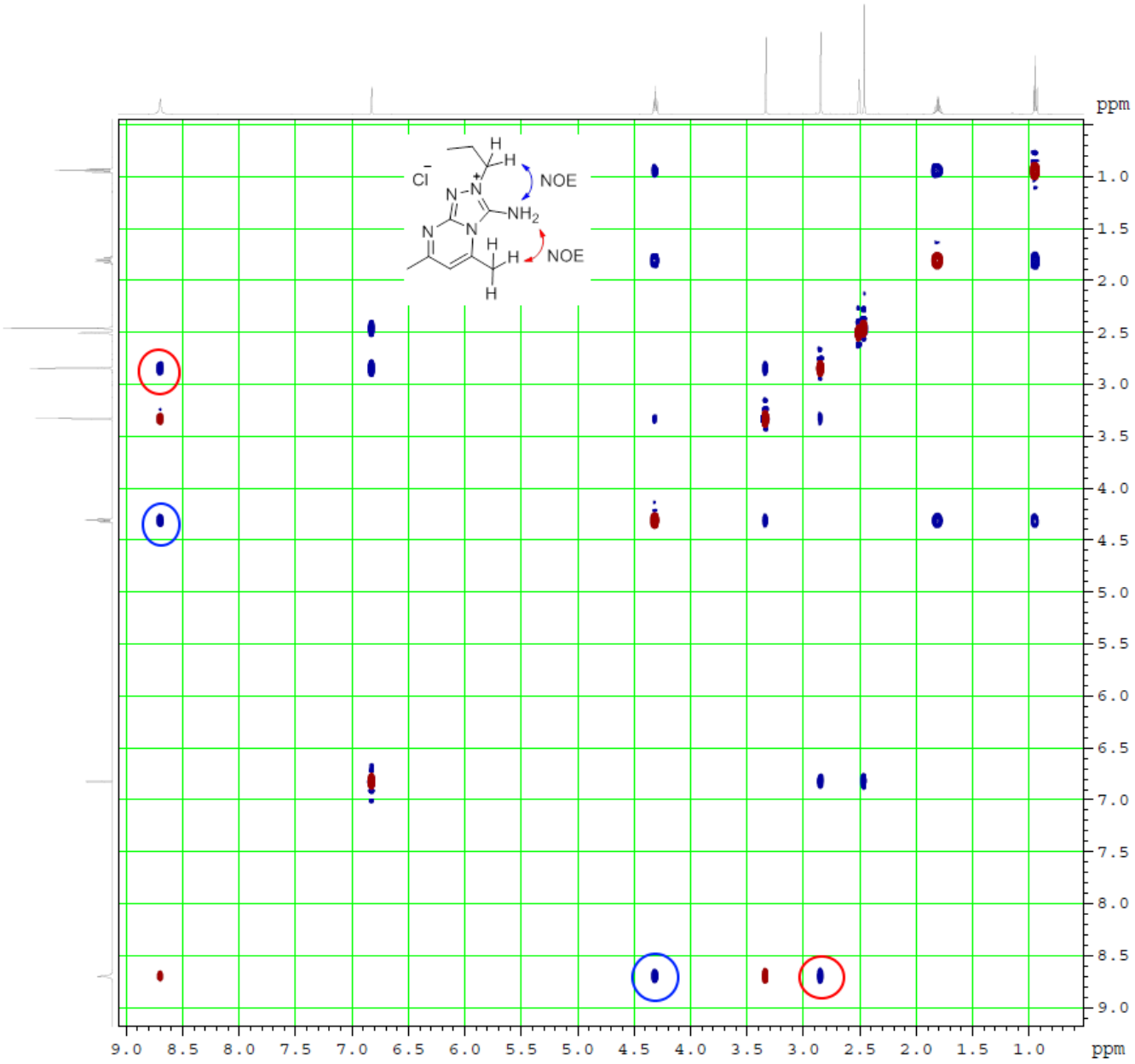


Figure S66. NOESY spectrum of compound **5e** (DMSO-d_6)

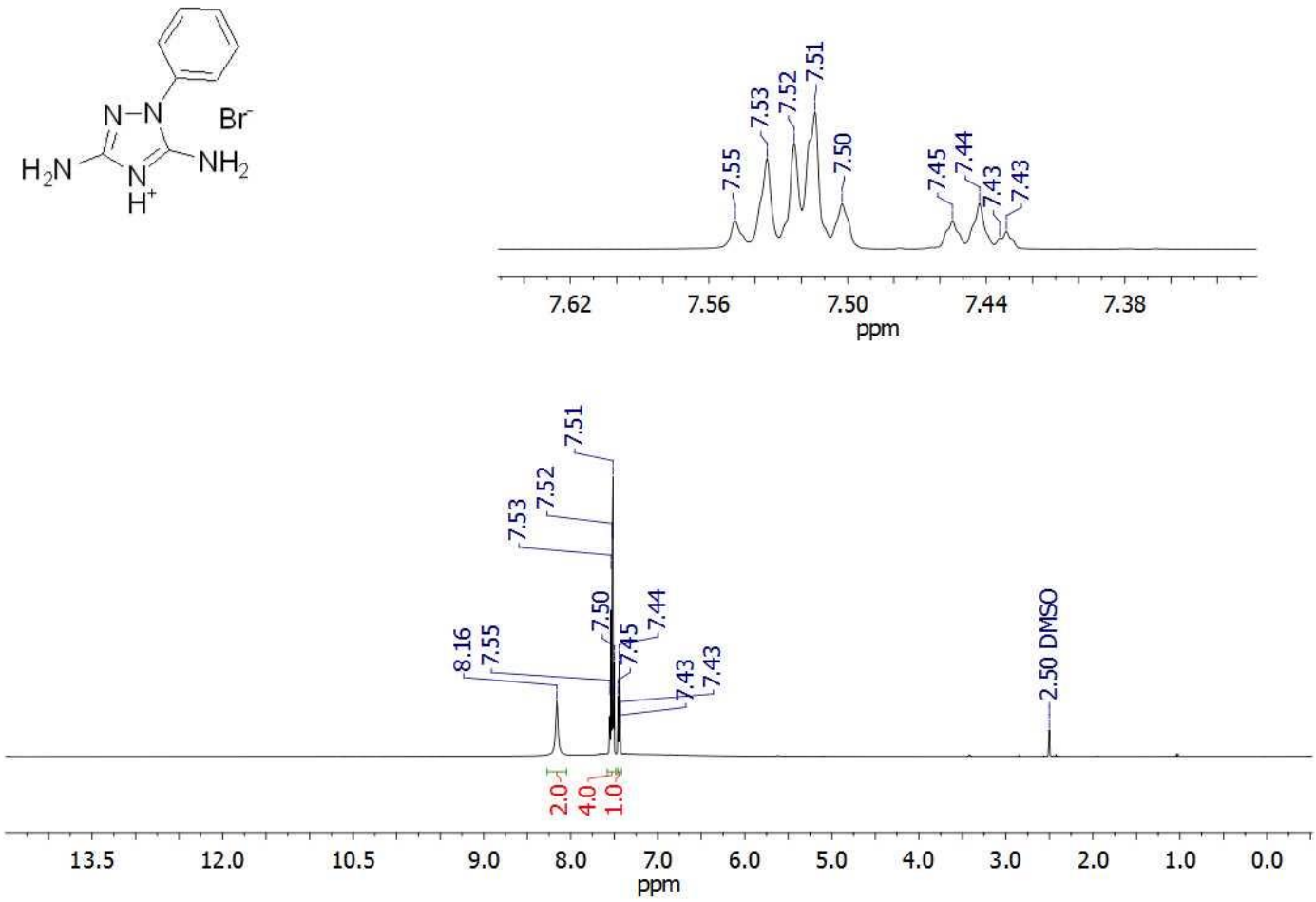


Figure S67. [1]H NMR spectrum of compound **6a** (DMSO-d_6)

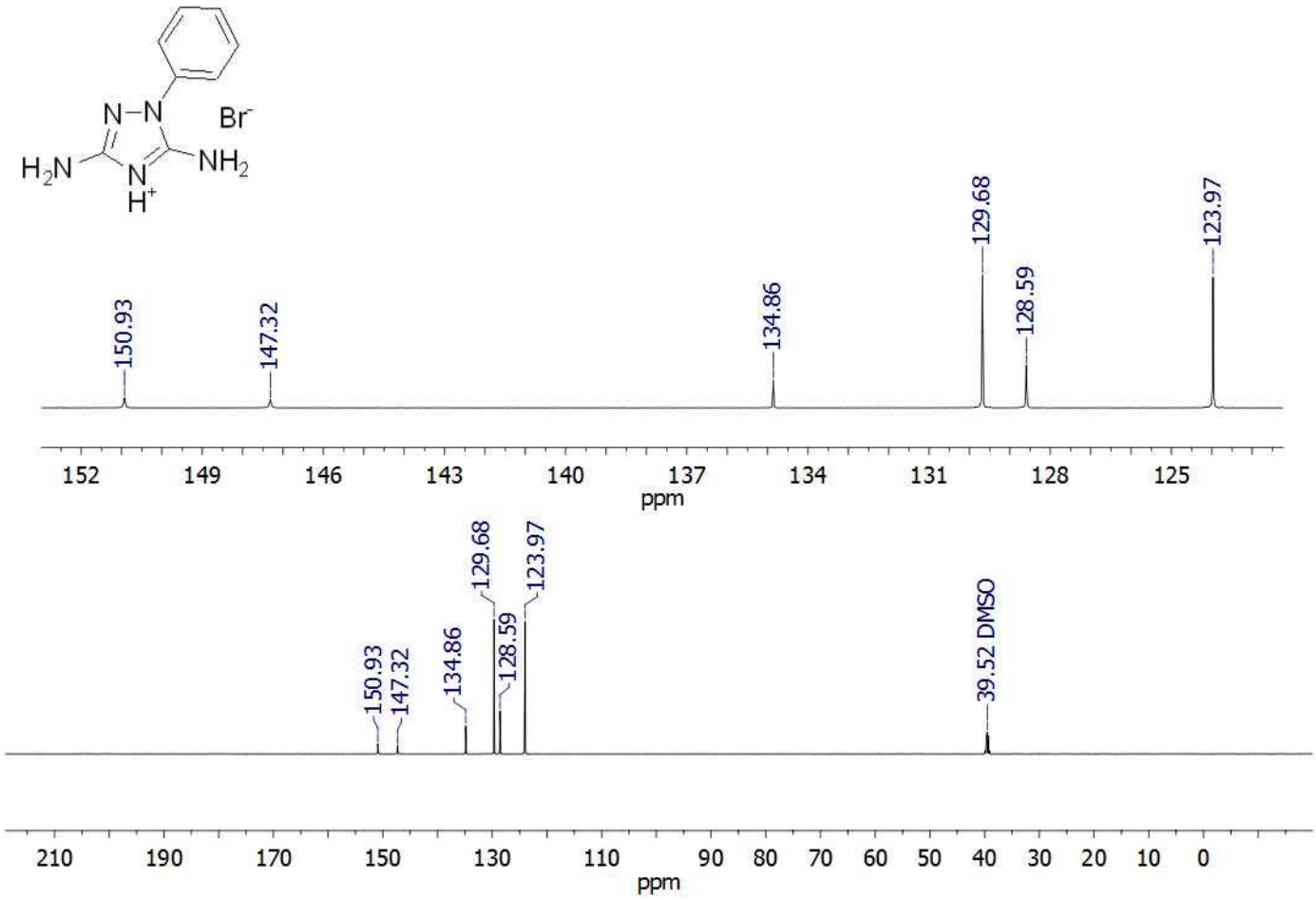


Figure S68. [13]C NMR spectrum of compound **6a** (DMSO-d_6)

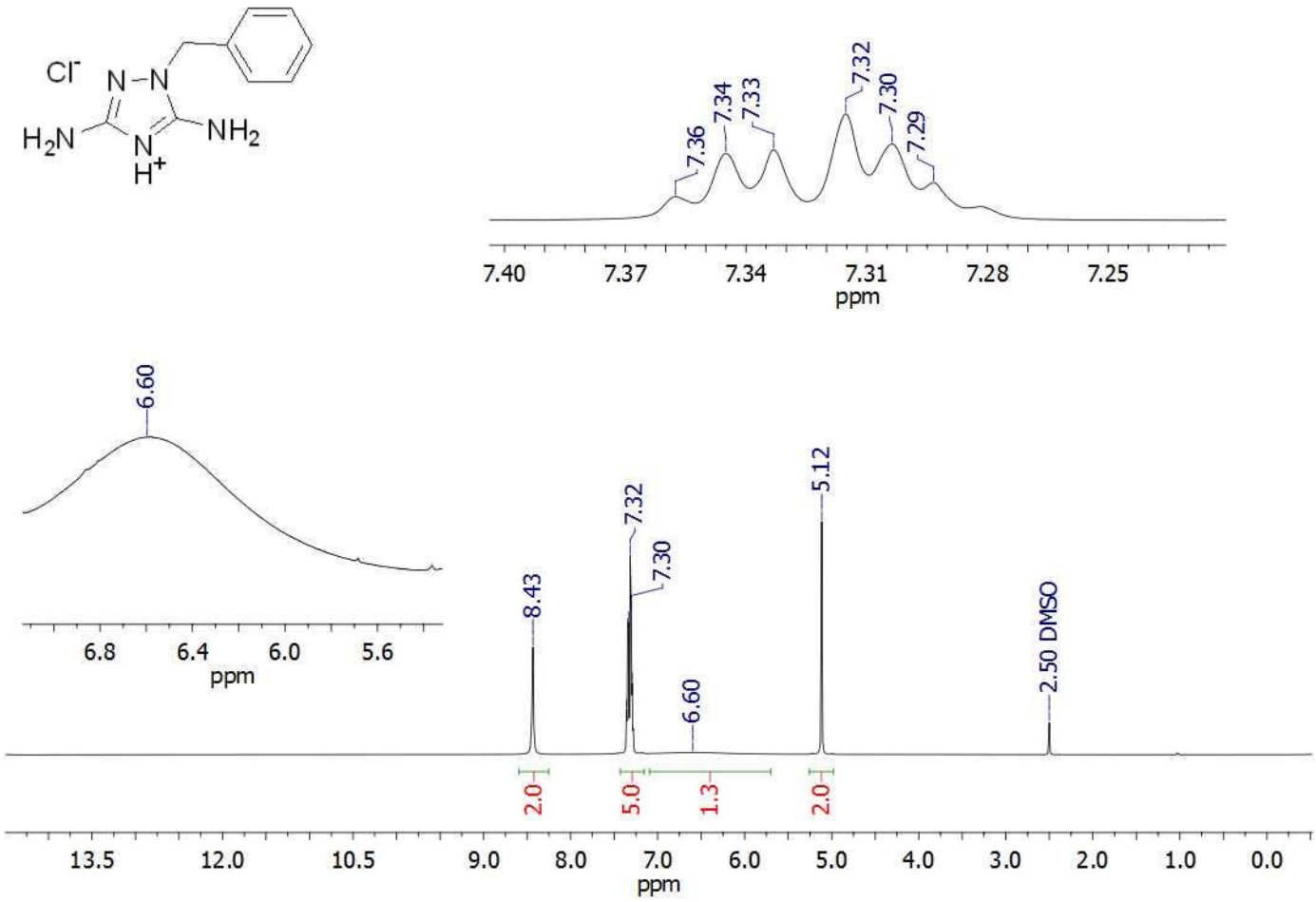


Figure S69. ^{1}H NMR spectrum of compound **6b** (DMSO-d_6)

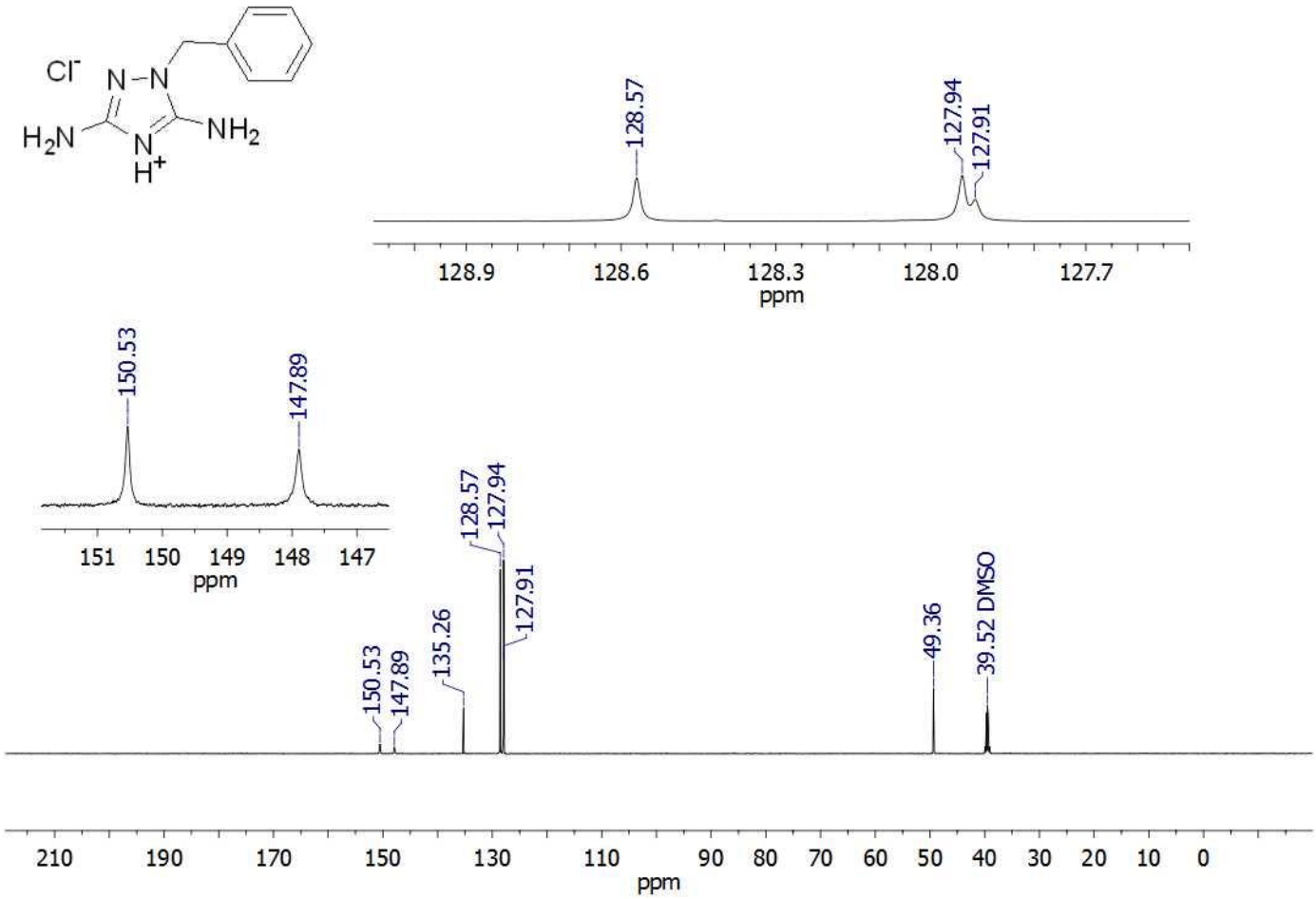


Figure S70. ^{13}C NMR spectrum of compound **6b** (DMSO-d_6)

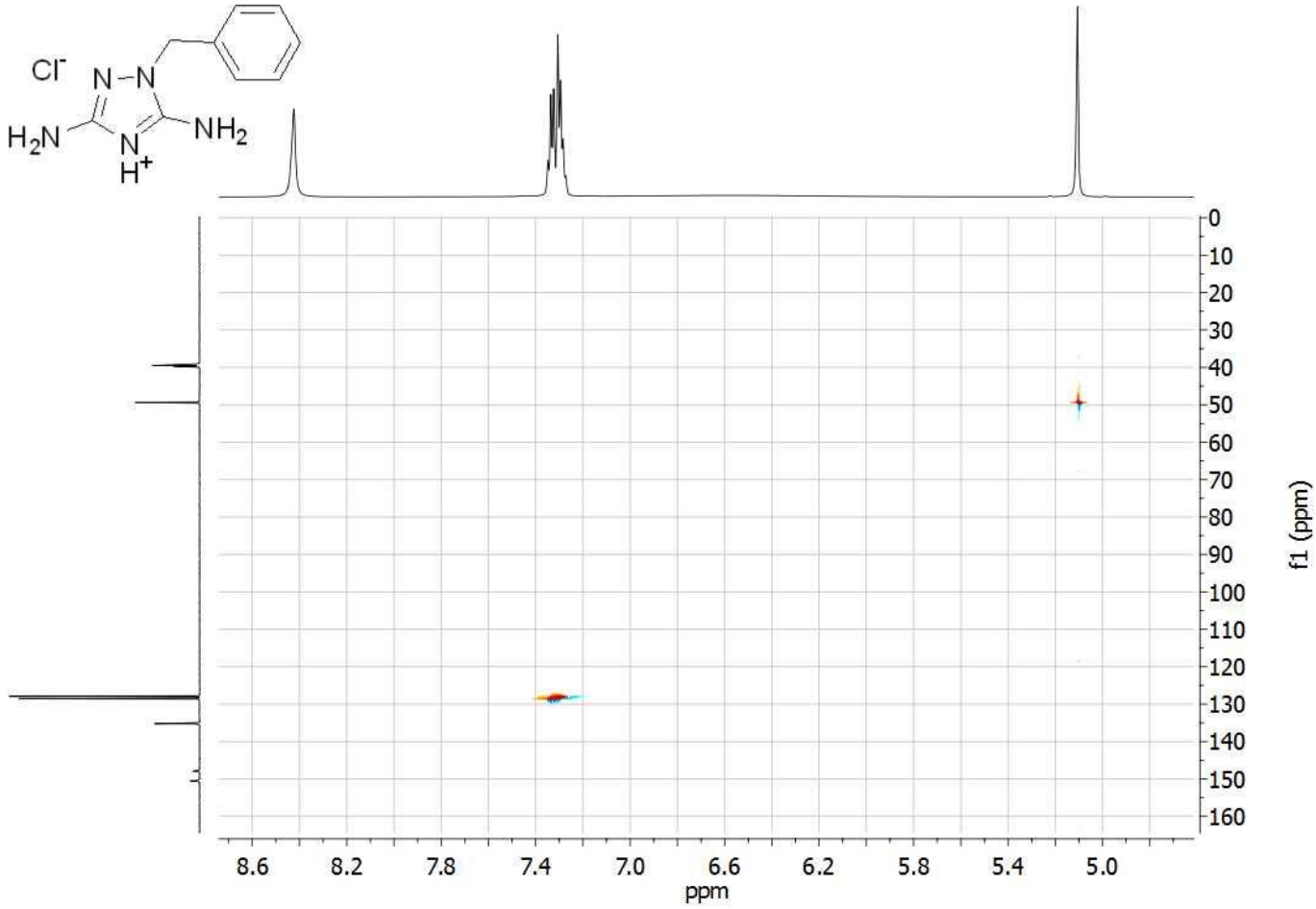


Figure S71. ^{1}H-^{13}C HSQC spectrum of compound **6b** (DMSO-d_6)

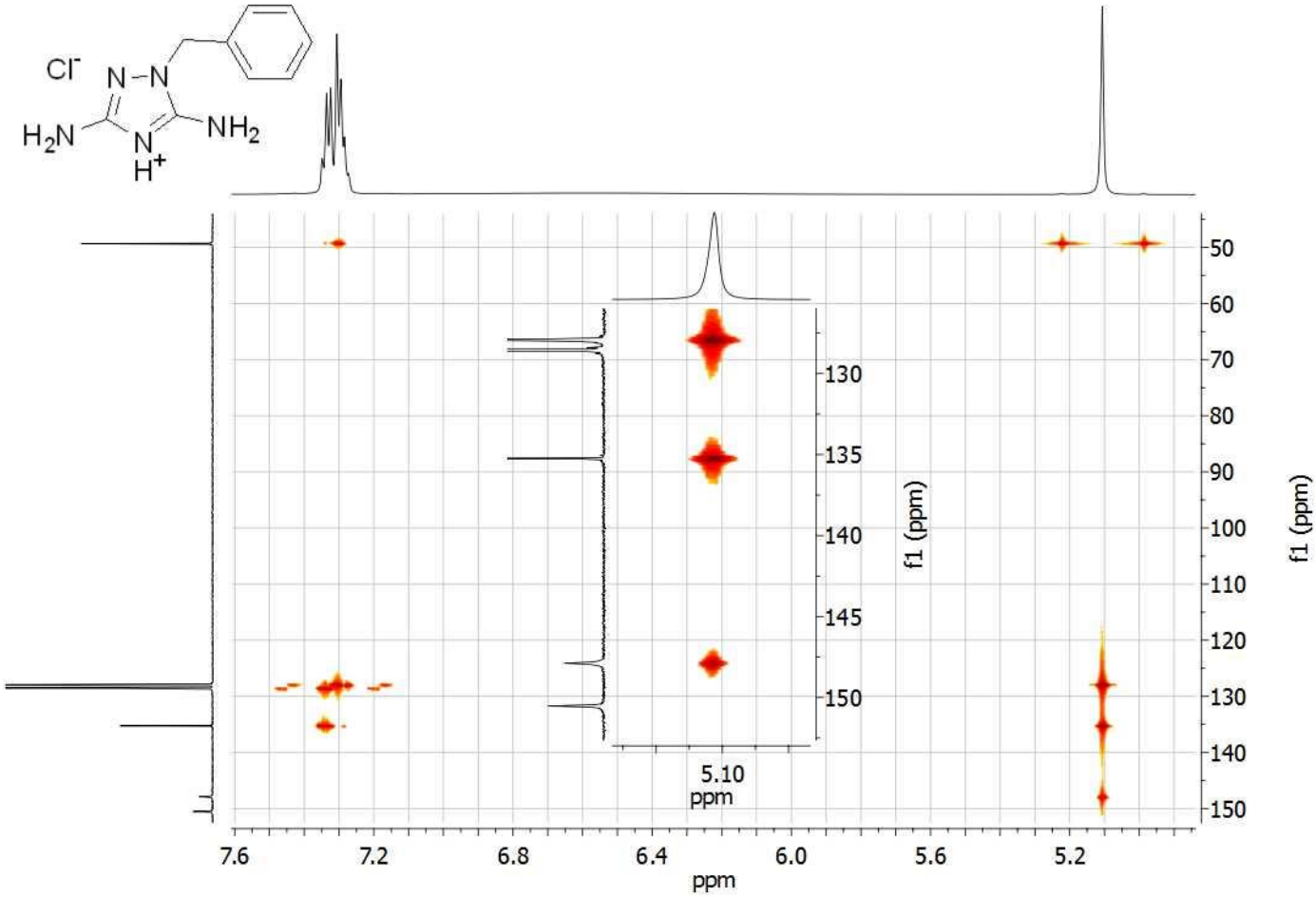


Figure S72. ^{1}H-^{13}C HMBC spectrum of compound **6b** (DMSO-d_6)