

## Electronic Supplementary Information (ESI)

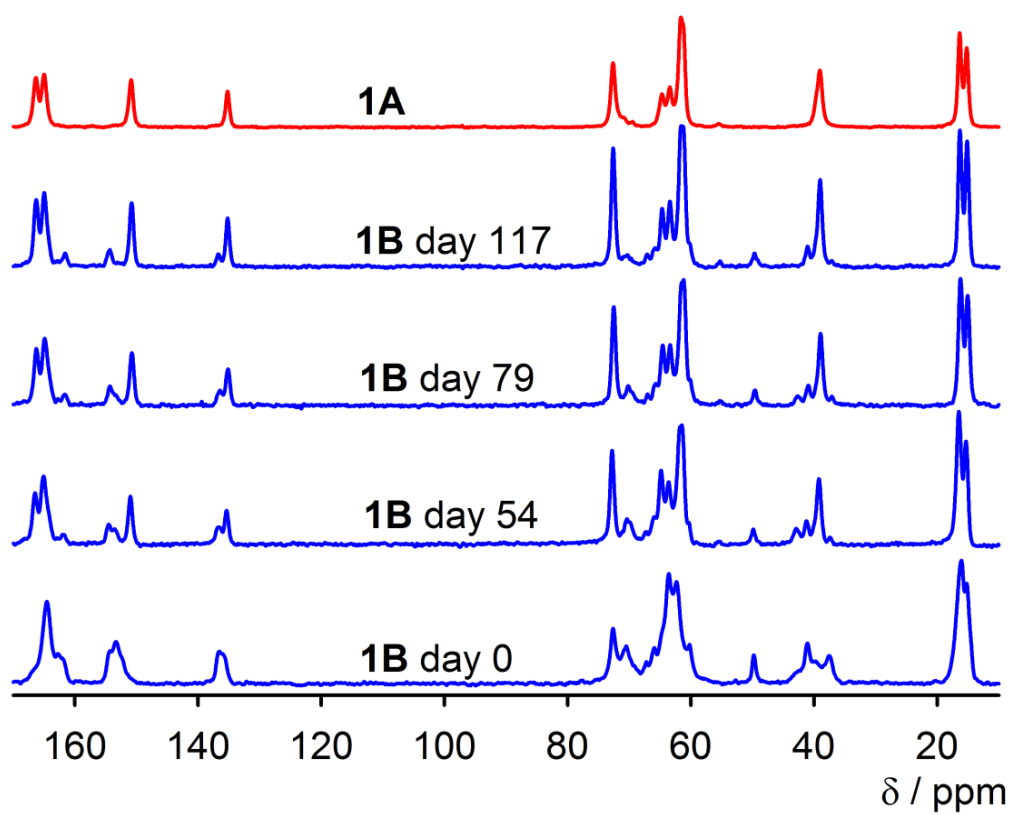
# Separation of Planar Rotamers Through Intramolecular Hydrogen Bonding in Polysubstituted 5-Nitrosopyrimidines

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**Fig. S1.**  $^{13}\text{C}$  CP-MAS solid-state NMR spectra of rotamers **1A** and **1B**. Solid amorphous **1B** slowly transforms into solid crystalline **1A**.

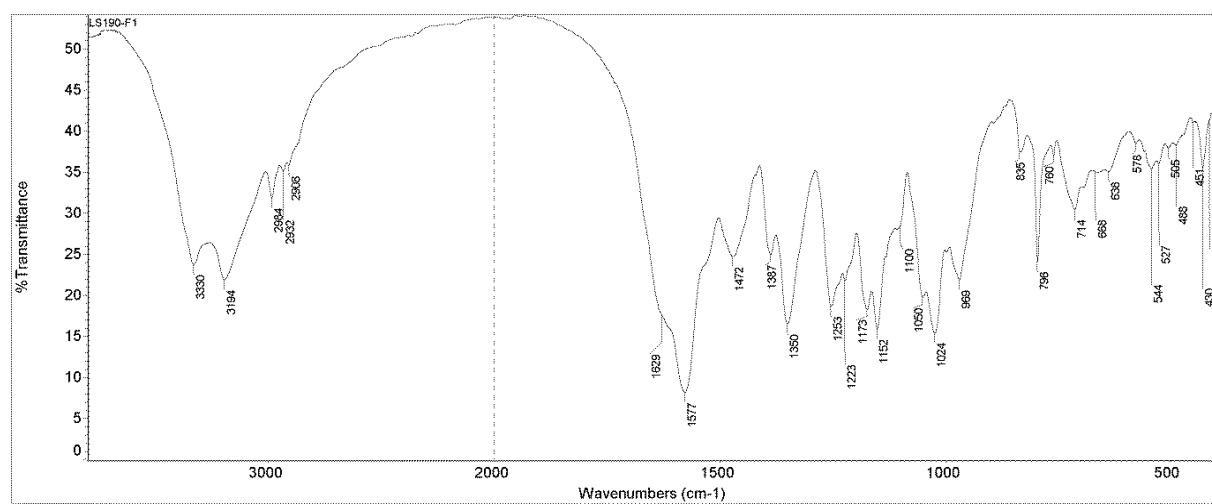
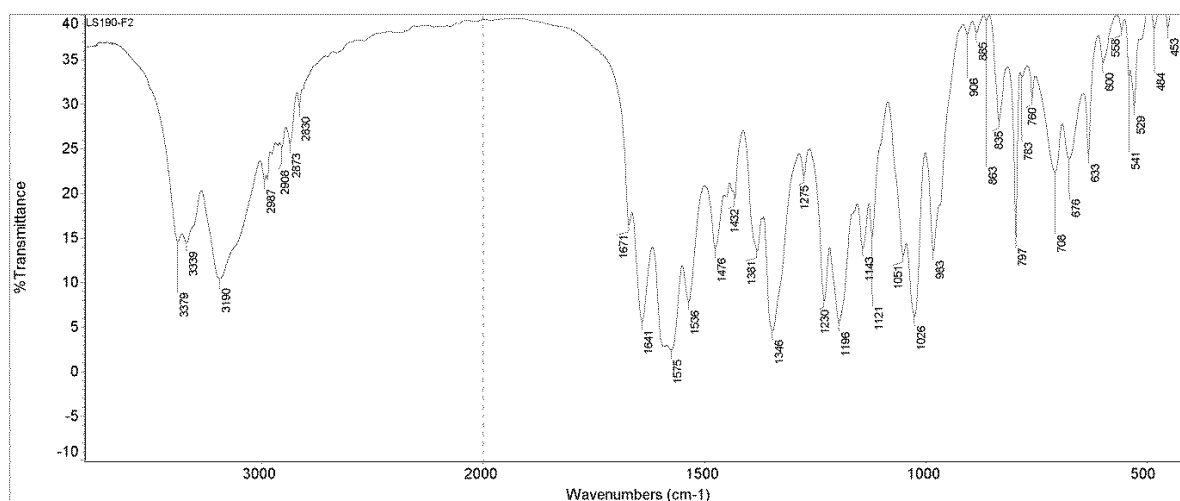
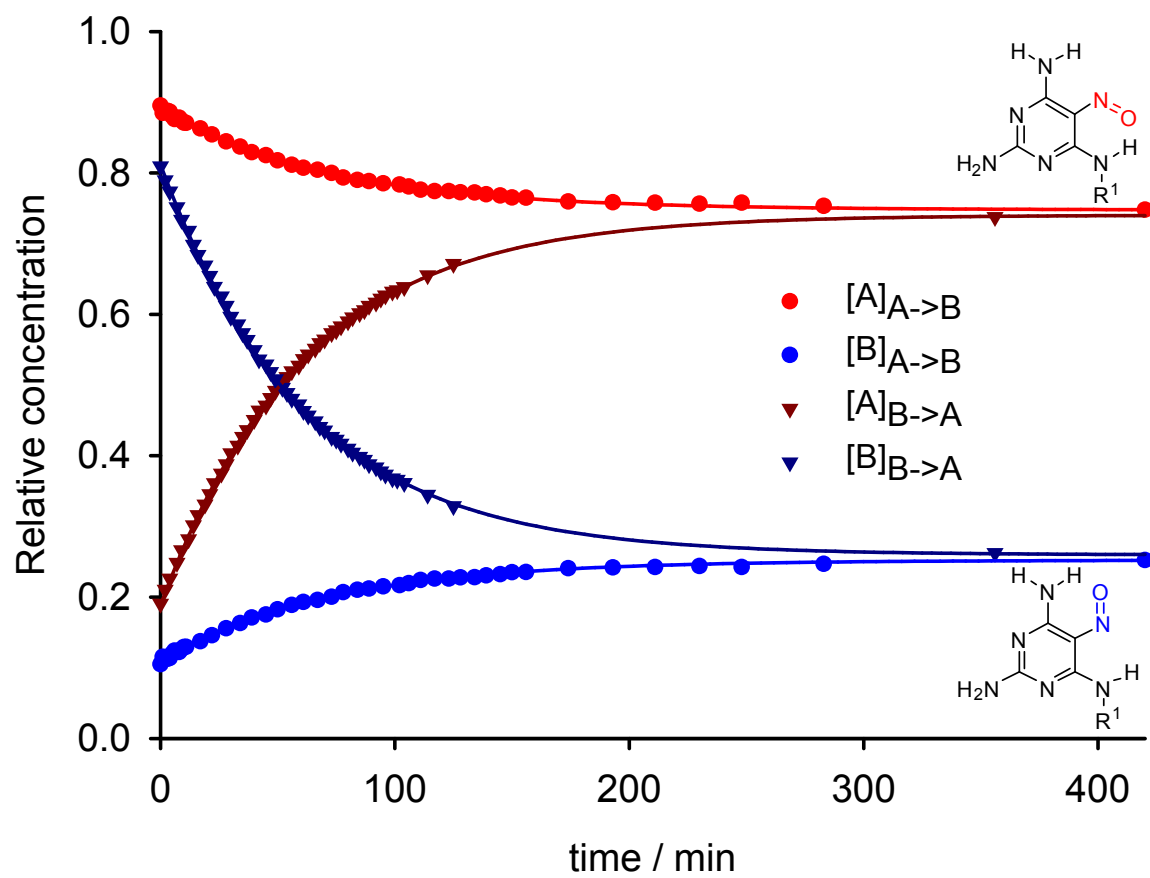
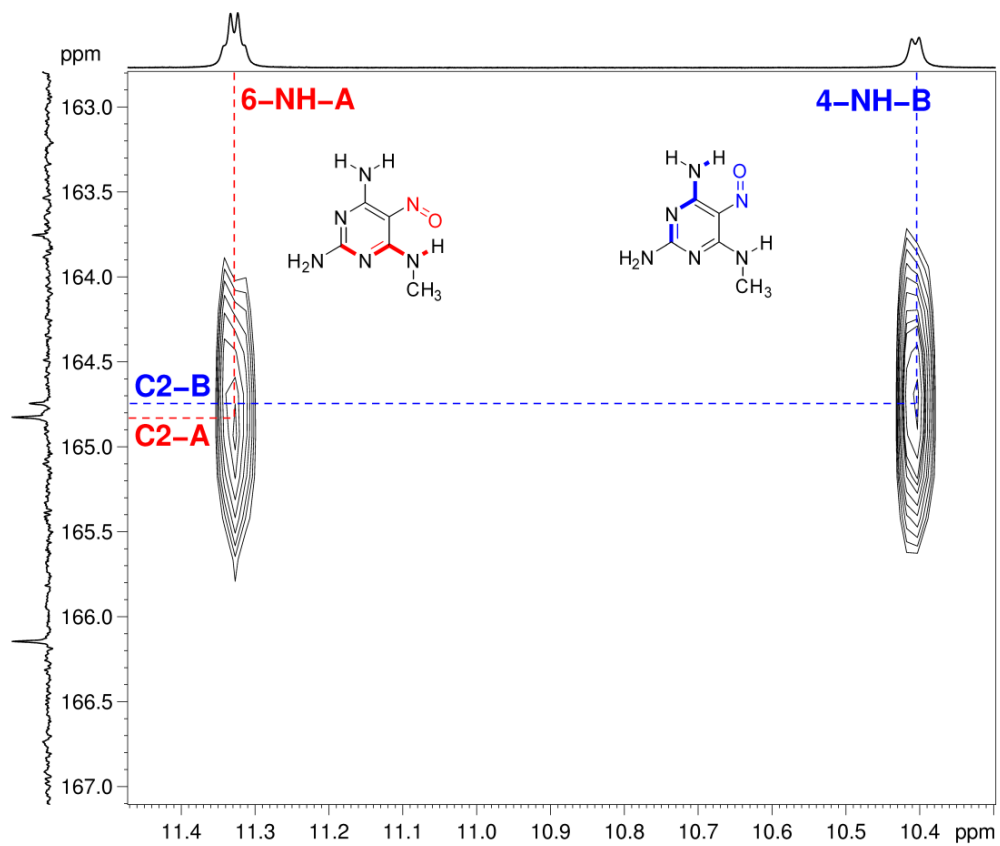


Fig. S2. IR spectra of rotamers **1A** and **1B** dispersed in KBr pellets.



**Fig. S3.** Interconversion of rotamers **2A** and **2B**. Interconversion was monitored by <sup>1</sup>H NMR spectroscopy in DMSO-*d*<sub>6</sub> solution. R<sup>1</sup> = CH<sub>2</sub>-CH<sub>2</sub>-O-CH<sub>3</sub>.



**Fig. S4.** HMBC spectrum of compound 3. W-like arrangement between the NH hydrogens and C2 is observed.

**Table S1.** Relative concentration of **A** in equilibrium and the rate constant of planamer interconversion. The data were determined from <sup>1</sup>H NMR spectra of compounds **1–4** in various solvents. (Errors in the rotamer ratios and rate constants are estimated to be lower than 2% and 5%, respectively.)

Compound	Solvent	% <b>A</b> in equilibrium	$k_{A \rightarrow B} / 10^{-4} \text{ s}^{-1}$
<b>1</b>	DMSO	71	1.21
<b>1</b>	methanol	67	1.07
<b>1</b>	acetone	71	1.64
<b>2</b>	DMSO	74	0.66
<b>3</b>	DMSO	64	0.92
<b>4</b>	DMSO	63	0.39
<b>4</b>	methanol	52	0.19

### Single-crystal X-ray diffraction data

Single-crystal X-ray diffraction data for **1A** and **1** (as a mixture of **1A** and **1B**) were obtained from Nonius Kappa CCD diffractometer equipped with Bruker ApexII-CCD detector by monochromatized MoK $\alpha$  radiation ( $\lambda = 0.71073 \text{ \AA}$ ) at 150(2)K. The structures were solved by direct methods and refined by full-matrix least squares based on  $F^2$  (SHELXS; SHELXL97)<sup>1</sup>. The hydrogen atoms were found on difference Fourier map and recalculated into idealised positions (riding model) with assigned temperature factors either  $H_{\text{iso}}(\text{H}) = 1.2 U_{\text{eq}}(\text{pivot atom})$  or  $1.5 U_{\text{eq}}$  for methyl moiety.

In both cases, the quality of measured single crystal and consequently precision of structure determination were affected by disorder of ethyl moieties. However, the pyrimidine parts were unambiguously determined including the position of hydrogen atoms.

Crystal data for **1A**:  $\text{C}_{11}\text{H}_{21}\text{N}_6\text{O}_5\text{P}$ ,  $M_r = 348.31$ , Monoclinic,  $P2/c$  (No 13),  $a = 15.1845$  (4)  $\text{ \AA}$ ,  $b = 13.7904$  (4)  $\text{ \AA}$ ,  $c = 16.3311$  (4)  $\text{ \AA}$ ,  $\beta = 104.6734$  (10) $^\circ$ ,  $V = 3308.20$  (15)  $\text{ \AA}^3$ ,  $Z = 8$ ,  $D_x = 1.399 \text{ Mg m}^{-3}$ , red prism of dimensions  $0.54 \times 0.38 \times 0.32 \text{ mm}$ , multi-scan absorption correction ( $\mu = 0.20 \text{ mm}^{-1}$ )  $T_{\text{min}} = 0.900$ ,  $T_{\text{max}} = 0.939$ ; a total of 30510 measured reflections ( $\theta_{\text{max}} = 27.5^\circ$ ), from which 7598 were unique ( $R_{\text{int}} = 0.034$ ) and 5611 observed according to the  $I > 2\sigma(I)$  criterion. The refinement converged ( $\Delta/\sigma_{\text{max}} \leq 0.001$ ) to  $R = 0.068$  for observed reflections and  $wR(F^2) = 0.206$ ,  $GOF = 1.04$  for 459 parameters and all 7598 reflections. The final difference map displayed no peaks of chemical significance ( $\Delta\rho_{\text{max}} = 1.05$ ,  $\Delta\rho_{\text{min}} = -0.41 \text{ e. \AA}^{-3}$ ), both peaks being in the vicinity of disordered atoms.

Crystal data for **1 (1A + 1B)**:  $\text{C}_{11}\text{H}_{21}\text{N}_6\text{O}_5\text{P} \cdot \text{H}_2\text{O}$ ,  $M_r = 366.32$ ,  $P-1$  (No 2),  $a = 8.5829$  (2)  $\text{ \AA}$ ,  $b = 10.4800$  (3)  $\text{ \AA}$ ,  $c = 11.4529$  (3)  $\text{ \AA}$ ,  $\alpha = 113.4116$  (10) $^\circ$ ,  $\beta = 92.8654$  (11) $^\circ$ ,  $\gamma = 108.2169$  (10) $^\circ$ ,  $V = 879.87$  (4)  $\text{ \AA}^3$ ,  $Z = 2$ ,  $D_x = 1.383 \text{ Mg m}^{-3}$ , violet prism of dimensions  $0.68 \times 0.30 \times 0.12 \text{ mm}$ , multi-scan absorption correction ( $\mu = 0.20 \text{ mm}^{-1}$ )  $T_{\text{min}} = 0.879$ ,  $T_{\text{max}} = 0.976$ ; a total

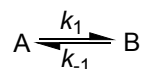
of 9450 measured reflections ( $\theta_{\max} = 27.5^\circ$ ), from which 3951 were unique ( $R_{\text{int}} = 0.019$ ) and 3327 observed according to the  $I > 2\sigma(I)$  criterion. The refinement converged ( $\Delta/\sigma_{\max} \leq 0.001$ ) to  $R = 0.046$  for observed reflections and  $wR(F^2) = 0.119$ ,  $GOF = 1.04$  for 229 parameters and all 3951 reflections. The final difference map displayed no peaks of chemical significance ( $\Delta\rho_{\max} = 0.55$ ,  $\Delta\rho_{\min} -0.54$  e.Å<sup>-3</sup>). Both orientations of the nitroso group are present with the statistical distribution in the crystal. The occupational factor of syn position was refined as free variable, whereas the second one was restrained to give the sum of both equal to 1. The refinement results to the ration of syn- and anti- position equal 0.787(2):0.213(2).

Crystallographic data (excluding structure factors) for the structures **1A** and **1** have been deposited with the Cambridge Crystallographic Data Centre with CCDC numbers 1001296 and 1001297, respectively. Copies of the data can be obtained, free of charge, on application to Cambridge Crystallographic Data Centre, 12 Union Road, Cambridge CB2 1EZ, UK, (fax: +44-(0)1223-336033 or e-mail: [deposit@ccdc.cam.ac.Uk](mailto:deposit@ccdc.cam.ac.Uk)).



## Kinetics of equilibrium reactions

A unimolecular reaction in which a molecule fluctuates between two conformations can be written as



The rate equations that describe the change in populations of A and B are:

$$\frac{d[A]}{dt} = -k_1[A] + k_{-1}[B] \quad \text{and} \quad \frac{d[B]}{dt} = k_1[A] - k_{-1}[B] \quad (1)$$

At equilibrium, the forward reaction rate is equal to the reverse reaction rate:

$$k_1[A]_{\text{eq}} = k_{-1}[B]_{\text{eq}}$$

This can be rearranged to:

$$k_1 / k_{-1} = [B]_{\text{eq}} / [A]_{\text{eq}} = K_{\text{eq}} \quad (2)$$

where  $K_{\text{eq}}$  is the equilibrium constant.

If the system is initially in non-equilibrium state, the populations of A and B will change as a function of time until equilibrium is reached. The solution of the rate equations (1) can be written as

$$x_A(t) = x_A(0)\exp(-k_r t) \quad \text{and} \quad x_B(t) = x_B(0)\exp(-k_r t)$$

where  $x_A$  and  $x_B$  are the populations of A and B, respectively, that deviate from the equilibrium populations ( $x_A(t) = [A]_t - [A]_{\text{eq}}$ ) and  $k_r = k_1 + k_{-1}$ .

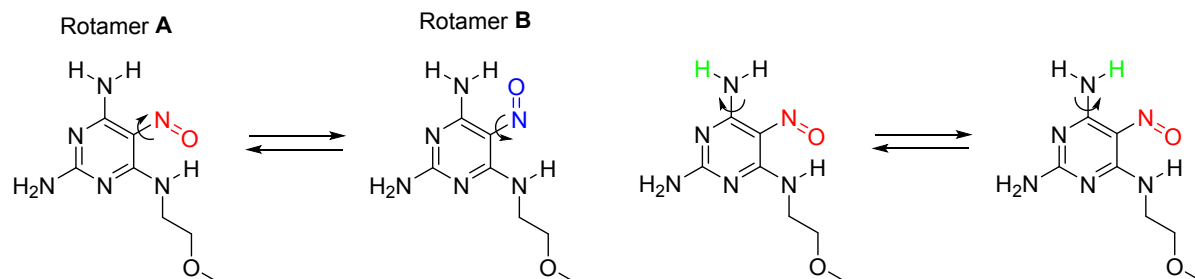
Logarithmic form of the solution is

$$\ln x_A(t) = \ln x_A(0) - k_r t$$

Therefore, plotting experimental values of  $\ln x_A(t)$  against time will provide a straight line with the slope of  $k_r$ . The rate constants  $k_1$  and  $k_{-1}$  can be then calculated by applying equation (2).

## DFT calculations

We were looking for transition-state structures for the planamer interconversion and for the 4-amino group rotation around the C4-N single bond (Figure S5). The first-order saddle-point structures on the reaction coordinates of the compound **2** were localized by using the QST3 method<sup>2,3</sup> at the DFT level of theory, using the B3LYP functional<sup>4,5</sup> and a standard 6-31+G(d,p) basis set, and the free-energy barriers to transition were calculated. The free-energy barrier heights calculated in vacuum were 27.4 and 21.8 kcal/mol, respectively. The Gaussian09 program package was used for the calculations<sup>6</sup>.

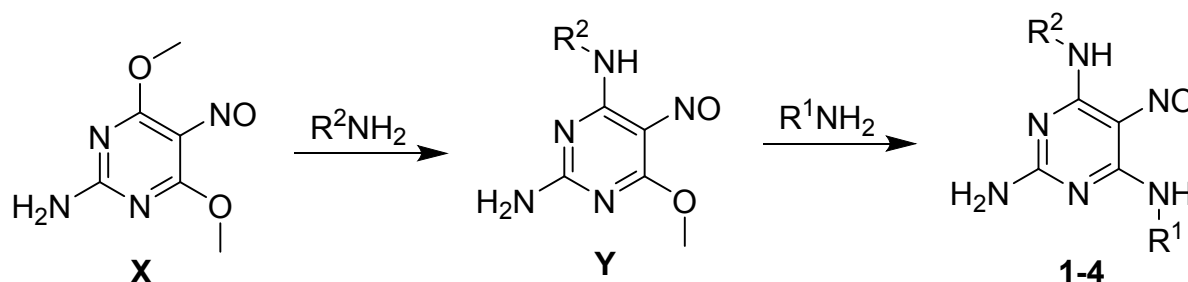


**Fig. S5.** Rotation around the C5-N and C4-N bonds.

## Synthesis and characterization of compounds 1-4 and their intermediates

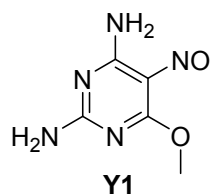
### METHODS

NMR spectra were measured on Bruker AVANCE II 500 spectrometer operating at 499.9 MHz for  $^1\text{H}$  and 125.7 MHz for  $^{13}\text{C}$  in  $\text{DMSO-}d_6$ . A combination of 1D and 2D experiments (COSY, HSQC, HMBC) was used for the assignment of  $^1\text{H}$  and  $^{13}\text{C}$  resonances. High resolution electrospray mass spectra (HR-MS) were measured using LTQ Orbitrap XL (Thermo Fisher Scientific). A Thermo-Nicolet 6700 FTIR spectrometer was used to record IR spectra on samples dispersed in KBr pellets.



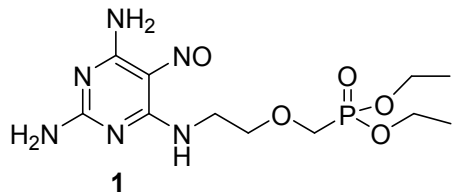
### 6-Methoxy-5-nitrosopyrimidine-2,4-diamine (Y1).

A solution of 2-amino-4,6-dimethoxy-5-nitrosopyrimidine **X** (327 mg, 1.8 mmol) in a mixture of aqueous ammonia (25% solution, 7 mL) and water (7 mL) was stirred at room temperature for 30 min and evaporated *in vacuum*. Silica gel column chromatography (15 %,  $\text{MeOH}/\text{CHCl}_3$ ) gave 156 mg (51%) of violet solid; m.p.= 250 °C.  $^1\text{H}$  NMR ( $\text{DMSO-}d_6$ ): 10.07 (1H, d,  $J_{\text{GEM}} = 3.8$ ,  $\text{NH}^a$ ), 8.00 (1H, d,  $J_{\text{GEM}} = 3.8$ ,  $\text{NH}^b$ ), 7.85 (1H, bs, 2- $\text{NH}^a$ ), 7.79 (1H, bs, 2- $\text{NH}^b$ ), 4.05 (3H, s, 6-O- $\text{CH}_3$ ).  $^{13}\text{C}$  NMR ( $\text{DMSO-}d_6$ ): 171.2 (C-6), 163.6 (C-2), 150.9 (C-4), 139.8 (C-5), 54.3 (O- $\text{CH}_3$ ). ESI MS,  $m/z$  (%): 192.0 [ $\text{M} + \text{Na}$ ] $^+$ , 170.1 [ $\text{M} + \text{H}$ ] $^+$ ; HRMS (ESI) calcd for  $\text{C}_5\text{H}_8\text{N}_5\text{O}_2$  [ $\text{M} + \text{H}$ ] $^+$  170.0672, found 170.0671.



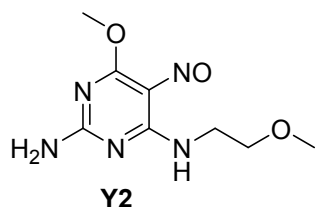
**Diethyl {(2-[(2,4-diamino-5-nitrosopyrimidin-6-yl)amino]ethoxy)methyl}phosphonate (1).**

A mixture of 6-methoxy-5-nitrosopyrimidine-2,4-diamine **Y1** (281 mg, 1.7 mmol) and diethyl [(2-aminoethoxy)methyl]phosphonate<sup>6</sup> (538 mg, 2.5 mmol) in DMF (15 mL) was stirred at 60 °C for 48 h. Solvents were evaporated *in vacuum* and silica gel column chromatography (15 %, MeOH/CHCl<sub>3</sub>) gave 374 mg (63%) of pink solid; m.p. = 165-167 °C. <sup>1</sup>H NMR (DMSO-*d*<sub>6</sub>): Rotamers A and B: 11.50 (1H, t,  $J_{NH-1'}$  = 5.7, 6-NH, A), 10.35 (1H, d,  $J_{GEM}$  = 5.1, 4-NH<sup>a</sup>, B), 8.59 (1H, t,  $J_{NH-1'}$  = 5.8, 6-NH, B), 8.15 (1H, s, 4-NH<sup>a</sup>, A), 7.78 (1H, d,  $J_{GEM}$  = 5.1, 4-NH<sup>b</sup>, B), 7.26-7.39 (5H, m, 4-NH<sup>b</sup> A, 2-NH<sub>2</sub> A, 2-NH<sub>2</sub> B), 3.98 -4.08 (8H, m, O-CH<sub>2</sub>-CH<sub>3</sub>, A and B), 3.85 (1H, d,  $J_{3'-P}$  = 8.4, H-3', B), 3.85 (1H, d,  $J_{3'-P}$  = 8.3, H-3', A), 3.72 (2H, m, H-2', B), 3.63-3.67 (4H, m, H-1' B and H-2' A), 3.55 (2H, m, H-1', A), 1.23 (3H, t,  $J_{CH3-CH2}$  = 7.1, O-CH<sub>2</sub>-CH<sub>3</sub>, A), 1.19 (3H, t,  $J_{CH3-CH2}$  = 7.1 O-CH<sub>2</sub>-CH<sub>3</sub>, B). <sup>13</sup>C NMR (DMSO-*d*<sub>6</sub>): Rotamer A: 166.1 (C-4), 164.8 (C-2), 150.8 (C-6), 136.7 (C-5), 70.7 (d,  $J_{2'-P}$  = 11.7, C-2'), 64.1 (d,  $J_{3'-P}$  = 162.6, C-3'), 61.9 (d,  $J_{CH2-P}$  = 6.2, O-CH<sub>2</sub>-CH<sub>3</sub>), 38.3 (C-1'), 16.4 (d,  $J_{CH3-P}$  = 5.6, O-CH<sub>2</sub>-CH<sub>3</sub>); Rotamer B: 164.6 (C-2), 163.5 (C-6), 151.2 (C-4), 137.3 (C-5), 70.8 (d,  $J_{2'-P}$  = 12.3, C-2'), 64.0 (d,  $J_{3'-P}$  = 162.6, C-3'), 61.9 (d,  $J_{CH2-P}$  = 6.2, O-CH<sub>2</sub>-CH<sub>3</sub>), 38.3 (C-1'), 16.4 ( $J_{CH3-P}$  = 5.6, O-CH<sub>2</sub>-CH<sub>3</sub>). ESI MS, *m/z* (%): 371.2 [M + Na]<sup>+</sup>, 349.2 [M + H]<sup>+</sup>; HRMS (ESI) calcd for C<sub>11</sub>H<sub>22</sub>N<sub>6</sub>O<sub>5</sub>P [M + H]<sup>+</sup> 349.1383, found 349.1384.



#### 4-Methoxy-*N*<sup>6</sup>-(2-methoxyethyl)-5-nitrosopyrimidine-2,6-diamine (**Y2**).

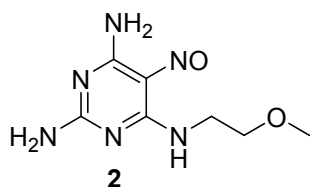
2-Methoxyethan-1-amine (446 mg, 5.9 mmol) was added dropwise to a solution of 2-amino-4,6-dimethoxy-5-nitrosopyrimidine **X** (1.00 g, 5.4 mmol) in DMF (60 mL). The reaction mixture was stirred at room temperature overnight and solvents were evaporated *in vacuum*. Silica gel column chromatography (5 %, MeOH/CHCl<sub>3</sub>) gave 1.04 g (84%) of violet solid; m.p. = 161 °C. <sup>1</sup>H NMR (DMSO-*d*<sub>6</sub>): 11.33 (1H, t, *J*<sub>NH-CH<sub>2</sub></sub> = 5.4, NH), 8.00 (2H, bs, 2-NH<sub>2</sub>), 4.04 (3H, s, 4-O-CH<sub>3</sub>), 3.55 (2H, m, NH-CH<sub>2</sub>), 3.46 (2H, m, NH-CH<sub>2</sub>), 3.28 (3H, s, CH<sub>2</sub>-O-CH<sub>3</sub>). <sup>13</sup>C NMR (DMSO-*d*<sub>6</sub>): 171.2 (C-4), 163.5 (C-2), 150.6 (C-6), 138.8 (C-5), 69.9 (CH<sub>2</sub>-O), 58.2 (CH<sub>2</sub>-O-CH<sub>3</sub>), 54.4 (4-O-CH<sub>3</sub>), 38.9 (CH<sub>2</sub>-NH). ESI MS, *m/z* (%): 250.1 [M + Na]<sup>+</sup>, 228.1 [M + H]<sup>+</sup>; HRMS (ESI) calcd for C<sub>8</sub>H<sub>14</sub>N<sub>5</sub>O<sub>3</sub> [M + H]<sup>+</sup> 228.1091, found 228.1091.



#### *N*<sup>6</sup>-(2-Methoxyethyl)-5-nitrosopyrimidine-2,4,6-triamine (**2**).

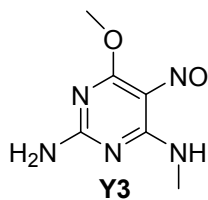
A solution of 4-methoxy-*N*<sup>6</sup>-(2-methoxyethyl)-5-nitrosopyrimidine-2,6-diamine **Y2** (400 mg, 1.8 mmol) in aqueous ammonia (25% solution, 40 mL) was stirred at room temperature for 2 h. Solvents were evaporated *in vacuum*. Silica gel column chromatography (10 %, MeOH/CHCl<sub>3</sub>)

gave 280 mg (74%) of pink solid; m.p. = 210 °C. <sup>1</sup>H NMR (DMSO-*d*<sub>6</sub>): Rotamers A and B: 11.52 (1H, t,  $J_{NH-1'}$  = 5.4, 6-NH, A), 10.35 (1H, d,  $J_{GEM}$  = 4.9, 4-NH<sup>b</sup>, B), 8.54 (1H, t,  $J_{NH-1'}$  = 5.8, 6-NH, B), 8.15 (1H, s, 4-NH<sup>b</sup>, A), 7.78 (1H, d,  $J_{GEM}$  = 4.9, 4-NH<sup>a</sup>, B), 7.27-7.37 (5H, m, 2-NH<sub>2</sub> A and B, 4-NH<sup>a</sup> A), 3.63 (2H, m, H-1', B), 3.51-3.54 (4H, m, H-1' A and H-2' B), 3.45 (2H, m, H-2', A), 3.29 (3H, s, O-CH<sub>3</sub>, A), 3.27 (3H, s, O-CH<sub>3</sub>, B). <sup>13</sup>C NMR (DMSO-*d*<sub>6</sub>): Rotamer A: 166.1 (C-4), 164.8 (C-2), 150.8 (C-6), 136.7 (C-5), 70.1 (C-2'), 58.2 (O-CH<sub>3</sub>), 38.5 (C-1'); Rotamer B: 164.7 (C-2), 163.4 (C-6), 151.2 (C-4), 137.3 (C-5), 70.3 (C-2'), 58.1 (O-CH<sub>3</sub>), 39.6 (C-1'). ESI MS, *m/z* (%): 235.1 [M + Na]<sup>+</sup>, 213.1 [M + H]<sup>+</sup>; HRMS (ESI) calcd for C<sub>7</sub>H<sub>13</sub>N<sub>6</sub>O<sub>2</sub> [M + H]<sup>+</sup> 213.1094, found 213.1094.



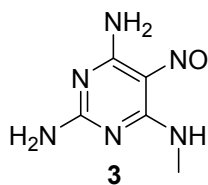
#### 4-Methoxy-N<sup>6</sup>-methyl-5-nitrosopyrimidine-2,6-diamine (Y3).

A mixture of 2-amino-4,6-dimethoxy-5-nitrosopyrimidine **X** (737 mg, 4.0 mmol) and methylamine (8 M ethanolic solution, 0.5 mL) in DMF (40 mL) was stirred at room temperature for 3 h. Solvents were evaporated *in vacuo* and the residue was codistilled with toluene (2 x 5 mL). Silica gel column chromatography (3 %, MeOH/CHCl<sub>3</sub>) gave 680 mg (93%) of violet solid; m.p.= 213 °C. <sup>1</sup>H NMR (DMSO-*d*<sub>6</sub>): 11.13 (1H, m, NH-CH<sub>3</sub>), 7.97 (2H, m, 2-NH<sub>2</sub>), 4.04 (3H, s, O-CH<sub>3</sub>), 2.86 (3H, d,  $J_{CH3-NH}$  = 5.0, N-CH<sub>3</sub>). <sup>13</sup>C NMR (DMSO-*d*<sub>6</sub>): 171.2 (C-4), 163.5 (C-2), 151.3 (C-6), 139.0 (C-5), 54.4 (O-CH<sub>3</sub>), 26.5 (N-CH<sub>3</sub>). ESI MS, *m/z* (%): 206.1 [M + Na]<sup>+</sup>, 184.1 [M + H]<sup>+</sup>; HRMS (ESI) calcd for C<sub>6</sub>H<sub>9</sub>N<sub>5</sub>O<sub>2</sub>Na [M + Na]<sup>+</sup> 206.0648, found 206.0647.



***N*<sup>6</sup>-Methyl-5-nitrosopyrimidine-2,4,6-triamine (3).**

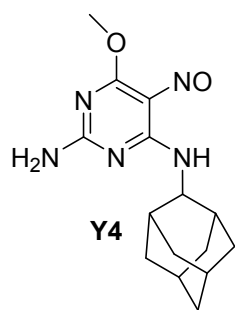
4-Methoxy-*N*<sup>6</sup>-methyl-5-nitrosopyrimidine-2,6-diamine **Y3** (325 mg, 1.8 mmol) was dissolved in DMF (7 mL) and methanolic ammonia solution (25 %, 10 ml) was added. The reaction mixture was sealed and heated at 85 °C for 18 h. Solvents were evaporated *in vacuo* and the residue crystallized from MeOH to give 263 mg (88%) of orange crystals; m.p.= 246-248 °C. <sup>1</sup>H NMR (DMSO-*d*<sub>6</sub>): 11.33 (1H, q, *J*<sub>NH-CH<sub>3</sub></sub> = 5.0, 6-NH, A), 10.41 (1H, d, *J*<sub>GEM</sub> = 4.9, 4-NH<sup>b</sup>, B), 8.7 (1H, q, *J*<sub>NH-CH<sub>3</sub></sub> = 4.8, 6-NH, B), 8.11 (1H, s, 4-NH<sup>b</sup>, A), 7.75 (1H, d, *J*<sub>GEM</sub> = 4.9), 7.25-7.37 (5H, m, 4-NH<sup>a</sup> A, 2-NH<sub>2</sub> A and 2-NH<sub>2</sub> B), 2.92 (3H, d, NH-CH<sub>3</sub>, B), 2.84 (3H, d, NH-CH<sub>3</sub>, A). <sup>13</sup>C NMR (DMSO-*d*<sub>6</sub>): 166.1 (C-4, A), 164.8 (C-2, A), 164.7 (C-2, B), 163.7 (C-6, B), 151.5 (C-6, A), 151.2 (C-4, B), 137.5 (C-5, B), 136.8 (C-5, A), 27.55 (CH<sub>3</sub>, B), 26.0 (CH<sub>3</sub>, A). ESI MS, *m/z* (%): 191.1 [M + Na]<sup>+</sup>, 169.1 [M + H]<sup>+</sup>; HRMS (ESI) calcd for C<sub>5</sub>H<sub>9</sub>N<sub>6</sub>O [M + H]<sup>+</sup> 169.0832, found 169.0830.



***N*<sup>6</sup>-(Adamantan-2-yl)-4-methoxy-5-nitrosopyrimidine-2,6-diamine (Y4).**

A mixture of 2-amino-4,6-dimethoxy-5-nitrosopyrimidine **X** (921 mg, 5.0 mmol), 1-adamantylamine (939 mg, 5.0 mmol), and potassium carbonate (691 mg, 5.0 mmol) in DMF (40

mL) was stirred at room temperature overnight. Solids were filtered off and filtrate was evaporated *in vacuum*. The residue was codistilled with toluene (3 x 5 mL) and purified by silica gel column chromatography (3% MeOH/CHCl<sub>3</sub>) to give 1.40 g (92%) of blue solid; m.p.= 240-242 °C. <sup>1</sup>H NMR (DMSO-*d*<sub>6</sub>): 12.20 (1H, d,  $J_{\text{NH-2}'} = 8.4$ , **NH-CH**), 8.02 (2H, bs, 2-NH<sub>2</sub>), 4.28 (1H,  $J_{2'-\text{NH}} = 8.4$ , H-2'), 4.03 (3H, s, O-CH<sub>3</sub>), 1.62-1.89 (14H, m, H-1' and H-3' – H-10'). <sup>13</sup>C NMR (DMSO-*d*<sub>6</sub>): 171.1 (C-4), 163.8 (C-2), 150.0 (C-6), 138.7 (C-5), 54.4 (O-CH<sub>3</sub>), 52.9 (C-2'), 37.0 (C-6'), 36.6 (C-8' and C-9') or (C-4' and C-10'), 31.6 (C-4' and C-10') or (C-8' and C-9'), 31.3 (C-5' and C-7'), 26.7 and 26.6 (C-1' and C-3'). ESI MS, *m/z* (%): 326.1 [M + Na]<sup>+</sup>, 304.1 [M + H]<sup>+</sup>; HRMS (ESI) calcd for C<sub>15</sub>H<sub>22</sub>N<sub>5</sub>O<sub>2</sub> [M + H]<sup>+</sup> 304.1768, found 304.1769.

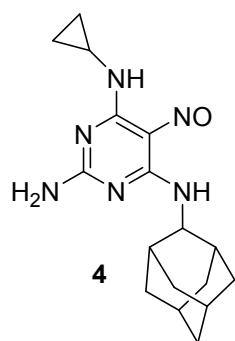


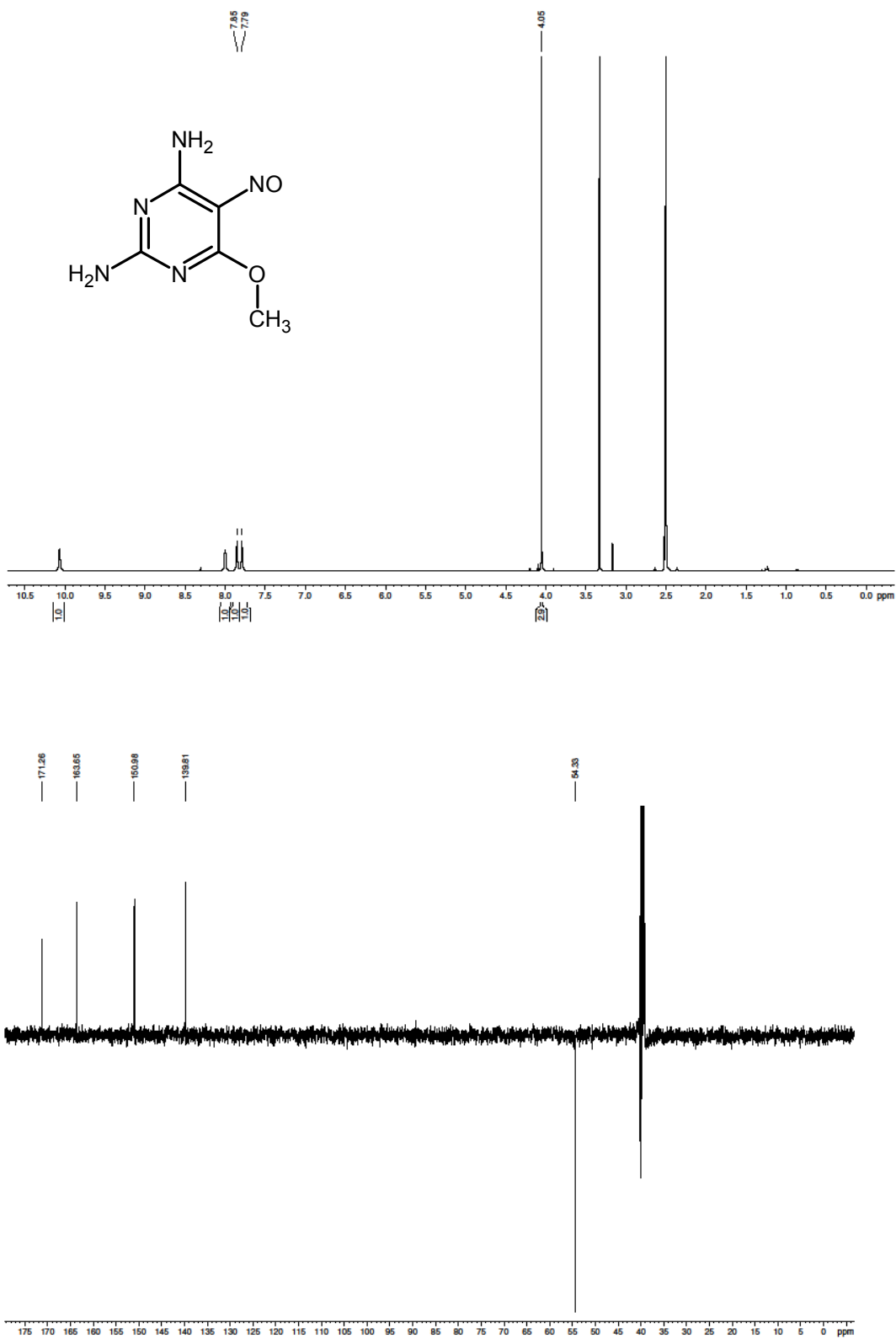
***N*<sup>6</sup>-(Adamantan-2-yl)-*N*<sup>4</sup>-cyclopropyl-5-nitrosopyrimidine-2,4,6-triamine (4).**

A mixture of *N*<sup>6</sup>-(adamantan-2-yl)-4-methoxy-5-nitrosopyrimidine-2,6-diamine **B4** (364 mg, 1.2 mmol) and cyclopropylamine (1.5 mL) in DMF (30 mL) was heated at 80 °C for 22 h. One more portion of cyclopropylamine (1.5 mL) was added and the mixture was heated at 80 °C overnight. Solvents were evaporated and the residue was codistilled with toluene (3 x 5 mL). Crystallization from MeOH gave 323 mg (82%) of violet crystals; m.p.= 271 °C. <sup>1</sup>H NMR (DMSO-*d*<sub>6</sub>): Rotamer A: 12.56 (1H, d,  $J_{\text{NH-2}} = 8.5$ , 6-NH), 8.64 (1H, d,  $J_{\text{NH-CH}} = 5.4$ , 4-NH), 7.47 (2H, m, 2-NH<sub>2</sub>), 4.28 (1H, dm,  $J_{2'-\text{NH}} = 8.5$ , H-2'), 3.12 (1H, m, CH<sup>cyp</sup>), 1.61-1.87 (14H, m, H-1' and H-3' -



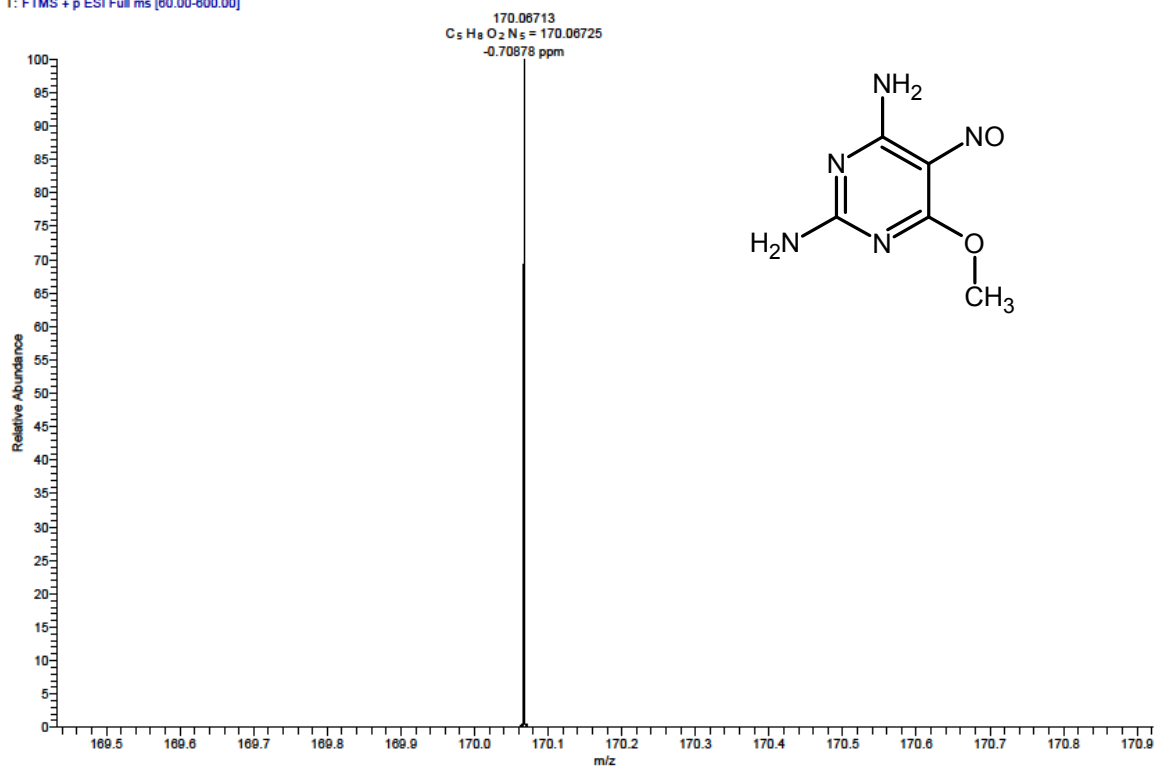
H-10'), 0.74 (2H, m, CH<sub>2</sub><sup>cypr a</sup>), 0.69 (2H, m, CH<sub>2</sub><sup>cypr b</sup>); Rotamer B: 11.63 (1H, d,  $J_{NH-CH} = 5.7$ , 4-NH), 7.88 (1H, d,  $J_{NH-2'} = 8.0$ , 6-NH), 7.63 and 7.58 (2H, bs, 2-NH<sub>2</sub>), 4.28 (1H, m, H-2'), 3.03 (1H, m, CH<sup>cypr</sup>), 1.61-1.87 (14H, m, H-1' and H-3' – H-10'), 0.77 and 0.59 (4H, m, CH<sub>2</sub><sup>cypr</sup>). <sup>13</sup>C NMR (DMSO-*d*<sub>6</sub>): Rotamer A: 164.7 (C-2), 164.2 (C-4), 150.1 (C-6), 136.2 (C-5), 52.5 (C-2'), 37.1 (C-6'), 36.6 and 31.6 (C-8' and C-9') and (C-4' and C-10'), 31.5 (C-5' and C-7'), 26.8 and 26.7 (C-1' and C-3'), 24.3 (CH<sup>cypr</sup>), 6.2 (CH<sub>2</sub><sup>cypr</sup>); Rotamer B: 164.6 (C-2), 162.0 (C-6), 152.2 (C-4), 135.5 (C-5), 53.6 (C-2'), 37.1 (C-6'), 36.9 and 31.6 (C-8' and C-9') and (C-4' and C-10'), 31.5 (C-5' and C-7'), 26.8 (C-1' and C-3'), 22.7 (CH<sup>cypr</sup>), 7.0 (CH<sub>2</sub><sup>cypr</sup>). ESI MS, *m/z* (%): 351.2 [M + Na]<sup>+</sup>, 329.2 [M + H]<sup>+</sup>; HRMS (ESI) calcd for C<sub>17</sub>H<sub>25</sub>N<sub>6</sub>O [M + H]<sup>+</sup> 329.2084, found 329.2085.





**Fig. S6.** <sup>1</sup>H (top) and <sup>13</sup>C (bottom) NMR spectra of compound Y1.

070214servisHR\_2+ #61-64 RT: 1.67-1.76 AV: 4 NL: 3.19E8  
T: FTMS + p ESI Full ms [60.00-600.00]



**Fig. S7.** High resolution mass spectrum (HR-MS) of compound **Y1**.

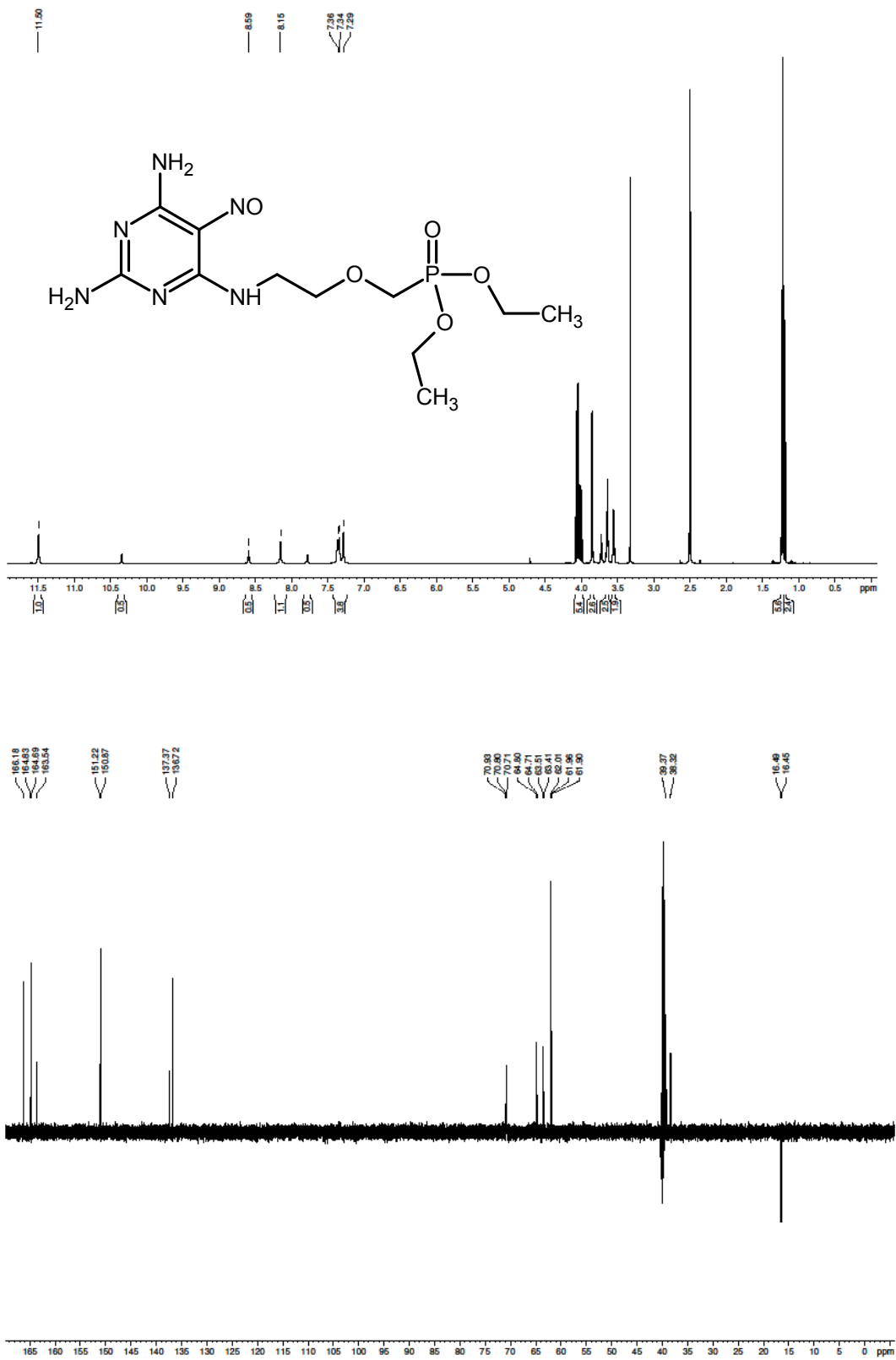
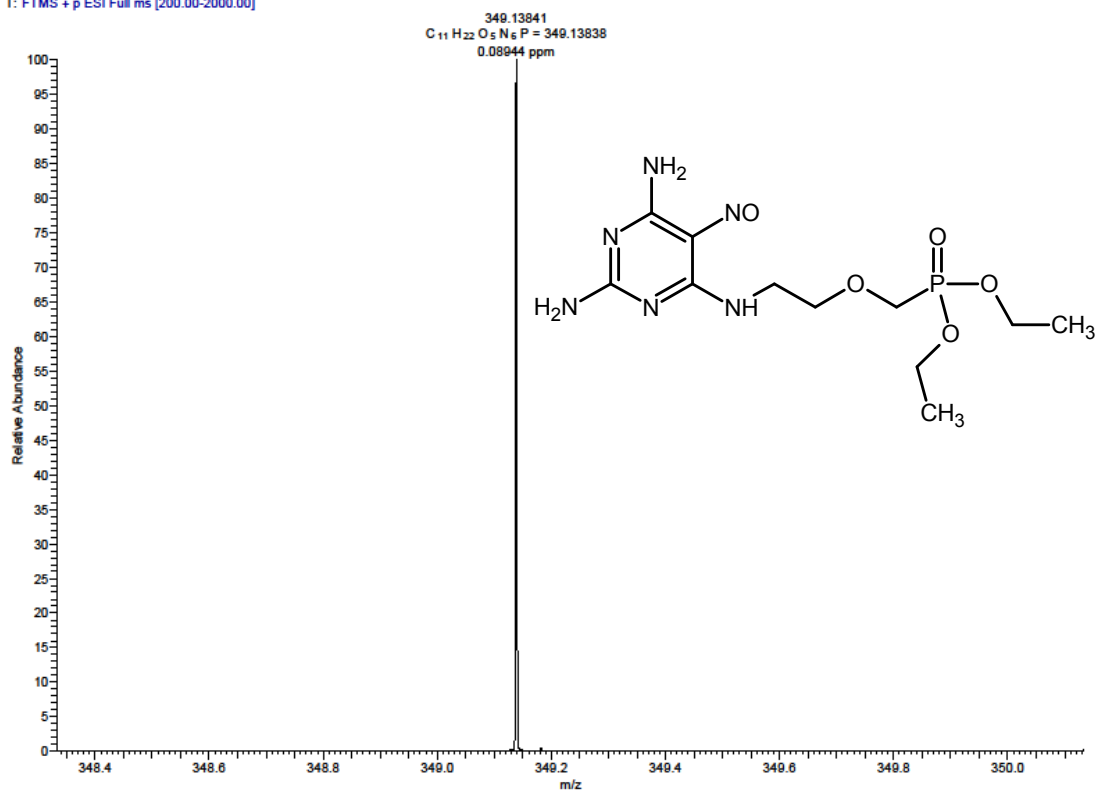
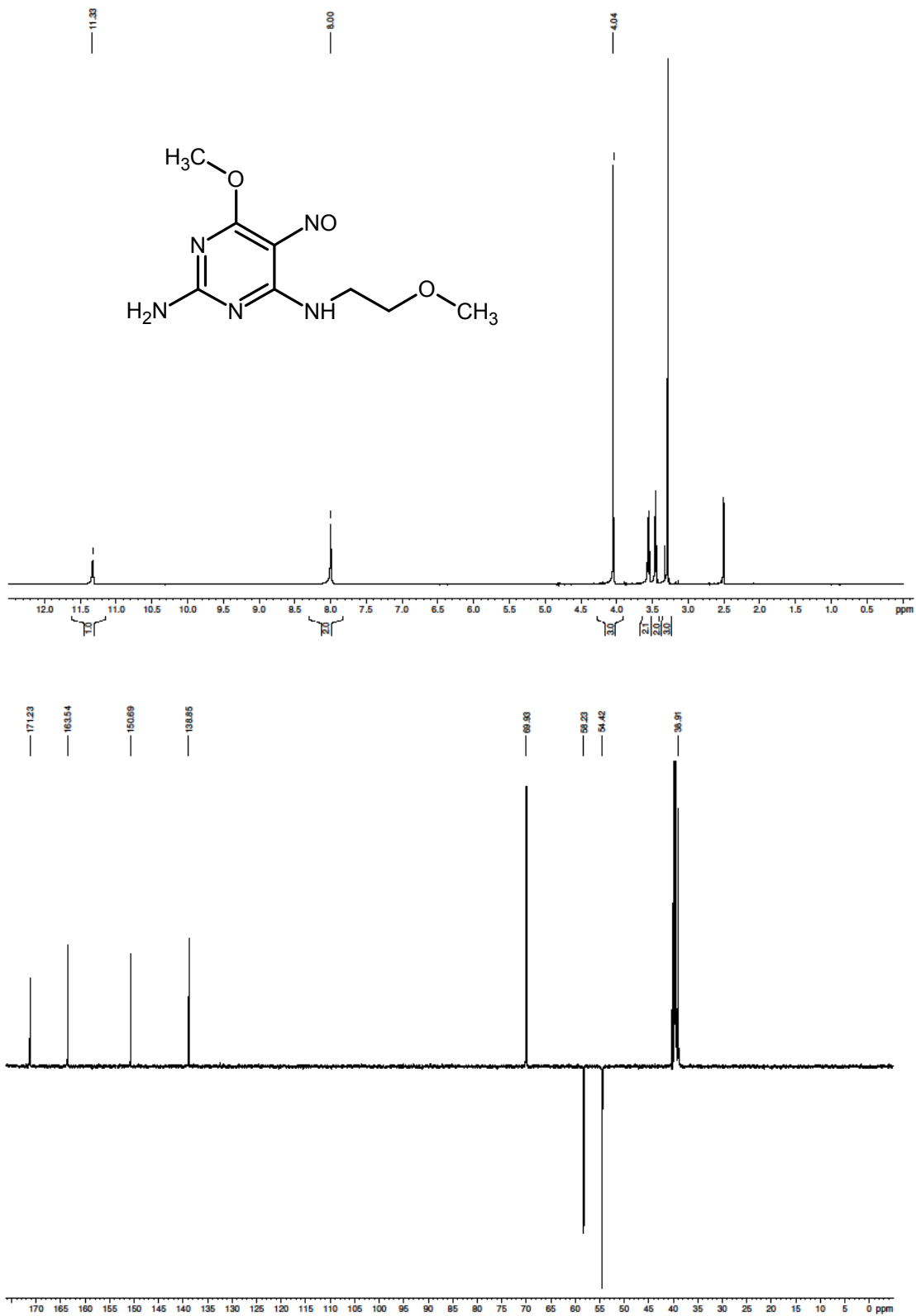


Fig. S8.  $^1\text{H}$  (top) and  $^{13}\text{C}$  (bottom) NMR spectra of compound 1.

080612servis\_12+\_120609080920 #43-55 RT: 1.20-1.54 AV: 13 NL: 1.20E6  
T: FTMS + p ESI Full ms [200.00-2000.00]

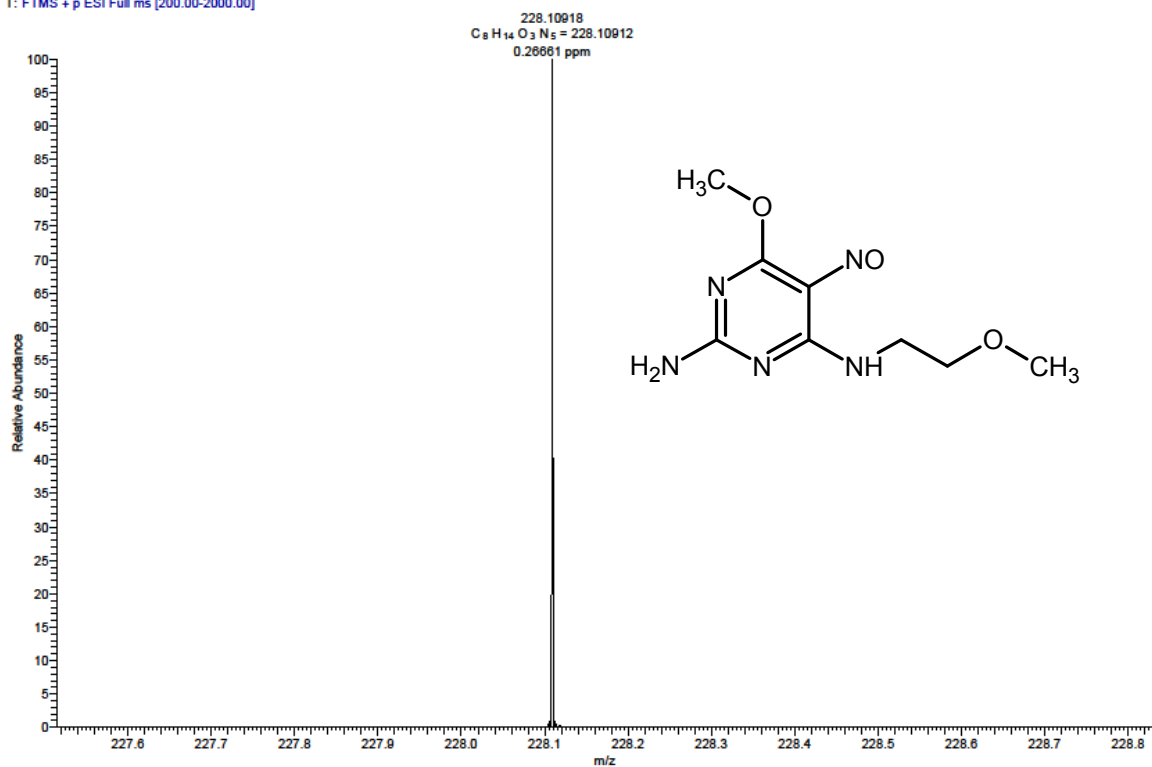


**Fig. S9.** High resolution mass spectrum (HR-MS) of compound **1**.



**Fig. S10.**  $^1\text{H}$  (top) and  $^{13}\text{C}$  (bottom) NMR spectra of compound Y2.

070214servisHR\_3+ #62 RT: 1.72 AV: 1 SB: 17 0.12-0.32 , 0.04-0.26 NL: 8.47E6  
T: FTMS + p ESI Full ms [200.00-2000.00]



**Fig. S11.** High resolution mass spectrum (HR-MS) of compound **Y2**.

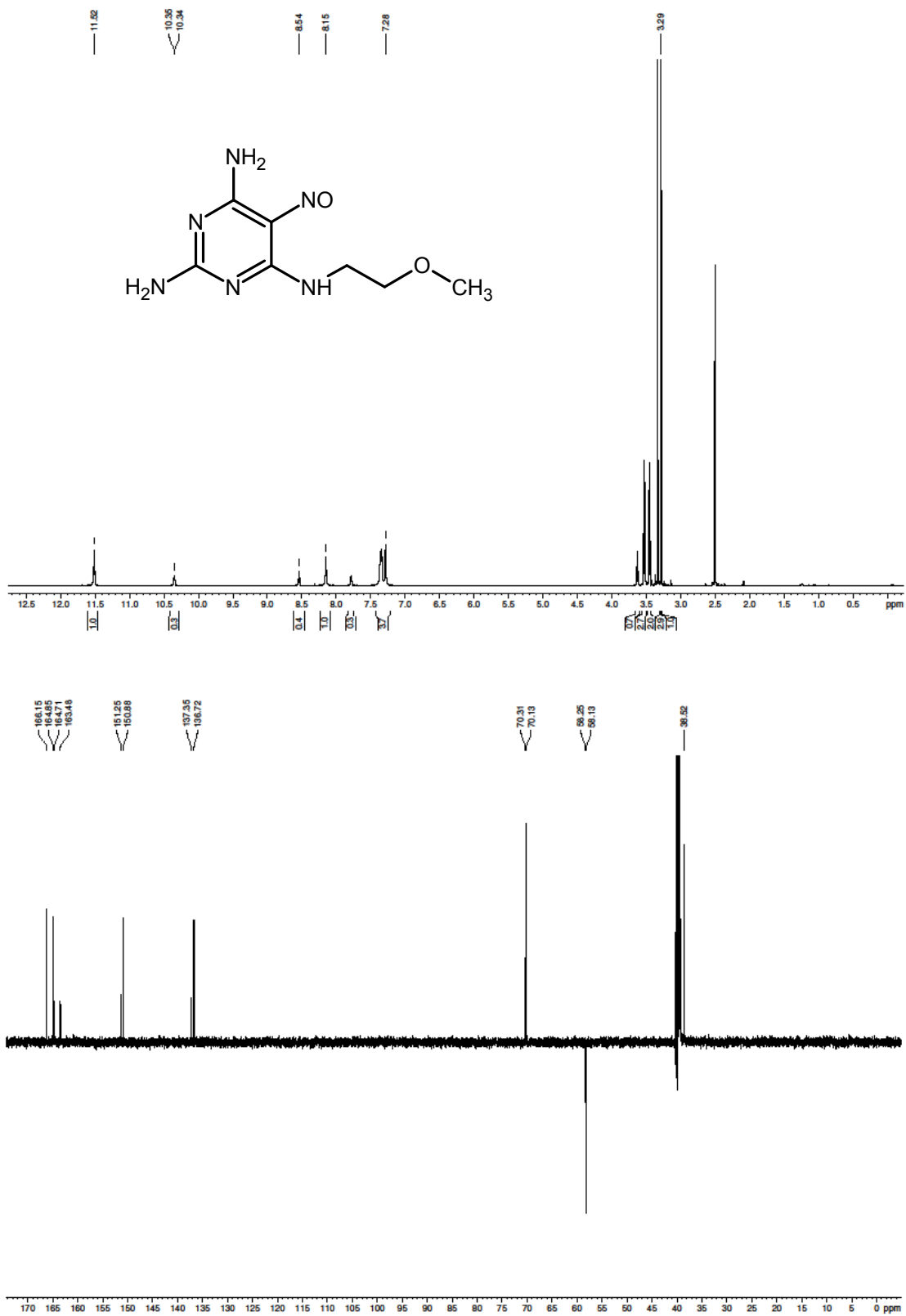
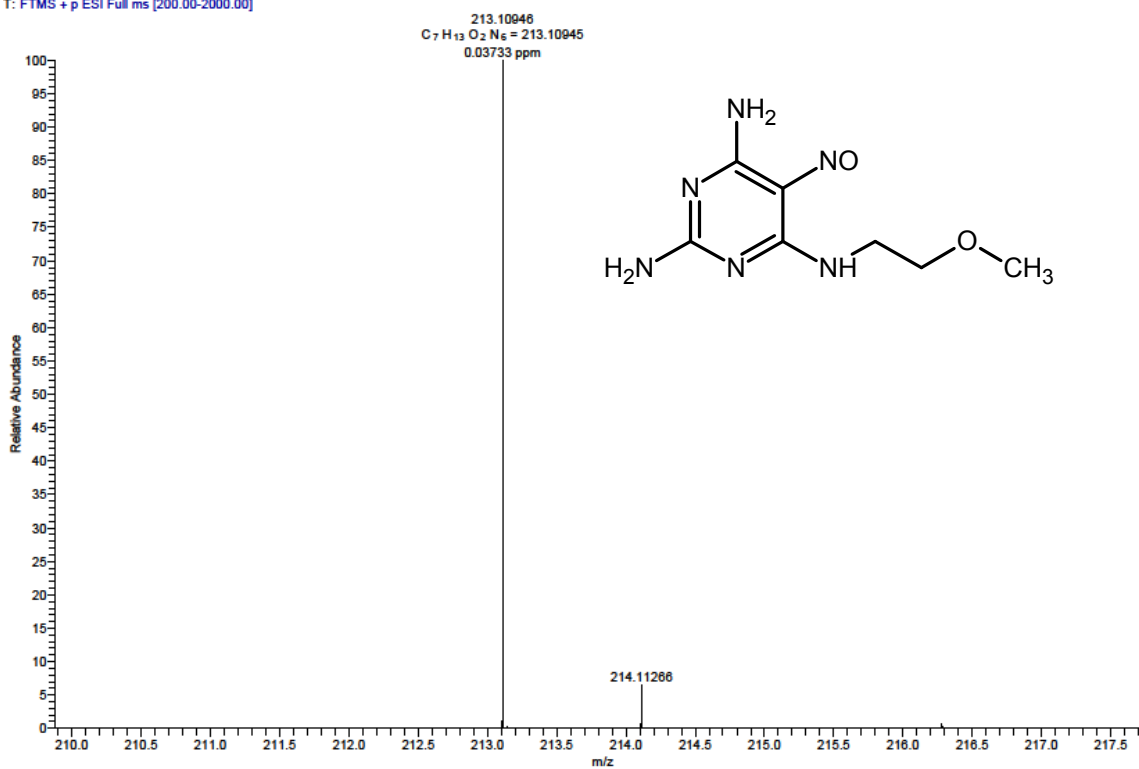


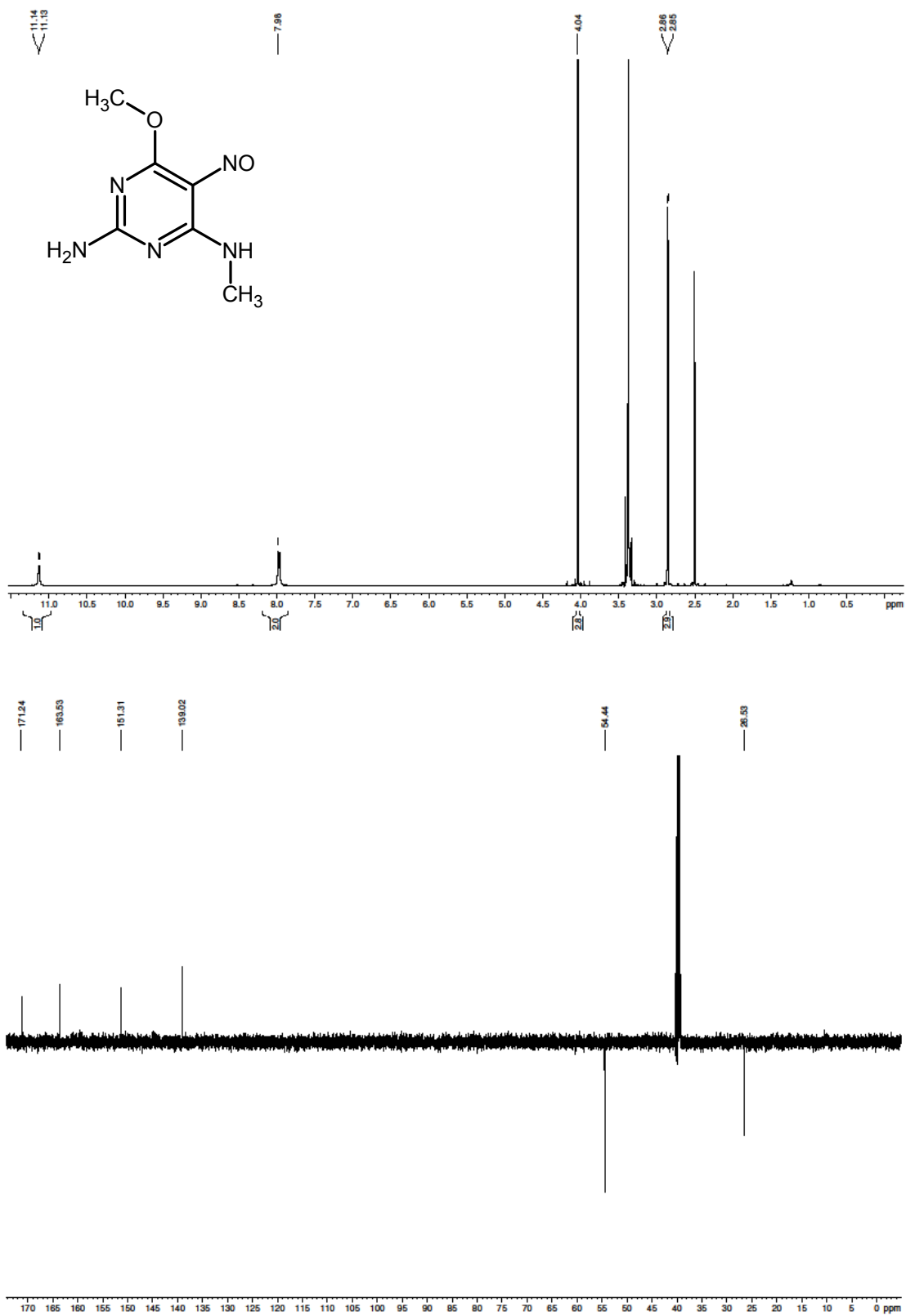
Fig. S12.  $^1\text{H}$  (top) and  $^{13}\text{C}$  (bottom) NMR spectra of compound 2.



070214servisHR\_4+ #59-68 RT: 1.64-1.89 AV: 10 NL: 6.20E6  
T: FTMS + p ESI Full ms [200.00-2000.00]

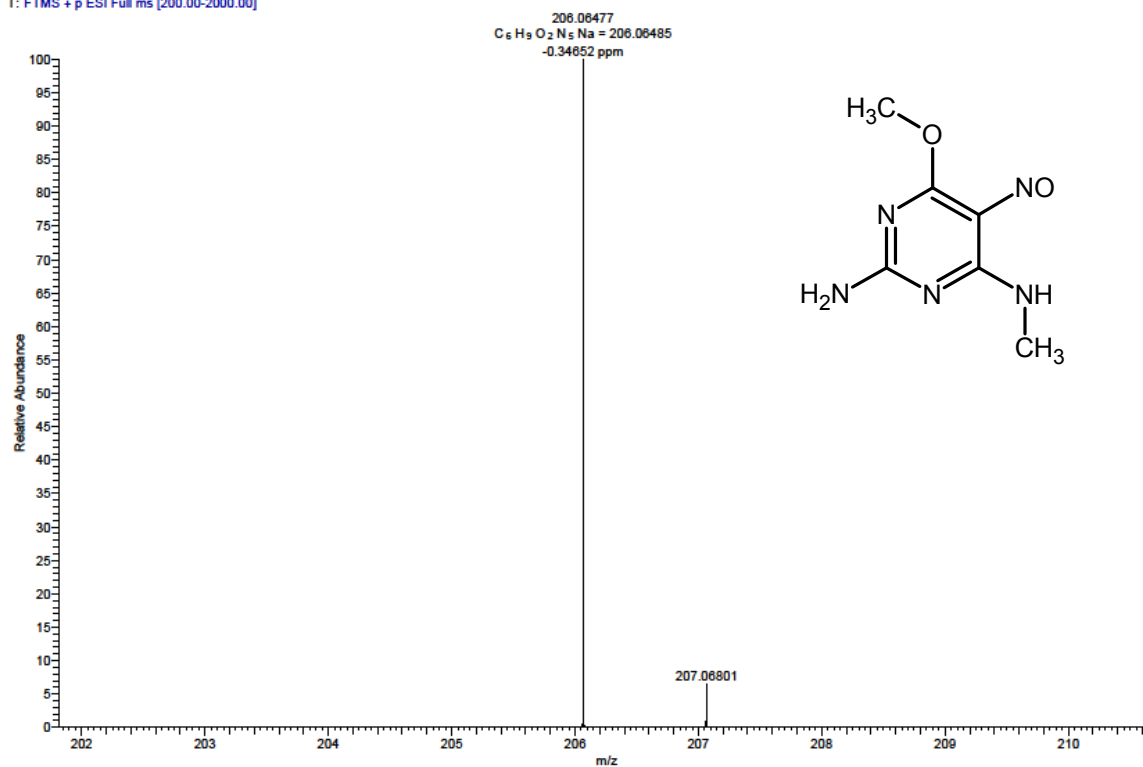


**Fig. S13.** High resolution mass spectrum (HR-MS) of compound 2.

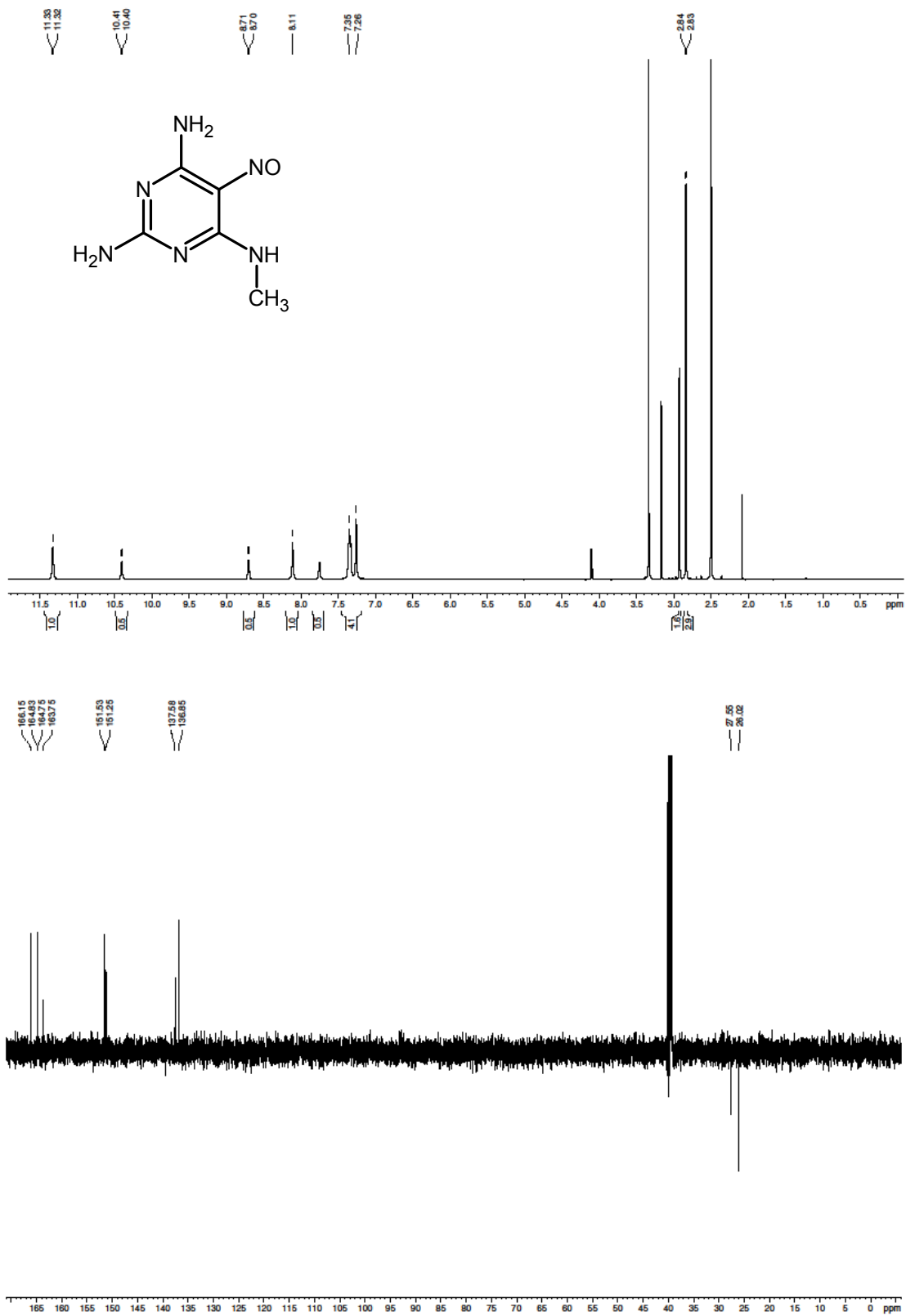


**Fig. S14.**  $^1\text{H}$  (top) and  $^{13}\text{C}$  (bottom) NMR spectra of compound Y3.

050214servisHR\_4+ #60-73 RT: 1.66-2.02 AV: 14 NL: 1.83E7  
T: FTMS + p ESI Full ms [200.00-2000.00]

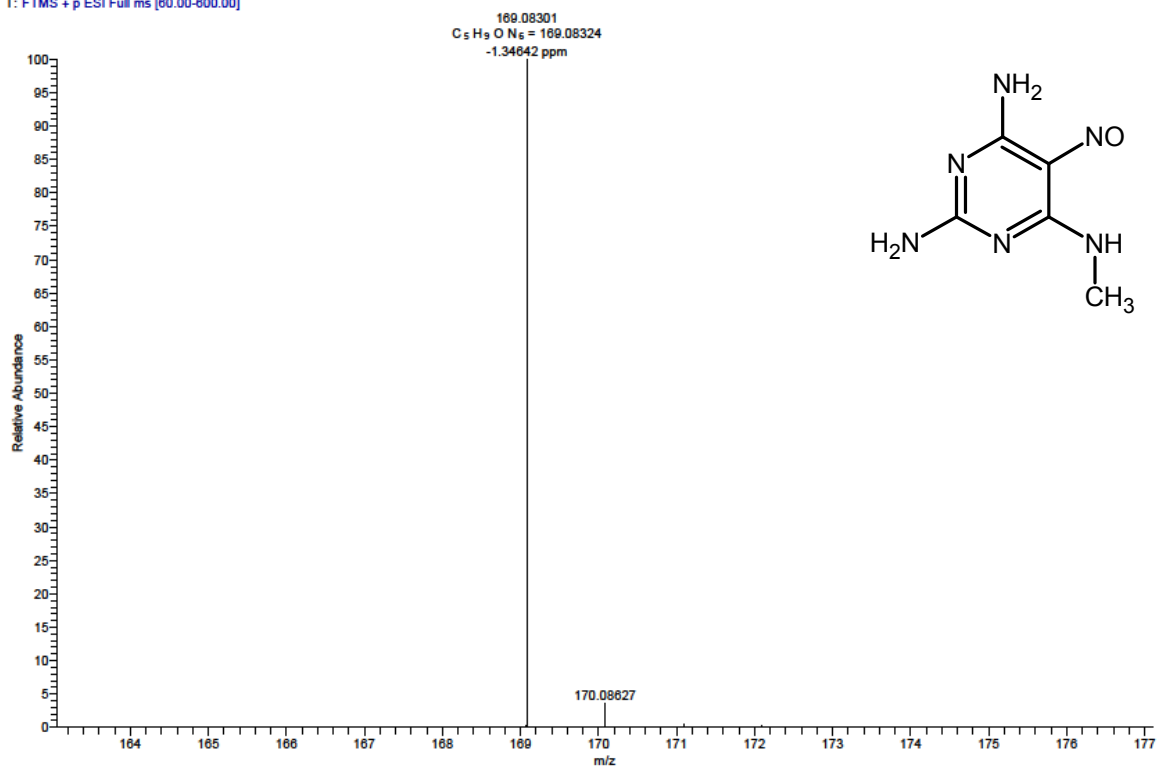


**Fig. S15.** High resolution mass spectrum (HR-MS) of compound **Y3**.

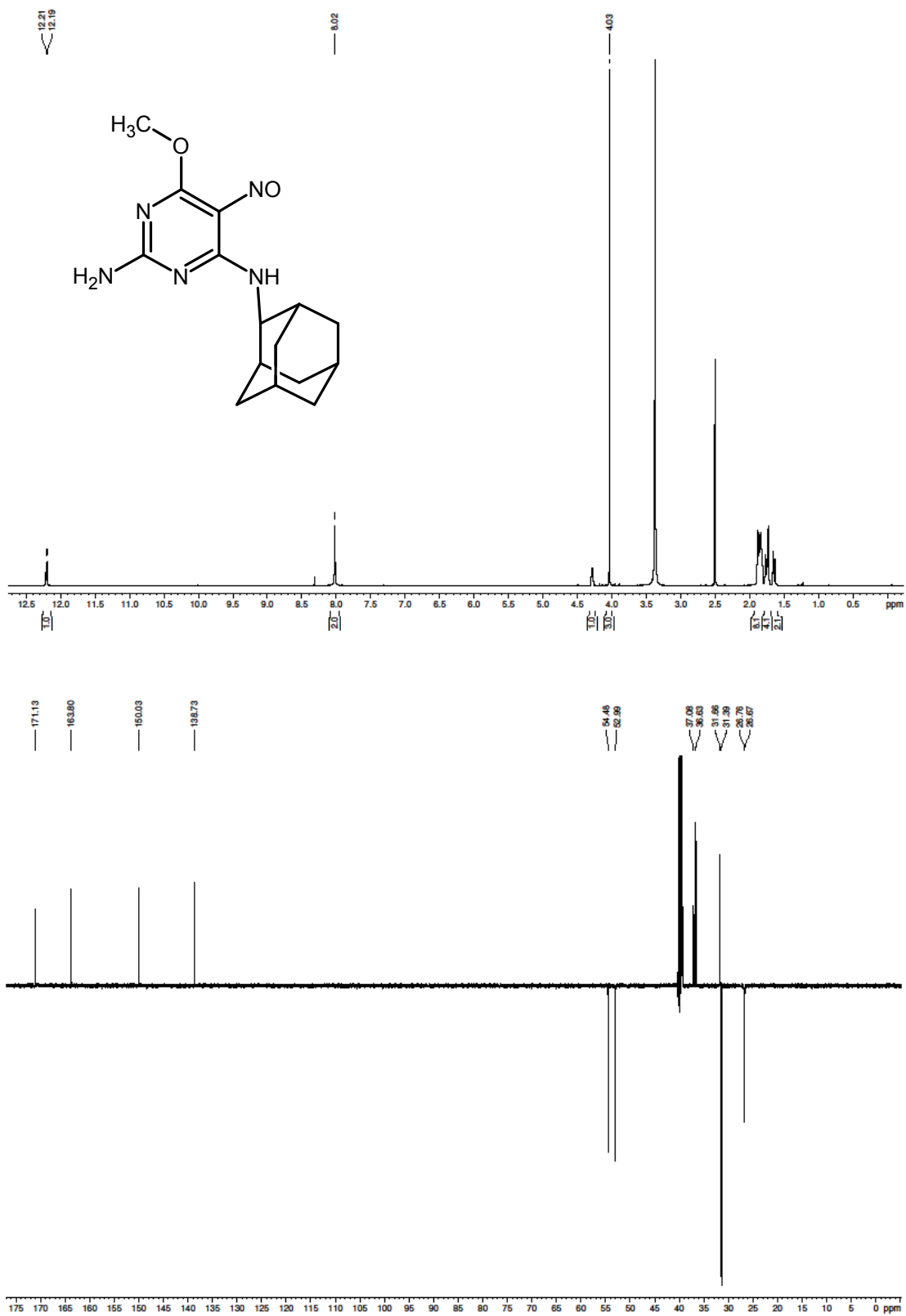


**Fig. S16.** <sup>1</sup>H (top) and <sup>13</sup>C (bottom) NMR spectra of compound 3.

050214servisHR\_2+ #64 RT: 1.81 AV: 1 NL: 4.83E6  
T: FTMS + p ESI Full ms [80.00-800.00]

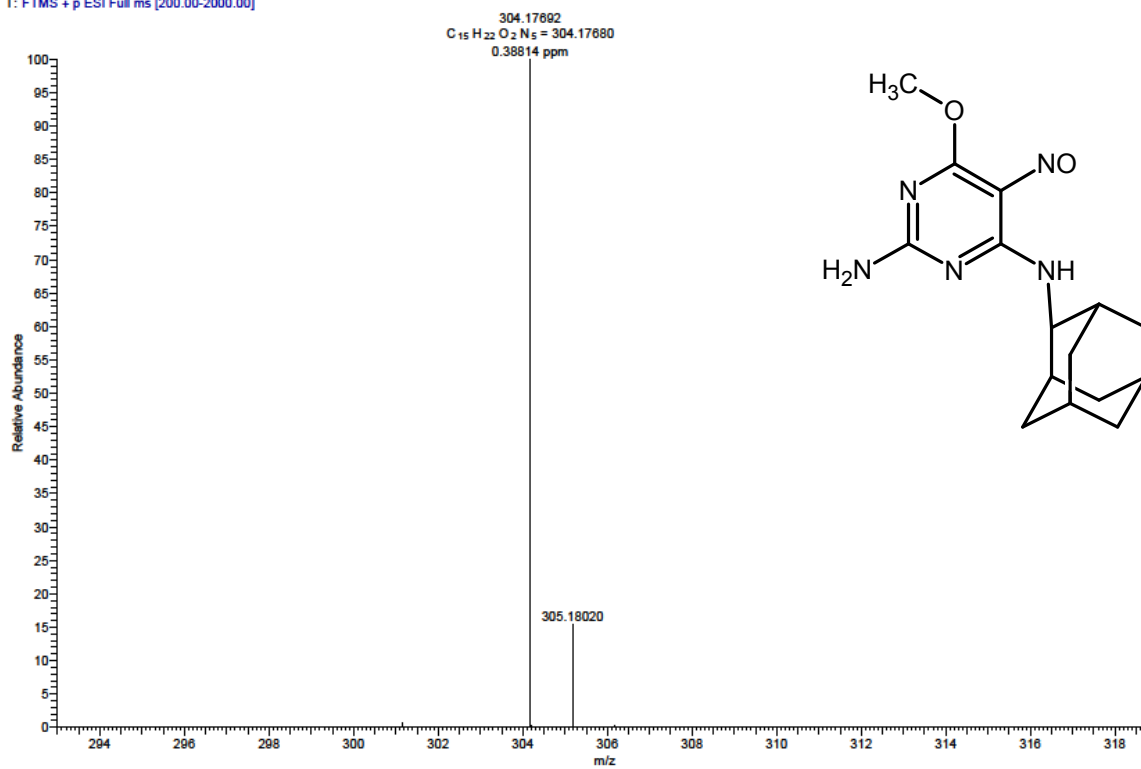


**Fig. S17.** High resolution mass spectrum (HR-MS) of compound **3**.

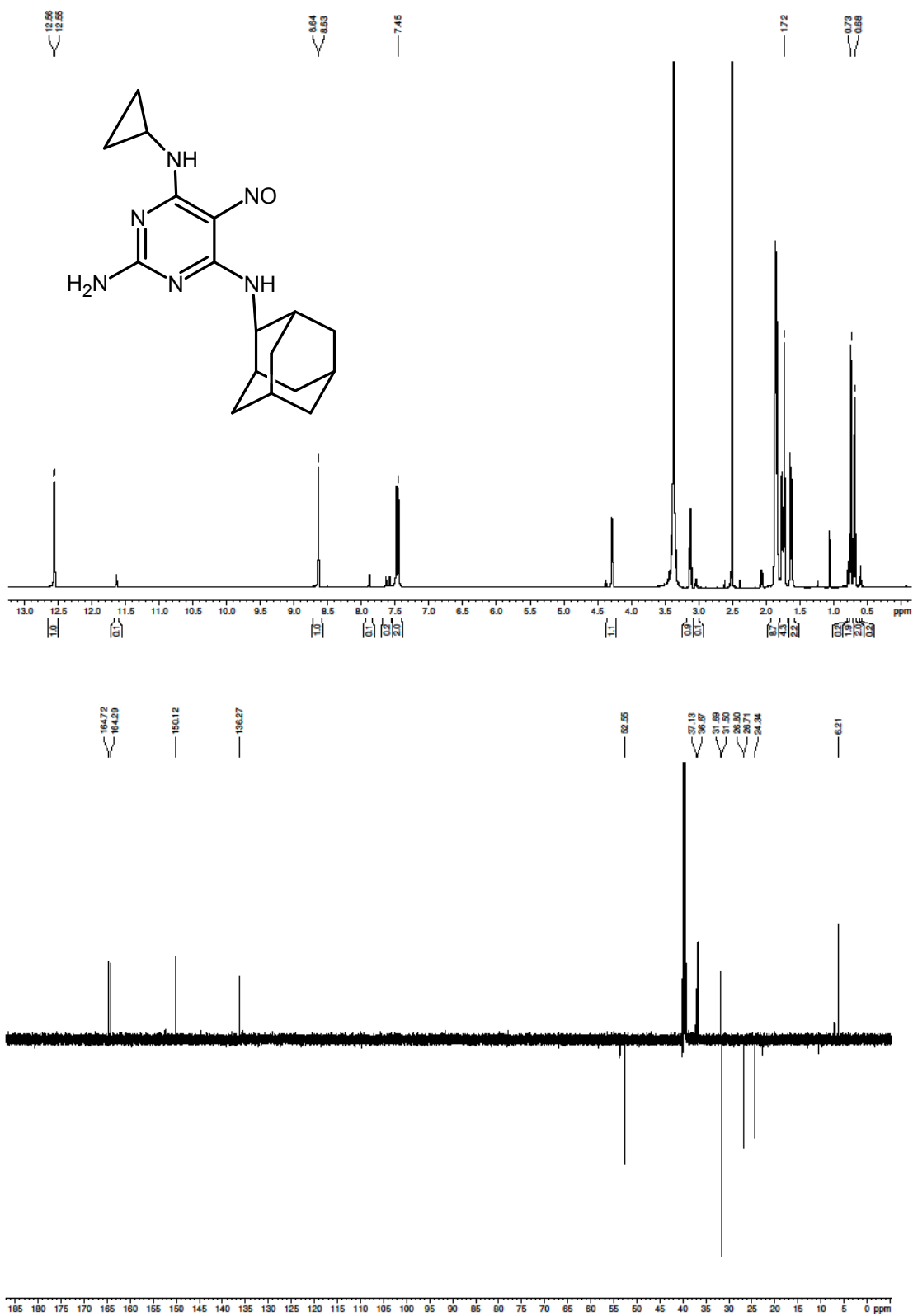


**Fig. S18.**  $^1\text{H}$  (top) and  $^{13}\text{C}$  (bottom) NMR spectra of compound Y4.

050214servisHR\_5+ #59-75 RT: 1.64-2.11 AV: 17 NL: 3.67E6  
T: FTMS + p ESI Full ms [200.00-2000.00]



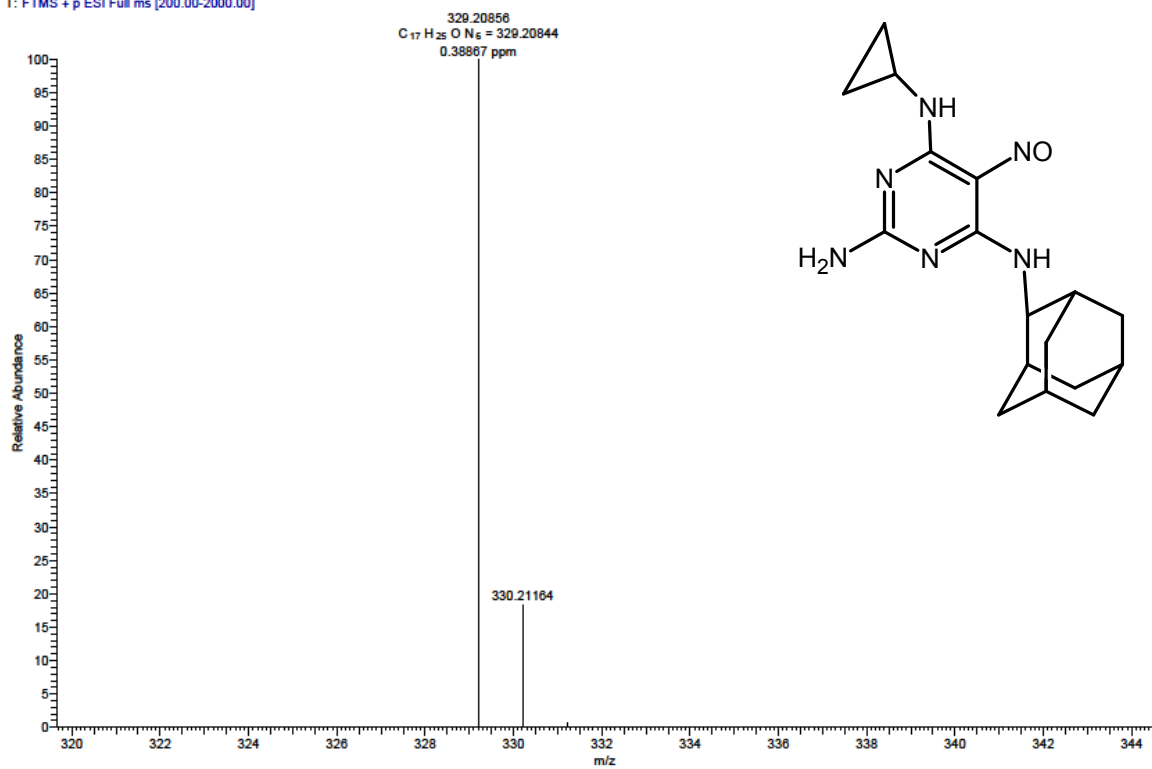
**Fig. S19.** High resolution mass spectrum (HR-MS) of compound **Y4**.



**Fig. S20.** <sup>1</sup>H (top) and <sup>13</sup>C (bottom) NMR spectra of compound 4.



050214servisHR\_6+ #59-71 RT: 1.64-1.98 AV: 13 NL: 1.22E7  
T: FTMS + p ESI Full ms [200.00-2000.00]



**Fig. S21.** High resolution mass spectrum (HR-MS) of compound **4**.

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