Supporting Information

Reactivity and Mechanism of α-Nucleophile Scaffolds as Catalytic Organophosphate Scavengers

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1. Materials and Anlyatical Methods

Materials

All reagents and solvents were purchased from commercial suppliers and used as received. These include paraoxon (purity ≥90% oil), butane-2,3-dione monoxime (DAM, ≥98%), pralidoxime chloride (2-PAM, 99%), 4-pyridinealdoxime (98%), 3-pyridinealdoxime (98%), hydroxylamine hydrochloride (98%), acetone, methanol, dichloromethane, and ethyl acetate, each from Sigma-Aldrich. NMR spectra were acquired in deuterium-labeled solvents including $CDCl_3$, DMSO-d_6 and CD_3OD, and D_2O (99.9 atom % D) containing 0.05 wt/wt % 3-(trimethylsilyl)propionic-2,2,3,3-d_4 acid sodium salt (DSS), each purchased from Sigma-Aldrich or Cambridge Isotope Laboratories. Column chromatography for compound purification was performed using silica gel (200–400 mesh), and fractions were assessed by thin layer chromatography (TLC) using silica plates (250 μm thick, Merck).

Analytical Methods

Compound characterization for structural identity and homogeneity was performed by standard instrumental analysis including mass spectrometry, high resolution mass spectrometry, ^{1}H and ^{13}C NMR spectroscopy, and ultrahigh performance liquid chromatography (UPLC).[1]

Mass Spectroscopy. Compound identification was performed in a Micromass AutoSpec Ultima magnetic sector mass spectrometer using a positive or negative electrospray ionization (ESI) mode. Measurement of an exact molecular mass was performed in a high resolution VG 70-250-S mass spectrometer with an electron ionization (EI) mode.

NMR Spectroscopy. Spectral analysis was performed in a Varian spectrometer at 500 MHz for ^{1}H NMR and at 100 MHz for ^{13}C NMR spectra. Chemical shift (δ) values for NMR spectra are reported in ppm relative to tetramethylsilane (TMS) or 3-(trimethylsilyl)propionic-2,2,3,3-d_4 acid sodium salt (DSS), each set as an internal standard (δ = 0.00 ppm), or to residual signals from an NMR solvent used.

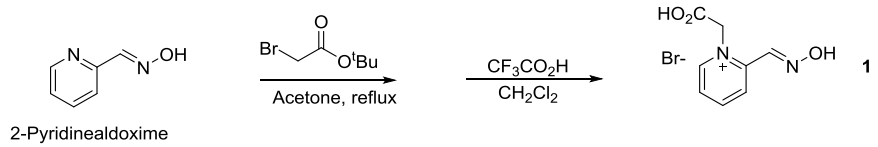
UV/vis Spectrometry. Absorption spectra were recorded in a Perkin Elmer Lambda 20 spectrophotometer.

Ultrahigh Performance Liquid Chromatography (UPLC). Compound purity was assessed by UPLC performed on a Waters Acquity System using a photodiode array detector (detection at 210 and 285 nm). Each sample solution prepared at 0.2–0.5 mg/mL was injected (3 μL) into a BEH C_{18} column (100 × 2.1 mm, 1.7 μm), and elution was performed at a flow rate of 0.2 mL/min with a linear gradient mode. This linear gradient is made of two mobile solvents, water and acetonitrile, each containing TFA (0.1% vol/vol), which are referred to as eluent A and B, respectively. The elution method begins with an initial mobile phase 1% B (0–2.0 min), followed by a linear increase to 80% B (13.4 min), a decrease to 50% B (13.8 min), a decrease to 1% B (14.4 min) and finally an isocratic elution at 1% B (18 min).

2. Synthetic Methods

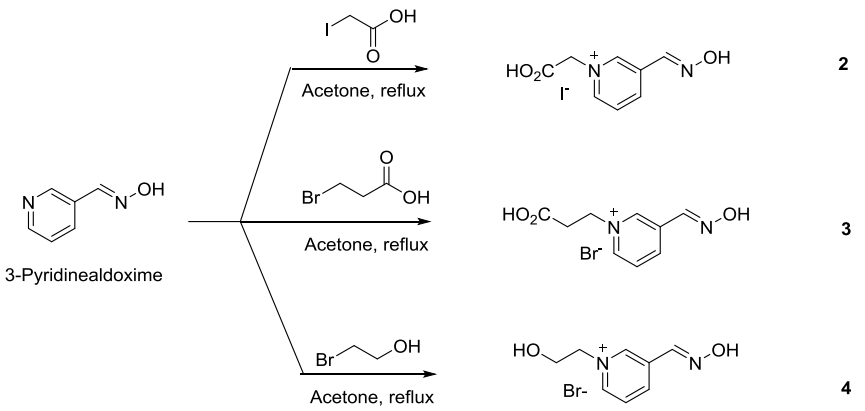
Pyrinidium Aldoxime (PAM) Class

Scheme 1



1. A mixture of hydroxyiminomethylpyridine (6 mmol) and tert-butyl bromoacetate (15 mmol) in acetone (10 mL) was stirred at 65–70 ^{o}C for ~40 h. The mixture was cooled to room temp and the precipitate was collected via centrifugation. It was washed with acetone (2 × 10 mL). In the subsequently step, the solid was dissolved in dichloromethane (2 ml) and trifluoroacetic acid (1.5 mL) was added slowly. The reaction mixture was stirred at room temperature for 2 h and then reaction mixture was dried under reduced pressure and washed with acetone (2 × 10 mL). Collected solid was dried under vacuum, and the product (1-(Carboxymethyl)-2-((hydroxyimino)methyl)pyridin-1-ium bromide) was obtained as white solid (yield = 18%). ^{1}H NMR (500 MHz, CD_3OD): δ 8.94 (d, J = 6.23 Hz, 1H), 8.63 (t, J = 7.93 Hz 1H), 8.53 (s, 1H), 8.46 (d, J = 8.2 Hz, 1H), 8.07 (t, J = 6.97 Hz, 1H), 5.74 (s, 2H) ppm; ^{13}C NMR (100 MHz, CD_3OD): δ 169.1, 147.3, 146.9, 146.5, 142.7, 128.1, 127.5, 60.6 ppm; ESI-MS: m/z 181.0606 $[M]^+$ (calculated for $[C_8H_9N_2O_3]^+$ 181.0608). Purity (UPLC): ≥95% (t_R = 1.79 min).

Scheme 2

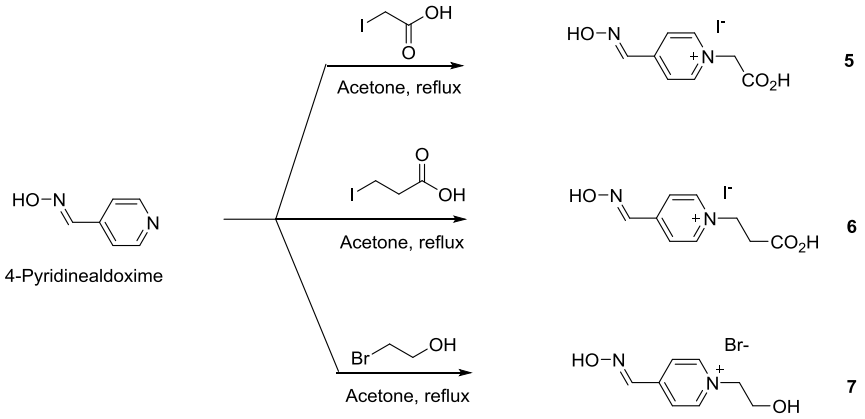


2. Oxime **2**[2] was prepared by stirring a mixture of 3-hydroxyiminomethylpyridine (6.0 mmol) and iodoacetic acid (15.0 mmol) in acetone (10 mL) at 65–70 ^{o}C for 40 h. The mixture was cooled to room temp and the precipitate was collected via centrifugation. It was washed with acetone (3 × 10 mL), and dried under vacuum. The product 1-(carboxymethyl)-3-((hydroxyimino)methyl)pyridin-1-ium bromide was obtained as pale yellow solid; yield: 95%. ^{1}H NMR (500 MHz, CD_3OD): δ 9.11 (s, 1H), 8.84 (d, J = 6.1 Hz 1H), 8.76 (d, J = 8.2 Hz, 1H), 8.26 (s, 1H), 8.08 (dd, J = 6.17 Hz, 1H), 5.37 (s, 2H) ppm; ^{13}C NMR (100 MHz, CD_3OD): δ 169.5, 145.4, 144.7, 143.5, 142.8, 133.3, 127.9, 62.4 ppm; ESI-MS: m/z 181.0605 $[M]^+$ (Calculated for $[C_8H_9N_2O_3]^+$ 181.0608) ppm. Purity (UPLC): ≥95% (t_R = 1.79 min).

3. Oxime **3**[2] was prepared by stirring a mixture of 3-hydroxyiminomethylpyridine (6.0 mmol) and 3-bromopropionic acid (15.0 mmol) in acetone (10 mL) at 65–70 ^{o}C for 40 h. The mixture was cooled to room temp and the precipitate was collected via centrifugation. It was washed with acetone (3 × 10 mL), and dried under vacuum. The product 1-(2-carboxyethyl)-3-((hydroxyimino)methyl)pyridin-1-ium bromide was obtained as white solid (yield 39%) (500 MHz, CD_3OD): δ 9.24 (s, 1H), 8.98 (d, J = 6.10 Hz, 1H), 8.74 (d, J = 8.19 Hz, 1H), 8.26 (s, 1H), 8.07 (dd, J = 6.23 Hz, 1H), 4.83 (t, J = 6.34 Hz, 2H), 3.13 (t, J = 6.33 Hz, 2H) ppm; ^{13}C NMR (100 MHz, CD_3OD): δ 171.1, 142.4, 142.3, 140.5, 140.2, 131.0, 125.7, 54.9, 31.9 ppm; ESI-MS: m/z 195.0764 $[M]^+$ (calculated for $[C_9H_{11}N_2O_3]^+$ 195.0764). Purity (UPLC): ≥95% (t_R = 2.82 min).

4. A mixture of 3-hydroxyiminomethylpyridine (6.0 mmol) and 2-bromoethanol (15.0 mmol) in acetone (10 mL) was stirred at 65–70 ^{o}C for 40 h. The mixture was cooled to room temp and the precipitate was collected via centrifugation. It was washed with acetone (3 × 10 mL), and dried under vacuum. The product 1-(2'-hydroxyethyl)-3-((hydroxyimino)methyl)pyridin-1-ium bromide was obtained as white solid (yield 34%). ^{1}H NMR (500 MHz, CD_3OD): δ 9.16 (s, 1H), 8.90 (d, J = 5.70 Hz 1H), 8.77 (d, J = 8.06 Hz, 1H), 8.28 (s, 1H), 8.09 (t, J = 6.92 Hz, 1H), 4.73 (t, J = 4.65 Hz, 2H), 4.01 (t, J = 4.23 Hz, 2H) ppm; ^{13}C NMR (100 MHz, CD_3OD): δ 146.4, 144.5, 143.8, 142.4, 139.9, 122.2, 60.6, 57.8 ppm; ESI-MS: m/z 167.0816 $[M]^+$ (calculated for $[C_8H_{11}N_2O_2]^+$ 167.0815) ppm. Purity (UPLC): ≥95% (t_R = 2.37 min).

Scheme 3



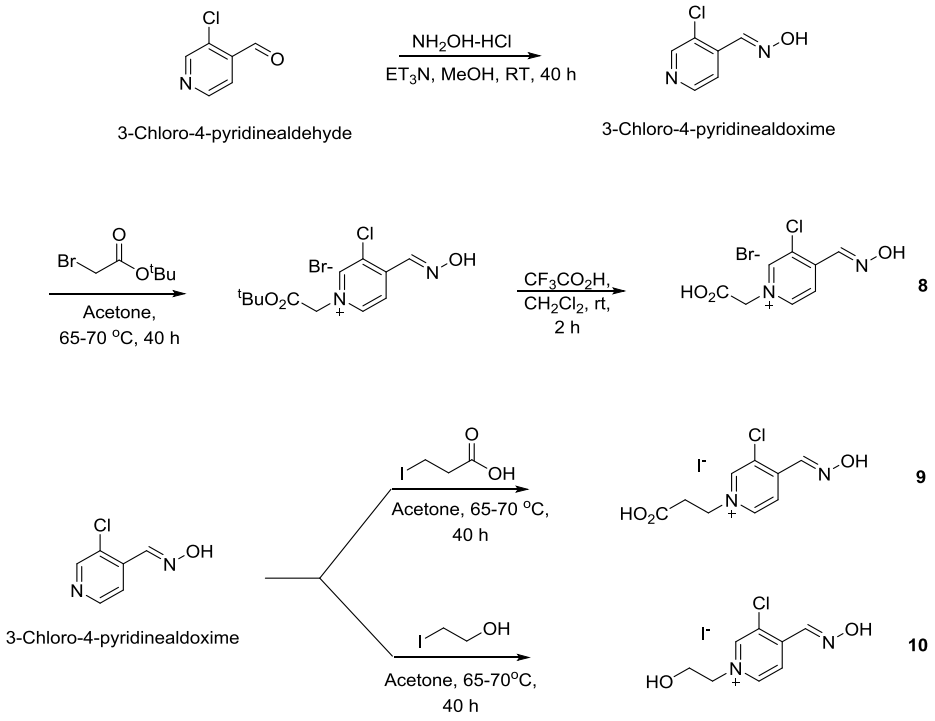
5. Oxime **5**[3] was prepared by stirring a mixture of 4-hydroxyiminomethylpyridine (0.733, 6.0 mmol) and 2-iodoacetic acid (2.789 g, 15.0 mmol) in acetone (10 mL) at 65–70 ^{o}C (oil bath temperature) for 40 h. The mixture was cooled to room temp, and the precipitate was collected via centrifugation. It was washed with acetone (10 × 10 mL). Collected solid was dried under vacuum, and the product 1-(carboxymethyl)-4-((hydroxyimino)methyl)pyridin-1-ium iodide was obtained as yellow solid (93%). ^{1}H NMR (500 MHz, CD_3OD): 8.85 (d, *J* = 6.83 Hz, 2H), 8.33 (s, 1H), 8.24 (d, *J* = 6.79 Hz, 2H), 5.42 (s, 2H); ESI-MS: m/z 181.0605 $[M]^+$ (Calculated for $[C_8H_9N_2O_3]^+$ 181.0608). Purity (UPLC): ≥95% (t_R = 1.75 min).

6. A solution of in acetone (10 mL) that contained 4-hydroxyiminomethylpyridine (0.733, 6.0 mmol) and 3-iodopropionic acid (3.0 g, 15.0 mmol) were stirred at 65–70 ^{o}C (oil bath temperature) for 40 h. The mixture was cooled to room temp and the precipitate was collected

via centrifugation. It was washed with acetone (10 × 10 mL). Collected solid was dried under vacuum. The product 1-(2-carboxyethyl)-4-((hydroxyimino)methyl)pyridin-1-ium iodide was obtained as brownish yellow solid (yield: 95%). ^{1}H NMR (500 MHz, CD_3OD): 8.81 (d, J = 6.79 Hz, 2H), 8.30 (s, 1H), 8.12 (d, J = 6.72 Hz, 2H), 4.79 (t, J = 6.33 Hz, 2H), 3.10 (t, J = 6.34 Hz, 2H); ESI-MS: m/z 195.0766 $[M]^+$ (Calculated for $[C_9H_{11}N_2O_3]^+$ 195.0764). Purity (UPLC): ≥95% (t_R = 2.55 min).

7. Oxime **7**[2, 4] was prepared by stirring a mixture of 4-hydroxyiminomethylpyridine (6.0 mmol) and 2-bromoethanol (15.0 mmol) in acetone (10 mL) at 65–70 ^{o}C for 40 h. The mixture was cooled to room temp and the precipitate was collected via centrifugation. It was washed with acetone (3 × 10 mL), and dried under vacuum. The product 1-(2'-hydroxyethyl)-4-((hydroxyimino)methyl)pyridin-1-ium bromide was obtained as white solid (yield 87%). ^{1}H NMR (500 MHz, CD_3OD): δ 8.89 (d, J = 6.80 2H), 8.32 (s, 1H), 8.23 (d, J = 6.73 Hz, 2H), 4.68 (t, J = 4.93 Hz, 2H), 4.00 (t, J = 4.93 Hz, 2H) ppm; ^{13}C NMR (100 MHz, CD_3OD): δ 142.4, 140.2, 131.0, 125.7, 61.4, 57.7 ppm; ESI-MS: m/z 167.0817 $[M]^+$ (calculated for $[C_8H_{11}N_2O_2]^+$167.0815) ppm. Purity (UPLC): ≥95% (t_R = 2.74 min).

Scheme 4



3-Chloro-4-hydroxyiminomethylpyridine. Hydroxylamine hydrochloride (11.25 mmol, 2.5 eq.) and trimethylamine (11.25 mmol, 2.5 eq.) were mixed in dry MeOH and allowed to stir for 30 min. Subsequently, 3-chloroisonicotinaldehyde (4.5 mmol, 1 eq.) was added slowly to the above hydroxylamine solution and stirred at room temperature for ~40 h. Reaction mixture was dried under reduced pressure and then purified by flash chromatogram using 2:1 hexanes and ethyl acetate (R_f = 0.7 in 1:1 hexanes and ethyl acetate) to afford white solid as desired product in 80% yield. ^{1}H NMR (500 MHz, CD_3OD): δ 8.58 (s, 1H), 8.41 (d, J = 5.20 Hz, 1H), 8.40 (s, 1H),

7.82 (d, J = 5.18 Hz, 1H) ppm; ^{13}C NMR (100 MHz, D_2O): δ 150.9, 148.8,144.3, 138.6, 125.9, 120.9 ppm; ESI-MS: m/z 157.0163 $[M + H]^+$ (calculated for $[C_6H_6N_2OCl]^+$ 157.0168), Purity (UPLC): ≥95% (t_R = 5.83 min).

8. A mixture of 3-chloro-4-hydroxyiminomethylpyridine (1.25 mmol, 1 eq.) and tert-butyl bromoacetate (3.13 mmol, 2.5 eq.) in acetone (3 mL) was stirred at 65–70 ^oC (oil bath temperature) in a seal tube for ~40 h. The mixture was cooled to room tempetature and the precipitate was collected via centrifugation. It was washed with acetone (2 × 7.5 mL) and remove the residual solvent under reduce pressure.

In a subsequent step, the solid was dissolved in dichloromethane (2 mL) and then trifluoroacetic acid (1.5 mL) was added slowly. The reaction mixture was stirred at room temperature for 2 h and dried to obtained brown liquid. Next, acetone was added to the brown liquid resulting in solid precipitation which was washed with acetone (6 × 7.5 mL). Collected solid was dried under vacuum, and the product, (E)-1-(carboxymethyl)-3-chloro-4-((hydroxyimino)methyl)pyridin-1-ium bromide was obtained as pale brown solid (110 mg, yield = 57%). ^{1}H NMR (500 MHz, CD_3OD): δ 9.27 (s, 1H), 8.81 (d, J = 6.56 Hz, 1H), 8.56 (s, 1H), 8.48 (d, J = 6.53 Hz, 1H), 4.50 (s, 2H) ppm; ^{13}C NMR (100 MHz, D_2O): δ 168.0, 147.5, 146.2, 143.2, 143.3, 143.1, 132.8, 123.3, 60.6 ppm; ESI-MS: m/z 215.0218 $[M + H]^+$ (calculated for $[C_8H_8N_2O_3Cl]^+$ 215.0223). Purity (UPLC): ≥95% (t_R = 3.33 min).

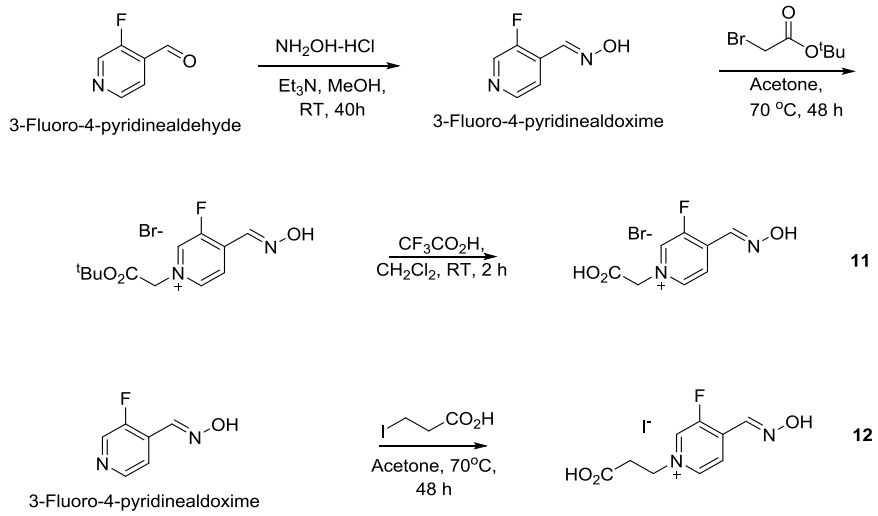
9. A mixture of 3-chloro-4-hydroxyiminomethylpyridine (1.25 mmol, 1 eq.) and 3-iodopropionic acid (3.13 mmol, 2.5 eq.) in acetone (3 mL) were stirred at 65–70 ^oC (oil bath temperature) in a seal tube for ~40 h. The mixture was cooled to room temperature and the solid precipitate was collected via centrifugation and subsequently, washed with acetone (6 × 7.5 mL). Collected solid was dried under vacuum, and the product, (E)-1-(2-carboxyethyl)-3-chloro-4-((hydroxyimino)methyl)pyridin-1-ium iodide was obtained as yellow solid (100 mg, yield = 56%). ^{1}H NMR (500 MHz, CD_3OD): δ 9.33 (s, 1H), 8.88 (d, J = 6.56 Hz, 1H), 8.53 (s, 1H), 8.41 (d, J = 6.53 Hz, 1H), 4.83 (t, J = 6.35 Hz, 2H), 3.14 (t, J = 6.29 Hz, 2H) ppm; ^{13}C NMR (100 MHz, D_2O): δ 173.7, 146.9, 145.6, 143.5, 142.6, 133.1, 123.7, 57.0, 34.5 ppm; ESI-MS: m/z 229.0378 $[M]^+$ (calculated for $[C_9H_{10}N_2O_3Cl]^+$ 229.0379). Purity (UPLC): ≥95% (t_R = 4.23 min).

10. A mixture of 3-chloro-4-hydroxyiminomethylpyridine (1.25 mmol, 1 eq.) and 2-iodoethanol (3.13 mmol, 2.5 eq.) in acetone (3 mL) was stirred at 65–70 ^oC (oil bath temperature) in a seal tube for ~40 h. The mixture was cooled to room temperature and the solid precipitate was collected via centrifugation. Subsequently, it was washed with acetone (6 × 7.5 mL). Collected solid was dried under vacuum, and the product, (E)-3-chloro-1-(2-hydroxyethyl)-4-((hydroxyimino)methyl)pyridin-1-ium iodide was obtained as yellow solid (217 mg, yield = 61%). ^{1}H NMR (500 MHz, CD_3OD): δ 9.24 (s, 1H), 8.81 (d, J = 6.51 Hz, 1H), 8.58 (s, 1H), 8.47 (d, J = 6.51 Hz, 1H), 4.69 (t, J = 4.88 Hz, 2H), 4.02 (t, J = 4.83 Hz, 2H) ppm; ^{13}C NMR (100 MHz, D_2O): δ 146.9, 145.3, 143.5, 142.4, 133.1, 123.7, 63.4, 60.0 ppm; ESI-MS: m/z 201.0430 $[M]^+$ (calculated for $[C_8H_{10}N_2O_2Cl]^+$ 201.0430). Purity (UPLC): ≥95% (t_R = 4.01 min).

3-Fluoroisonicotinaldehyde Oxime: Hydroxylamine hydrochloride (8 mmol, 2 eq.) and trimethylamine (8 mmol, 2 eq.) were mixed in dry MeOH and allowed to stir for 30 min. Subsequently, 3-fluoroisonicotinaldehyde (4.0 mmol, 1 eq.) was added slowly to the above hydroxylamine solution and stirred at room temperature for ~40 h. Reaction mixture was dried

under reduced pressure and then purified by flash chromatogram using 2:1 hexanes and ethyl acetate (R_f = 0.256 in 2:1 hexanes and ethyl acetate) to afford white solid as desired product in 92 % yield. ^{1}H NMR (500 MHz, CD_3OD): δ 8.49 (d, *J* = 2.23 Hz, 1H), 8.35 (d, *J* = 5.09 Hz, 1H), 8.26 (s, 1H), 7.80 (t, *J* = 5.66 Hz, 1H) ppm; ^{13}C NMR (125 MHz, D_2O): δ 150.9, 148.8,144.3, 138.6, 125.9, 120.9 ppm; ESI-MS: m/z $[M + H]^+$ 141.0466 (calculated for $[C_6H_5N_2OF+H]^+$ 141.0464), Purity (UPLC): ≥95% (t_R = 5.83 min).

Scheme 5

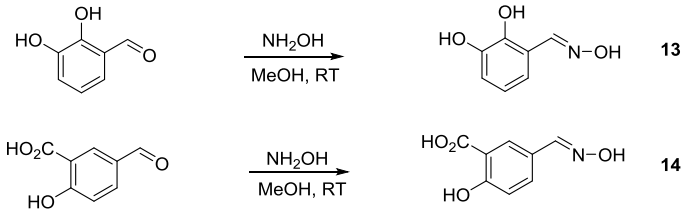


11. A mixture of 3-fluoroisonicotinaldehyde Oxime (0.85 mmol, 1 eq.) and tert-butyl bromoacetate (2.55 mmol, 3.0 eq.) in acetone (1.5 mL) was stirred at 65–70 °C (oil bath temperature) in a seal tube for ~48 h. The mixture was cooled to room temperature and the precipitate was collected via centrifugation. It was washed with acetone (3 × 7.5 mL) and remove the residual solvent under reduce pressure. In a subsequent step, the solid was dissolved in dichloromethane (2 mL) and then trifluoroacetic acid (1.5 mL) was added slowly. The reaction mixture was stirred at room temperature for 2 h and dried to obtained brown liquid. Next, acetone was added to the brown liquid resulting in solid precipitation which was washed with acetone (6 × 7.5 mL). Collected solid was dried under vacuum, and the product, 1-(carboxymethyl)-3-fluoro-4-((hydroxyimino)methyl)pyridin-1-ium bromide was obtained as brown solid (154 mg, yield = 90 %). ^{1}H NMR (500 MHz, CD_3OD): δ 9.18 (d, *J* = 4.11 Hz, 1H), 8.75 (d, *J* = 6.32 Hz, 1H), 8.43 (t, *J* = 6.72 Hz, 1H), 8.42 (s, 1H), 5.32 (s, 2H) ppm; ^{13}C NMR (100 MHz, D_2O): δ162.3, 151.4, 148.9, 135.1, 133.6, 130.9, 130.8, 129.4, 129.0, 117.3, 117.2, 55.4 ppm; ESI-MS: m/z of $[M]^+$ 199.0514 (calculated for $[C_8H_8FN_2O_3]^+$ 199.0514). Purity (UPLC): ≥ 95% (t_R = 1.96 min).

12. A mixture of 3-fluoroisonicotinaldehyde Oxime (1.16 mmol, 1 eq.) and 3-iodopropionic acid (3.48 mmol, 3 eq.) in acetone (1.5 mL) were stirred at 65–70 °C (oil bath temperature) in a seal tube for ~40 h. The mixture was cooled to room temperature and the solid precipitate was collected via centrifugation and subsequently, washed with acetone (6 × 7.5 mL). Collected solid was dried under vacuum, and the product, 1-(2-carboxyethyl)-3-fluoro-4-((hydroxyimino)methyl) pyridin-1-ium iodide was obtained as yellow solid (179 mg, yield = 73 %). ^{1}H NMR (500 MHz, CD_3OD): δ 9.30 (d, *J* = 4.85 Hz, 1H), 8.86 (d, J = 6.47 Hz, 1H), 8.41(t,

J = 6.7 Hz, 1H), 8.40(s, 1H), 4.83 (t, *J* = could not be detected due to overlap with water peak, 2H), 3.14 (t, *J* = 6.27 Hz, 2H) ppm; ^{13}C NMR (100 MHz, D_2O): δ 173.3, 158.4, 155.9, 141.5, 140.6, 137.5, 137.4, 135.9, 135.5, 124.5, 57.3, 34.4 ppm; ESI-MS: m/z of $[M]^+$ 213.0733 (calculated for $[C_9H_{10}FN_2O_3]^+$ 213.0670). Purity (UPLC): ≥ 95% (t_R = 2.99 min).

Scheme 6



Representative procedure: To a glass scintillation vial (25 mL) was weighed 0.5 g of aldehyde (2,3-dihydroxybenzaldehyde, 5-formyl salicylic acid), and then methanol (5 mL) was added to dissolve the compound. To this solution was added 2.0 equiv. of hydroxylamine in methanol (3.0 M). The mixture was gently shaken overnight. The solution was concentrated and the product was crystalized from methanol.

13 (2,3-Dihydroxybenzaldehyde aldoxime). MS (ESI) *m/z* (relative intensity, %) = 154.050 (53 %) $[M + H]^+$. ^{1}H NMR (500 MHz, DMSO-d_6): δ 11.304 (s, 1H), 9.571 (s, 1H), 9.275 (s, 1H), 8.304 (s, 1H, CH=NOH)), 6.925 (dd, 1H, *J* = 2, 8 Hz, C_6H), 6.796 (dd, 1H, *J* = 2, 8 Hz, C_4H), 6.673 (t, 1H, *J* = 8 Hz, C_5H) ppm.

14 (5-Formyl salicylic acid aldoxime). MS (ESI, negative ion mode) *m/z* (relative intensity, %) = 180.031 (100 %) $[M - H]^+$. ^{1}H NMR (500 MHz, DMSO-d_6): δ 11.065 (s, 1H), 8.111 (s, 1H, CH=NOH), 7.985 (d, 1H, *J* = 2 Hz, C_6H), 7.764 (dd, 1H, *J* = 2, 8.5 Hz, C_4H), 6.990 (d, 1H, *J* = 8.5 Hz, C_3H) ppm.

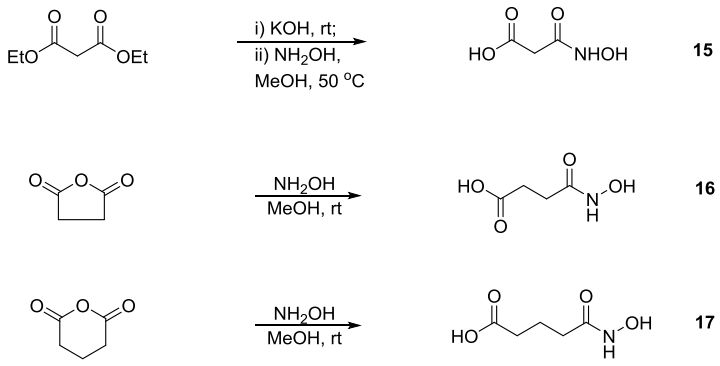
Hydroxamic Acid (HA) Class

15 (Scheme 7). To diethyl malonate (0.5 g, 3.12 mmol) was added 3.0 M KOH (1.09 mL). As soon as the KOH was added, yellow precipitates were formed. The mixture was stirred at room temp for 24 h, and methanol was evaporated. The residue was washed with acetonitrile (2 mL), and dried. The solid material was suspended in methanol (1.0 mL), and 2.72 M hydroxylamine in methanol (1.21 mL; 1.05 mol equiv) was added, and the mixture was incubated at 50 °C for 24 h. Methanol was evaporated, and the solid residue was washed with methanol (2 × 1 mL). Yield = 108 mg. MS (ESI, negative ion mode) *m/z* (relative intensity, %) = 118.01 (100%) $[M - H]^-$. ^{1}H NMR (500 MHz, D_2O): δ 3.00 (s, 2H, CH_2) ppm. ^{13}C NMR (500 MHz, D_2O): δ 174.45, 167.89, 42.17, 42.08, 41.92 ppm.

16. To succinic anhydride (0.5 g, 5.0 mmol) in methanol (1.0 mL) was added hydroxylamine in methanol (2.72 M, 1.84 mL; 1.0 equiv.). The mixture was stirred for 1 h at room temp, and followed by addition of 3.0 M KOH in methanol (1.666 mL). After stirred for 5 min, methanol was slowly evaporated, and the product was precipitated as a while solid. It was collected and washed with methanol. Yield = 0.729 g. R_f = 0.2 (10% MeOH/CH_2Cl_2). MS (ESI, negative ion

mode) *m/z* (relative intensity, %) = 132.025 (100 %) $[M - H]^+$. ^{1}H NMR (500 MHz, CD_3OD): δ 2.483–2.468 (m, 2H, $\underline{CH_2}CO_2H$), 2.397–2.368 (m, 2H, $\underline{CH_2}C(=O)NHOH$) ppm. ^{13}C NMR (100 MHz, CD_3OD): δ 180.419, 172.334, 32.255, 28.819 ppm.

Scheme 7

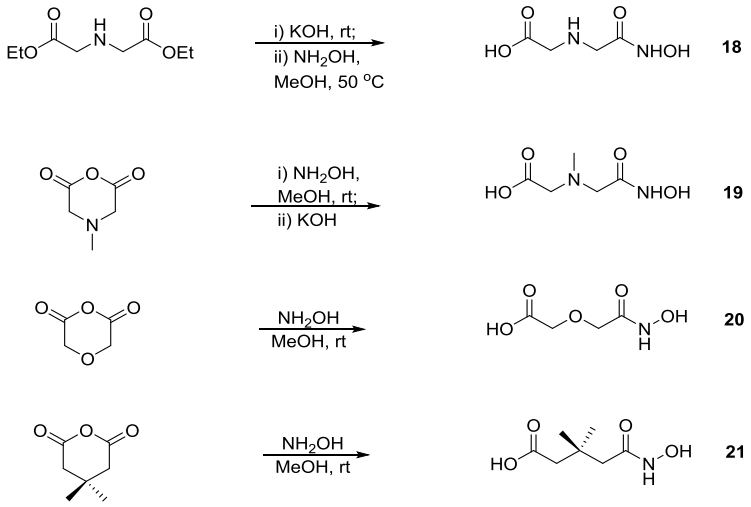


17. To glutaric anhydride (0.5 g, 4.38 mmol) in methanol (1.0 mL) was added hydroxylamine in methanol (2.72 M, 1.61 mL; 1.0 equiv.). The mixture was stirred at room temp for 1 h, and followed by addition of 3.0 M KOH in methanol (1.462 mL). After stirred for 5 min, methanol was slowly evaporated, and the product was precipitated as a while solid. It was collected and washed with methanol. Yield = 0.655 g. R_f = 0.38 (10% $MeOH/CH_2Cl_2$). MS (ESI, negative ion mode) *m/z* (relative intensity, %) = 146.046 (100 %) $[M - H]^+$. ^{1}H NMR (500 MHz, CD_3OD): δ 2.238–2.168 (m, 4H, $C(=O)\underline{CH_2}$), 1.850–1.820 (m, 2H, *J* = 8 Hz, $CH_2\underline{CH_2}CH_2$) ppm. ^{13}C NMR (100 MHz, CD_3OD): δ 181.708, 172.615, 35.857, 31.739, 21.629 ppm.

18 (Scheme 8). To diethyl imminodiacetate (0.5 g, 2.64 mmol) was added 3.0 M KOH (0.925 mL). As soon as the KOH was added, yellow precipitates were formed. The mixture was stirred at room temp for 24 h (5:15 pm-), and methanol was evaporated. The residue was washed with acetonitrile (2 mL), and dried. The solid material was suspended in methanol (1.0 mL), and 2.72 M hydroxylamine in methanol (1.02 mL; 1.05 mol equiv) was added, and the mixture was incubated at 50 °C for 12-24 h. Methanol was evaporated, and the solid material was washed with methanol (2 × 1 mL). Yield = 180 mg. MS (ESI, negative ion mode) *m/z* (relative intensity, %) =147.04 (100%) $[M-H]^-$. ^{1}H NMR (500 MHz, CD_3OD or $CDCl_3$): δ 4.05 (s, 2H, $\underline{CH_2}$), 3.85 (s, 2H, $\underline{CH_2}$), ppm. ^{13}C NMR (500 MHz, D_2O): δ 174.54, 171.25, 165.53, 50.20, 49.44, 48.85 ppm.

19. To N-methyl morpholine-2,6-dione (0.5 g, 3.87 mmol) was added 2.72 M hydroxylamine in methanol (1.5 mL; 1.05 mol equiv) and methanol (1.0 mL) (5:5 pm). It was stirred for 2.5 h at room temp, and followed by addition of 3.0 M KOH in methanol (1.36 mL). The mixture was placed in a ventilation hood in which methanol was slowly evaporated, leading to precipitation of white solids. The crystals precipitated were collected and washed with methanol (2 × 1 mL). Yield = 75 mg. MS (ESI, negative ion mode) *m/z* (relative intensity, %) = 161.05 (100%) $[M - H]^-$. ^{1}H NMR (500 MHz, D_2O): δ 2.94 (s, 2H, $\underline{CH_2}$), 2.93 (s, 2H, $\underline{CH_2}$), 2.12 (s, 3H, CH_3) ppm. ^{13}C NMR (500 MHz, D_2O: δ 170.69, 60.66, 58.51, 57.95, 42.20, 41.87 ppm.

Scheme 8



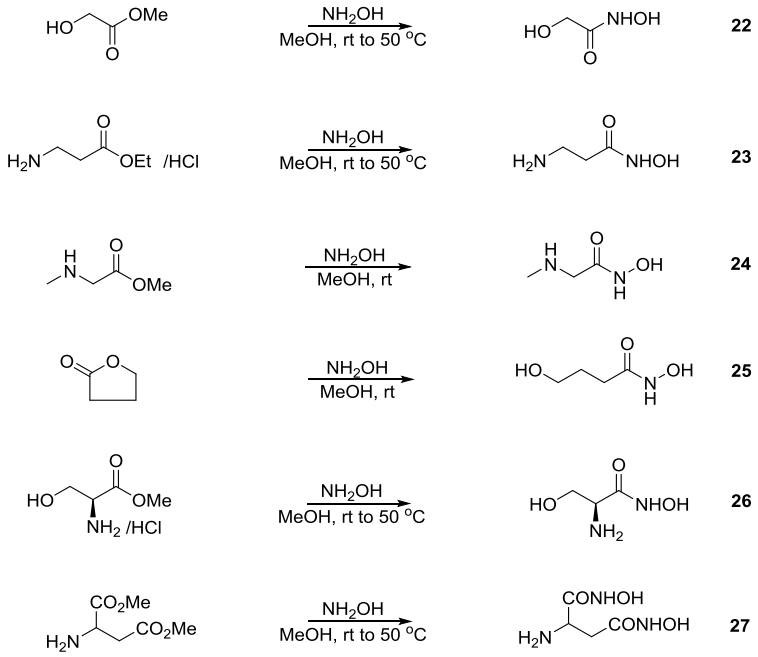
20. To diglycolic anhydride (0.5 g, 3.35 mmol) in methanol (1.0 mL) was added hydroxylamine in methanol (2.72 M, 1.23 mL). It was stirred at room temp for 1 h, and followed by the addition of 3.0 M KOH in methanol (1.12 mL). After stirred for 5 min, methanol was slowly evaporated, precipitating the product. The white precipitates were collected, washed with acetonitrile (1 mL), and then methanol (0.5 mL). Yield = 0.38 g. MS (ESI, negative ion mode) *m/z* (relative intensity, %) = 148.025(100 %) $[M - H]^+$. ^{1}H NMR (500 MHz, CD_3OD): δ 4.068, 4.004 ppm.

21. To 3,3-dimethylglutaric anhydride (0.5 g, 3.52 mmol) was added hydroxylamine in methanol (2.72 M, 1.30 mL). The reaction mixture was stirred at room temp for 1 h and followed by the addition of 3.0 M KOH (2.34 mL; 2.0 equiv). The solution was stirred for 5 min and methanol was slowly evaporated to dryness, yielding an oil residue. The product was washed with methanol and dried (yield = 0.61 g). MS (ESI, negative ion mode) *m/z* (relative intensity, %) = 174.077 (100 %) $[M - H]^+$. ^{1}H NMR (500 MHz, CD_3OD): δ 2.354 (s, 2H, $\underline{CH_2}CO_2H$), 2.173 (s, 2H, $CH_2C(=O)NHOH$), 1.106 (s, 3H, CH_3), 1.093 (s, 3H, CH_3) ppm. ^{13}C NMR (100 MHz, CD_3OD): δ 178.083, 171.895, 46.293, 45.209, 27.431, 26.309 ppm.

22 (Scheme 9). To methyl glycolate (0.5 g, 5.55 mmol) was added a solution of NH_2OH (2.04 mL; 2.72 M) in methanol. After addition of NH_2OH, the reaction mixture was stirred at room temp volatile solvent was evaporated and the solid residue was washed with methanol (3 × 1 mL). The product was dried *in vacuo*, and obtained as brown solid (0.218 g). MS (ESI) *m/z* (relative intensity, %) = 114.89 (42 %) $[M + Na]^+$. ^{1}H NMR (500 MHz, D_2O): δ 3.92 (s, 2H, $\underline{CH_2}$) ppm. ^{13}C NMR (500 MHz, D_2O): δ 178.90, 61.67, 60.51 ppm.

23. To beta-alanine ethyl ester hydrochloride (0.5 g, 3.25 mmol) was added a solution of NH_2OH (1.26 mL; 2.717 M). After solubilization of the ester, a solution of KOH (1.08 mL; 3.0 M) in methanol was added, resulting in formation of white precipitates. The solid material (KCl salt) was removed immediately by centrifugation (10,000 rpm; 5 min), and the supernatant was collected. It was stirred at room temp for 6 h and at 50 °C overnight until the reaction was completed. Methanol was evaporated, resulting in white solid. It was washed with methanol (2 × 1 mL), and dried *in vacuo* (240 mg). MS (ESI) *m/z* (relative intensity, %) = 105.06 (79 %) $[M + H]^+$. ^{1}H NMR (500 MHz, D_2O): δ 3.15–3.13 (t, J = 5 Hz, 2H $\underline{CH_2}N$), 2.43–2.41 (t, J = 5 Hz, 2H $\underline{CH_2}$) ppm. ^{13}C NMR (500 MHz, D_2O): δ 166.47, 36.42, 31.18 ppm.

Scheme 9



24. To sarcosine methyl ester hydrochloride (0.5 g, 3.58 mmol) was added hydroxylamine in methanol (2.72 M, 1.32 mL) and then potassium hydroxide in methanol (3.0 M, 1.19 mL). Immediately after the addition, white precipitates were formed. This solid which is mostly potassium chloride was removed by centrifugation. The supernatant alone was stirred at room temp overnight, and heated at 50 °C for 12 h, yielding white precipitates. After solvent evaporation, the product was isolated as a white solid (yield = 101 mg). MS (ESI, negative ion mode) *m/z* (relative intensity, %) = 105.066 (61 %) $[M - H]^+$. ^{1}H NMR (500 MHz, D_2O): δ 3.407 (s, 3H, $\underline{CH_3}NH$), 2.546 (s, 2H, $\underline{CH_2}C(=O)NHOH$) ppm. ^{13}C NMR (100 MHz, D_2O): δ 164.644, 50.624, 33.461 ppm.

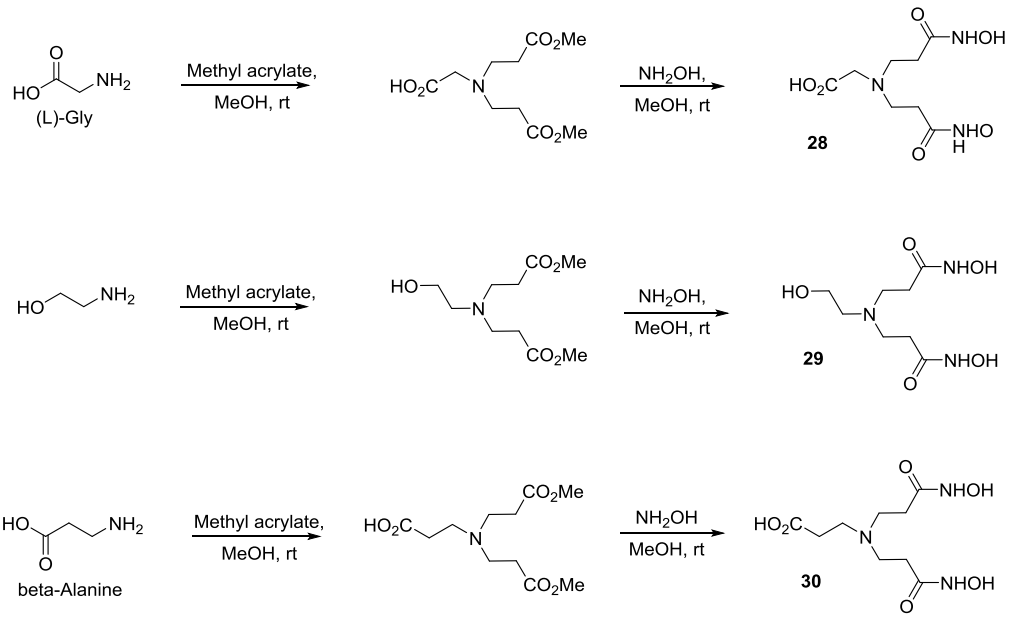
25. To γ-butyrolactone (0.5 g, 5.81 mmol) was added hydroxylamine solution in methanol (2.72 M, 2.14 mL; 1.0 equiv). The mixture was stirred at room temp for 30 min, and heated at 50 °C for 12 h. To this solution was added 3.0 M KOH (1.937 mL, 1 equiv). Methanol was evaporated slowly, precipating a pale brown solid. It was washed with methanol and dried. Yield = 0.65 g. R_f = 0.2 (10% MeOH/CH_2Cl_2). MS (ESI, negative ion mode) *m/z* (relative intensity, %) = 120.065 (76 %) $[M - H]^+$. ^{1}H NMR (500 MHz, CD_3OD): δ 3.584–3.545 (m, 2H, $\underline{CH_2}OH$), 2.178–2.148 (m, 2H, $\underline{CH_2}C(=O)NHOH$), 1.834–1.778 (m, 2H, $\underline{CH_2}CH_2OH$) ppm. ^{13}C NMR (100 MHz, CD_3OD): δ 169.172, 60.627, 29.062, 27.651 ppm.

26. To L-serine methyl ester hydrochloride (0.5 g, 3.21 mmol) was added a solution of NH_2OH (1.24 mL; 2.717 M) and then KOH (1.07 mL; 3.0 M) in methanol. After this addition, white precipitate was formed. After stirring for 5 min, the solid material (KCl salt) was removed by centrifugation (10,000 rpm, 5 min), and the supernatant was collected. It was stirred at room temp for 6 h, and incubated at 50 °C overnight until the reaction was completed. Methanol was evaporated, resulting in white solid. It was washed with methanol (2 × 1 mL), and dried *in vacuo* (572 mg). MS (ESI, negative ion mode) *m/z* (relative intensity, %) = 119.04 (100%) $[M - H]^-$. ^{1}H

NMR (500 MHz, D_2O): δ δ 3.76–3.75 (d, *J* = 5 Hz, 2H $\underline{CH_2}O$), 3.62–3.60 (t, *J* = 5 Hz, 2H $\underline{CH_2}N$) ppm. ^{13}C NMR (500 MHz, D_2O): δ 168.26, 61.77, 60.69, 60.24, 55.65, 53.83, 52.71 ppm.

27. To (D/L)-aspartate dimethyl ester hydrochloride (0.5 g, 2.53 mmol) was added a solution of NH_2OH (1.864 mL; 2.717 M) and KOH (0.844 mL; 3.0 M), each prepared in methanol. Addition of these solutions led to the formation of white precipitates which contained mostly KCl, and the precipitate was removed by centrifugation. The supernatant was collected, and it was stirred at room temp overnight and further incubated at 50 °C for 12 h. After the reaction, methanol was slowly evaporated, and the product was isolated as a white solid. It was washed with methanol and dried *in vacuo* (226 mg). MS (ESI, negative ion mode) *m/z* (relative intensity, %) = 162.07 (52 %) $[M - H]^-$. ^1H NMR (500 MHz, D_2O): δ 4.23–4.20 (m, 1H, $\underline{CH}$), 3.11–3.06 (dd, J_1= 10 Hz, J_2= 20 Hz, 1H, $\underline{CH_2}$) and 2.64–2.59 (dd, J_1= 10 Hz, J_2= 20 Hz, 1H, $\underline{CH_2}$) ppm. ^{13}C NMR (500 MHz, DMSO-D_6): δ 171.06, 47.52, 35.07 ppm.

Scheme 10



28 (Scheme 10). To a suspension of (L)-glycine (0.50 g, 6.66 mmol) in methanol (3 mL) was added a KOH solution in methanol (2.22 mL, 3 M). It was fully solubilized after stirred for 10 min. To this clear solution was added methyl acrylate (1.8 mL, 20.0 mmol). The mixture was stirred for 3 days under nitrogen gas atmosphere at room temperature. After concentrated at room temperature, the resulting clear viscous residue was redissolved in methanol (5 mL), concentrated and then dried under higher vacuum. The viscous residue was saturated with nitrogen for 1 h. The resulting residue was dissolved in methanol (2 mL) and then poured into a solution of 1:1 ethhyl acetate/hexane (20 mL). A white precipitate was formed, and it was collected and dried *in vacuo* to give the desired product bis(3-methoxy-3-oxopropyl)glycine as a white solid (1.42 g). This was used in the next reaction without further treatment.

To the white solid (150 mg, 0.61 mmol) in MeOH (1.5 mL) was added a fresh hydroxylamine solution in methanol (4.49 mL, 2.717 M). The mixture was stirred under nitrogen gas atmosphere

at room temperature for 5 days. After concentrated and then dried under higher vaccum, the white solid residue was sonicated in methanol (5 mL, 3 mL). The methanol extracts were combined, and it was frozen overnight. A white salt was filtered off, and the filtrate was concentrated. The residue was washed with hot ethanol (3 × 2 mL) and then the remaining solid was dried *in vacuo* to give the product **28** as white solid (100 mg). MS (ESI, negative ion mode) *m/z* (relative intensity, %) = 248.08 (100 %) $[M - H]^-$. ^{1}H NMR (500 MHz, D_2O): δ 3.77 (s, 2H, NCH_2), 3.52–3.54 (t, *J* = 5 Hz, 4H, $N(CH_2)_2$), 2.68–2.71 (t, *J* = 5 Hz, 4H, 2 $(CH_2)(C=O)$) ppm. ^{13}C NMR (500 MHz, D_2O): δ 170.01, 168.34, 56.10, 51.06, 26.55 ppm.

29. To a solution of ethanolamine (0.50 g, 8.19 mmol) in methanol (3 mL) was added methyl acrylate (2.21 mL, 24.57 mmol). The mixture was stirred under nitrogen gas atmosphere at room temperature for 3 days. After concentrated at room temperature, the resulting clear viscous residue was redissolved in methanol (3 mL), concentrated *in vacuo* and then dried under higher vacuum. The viscous residue was saturated with nitrogen for 1 h, and the desired product, dimethyl 3,3'-((2-hydroxyethyl)azanediyl)dipropionate, was obtained as white oil (1.91 g). This product was used in the next step without further purification.

To the white oil (175 mg, 0.75 mmol) in MeOH (2 mL) was added a fresh solution of hydroxylamine in methanol (5.52 mL, 2.717 M). The mixture was stirred under nitrogen gas atmosphere at room temperature for 5 days. After concentrated and then dried under higher vaccum, the white solid residue was obtained and it was sonicated in methanol (10 mL, 5 mL). The methanol extract was combined and was frozen overnight. White salt was filtered off, and the filtrate was concentrated *in vacuo*. The residue was purified by column chromatography using 20% methanol in dichloromethane as an eluent. The product **29** was obtained as solid (103 mg). MS (ESI, negative ion mode) *m/z* (relative intensity, %) = 234.11 (100 %) $[M - H]^-$. ^{1}H NMR (500 MHz, D_2O): δ 3.74–3.72 (t, *J* = 5 Hz, 2H, $HO\underline{CH_2}$), 3.03–3.01 (t, *J* = 5 Hz, 4H, $N(CH_2)_2$), 2.85–2.83 (t, *J* = 5 Hz, 2H, NCH_2), 2.46–2.44 (t, *J* = 5 Hz, 4H, 2 $(CH_2)(C=O)$) ppm. ^{13}C NMR (500 MHz, D_2O): δ 169.30, 56.35, 55.85, 54.93, 49.54, 49.06, 43.15, 27.97, 26.85 ppm.

30. To a suspension of beta-alanine (0.50 g, 5.61 mmol) in methanol (3 mL) was added a KOH solution (1.87 mL, 3 M). It was fully solubilized after stirring for 10 min. To this clear solution was added methyl acrylate (1.51 mL, 16.83 mmol). The mixture was stirred under nitrogen gas atmosphere at room temperature for 3 days. After concentrated at room temperature, the resulting clear viscous residue was redissolved in methanol (5 mL), concentrated and then dried under higher vacuum. The viscous residue was saturated with nitrogen for 1 h. The resulting residue was dissolved in methanol (2 mL) and then poured into a solution of 1:1 ethhyl acetate/hexane (20 mL). A white precipitate was formed and it was collected by centrifugation and dried *in vacuo* to give a desired product 3-(bis(3-methoxy-3-oxopropyl)amino)propanoic acid as clear oil (1.32 g), which was used in the next step as prepared.

To the oil (196 mg, 0.75 mmol) in MeOH (2 mL) was added a fresh hydroxylamine solution in methanol (5.52 mL, 2.717 M). The mixture was stirred under nitrogen gas atmosphere at room temperature for 5 days. After concentrated and then dried under higher vaccum, a white solid residue was obtained and it was sonicated in methanol (5 mL, 3 mL). The methanol extracts were combined and frozen overnight. A white salt was filtered off, and the filtrate was concentrated. The residue was washed with hot ethanol (3 × 2 mL) and then dried *in vacuo* to give product **30**

as a white solid (182 mg). MS (ESI, negative ion mode) *m/z* (relative intensity, %) = 262.10 (100 %) $[M - H]^-$. ^{1}H NMR (500 MHz, D_2O): δ δ 3.49–3.47 (t, *J* = 5 Hz, 4H, $N(CH_2)_2$), 3.37–3.35 (t, *J* = 5 Hz, 2H, NCH_2), 2.75–2.73 (t, *J* = 5 Hz, 4H, 2 $(CH_2)(C=O)$), 2.66–2.64 (t, *J* = 5 Hz, 2H, $(\underline{CH_2})(CO_2H)$ ppm. ^{13}C NMR (500 MHz, D_2O): δ177.93, 168.58, 51.01, 50.51, 49.13, 30.00, 26.31 ppm.

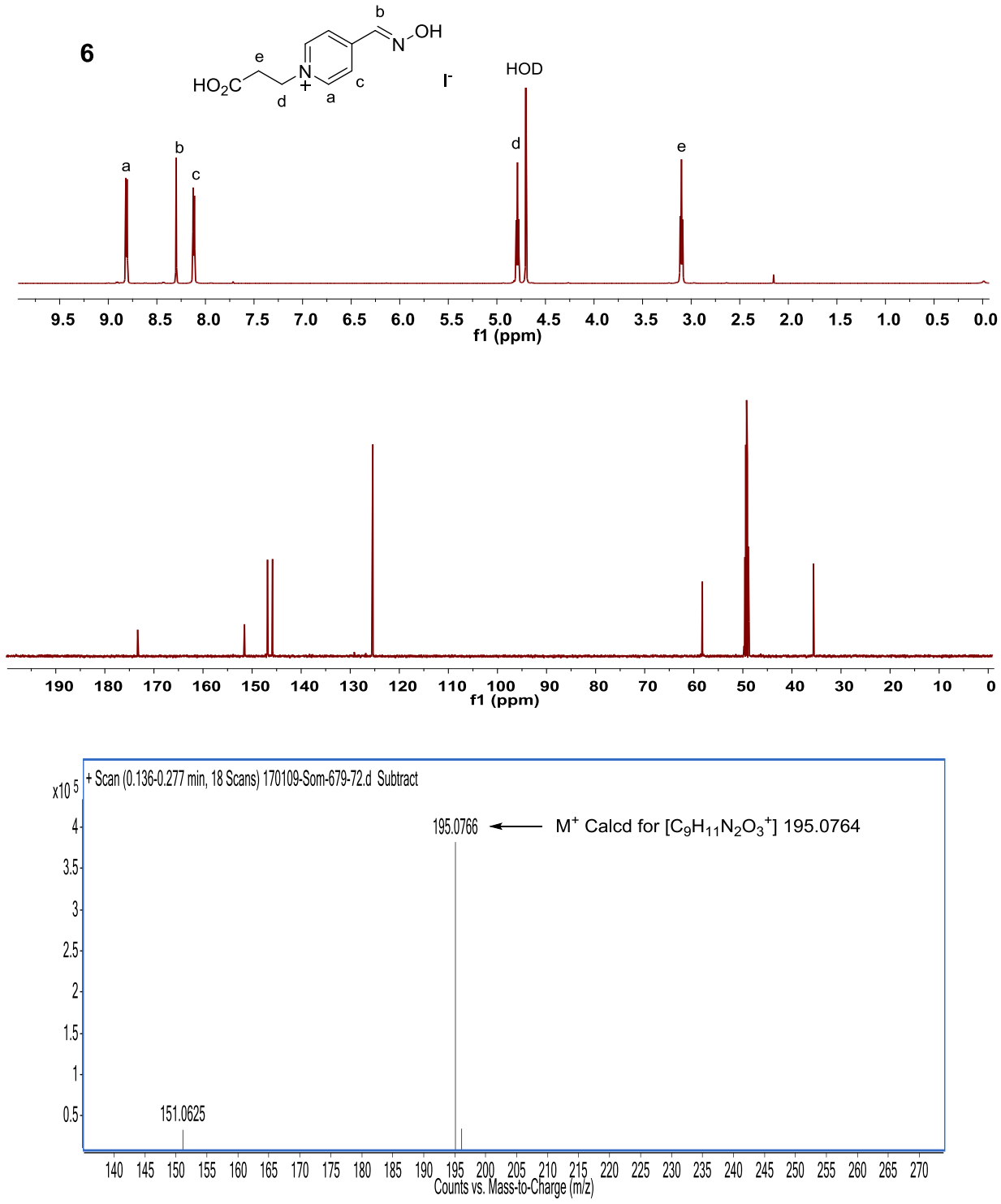


Figure S1. ^{1}H NMR (D_2O, 500 MHz; top), ^{13}C NMR (100 MHz; middle) and HRMS spectra (bottom) of **6**.

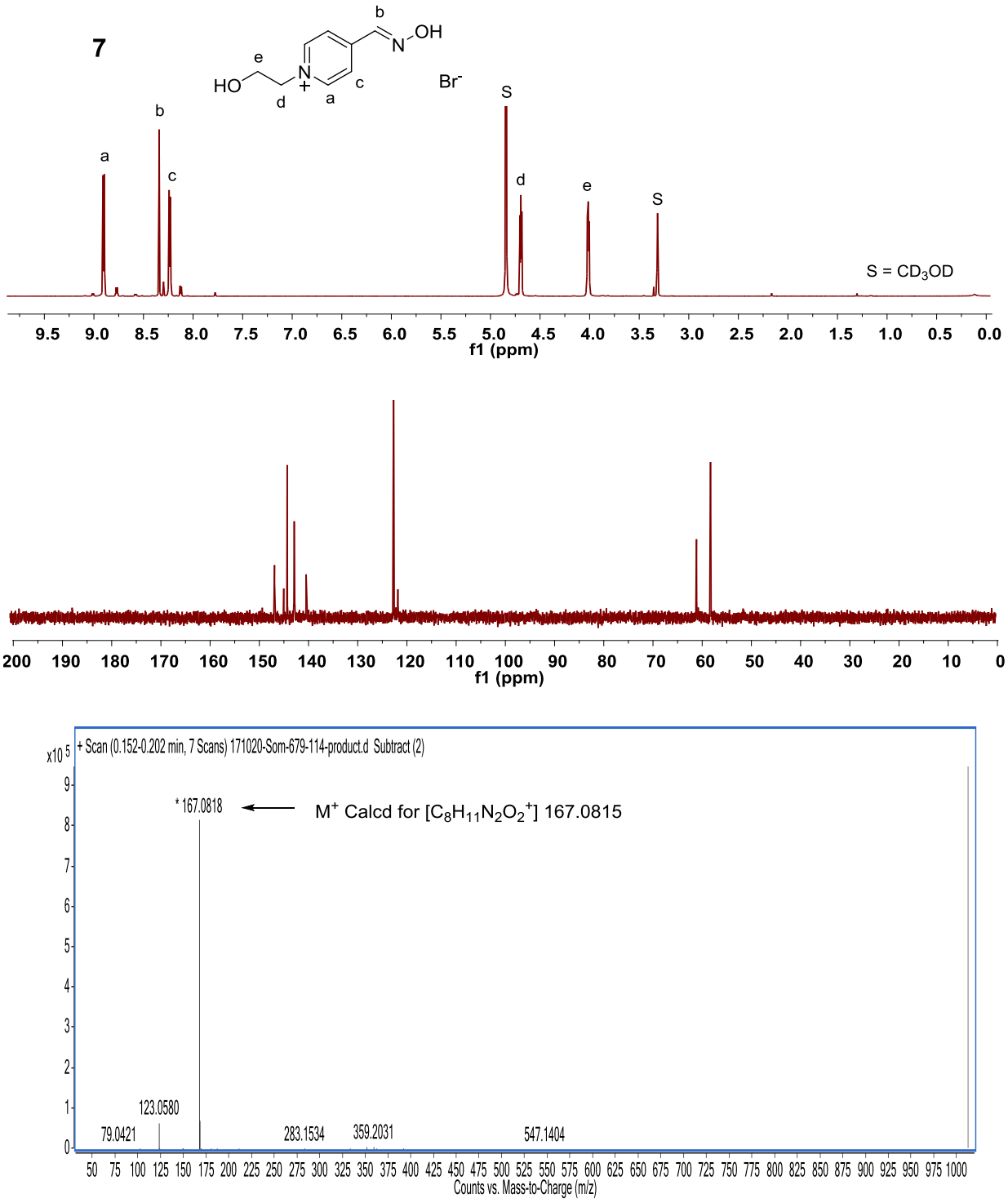


Figure S1. ^{1}H NMR (CD_3OD, 500 MHz; top), ^{13}C NMR (100 MHz; middle) and HRMS spectra (bottom) of **7**.

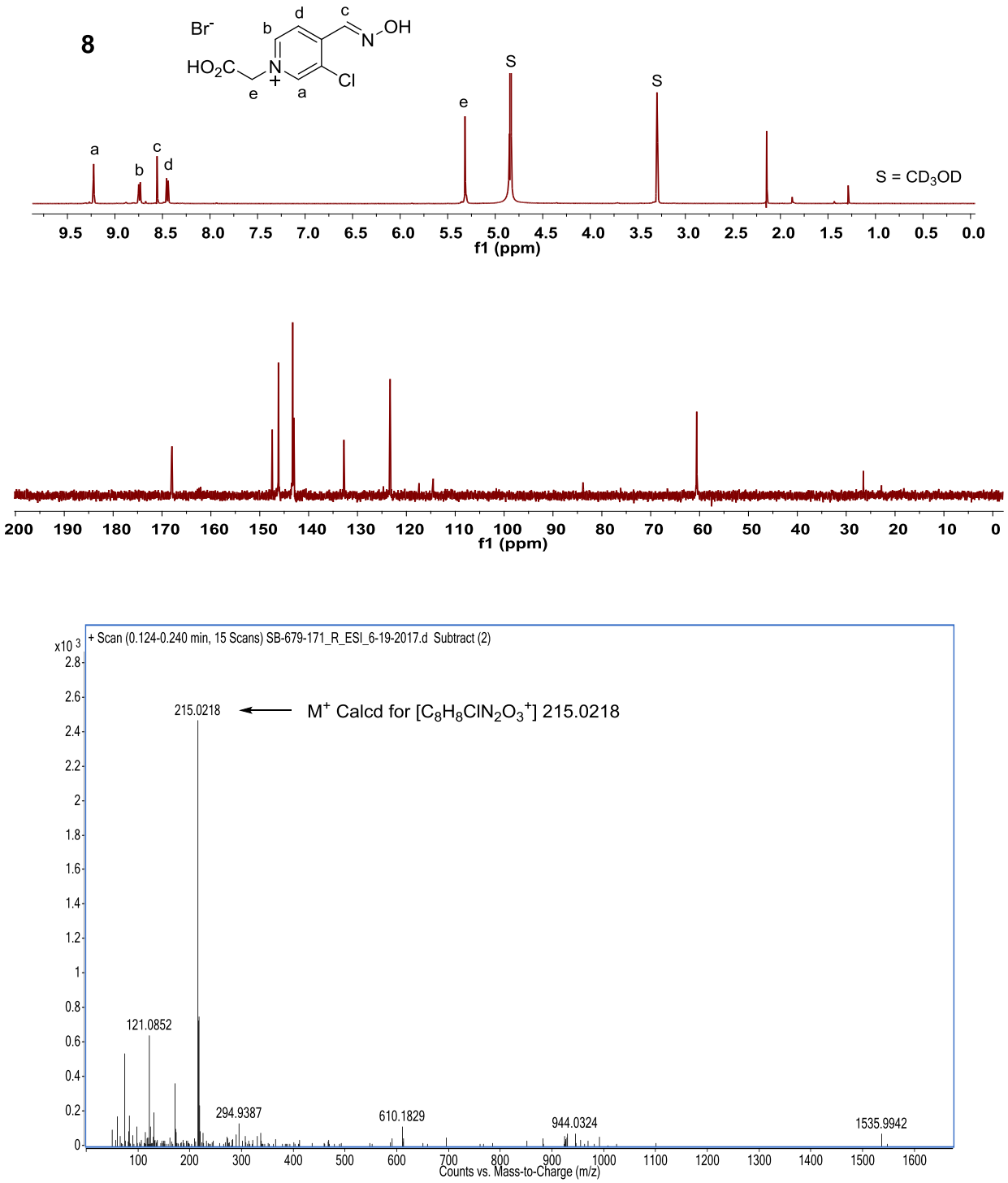


Figure S1. ^{1}H NMR (CD_3OD, 500 MHz; top), ^{13}C NMR (100 MHz; middle) and HRMS spectra (bottom) of **8**.

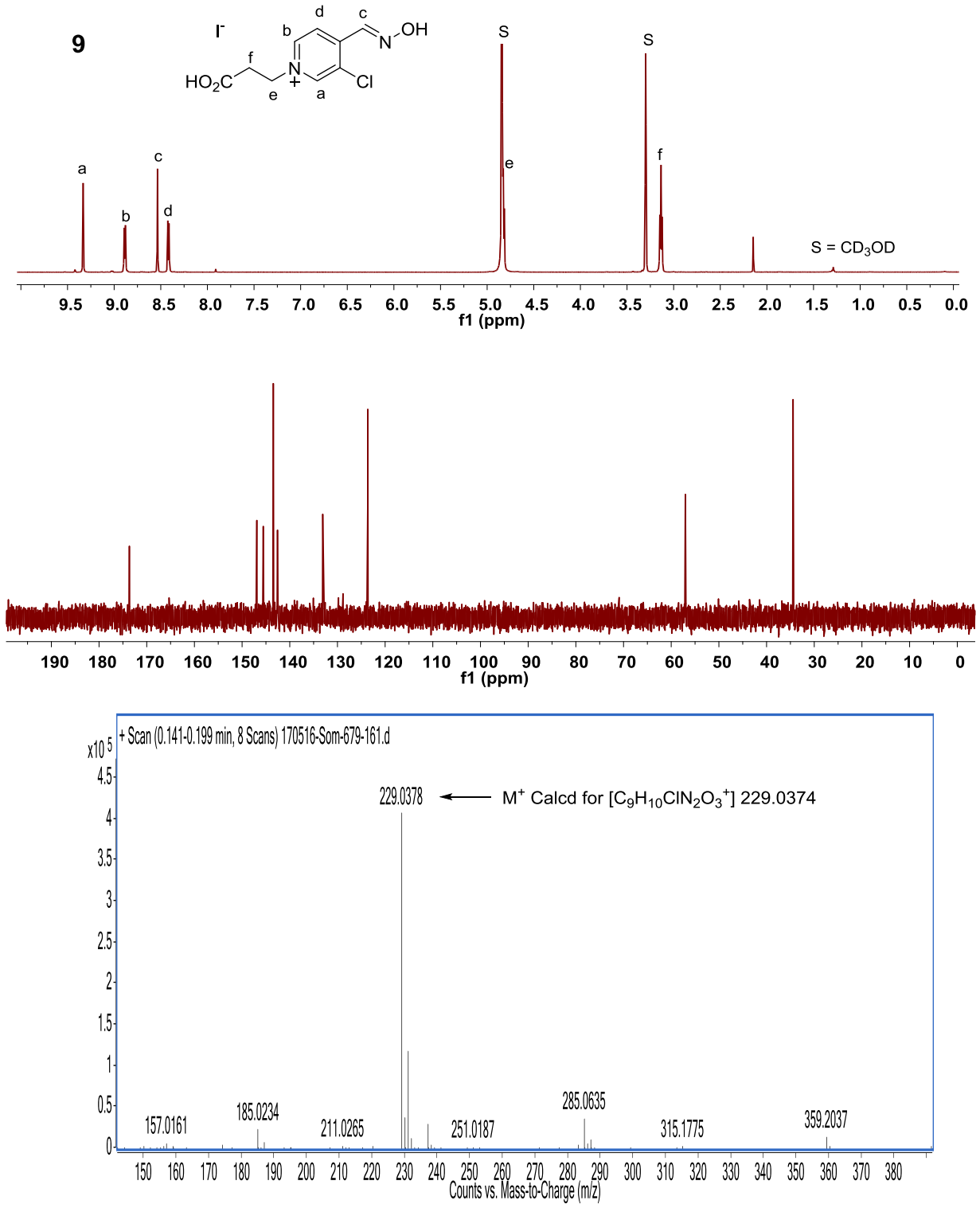


Figure S1. ^{1}H NMR (CD_3OD, 500 MHz; top), ^{13}C NMR (100 MHz; middle) and HRMS spectra (bottom) of **9**.

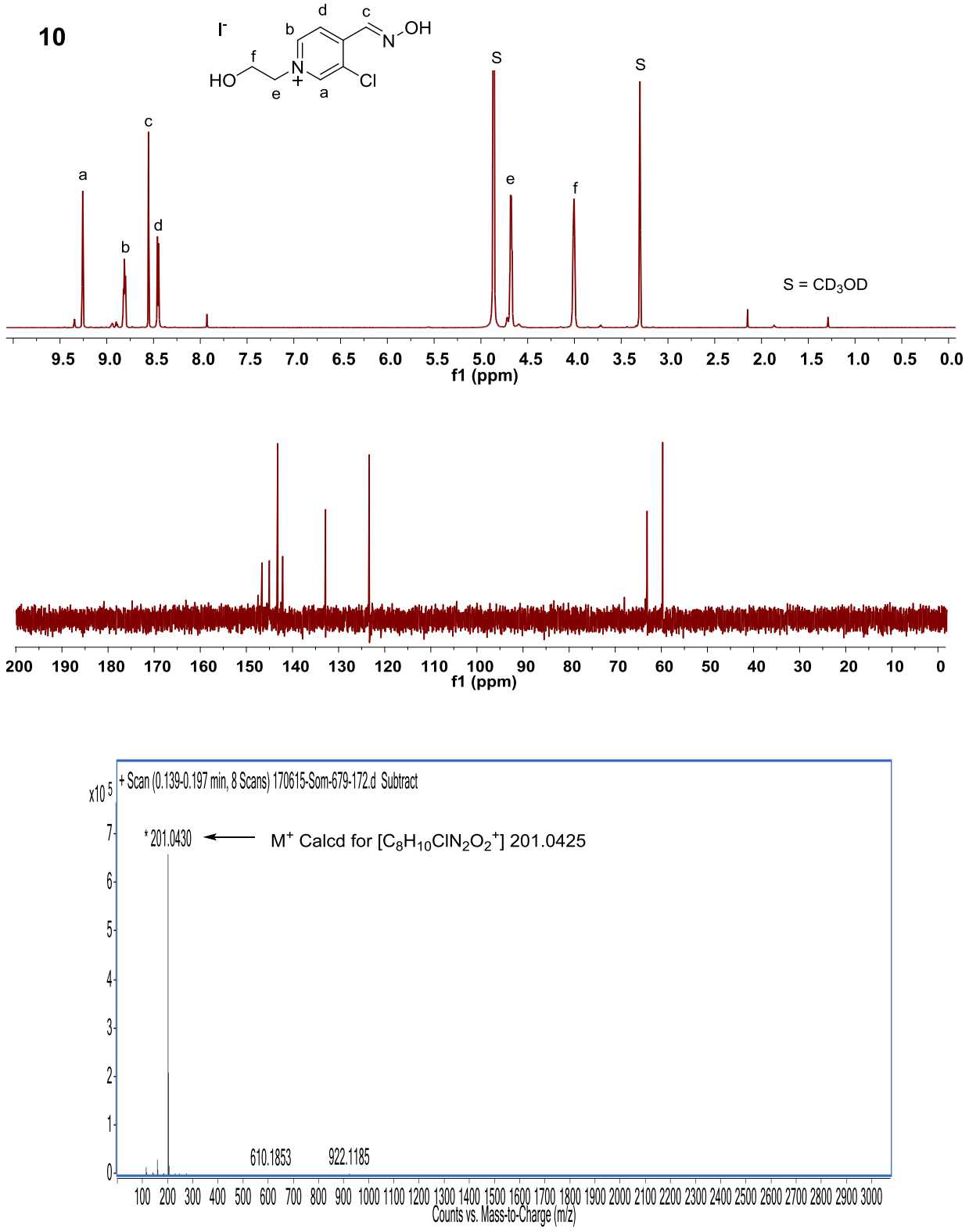


Figure S1. ^{1}H NMR (CD_3OD, 500 MHz; top), ^{13}C NMR (100 MHz; middle) and HRMS spectra (bottom) of **10**.

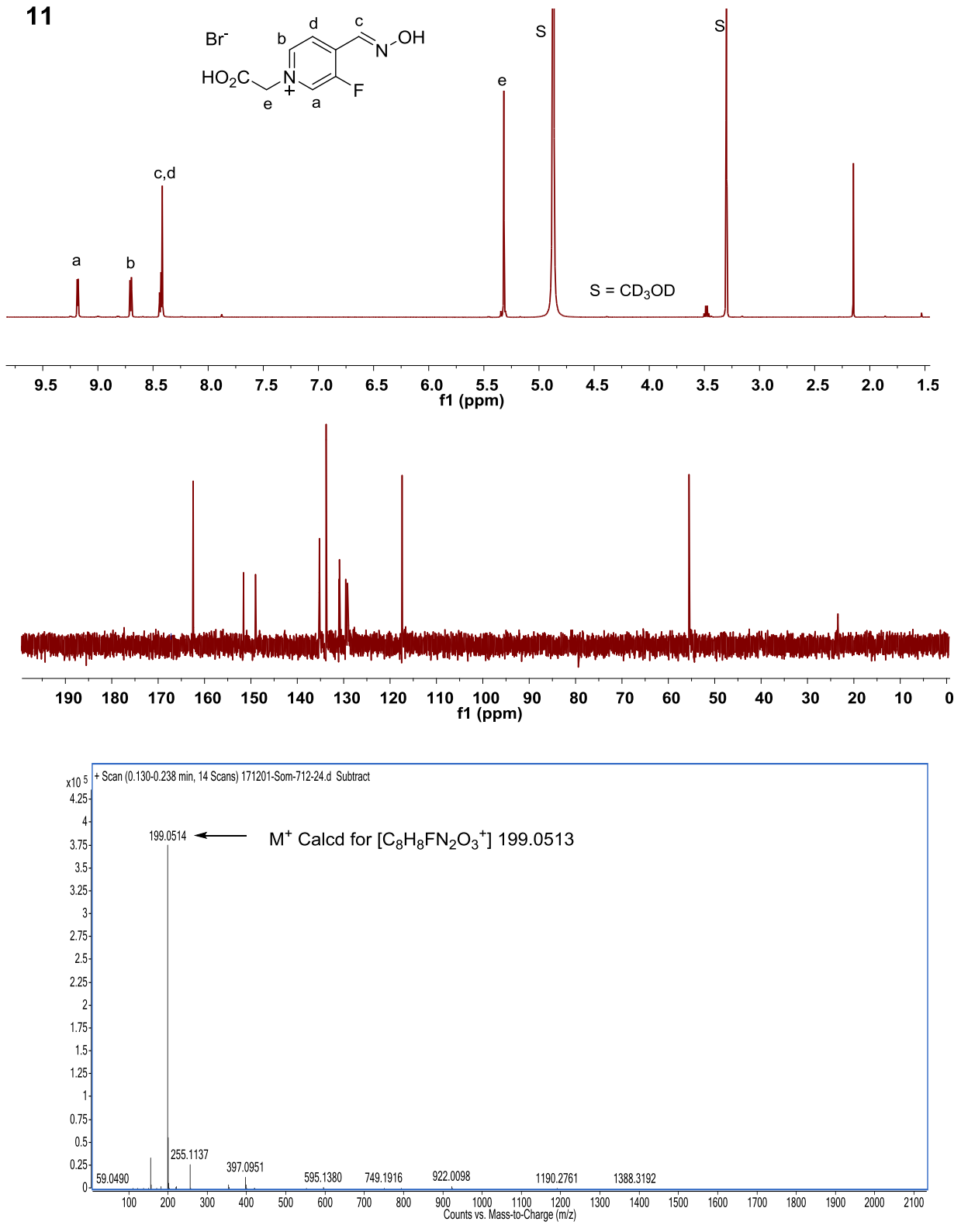


Figure S1. ^{1}H NMR (CD_3OD, 500 MHz; top), ^{13}C NMR (100 MHz; middle) and HRMS spectra (bottom) of **11**.

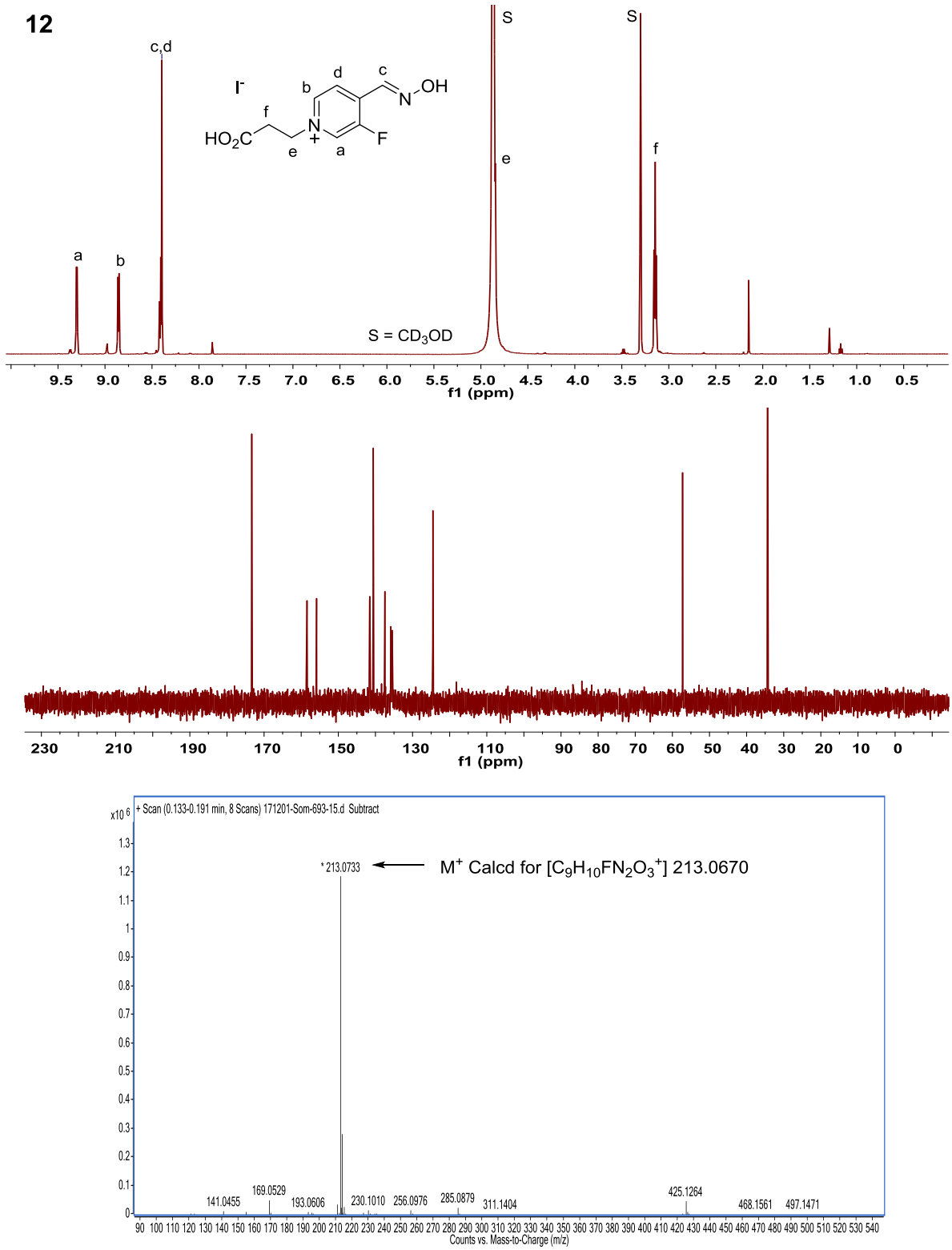


Figure S1. ^{1}H NMR (CD_3OD, 500 MHz; top), ^{13}C NMR (100 MHz; middle) and HRMS spectra (bottom) of **12**.

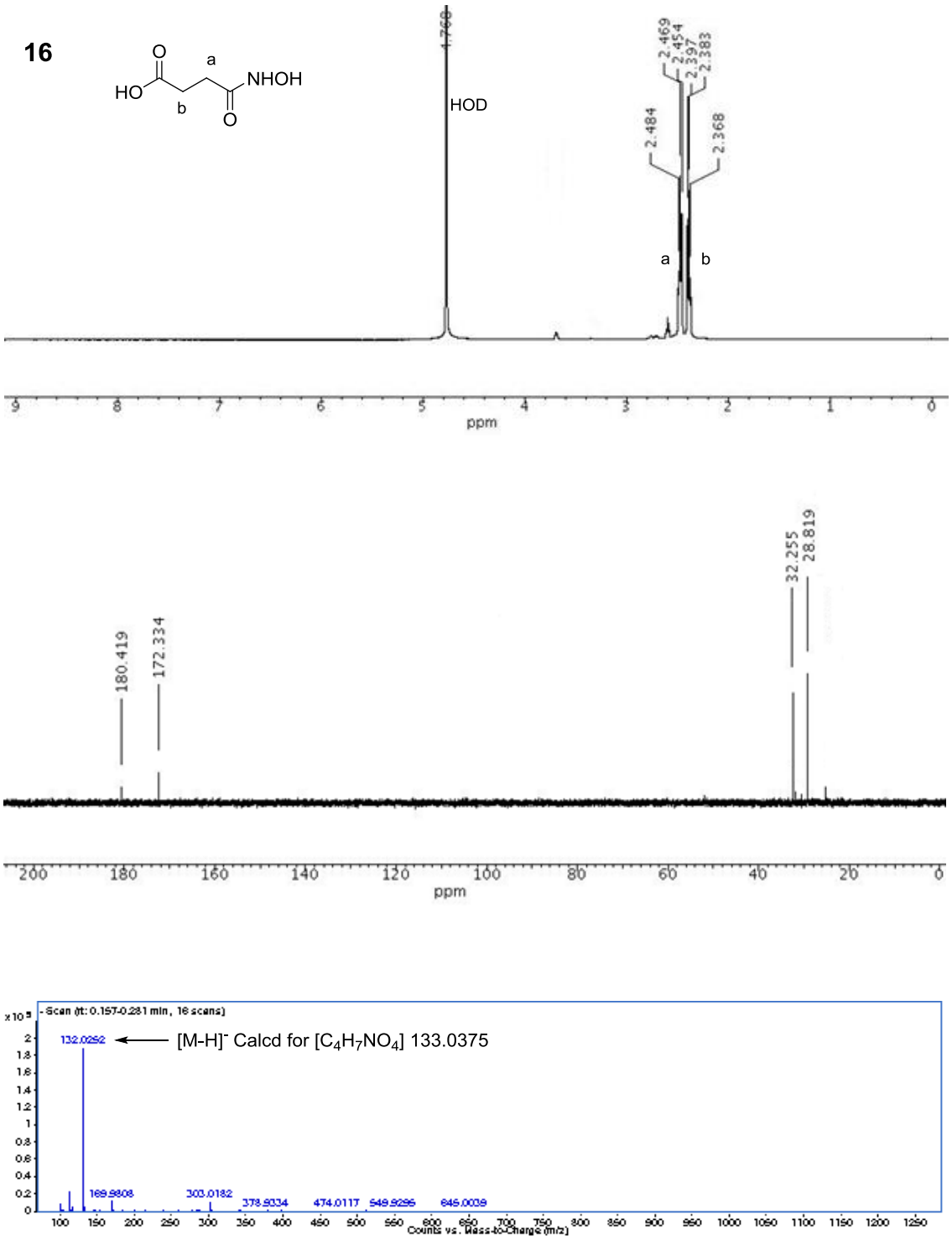


Figure S1. ^{1}H NMR (D_2O, 500 MHz; top), ^{13}C NMR (100 MHz; middle) and HRMS spectra (bottom; negative ion mode) of **16**.

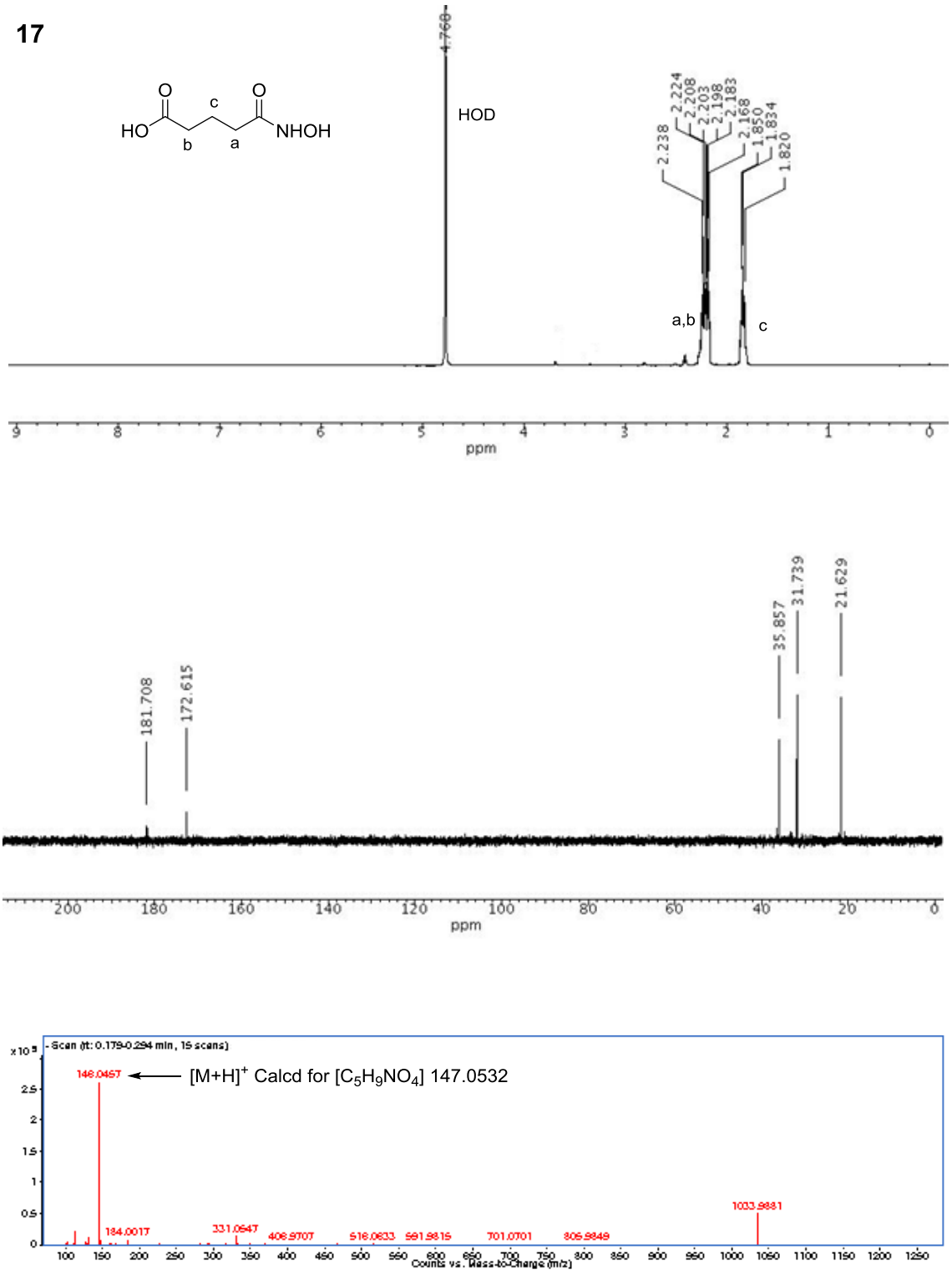


Figure S1. ^{1}H NMR (D_2O, 500 MHz; top), ^{13}C NMR (100 MHz; middle) and HRMS spectra (bottom) of **17**.

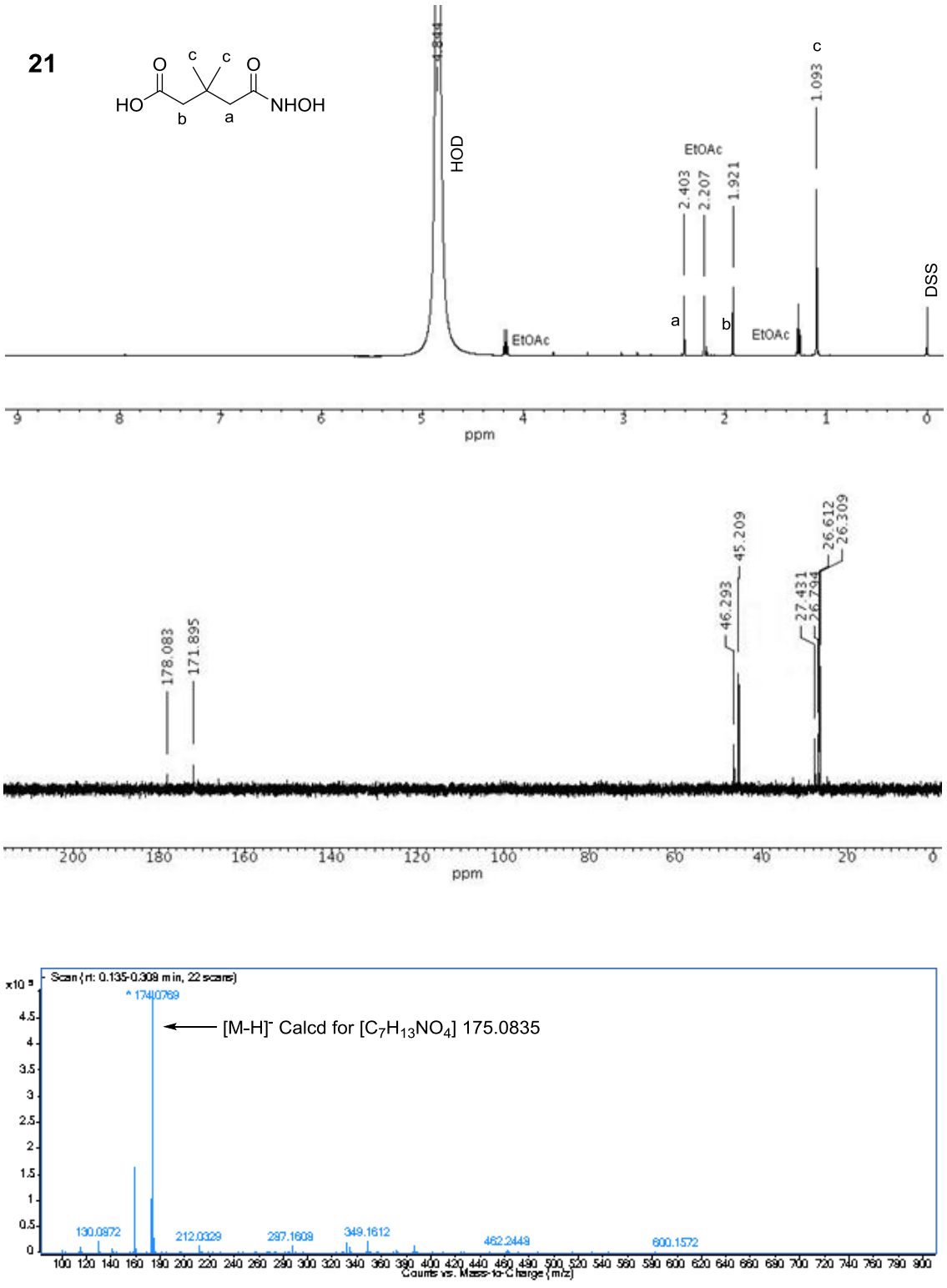


Figure S1. ^{1}H NMR (D_2O, 500 MHz; top), ^{13}C NMR (100 MHz; middle) and HRMS spectra (bottom; negative ion mode) of **21**.

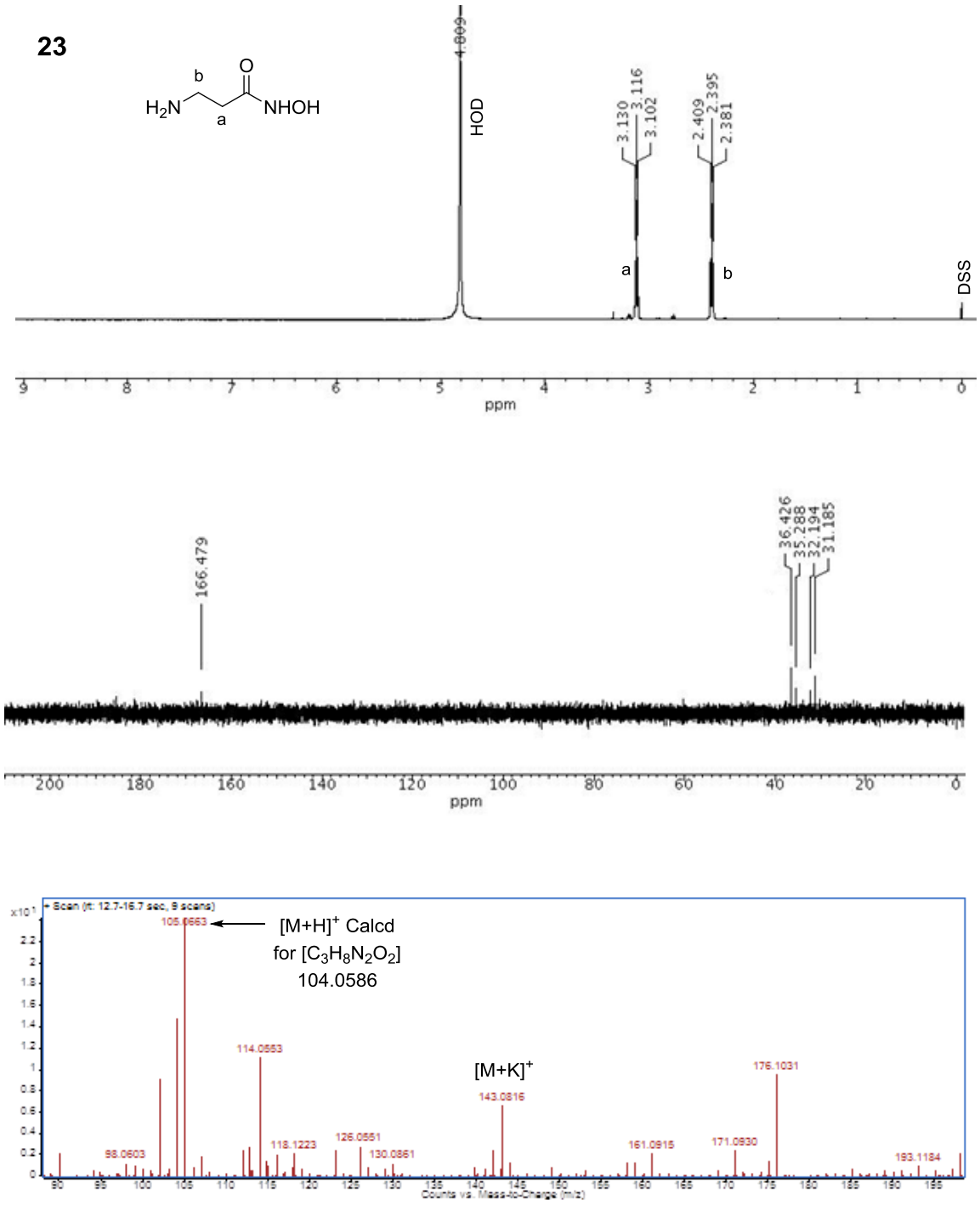


Figure S1. ^{1}H NMR (D_2O, 500 MHz; top), ^{13}C NMR (100 MHz; middle) and HRMS spectra (bottom) of **23**.

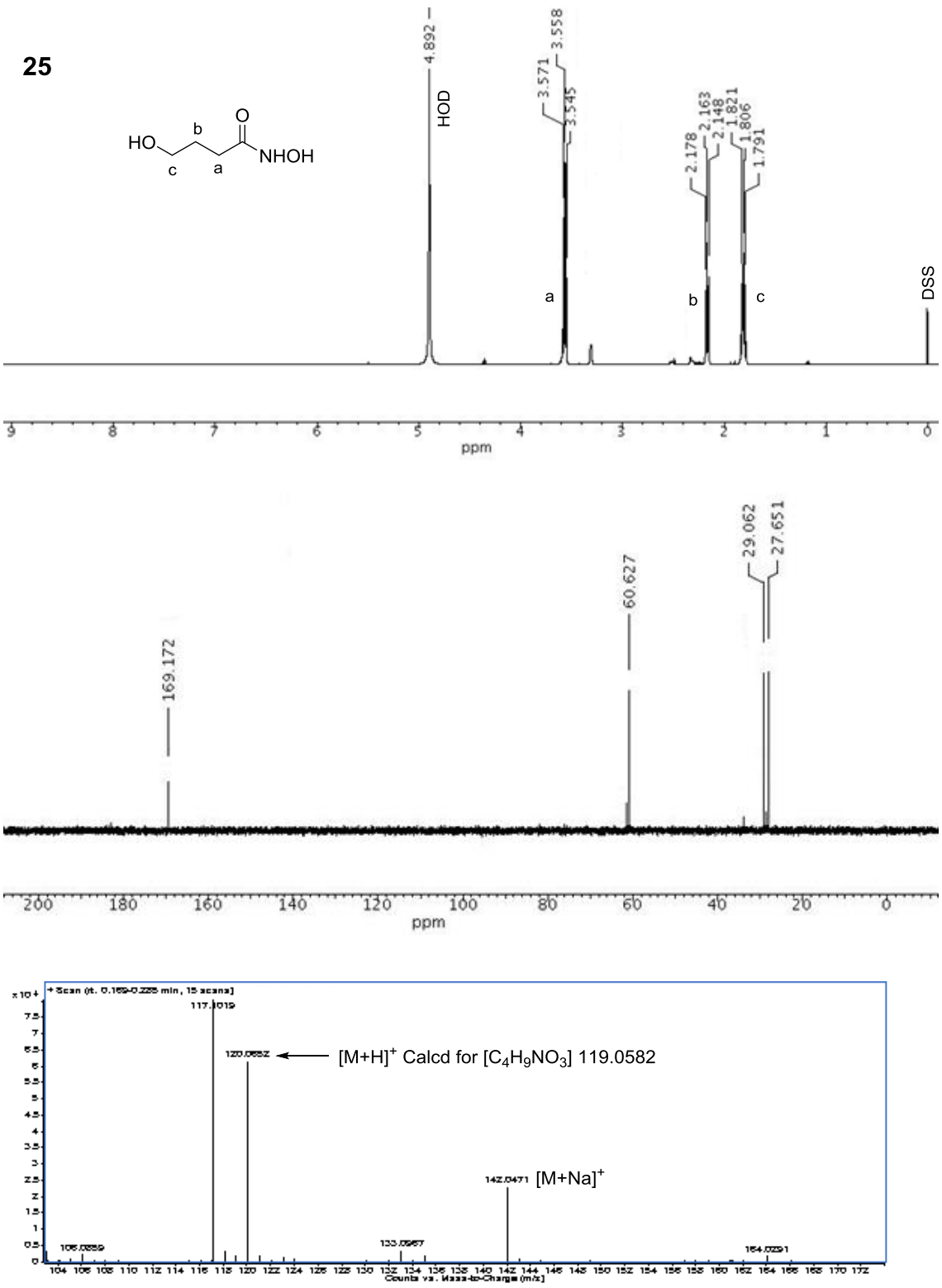


Figure S1. ^{1}H NMR (D_2O, 500 MHz; top), ^{13}C NMR (100 MHz; middle) and HRMS spectra (bottom) of **25**.

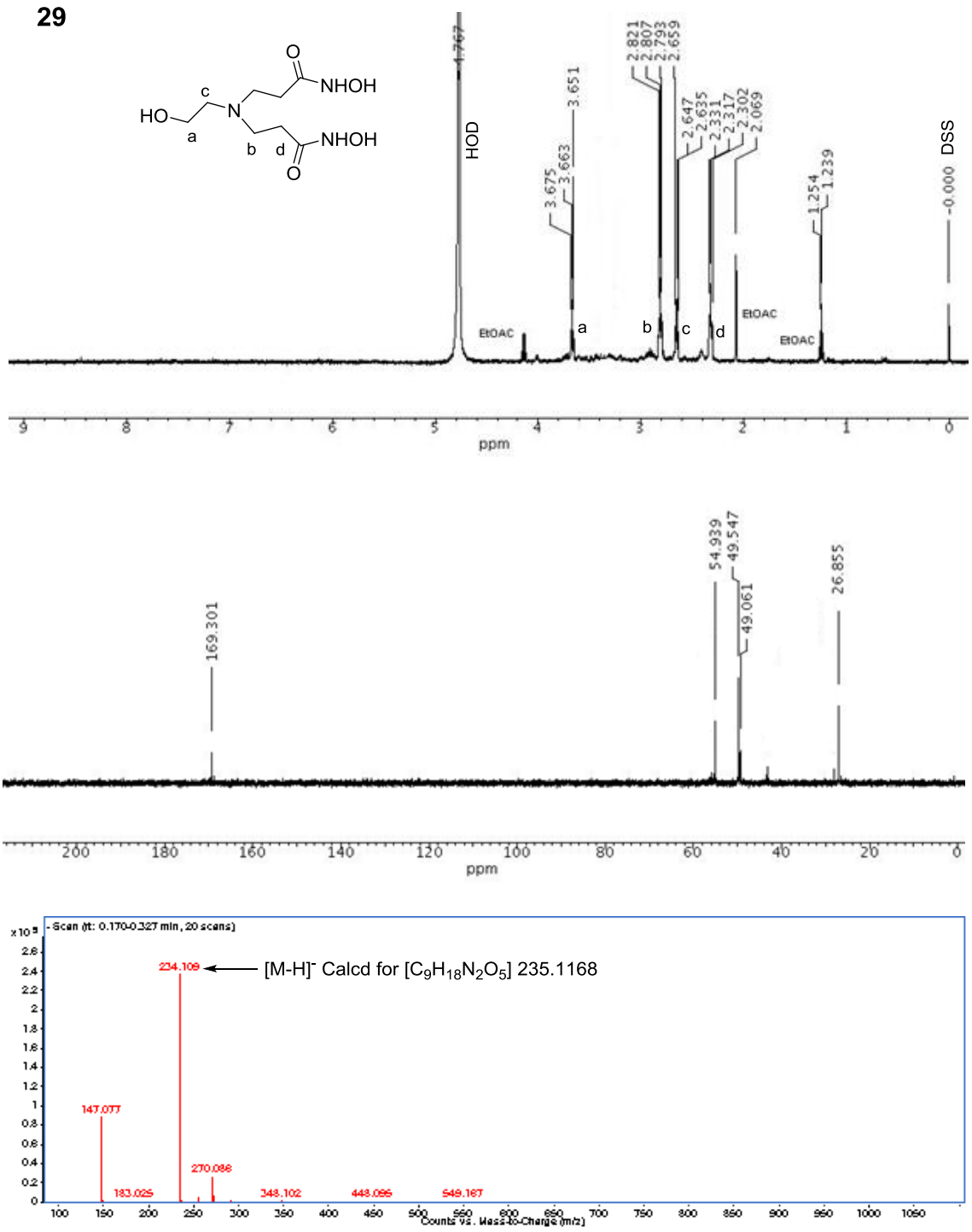


Figure S1. ^{1}H NMR (D_2O, 500 MHz; top), ^{13}C NMR (100 MHz; middle) and HRMS spectra (bottom; negative ion mode) of **29**.

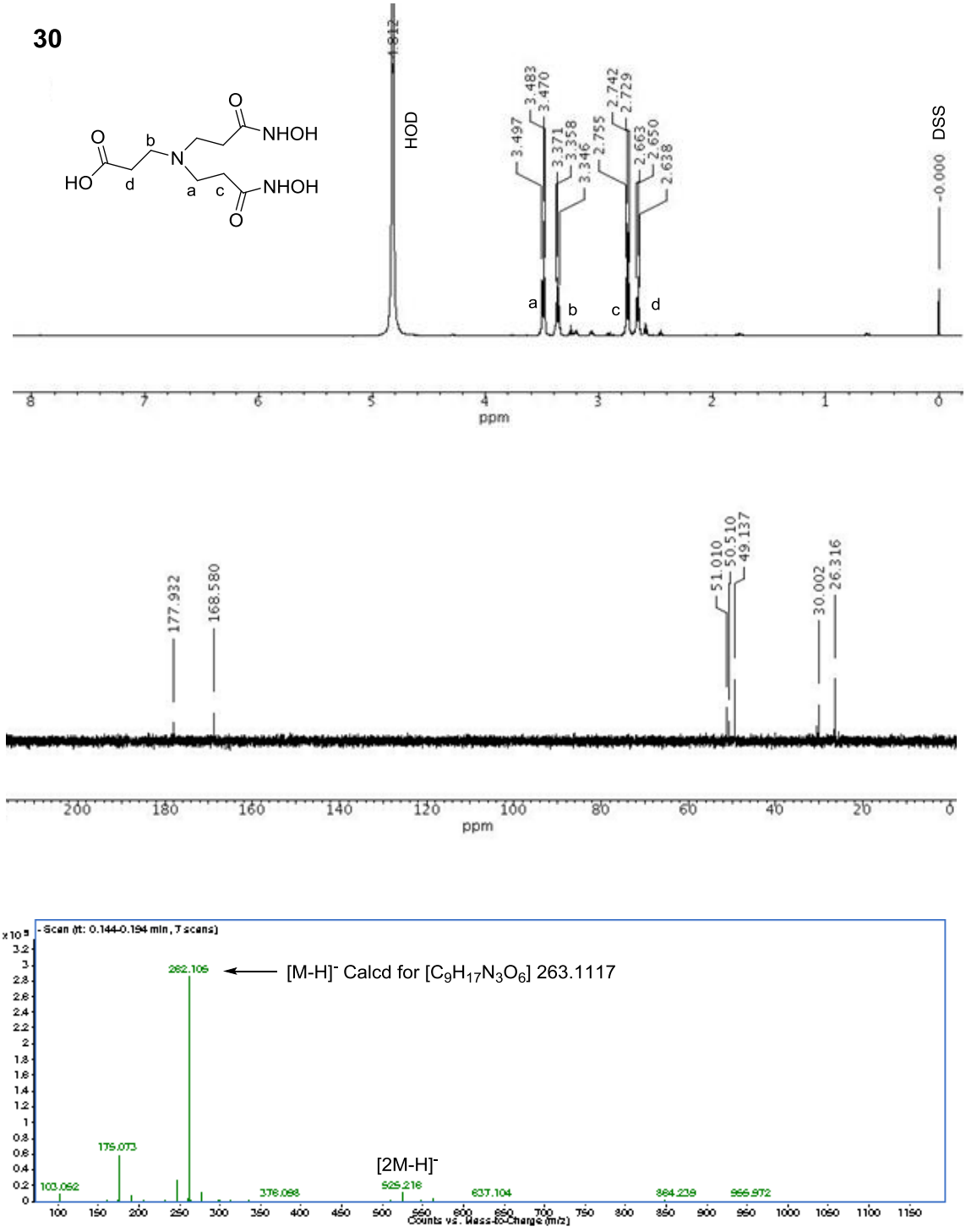


Figure S1. ^{1}H NMR (D_2O, 500 MHz; top), ^{13}C NMR (100 MHz; middle) and HRMS spectra (bottom; negative ion mode) of **30**.

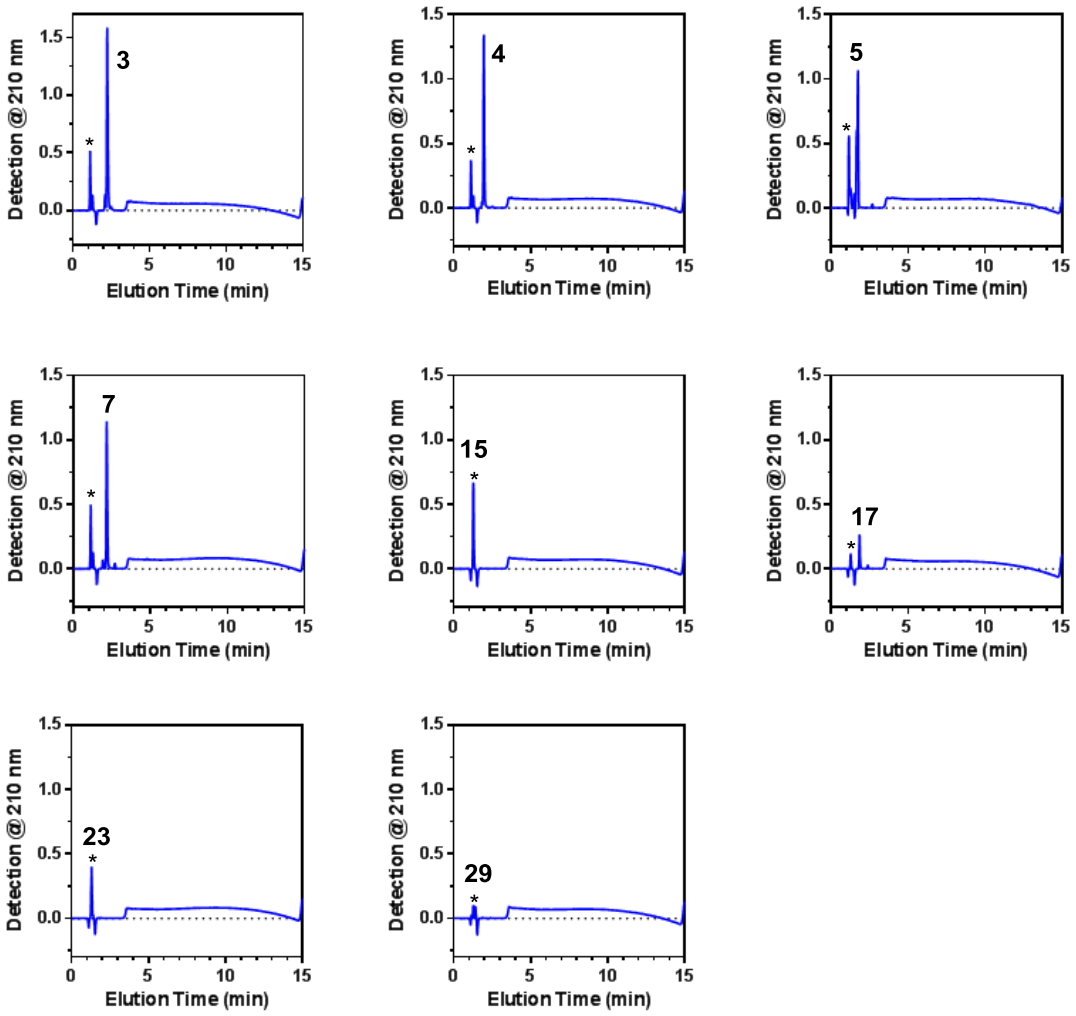


Figure S2. UPLC traces of selected compounds **3**–**5**, **7**, **15**, **17**, **23**, **29** in PBS pH 10.5 after incubation at 23 °C for 3 days. *denotes a void volume (solvent front), which is often overlapped with compound peaks.

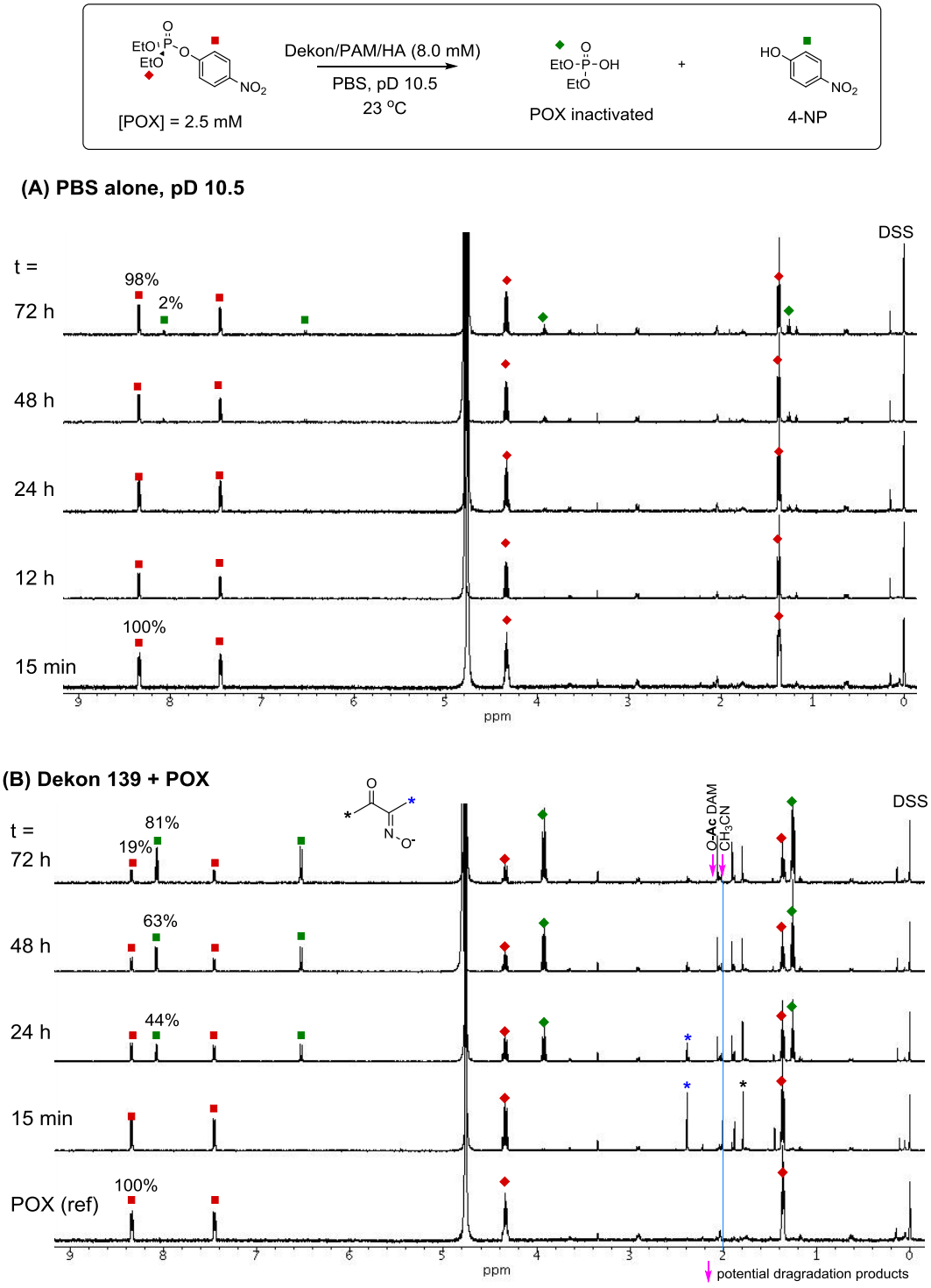


Figure S3. ^{1}H NMR spectral traces of the hydrolysis of POX (2.5 mM) in a deuterated phosphate buffered saline (dPBS, pD 10.5) alone (A), or catalyzed by Dekon 139 (8.0 mM; B), each in pD 10.5 at 23 °C. The fraction of POX hydrolysis is noted as the percentage value (%) as a function of incubation time. It was quantified by the integration of signals from free 4-nitrophenol (4-NP) relative to those in intact POX. DSS (4,4-dimethyl-4-silapentane-1-sulfonate) was added as the internal standard (δ = 0 ppm).

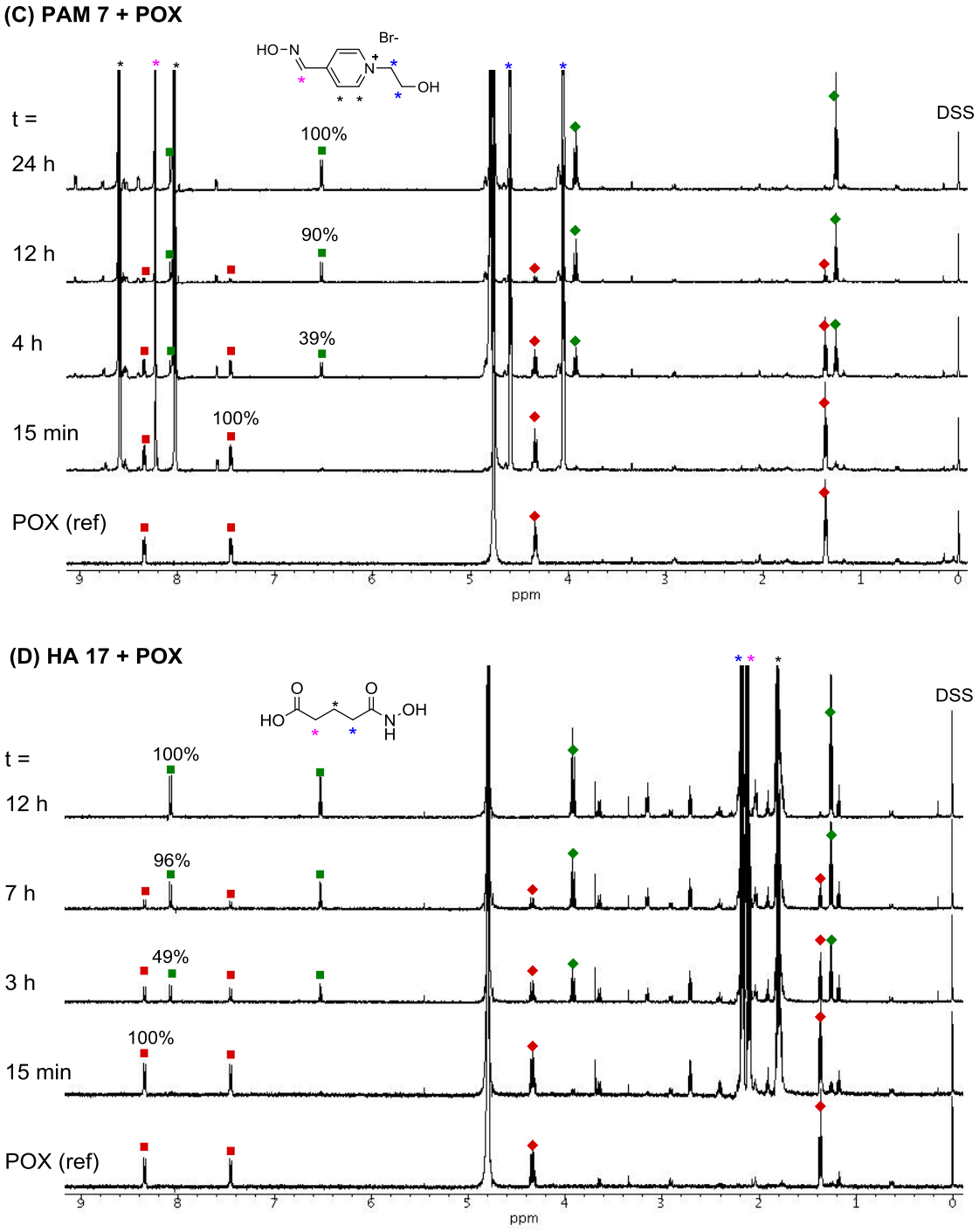


Figure S3 (continued). ^{1}H NMR spectral traces of the hydrolysis of POX (2.5 mM) in a deuterated phosphate buffered saline (dPBS, pD 10.5) catalyzed by **7** (8.0 mM; C), and **17** (8.0 mM; D), each in pD 10.5 at 23 °C. The fraction of POX hydrolysis is noted as the percentage value (%) as a function of incubation time.

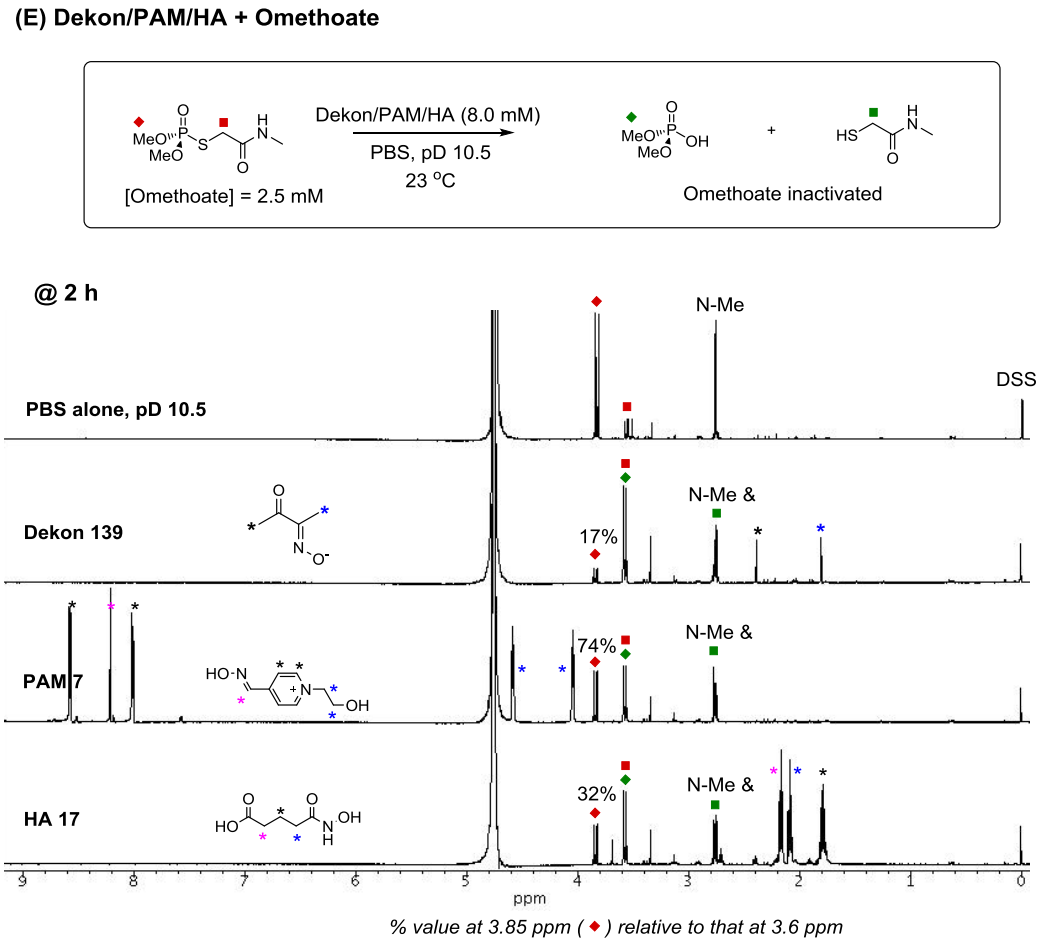
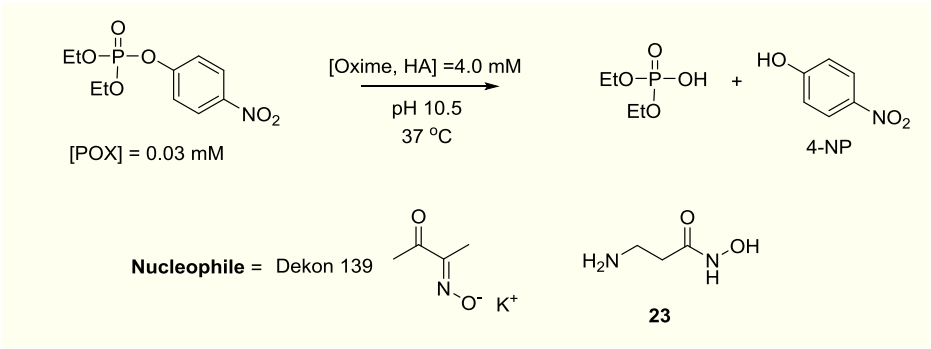


Figure S3 (Continued). ^{1}H NMR spectral traces of the hydrolysis of omethoate (2.5 mM) in a deuterated phosphate buffered saline (dPBS, pD 10.5) alone, or catalyzed by Dekon 139 (8.0 mM), **7** (8.0 mM), and **17** (8.0 mM), each in pD 10.5 at 23 °C after 2 h (E). The fraction (%) of omethoate intact was estimated by the integration of its signals for OMe groups.



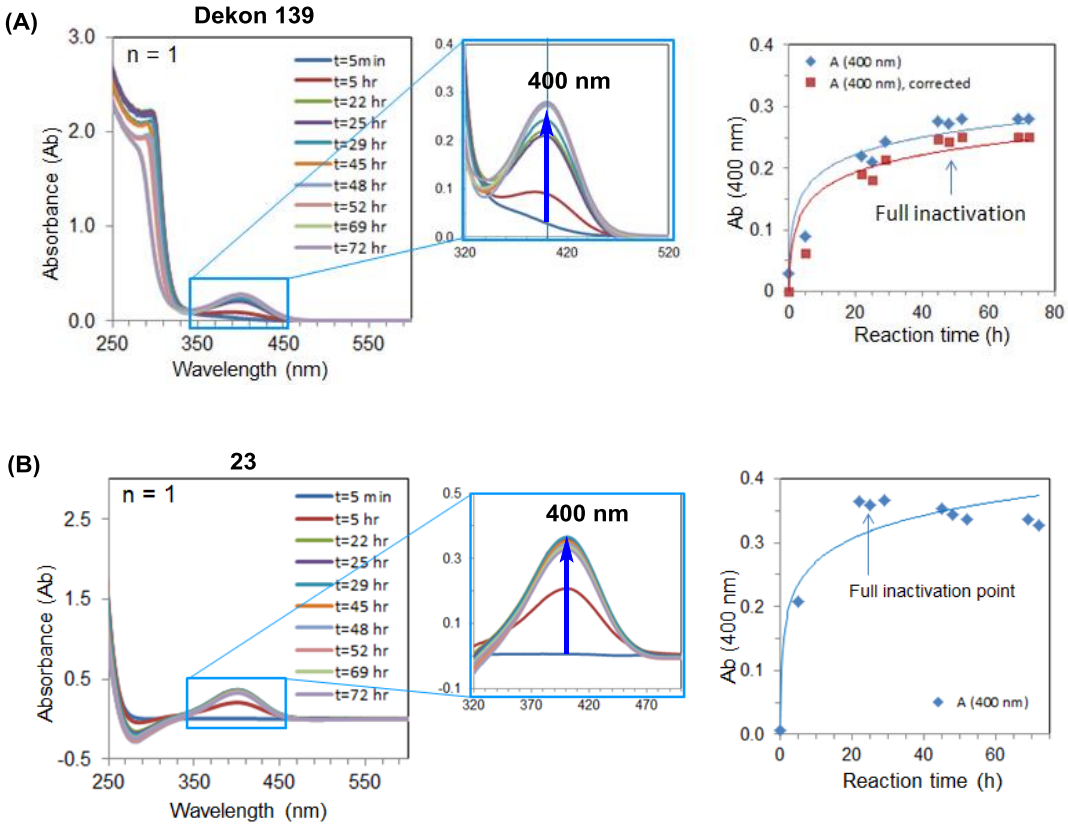


Figure S4. UV/vis spectral traces of POX inactivation. Paraoxon (POX; 30 μM) was incubated with Dekon 139 (4.0 mM; A) and **23** (4.0 mM; B) in PBS, pH 10.5 at 37 °C.

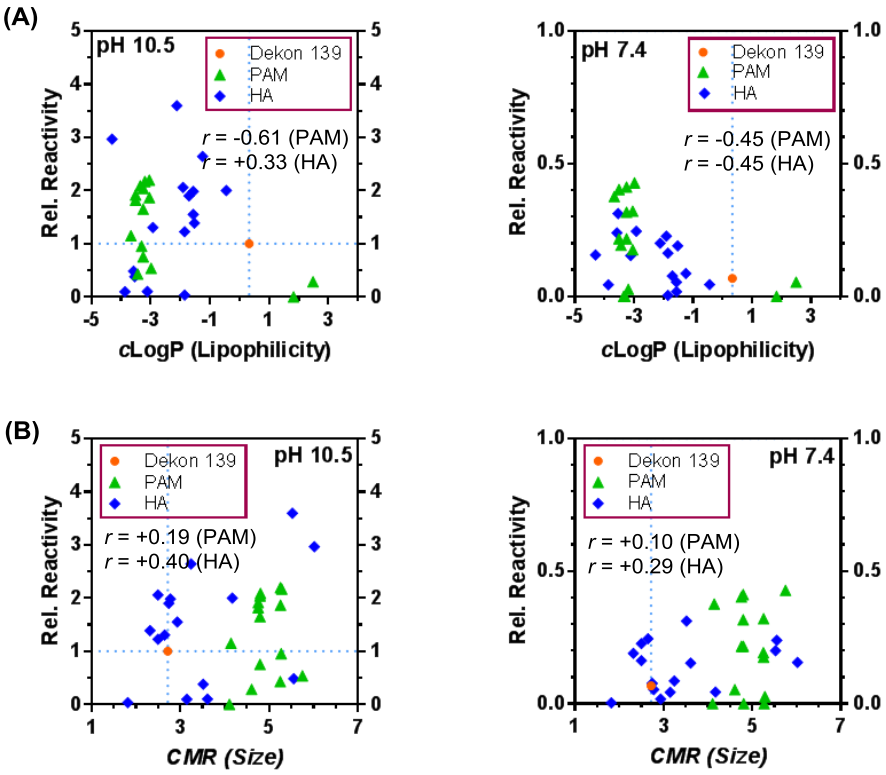


Figure S5. Plots of compound reactivity versus its lipophilicity (*c*log*P*) (A) and calculated molar refractivity (CMR) (B). Relative reactivity refers to the ratio of k_1(test compound)/k_1(Dekon 139, pH 10.5). *r* = correlation coefficient (Pearson)

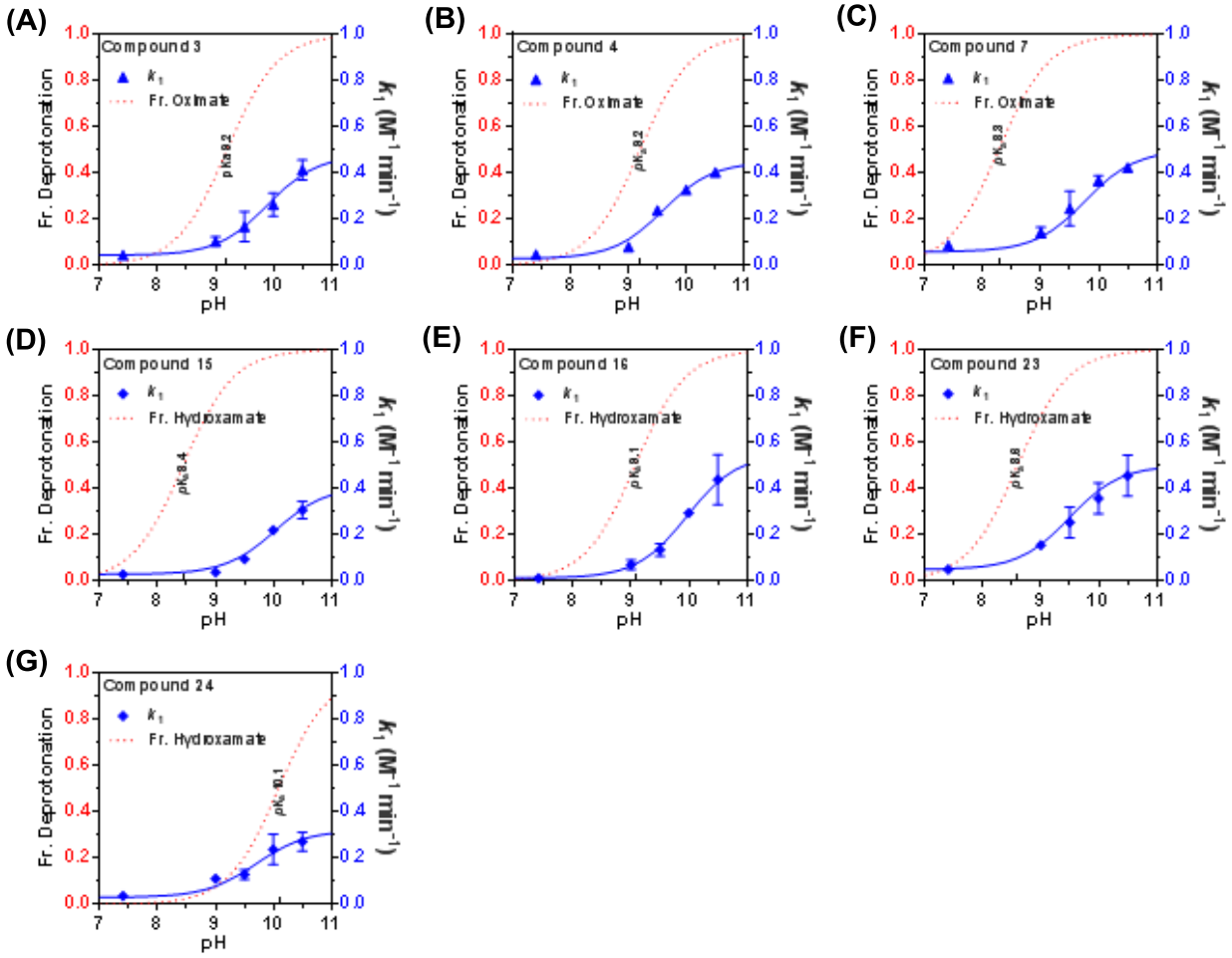


Figure S6. (A–G) Plots of k_1 (37 ^{o}C) and the fraction of deprotonation as a function of medium pH for Dekon 139 and selected compounds in the PAM (**3**, **4**, **7**) and hydroxamic acid (**15**, **16**, **23**, **24**) class.

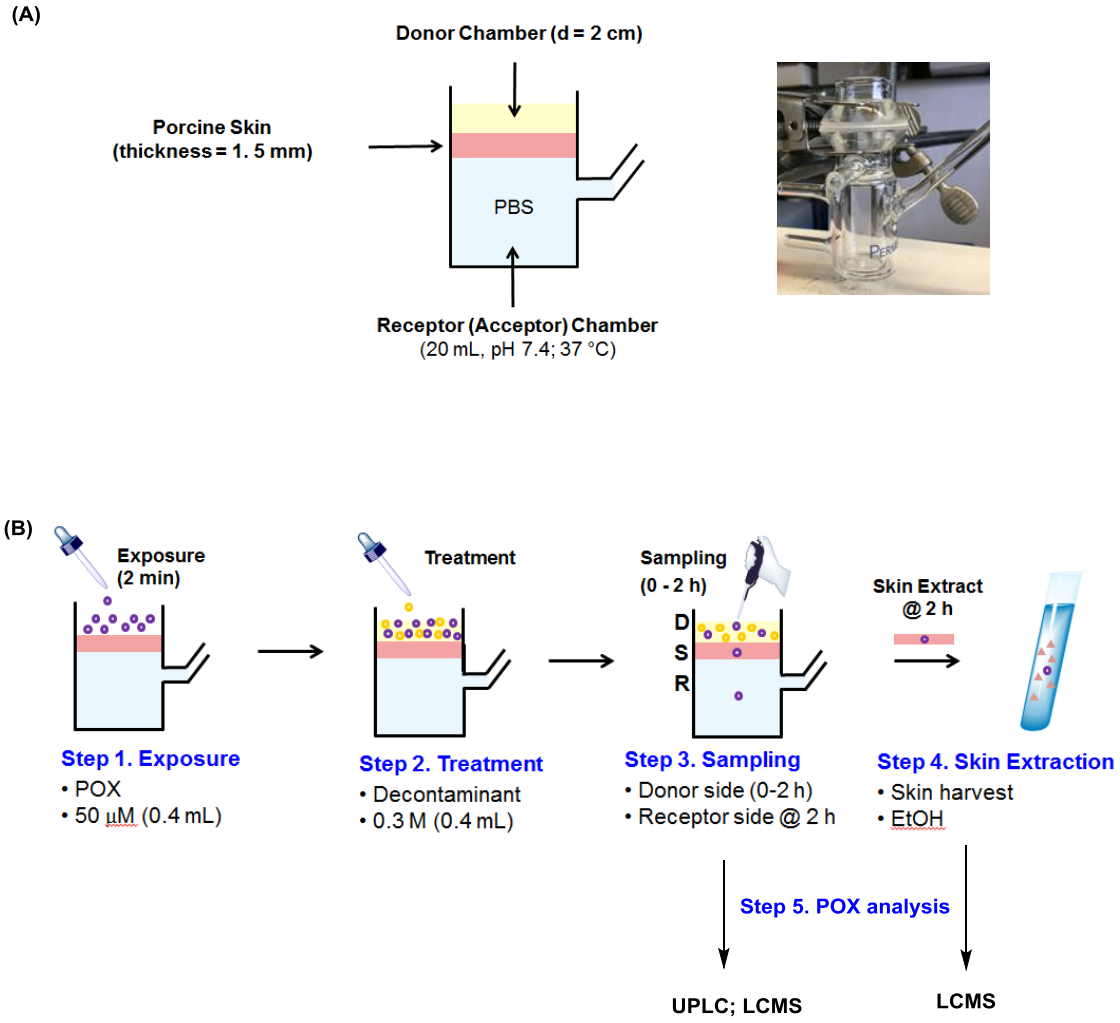


Figure S7. Schematic for POX decontamination using porcine skin in a Franz cell. (A) A photograph of a Franz cell, and (B) Process of POX decontamination and sample analysis. D = donor chamber; S = skin; R = receptor chamber

Table S1. The values of observed rate constant (k_{obsd}, min^{-1}) and bimolecular rate constant (k_1, M^{-1} min^{-1}) determined for the hydrolysis of paraoxon ([POX] = 30 μM) at pH 10.5 and 37 ± 1 °C.[a]

pH 10.5; 37 ± 1 °C	**k_{obsd} (min^{-1}) × 10^4**				**k_1 (M^{-1} min^{-1})**
	[Oxime]				
	0.5 mM	**1.0 mM**	**2.0 mM**	**4.0 mM**	
Dekon 139	1.41(±0.23)	2.58(±0.66)	5.13(±0.64)	8.38(±1.35)	0.221(±0.08)
2-PAM	1.89(±0.11)	3.36(0.26)	5.76(±0.88)	16.13(±1.27)	0.255
1	0.81(±0.018)	1.45(0.04)	2.29(±0.07)	3.27(±0.10)	0.167(±0.037)
2	2.03(±0.079)	5.60(0.27)	7.86(±0.14)	18.60(±10.70)	0.365
3	3.81(±0.66)	7.06(0.04)	9.62(±1.24)	17.63(±3.81)	0.413(±0.043)
4	1.57(±0.22)	3.97(0.46)	8.87(±1.05)	13.63(±1.67)	0.403(±0.002)
5	1.47(±0.13)	2.87(0.14)	6.13(±0.09)	20.00(±0.71)	0.452(±0.019)
6	3.71(±0.98)	7.74(2.09)	7.47(±1.81)	21.60(±3.05)	0.486
7	1.53(±0.11)	3.54(0.25)	6.90(±0.57)	20.53(±1.88)	0.424(±0.0027)
8	1.18(±0.067)	4.60(2.84)	9.76(±0.86)	18.33(±2.32)	0.48
9	1.26(±0.064)	1.82(0.08)	3.04(±0.07)	2.75(±0.93)	0.119
10	0.70(±0.016)	1.18(0.08)			0.095
11	1.72(±0.16)	4.01(0.64)	8.64(±3.78)	10.95(±1.26)	0.462
12	3.28(±0.82)	4.33(0.25)	5.01(±0.53)	6.42(±0.82)	0.211
13	-	-	-		-
14	1.87(±0.79)	2.72(0.27)	3.46(±1.07)	4.27(±1.32)	0.063
15	1.46(±0.22)	3.96(0.46)	8.87(±1.05)	13.6(±1.67)	0.307(±0.037)
16	3.58(±0.34)	6.23(±1.00)	10.43(±2.08)	21.13(±1.69)	0.439(±0.108)

17	5.63(±0.87)	9.04(±2.02)	16.73(±1.43)	26.47(±6.47)	0.584(±0.09)
18	0.097(±0.0028)	0.13(±0.01)	0.35(±0.01)	0.82(±0.02)	0.021
19	0.809(±0.14)	0.90(±0.11)	1.16(±0.08)	1.57(±0.19)	0.022
20	1.00(±0.062)	2.34(±0.12)	7.29(±1.06)	12.77(±1.61)	0.343
21	0.982(±0.38)	2.10(±0.38)	7.08(±0.15)	16.03(±0.42)	0.442
22	0.188(±0.040)	0.15(±0.01)	0.23(±0.02)	0.39(±0.05)	0.008
23	2.55(±0.15)	4.91(±0.54)	9.46(±0.65)	19.92(±2.34)	0.455(±0.089)
24	1.95(±0.16)	3.24(±0.15)	5.84(±0.43)	9.67(±1.41)	0.271(±0.041)
25	0.917(±0.12)	2.41(±0.10)	7.81(±1.16)	19.63(±1.01)	0.42
26	0.456(±0.019)	1.14(±0.09)	3.05(±0.38)	10.36(±2.06)	0.289
27	0.407(±0.0095)	0.81(±0.03)	1.62(±0.12)	3.35(±0.34)	0.084
28	2.03(±0.112)	3.82(±0.30)	4.15(±1.84)	6.26(±1.06)	0.107
29	11.0(±0.85)	15.10(±1.04)	19.33(±7.01)	39.1(±17.80)	0.795
30	10.5(±0.64)	17.07(±0.32)	21.00(±2.65)	ND(>39.1)	0.656

[a] Each reaction was performed in a PBS buffer (pH 10.5) and catalyzed by an oxime compound ($[\text{Oxime}]_{\text{variable}}$ = 0.5 – 4.0 mM). Each k_{obsd} value represents a mean ± standard deviation ($n \geq 3$). ND = not determined

Table S2. Values of observed rate constant (k_{obsd}, min^{-1}) and bimolecular rate constant (k_1, M^{-1} min^{-1}) determined for the hydrolysis of paraoxon ([POX] = 30 μM) at pH 7.4 and 37 ± 1 °C.[a]

pH 7.4; 37 ± 1 °C	**k_{obsd} (min^{-1}) × 10^4**			**k_1 (M^{-1} min^{-1})**
	[Oxime]			
	1.0 mM	**2.0 mM**	**4.0 mM**	
Dekon 139	0.275(±0.040)	0.339(±0.108)	0.553(±0.081)	0.015
2-PAM	1.187(±0.031)	1.737(±0.163)	3.393(±1.010)	0.083
1	0.523(±0.008)	1.375(±0.035)	4.350(±0.184)	0.070
2	0.219(±0.127)	0.591(±0.098)	1.737(±0.144)	0.048
3	0.216	0.669	1.4	0.039
4	0.508(±0.017)	0.748(±0.101)	1.770(±0.061)	0.048
5	1.056(±0.309)	2.383(±0.380)	3.793(±0.628)	0.091
6	0.449(±0.029)	1.009(±0.045)	2.810(±0.125)	0.071
7	0.859(±0.033)	2.397(±0.046)	4.467(±0.258)	0.089
8	0.523(±0.012)	0.432(±0.544)	0.238(±0.009)	0.006
9	0.600(±0.009)	1.460(±0.040)	3.420(±0.075)	0.095
10	0.509(±0.013)	0.935(±0.069)	1.180(±0.052)	0.043
11	NA	NA	NA	NA
12	NA	NA	NA	NA
13	NA	NA	NA	NA
14	0.607(±0.203)	0.592(±0.060)	0.571(±0.135)	0.012
15	0.152(±0.020)	0.316(±0.050)	0.783(±0.027)	0.042
16	0.451(±0.158)	0.528(±0.015)	0.811(±0.205)	0.012
17	0.481(±0.058)	0.703(±0.119)	0.739(±0.143)	0.019

18	0.139(±0.017)	0.151(±0.009)	0.429(±0.072)	0.010
19	0.195(±0.077)	0.198(±0.002)	0.482(±0.092)	0.034
20	0.425(±0.061)	0.207(±0.003)	0.348(±0.054)	0.004
21	0.328(±0.032)	0.326(±0.057)	0.638(±0.120)	0.010
22	NA	NA	0.11	0.001
23	0.650(±0.062)	1.027(±0.015)	2.790(±0.104)	0.050
24	0.643(±0.247)	1.583(±0.055)	1.847(±0.235)	0.036
25	0.198(±0.008)	0.324(±0.032)	0.774(±0.196)	0.017
26	0.206(±0.028)	0.485(±0.058)	1.923(±0.692)	0.054
27	0.317(±0.046)	1.027(±0.184)	2.503(±0.972)	0.069
28	0.461(±0.027)	0.882(±0.038)	1.797(±0.012)	0.053
29	0.385(±0.031)	1.119(±0.417)	1.843(±0.050)	0.044
30	0.346(±0.004)	0.556(±0.014)	1.260(±0.040)	0.034

[a] Each reaction was performed in a PBS buffer (pH 7.4) and catalyzed by an oxime compound ($[Oxime]_{variable}$ = 1.0 – 4.0 mM). Each k_{obsd} value represents a mean ± standard deviation ($n \geq 3$). NA = not active

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