

Supporting Information

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1. General Information

All experiments were carried out using standard conditions. All solvents were reagent grade or better and were purified [S1]. Milli Q water was used for preparing the buffers. Salts used for preparing buffers were Analytical grade or biochemical grade. pH was adjusted using NaOH. All buffer solutions were prepared according to standard procedure and stored at 0 °C. Deuterated solvents were used as received without any further purification. Chloroacetyl chloride was distilled and stored under Argon. TEA and Pyridine were freshly distilled prior to use. Thin layer chromatography (TLC) analyses were performed on Merck Analytical Chromatography aluminum plates bearing a 0.25 mm layer of Merck Silica gel 60 F₂₅₄, which were visualized with UV light at 254 nm or developed using iodine. Ninhydrin (0.2 g in 100 mL EtOH) spraying and drying (110 °C) was performed as per standard TLC visualizing conditions for amines, amino alcohols and amino acids. Bromophenol blue (0.1 gm in 500 mL EtOH) (similar to bromocresol green) spraying and dipping in NaOH (0.1 M) was performed as per standard TLC visualizing conditions for detecting unreacted chloroacetyl chloride or formation of chloroacetic acid (pale yellow spot). Column chromatography was performed with SiO₂ (Fisher Scientific Silicagel (100-200 mesh). NMR was measured using ¹H NMR (500 MHz), ¹³C NMR spectra were recorded on the 125 MHz NMR Bruker AVANCE III spectrometer. Deuterated chloroform or DMSO was used as the solvent, and chemical shift values (δ) are reported in parts per million relatives to the residual signals. Abbreviations used in the NMR follow-up experiments: br, broad; s, singlet; d, doublet; t, triplet; m, multiplet. NMR spectra were processed using ACD/NMR processor Academic Edition, version 12.01 [S2]. Mass spectra were obtained on Waters SYNAPT G2 with 2D nano ACQUITY System with ionization voltages of 70 eV. High-resolution mass spectra (HRMS) were obtained by fast atom bombardment (FAB) using a double focusing magnetic sector mass spectrometer and electron impact (EI) ionization technique (magnetic sector-electric sector double focusing mass analyzer).

Abbreviations used: ABA – Amino benzyl alcohol; CAC – Chloroacetyl Chloride

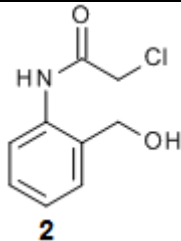
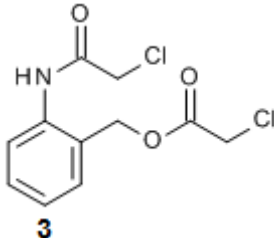
[S1] W. L. F. Armarego and D. D. Perrin, Purification of Laboratory Chemicals, Pergamon Press, Oxford, ed 3. 1988.

[S2] ACD/NMR processor Academic Edition, version 12.01. Advanced Chemistry Development, Inc., Toronto, ON, Canada, www.acdlabs.com, 2015.

EXPERIMENTS

2.1 Procedure to study the effect of base:

In a two neck 25 mL round-bottom flask, fitted with a two way stop-cock and septa, ABA (100 mg, 0.80 mmol) was taken. The flask was evacuated and filled with Argon. CH₂Cl₂ (2 mL) was added through syringe. The base (1.60 mmol) in CH₂Cl₂(500 μL) was added via syringe. The contents of the reaction were cooled in an ice bath (0-5 °C). Then CAC (0.80 mmol) in CH₂Cl₂ (500 μL) was added drop wise to the solution at 0-5 °C. Once the addition was over, the mixture was allowed to come to room temperature till the starting material was consumed (TLC analysis). The mixture was diluted with CH₂Cl₂ (5 mL) and washed with NaHCO₃ (1 X 2 mL) and washed with water followed by brine and dried over Na₂SO₄ and concentrated *in vacuo*. The crude mixture was analysed by NMR and the ratio of the products were obtained.

 2	White solid, m.p. 103 °C; (J. Biol. Chem., 1915, 21, 103) ¹ H NMR (500 MHz, CDCl ₃) δ ppm 4.22 (s, 2H), 4.78 (s, 2H), 7.15-7.17 (m, 1H), 7.24-7.26 (m, 1H), 7.33 - 7.44 (m, 1H), 8.10 (d, <i>J</i> =8.20 Hz, 1H), 9.67 (br. s., 1H). ¹³ C NMR (125 MHz, CDCl ₃) δ ppm 43.01, 64.31, 122.42, 125.08, 128.91, 129.25, 129.86, 136.58, 164.80. ESI-MS calcd for C ₉ H ₁₀ ClNO ₂ (M+H) ⁺ 200.0478, found 200.0812, 202.0779 (M+H+2) ⁺
 3	White solid, m.p. 80-82 °C; (EdizioneScientifica, 1965, 20, 323) ¹ H NMR (500 MHz, CDCl ₃) δ ppm 4.10 (s, 2H), 4.23 (s, 2H), 5.22 (s, 2H), 7.22 - 7.25 (m, 1H), 7.40 - 7.43 (m, 2H), 7.85 (d, <i>J</i> =7.88 Hz, 1H), 9.01 (br. s., 1H) ¹³ C NMR (125 MHz, CDCl ₃) δ ppm 40.73, 43.09, 65.09, 124.41, 126.14, 126.87, 130.07, 130.90, 135.55, 164.90, 167.38.

2.2 Procedure to study the effect of buffers:

In a 5 mL round-bottom flask, the ABA (100 mg, 0.80 mmol) was mixed with water or buffer (500 μL). The CAC (0.80 mmol) was added drop wise to the solution. Once the addition was over, the mixture was stirred for a min and the TLC analysis was performed. The mixture extracted with Ethyl acetate (3 X 2 mL) washed with brine (1 X 2 mL) dried over Na₂SO₄ and concentrated *in vacuo*. The crude mixture was analysed by NMR and the ratio of the products were obtained.

2.3 Procedure to study the effect of metal salts:

In a 5 mL round-bottom flask, the ABA (100 mg, 0.80 mmol) was mixed with buffer (500 μ L). The metal salt (0.80 mmol) was added to the reaction mixture. The contents were allowed to stir for 20-30 min. Then the mixture was cooled and CAC (0.80 mmol) was added drop wise to the solution. Once the addition was over, the mixture was stirred and TLC analysis was performed. The metal salt was removed by filtration using celite. The celite bed was washed with Ethyl acetate (3 X 2 mL). The aqueous layer was separated and extracted with Ethyl acetate (2 X 2 mL). The organic layers were combined and washed with brine (1 X 2 mL) dried over Na_2SO_4 and concentrated *in vacuo*. The crude mixture was analysed by NMR and the ratio of the products were obtained.

2.4 Procedure to study the effect of scavengers:

In a 5 mL round-bottom flask, the ABA (100 mg, 0.80 mmol) was mixed with buffer (500 μ L). The scavenger (1-3 equiv.) was added to the reaction mixture. Then the mixture was cooled and CAC (0.80 mmol) was added drop wise to the solution. Once the addition was over, the mixture was stirred and TLC analysis was performed. The aqueous layer was extracted with Ethyl acetate (3 X 2 mL). The organic layers were washed with brine (1 X 2 mL) dried over Na_2SO_4 and concentrated *in vacuo*. The crude mixture was analysed by NMR and the ratio of the products were obtained.

2.5 Procedure for the competitive reaction between aniline and alcohol/phenols:

In a 5 mL round-bottom flask, the aniline and alcohol/phenol (0.50 mmol each) was mixed with buffer (10 μ L/mg). Additives were added (if used, as per Table 7). Then the mixture was cooled and CAC (0.50 mmol) was added drop wise to the solution. Once the addition was over, the mixture was stirred and TLC analysis was performed. The aqueous layer was extracted with Ethyl acetate (5 X 2 mL). The organic layers were washed with brine (1 X 2 mL) dried over Na_2SO_4 and concentrated *in vacuo*. The crude mixture was analysed by NMR and the ratio of the products were obtained.

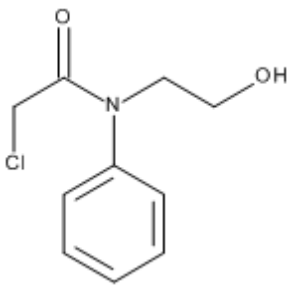
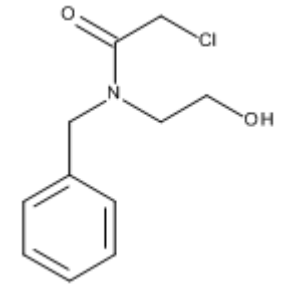
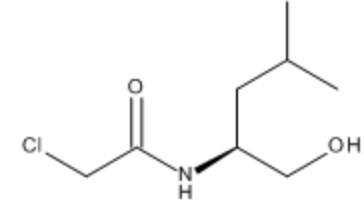
2.6 Procedure for the competitive reaction between amine and alcohol/phenols:

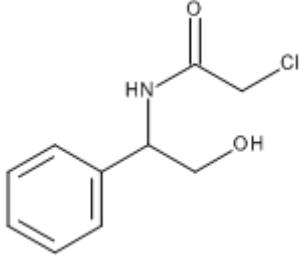
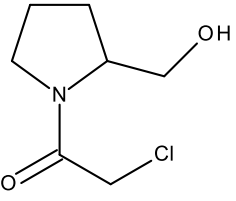
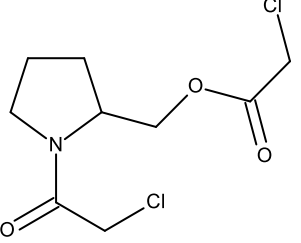
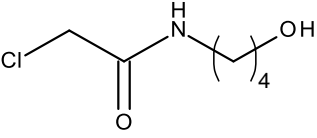
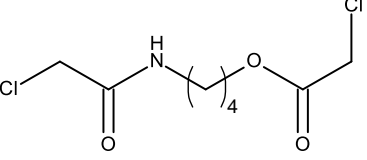
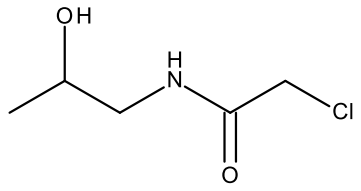
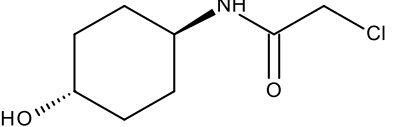
In a 5 mL round-bottom flask, the amine and alcohol/phenol (0.50 mmol each) were mixed with buffer (10 μ L/1mg of substrate). Additives were added (if used, as per Table 8). Then the mixture was cooled and CAC (0.50 mmol) was added drop wise to the solution. Once the addition was over, the mixture was stirred and TLC analysis was performed. The aqueous layer was extracted

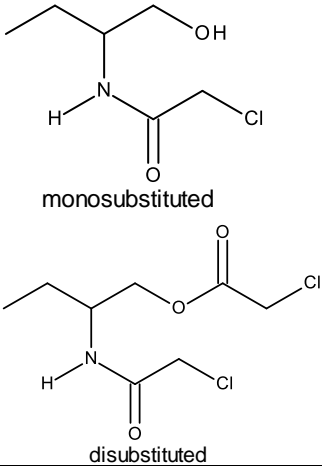
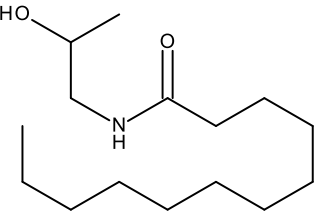
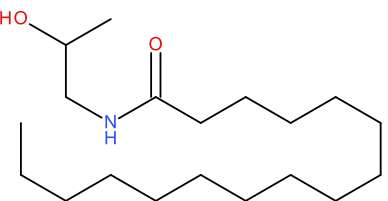
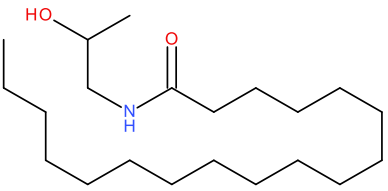
with Ethyl acetate (5 X 2 mL). The organic layers were washed with brine (1 X 2 mL) dried over Na₂SO₄ and concentrated *in vacuo*. The crude mixture was analysed by NMR and the ratio of the products were obtained.

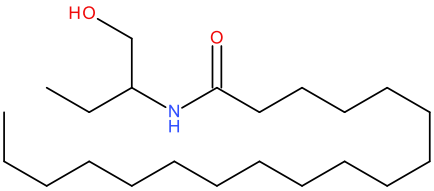
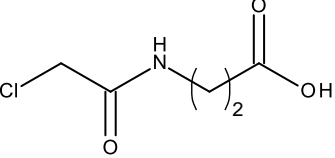
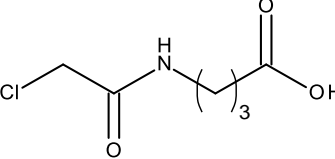
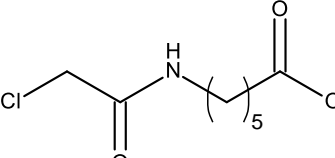
2.9 Procedure for the reaction of amino alcohols or amino acids:

In a 5 mL round-bottom flask, amino alcohol or amino acid (50 mg) was mixed with buffer (10µL/mg). Propylene oxide (2 equiv.) was added to the reaction mixture. Then the mixture was cooled and CAC (1.1 eq) was added drop wise to the solution. Once the addition was over, the mixture was stirred and TLC analysis was performed. The aqueous layer was extracted with Ethyl acetate (5 X 2 mL). The organic layers were washed with brine (1 X 2 mL) dried over Na₂SO₄ and concentrated *in vacuo*. The crude mixture was analysed by NMR and the ratio of the products were obtained. Physical parameters of thus obtained N-chloroacylated compounds are shown in the below table.

	<p>m.p. 67.5-68.5°C(J. Biol. Chem.1915, 21, 403-37) ¹H NMR (500 MHz, CDCl₃) δ ppm 3.80 (t, <i>J</i>=5.20 Hz, 2H) 3.88 (s, 2H) 3.92 - 3.95 (m, 2H) 7.28 - 7.34 (m, 2H) 7.44 (d, <i>J</i>=7.25 Hz, 1H) 7.46 - 7.51 (m, 2H) ¹³C NMR (125 MHz, CDCl₃) δ ppm 42.13, 52.82, 60.18, 128.04, 128.96, 130.17, 141.07, 167.81 LC-MS C₁₀H₁₂ClNO₂ (M-OH)⁺Calcd. 196.0381, found 196.0529</p>
	<p>m.p. 85.3-87.9 °C (USPTO 2771468) ¹H NMR (500 MHz, CDCl₃) δ ppm 3.42-3.47 (m, 2H), 3.56 - 3.62 (m, 2H), 4.14 (s, 2H), 4.38 (s, 2H), 7.28 - 7.40 (m, 5H) ¹³C NMR (125 MHz, CDCl₃) δ ppm 42.87, 48.78, 51.14, 57.07, 126.30, 129.04, 130.01, 130.51, 172.00 ESI-MS calcd for C₁₁H₁₄ClNO₂ (M+H)⁺228.0791, found 228.0479, 230.0508 (M+H+2)⁺</p>
	<p>¹H NMR (500 MHz, CDCl₃) δ ppm 1.37 - 1.53 (m, 2H) 1.64 (d, <i>J</i>=5.99 Hz, 1H) 3.56 (dt, <i>J</i>=10.72, 5.36 Hz, 1H) 3.61 - 3.77 (m, 1H) 4.07 (s, 3H), 6.76 (br. s., 1H) ¹³C NMR (125 MHz, CDCl₃) δ ppm 22.15, 23.00, 24.84, 39.97, 42.68, 50.22, 64.97, 166.62 HRMS (EI⁺) calcd for C₈H₁₆ClNO₂(M-OH)⁺ 176.0842, found 176.0841</p>

	$^1\text{H NMR}$ (500 MHz, CDCl_3) δ ppm 3.68 - 3.78 (m, 2H), 4.01 (s, 2H), 4.4 (t, $J=5.83\text{Hz}$, 1H), 4.92 (br. s, 1H), 7.14 - 7.20 (m, 1H), 7.23 - 7.28 (m, 4 H), 7.77 (br. s, 1H) $^{13}\text{C NMR}$ (125 MHz, CDCl_3) δ ppm 41.67, 54.65, 63.72, 125.71, 126.07, 127.19, 138.82, 165.01 HRMS (EI^+) calcd for $\text{C}_{10}\text{H}_{12}\text{ClNO}_2(\text{M-OH})^+$ 196.0529, found. 196.0497
	$^1\text{H NMR}$ (500 MHz, CDCl_3) δ ppm 1.53- 1.85 (m, 3H), 2.24 - 2.5 (m, 1H), 3.34 -3.57 (m, 2H), 3.68-3.83 (m, 2H), 4.09 (s, 2H), 4.24-4.35 (m, 1H), 6.65 (br. s, 1H) $^{13}\text{C NMR}$ (125 MHz, CDCl_3) δ ppm 24.37, 28.00, 42.41, 47.95, 55.92, 65.21, 167.10 ESI-MS calcd for $\text{C}_7\text{H}_{12}\text{ClNO}_2(\text{M-OH})^+$ 160.0529, found 160.0535
	$^1\text{H NMR}$ (500 MHz, CDCl_3) δ ppm 1.57 - 1.89 (m, 4H), 3.38 (d, $J=6.62\text{Hz}$, 2H) 4.06 (s, 2H), 4.07 (s, 2H), 4.24 (t, $J=6.31\text{Hz}$, 1H) 6.65 (br. s, 1H) $^{13}\text{C NMR}$ (125 MHz, CDCl_3) δ ppm 24.22, 27.16, 40.71, 42.21, 47.14, 61.79, 66.04, 165.48, 167.16 ESI-MS calcd for $\text{C}_9\text{H}_{13}\text{Cl}_2\text{NO}_3(\text{M+H})^+$ 254.0352, found 254.2482
	$^1\text{H NMR}$ (500 MHz, CDCl_3) δ ppm 1.53 (d, $J=8.67$, 4.89 Hz, 4 H) 3.24 (d, $J=5.04$ Hz, 2H) 3.54 (d, $J=4.10$ Hz, 2H) 3.96 (br. s., 2H), 6.35 (br. s, 1H) HRMS (EI^+) calcd for $\text{C}_6\text{H}_{12}\text{ClNO}_2(\text{M-OH})^+$ 148.0529, found 148.0509
	$^1\text{H NMR}$ (500 MHz, CDCl_3) δ ppm 1.68 - 1.75 (m, 4 H) 3.39 (br. s., 2H) 4.09 (s., 4 H), 4.25 (s, 2H), 6.7 (br. s, 1H) $^{13}\text{C NMR}$ (125 MHz, CDCl_3) δ ppm 25.79, 25.95, 39.31, 40.86, 42.66, 65.64, 165.99, 167.35 ESI-MS calcd for $\text{C}_8\text{H}_{13}\text{Cl}_2\text{NO}_3(\text{M+H})^+$ 242.0352, found 242.2432
	$^1\text{H NMR}$ (500 MHz, CDCl_3) δ ppm 1.21 (t, $J=7.4\text{Hz}$, 3H), 3.13-3.19 (m, 1H), 3.46-3.50 (m, 1H), 3.94-4.03 (m, 2H), 4.08 (s, 2H), 7.24 (s, 1H) $^{13}\text{C NMR}$ (125 MHz, CDCl_3) δ ppm 20.75, 42.54, 46.95, 66.93, 167.27 ESI-MS calcd for $\text{C}_5\text{H}_{10}\text{ClNO}_2(\text{M+H})^+$ 152.0478, found 152.0697, 154.00 ($\text{M+H}+2$) ⁺
	$^1\text{H NMR}$ (500 MHz, CDCl_3) δ ppm 1.26-1.44 (m, 4H), 1.88-2.07 (m, 4H), 3.11-3.18 (m, 1H), 3.52-3.62 (m, 1H), 4.08 (s, 2H), 4.75 (br, 1H) $^{13}\text{C NMR}$ (125 MHz, CDCl_3) δ ppm 28.87, 32.84, 41.14,

	<p>47.53, 68.25, 169.08</p> <p>ESI-MS calcd for $C_3H_{14}ClNO_2(M+H)^+$ 192.0791, found 192.0402, 194.0364 ($M+H+2$)⁺</p>
 <p>monosubstituted</p> <p>disubstituted</p>	<p>monosubstituted</p> <p>¹H NMR (500 MHz, CDCl₃) δ ppm 0.95 (t, <i>J</i>=7.6 Hz, 3H), 1.50-1.57 (m, 1H), 1.61-1.68 (m, 1H), 3.57-3.62 (m, 1H), 3.65-3.69 (m, 1H), 3.86-3.91 (m, 1H), 4.08 (s, 2H), 6.93 (br, 1H)</p> <p>¹³C NMR (125 MHz, CDCl₃) δ ppm 10.27, 23.83, 42.57, 53.33, 63.78, 166.69</p> <p>ESI-MS calcd for $C_6H_{12}ClNO_2(M-OH)^+$ 148.0529, found 148.0399</p> <p>Disubstituted</p> <p>¹³C NMR (125 MHz, CDCl₃) δ ppm 10.08, 24.00, 40.56, 42.41, 50.06, 66.59, 166.22, 167.29</p>
	<p>Fluffy White powder</p> <p>¹H NMR (500 MHz, DMSO-<i>d</i>₆) δ ppm 0.88 (t, <i>J</i>=7.6 Hz, 3H) 1.15-1.17 (d, 3 H), 1.27-1.38 (m, 15 H), 1.62 (br. s., 2 H), 2.14 - 2.36 (m, 2 H), 3.06 (br. s., 1 H), 3.37 (br. s., 1 H), 3.85 – 3.90 (m, 1H), 7.11 (br. s., 1 H)</p> <p>¹³C NMR (125 MHz, CDCl₃) δ ppm 13.68, 20.33, 22.14, 24.44, 25.35, 28.57, 28.72, 28.79, 28.82, 28.9, 28.99, 29.07, 31.36, 36.01, 46.52, 66.18, 173.61</p> <p>HRMS (EI⁺) calcd for $C_{15}H_{31}NO_2 (M-OH)^+$ 240.2327, found 240.2304</p>
	<p>White powder</p> <p>¹H NMR (500 MHz, CDCl₃) δ ppm 0.89 (t, , <i>J</i>=7.32 Hz, 3H), 1.19 (d, , <i>J</i>=6.44 Hz, 3H), 1.22 - 1.32 (m, 24 H) 1.62 - 1.65 (m, 2 H) 2.22 (t, <i>J</i>=7.80 Hz, 2H), 3.13 (ddd, <i>J</i>=13.87, 7.57, 5.36 Hz, 1 H), 3.43 (td, <i>J</i>=7.01, 2.99 Hz, 1 H), 3.89 - 3.93 (m, 1 H) 6.22 (br. s., 1 H)</p> <p>¹³C NMR (125 MHz, CDCl₃) δ ppm 14.13, 20.89, 22.7, 25.8, 29.32, 29.37, 29.52, 29.64, 29.67, 29.71, 31.93, 36.73, 47.02, 67.47, 174.58</p> <p>HRMS (EI⁺) calcd for $C_{19}H_{39}NO_2 (M+H)^+$ 314.3059, found 314.3038</p>
	<p>¹H NMR (500 MHz, CDCl₃) δ ppm 0.87 (t, , <i>J</i>=7.32 Hz, 3H), 1.16 (d, , <i>J</i>=6.44 Hz, 3H), 1.22 - 1.28 (m, 28 H) 1.62 - 1.65 (m, 2 H) 2.17 – 2.22 (m, 2H), 3.04 - 3.08 (m, 2H), 3.39 – 3.41 (m, 1H), 3.86 (br., 1 H) 6.71 (br., 1 H)</p> <p>¹³C NMR (125 MHz, CDCl₃) δ ppm 13.87, 20.54, 20.62, 22.41, 25.56, 29.07, 29.13, 29.25, 29.37, 29.38, 29.41, 31.64, 36.4, 46.77, 66.76, 174.00</p> <p>HRMS (EI⁺) calcd for $C_{21}H_{43}NO_2 (M+H)^+$ 342.3372,</p>

	<p>found 342.3348</p> <p>$^1\text{H NMR}$ (500 MHz, CDCl_3) δ ppm 0.82 - 0.98 (m, 6 H), 1.21 - 1.34 (m, 30 H), 1.59 - 1.62 (m, 4 H), 2.16 - 2.19 (m, 2 H), 3.55 - 3.62 (m, 2 H), 3.79 - 3.82 (m, 1 H), 6.66 (br. s., 1 H).</p> <p>$^{13}\text{C NMR}$ (125 MHz, CDCl_3) δ ppm 10.22, 13.7, 22.21, 23.66, 25.5, 28.87, 28.97, 29.07, 29.21, 31.44, 36.32, 52.37, 63.81, 173.45</p> <p>HRMS (EI^+) calcd for $\text{C}_{22}\text{H}_{45}\text{NO}_2$ ($\text{M}+\text{H}^+$) 356.3528, found 356.3501</p>
	<p>m.p. 95 °C (J. Biol. Chem. 1948, 175, 833-48)</p> <p>$^1\text{H NMR}$ (500 MHz, CDCl_3) δ ppm 2.52 (t, $J = 6.3$ Hz, 2H), 3.48 (t, $J = 6.3$ Hz, 2H), 4.05 (s, 2H), 7.89 (br. s. 1H), 9.50 (br. s. 1H)</p> <p>$^{13}\text{C NMR}$ (125 MHz, CDCl_3) δ ppm 32.61, 34.37, 41.57, 165.40, 172.73</p> <p>ESI-MS calcd for $\text{C}_5\text{H}_8\text{ClNO}_3$ ($\text{M}-\text{OH}^+$) 148.5676, found 148.4922</p>
	<p>$^1\text{H NMR}$ (500 MHz, CDCl_3) δ ppm 2.07 (quin, $J=7.49$ Hz, 2H), 2.25 - 2.38 (m, 2H), 3.37 (t, $J=6.94$ Hz, 2H), 4.02 (s, 2H), 7.47 (br. s., 1H), 9.20 (br. s., 1H)</p> <p>$^{13}\text{C NMR}$ (125 MHz, CDCl_3) δ ppm 19.96, 30.13, 40.74, 43.34, 167.97, 178.81</p> <p>ESI-MS calcd for $\text{C}_8\text{H}_{14}\text{ClNO}$ ($\text{M}+\text{H}^+$) 180.0427, found 180.2152</p>
	<p>m.p. 86 °C (Acta Crystallographica, Section C: Crystal Structure Communications 2006, 62, 498-500)</p> <p>$^1\text{H NMR}$ (500 MHz, CDCl_3) δ ppm 1.35 - 1.47 (m, 2 H), 1.55 - 1.63 (m, 2 H), 1.66 - 1.73 (m, 2 H), 2.33 - 2.45 (m, 2 H), 3.34 (q, $J=6.73$ Hz, 2 H), 4.08 (s, 2 H), 6.7 (br. s. 1H)</p> <p>$^{13}\text{C NMR}$ (125 MHz, CDCl_3) δ ppm 24.19, 26.14, 28.90, 33.79, 39.66, 42.63, 166.39, 178.64</p> <p>ESI-MS calcd for $\text{C}_8\text{H}_{14}\text{ClNO}_3$ ($\text{M}+\text{H}^+$) 208.0740, found 208.1424</p>

NH2-BN-DCM-DABCO.001.1R.ESP

TMS

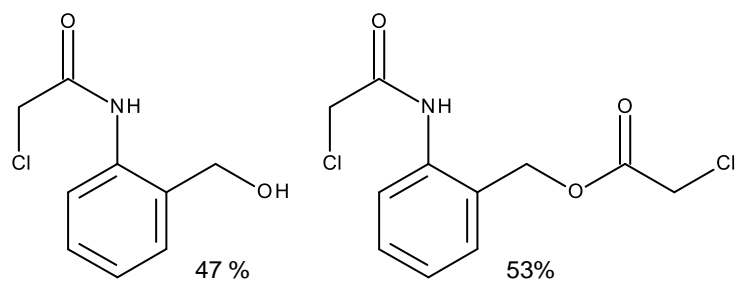
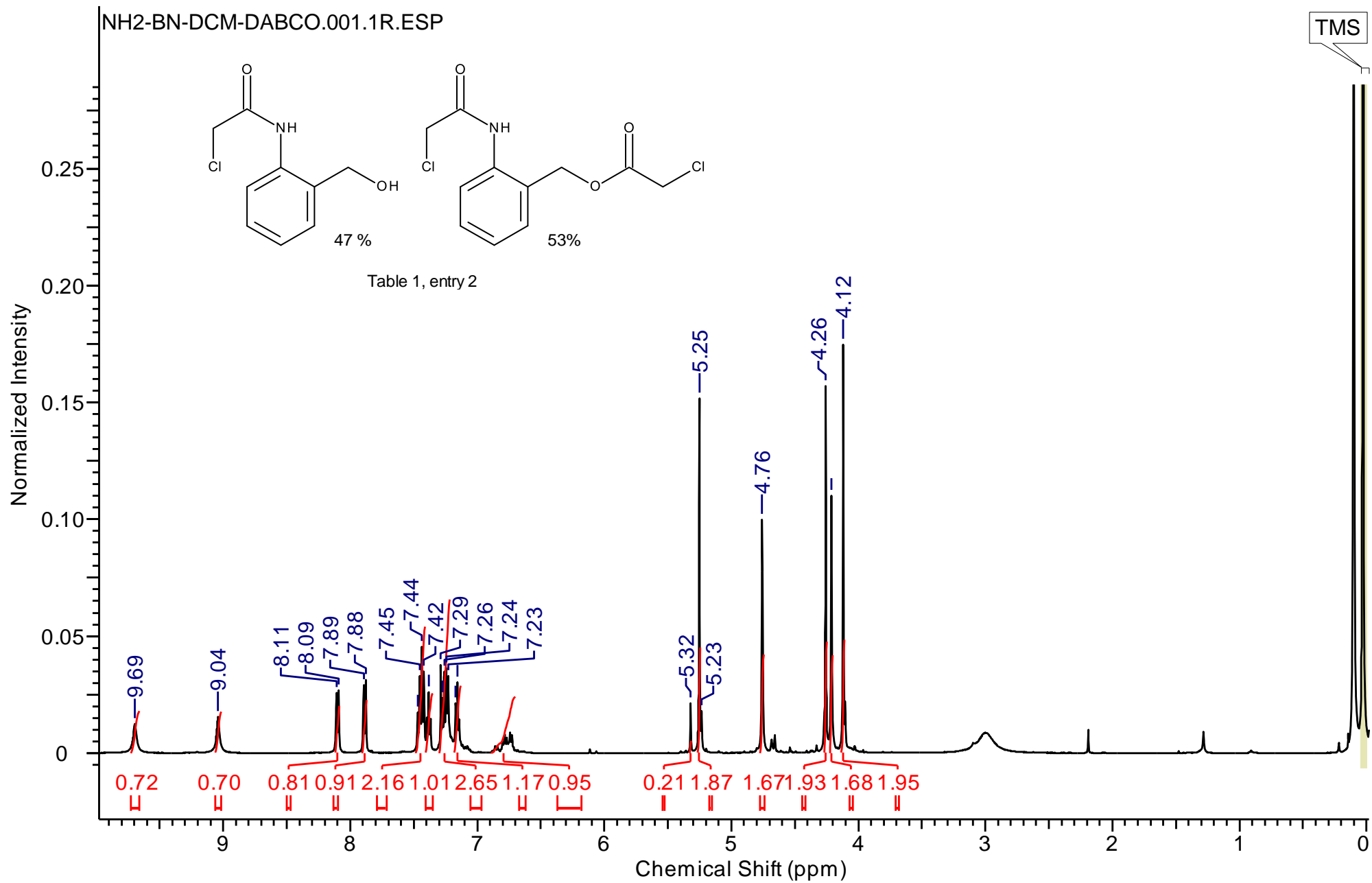
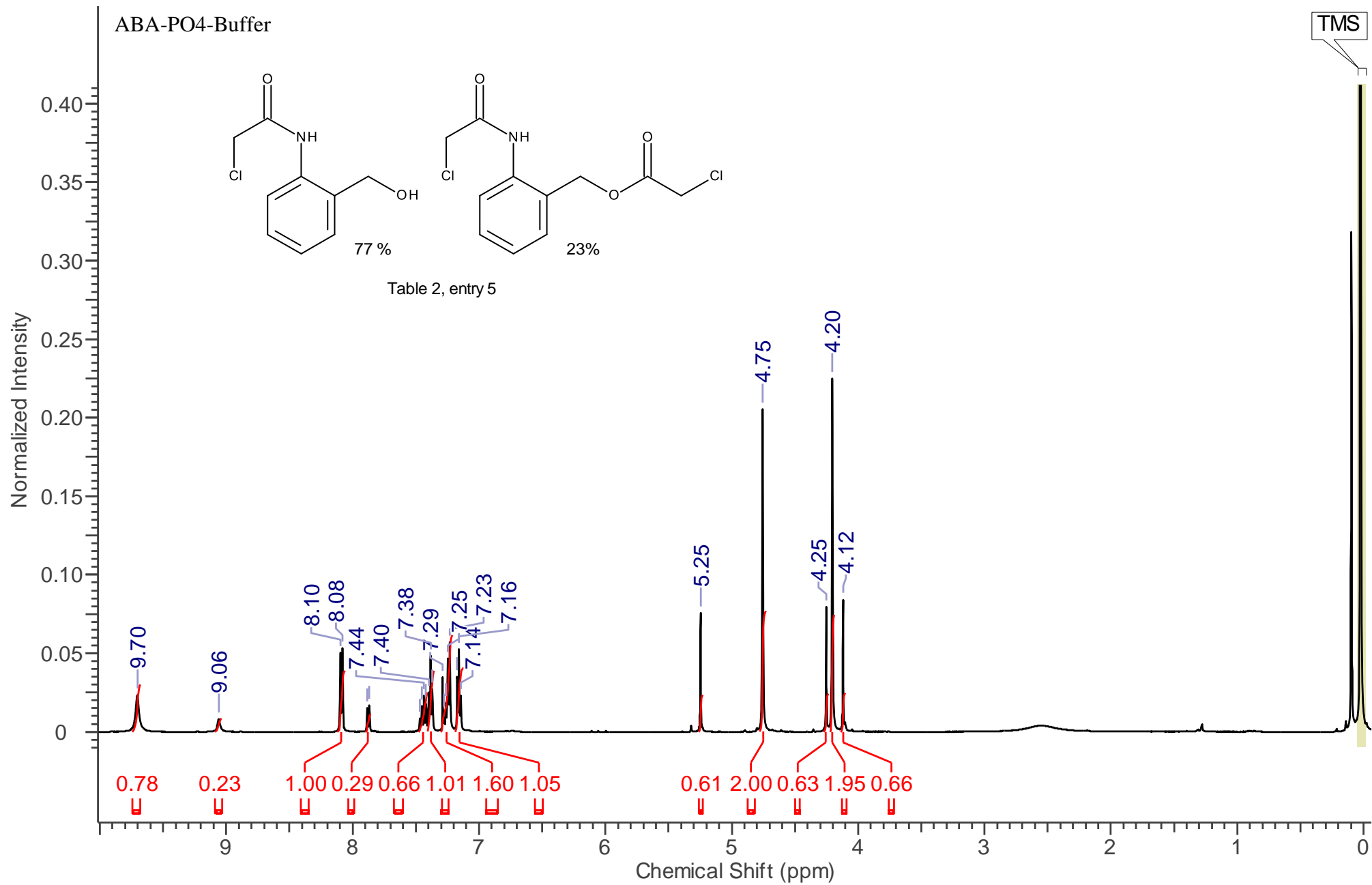


Table 1, entry 2





NH2-BN-PO4-BUFFER-MG2.001.1R.esp

