molecules

MDPI

*Supplementary Materials*

# Efficient Method of *(S)*-Nicotine Synthesis

**Nazar Trotsko[1]*, Barbara Miroslaw[2], Radomir Jasiński[3], Mateusz Długosz[4], Małgorzata Sadczuk[5] and Oleg M. Demchuk[6]***

[1] Department of Organic Chemistry, Medical University of Lublin, Witolda Chodźki 4A, 20-093 Lublin, Poland
[2] Department of General and Coordination Chemistry and Crystallography, Institute of Chemical Sciences, Faculty of Chemistry, Maria Curie-Sklodowska University in Lublin, Marii Skłodowskiej-Curie, 2, 20-031 Lublin, Poland, barbara.miroslaw@mail.umcs.pl
[3] Department of Organic Chemistry and Technology, University of Technology in Cracow, Warszawska 24, 31-155 Kraków, Poland, radomir.jasinski@pk.edu.pl
[4] A-Sense sp. z o.o, Przemysłowa 46, 24-320 Poniatowa, Poland, mateusz.dlugosz@a-sense.pl
[5] Chair and Department of Synthesis and Chemical Technology of Pharmaceutical Substances, Medical Univer-sity of Lublin, Witolda Chodźki 4A, 20-093 Lublin, Poland; malgorzta.sadczuk@umlub.pl
[6] Faculty of Medicine, The John Paul II Catholic University of Lublin, Konstantynów 1J/4.03, 20-708 Lublin, Poland

* Correspondence: nazar.trotsko@umlub.pl (N.T.); Oleh.Demchuk@KUL.Lublin.pl (O.D.)

**Table of contents:**

Figure S1. Molecular structure of *N*-lauroyl-*(S)*-alanine *(S)*-nornicotine salt with atom numbering scheme 2
Figure S2. Molecular structure of *N*-lauroyl-*(S)*-alanine *(R)*-nornicotine salt with atom numbering scheme 2
Table S1 Crystal data and structure refinement for *N*-lauroyl-*S*-alanine (*S*)- and *(R)*-nornicotine salts 3
Table S2 Bond Lengths for *N*-lauroyl-S-alanine (*S*)- and *(R)*-nornicotine salts 4
Table S3 Bond Angles for *N*-lauroyl-*S*-alanine (*S*)- and *(R)*-nornicotine salts 5
Table S4 Torsion Angles for *N*-lauroyl-*S*-alanine *(S)*- and *(R)*-nornicotine salts 6
Figures S3 and S4. $^{1}H$ and $^{13}C$ NMR spectra of *N*-lauroyl-(*S*)-alanine *(R)*-nornicotine salt 7
Figures S5 and S6. $^{1}H$ and $^{13}C$ NMR spectra of *N*-lauroyl-(*R*)-alanine *(S)*-nornicotine salt 8
Figure S7 and S8. $^{1}H$ and $^{13}C$ NMR spectra of *(R)*-nornicotine 9
Figures S9 and S10. $^{1}H$ and $^{13}C$ NMR spectra of *(S)*-nornicotine 10
Figures S11 and S12. $^{1}H$ and $^{13}C$ NMR spectra of *(S)*-nicotine 11
Figure S13 and S14. $^{1}H$ and $^{13}C$ NMR spectra of myosmine 12
Figure S15. HRMS analysis of myosmine (Q-Tof) 15
Figure S16. HRMS analysis of nornicotine (Q-Tof) 14
Figure S17. HRMS analysis of nicotine (Q-Tof) 15
Figure S18. GCMS analysis of reaction mixture of incomplete oxidation of nornicotine to myosmine 16
Figure S19. GCMS analysis of reaction mixture of incomplete reduction of myosmine 17
Figure S20. GCMS analysis of nicotine 18
Figure S21. Comparision of DEPT135 spectra of rac-nornicotine and rac-nornicotine in the presence of naproxen 19
Figure S22. Comparision of $^{1}H$ NMR spectra of rac-nornicotine and rac-nornicotine in the presence of naproxen 20

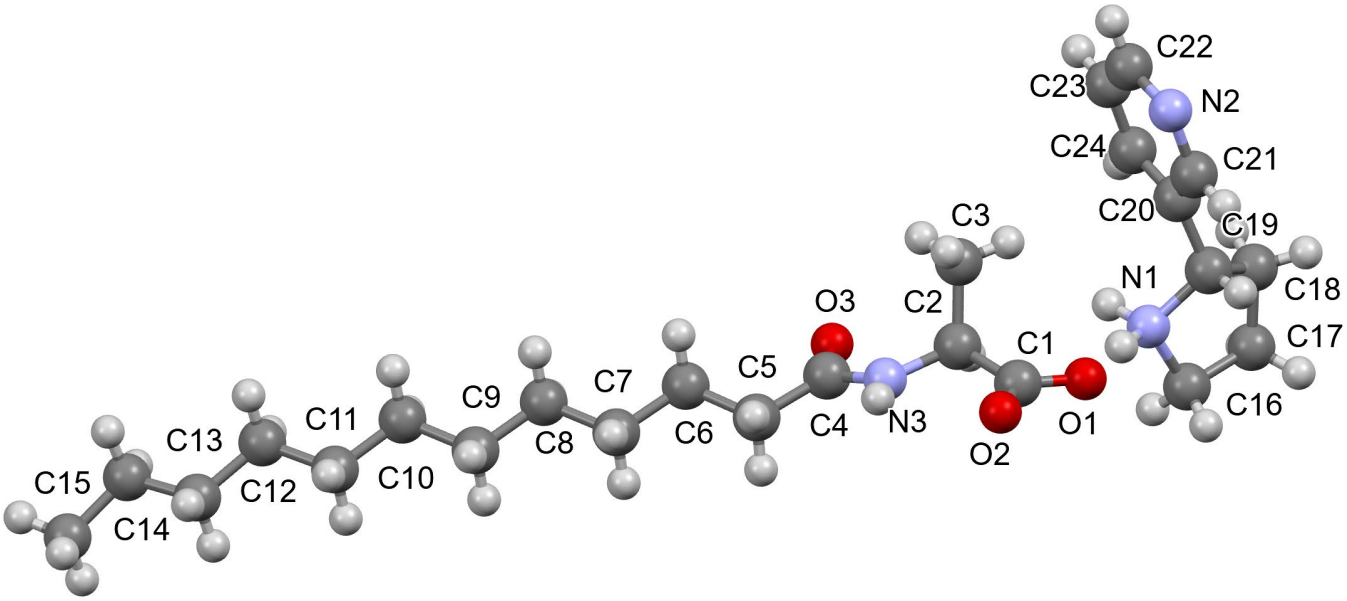



**Figure S1. Molecular structure of *N*-lauroyl-*(S)*-alanine *(S)*-nornicotine salt with atom numbering scheme.**

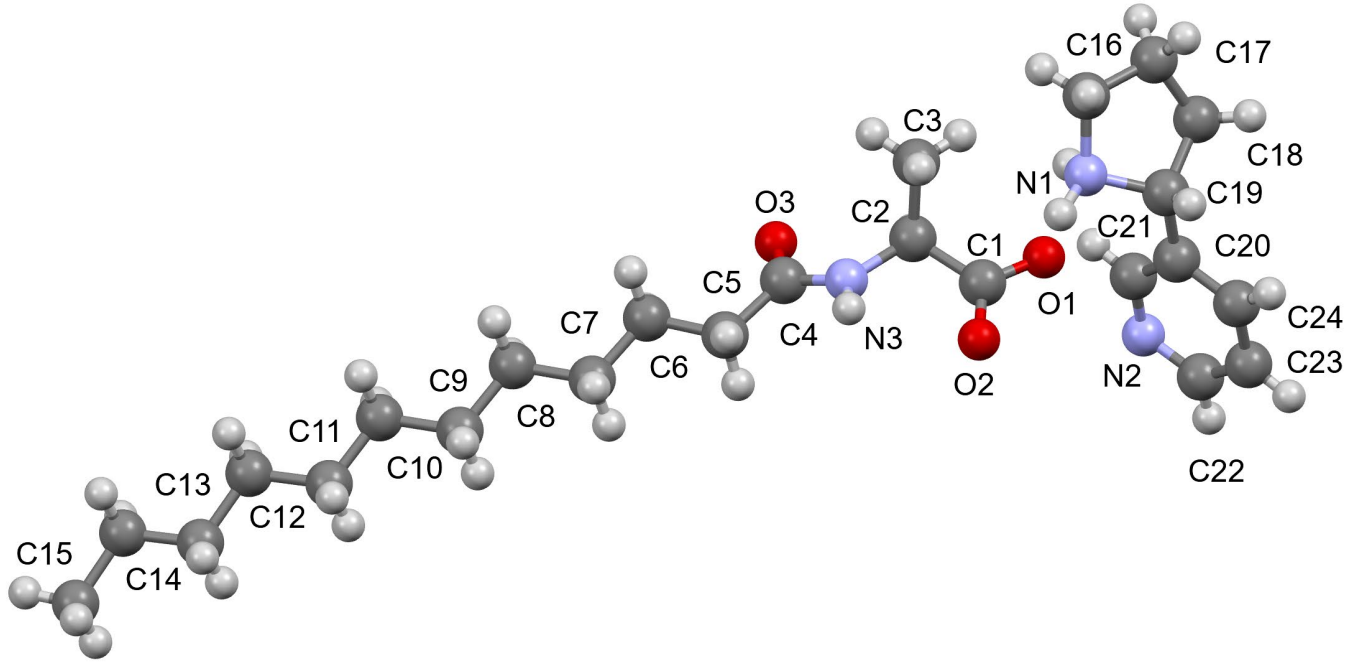



**Figure S2. Molecular structure of *N*-lauroyl-*(S)*-alanine *(R)*-nornicotine salt with atom numbering scheme.**

**Table S1 Crystal data and structure refinement for *N*-lauroyl-*(S)*-alanine *(S)*- and *(R)*- nornicotine salts.**

| Identification code | *N*-lauroyl-(*S*)-alanine (*S*)-nornicotine | *N*-lauroyl-(*S*)-alanine (*R*)-nornicotine |
|---|---|---|
| Empirical formula | $C_{24}H_{41}N_3O_3$ | $C_{24}H_{41}N_3O_3$ |
| Formula weight | 419.60 | 419.60 |
| Temperature/K | 293 | 293 |
| Crystal system | orthorhombic | orthorhombic |
| Space group | $P2_12_12_1$ | $P2_12_12_1$ |
| *a*/Å | 5.3833(3) | 5.0002(2) |
| *b*/Å | 12.433(1) | 12.6394(7) |
| *c*/Å | 38.203(3) | 39.897(2) |
| *α*/° | 90 | 90 |
| *β*/° | 90 | 90 |
| *γ*/° | 90 | 90 |
| Volume/Å$^3$ | 2556.9(3) | 2521.4(2) |
| Z | 4 | 4 |
| $\rho_{calc}$ g/cm$^3$ | 1.090 | 1.105 |
| $\mu$/mm$^{-1}$ | 0.566 | 0.574 |
| *F*(000) | 920.0 | 920.0 |
| Crystal size/mm$^3$ | 0.25 × 0.1 × 0.05 | 0.25 × 0.08 × 0.05 |
| Radiation | Cu Kα (λ = 1.54184) | Cu Kα (λ = 1.54184) |
| 2*Θ* range for data collection/° | 7.478 to 161.23 | 7.336 to 152.022 |
| Index ranges | $-6 \le h \le 6$, $-14 \le k \le 15$, $-44 \le l \le 47$ | $-5 \le h \le 6$, $-13 \le k \le 15$, $-49 \le l \le 47$ |
| Reflections collected | 17375 | 6729 |
| Independent reflections | 5236 [$R_{int}$ = 0.0361, $R_{sigma}$ = 0.0365] | 4262 [$R_{int}$ = 0.0196, $R_{sigma}$ = 0.0367] |
| Data/restraints/parameters | 5236/0/285 | 4262/0/285 |
| Goodness-of-fit on $F^2$ | 1.119 | 1.034 |
| Final *R* indexes [*I*>=2*σ*(*I*)] | $R_1$ = 0.0554, $wR_2$ = 0.1464 | $R_1$ = 0.0575, $wR_2$ = 0.1480 |
| Final *R* indexes [all data] | $R_1$ = 0.0798, $wR_2$ = 0.1718 | $R_1$ = 0.0821, $wR_2$ = 0.1707 |
| Largest diff. peak/hole / e Å$^{-3}$ | 0.15/-0.19 | 0.18/-0.14 |
| Flack parameter | -0.04(16) | -0.2(3) |
| CCDC No. | 2377057 | 2377056 |

**Table S2 Bond Lengths for *N*-lauroyl-(*S*)-alanine (*S*)- and (*R*)- nornicotine salts**.

| ***N*-lauroyl-(*S*)-alanine (*S*)-nornicotine** | | | ***N*-lauroyl-(*S*)-alanine (*R*)-nornicotine** | | |
|---|---|---|---|---|---|
| O1 | C1 | 1.259(4) | O1 | C1 | 1.272(5) |
| O2 | C1 | 1.225(4) | O2 | C1 | 1.225(5) |
| O3 | C4 | 1.227(4) | O3 | C4 | 1.225(4) |
| N1 | C19 | 1.503(4) | N1 | C19 | 1.497(6) |
| N1 | C16 | 1.487(5) | N1 | C16 | 1.501(6) |
| N2 | C21 | 1.331(7) | N2 | C21 | 1.334(7) |
| N2 | C22 | 1.318(8) | N2 | C22 | 1.294(10) |
| N3 | C2 | 1.444(5) | N3 | C2 | 1.455(4) |
| N3 | C4 | 1.344(5) | N3 | C4 | 1.337(5) |
| C1 | C2 | 1.519(4) | C1 | C2 | 1.514(5) |
| C2 | C3 | 1.510(6) | C2 | C3 | 1.525(5) |
| C4 | C5 | 1.513(5) | C4 | C5 | 1.506(5) |
| C5 | C6 | 1.487(5) | C5 | C6 | 1.493(5) |
| C6 | C7 | 1.516(6) | C6 | C7 | 1.504(5) |
| C7 | C8 | 1.505(6) | C7 | C8 | 1.497(5) |
| C8 | C9 | 1.506(7) | C8 | C9 | 1.516(5) |
| C9 | C10 | 1.510(6) | C9 | C10 | 1.496(5) |
| C10 | C11 | 1.505(7) | C10 | C11 | 1.503(5) |
| C11 | C12 | 1.495(7) | C11 | C12 | 1.485(6) |
| C12 | C13 | 1.518(8) | C12 | C13 | 1.522(6) |
| C13 | C14 | 1.444(8) | C13 | C14 | 1.450(7) |
| C14 | C15 | 1.498(9) | C14 | C15 | 1.521(7) |
| C16 | C17 | 1.525(6) | C16 | C17 | 1.483(7) |
| C17 | C18 | 1.519(6) | C17 | C18 | 1.491(8) |
| C18 | C19 | 1.519(5) | C18 | C19 | 1.496(7) |
| C19 | C20 | 1.492(5) | C19 | C20 | 1.503(7) |
| C20 | C21 | 1.389(5) | C20 | C21 | 1.355(7) |
| C20 | C24 | 1.387(6) | C20 | C24 | 1.359(8) |
| C22 | C23 | 1.383(8) | C24 | C23 | 1.393(11) |
| C23 | C24 | 1.364(7) | C23 | C22 | 1.348(12) |

**Table S3 Bond Angles for *N*-lauroyl-*S*-alanine (*S*)- and (*R*)- nornicotine salts**.

| ***N*-lauroyl-*S*-alanine (*R*)-nornicotine** | | | | ***N*-lauroyl-*S*-alanine (*S*)-nornicotine** | | | |
|---|---|---|---|---|---|---|---|
| O1 | C1 | O2 | 122.1(3) | O1 | C1 | O2 | 122.8(4) |
| O1 | C1 | C2 | 118.3(2) | O1 | C1 | C2 | 116.4(4) |
| O2 | C1 | C2 | 119.3(3) | O2 | C1 | C2 | 120.8(3) |
| O3 | C4 | N3 | 122.1(4) | O3 | C4 | N3 | 122.6(4) |
| O3 | C4 | C5 | 121.9(3) | O3 | C4 | C5 | 122.5(4) |
| N1 | C16 | C17 | 105.3(3) | N1 | C16 | C17 | 106.4(4) |
| N1 | C19 | C18 | 101.9(3) | N1 | C19 | C18 | 103.0(4) |
| N1 | C19 | C20 | 112.5(3) | N1 | C19 | C20 | 114.0(4) |
| N2 | C21 | C20 | 125.6(5) | N2 | C21 | C20 | 125.5(6) |
| N2 | C22 | C23 | 124.5(5) | N2 | C22 | C23 | 123.7(8) |
| N3 | C2 | C1 | 109.6(3) | N3 | C2 | C1 | 110.1(3) |
| N3 | C2 | C3 | 112.4(3) | N3 | C2 | C3 | 111.6(3) |
| N3 | C4 | C5 | 115.8(3) | N3 | C4 | C5 | 114.8(3) |
| C1 | C2 | C3 | 109.3(3) | C1 | C2 | C3 | 109.7(4) |
| C2 | N3 | C4 | 122.2(3) | C2 | N3 | C4 | 122.8(3) |
| C4 | C5 | C6 | 114.3(3) | C4 | C5 | C6 | 115.8(3) |
| C5 | C6 | C7 | 113.8(4) | C5 | C6 | C7 | 113.5(3) |
| C6 | C7 | C8 | 115.0(4) | C6 | C7 | C8 | 116.1(4) |
| C7 | C8 | C9 | 114.9(4) | C7 | C8 | C9 | 114.8(4) |
| C8 | C9 | C10 | 115.1(4) | C8 | C9 | C10 | 116.0(4) |
| C9 | C10 | C11 | 114.6(5) | C9 | C10 | C11 | 114.9(4) |
| C10 | C11 | C12 | 116.1(5) | C10 | C11 | C12 | 116.5(4) |
| C11 | C12 | C13 | 114.6(5) | C11 | C12 | C13 | 115.0(5) |
| C12 | C13 | C14 | 117.2(6) | C12 | C13 | C14 | 115.0(5) |
| C13 | C14 | C15 | 114.0(7) | C13 | C14 | C15 | 114.2(6) |
| C16 | C17 | C18 | 106.0(3) | C16 | C17 | C18 | 106.8(4) |
| C16 | N1 | C19 | 105.6(3) | C16 | N1 | C19 | 105.1(4) |
| C17 | C18 | C19 | 105.5(3) | C17 | C18 | C19 | 106.6(5) |
| C19 | C20 | C21 | 120.2(4) | C19 | C20 | C21 | 125.6(5) |
| C19 | C20 | C24 | 123.2(3) | C19 | C20 | C24 | 117.3(6) |
| C20 | C19 | C18 | 117.8(3) | C20 | C19 | C18 | 117.1(5) |
| C20 | C24 | C23 | 119.3(4) | C20 | C24 | C23 | 118.2(8) |
| C21 | C20 | C24 | 116.5(4) | C21 | C20 | C24 | 117.1(6) |
| C21 | N2 | C22 | 115.4(5) | C21 | N2 | C22 | 116.2(7) |
| C22 | C23 | C24 | 118.7(5) | C22 | C23 | C24 | 119.3(7) |

**Table S4 Torsion Angles for *N*-lauroyl-*S*-alanine (*S*)- and (*R*)- nornicotine salts.**

| ***N*-lauroyl-*S*-alanine (*S*)-nornicotine** | | | | | ***N*-lauroyl-*S*-alanine (*R*)-nornicotine** | | | | |
|---|---|---|---|---|---|---|---|---|---|
| O1 | C1 | C2 | N3 | 159.2(3) | O1 | C1 | C2 | N3 | 171.2(3) |
| O1 | C1 | C2 | C3 | -77.1(4) | O1 | C1 | C2 | C3 | -65.6(5) |
| O2 | C1 | C2 | N3 | -26.2(5) | O2 | C1 | C2 | N3 | -10.8(5) |
| O2 | C1 | C2 | C3 | 97.5(4) | O2 | C1 | C2 | C3 | 112.4(5) |
| O3 | C4 | C5 | C6 | -31.5(6) | O3 | C4 | C5 | C6 | -26.3(7) |
| N1 | C16 | C17 | C18 | 8.2(4) | N1 | C16 | C17 | C18 | -6.4(7) |
| N1 | C19 | C18 | C17 | -34.4(4) | N1 | C19 | C18 | C17 | 31.0(6) |
| N1 | C19 | C20 | C21 | 117.9(3) | N1 | C19 | C20 | C21 | 38.0(7) |
| N1 | C19 | C20 | C24 | -64.2(4) | N1 | C19 | C20 | C24 | -145.0(6) |
| N2 | C21 | C20 | C24 | 0.5(6) | N2 | C21 | C20 | C24 | 2.5(10) |
| N2 | C21 | C20 | C19 | 178.4(4) | N2 | C21 | C20 | C19 | 179.5(6) |
| N2 | C22 | C23 | C24 | -0.6(9) | N2 | C22 | C23 | C24 | 0.5(16) |
| N3 | C4 | C5 | C6 | 152.7(4) | N3 | C4 | C5 | C6 | 157.6(4) |
| C2 | N3 | C4 | O3 | 0.4(6) | C2 | N3 | C4 | O3 | -4.3(7) |
| C2 | N3 | C4 | C5 | 176.2(3) | C2 | N3 | C4 | C5 | 171.8(4) |
| C4 | N3 | C2 | C1 | -158.2(3) | C4 | N3 | C2 | C1 | -141.7(4) |
| C4 | N3 | C2 | C3 | 80.0(5) | C4 | N3 | C2 | C3 | 96.2(5) |
| C4 | C5 | C6 | C7 | 174.7(4) | C4 | C5 | C6 | C7 | 172.3(4) |
| C5 | C6 | C7 | C8 | -179.4(4) | C5 | C6 | C7 | C8 | -179.9(4) |
| C6 | C7 | C8 | C9 | 177.2(4) | C6 | C7 | C8 | C9 | 176.2(4) |
| C7 | C8 | C9 | C10 | 179.4(5) | C7 | C8 | C9 | C10 | 178.5(4) |
| C8 | C9 | C10 | C11 | 178.3(5) | C8 | C9 | C10 | C11 | 177.6(4) |
| C9 | C10 | C11 | C12 | -177.7(5) | C9 | C10 | C11 | C12 | -179.6(4) |
| C10 | C11 | C12 | C13 | 174.5(5) | C10 | C11 | C12 | C13 | 177.0(4) |
| C11 | C12 | C13 | C14 | -175.5(6) | C11 | C12 | C13 | C14 | -178.0(5) |
| C12 | C13 | C14 | C15 | 175.0(6) | C12 | C13 | C14 | C15 | 178.8(5) |
| C16 | N1 | C19 | C18 | 40.2(3) | C16 | N1 | C19 | C20 | -162.6(4) |
| C16 | N1 | C19 | C20 | 167.3(3) | C16 | N1 | C19 | C18 | -34.7(5) |
| C16 | C17 | C18 | C19 | 16.5(4) | C16 | C17 | C18 | C19 | -15.5(8) |
| C18 | C19 | C20 | C24 | 53.8(5) | C18 | C19 | C20 | C24 | 94.7(7) |
| C18 | C19 | C20 | C21 | -124.0(4) | C18 | C19 | C20 | C21 | -82.2(6) |
| C19 | N1 | C16 | C17 | -30.3(4) | C19 | N1 | C16 | C17 | 25.8(6) |
| C19 | C20 | C24 | C23 | -177.9(4) | C19 | C20 | C24 | C23 | -178.9(7) |
| C20 | C19 | C18 | C17 | -158.0(3) | C20 | C19 | C18 | C17 | 156.9(5) |
| C20 | C24 | C23 | C22 | 0.1(7) | C20 | C24 | C23 | C22 | 0.3(14) |
| C21 | N2 | C22 | C23 | 1.0(9) | C21 | N2 | C22 | C23 | 0.2(13) |
| C21 | C20 | C24 | C23 | 0.0(6) | C21 | C20 | C24 | C23 | -1.7(11) |
| C22 | N2 | C21 | C20 | -0.9(8) | C22 | N2 | C21 | C20 | -1.8(11) |

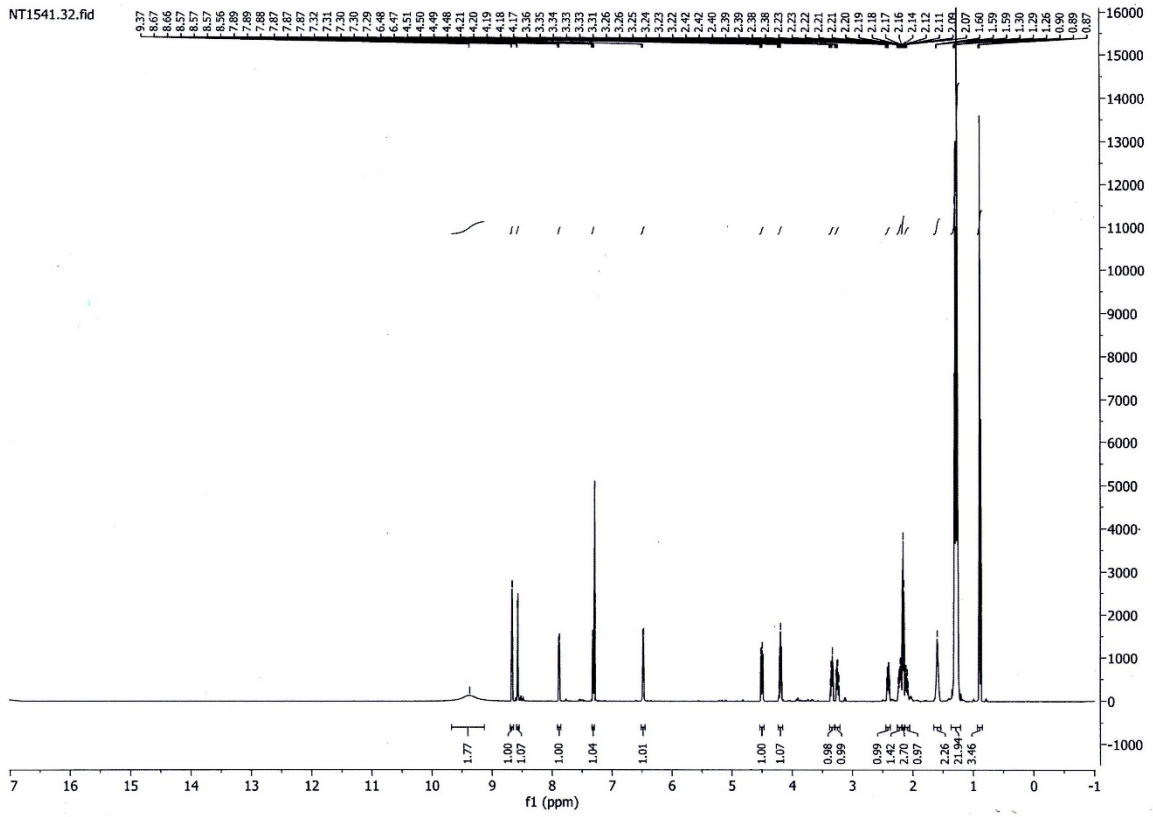



**Figure S3.** [1]H NMR spectrum of *N*-lauroyl-*(S)*-alanine•*(R)*-nornicotine salt

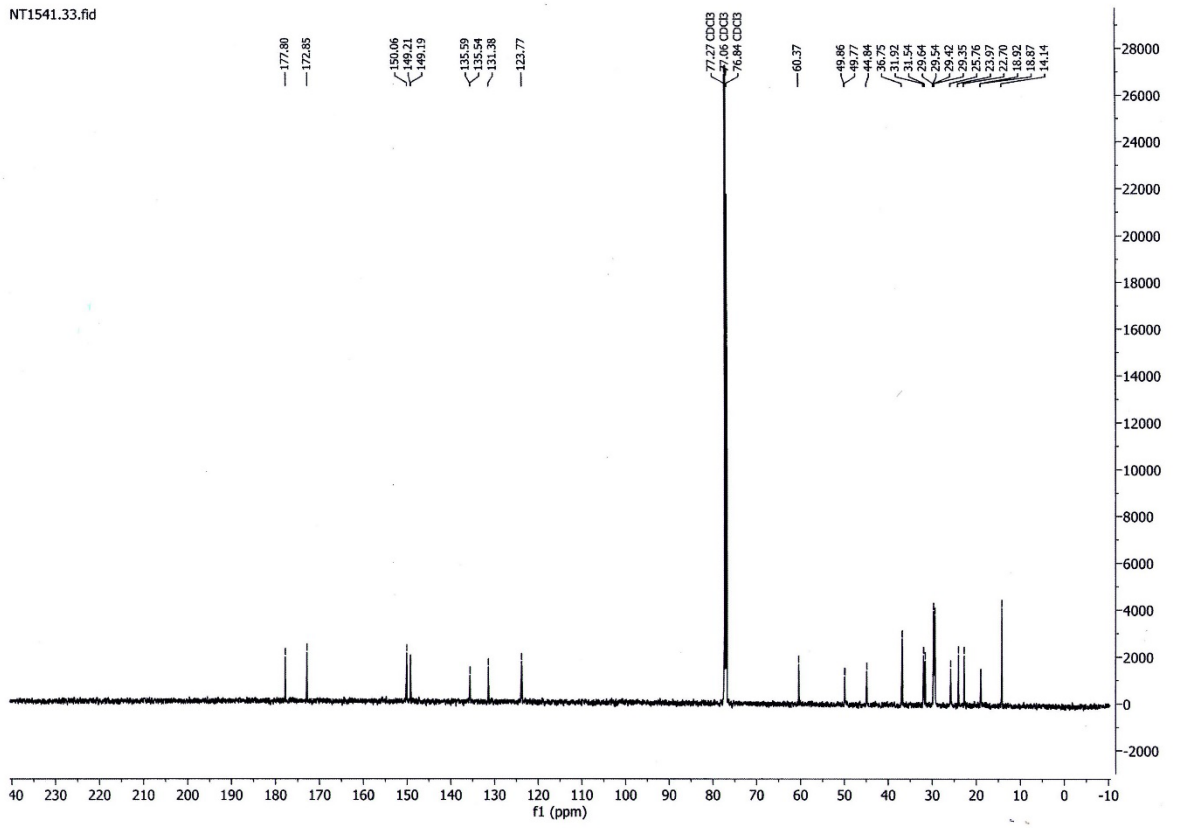



**Figure S4.** [13]C NMR spectrum of *N*-lauroyl-*(S)*-alanine•*(R)*-nornicotine salt

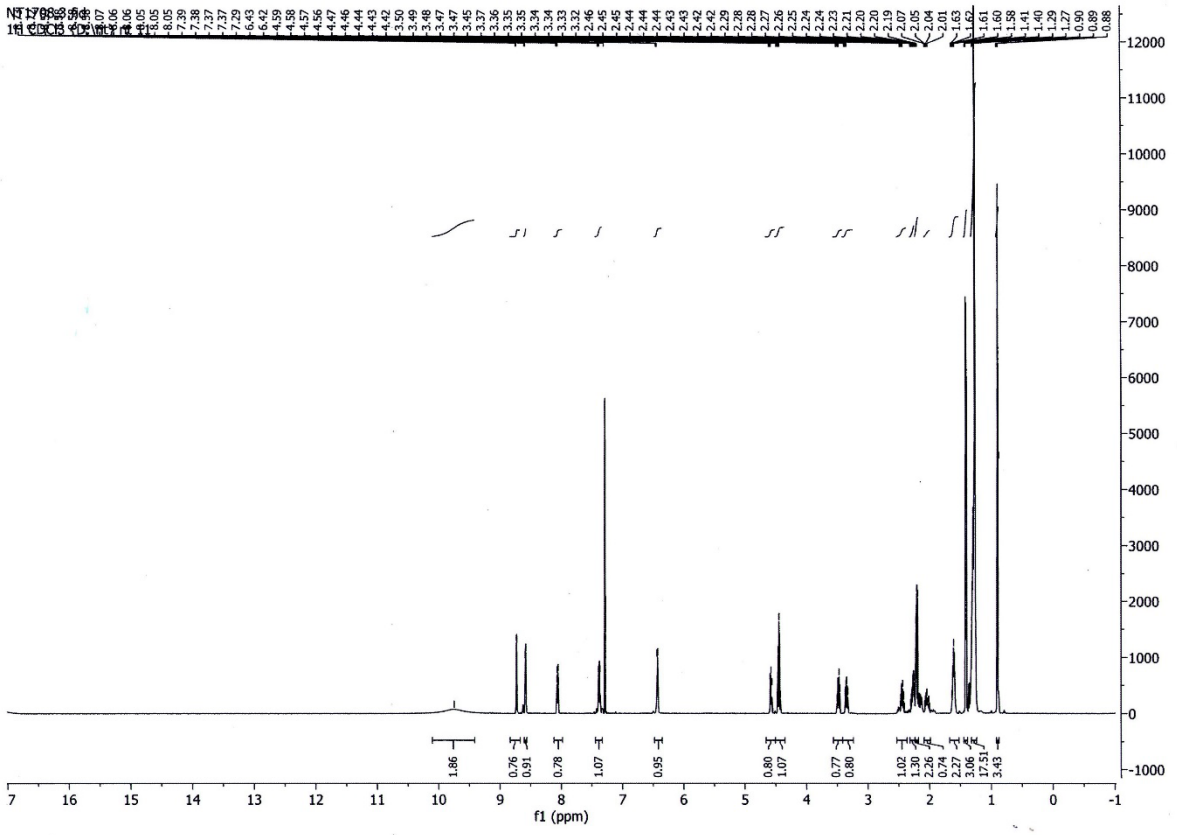



**Figure S5.** $^{1}$H NMR spectrum of *N*-lauroyl-*(R)*-alanine•*(S)*-nornicotine salt

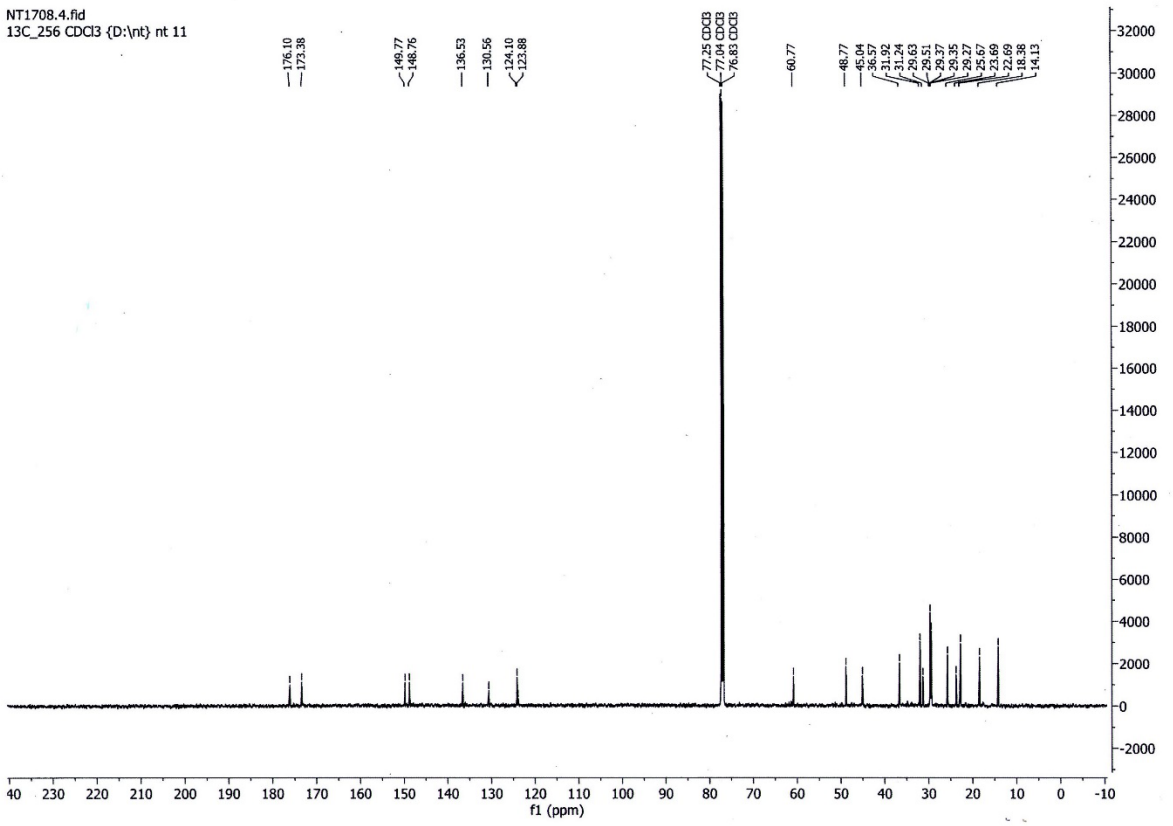



**Figure S6.** $^{13}$C NMR spectrum of *N*-lauroyl-*(R)*-alanine•*(S)*-nornicotine salt

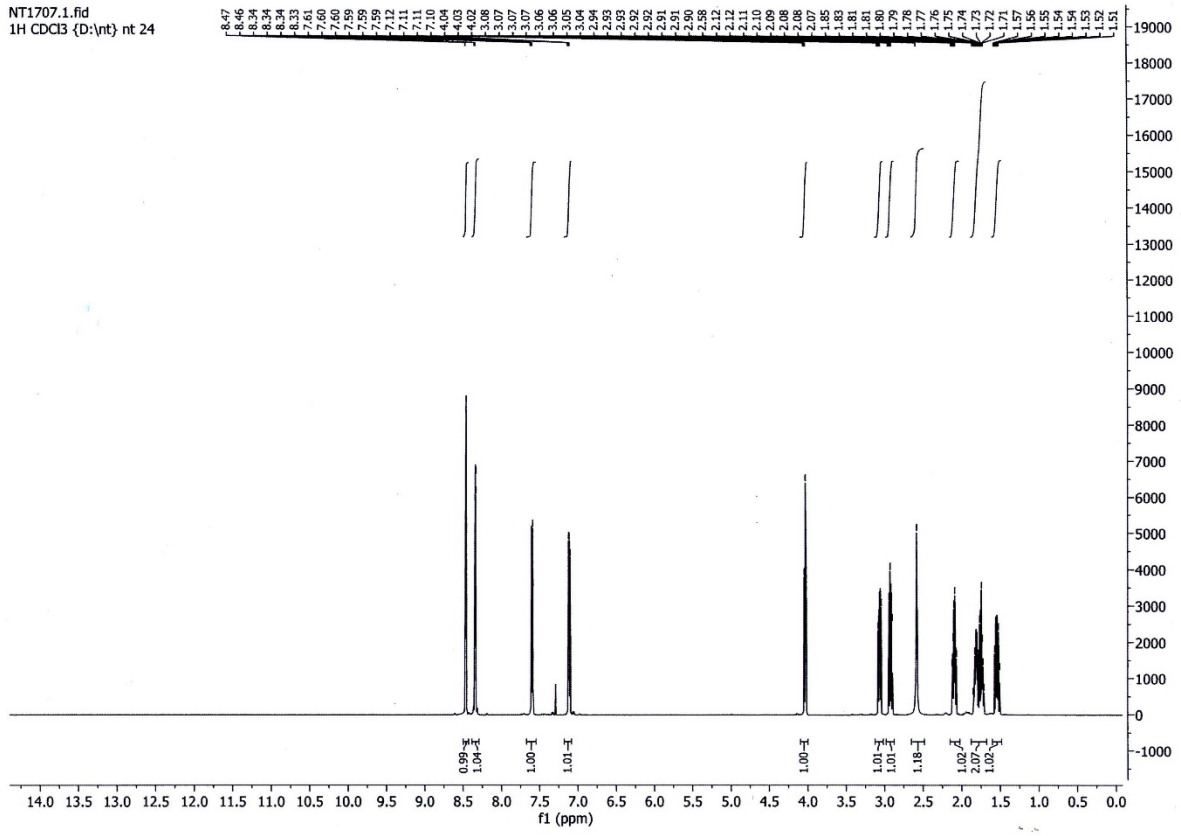



**Figure S7.** $^{1}$H NMR spectrum of (*R*)-nornicotine

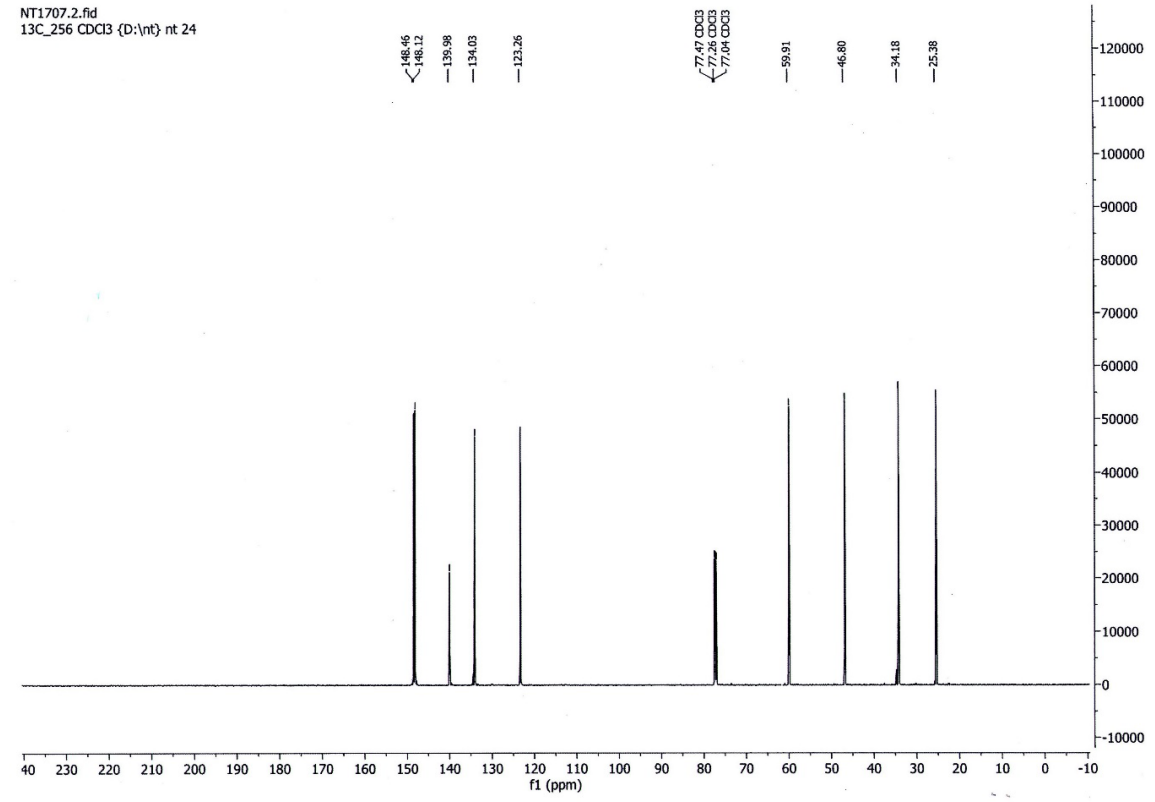



**Figure S8.** $^{13}$C NMR spectrum of (*R*)-nornicotine

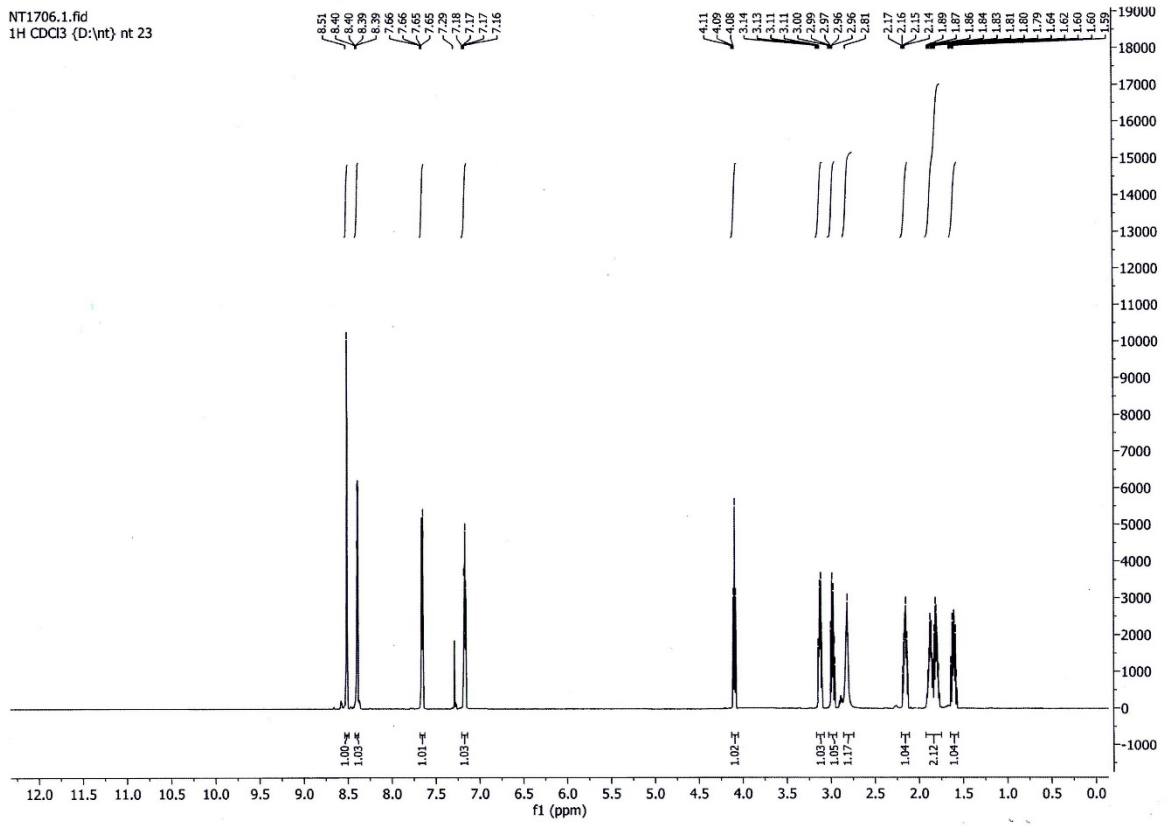



**Figure S9.** $^{1}$H NMR spectrum of (*S*)-nornicotine

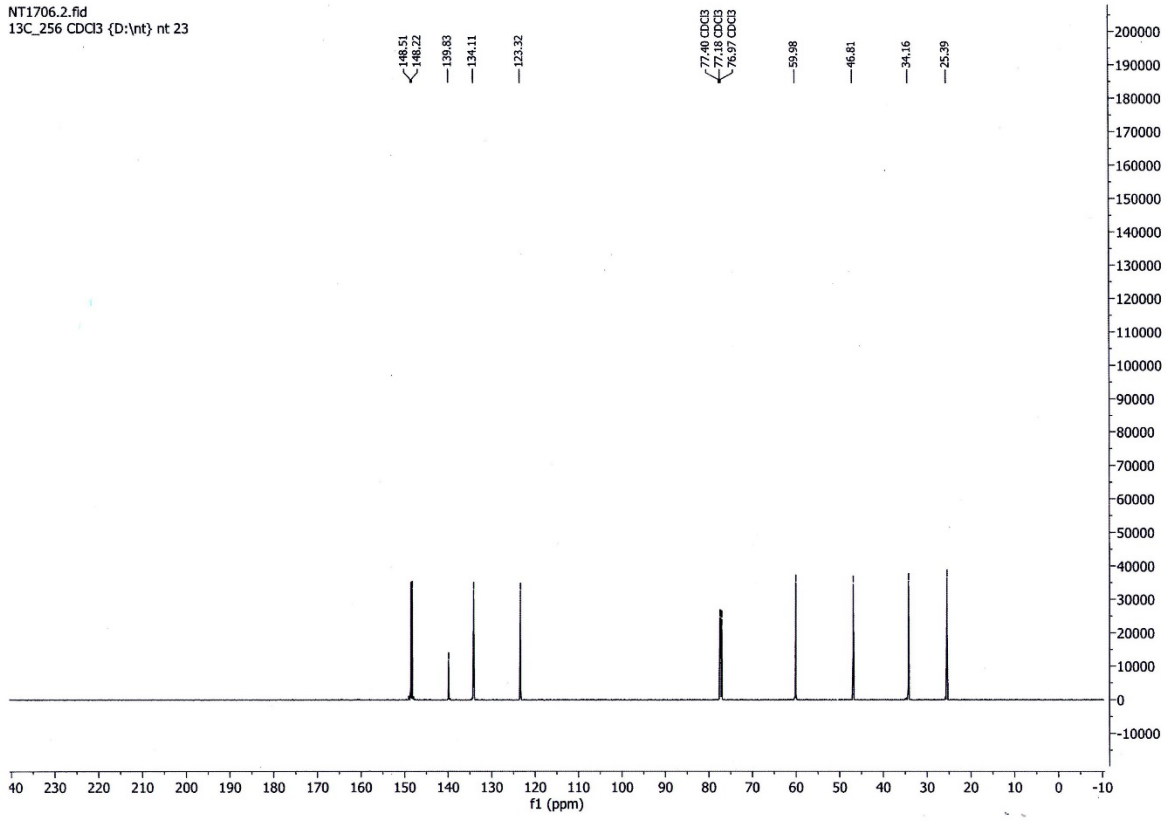



**Figure S10.** $^{13}$C NMR spectrum of (*S*)-nornicotine

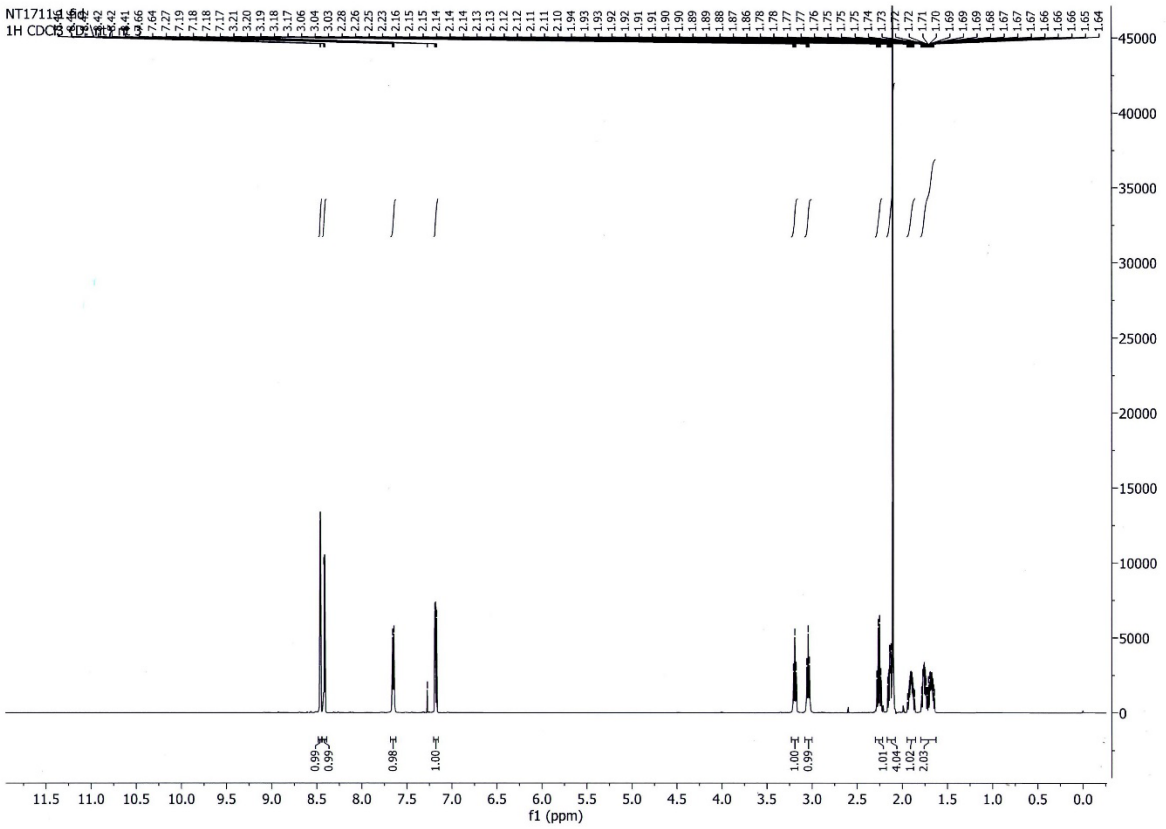



**Figure S11.** $^{1}$H NMR spectrum of (*S*)-nicotine

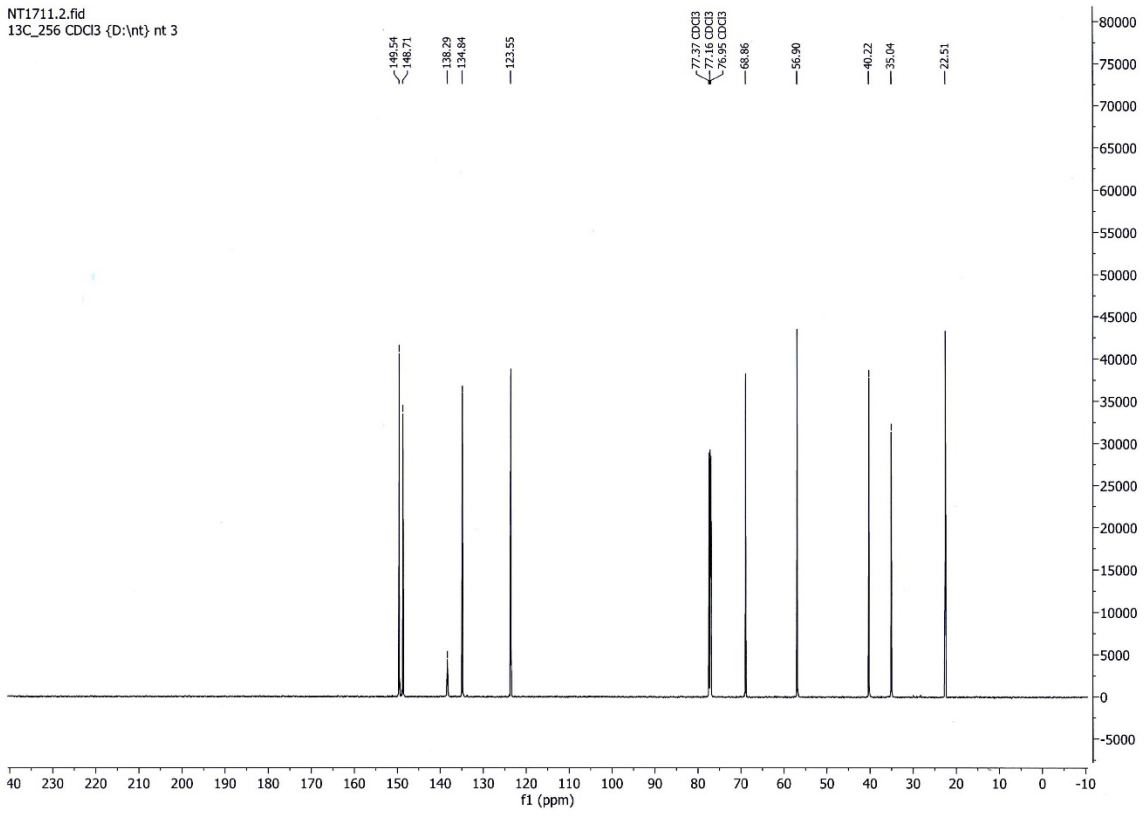



**Figure S12.** $^{13}$C NMR spectrum of (*S*)-nicotine

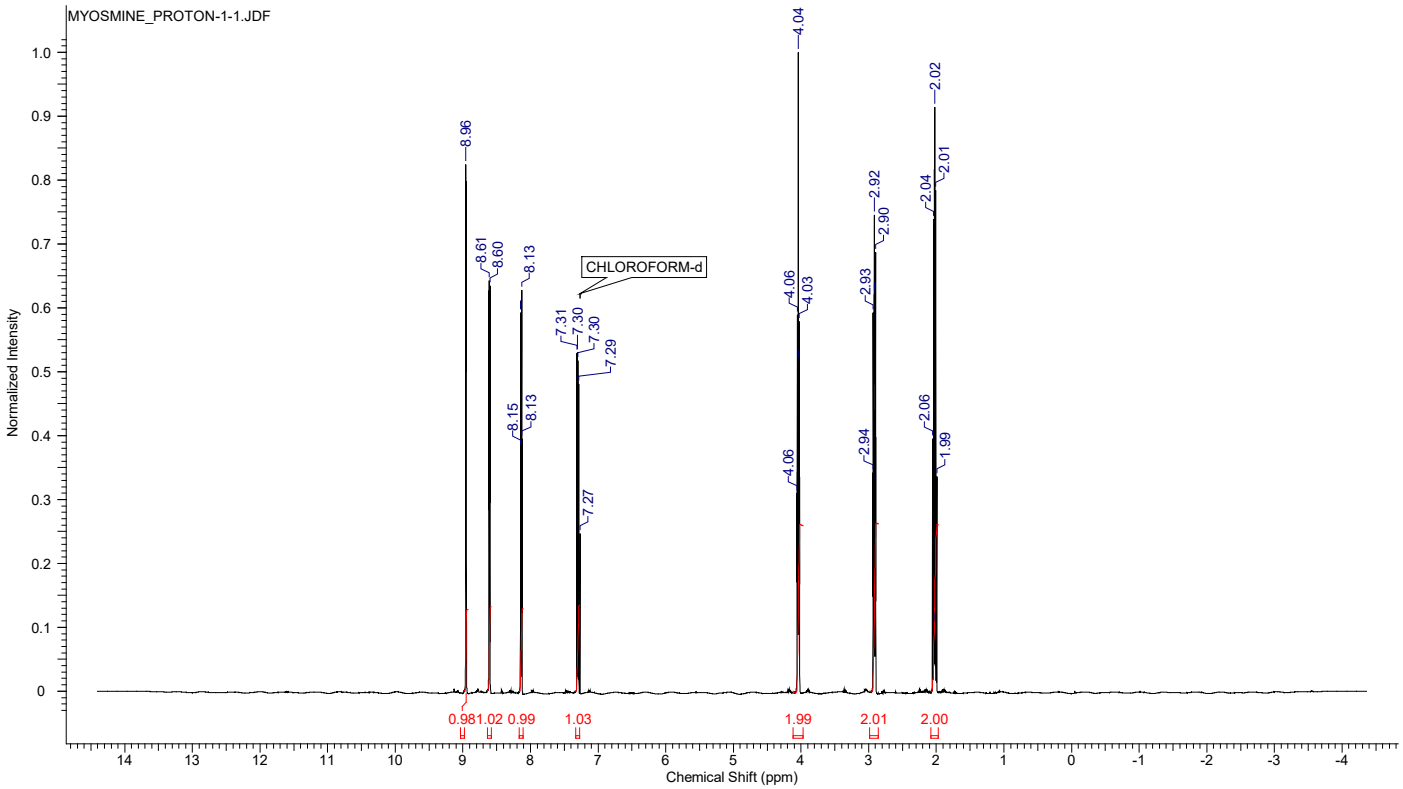



**Figure S13.** $^{1}$H NMR spectrum of myosmine

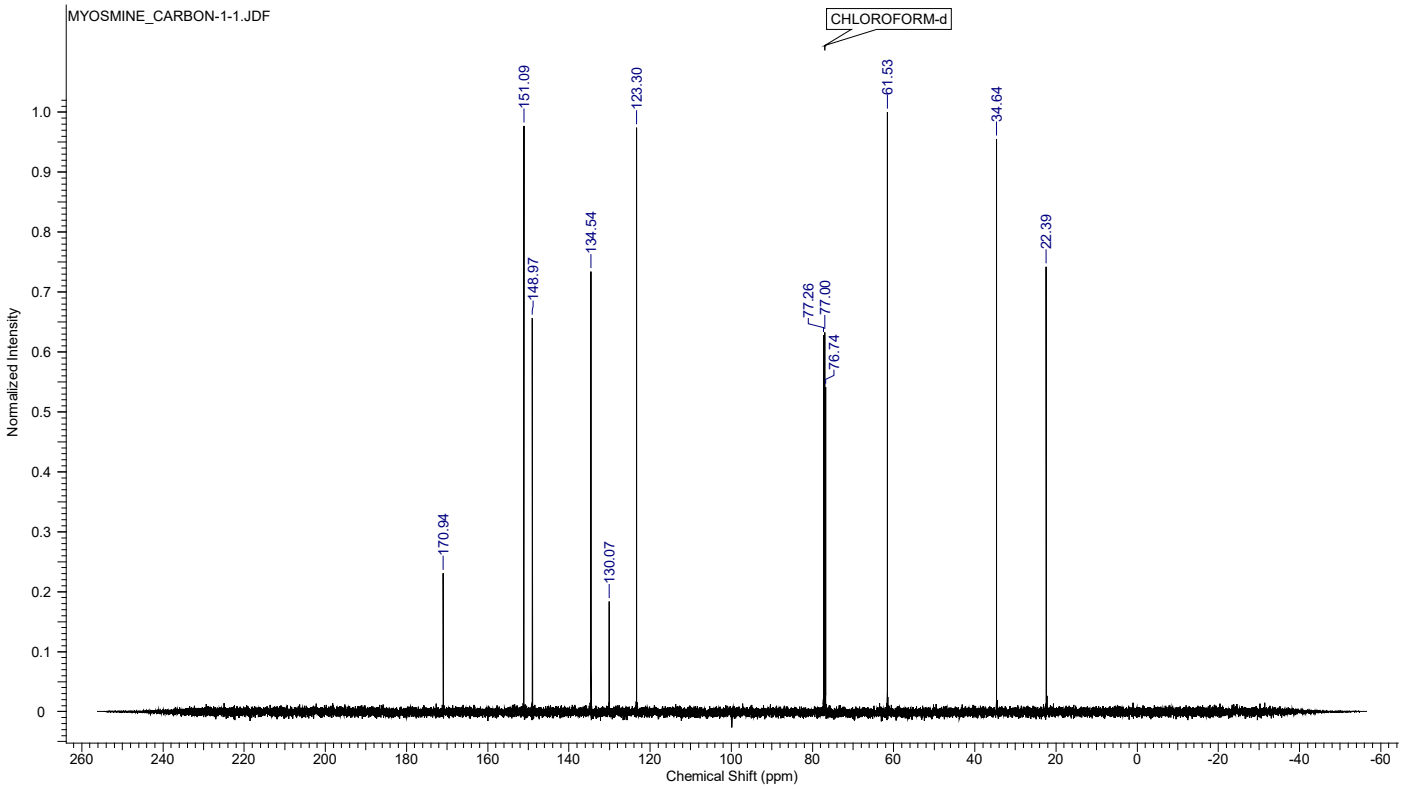
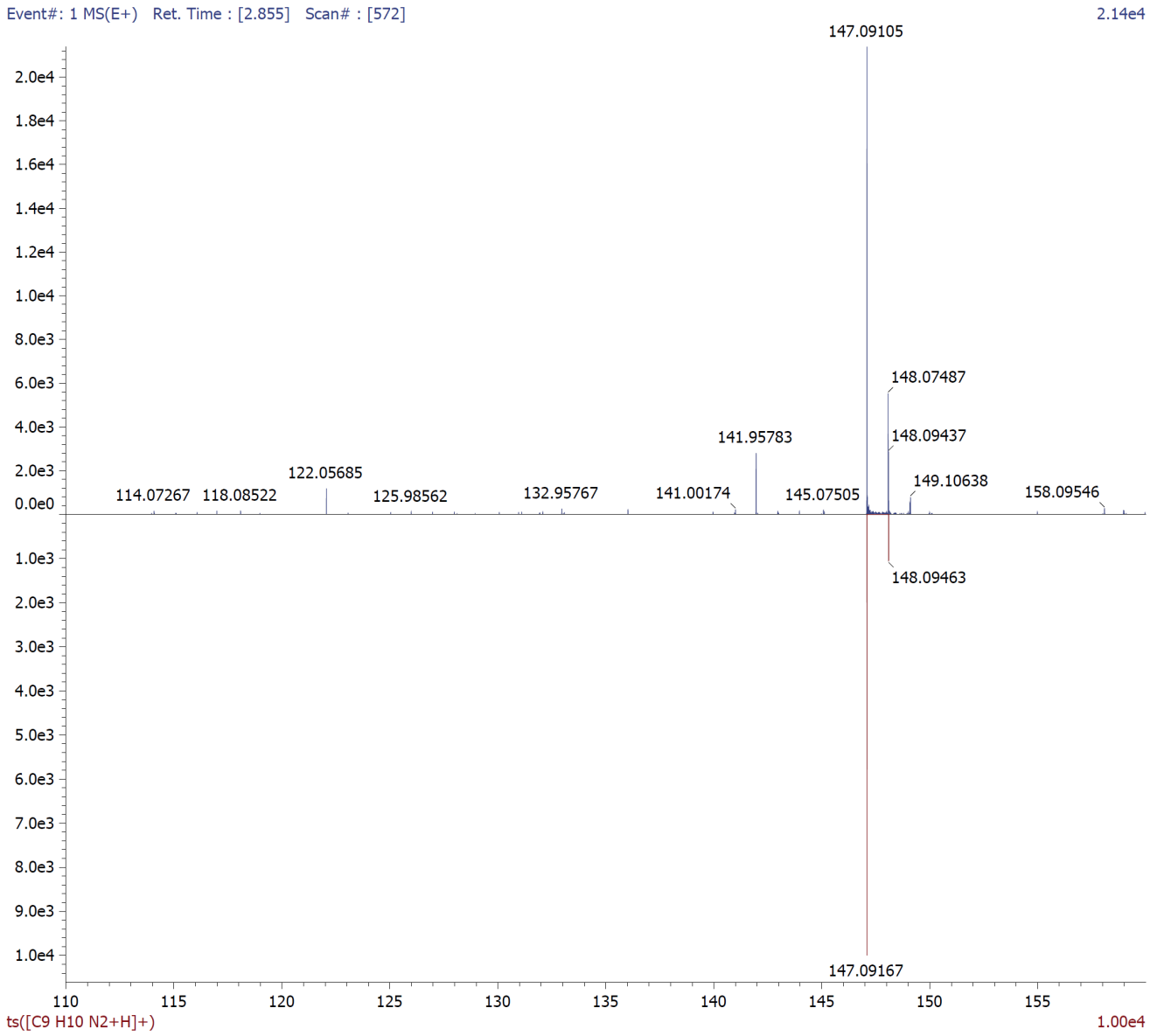



**Figure S14.** $^{13}$C NMR spectrum of myosmine

**Formula Predictor Report** **Printed at 08.11.2024 12:12:43**

| | |
|---|---|
| Formula Predictor Result | **C9 H10 N2** |
| Mass | 147.09105 |
| Error Margin | 30 ppm |
| DBE Range | Not Used |
| Electron Ions | Both configurations |
| HC Ratio | Not Used |
| Nitrogen Rule | Not Used |

| # | Score | Pred. (M) | Pred. m/z | Meas. m/z | Diff. (mDa) | Formulae (M) | Ion | Diff. (ppm) | Iso Score | DBE |
|---|---|---|---|---|---|---|---|---|---|---|
| 1 | 97.37 | 146.08440 | 147.09167 | 147.09105 | -0.62 | C9 H10 N2 | [M+H]+ | -4.248 | 97.08 | 6.0 |




**Page 1 of 1**

**Figure S15.** HRMS analysis of myosmine (Q-Tof)

# Formula Predictor Report

**Printed at 08.11.2024 12:14:08**

| | |
|---|---|
| Formula Predictor Result | **C9 H12 N2** |
| Mass | 149.10677 |
| Error Margin | 30 ppm |
| DBE Range | Not Used |
| Electron Ions | Both configurations |
| HC Ratio | Not Used |
| Nitrogen Rule | Not Used |

| # | Score | Pred. (M) | Pred. m/z | Meas. m/z | Diff. (mDa) | Formulae (M) | Ion | Diff. (ppm) | Iso Score | DBE |
|---|---|---|---|---|---|---|---|---|---|---|
| 1 | 88.95 | 148.10005 | 149.10732 | 149.10677 | -0.55 | C9 H12 N2 | [M+H]+ | -3.721 | 87.72 | 5.0 |

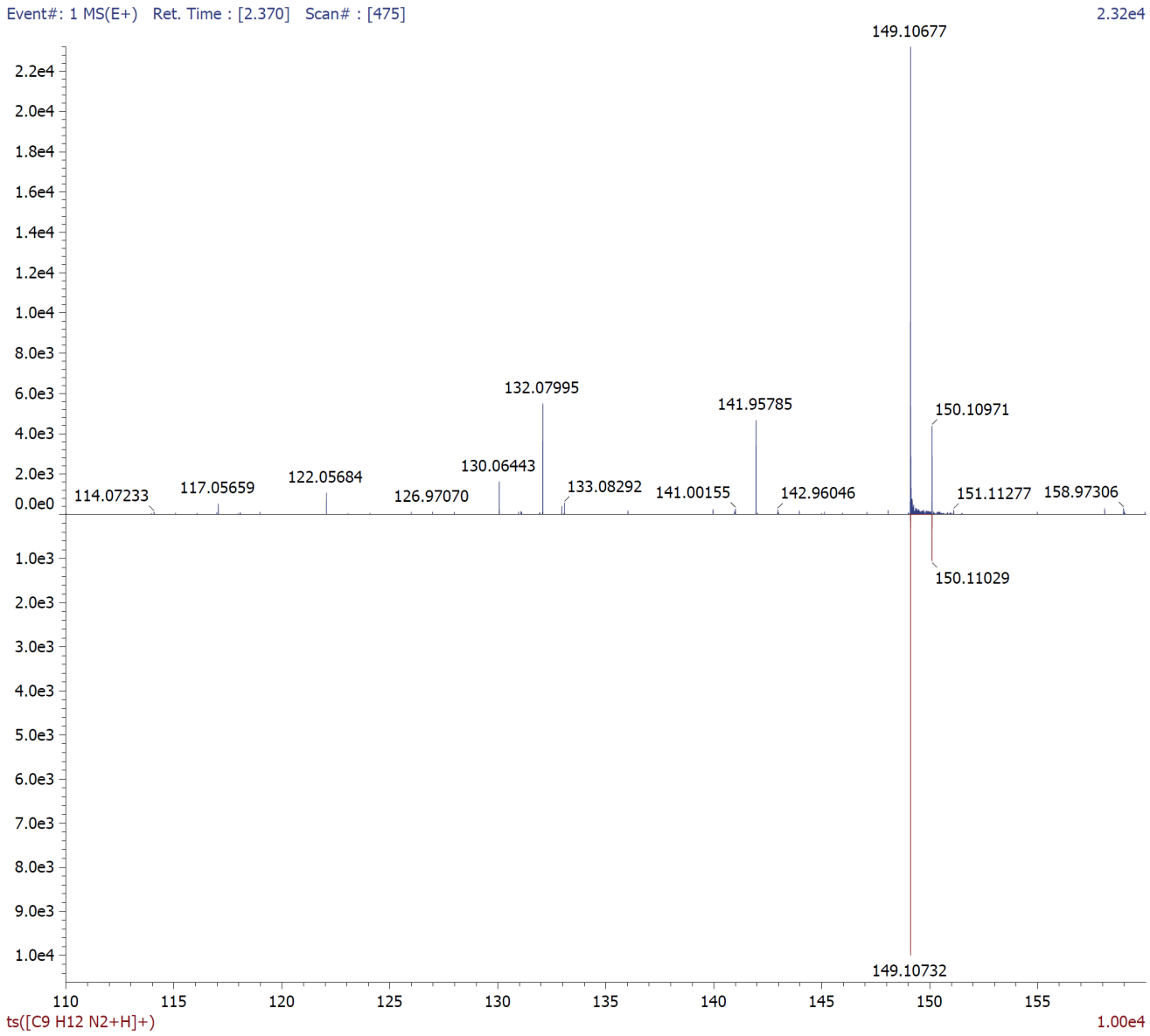


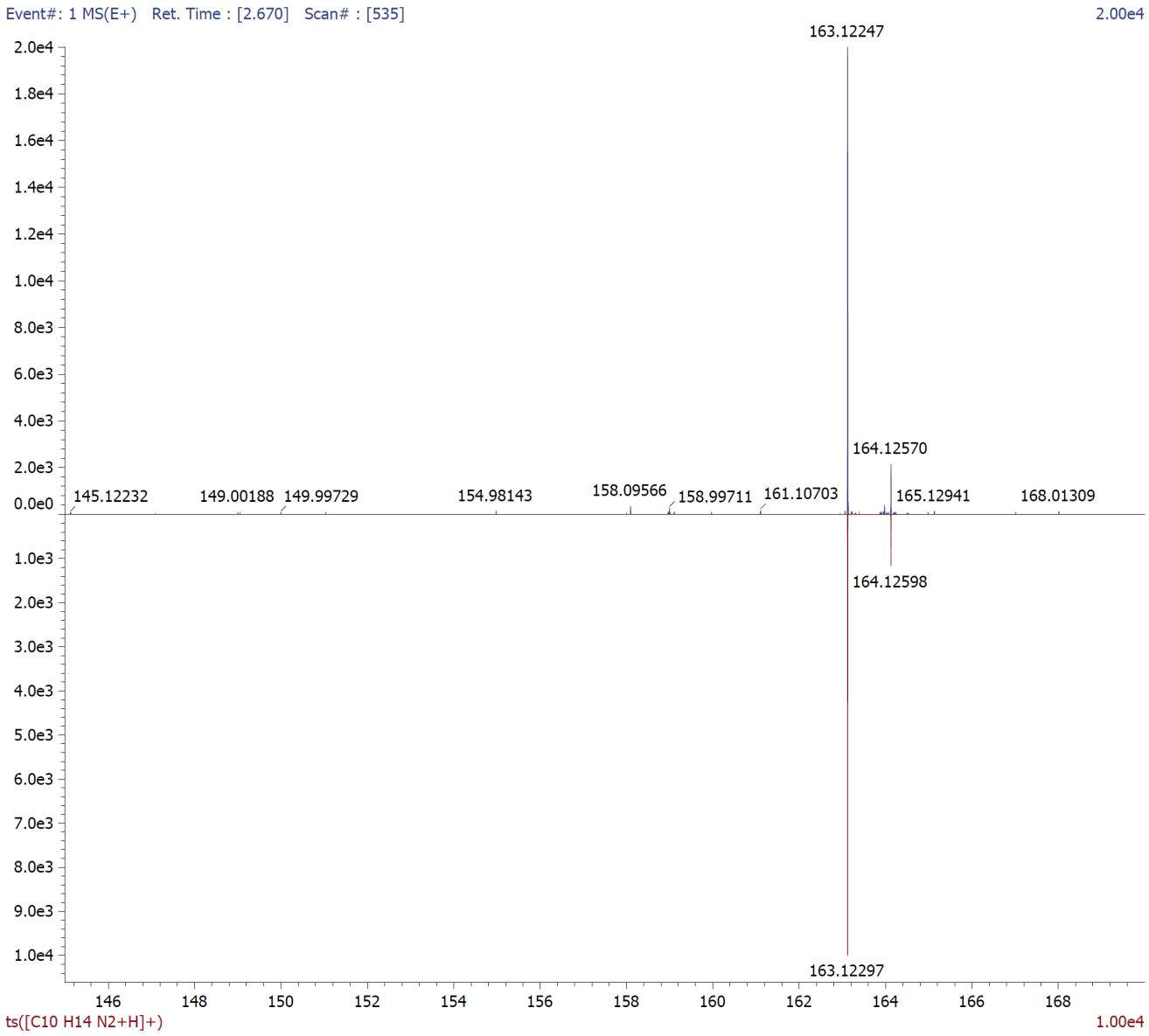



**Figure S16.** HRMS analysis of nornicotine (Q-Tof)

**Formula Predictor Report** **Printed at 08.11.2024 12:37:24**

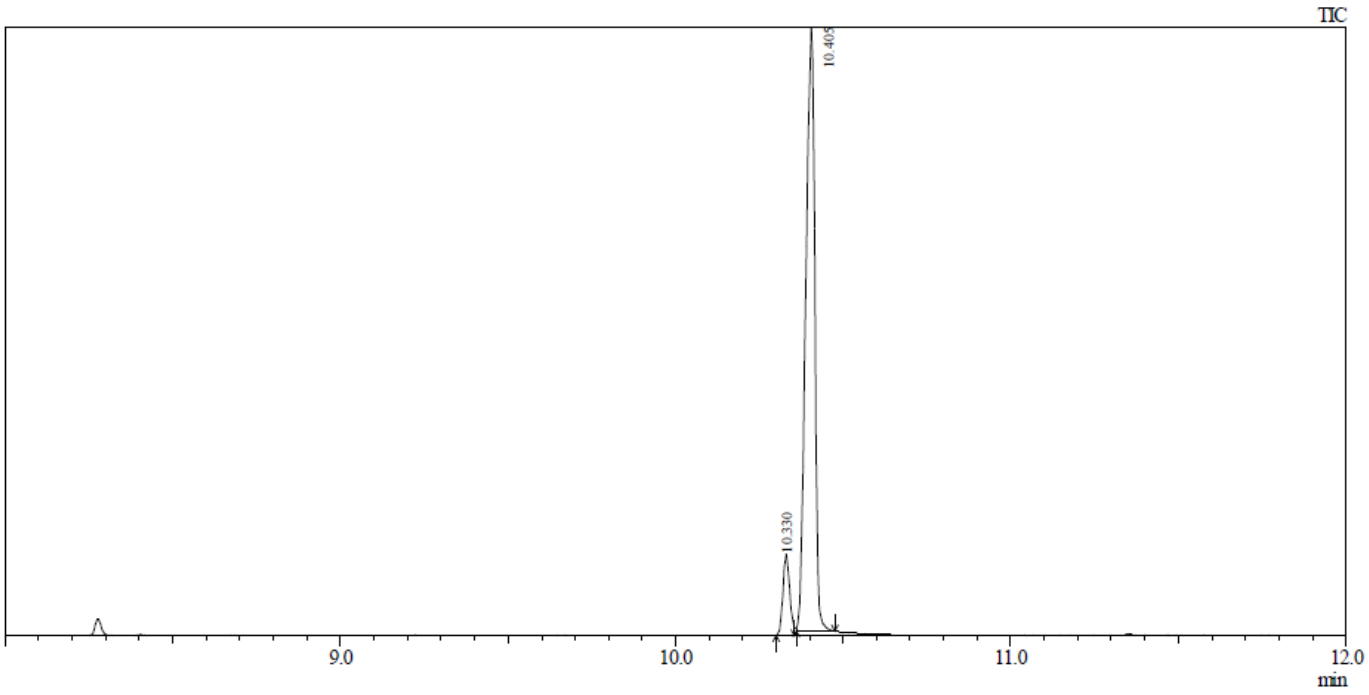
| | |
|---|---|
| Formula Predictor Result | **C10 H14 N2** |
| Mass | 163.12247 |
| Error Margin | 30 ppm |
| DBE Range | Not Used |
| Electron Ions | Both configurations |
| HC Ratio | Not Used |
| Nitrogen Rule | Not Used |

| # | Score | Pred. (M) | Pred. m/z | Meas. m/z | Diff. (mDa) | Formulae (M) | Ion | Diff. (ppm) | Iso Score | DBE |
|---|---|---|---|---|---|---|---|---|---|---|
| 1 | 98.16 | 162.11570 | 163.12297 | 163.12247 | -0.50 | C10 H14 N2 | [M+H]+ | -3.095 | 97.96 | 5.0 |




**Page 1 of 1**

**Figure S17.** HRMS analysis of nicotine (Q-Tof)

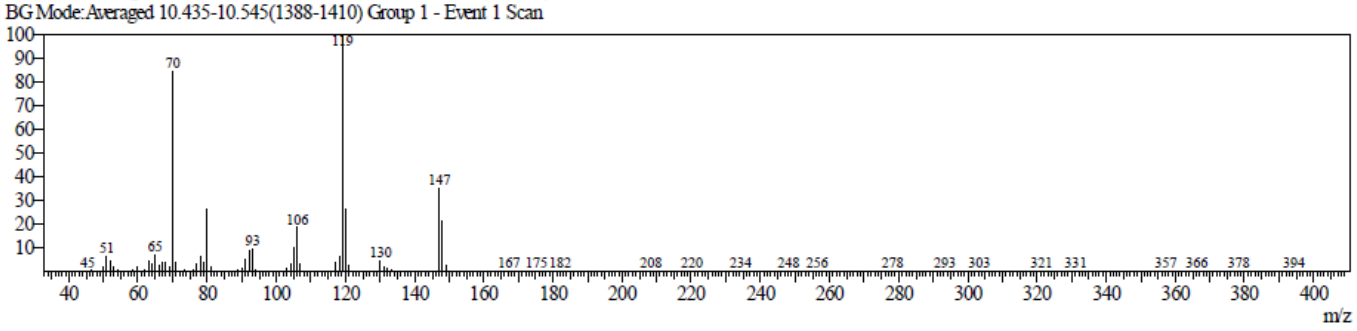



Peak Report TIC

| Peak# | R.Time | I.Time | F.Time | Area | Area% | Height | Height% | A/H | Mark | Name |
|---|---|---|---|---|---|---|---|---|---|---|
| 1 | 10.330 | 10.300 | 10.355 | 2753470 | 8.95 | 1971287 | 11.88 | 1.40 | MI | |
| 2 | 10.405 | 10.360 | 10.475 | 28018116 | 91.05 | 14619001 | 88.12 | 1.92 | MI | |
| | | | | 30771586 | 100.00 | 16590288 | 100.00 | | | |

Spectrum

Line#:1 R.Time:10.330(Scan#:1367)
MassPeaks:150
RawMode:Averaged 10.320-10.340(1365-1369) BasePeak:119(312170)
BG Mode:Averaged 10.435-10.545(1388-1410) Group 1 - Event 1 Scan




Line#:2 R.Time:10.400(Scan#:1381)
MassPeaks:254
RawMode:Averaged 10.395-10.405(1380-1382) BasePeak:118(3269964)
BG Mode:Averaged 10.725-10.955(1446-1492) Group 1 - Event 1 Scan

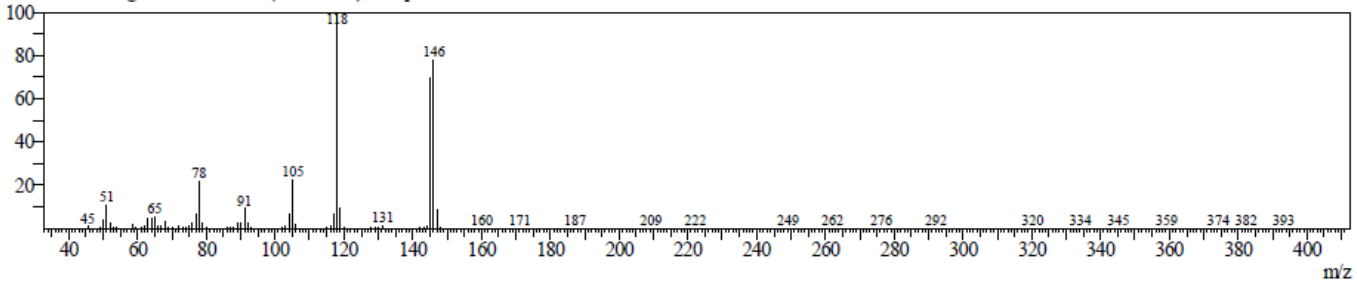
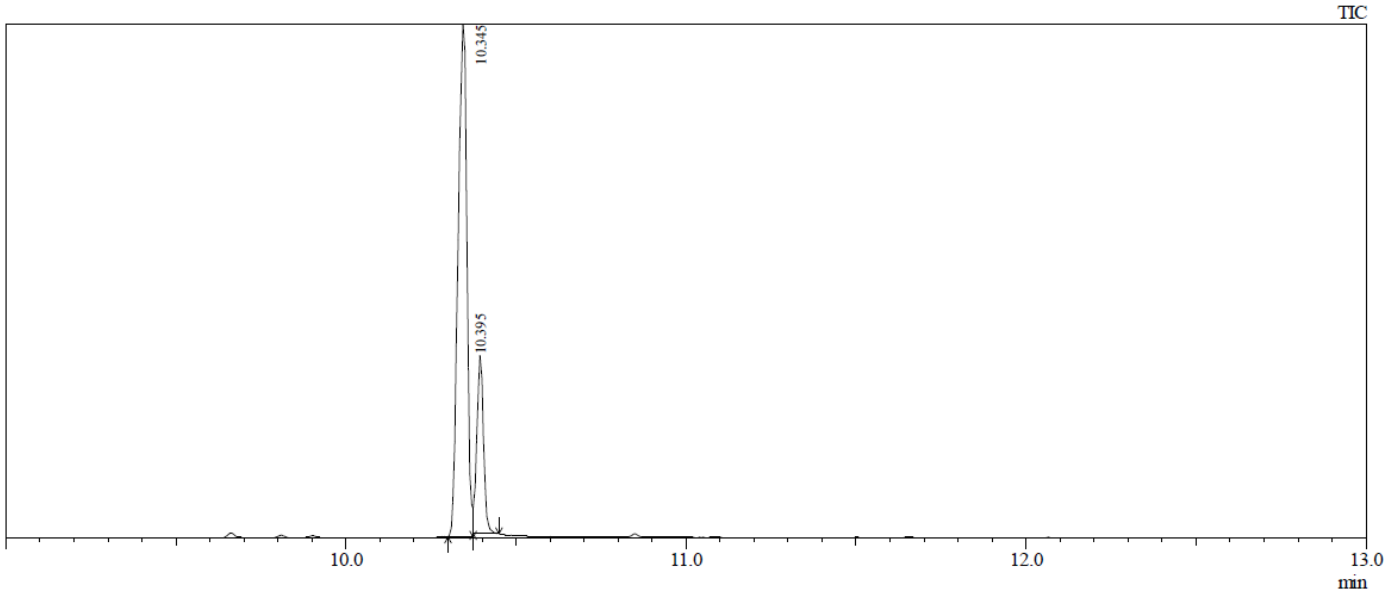



**Figure S18.** GCMS analysis of reaction mixture of incomplete oxidation of nornicotine to myosmine

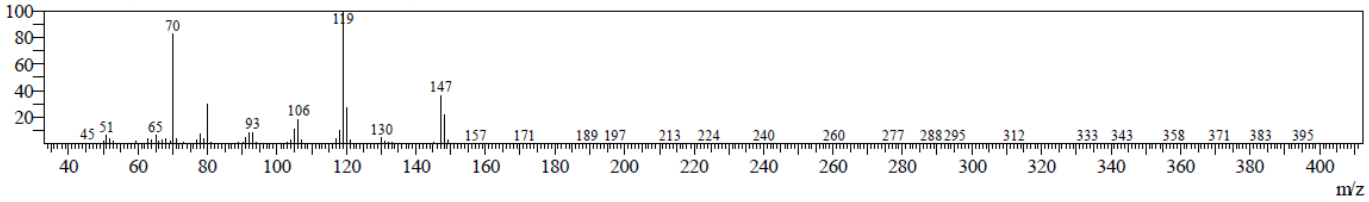



Peak Report TIC

| Peak# | R.Time | I.Time | F.Time | Area | Area% | Height | Height% | A/H | Mark | Name |
|---|---|---|---|---|---|---|---|---|---|---|
| 1 | 10.345 | 10.300 | 10.375 | 26456909 | 79.58 | 14494473 | 74.18 | 1.83 | MI | |
| 2 | 10.395 | 10.375 | 10.450 | 6788131 | 20.42 | 5045527 | 25.82 | 1.35 | MI | |
| | | | | 33245040 | 100.00 | 19540000 | 100.00 | | | |

Spectrum

Line#:1 R.Time:10.345(Scan#:1370)
MassPeaks:280
RawMode:Averaged 10.340-10.350(1369-1371) BasePeak:119(2962176)
BG Mode:Averaged 10.405-10.540(1382-1409) Group 1 - Event 1 Scan




Line#:2 R.Time:10.395(Scan#:1380)
MassPeaks:231
RawMode:Averaged 10.390-10.405(1379-1382) BasePeak:118(942120)
BG Mode:Averaged 10.265-10.320(1354-1365) Group 1 - Event 1 Scan

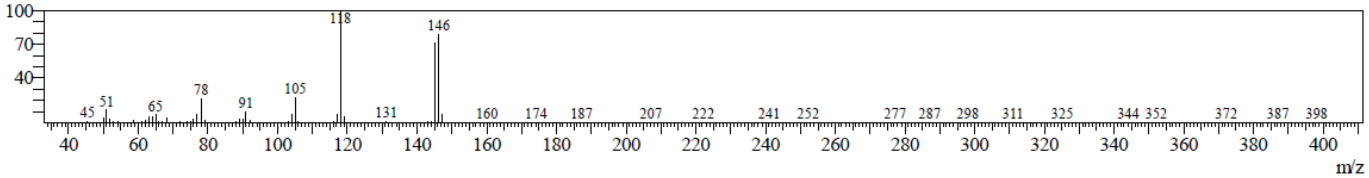
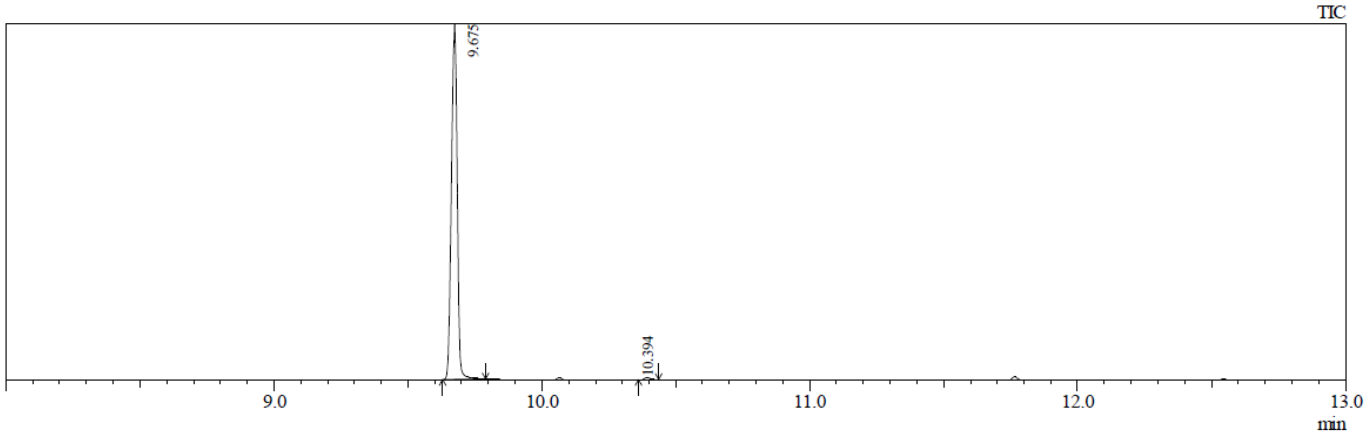



**Figure S19.** GCMS analysis of reaction mixture of incomplete reduction of myosmine

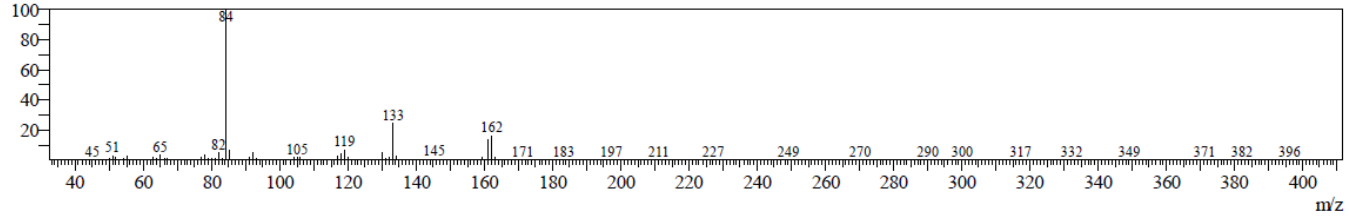



Peak Report TIC

| Peak# | R.Time | I.Time | F.Time | Area | Area% | Height | Height% | A/H | Mark | Name |
|---|---|---|---|---|---|---|---|---|---|---|
| 1 | 9.675 | 9.630 | 9.790 | 25469432 | 99.48 | 17000267 | 99.47 | 1.50 | | Pyridine, 3-(1-methyl-2-pyrrolidinyl)-, (S)- |
| 2 | 10.394 | 10.360 | 10.435 | 134116 | 0.52 | 91330 | 0.53 | 1.47 | | Pyridine, 3-(3,4-dihydro-2H-pyrrol-5-yl)- |
| | | | | 25603548 | 100.00 | 17091597 | 100.00 | | | |

Spectrum

Line#:1 R.Time:9.675(Scan#:1236)
MassPeaks:232
RawMode:Averaged 9.670-9.680(1235-1237) BasePeak:84(6588287)
BG Mode:Calc. from Peak Group 1 - Event 1 Scan




Line#:2 R.Time:10.395(Scan#:1380)
MassPeaks:217
RawMode:Averaged 10.390-10.400(1379-1381) BasePeak:118(20129)
BG Mode:Calc. from Peak Group 1 - Event 1 Scan

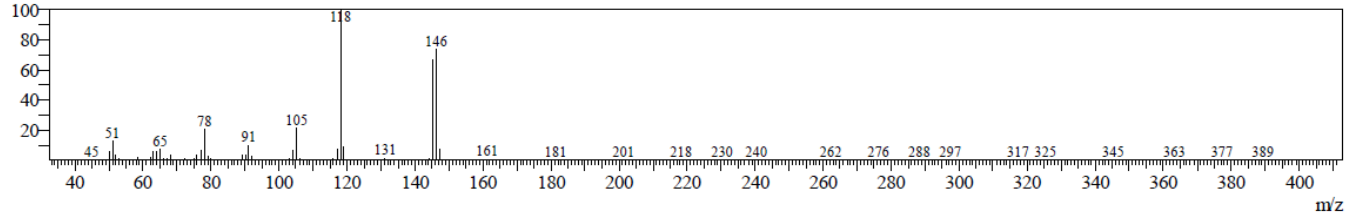



**Figure S20.** GCMS analysis of nicotine

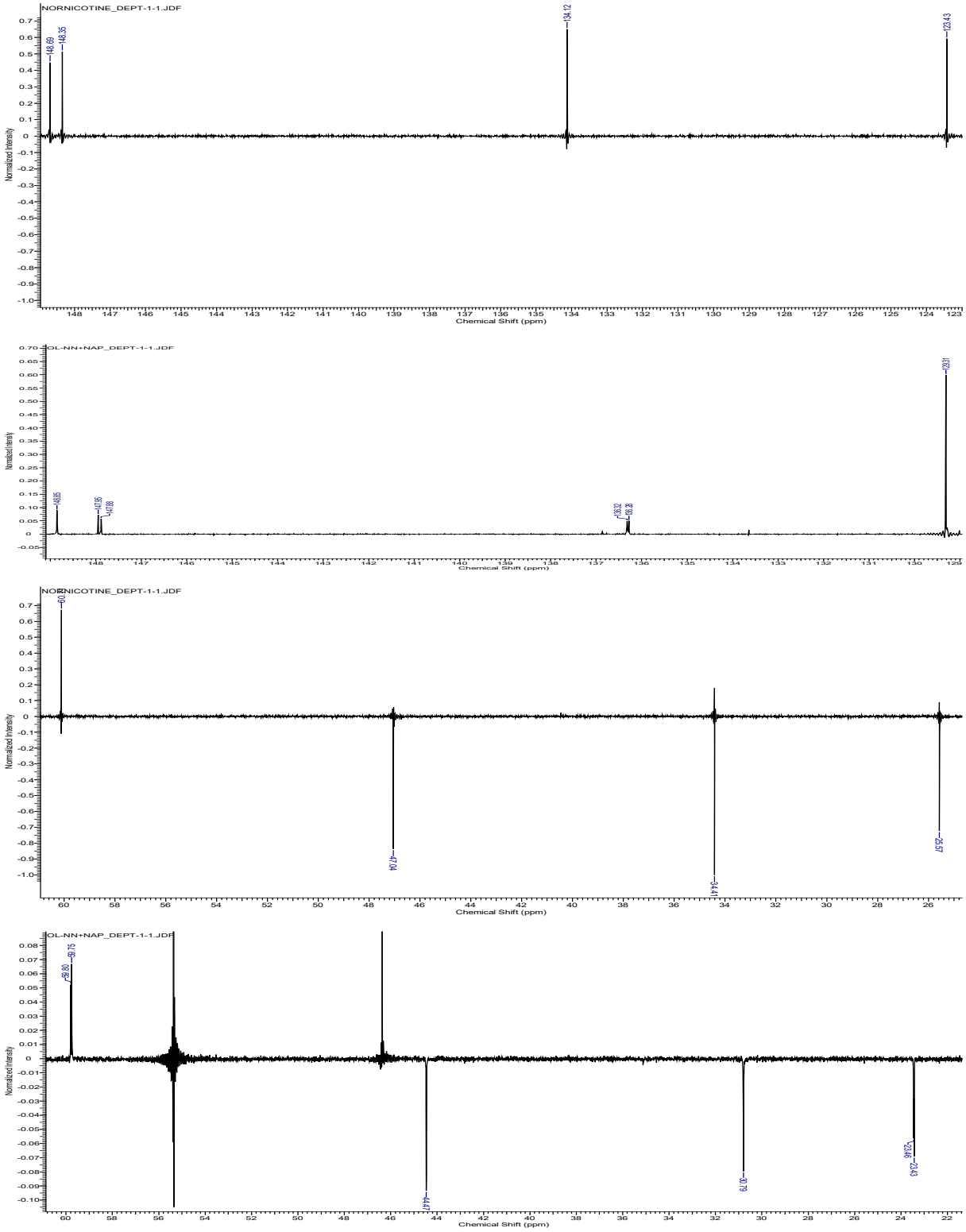



**Figure S21**. Comparision of charactiristic regions in DEPT135 spectra of rac-nornicotine and *rac*-nornicotine in the presence of naproxen

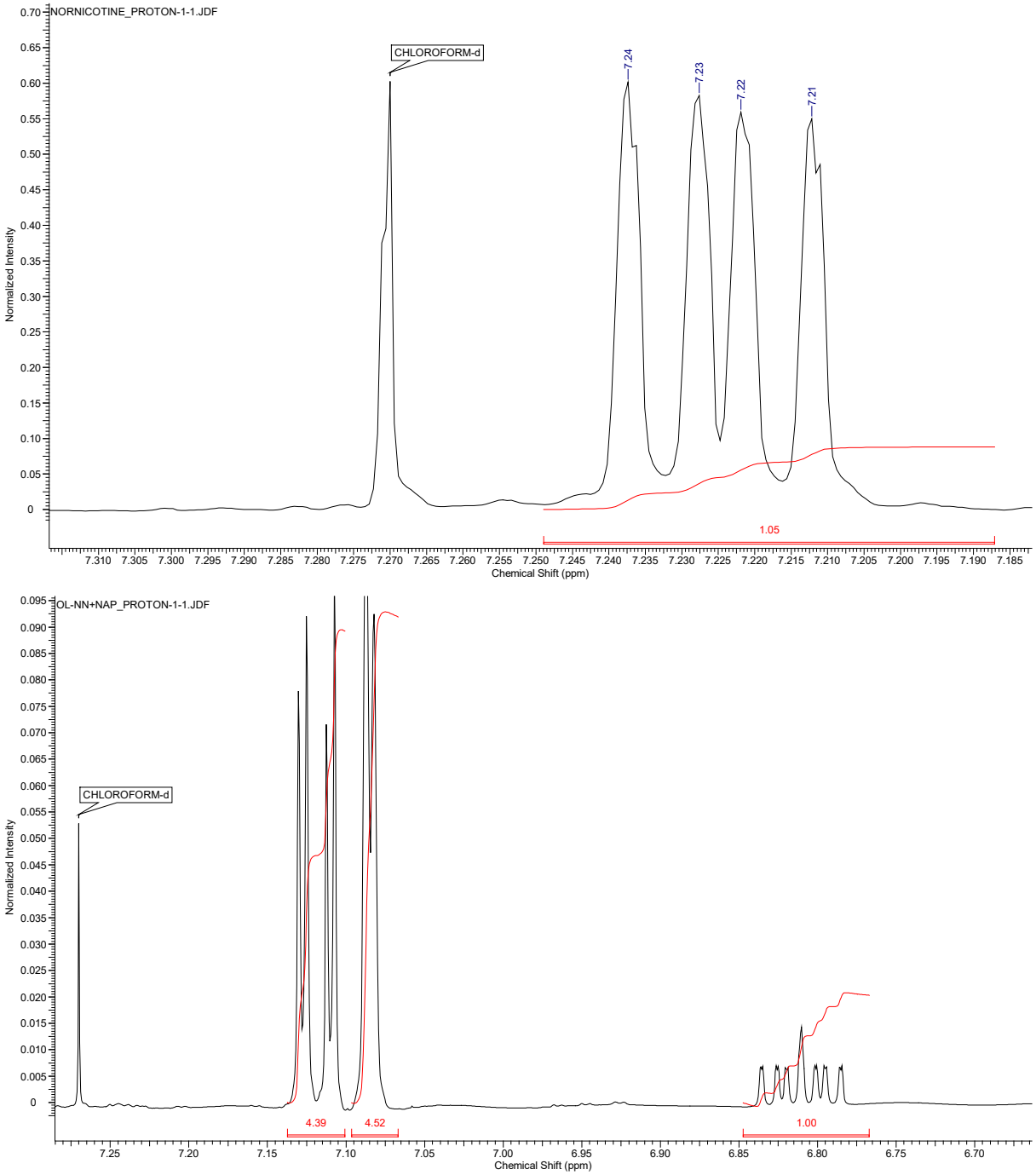



**Figure S22**. Comparision of charactiristic region in $^{1}$H NMR spectra of rac-nornicotine and *rac*-nornicotine in the presence of naproxen.