Synthesis and some chemical transformations of novel 1-oxo-3,4-dihydro-1*H*-pyrrolo[2,1-*c*][1,4]oxazine-8-carboxylic acids and their benzoannelated analogues

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Supplemental Materials

Contents

Materials and Methods

All commercially available chemicals were purchased from Sigma-Aldrich Chemicals (Steinheim, Germany), Merck Chemicals (Darmstadt, Germany), Enamine Ltd (Kyiv, Ukraine). Melting points were determined on a Kofler bench and are uncorrected. ^{1}H NMR spectra were acquired on a Varian UNITY INOVA 400 spectrometer (400 MHz) in $CDCl_3$ solution (for compounds **1b**, **1c**, **6b**, **6c**, **6d**, **8a-e**, **13a**, **13b**, **17**) and in DMSO-d_6 solution (for compounds **4a-e**, **5b**, **5d**, **6e**, **7a**, **7c-7f**, **9a**, **9e**, **9f**, **11e**, **11g**, **12b**, **12d**, **16**) and a Varian Mercury 300 spectrometer (300 MHz) in $CDCl_3$ solution (for compounds **6a**, **7b**, **9b**, **11b**, **11c**, **11d**, **15**, **18**, **19**, **20**) and in DMSO-d_6 solution (for compounds **5a**, **5c**, **5e**, **5f**, **9c**, **9d**, **11a**, **11f**, **11h**, **11i**, **12a**, **12c**, **14**) with TMS as an internal standard. ^{13}C NMR spectra were acquired on a Varian Mercury 300 spectrometer (76 MHz) in $CDCl_3$ solution (for compounds **9b**), in DMSO-d_6 solution (for compounds **9c**) and in CF_3COOD solution (for compounds **14**), Bruker AVANCE DRX 500 spectrometer (125 MHz) in $CDCl_3$ solution (for compounds **1b**, **7a-f**, **8b**, **8c**, **8d**, **8e**, **9d**, **9e**, **11b**, **12a**, **12c**, **13a**, **13b**, **15**, **17**, **19**, **20**) and in DMSO-d_6 solution (for compounds **4a**, **4c-4e**, **5a**, **9f**, **11a**, **11c**, **11f**, **11g**, **11i**, 18) and a Agilent 600MHz spectrometer (150 MHz) in $CDCl_3$ solution (for compounds **6b-6e**, **8a**, **9a**) and in DMSO-d_6 solution (for compounds **1c**, **4b**, **5b**, **5d**, **5e**, **5f**, **11d**, **11e**, **11h**), Bruker AVANCE III 400 (101 MHz) in CF_3COOD solution (for compounds **12b**), with TMS as an internal standard. ^{19}F NMR spectra were acquired on a Varian Mercury-400 spectrometer (376 MHz) in $CDCl_3$ solution (for compounds **11c**, **11d**, **12c**) and in DMSO-d_6 solution (for compounds **5e**, **7e**, **9e**, **11i**, **12d**). Mass spectra were recorded on an Agilent LC/MSD SL instrument; column Zorbax SB-C18, 4.6 × 15 mm, 1.8 μm (PN 82(c) 75-932); solvent DMSO, at atmospheric pressure, electrospray ionization. Merck 60 (40–63 μ) silica gel was used for column chromatography. X-ray difraction study of (4*S*)-*N*-(4-bromophenyl)-4-(1-methylethyl)-1-oxo-3,4-dihydro-1*H*-pyrrolo[2,1-*c*][1,4]oxazine-8-carboxamide **11b** was solved by direct method using SHELXTL package. All reactions were monitored using thin layer chromatography TLC on TLC-sheets ALUGRAM Xtra SIL G/UV_{254} (MACHEREY-NAGEL) (eluent CH_2Cl_2–MeOH, 50:1).

Synthesis and chemical characterization of 1a-e

General procedure for the synthesis of methyl (2-oxomorpholin-3-ylidene)ethanoates **1a-e**. To a cooled (0°C) solution of DMAD (81.4 mmol) in 100 cm^3 MeOH, a solution of 2-aminoethanoles (1-aminopropan-2-ol, 2-amino-2-methylpropan-1-ol, (2*S*)-2-amino-3-methylbutan-1-ol, 2-amino-1-phenylethanol, (1*S*,2*S*)-2-aminocyclohexanol) or 2-aminophenoles) (81.4 mmol) in 80 cm^3 MeOH was added. After completion of the reaction for compounds **1a-e**, the resulting mixture is evaporated to 1/3 of the volume under reduced pressure and cooled at 0°C for 12 hours. The insoluble materials were filtered off, washed with cold MeOH (2 × 3 cm^3), hexane (2 × 5 cm^3), and dried under reduced pressure.

For the (2-oxomorpholine-3-ylidene)ethanoates **1a,b,d,e**[40,41,42] the ^{1}H-NMR and ^{13}C, NMR spectra were found to be identical with the ones described in Ref.[40-44].

Chemical characterization of methyl [(5S)-5-(1-methylethyl)-2-oxomorpholin-3-ylidene]ethanoate (**1c**). Yellow oil; yield 64%. ^{1}H-NMR (400 MHz, $CDCl_3$): δ 1.03 (d, $^{3}J_{HH}$ = 6.7 Hz, 3H, CHC<u>H</u>$_3$), 1.07 (d, $^{3}J_{HH}$ = 6.7 Hz, 3H, CHC<u>H</u>$_3$), 1.82-1.91 (m, 1H, C<u>H</u>$(CH_3)_2$), 3.26-3.32 (m, 1H, C^{5}H), 3.71 (s, 3H, OCH_3), 4.33 (dd, $^{2}J_{HH}$ = 11.2, $^{3}J_{HH}$ = 7.7 Hz, 1H, C^{6}<u>H</u>H), 4.48 (dd, $^{2}J_{HH}$ = 11.1, $^{3}J_{HH}$ = 3.3 Hz, 1H, C^{6}H<u>H</u>), 5.64 (s, 1H, CH), 8.56 (s, 1H, NH). ^{13}C, NMR (151 MHz, DMSO-d_6): δ = 18.24, 18.47, 29.46, 50.59, 52.64, 68.92, 86.31, 144.64, 160.19, 169.39. MS: m/z 214 (M + H). Anal. Calcd. for $C_{10}H_{15}NO_4$ (%): C, 56.33; H, 7.09; N, 6.57. Found: C, 56.15; H, 7.05; N, 6.62.

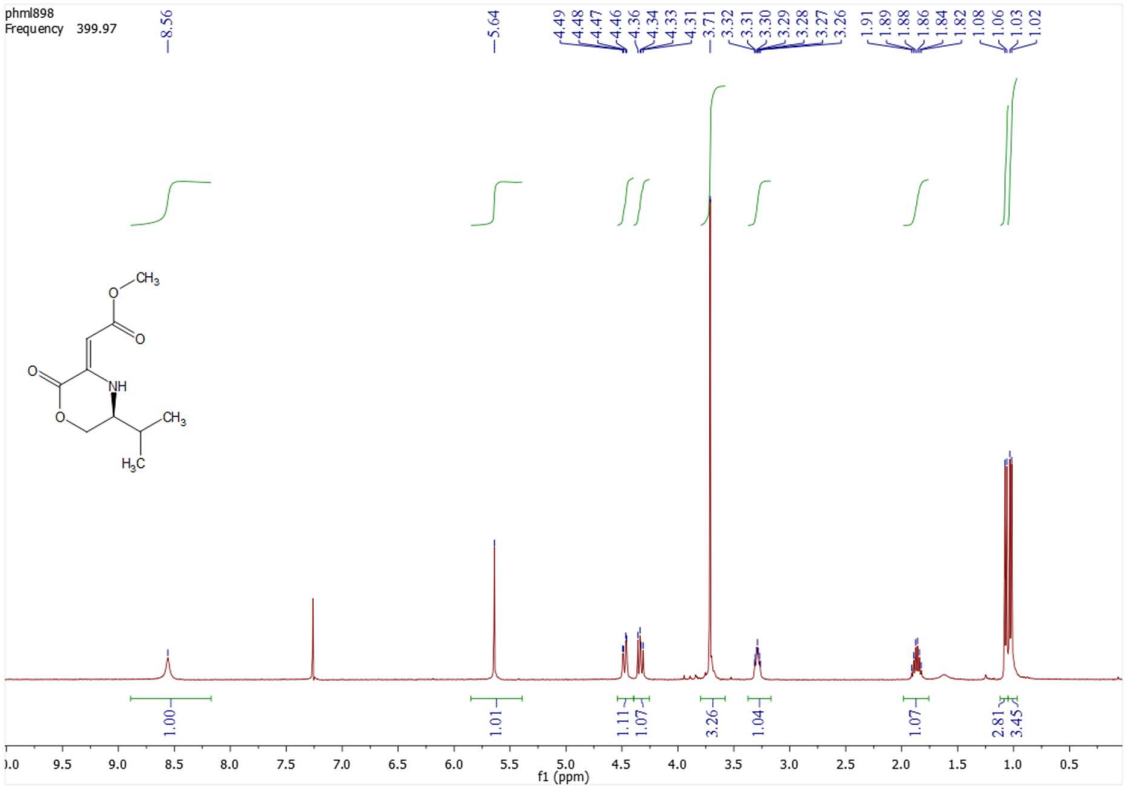

Figure S1. ^{1}H-NMR spectrum of methyl [(5*S*)-5-(1-methylethyl)-2-oxomorpholin-3-ylidene]ethanoate in $CDCl_3$

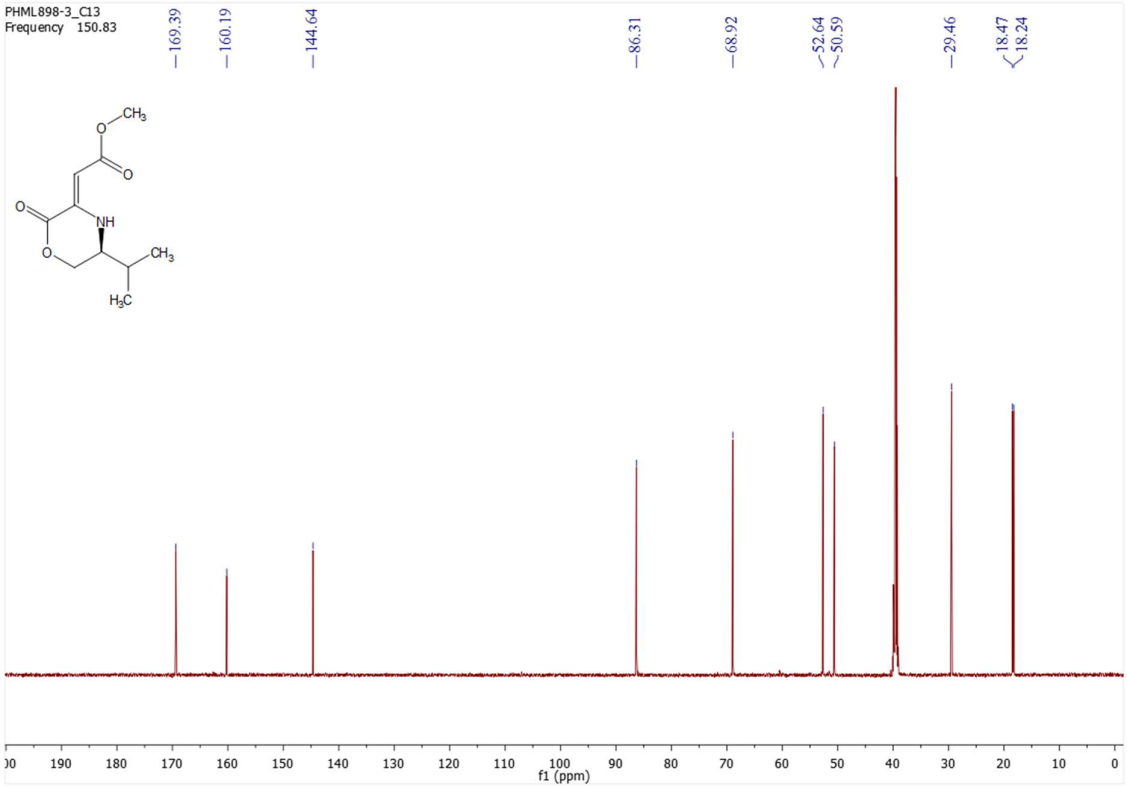

Figure S2. ^{13}C, NMR spectrum of methyl [(5*S*)-5-(1-methylethyl)-2-oxomorpholin-3-ylidene]ethanoate in DMSO-d_6

Synthesis and chemical characterization of 2a-f

General procedure for the synthesis of methyl (2-oxo-2H-1,4-benzoxazin-3(4H)-ylidene)ethanoates **2a-f**. To a cooled (0°C) solution of 2-aminophenoles (2-aminophenol, 2-amino-3-methylphenol, 2-amino-4-chlorophenol, 2-amino-4-*tert*-butylphenol, 2-amino-5-fluorophenol, 2-amino-6-bromophenol) (81.4 mmol) in 100 cm^3 MeOH, a solution of DMAD (81.4 mmol) in 100 cm^3 MeOH was added. After completion of the reaction the insoluble materials were filtered off, washed with cold MeOH (2 × 5 cm^3), hexane (2 × 5 cm^3), and dried under reduced pressure. For the (2-oxo-1,4-benzoxazine-3(4*H*)-ylidene)ethanoates **2a-e**[42,43,44], the ^{1}H-NMR and ^{13}C, NMR spectra were found to be identical with the ones described in Ref.[40-44].

Chemical characterization of methyl (8-bromo-2-oxo-2H-1,4-benzoxazin-3(4H)-ylidene)ethanoate (**2f**). Yellow solid, mp 164-165°C; yield 93%. ^{1}H-NMR (400 MHz, $CDCl_3$): δ 3.79 (s, 3H, CH_3), 5.98 (s, 1H, CH), 6.91 (d, $^3J_{HH}$ = 8.0 Hz, 1H, $1H_{Ar}$), 7.01 (t, $^3J_{HH}$ = 8.0 Hz, 1H, $1H_{Ar}$), 7.24 (d, $^3J_{HH}$ = 8.0 Hz, 1H, $1H_{Ar}$), 10.68 (s, 1H, NH).^{13}C, NMR (126 MHz, $CDCl_3$): δ = 51.76, 91.86, 110.67, 114.06, 125.56, 126.27, 126.60, 137.42, 137.59, 155.16, 170.22. MS: m/z 298, 300 (M + H). Anal. Calcd. for $C_{11}H_8BrNO_4$ (%): C, 44.32; H, 2.71; N, 4.70. Found: C, 44.56; H, 2.74; N, 4.59.

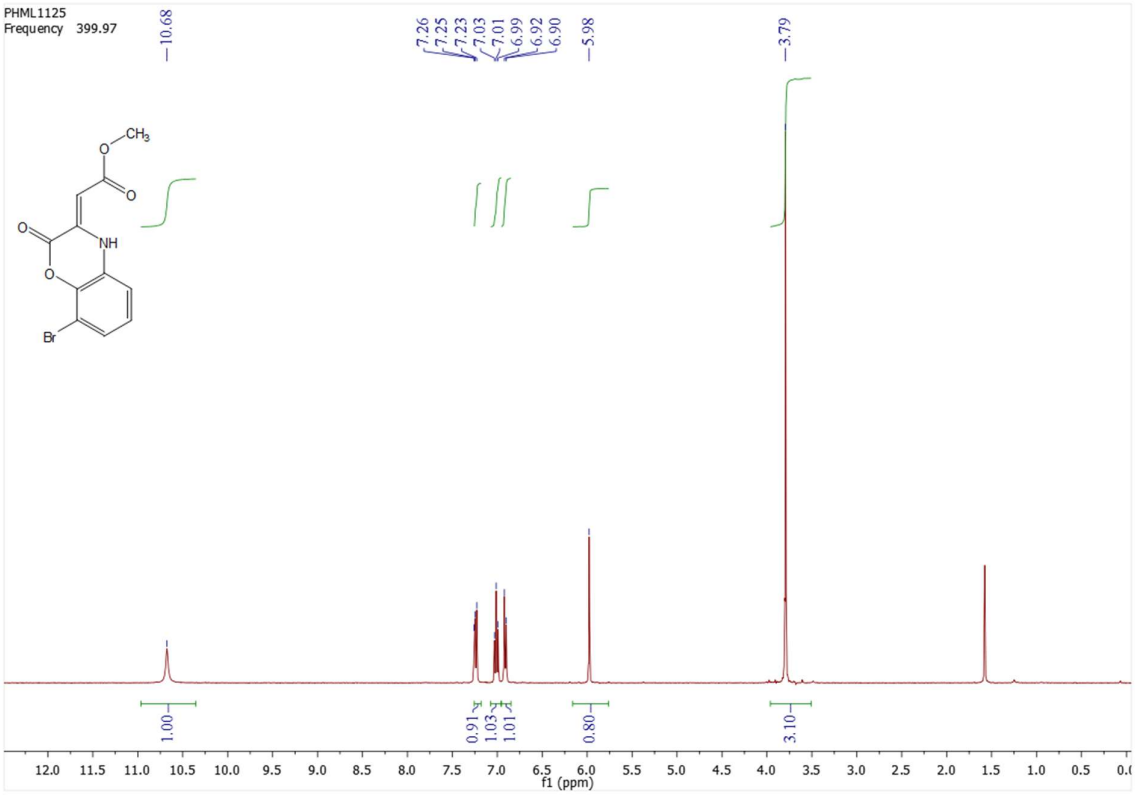

Figure S3. ^{1}H-NMR spectrum of methyl (8-bromo-2-oxo-2*H*-1,4-benzoxazin-3(4*H*)-ylidene)ethanoate in $CDCl_3$

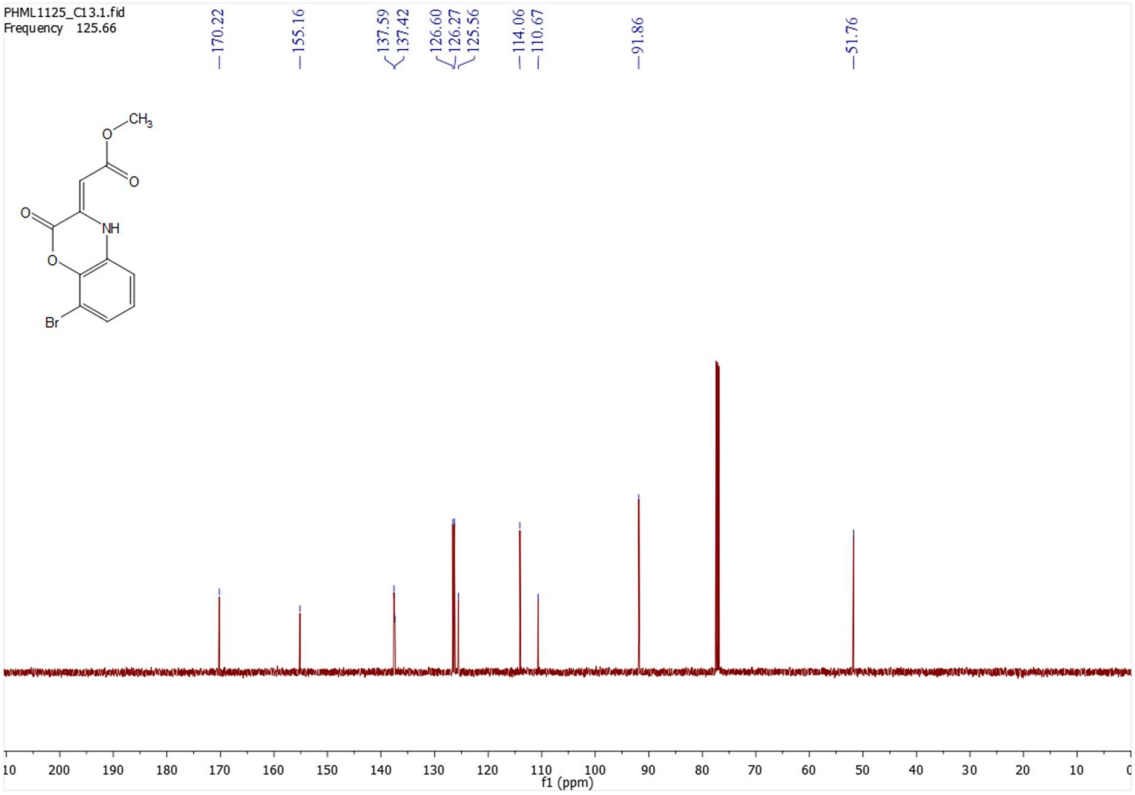

Figure S4. ^{13}C, NMR spectrum of methyl (8-bromo-2-oxo-2*H*-1,4-benzoxazin-3(4*H*)-ylidene)ethanoate in $CDCl_3$

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Synthesis and spectra characteristics of compounds 4a-e and 5a-f

*General procedure for the synthesis of 1-oxo-3,4-dihydro-1H-pyrrolo[2,1-c][1,4]oxazine-8-carboxylic acid **4a-e** and 4-oxo-4H-pyrrolo[2,1-c][1,4]benzoxazine-3-carboxylic acid **5a-f**.* To a solution of (32.5 mmol) methyl (2-oxomorpholin-3-ylidene)ethanoate **1a-e** or methyl (2-oxo-2*H*-1,4-benzoxazin-3(4*H*)-ylidene)ethanoate **2a-f** in 60 cm^3 AcOH, 6.41 g bromoacetaldehyde diethyl acetal (32.5 mmol) was added. The resulting mixture was stirred at 80°C for 6–12 h. After the reaction was completed, the mixture was cooled and the insoluble materials were filtered off, washed with AcOH (2 × 5 cm^3), MTBE (2 × 2 cm^3), hexane (2 × 4 cm^3) and dried under reduced pressure.

Chemical characterization of 3-methyl-1-oxo-3,4-dihydro-1H-pyrrolo[2,1-c][1,4]oxazine-8-carboxylic acid (**4a**). Beige solid, mp 204-205°C; yield 67%. ^{1}H-NMR (400 MHz, DMSO-d_6): δ = 1.43 (d, $^3J_{HH}$ = 6.3 Hz, 3H, CH_3), 4.11 (dd, $^2J_{HH}$ =13.6, $^3J_{HH}$ = 10.6 Hz, 1H, C^{4}HH), 4.48 (dd, $^2J_{HH}$ = 13.6, $^3J_{HH}$ = 3.2 Hz, 1H, C^{4}HH), 4.99-5.07 (m, 1H, C^{3}H), 6.76 (d, $^3J_{HH}$ = 2.7 Hz, 1H, C^{7}H), 7.33 (d, $^3J_{HH}$ = 2.7 Hz, 1H, C^{6}H), 13.15 (s, 1H, OH). ^{13}C, NMR (126 MHz, DMSO-d_6): δ = 17.25, 47.95, 75.38, 114.26, 117.07, 123.00, 126.05, 161.04, 162.19. MS: m/z 196 (M + H). Anal. Calcd. for $C_9H_9NO_4$ (%): C, 55.39; H, 4.65; N, 7.18. Found: C, 55.20; H, 4.62; N, 7.29.

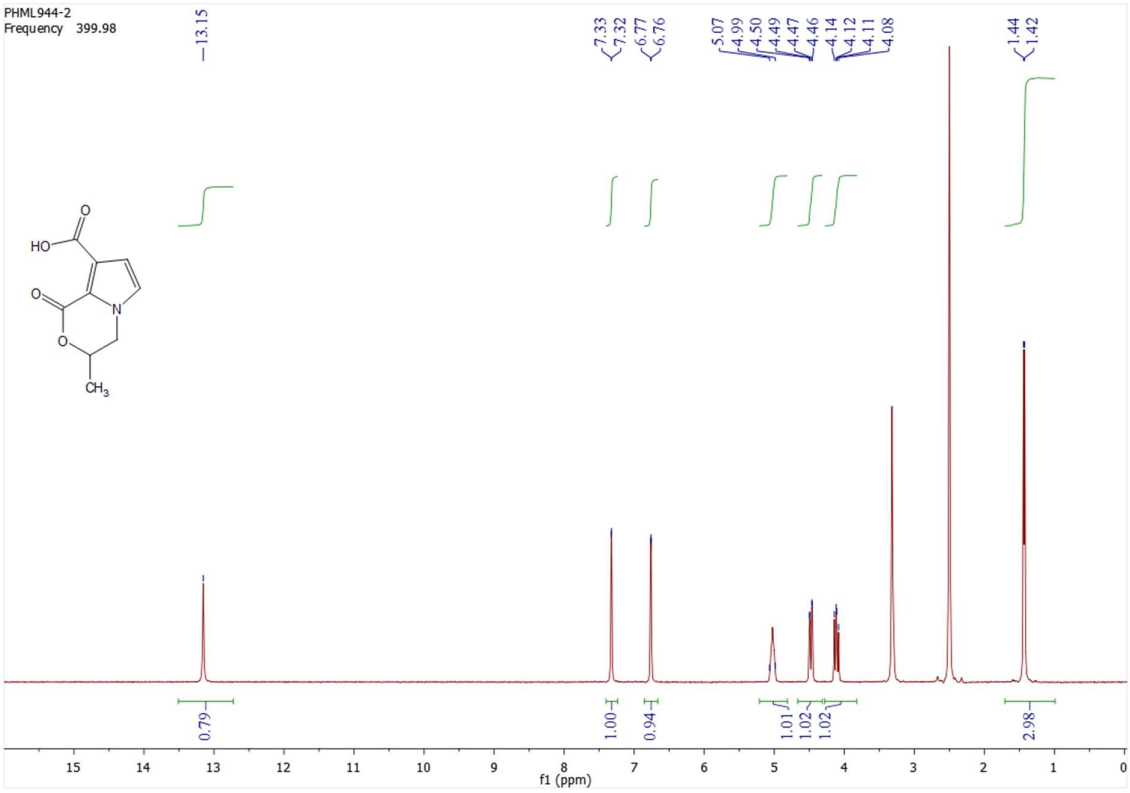

Figure S5. [1]H-NMR spectrum of 3-methyl-1-oxo-3,4-dihydro-1*H*-pyrrolo[2,1-*c*][1,4]oxazine-8-carboxylic acid (**4a**) in DMSO-d_6

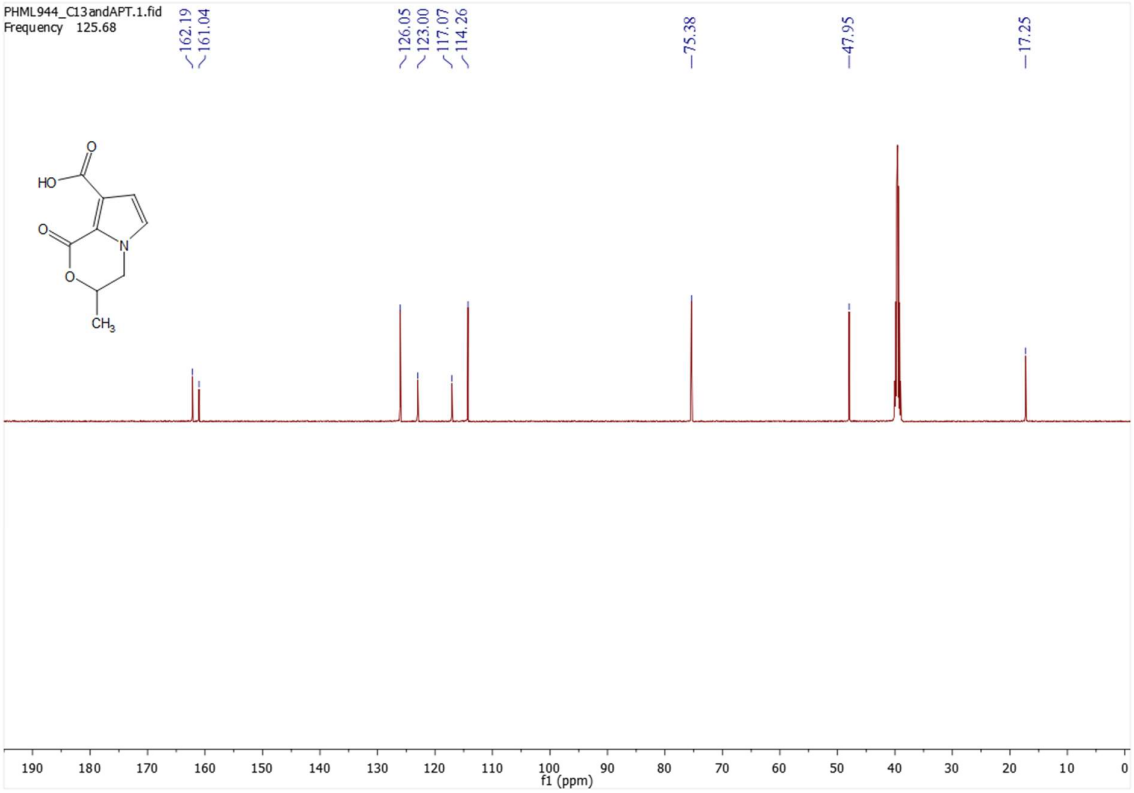

Figure S6. [13]C, NMR spectrum of 3-methyl-1-oxo-3,4-dihydro-1*H*-pyrrolo[2,1-*c*][1,4]oxazine-8-carboxylic acid (**4a**) in DMSO-d_6

Chemical characterization of 4,4-dimethyl-1-oxo-3,4-dihydro-1H-pyrrolo[2,1-c][1,4]oxazine-8-carboxylic acid (**4b**). White solid, mp 229-230°C; yield 84%. ^{1}H-NMR (400 MHz, DMSO-d_6): δ 1.52 (s, 6H, 2CH_3), 4.53 (s, 2H, C$^{3}H_2$), 6.79 (d, $^{3}J_{HH}$ = 1.5 Hz, 1H, C^{7}H), 7.52 (d, $^{3}J_{HH}$ = 1.7 Hz, 1H, C^{6}H), 13.14 (s, 1H, OH). ^{13}C, NMR (151 MHz, DMSO-d_6): δ = 23.61, 54.47, 75.07, 114.63, 116.21, 122.90, 124.05, 160.51, 162.41. MS: m/z 210 (M + H). Anal. Calcd. for $C_{10}H_{11}NO_4$ (%): C, 57.41; H, 5.30; N, 6.70. Found: C, 57.57; H, 5.26; N, 6.61.

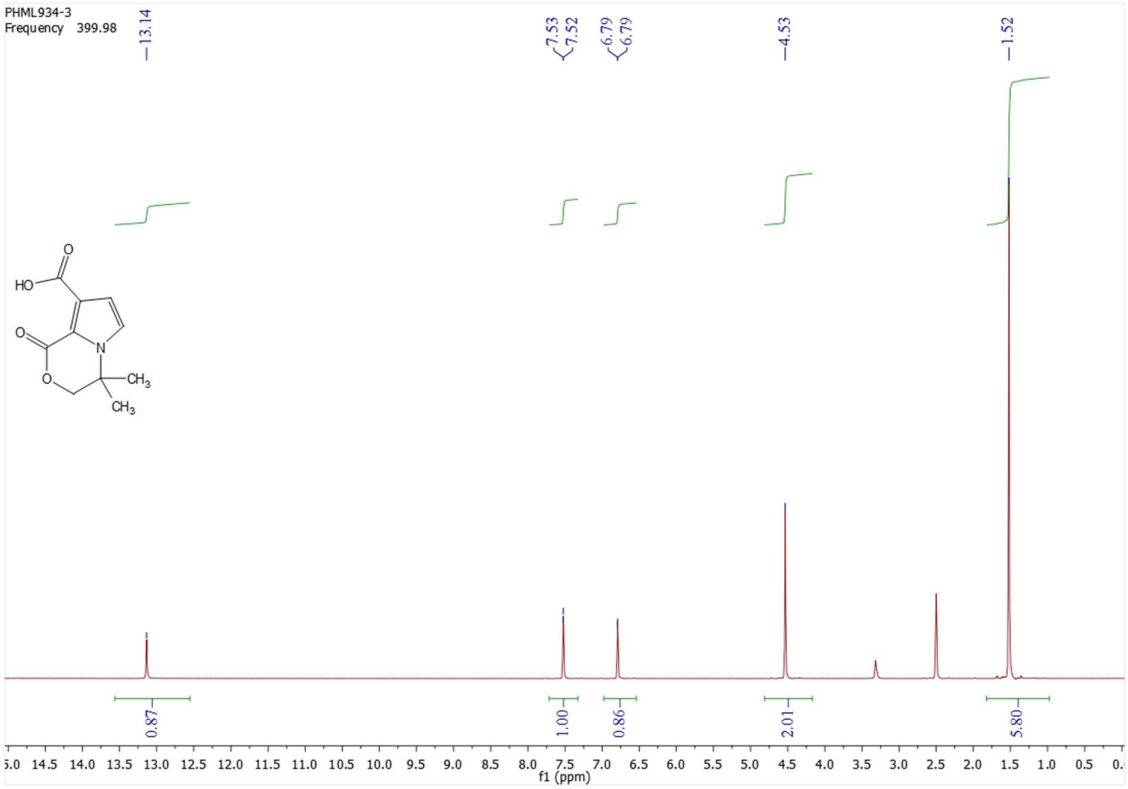

Figure S7. ^{1}H-NMR spectrum of 4,4-dimethyl-1-oxo-3,4-dihydro-1*H*-pyrrolo[2,1-*c*][1,4]oxazine-8-carboxylic acid (**4b**) in DMSO-d_6

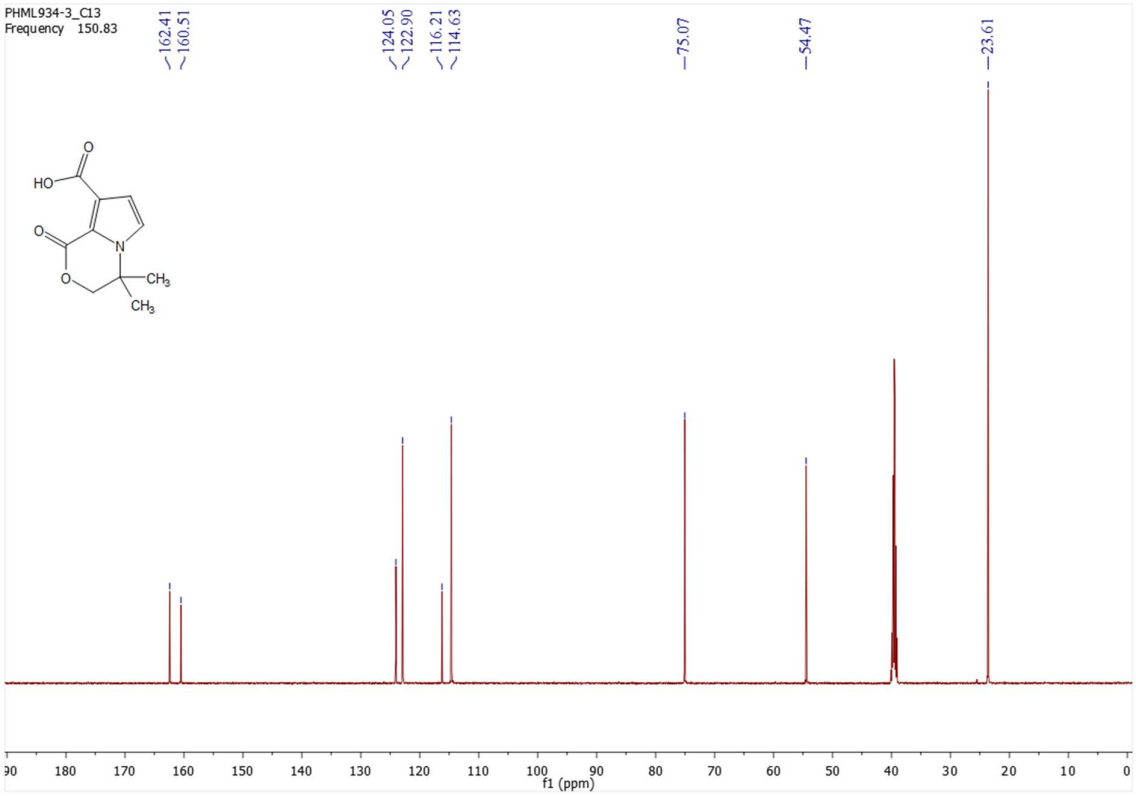

Figure S8. ^{13}C, NMR spectrum of 4,4-dimethyl-1-oxo-3,4-dihydro-1*H*-pyrrolo[2,1-*c*][1,4]oxazine-8-carboxylic acid (**4b**) in DMSO-d_6

Chemical characterization of (4S)-4-(1-methylethyl)-1-oxo-3,4-dihydro-1H-pyrrolo[2,1-c][1,4]oxazine-8-carboxylic acid (**4c**). White solid, mp 157-158°C; yield 73%. ^{1}H-NMR (400 MHz, DMSO-d_6): δ 0.85 (d, $^{3}J_{HH}$ = 6.8 Hz, 3H, CH_3), 0.95 (d, $^{3}J_{HH}$ = 6.8 Hz, 3H, CH_3), 2.07-2.18 (m, 1H, C<u>H</u>(CH_3)$_2$), 4.31-4.34 (m, C^{4}H), 4.77 (d, $^{3}J_{HH}$ = 2.8 Hz, 2H, C^{3}H$_2$), 6.77 (d, $^{3}J_{HH}$ = 2.7 Hz, 1H, C^{7}H), 7.40 (d, $^{3}J_{HH}$ = 2.7 Hz, 1H, C^{6}H), 13.07 (s, 1H, OH). ^{13}C, NMR (126 MHz, DMSO-d_6): δ = 18.69, 18.81, 30.21, 58.04, 68.54, 113.82, 116.88, 123.21, 126.47, 160.62, 162.31. MS: m/z 224 (M + H). Anal. Calcd. for $C_{11}H_{13}NO_4$ (%): C, 59.19; H, 5.87; N, 6.27. Found: C, 58.94; H, 5.91; N, 6.16.

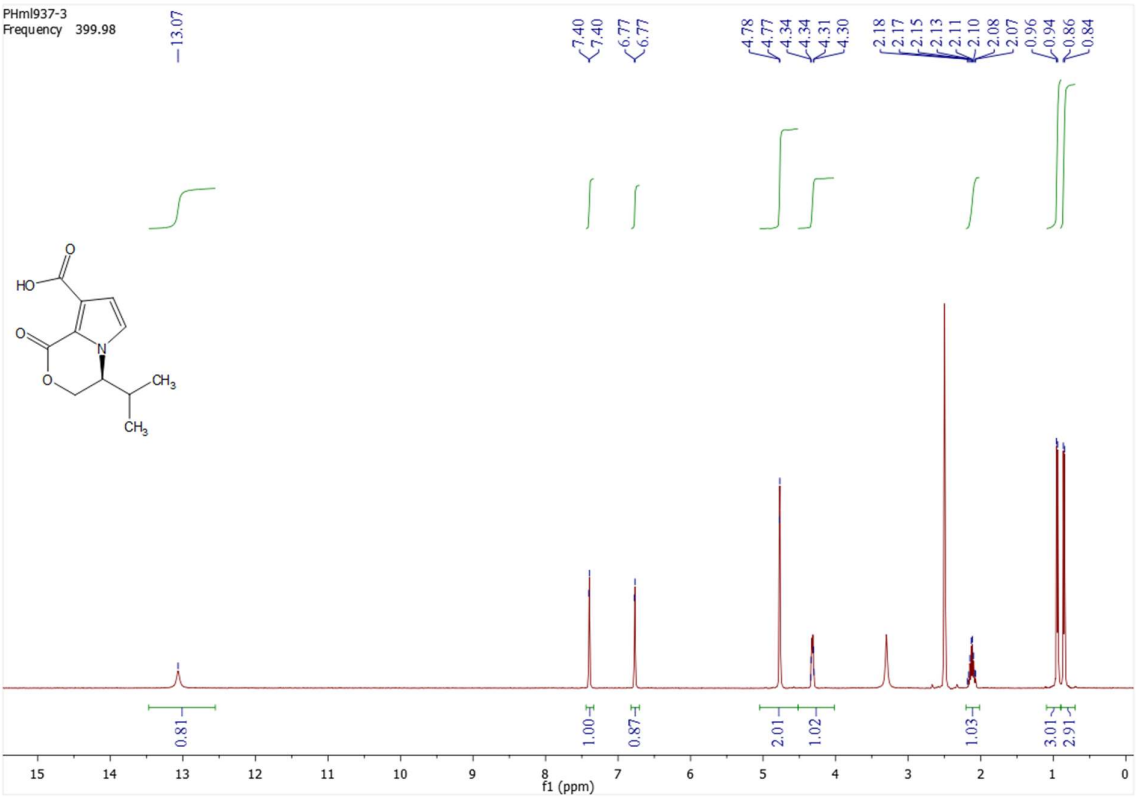

Figure S9. ^{1}H-NMR spectrum of (4*S*)-4-(1-methylethyl)-1-oxo-3,4-dihydro-1*H*-pyrrolo[2,1-*c*][1,4]oxazine-8-carboxylic acid (**4c**) in DMSO-d_6

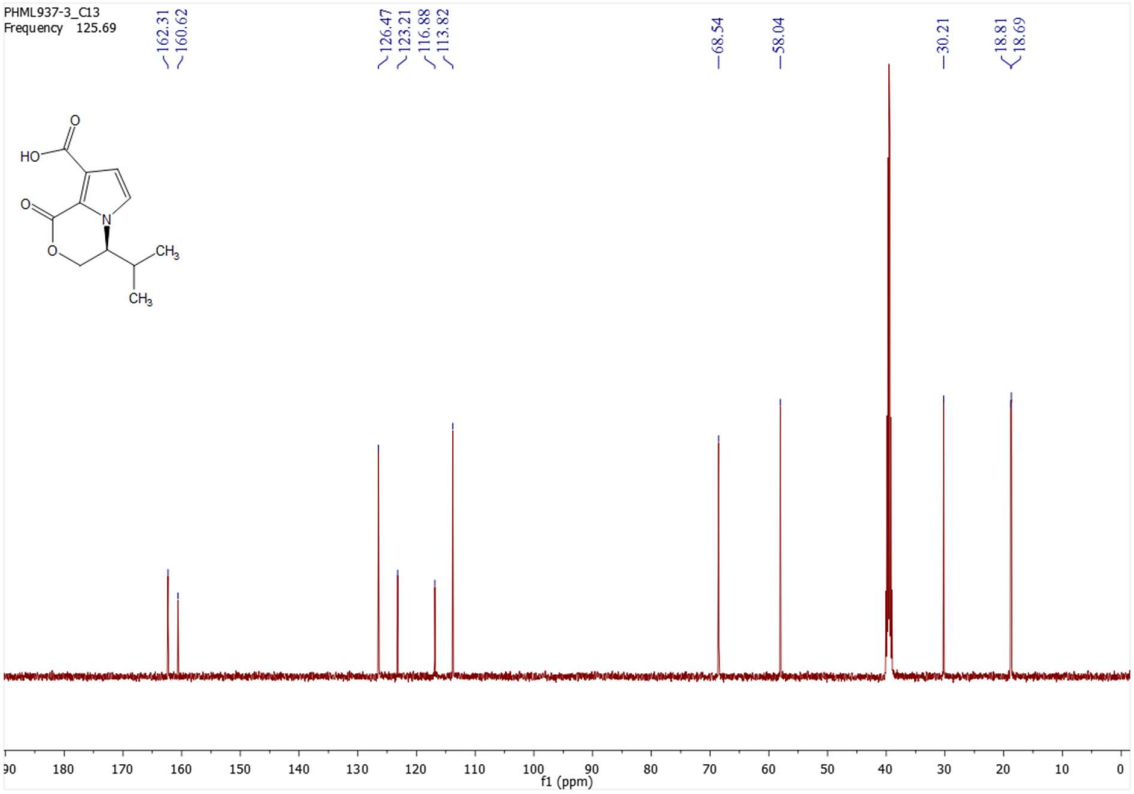

Figure S10. ^{13}C, NMR spectrum of *(4S)-4-(1-methylethyl)-1-oxo-3,4-dihydro-1H-pyrrolo[2,1-c][1,4]oxazine-8-carboxylic acid* (**4c**) in DMSO-d_6

Chemical characterization of 1-oxo-3-phenyl-3,4-dihydro-1H-pyrrolo[2,1-c][1,4]oxazine-8-carboxylic acid (**4d**). White solid, mp 237-238°C; yield 91%. ^{1}H-NMR (400 MHz, DMSO-d_6): δ 4.53 (dd, $^{2}J_{HH}$ = 13.7, $^{3}J_{HH}$ = 11.1 Hz, 1H, C^{4}HH), 4.68 (dd, $^{2}J_{HH}$ = 13.7, $^{3}J_{HH}$ = 3.3 Hz, 1H, C^{4}HH), 6.04 (dd, $^{3}J_{HH}$ = 11.0, $^{3}J_{HH}$ = 3.4 Hz, 1H, C^{3}H), 6.80 (d, $^{3}J_{HH}$ = 2.7 Hz, 1H, C^{7}H), 7.35 (d, $^{3}J_{HH}$ = 2.6 Hz, 1H, C^{6}H), 7.47-7.57 (m, 5H, Ph), 13.08 (s, 1H, OH). ^{13}C, NMR (126 MHz, DMSO-d_6): δ = 47.87, 79.22, 114.25, 117.30, 123.15, 125.89, 126.86, 128.71, 129.27, 135.03, 160.28, 162.33. MS: m/z 258 (M + H). Anal. Calcd. for $C_{14}H_{11}NO_4$ (%): C, 65.37; H, 4.31; N, 5.44. Found: C, 65.18; H, 4.33; N, 5.56.

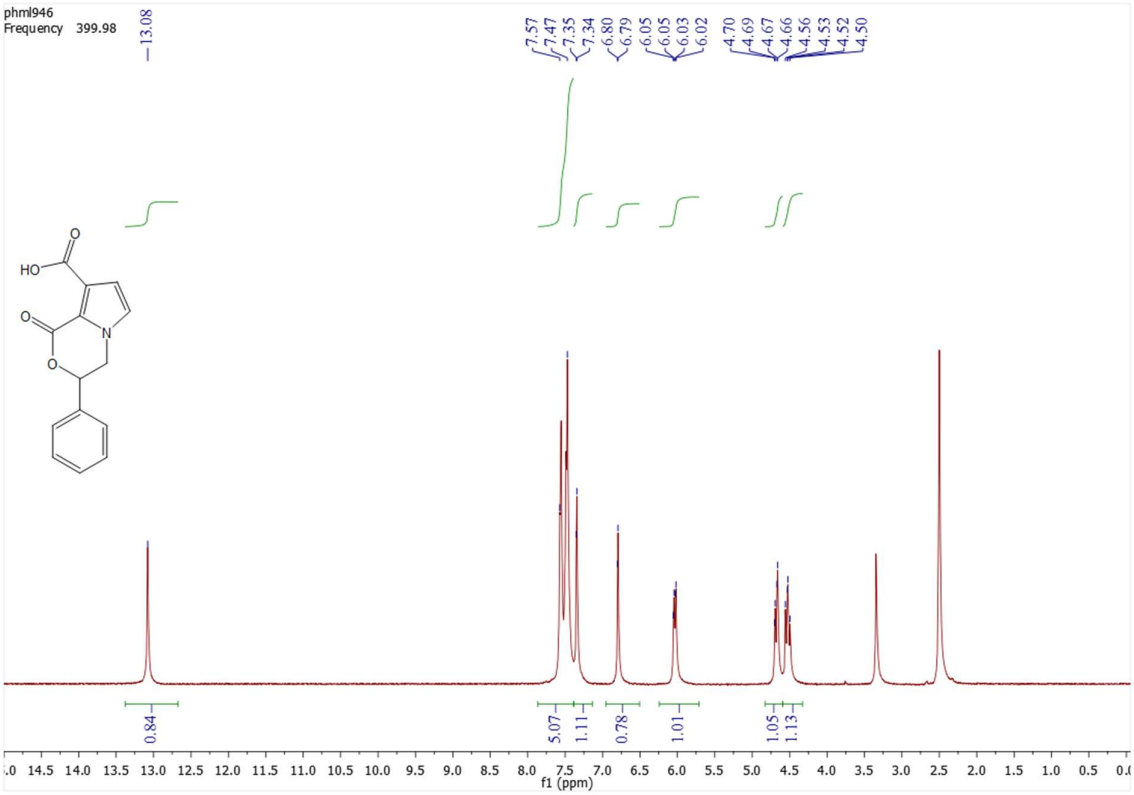

Figure S11. ^{1}H-NMR spectrum of 1-oxo-3-phenyl-3,4-dihydro-1*H*-pyrrolo[2,1-*c*][1,4]oxazine-8-carboxylic acid (**4d**) in DMSO-d_6

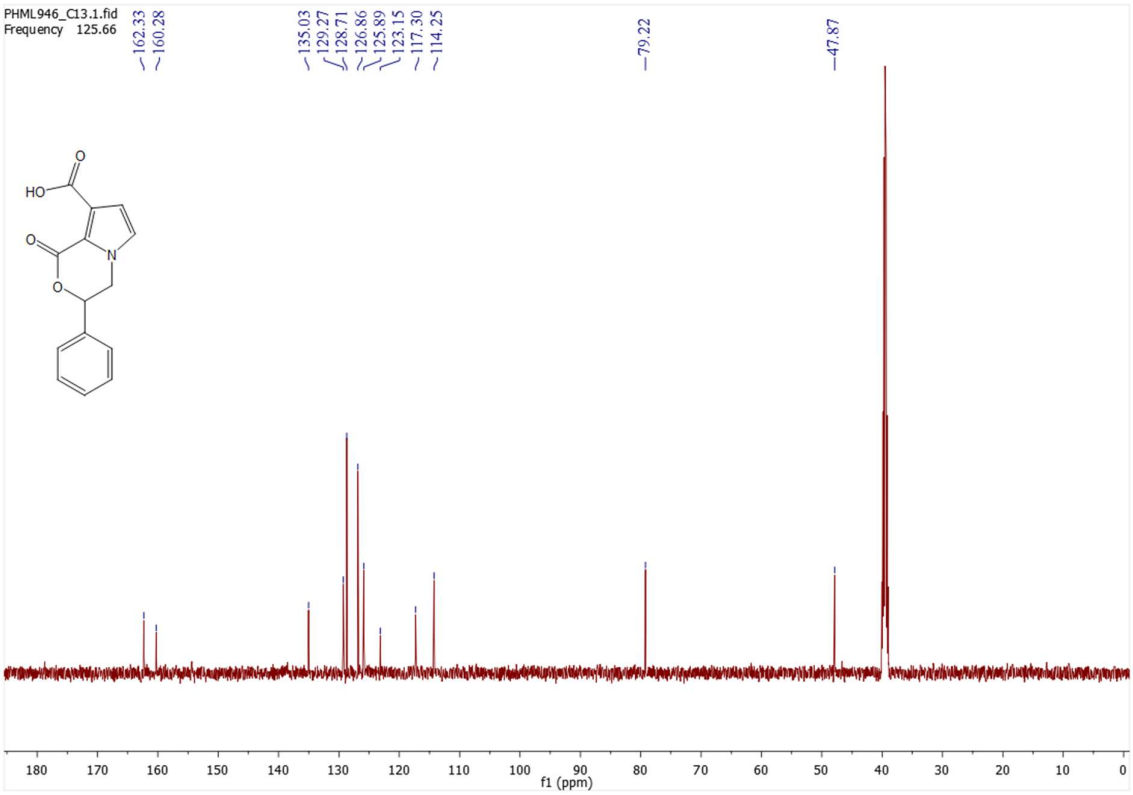

Figure S12. ^{13}C, NMR spectrum of 1-oxo-3-phenyl-3,4-dihydro-1*H*-pyrrolo[2,1-*c*][1,4]oxazine-8-carboxylic acid (**4d**) in DMSO-d_6

Chemical characterization of (5aS,9aS)-4-oxo-5a,6,7,8,9,9a-hexahydro-4H-pyrrolo[2,1-c][1,4]benzoxazine-3-carboxylic acid (**4e**). White solid, mp 217-218°C; yield 89%. ^{1}H-NMR (400 MHz, DMSO-d_6): δ 1.38-1.53 (m, 3H), 1.53-1.63 (m, 1H), 1.82-1.85 (m, 2H), 2.12-2.15 (m, 1H), 2.68-2.71 (m, 1H), 4.14 (td, $^3J_{HH}$ = 10.6, 4.4 Hz, 1H, C^{9a}H), 4.56 (td, $^3J_{HH}$ = 11.0, 4.4 Hz, 1H, C^{5a}H), 6.78 (d, $^3J_{HH}$ = 2.8 Hz, 1H, C^{2}H), 7.42 (d, $^3J_{HH}$ = 2.8 Hz, 1H, C^{1}H), 13.08 (s, 1H, OH). ^{13}C, NMR (126 MHz, DMSO-d_6): δ = 22.71, 22.84, 26.74, 28.96, 56.01, 81.07, 114.29, 117.84, 122.83, 123.74, 160.72, 162.42. MS: m/z 236 (M + H). Anal. Calcd. for $C_{12}H_{13}NO_4$ (%): C, 61.27; H, 5.57; N, 5.95. Found: C, 61.44; H, 5.61; N, 5.84.

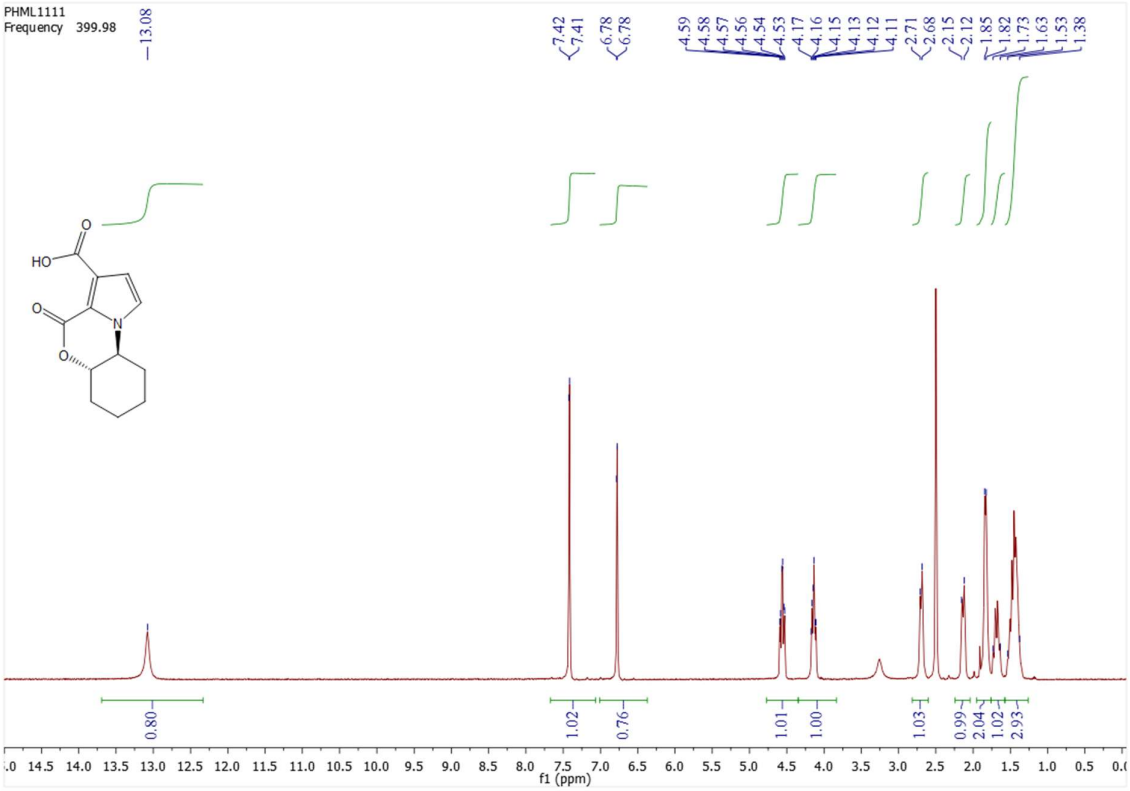

Figure S13. [1]H-NMR spectrum of (5*aS*,9*aS*)-4-oxo-5*a*,6,7,8,9,9*a*-hexahydro-4*H*-pyrrolo[2,1-*c*][1,4]benzoxazine-3-carboxylic acid (**4e**) in DMSO-d_6

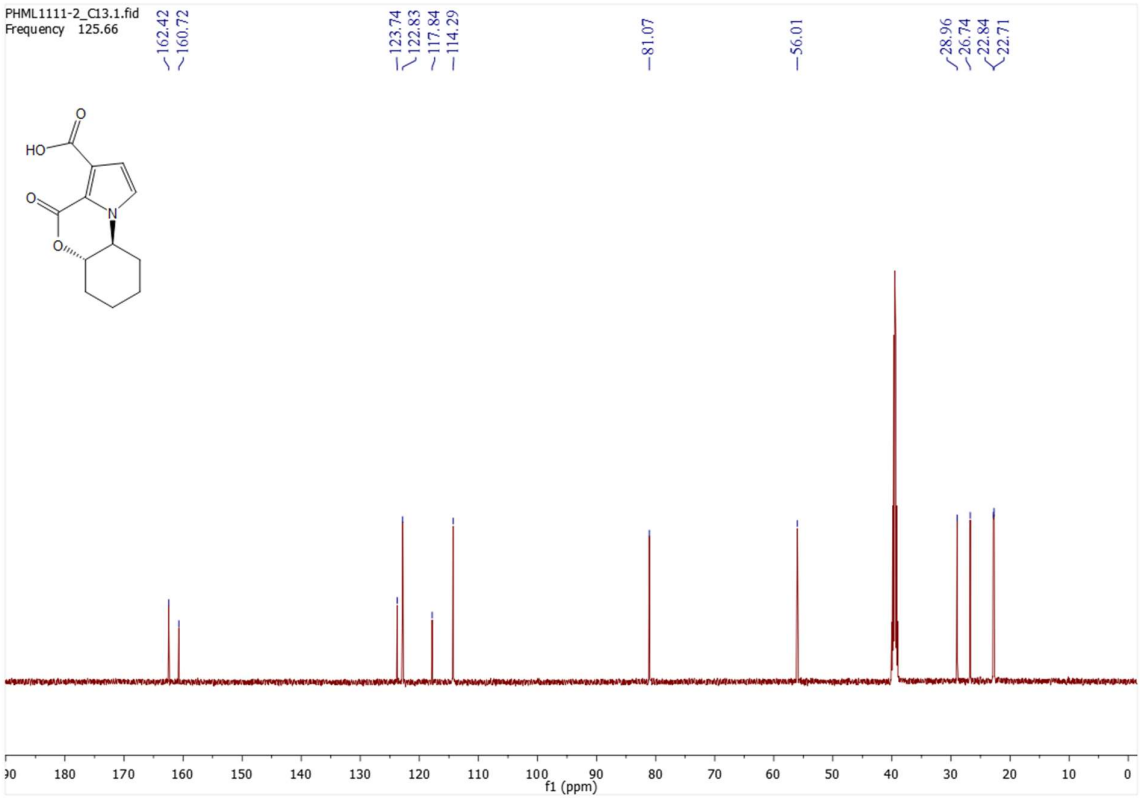

Figure S14. [13]C, NMR spectrum of (5*aS*,9*aS*)-4-oxo-5*a*,6,7,8,9,9*a*-hexahydro-4*H*-pyrrolo[2,1-*c*][1,4]benzoxazine-3-carboxylic acid (**4e**) in DMSO-d_6

Chemical characterization of 4-oxo-4H-pyrrolo[2,1-c][1,4]benzoxazine-3-carboxylic acid (**5a**). Gray solid, mp 246-247°C; yield 87%. ^{1}H-NMR (302 MHz, DMSO-d_6): δ 7.14 (d, $^{3}J_{HH}$ = 2.9 Hz, 1H, C^{2}H), 7.39–7.49 (m, 2H, 2H$_{Ar}$), 7.49–7.57 (m, 1H, 1H$_{Ar}$), 8.02–8.27 (m, 1H, 1H$_{Ar}$), 8.39 (d, $^{3}J_{HH}$ = 3.0 Hz, 1H, C^{1}H), 13.08 (s, 1H, OH). ^{13}C, NMR (126 MHz, DMSO-d_6): δ = 115.25, 115.94, 116.81, 117.61, 120.19, 121.83, 123.56, 125.39, 127.44, 142.44, 153.96, 162.67. MS: m/z 230 (M + H). Anal. Calcd. for $C_{12}H_7NO_4$ (%): C, 62.89; H, 3.08; N, 6.11. Found: 63.11; H, 3.06; N, 6.00.

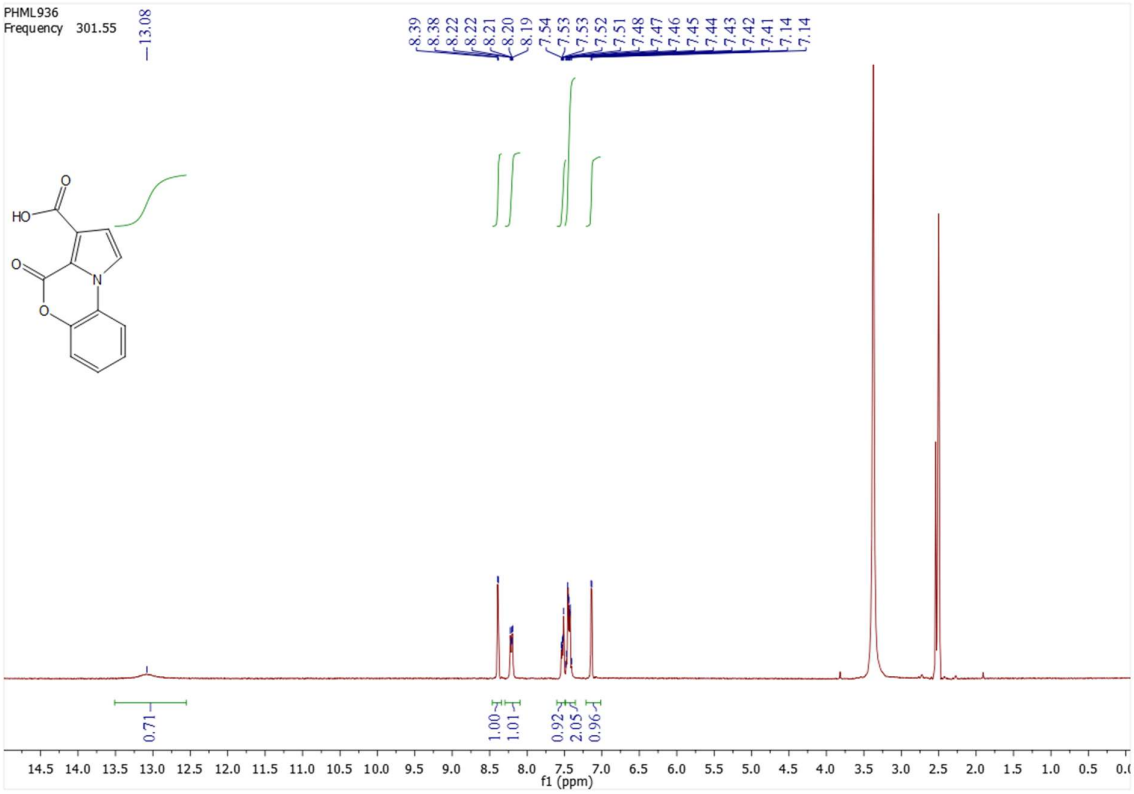

Figure S15. ^{1}H-NMR spectrum of 4-oxo-4*H*-pyrrolo[2,1-*c*][1,4]benzoxazine-3-carboxylic acid (**5a**) in DMSO-d_6

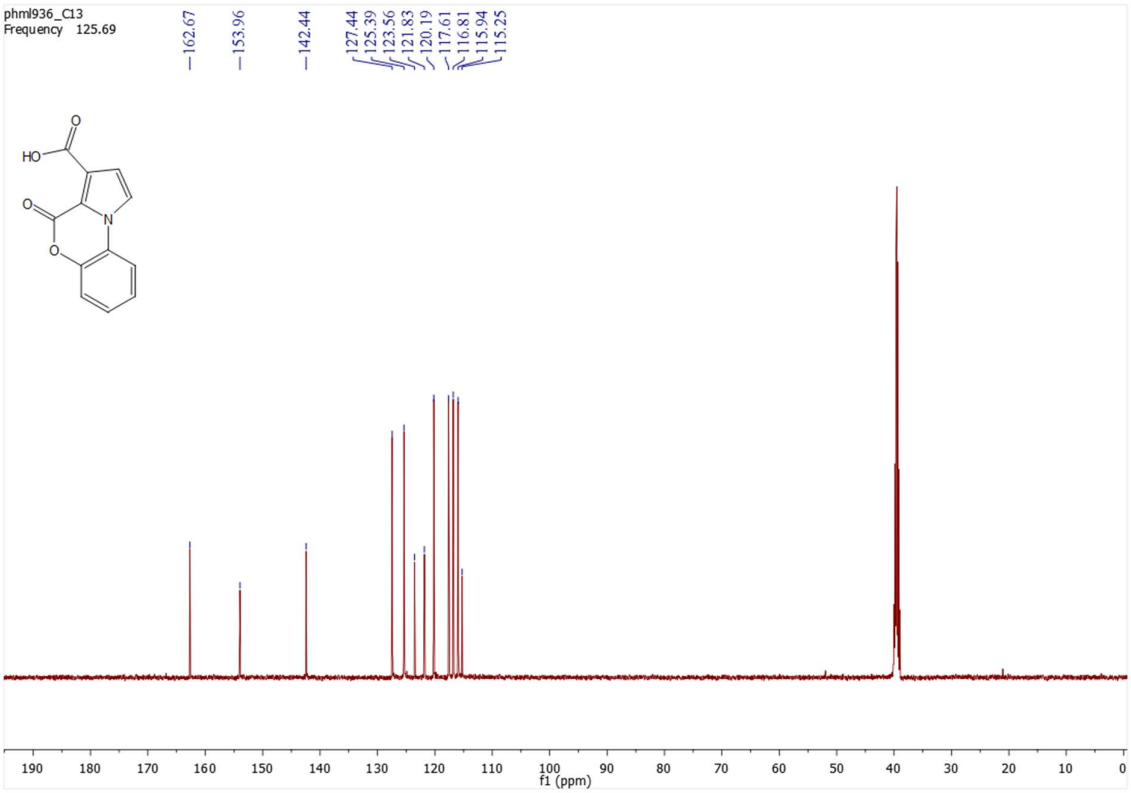

Figure S16. ^{13}C, NMR spectrum of 4-oxo-4*H*-pyrrolo[2,1-*c*][1,4]benzoxazine-3-carboxylic acid (**5a**) in DMSO-d_6

Chemical characterization of 9-methyl-4-oxo-4H-pyrrolo[2,1-c][1,4]benzoxazine-3-carboxylic acid (**5b**). Gray solid, mp >250°C; yield 75%. ^{1}H-NMR (400 MHz, DMSO-d_6): δ 2.80 (s, 3H, CH_3), 7.11 (d, $^{3}J_{HH}$ = 2.8 Hz, 1H, C^{2}H), 7.21–7.48 (m, 3H, 3H$_{Ar}$), 8.28 (d, $^{3}J_{HH}$ = 2.9 Hz, 1H, C^{1}H), 13.26 (s, 1H, OH). ^{13}C, NMR (151 MHz, DMSO-d_6): δ = 22.38, 115.80, 116.02, 116.19, 121.35, 123.43, 124.43, 126.66, 127.34, 129.27, 143.33, 154.16, 162.75. MS: m/z 244 (M + H). Anal. Calcd. for $C_{13}H_9NO_4$ (%): C, 64.20; H, 3.73; N, 5.76. Found: C, 64.01; H, 3.70; N, 5.84.

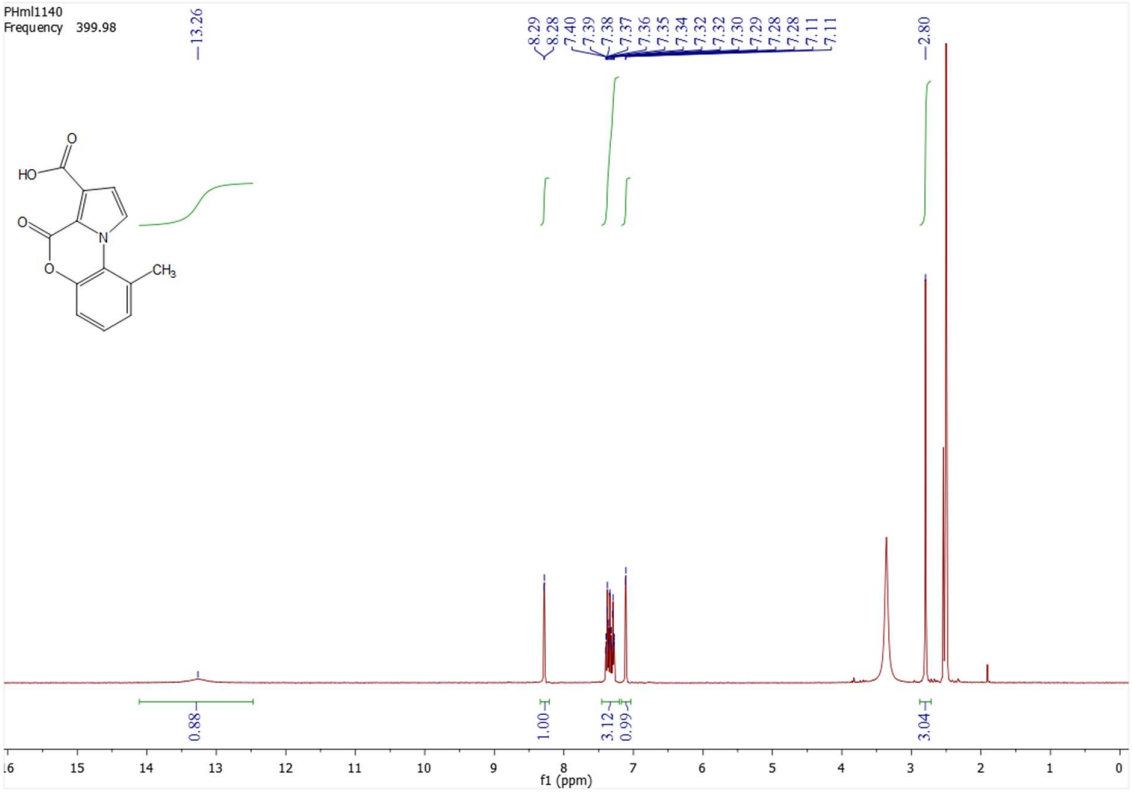

Figure S17. [1]H-NMR spectrum of 9-methyl-4-oxo-4*H*-pyrrolo[2,1-*c*][1,4]benzoxazine-3-carboxylic acid (**5b**) in DMSO-d_6

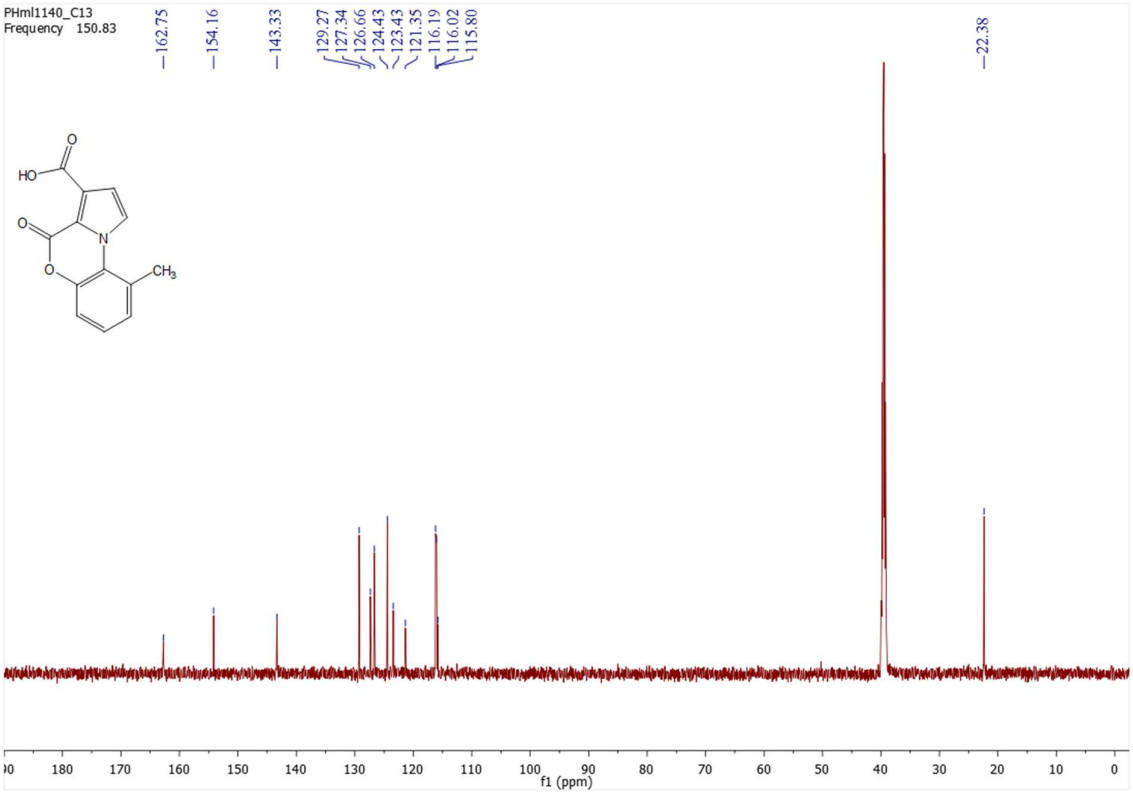

Figure S18. [13]C, NMR spectrum of 9-methyl-4-oxo-4*H*-pyrrolo[2,1-*c*][1,4]benzoxazine-3-carboxylic acid (**5b**) in DMSO-d_6

Chemical characterization of 8-chloro-4-oxo-4H-pyrrolo[2,1-c][1,4]benzoxazine-3-carboxylic acid (**5c**). Braun solid, mp >250°C; yield 69%. ^{1}H-NMR (302 MHz, DMSO-d_6): δ 7.12 (d, $^{3}J_{HH}$ = 2.9 Hz, 1H, C^{2}H), 7.48 (dd, $^{3}J_{HH}$ = 8.8, $^{4}J_{HH}$ = 2.2 Hz, 1H, 1H$_{Ar}$), 7.55 (d, $^{3}J_{HH}$ = 8.8 Hz, 1H, 1H$_{Ar}$), 8.40 (d, $^{3}J_{HH}$ = 3.0 Hz, 1H, C^{1}H), 8.43 (d, $^{4}J_{HH}$ = 2.2 Hz, 1H, 1H$_{Ar}$). MS: m/z 264 (M + H). Anal. Calcd. for $C_{12}H_6ClNO_4$ (%): C, 54.67; H, 2.29; N, 5.31. Found: C, 54.90; H, 2.34; N, 5.19.

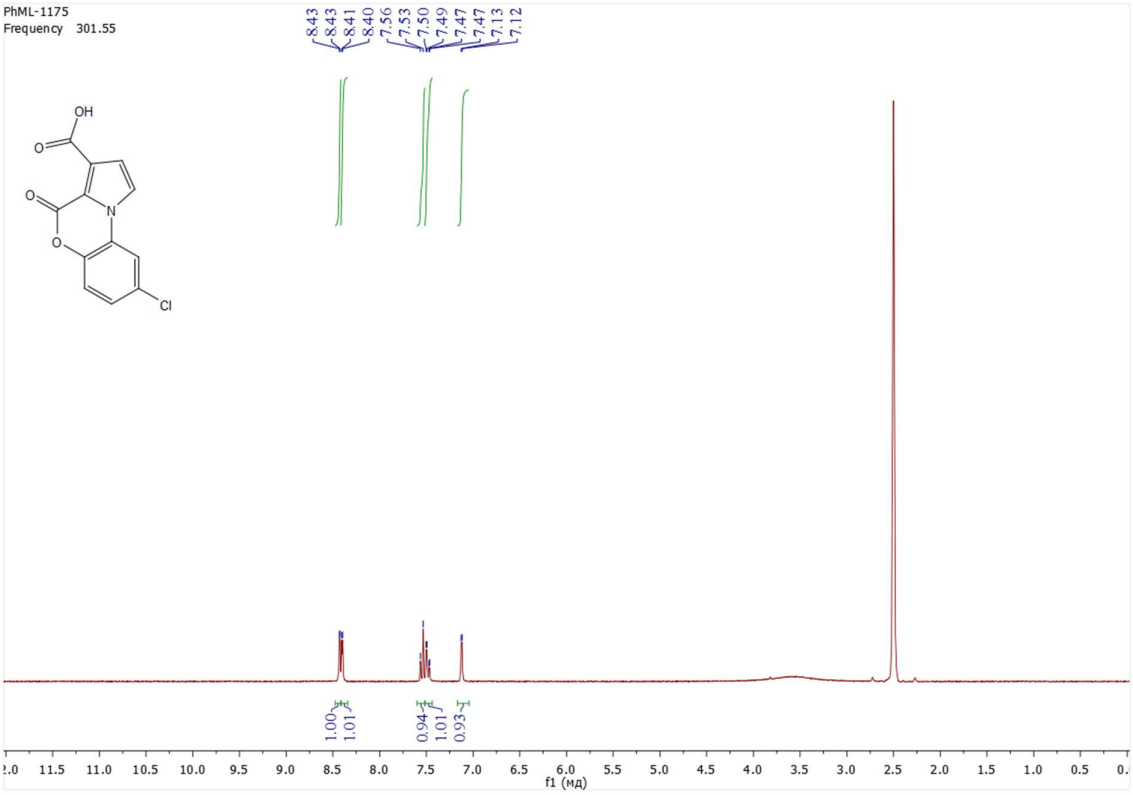

Figure S19. ^{1}H-NMR spectrum of 8-chloro-4-oxo-4*H*-pyrrolo[2,1-*c*][1,4]benzoxazine-3-carboxylic acid (**5c**) in DMSO-d_6

Chemical characterization of 8-tert-butyl-4-oxo-4H-pyrrolo[2,1-c][1,4]benzoxazine-3-carboxylic acid (**5d**). White solid, mp 247-248°C; yield 86%. ^{1}H-NMR (400 MHz, DMSO-d_6): δ 1.37 (s, 9H, 3CH$_3$), 7.15 (d, $^{3}J_{HH}$ = 2.9 Hz, 1H, C^{2}H), 7.30–7.60 (m, 2H, 2H$_{Ar}$), 8.14 (s, 1H, 1H$_{Ar}$), 8.58 (d, $^{3}J_{HH}$ = 3.0 Hz, C^{1}H), 13.10 (s, 1H, OH). ^{13}C, NMR (151 MHz, DMSO-d_6): δ = 31.11, 34.85, 112.86, 115.24, 116.76, 117.08, 120.52, 121.35, 123.50, 124.34, 140.35, 148.80, 154.51, 162.57. MS: m/z 286 (M + H). Anal. Calcd. for $C_{16}H_{15}NO_4$ (%): C, 67.36; H, 5.30; N, 4.91. Found: C, 67.15; H, 5.32; N, 5.00.

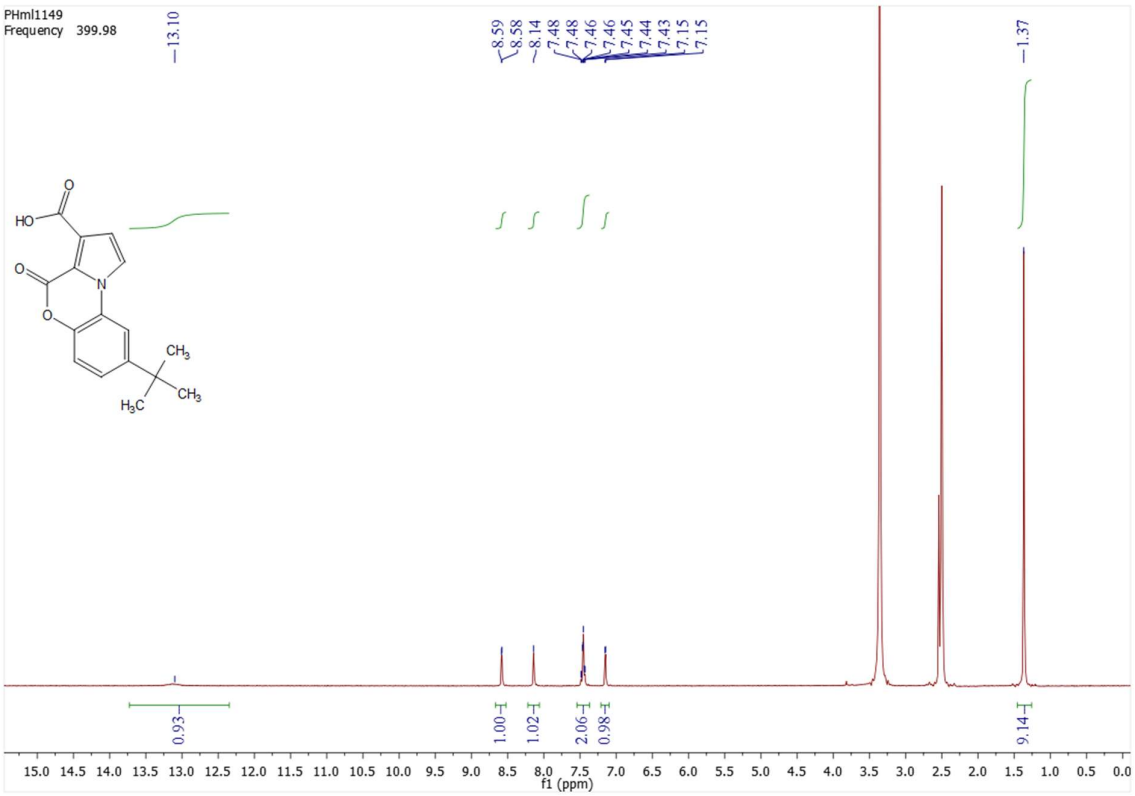

Figure S20. [1]H-NMR spectrum of 8-*tert*-butyl-4-oxo-4*H*-pyrrolo[2,1-*c*][1,4]benzoxazine-3-carboxylic acid (**5d**) in DMSO-d_6

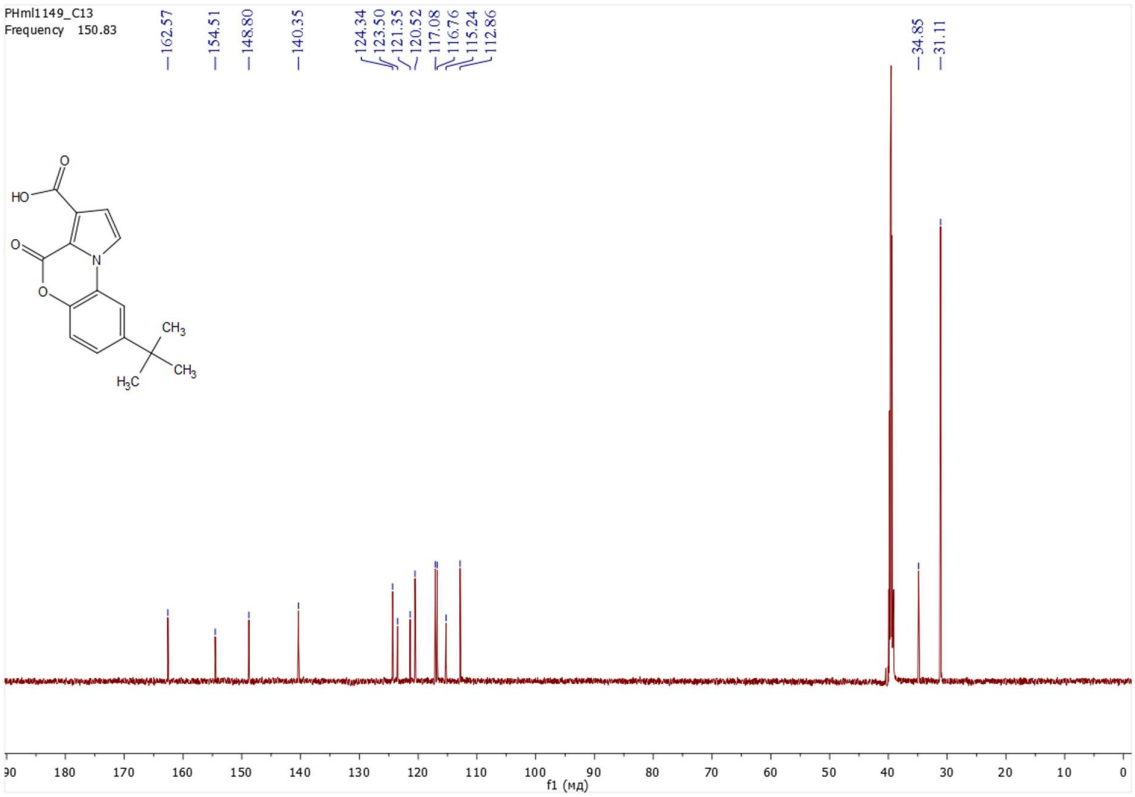

Figure S21. [13]C, NMR spectrum of 8-*tert*-butyl-4-oxo-4*H*-pyrrolo[2,1-*c*][1,4]benzoxazine-3-carboxylic acid (**5d**) in DMSO-d_6

Chemical characterization of 7-fluoro-4-oxo-4H-pyrrolo[2,1-c][1,4]benzoxazine-3-carboxylic acid (**5e**). Gray solid, mp >250°C; yield 81%. ^{1}H-NMR (302 MHz, DMSO-d_6): δ 7.12 (d, $^{3}J_{HH}$ = 2.9 Hz, 1H, 1H$_{Ar}$), 7.35 (ddd, $^{3}J_{HH}$ = 8.9, $^{3}J_{HF}$ = 8.9, $^{4}J_{HH}$ = 2.7 Hz, 1H, 1H$_{Ar}$), 7.55 (dd, $^{3}J_{HF}$ = 9.1, $^{4}J_{HH}$ = 2.7 Hz, 1H, 1H$_{Ar}$), 8.26 (dd, $^{3}J_{HH}$ = 9.1, $^{4}J_{HF}$ = 5.3 Hz, 1H, 1H$_{Ar}$), 8.35 (d, $^{3}J_{HH}$ = 3.0 Hz, 1H, 1H$_{Ar}$), 12.98 (s, 1H, OH). ^{13}C, NMR (151 MHz, DMSO-d_6): δ = 105.22 (d, $^{2}J_{CF}$ = 27.3 Hz, C^{6}), 112.33 (d, $^{2}J_{CF}$ = 23.5 Hz, C^{8}), 114.67, 116.61, 117.41 (d, $^{3}J_{CF}$ = 9.8 Hz, C^{9}), 118.95 (d, $^{4}J_{CF}$ = 2.9 Hz, C^{9a}), 120.23, 123.64, 143.37 (d, $^{3}J_{CF}$ = 12.9 Hz, C^{5a}), 152.91, 160.00 (d, $^{1}J_{CF}$ = 244.9 Hz, C^{7}), 162.82. ^{19}F, NMR (376 MHz, DMSO-d_6): δ -113.63. MS: m/z 248 (M + H). Anal. Calcd. for $C_{12}H_6FNO_4$ (%): C, 58.31; H, 2.45; N, 5.67. Found: C, 58.55; H, 2.41; N, 5.74.

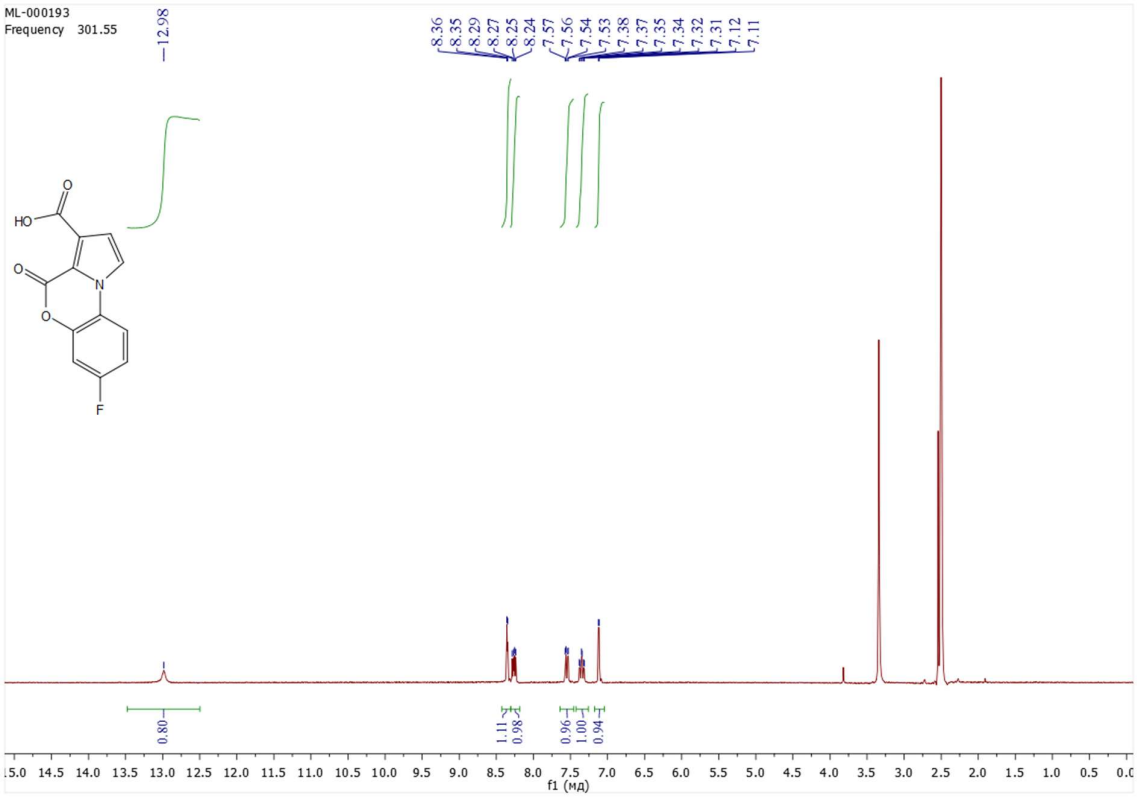

Figure S22. ^{1}H-NMR spectrum of 7-fluoro-4-oxo-4*H*-pyrrolo[2,1-*c*][1,4]benzoxazine-3-carboxylic acid (**5e**) in DMSO-d_6

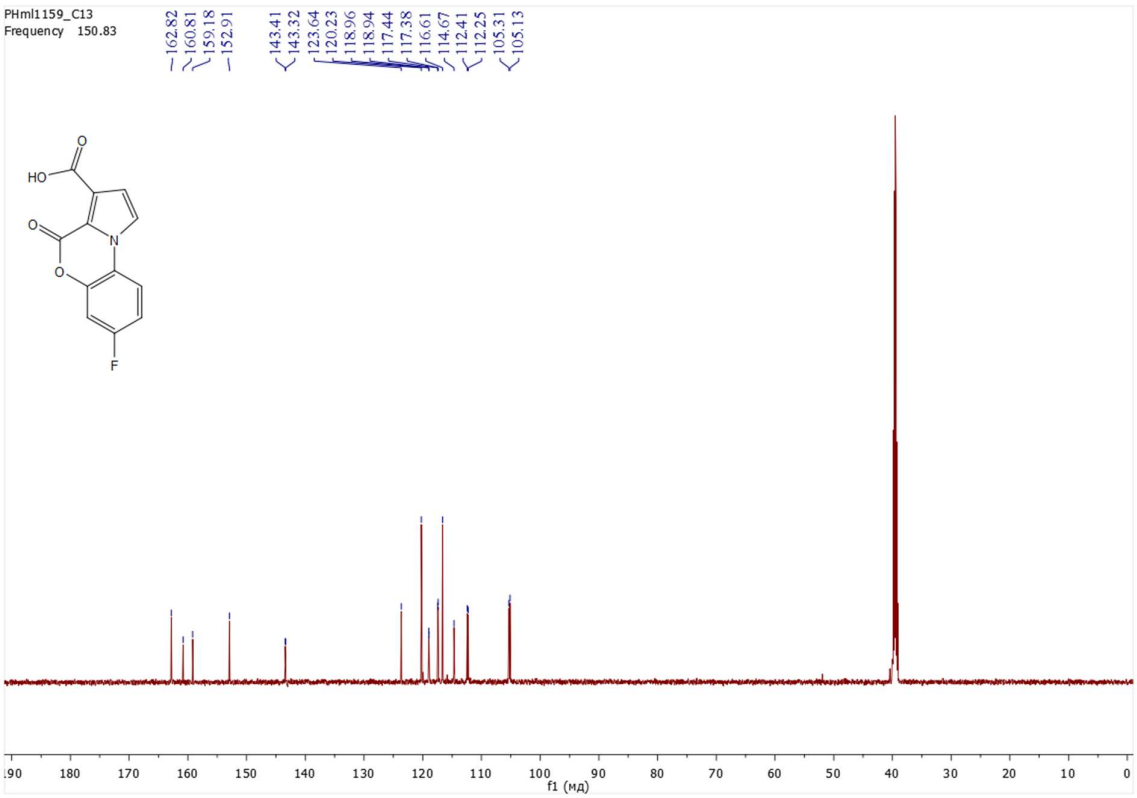

Figure S23. ^{13}C, NMR spectrum of 7-fluoro-4-oxo-4*H*-pyrrolo[2,1-*c*][1,4]benzoxazine-3-carboxylic acid (**5e**) in DMSO-d_6

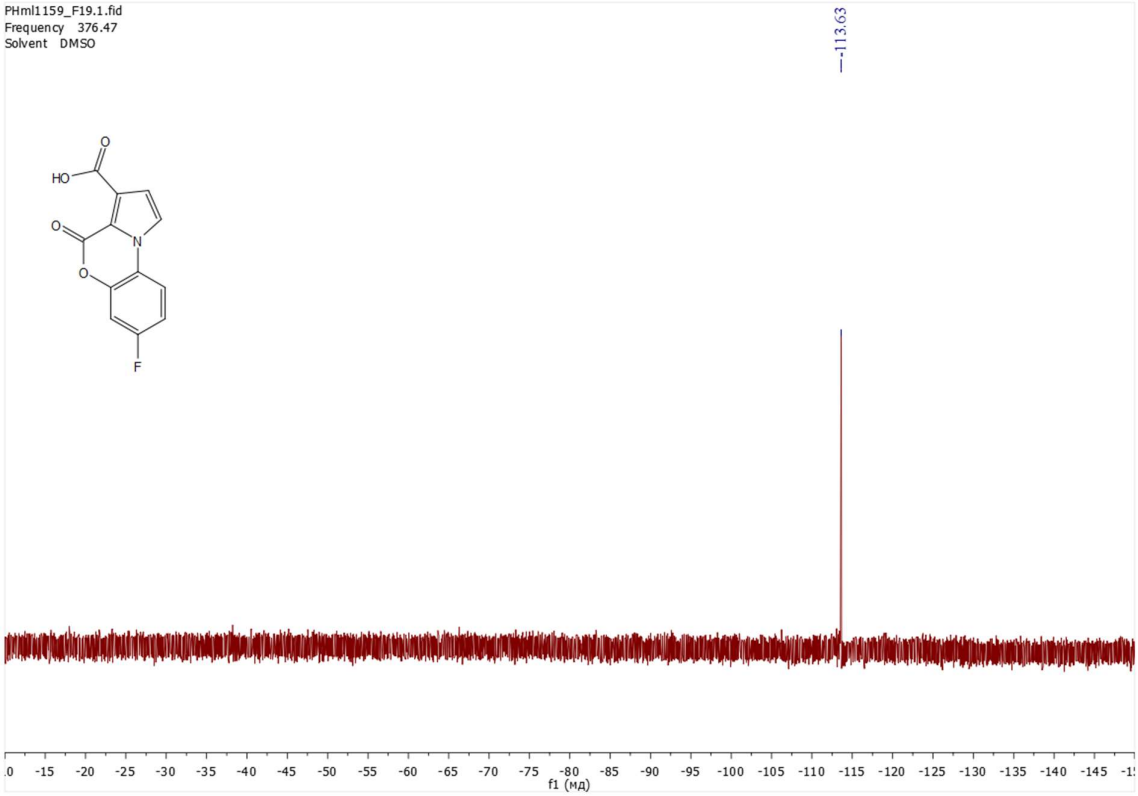

Figure S24. ^{19}F, NMR spectrum of 7-fluoro-4-oxo-4*H*-pyrrolo[2,1-*c*][1,4]benzoxazine-3-carboxylic acid (**5e**) in DMSO-d_6

Chemical characterization of 6-bromo-4-oxo-4H-pyrrolo[2,1-c][1,4]benzoxazine-3-carboxylic acid (**5f**). Braun solid, mp >250°C; yield 93%. ^{1}H-NMR (302 MHz, DMSO-d_6): δ 7.13 (d, $^{3}J_{HH}$ = 2.9 Hz, 1H, C^{2}H), 7.35 (t, $^{3}J_{HH}$ = 8.1 Hz, 1H, 1H$_{Ar}$), 7.72 (d, $^{3}J_{HH}$ = 8.0 Hz, 1H, 1H$_{Ar}$), 8.20 (d, $^{3}J_{HH}$ = 8.3 Hz, 1H, 1H$_{Ar}$), 8.37 (d, $^{3}J_{HH}$ = 3.0 Hz, 1H, C^{1}H), 12.92 (s, 1H, OH). ^{13}C, NMR (151 MHz, DMSO-d_6): δ = 110.09, 115.26, 115.47, 116.82, 120.43, 123.35, 123.94, 125.88, 130.51, 140.08, 152.09, 162.97. MS: m/z 308, 310 (M + H). Anal. Calcd. for $C_{12}H_6BrNO_4$ (%): C, 46.78; H, 1.96; N, 4.55. Found: C, 47.01; H, 2.00; N, 4.44.

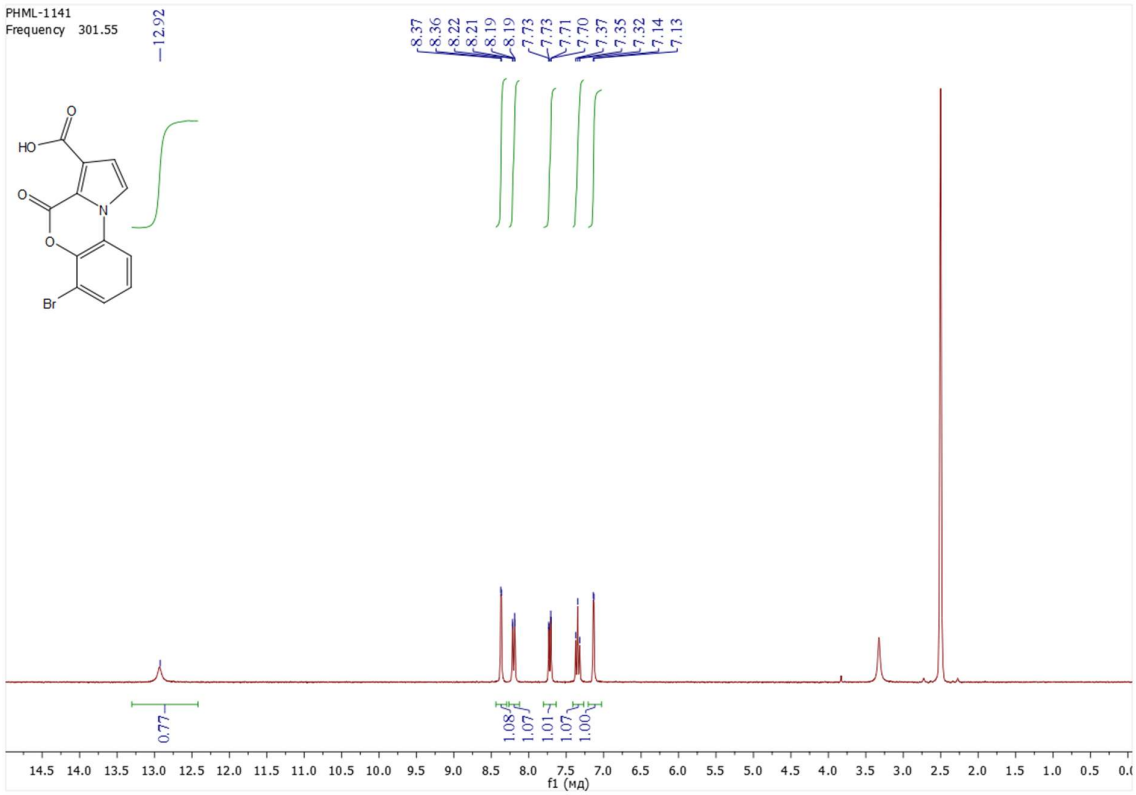

Figure S25. ^{1}H-NMR spectrum of 6-bromo-4-oxo-4*H*-pyrrolo[2,1-*c*][1,4]benzoxazine-3-carboxylic acid (**5f**) in DMSO-d_6

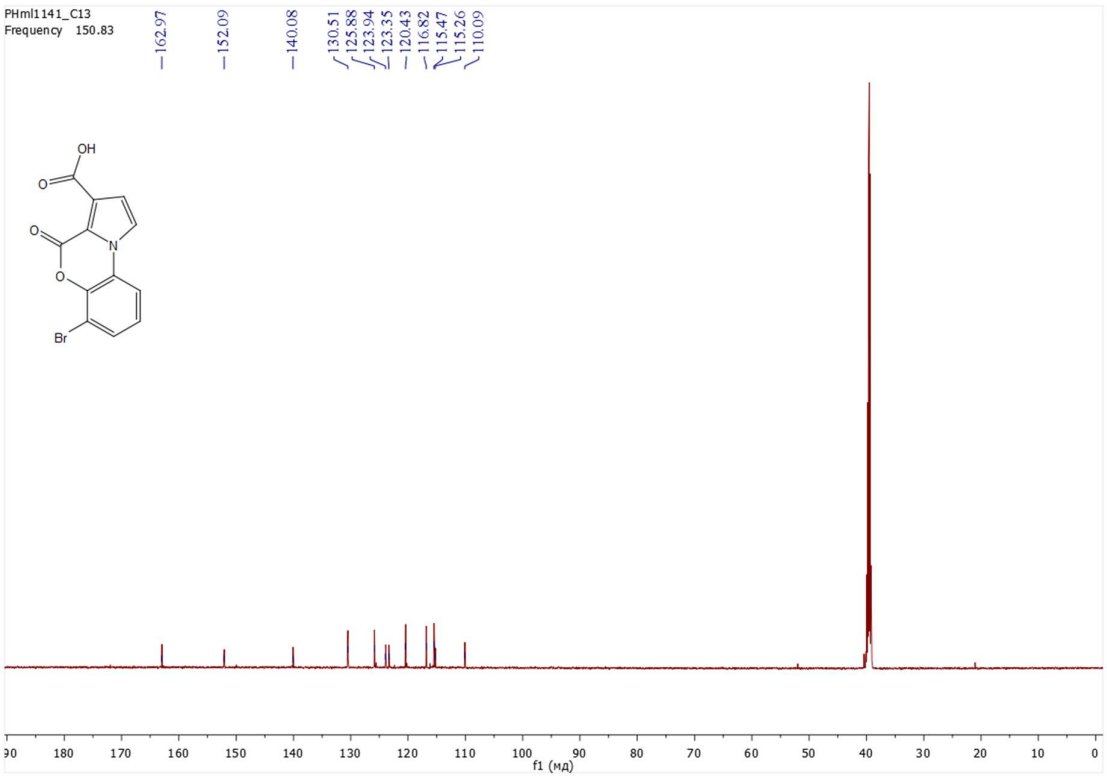

Figure S26. ^{13}C, NMR spectrum of 6-bromo-4-oxo-4*H*-pyrrolo[2,1-*c*][1,4]benzoxazine-3-carboxylic acid (**5f**) in DMSO-d_6

Synthesis and spectra characteristics of compounds 6a-e and 7a-f

General procedure for the synthesis of tert-butyl (1-oxo-3,4-dihydro-1H-pyrrolo[2,1-c][1,4]oxazin-8-yl)carbamate ***6a-e*** *and tert-butyl (4-oxo-4H-pyrrolo[2,1-c][1,4]benzoxazin-3-yl)carbamate* ***7a-f***. To a suspension of (7.2 mmol) 1-oxo-3,4-dihydro-1*H*-pyrrolo[2,1-*c*][1,4]oxazine-8-carboxylic acid **4a-e** or 4-oxo-4*H*-pyrrolo[2,1-*c*][1,4]benzoxazine-3-carboxylic acid **5a-f** in 50 cm^3 toluene, 0.95 g of TEA (1.3 mmol) and 2.14 g of *tert*-butyl alcohol (28.9 mmol) were added. To the resulting mixture was added 2.59 g of DPPA (9.4 mmol) dropwise. The resulting mixture was stirred at 110°C for 6–14 h. After the reaction was completed, the reaction mixture was cooled and washed with H_2O (2 × 10 cm^3) and brine (2 × 10 cm^3), the organic phase was dried over Na_2SO_4 and evaporated under reduced pressure. For the compounds **6a-e**, **7a**,**b**,**d**, formed precipitate was purified by column chromatography on silica gel, eluent CH_2Cl_2–MeOH, 100:1. For the compounds **7c**,**e**,**f**, formed precipitate was washed with boiling hexane (2 × 5 cm^3) and dried under reduced pressure.

Chemical characterization of tert-butyl (3-methyl-1-oxo-3,4-dihydro-1H-pyrrolo[2,1-c][1,4]oxazin-8-yl)carbamate (**6a**). Beige solid, mp 84-85°C; yield 77%. ^{1}H-NMR (302 MHz, $CDCl_3$): δ 1.50-1.51 (m, 12H, C^{3}C$\underline{H}_3$ + 3CH_3), 3.83 (dd, $^2J_{HH}$ = 12.9, $^3J_{HH}$ = 10.1 Hz, 1H, C$^4\underline{H}$H), 4.04 (dd, $^2J_{HH}$ = 12.9, $^3J_{HH}$ = 3.1 Hz, 1H, C^{4}H$\underline{H}$), 4.69-4.80 (m, 1H, C^{3}H), 6.71 (d, $^3J_{HH}$ = 2.7 Hz,1H, C^{7}H) 6.75 (s, 1H, NH), 8.13 (s, 1H, C^{6}H). ^{13}C, NMR (101 MHz, $CDCl_3$): δ = 18.10, 28.35, 48.68, 73.96, 80.68, 101.22,

104.69, 124.23, 134.32, 152.61, 160.05. MS: m/z 211 (M - t-Bu + H). Anal. Calcd. for $C_{13}H_{18}N_2O_4$ (%): C, 58.63; H, 6.81; N, 10.52. Found: C, 58.44; H, 6.78; N, 10.64.

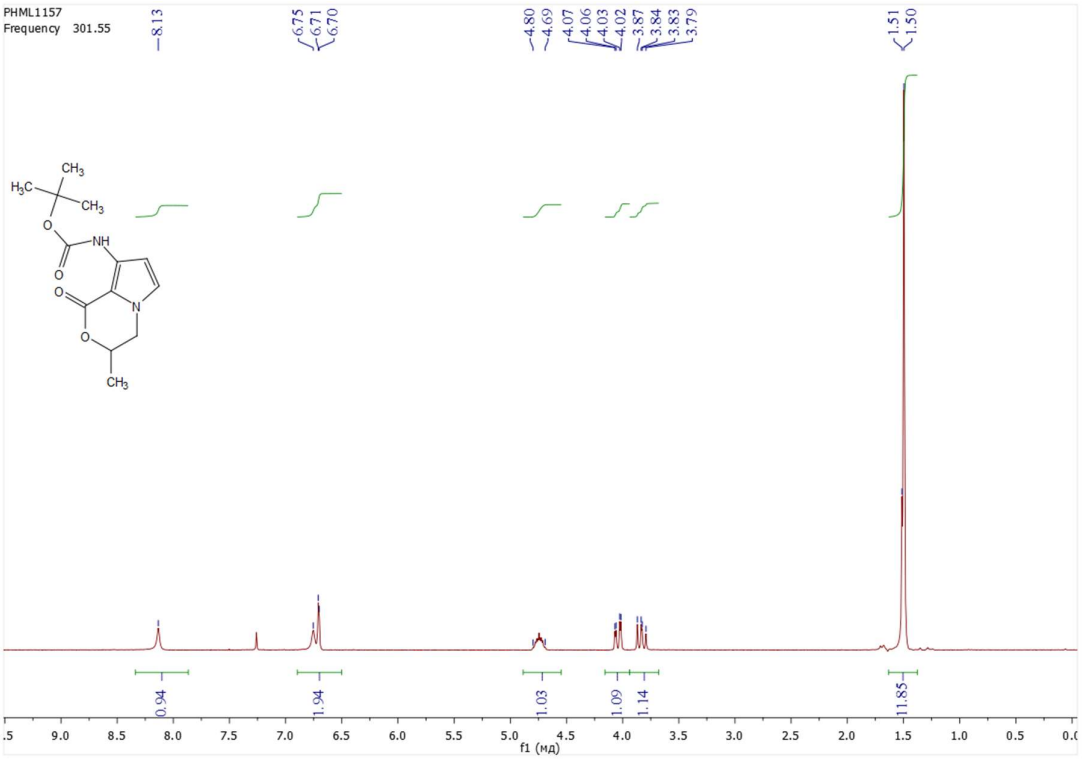

Figure S27. ^{1}H-NMR spectrum of *tert*-butyl (3-methyl-1-oxo-3,4-dihydro-1*H*-pyrrolo[2,1-*c*][1,4]oxazin-8-yl)carbamate (**6a**) in $CDCl_3$

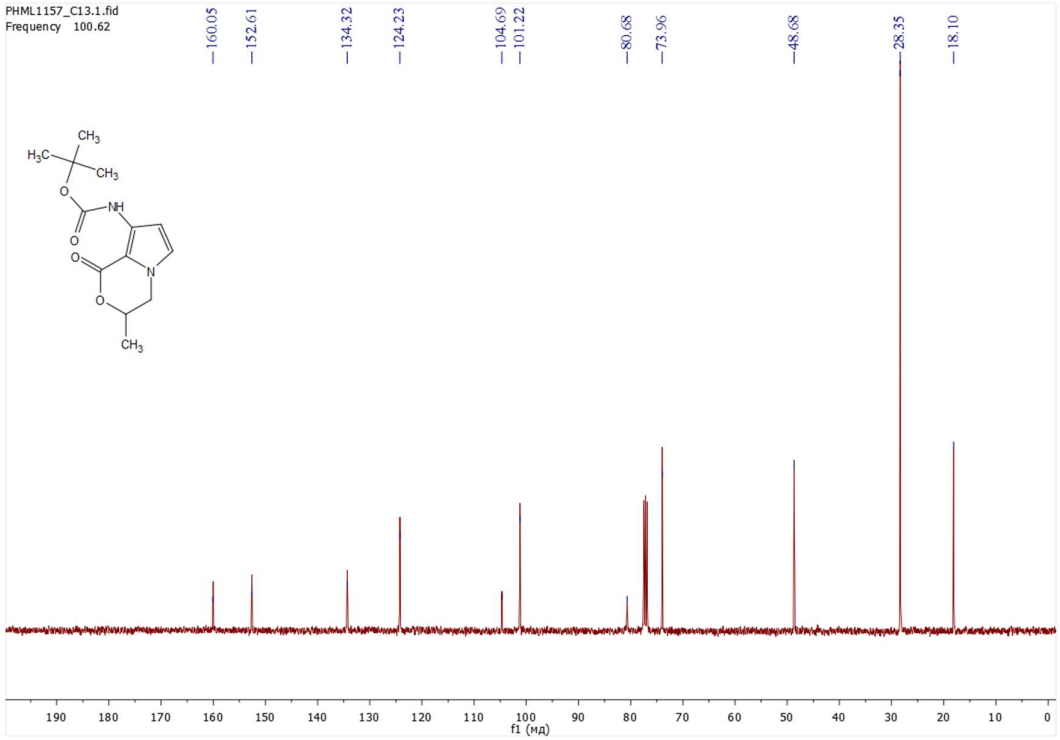

Figure S28. ^{13}C, NMR spectrum of *tert*-butyl (3-methyl-1-oxo-3,4-dihydro-1*H*-pyrrolo[2,1-*c*][1,4]oxazin-8-yl)carbamate (**6a**) in $CDCl_3$

Chemical characterization of tert-butyl (4,4-dimethyl-1-oxo-3,4-dihydro-1H-pyrrolo[2,1-c][1,4]oxazin-8-yl)carbamate (**6b**). White solid, mp 111-112°C; yield 81%. ^{1}H-NMR (400 MHz, $CDCl_3$): δ 1.50-1.51 (m, 15H, $2CH_3$ + $3CH_3$), 4.22 (s, 2H, C^3H_2), 6.57 – 6.93 (m, 2H, C^7H + NH), 8.23 (s, 1H, C^6H). ^{13}C, NMR (151 MHz, $CDCl_3$): δ = 24.33, 28.38, 53.46, 75.65, 80.65, 101.37, 104.11, 120.89, 135.09, 152.67, 159.81. MS: m/z 225 (M - t-Bu + H). Anal. Calcd. for $C_{14}H_{20}N_2O_4$ (%): C, 59.99; H, 7.19; N, 9.99. Found: C, 60.17; H, 7.16; N, 10.06.

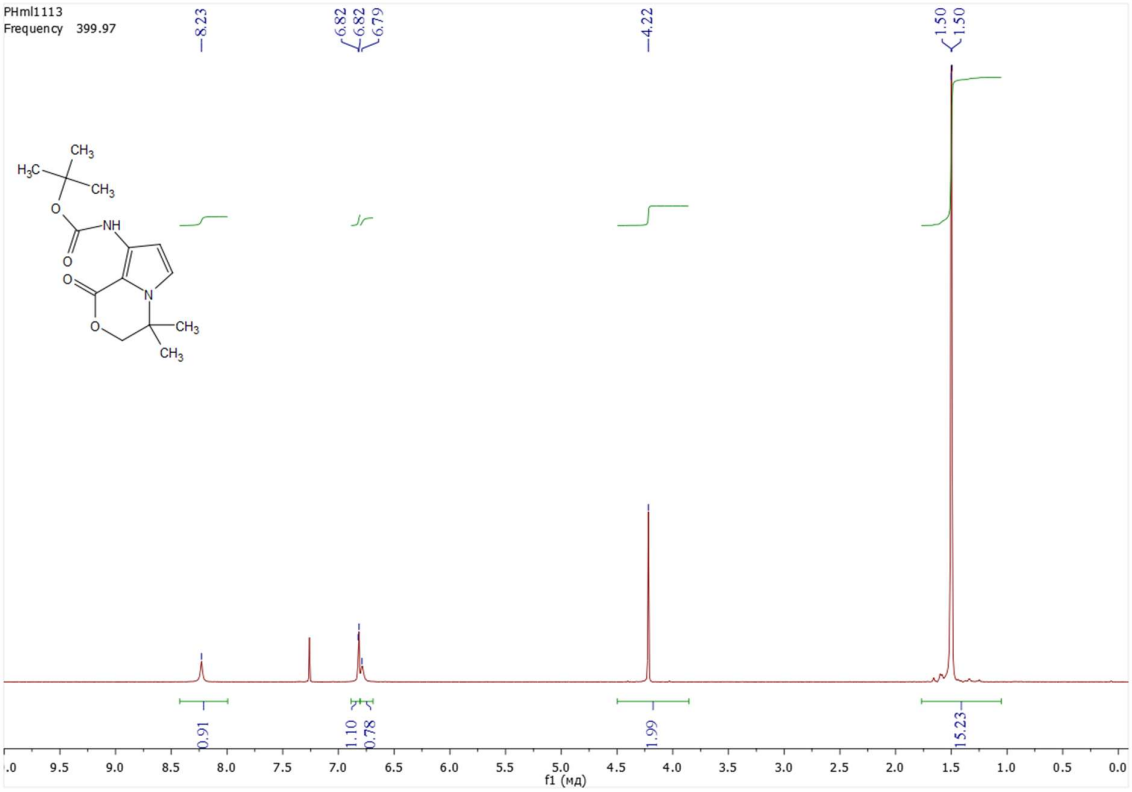

Figure S29. ^{1}H-NMR spectrum of *tert*-butyl (4,4-dimethyl-1-oxo-3,4-dihydro-1*H*-pyrrolo[2,1-*c*][1,4]oxazin-8-yl)carbamate (**6b**) in $CDCl_3$

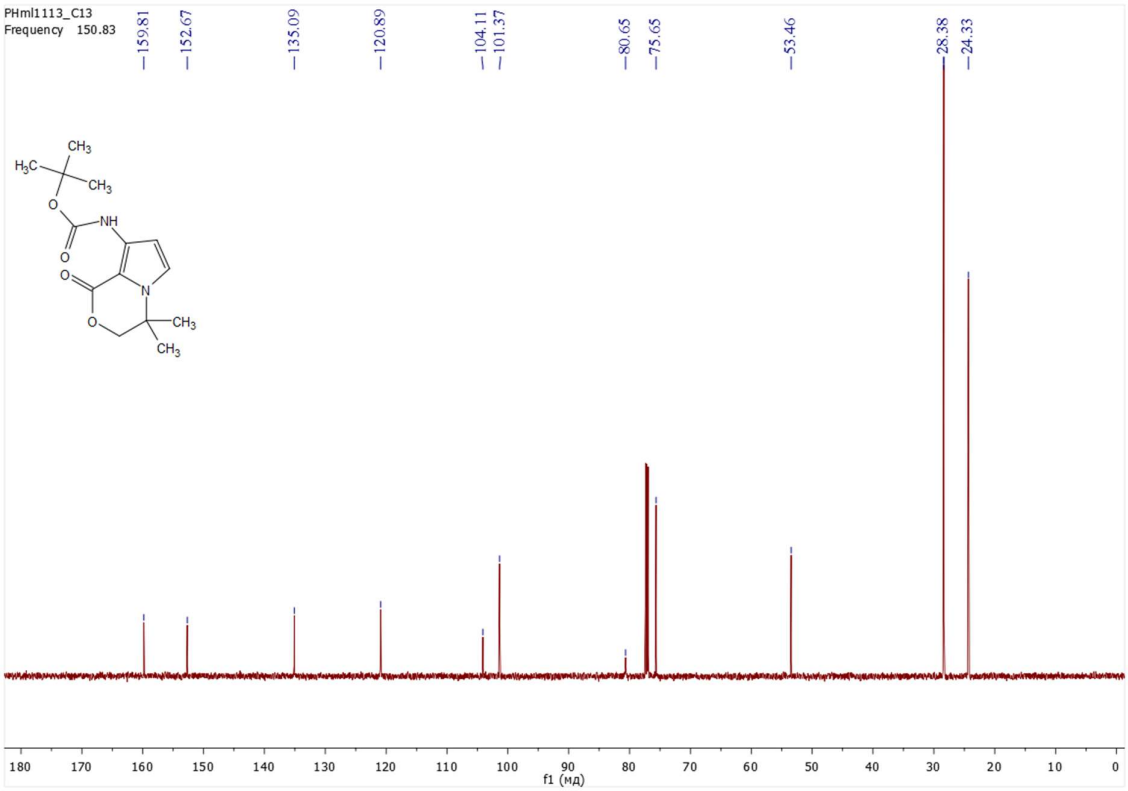

Figure S30. ^{13}C, NMR spectrum of *tert*-butyl (4,4-dimethyl-1-oxo-3,4-dihydro-1*H*-pyrrolo[2,1-*c*][1,4]oxazin-8-yl)carbamate (**6b**) in $CDCl_3$

Chemical characterization of tert-butyl [(4S)-4-(1-methylethyl)-1-oxo-3,4-dihydro-1H-pyrrolo[2,1-c][1,4]oxazin-8-yl]carbamate (**6c**). Beige solid, mp 84-85°C; yield 69%. ^{1}H-NMR (400 MHz, $CDCl_3$): δ 0.92 (d, $^3J_{HH}$ = 6.8 Hz, 3H, CHC<u>H</u>$_3$), 1.03 (d, $^3J_{HH}$ = 6.8 Hz, 3H, CHC<u>H</u>$_3$), 1.50 (s, 9H, 3CH_3), 2.13-2.22 (m, 1H, C<u>H</u>$(CH_3)_2$), 3.75 (dt, $^3J_{HH}$ = 6.6 Hz, $^3J_{HH}$ = 3.1 Hz, 1H, C^{4}H), 4.51 (dd, $^2J_{HH}$ = 11.8 Hz, $^3J_{HH}$ = 3.3 Hz, 1H, C^{3}H), 4.56 (dd, $^2J_{HH}$ = 11.8 Hz, $^3J_{HH}$ = 2.8 Hz, 1H, C^{3}H), 6.76 (s, 2H, C^{7}H + NH), 8.16 (s, 1H, C^{6}H). ^{13}C, NMR (151 MHz, $CDCl_3$): δ = 19.23, 19.49, 28.40, 30.46, 59.29, 68.07, 80.71, 100.72, 104.63, 124.58, 134.52, 152.68, 160.04. MS: m/z 239 (M -*t*-Bu + H). Anal. Calcd. for $C_{15}H_{22}N_2O_4$ (%): C, 61.21; H, 7.53; N, 9.52. Found: C, 61.04; H, 7.56; N, 9.43.

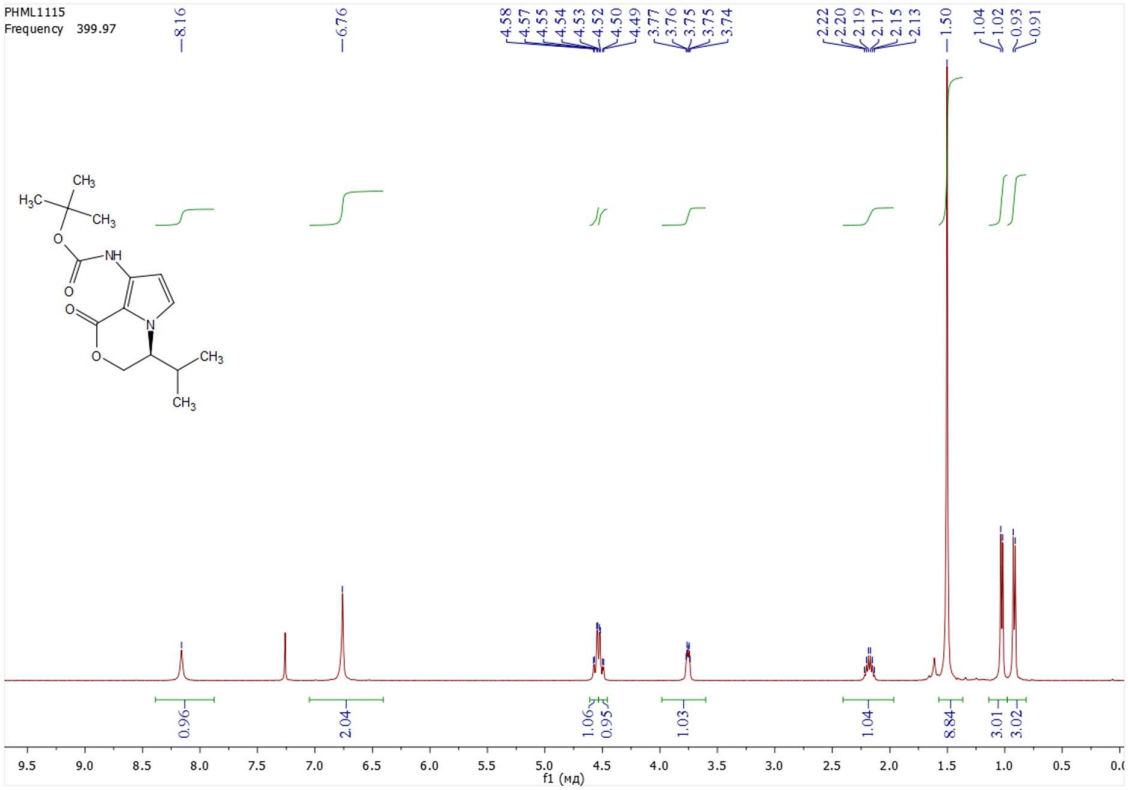

Figure S31. ^{1}H-NMR spectrum of *tert*-butyl [(4*S*)-4-(1-methylethyl)-1-oxo-3,4-dihydro-1*H*-pyrrolo[2,1-*c*][1,4]oxazin-8-yl]carbamate (**6c**) in $CDCl_3$

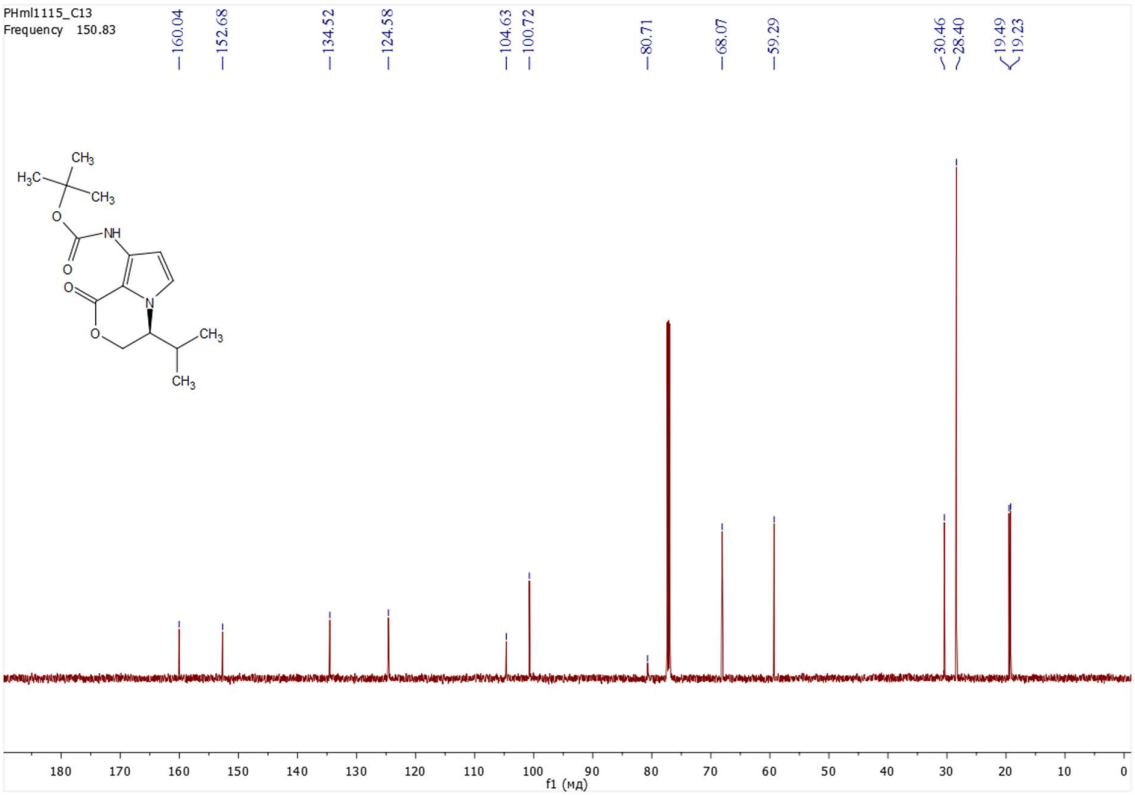

Figure S32. ^{13}C, NMR spectrum of *tert*-butyl [(4*S*)-4-(1-methylethyl)-1-oxo-3,4-dihydro-1*H*-pyrrolo[2,1-*c*][1,4]oxazin-8-yl]carbamate (**6c**) in $CDCl_3$

Chemical characterization of tert-butyl (1-oxo-3-phenyl-3,4-dihydro-1H-pyrrolo[2,1-c][1,4]oxazin-8-yl)carbamate (**6d**). White solid, mp 164-165°C; yield 85%. ^{1}H-NMR (400 MHz, $CDCl_3$): δ 1.52 (s, 9H, $3CH_3$), 4.13 (dd, $^{2}J_{HH}$ = 13.2, $^{3}J_{HH}$ = 10.3 Hz, 1H, C^{4}H), 4.21 (dd, $^{2}J_{HH}$ = 13.2, $^{3}J_{HH}$ = 3.6 Hz, 1H, C^{4}H), 5.62 (dd, $^{3}J_{HH}$ = 10.4, $^{3}J_{HH}$ = 3.6 Hz, 1H, C^{3}H), 6.75 (d, $^{3}J_{HH}$ = 2.8 Hz, 1H, C^{7}H), 6.81 (s, 1H, NH), 7.40–7.45 (m, 5H, $5H_{Ar}$), 8.18 (s, 1H, C^{6}H).^{13}C, NMR (151 MHz, $CDCl_3$): δ = 28.41, 49.19, 79.06, 80.82, 101.54, 104.90, 124.39, 126.45, 128.99, 129.41, 134.77, 135.42, 152.64, 159.85. MS: m/z 273 (M -*t*-Bu + H). Anal. Calcd. for $C_{18}H_{20}N_2O_4$ (%): C, 65.84; H, 6.14; N, 8.53. Found: C, 65.65; H, 6.18; N, 8.46.

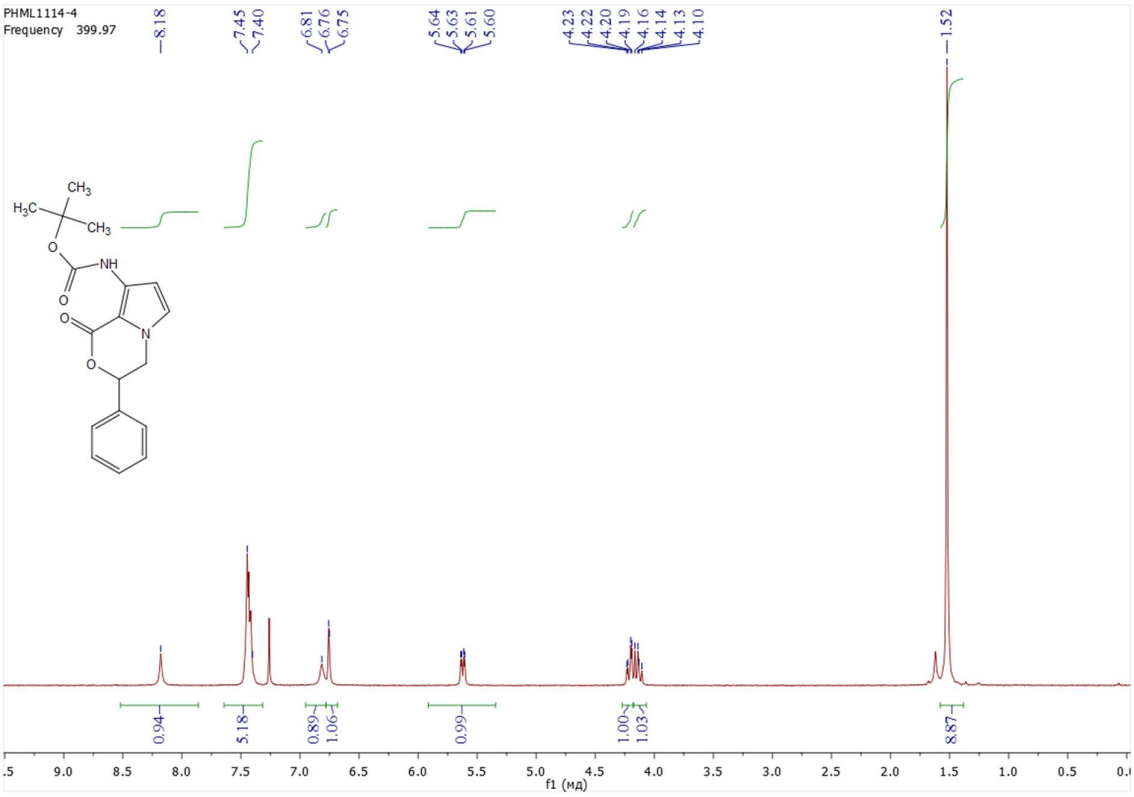

Figure S33. ^{1}H-NMR spectrum of *tert*-butyl (1-oxo-3-phenyl-3,4-dihydro-1*H*-pyrrolo[2,1-*c*][1,4]oxazin-8-yl)carbamate (**6d**) in $CDCl_3$

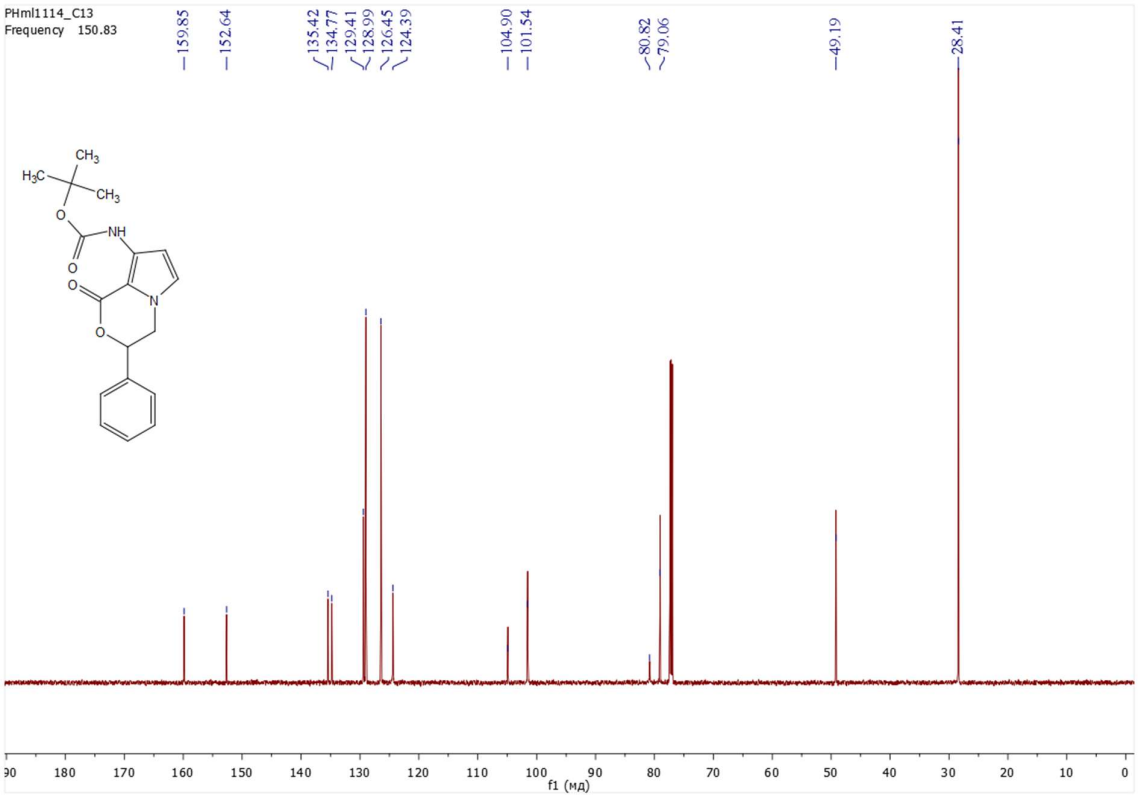

Figure S34. ^{13}C, NMR spectrum of *tert*-butyl (1-oxo-3-phenyl-3,4-dihydro-1*H*-pyrrolo[2,1-*c*][1,4]oxazin-8-yl)carbamate (**6d**) in $CDCl_3$

Chemical characterization of tert-butyl [(5aS,9aS)-4-oxo-5a,6,7,8,9,9a-hexahydro-4H-pyrrolo[2,1-c][1,4]benzoxazin-3-yl]carbamate (**6e**). White solid, mp 194-195°C; yield 87%. ^{1}H-NMR (400 MHz, DMSO-d_6): δ 1.30-1.43 (m, 3H), 1.47 (s, 9H, $3CH_3$), 1.55-1.67 (m, 1H), 1.74-1.85 (m, 2H), 2.05–2.08 (m, 1H), 2.60-2.67 (m, 1H), 3.71–4.01 (m, 1H, C^{9a}H), 4.26-4.34 (m, 1H, C^{5a}H), 6.54 (s, 1H, NH), 7.20 (s, 1H, C^{2}H), 8.13 (s, 1H, C^{1}H). ^{13}C, NMR (151 MHz, $CDCl_3$): δ = 23.40, 23.61, 27.29, 28.38, 29.79, 56.36, 80.63, 80.98, 101.15, 105.72, 120.86, 134.79, 152.66, 160.23. MS: m/z 251 (M -*t*-Bu + H). Anal. Calcd. for $C_{16}H_{22}N_2O_4$ (%): C, 62.73; H, 7.24; N, 9.14. Found: C, 62.50; H, 7.22; N, 9.23.

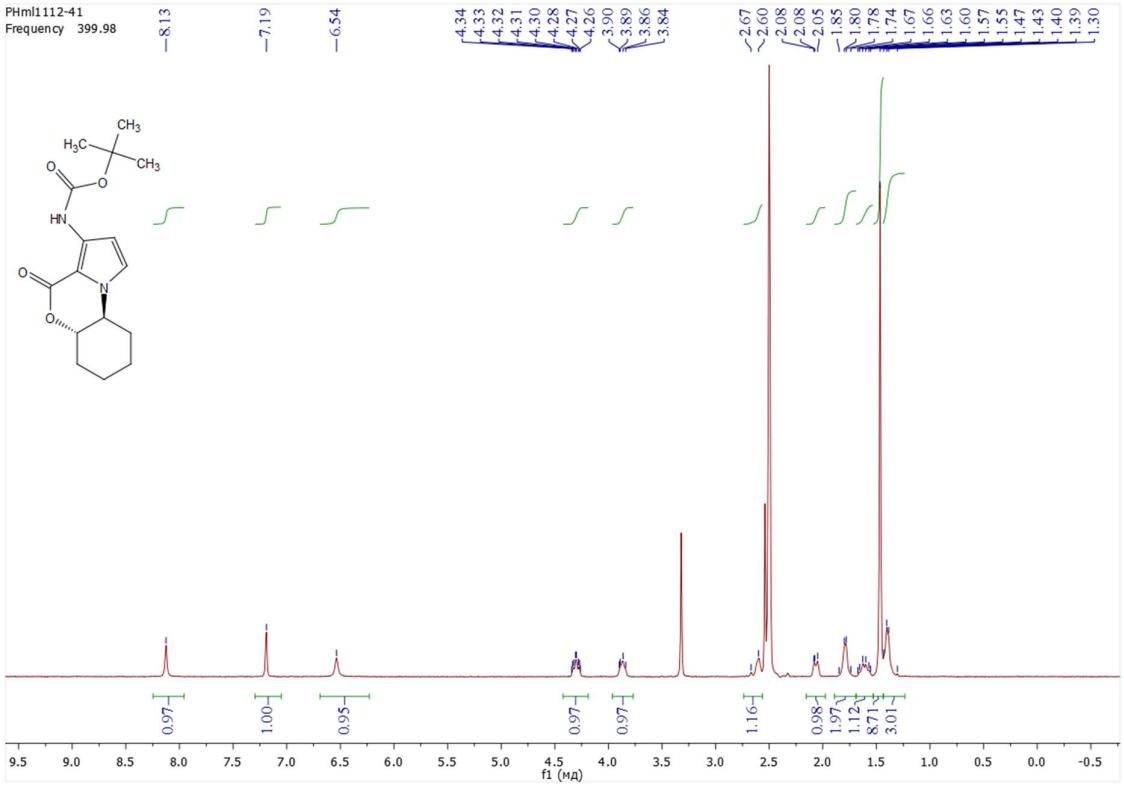

Figure S35. [1]H-NMR spectrum of *tert*-butyl [(5*aS*,9*aS*)-4-oxo-5*a*,6,7,8,9,9*a*-hexahydro-4*H*-pyrrolo[2,1-*c*][1,4]benzoxazin-3-yl]carbamate (**6e**) in DMSO-d_6

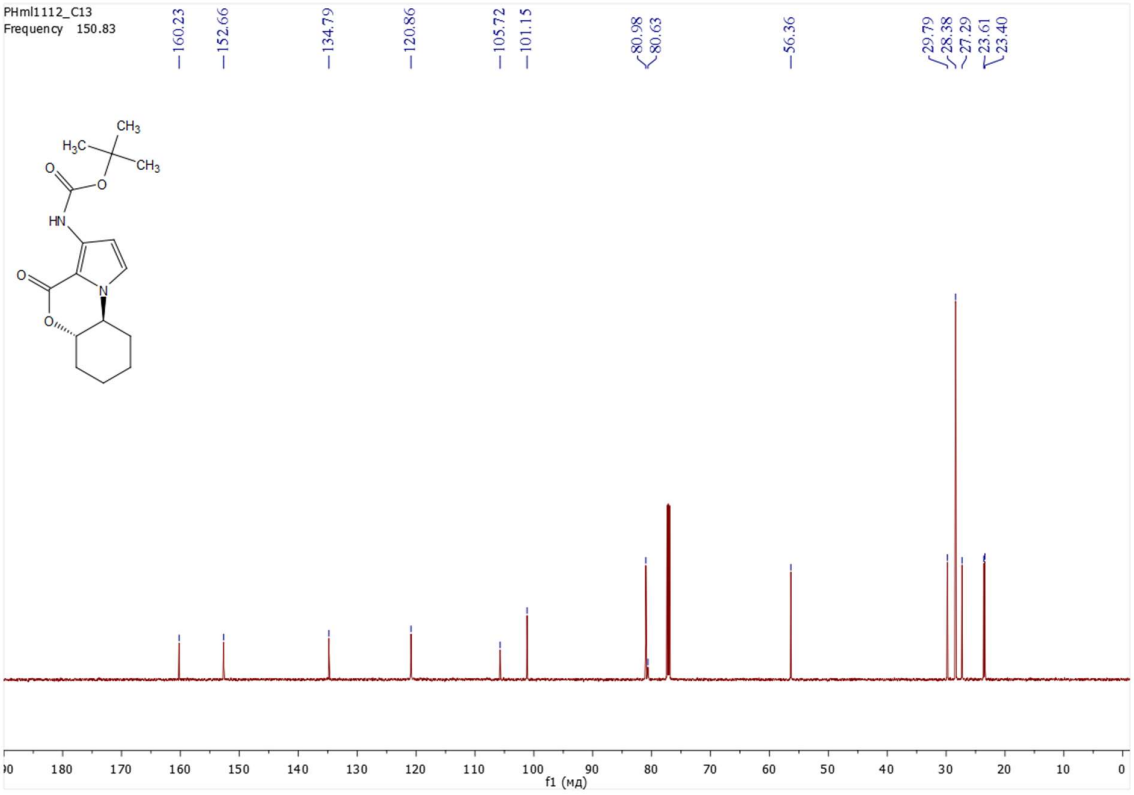

Figure 36 [13]C, NMR spectrum of *tert*-butyl [(5*aS*,9*aS*)-4-oxo-5*a*,6,7,8,9,9*a*-hexahydro-4*H*-pyrrolo[2,1-*c*][1,4]benzoxazin-3-yl]carbamate (**6e**) in $CDCl_3$

Chemical characterization of tert-butyl (4-oxo-4H-pyrrolo[2,1-c][1,4]benzoxazin-3-yl)carbamate (**7a**). Beige solid, mp 146-147°C; yield 61%. ^{1}H-NMR (400 MHz, DMSO-d_6): δ 1.50 (s, 9H, 3CH_3), 6.97 (s, 1H, C^2H), 7.29-7.36 (m, 2H, 2H_{Ar}), 7.39 (d, $^3J_{HH}$ = 7.7 Hz, 1H, 1H_{Ar}), 8.01 (d, $^3J_{HH}$ = 7.5 Hz, 1H, 1H_{Ar}), 8.15 + 8.23 (s + s, 2H, C^1H + NH). ^{13}C, NMR (126 MHz, $CDCl_3$): δ = 28.40, 81.24, 102.96, 104.60, 113.68, 117.89, 118.45, 122.64, 125.06, 125.98, 134.38, 142.76, 152.50, 155.33. MS: m/z 245 (M -*t*-Bu + H). Anal. Calcd. for $C_{16}H_{16}N_2O_4$ (%): C, 63.99; H, 5.37; N, 9.33. Found: C, 64.16; H, 5.40; N, 9.24.

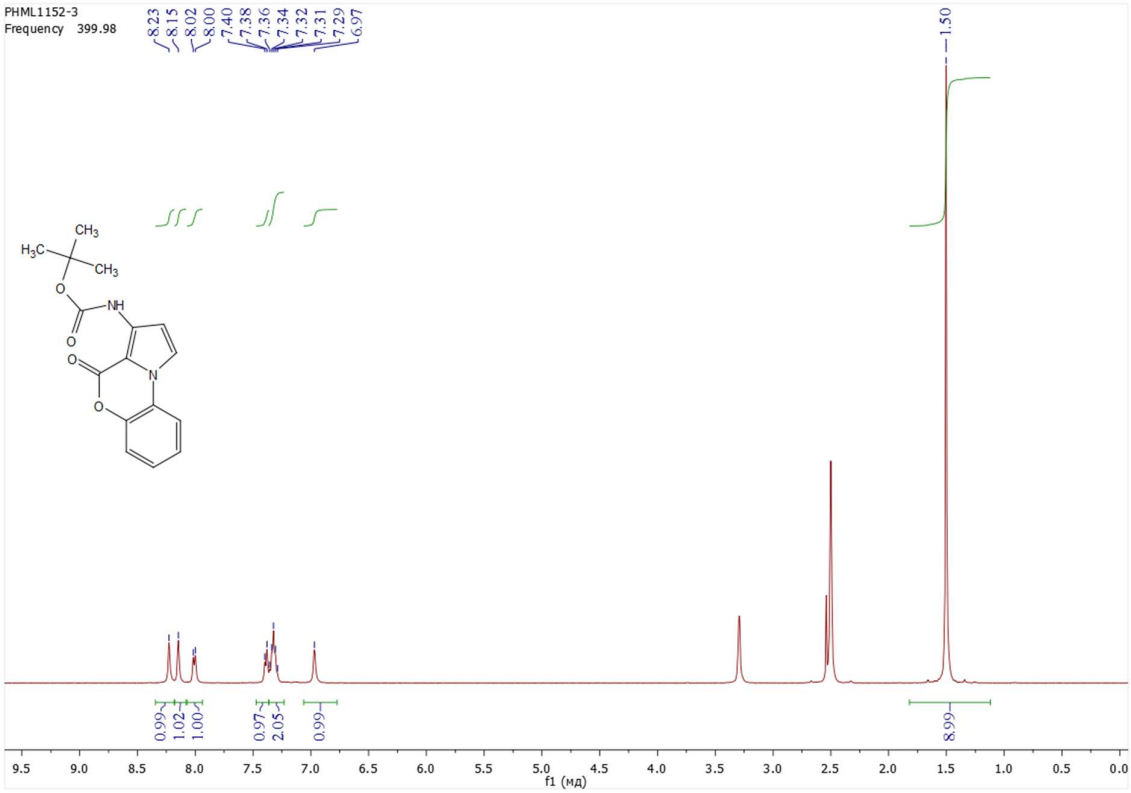

Figure S37. ^{1}H-NMR spectrum of *tert*-butyl (4-oxo-4*H*-pyrrolo[2,1-*c*][1,4]benzoxazin-3-yl)carbamate (**7a**) in DMSO-d_6

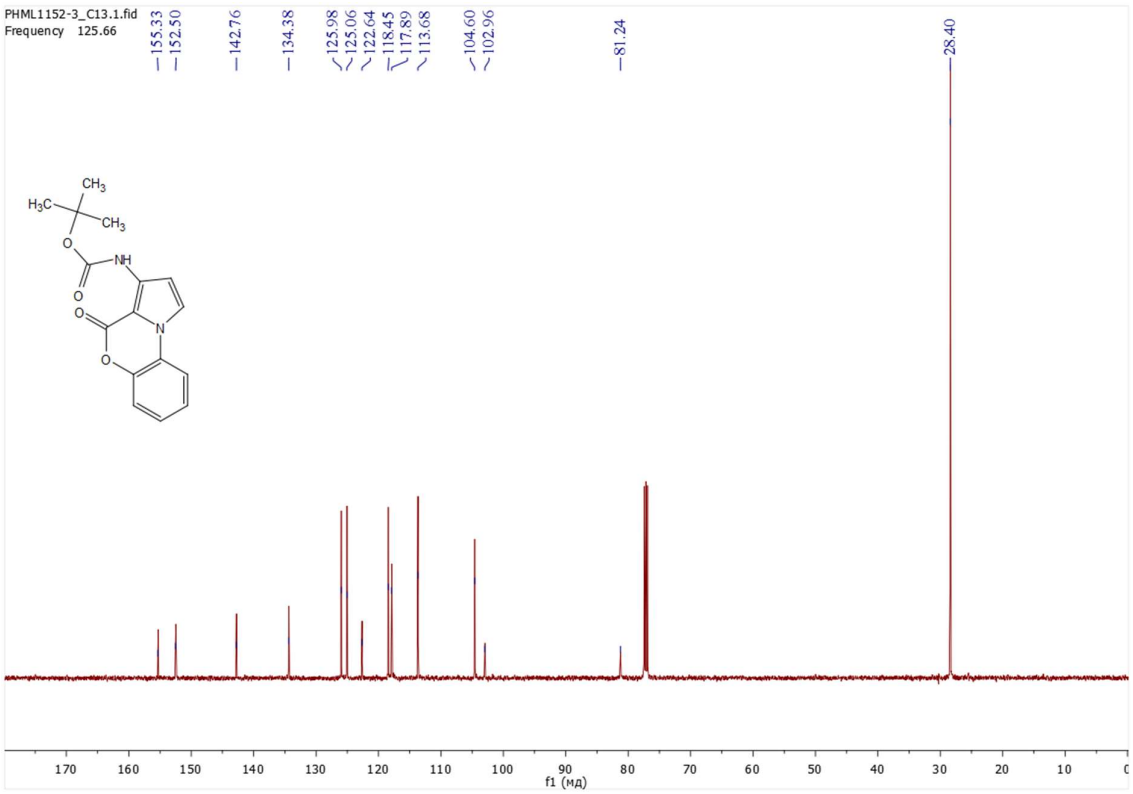

Figure S38. ^{13}C, NMR spectrum of *tert*-butyl (4-oxo-4*H*-pyrrolo[2,1-*c*][1,4]benzoxazin-3-yl)carbamate (**7a**) in $CDCl_3$

Chemical characterization of tert-butyl (9-methyl-4-oxo-4H-pyrrolo[2,1-c][1,4]benzoxazin-3-yl)carbamate (**7b**). White solid, mp 198-199°C; yield 54%. ^{1}H-NMR (302 MHz, $CDCl_3$): δ 1.54 (s, 9H, $3CH_3$), 2.75 (s, 3H, CH_3), 7.04-7.22 (m, 4H, $3H_{Ar}$ + C^2H), 7.80 (d, $^3J_{HH}$ = 3.2 Hz, 1H, C^1H), 8.45 (s, 1H, NH). ^{13}C, NMR (126 MHz, $CDCl_3$): δ = 22.90, 28.43, 81.18, 103.95, 104.18, 116.84, 122.45, 123.12, 125.28, 126.05, 128.85, 134.24, 143.81, 152.57, 155.50. MS: m/z 259 (M – *t*-Bu+ H). Anal. Calcd. for $C_{17}H_{18}N_2O_4$ (%): C, 64.96; H, 5.77; N, 8.91. Found: 65.17; H, 5.75; N, 8.83.

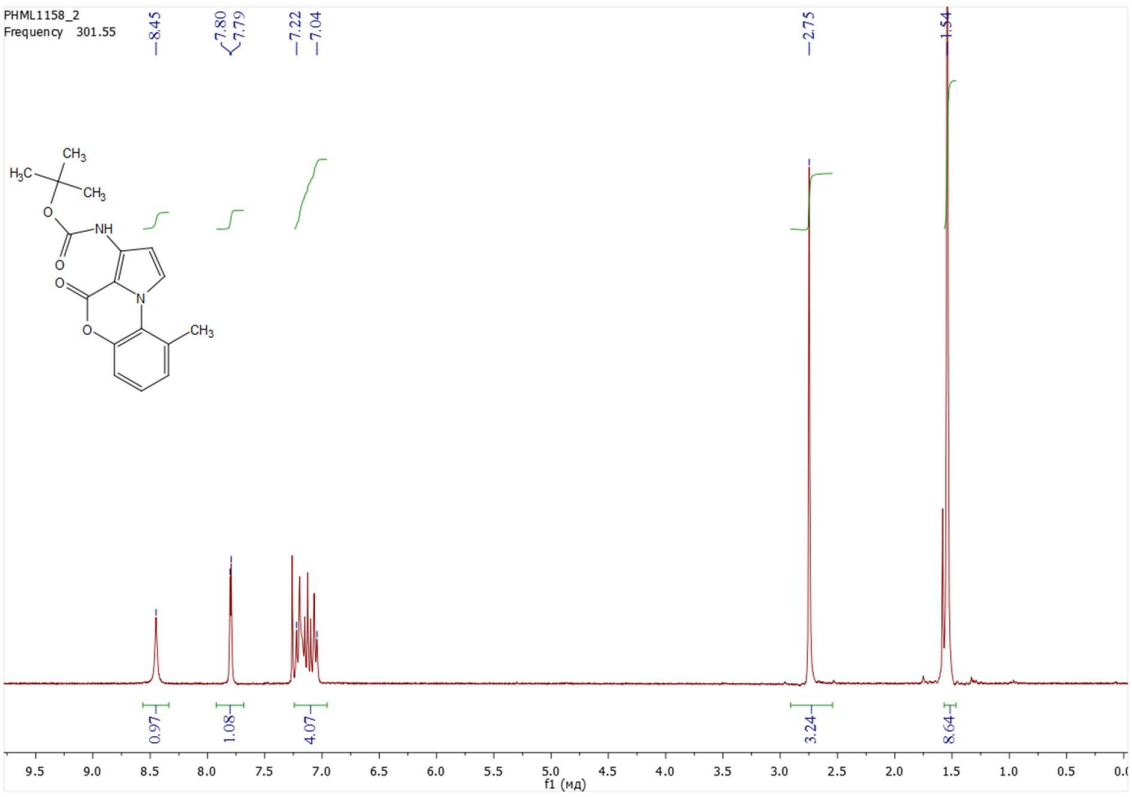

Figure S39. [1]H-NMR spectrum of *tert*-butyl (9-methyl-4-oxo-4*H*-pyrrolo[2,1-*c*][1,4]benzoxazin-3-yl)carbamate (**7b**) in $CDCl_3$

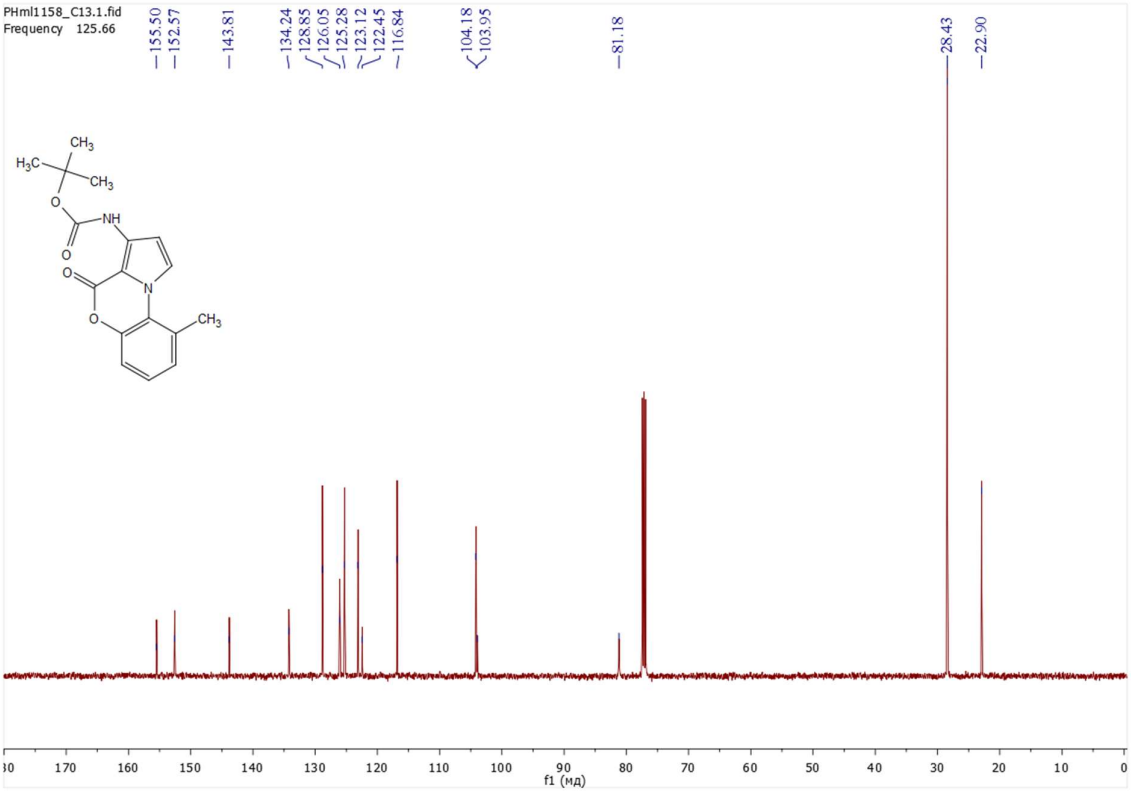

Figure S40. [13]C, NMR spectrum of *tert*-butyl (9-methyl-4-oxo-4*H*-pyrrolo[2,1-*c*][1,4]benzoxazin-3-yl)carbamate (**7b**) in $CDCl_3$

Chemical characterization of tert-butyl (8-chloro-4-oxo-4H-pyrrolo[2,1-c][1,4]benzoxazin-3-yl)carbamate (**7c**). Beige solid, mp 194-195°C; yield 49%. ^{1}H-NMR (400 MHz, DMSO-d_6): δ 1.50 (s, 9H, 3CH_3), 6.98 (s, 1H, C^2H), 7.34 (d, $^3J_{HH}$ = 8.4 Hz, 1H_{Ar}), 7.41 (d, $^3J_{HH}$ = 8.6 Hz, 1H_{Ar}), 8.20-8.23 (m, 3H, C^1H + NH + 1H_{Ar}). ^{13}C, NMR (126 MHz, $CDCl_3$): δ = 28.40, 81.48, 102.65, 105.36, 113.98, 118.16, 119.59, 123.48, 125.87, 130.41, 134.99, 141.38, 152.42, 154.77. MS: m/z 279 (M - *t*-Bu + H). Anal. Calcd. for $C_{16}H_{15}ClN_2O_4$ (%): C, 57.41; H, 4.52; N, 8.37. Found: C, 57.20; H, 4.55; N, 8.44.

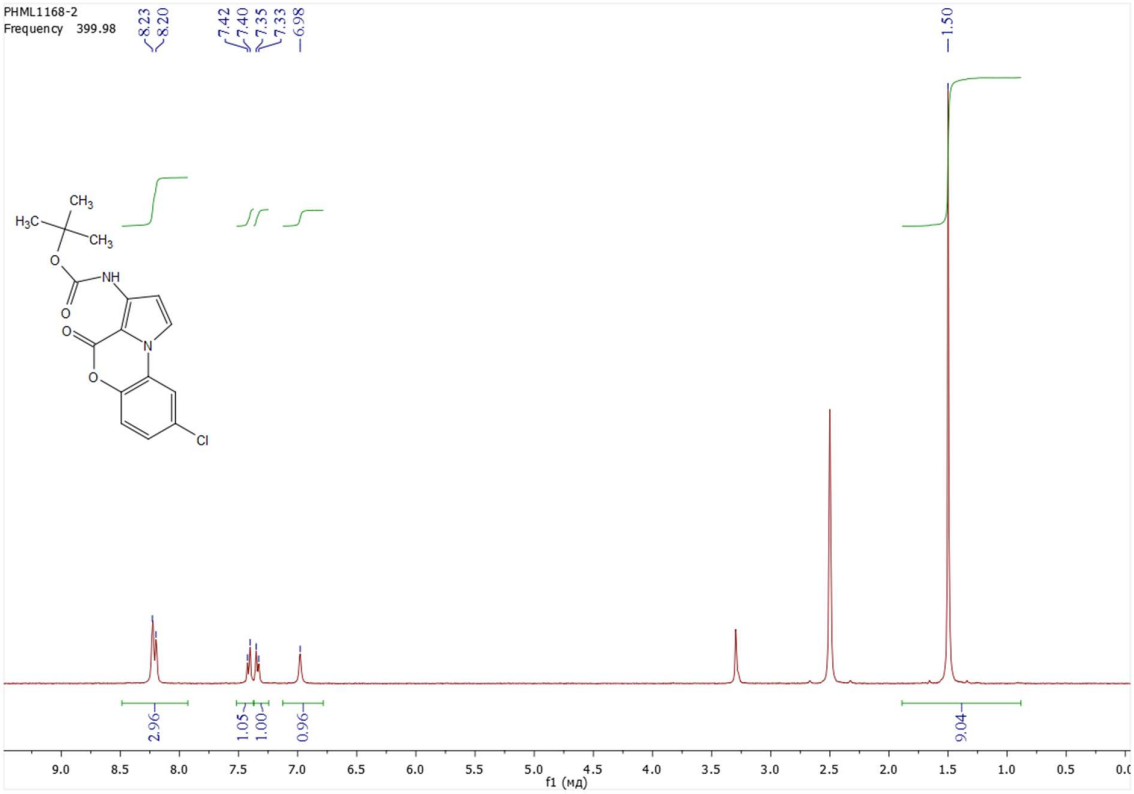

Figure S41. ^{1}H-NMR spectrum of *tert*-butyl (8-chloro-4-oxo-4*H*-pyrrolo[2,1-*c*][1,4]benzoxazin-3-yl)carbamate (**7c**) in DMSO-d_6

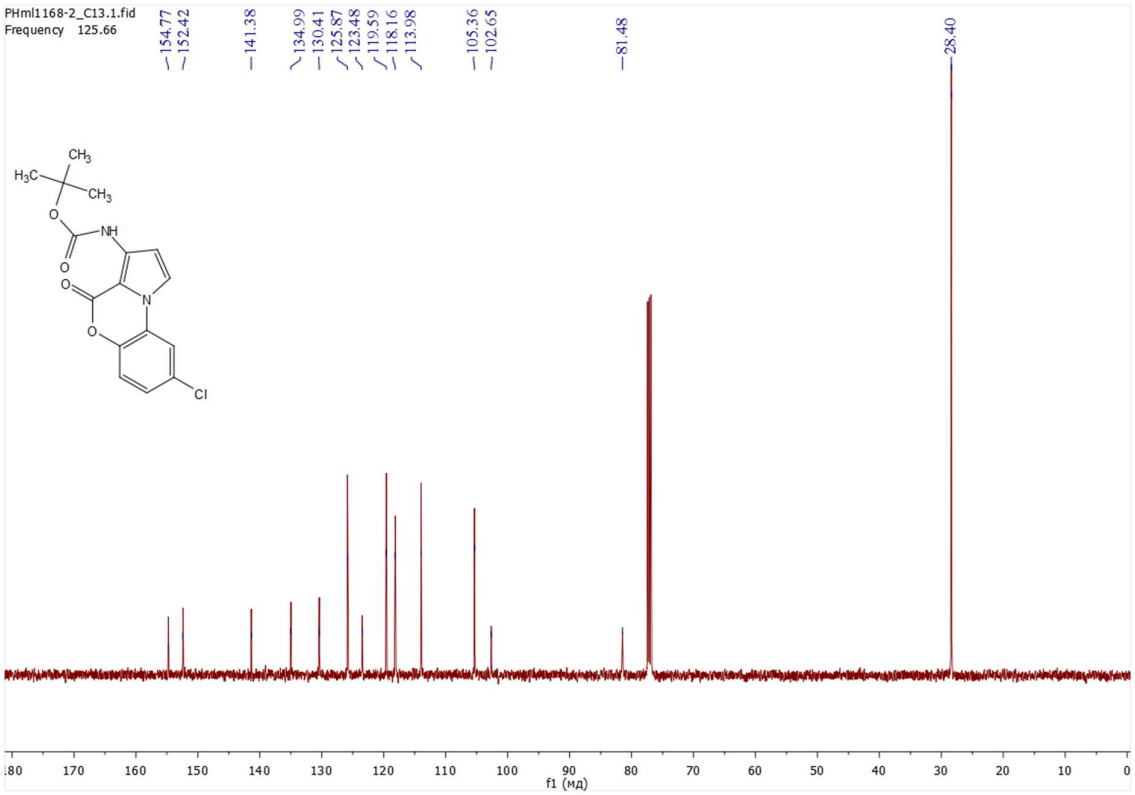

Figure S42. ^{13}C, NMR spectrum of *tert*-butyl (8-chloro-4-oxo-4*H*-pyrrolo[2,1-*c*][1,4]benzoxazin-3-yl)carbamate (**7c**) in $CDCl_3$

Chemical characterization of tert-butyl (8-tert-butyl-4-oxo-4H-pyrrolo[2,1-c][1,4]benzoxazin-3-yl)carbamate (**7d**). Beige solid, mp 176-177°C; yield 78%. ^{1}H-NMR (400 MHz, DMSO-d_6): δ 1.35 (s, 9H, 3CH_3-Ar), 1.50 (s, 9H, 3CH_3), 6.98 (s, 1H, C^{2}H), 7.29-7.34 (m, 2H, 2H_{Ar}), 7.97 (s, 1H, H_{Ar}), 8.25 (s, 1H, NH), 8.33 (d, $^3J_{HH}$ = 3.0 Hz, 1H, C^{1}H). ^{13}C, NMR (126 MHz, $CDCl_3$): δ = 28.43, 31.46, 34.90, 81.20, 103.12, 104.38, 110.43, 117.74, 117.98, 122.04, 123.29, 134.29, 140.63, 148.71, 152.61, 155.68. MS: m/z 301 (M – *t*-Bu + H). Anal. Calcd. for $C_{20}H_{24}N_2O_4$ (%): C, 67.40; H, 6.79; N, 7.86. Found: C, 67.62; H, 6.82; N, 7.78.

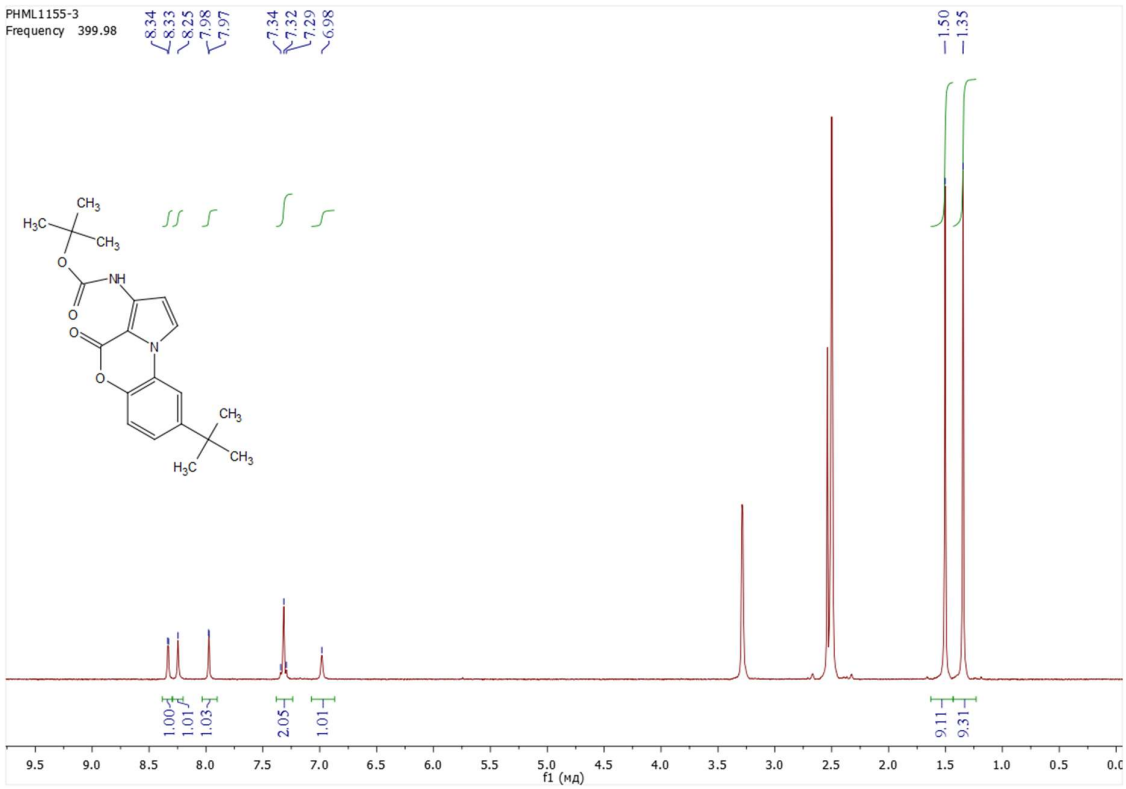

Figure S43. [1]H-NMR spectrum of *tert*-butyl (8-*tert*-butyl-4-oxo-4*H*-pyrrolo[2,1-*c*][1,4]benzoxazin-3-yl)carbamate (**7d**) in DMSO-d_6

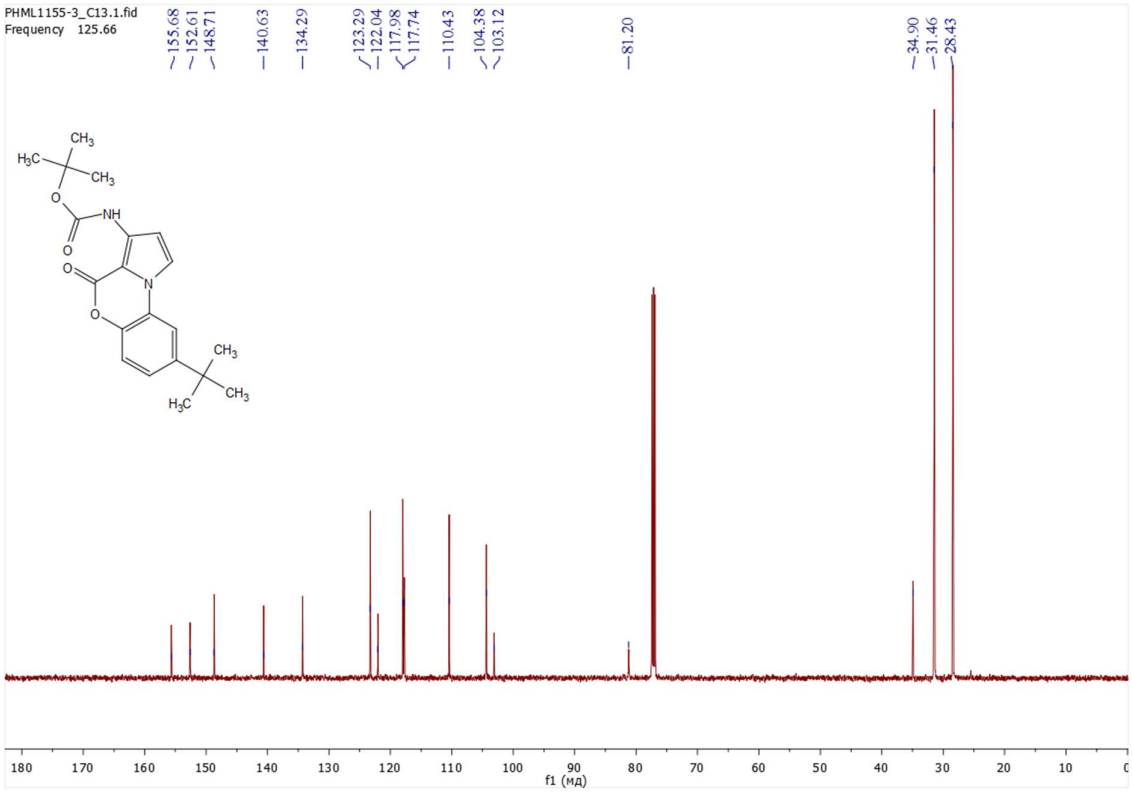

Figure S44. [13]C, NMR spectrum of *tert*-butyl (8-*tert*-butyl-4-oxo-4*H*-pyrrolo[2,1-*c*][1,4]benzoxazin-3-yl)carbamate (**7d**) in $CDCl_3$

Chemical characterization of tert-butyl (7-fluoro-4-oxo-4H-pyrrolo[2,1-c][1,4]benzoxazin-3-yl)carbamate (**7e**). White solid, mp 204-205°C; yield 65%. ^{1}H-NMR (400 MHz, DMSO-d_6): δ 1.50 (s, 9H, 3CH_3), 6.96 (s, 1H, C^2H), 7.22-7.28 (m, 1H, $1H_{Ar}$), 7.39-7.42 (m, 1H, $1H_{Ar}$), 8.05-8.09 (m, 1H, $1H_{Ar}$), 8.14 + 8.22 (s + s, 2H, C^1H + NH). ^{13}C, NMR (126 MHz, $CDCl_3$): δ = 28.38, 81.38, 102.41, 104.58, 106.18 (d, $^2J_{CF}$ = 26.7 Hz, C^6), 112.17 (d, $^2J_{CF}$ = 23.6 Hz, C^8), 114.61 (d, $^3J_{CF}$ = 9.5 Hz, C^9), 118.10, 119.42 (d, $^4J_{CF}$ = 3.1 Hz, C^{9a}), 134.64, 143.48 (d, $^3J_{CF}$ = 12.1 Hz, C^{5a}), 153.59 (d, $^1J_{CF}$ = 287.1 Hz, C^7), 158.96, 160.93. ^{19}F, NMR (376 MHz, DMSO-d_6) δ -115.30. MS: m/z 317 (M – *t*-Bu + H). Anal. Calcd. for $C_{16}H_{15}FN_2O_4$ (%): C, 60.37; H, 4.75; N, 8.80. Found: C, 60.14; H, 4.78; N, 8.74.

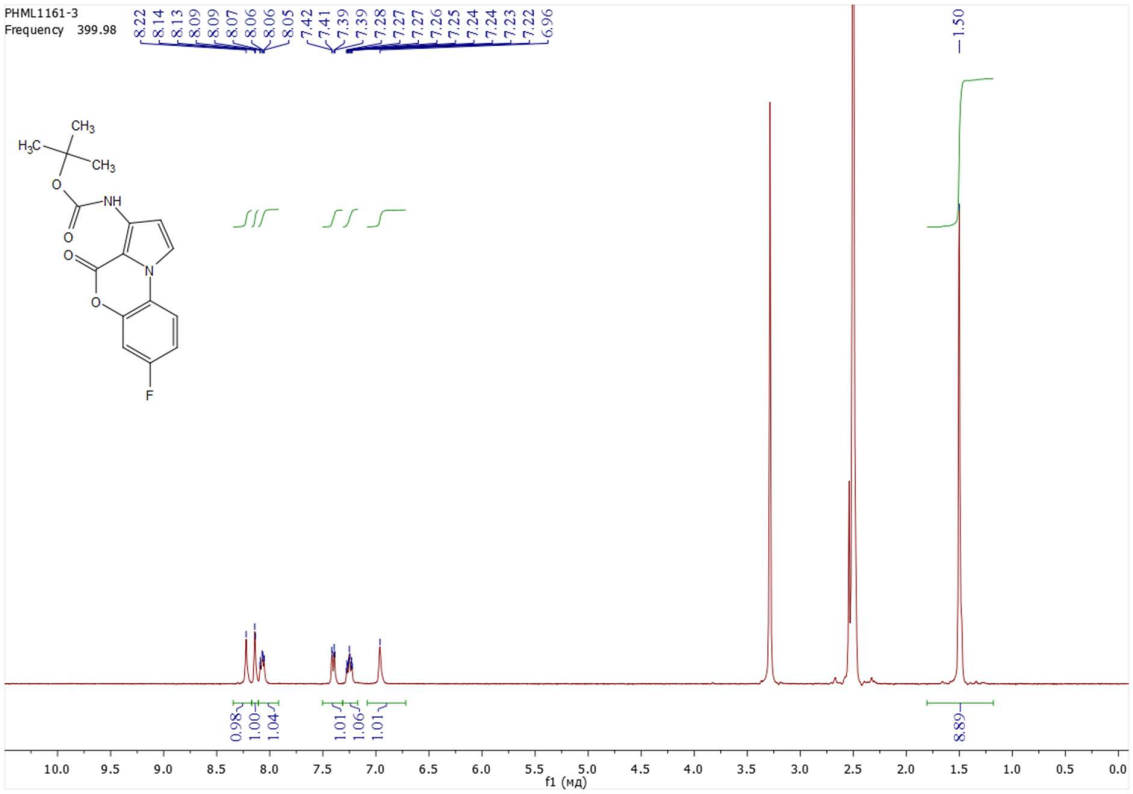

Figure S45. ^{1}H-NMR spectrum of *tert*-butyl (7-fluoro-4-oxo-4*H*-pyrrolo[2,1-*c*][1,4]benzoxazin-3-yl)carbamate (**7e**) in DMSO-d_6

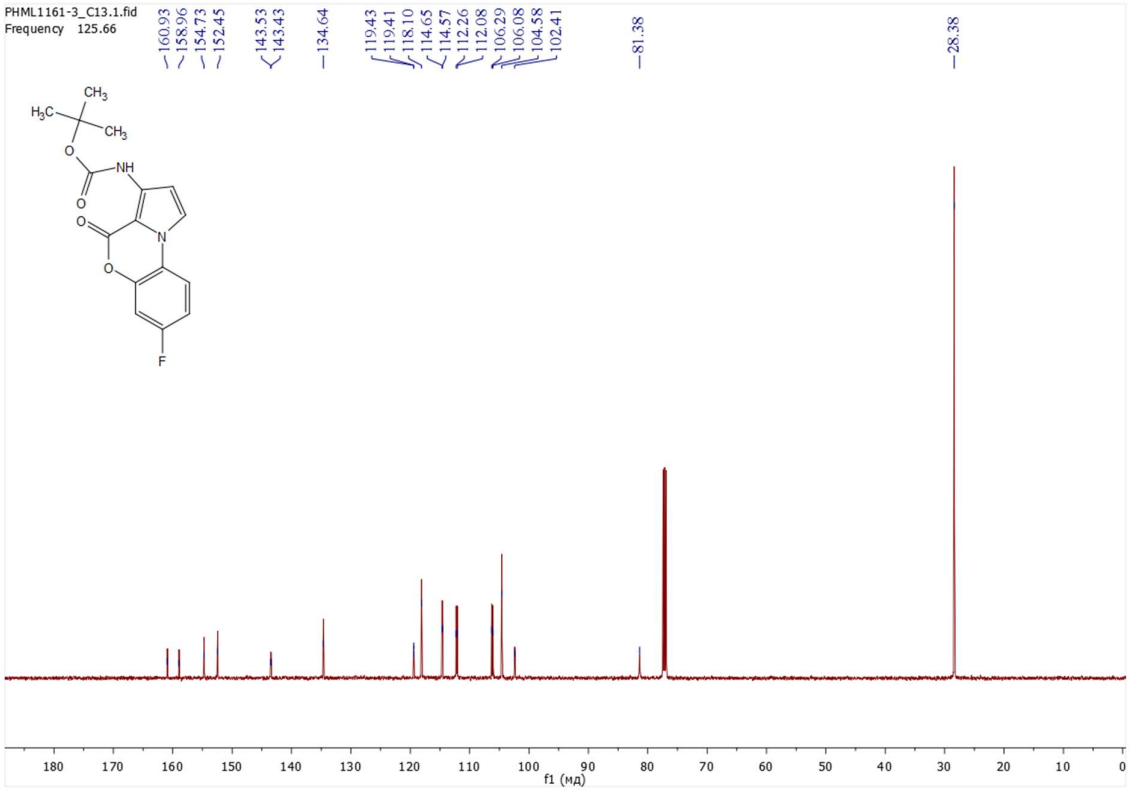

Figure S46. ^{13}C, NMR spectrum of *tert*-butyl (7-fluoro-4-oxo-4*H*-pyrrolo[2,1-*c*][1,4]benzoxazin-3-yl)carbamate (**7e**) in $CDCl_3$

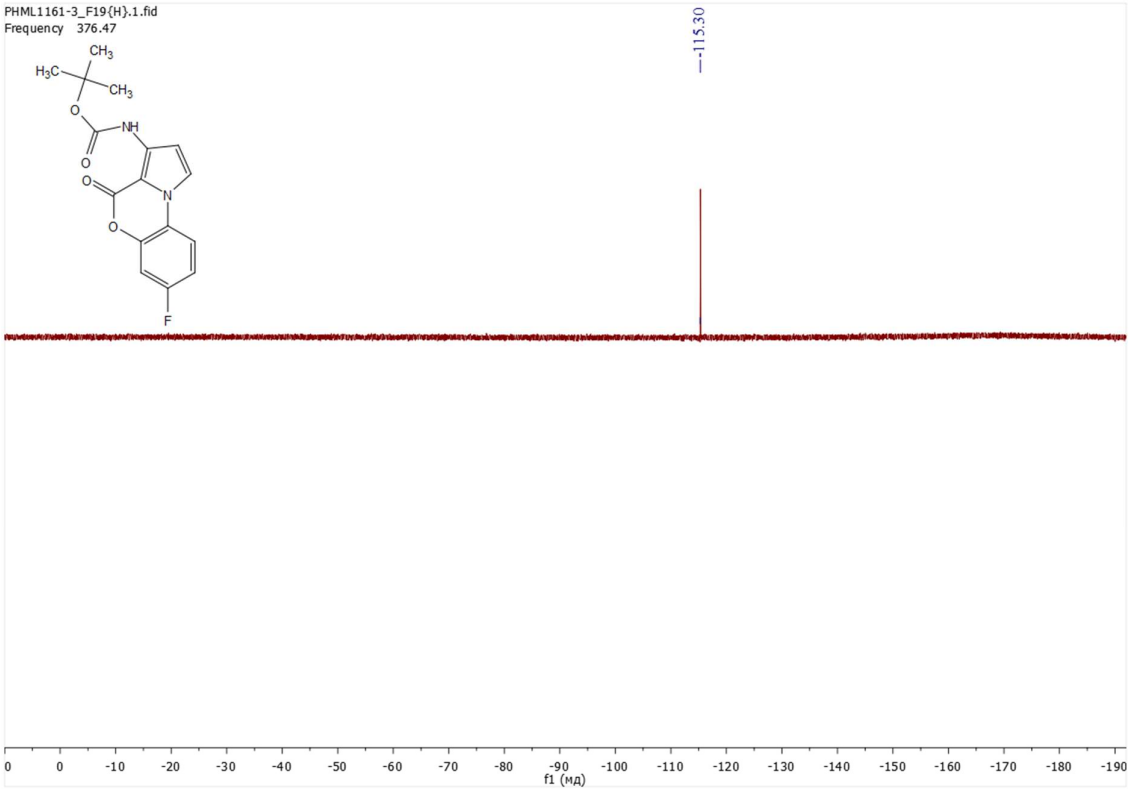

Figure S47. ^{19}F, NMR spectrum of *tert*-butyl (7-fluoro-4-oxo-4*H*-pyrrolo[2,1-*c*][1,4]benzoxazin-3-yl)carbamate (**7e**) in DMSO-d_6

Chemical characterization of tert-butyl (6-bromo-4-oxo-4H-pyrrolo[2,1-c][1,4]benzoxazin-3-yl)carbamate (**7f**). Beige solid, mp 215-216°C; yield 46%. ^{1}H-NMR (400 MHz, DMSO-d_6): δ 1.50 (s, 9H, 3CH_3), 7.01 (s, 1H, C^2H), 7.27 (t, $^{3}J_{HH}$ = 8.1 Hz, 1H, $1H_{Ar}$), 7.59 (d, $^{3}J_{HH}$ = 8.0 Hz, 1H, $1H_{Ar}$), 8.03 (d, $^{3}J_{HH}$ = 8.2 Hz, 1H, $1H_{Ar}$), 8.19 (d, $^{3}J_{HH}$ = 3.0 Hz, 1H, C^1H), 8.25 (s, 1H, NH). ^{13}C, NMR (126 MHz, $CDCl_3$): δ = 28.40, 81.47, 102.60, 105.29, 112.10, 112.80, 118.35, 123.78, 125.40, 129.74, 134.79, 140.32, 152.41, 154.12. MS: m/z 322, 324 (M -*t*-Bu + H). Anal. Calcd. for $C_{16}H_{15}BrN_2O_4$ (%): C, 50.68; H, 3.99; N, 7.39. Found: C, C, 50.84; H, 4.00; N, 7.31.

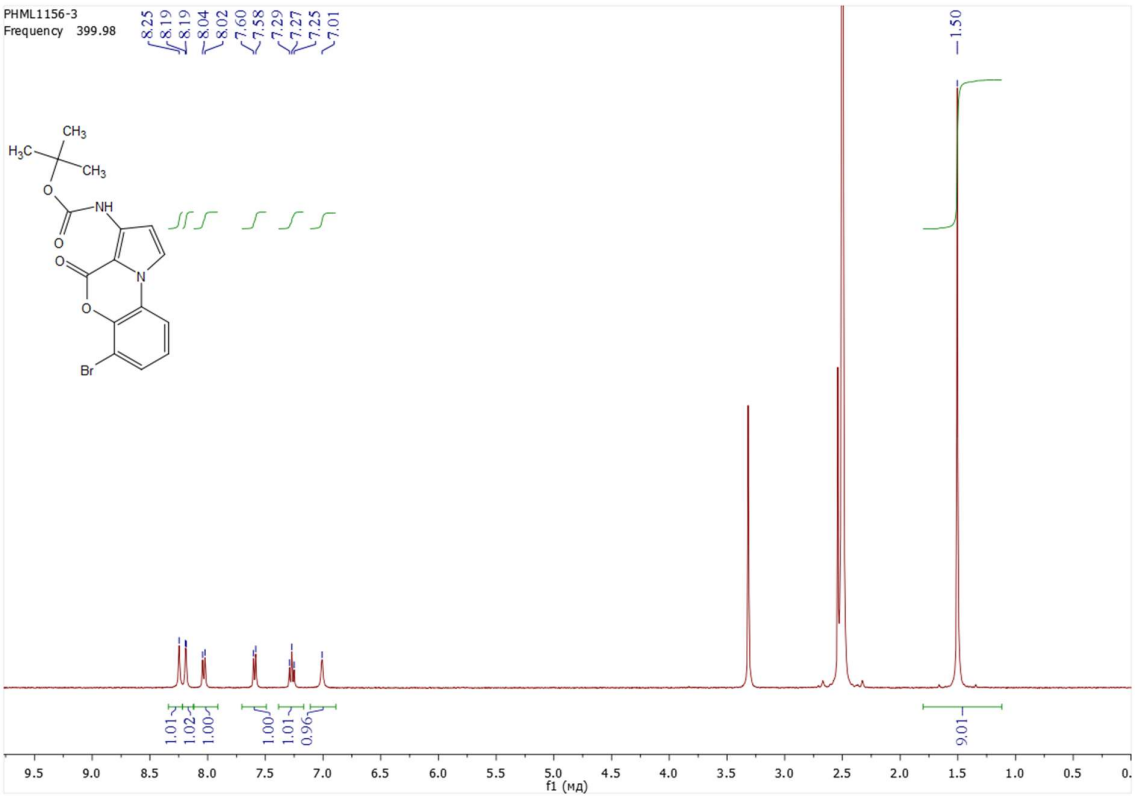

Figure S48. ^{1}H-NMR spectrum of *tert*-butyl (6-bromo-4-oxo-4*H*-pyrrolo[2,1-*c*][1,4]benzoxazin-3-yl)carbamate (**7f**) in DMSO-d_6

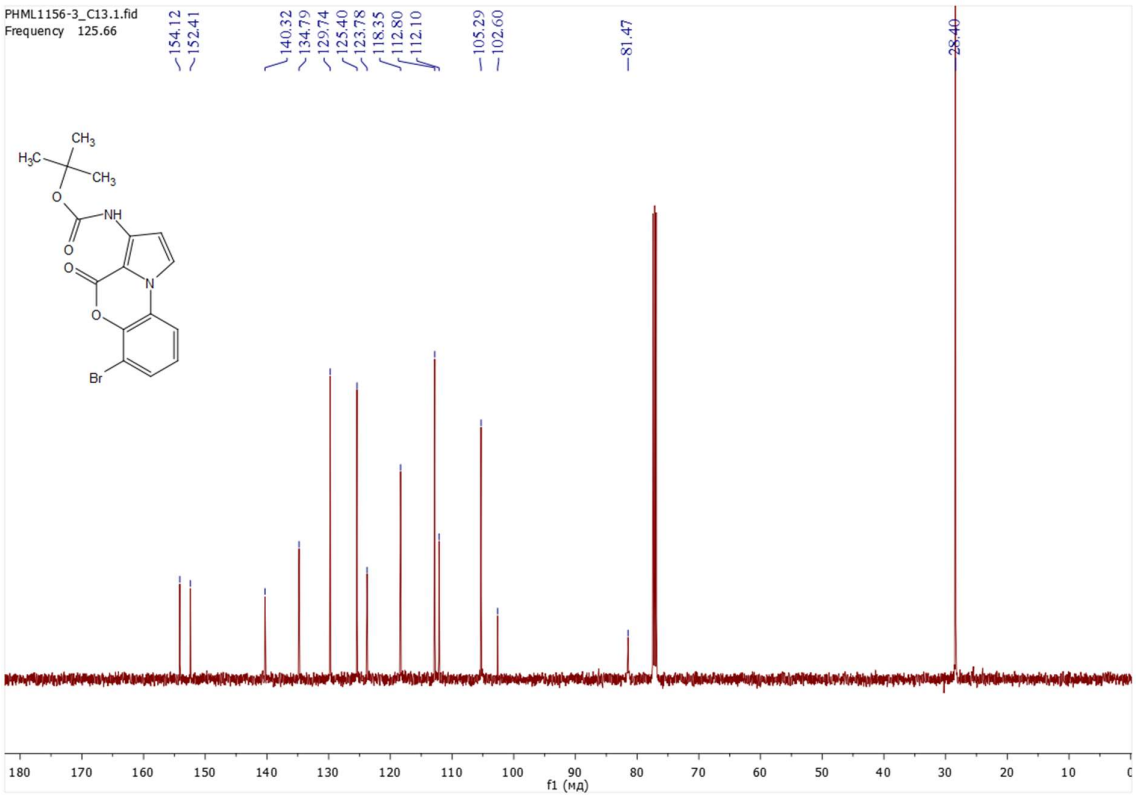

Figure S49. ^{13}C, NMR spectrum of *tert*-butyl (6-bromo-4-oxo-4*H*-pyrrolo[2,1-*c*][1,4]benzoxazin-3-yl)carbamate (**7f**) in $CDCl_3$

Synthesis and spectra characteristics of compounds 8a-e and 9a-f

General procedure for the synthesis of 8-amino-3,4-dihydro-1H-pyrrolo[2,1-c][1,4]oxazin-1-one ***8a-e*** *and 3-amino-4H-pyrrolo[2,1-c][1,4]benzoxazin-4-one* ***9a-f***. To a (2.8 mmol) *tert*-butyl (1-oxo-3,4-dihydro-1*H*-pyrrolo[2,1-*c*][1,4]oxazin-8-yl)carbamate **6a-e** or *tert*-butyl (4-oxo-4*H*-pyrrolo[2,1-*c*][1,4]benzoxazin-3-yl)carbamate **7a-f** 10 cm^3 of hydrogen chloride in dioxane, was added. The resulting mixture was stirred at room temperature for 4–6 h. After the reaction was completed, the obtained mixture was evaporated under reduced pressure. The formed precipitate was purified by column chromatography on silica gel, eluent CH_2Cl_2–MeOH, 50:1.

Chemical characterization of 8-amino-3-methyl-3,4-dihydro-1H-pyrrolo[2,1-c][1,4]oxazin-1-one (**8a**). Orange solid, mp 60-61°C; yield 64%. ^{1}H-NMR (400 MHz, $CDCl_3$): δ 1.47 (d, $^3J_{HH}$ = 6.4 Hz, 3H, CH_3), 3.73 (dd, $^2J_{HH}$ = 12.7, $^3J_{HH}$ = 10.0 Hz, 1H, C^{4}H), 3.94 (dd, $^2J_{HH}$ = 12.7, $^3J_{HH}$ = 3.1 Hz, 1H, C^{4}H) 3.70-3.76 (m, 1H, C^{4}HH), 3.90 (s, 2H, NH_2), 4.65-4.73 (m, 1H, C^{3}H), 5.67 (d, $^3J_{HH}$ = 2.6 Hz, 1H, C^{7}H), 6.57 (d, $^3J_{HH}$ = 2.6 Hz, 1H, C^{6}H). ^{13}C, NMR (151 MHz, $CDCl_3$): δ = 18.18, 48.81, 73.56, 98.30, 103.44, 124.53, 143.68, 160.24. MS: m/z 167 (M + H). Anal. Calcd. for $C_8H_{10}N_2O_2$ (%): C, 57.82; H, 6.07; N, 16.86. Found: C, 58.02; H, 6.10; N, 16.75.

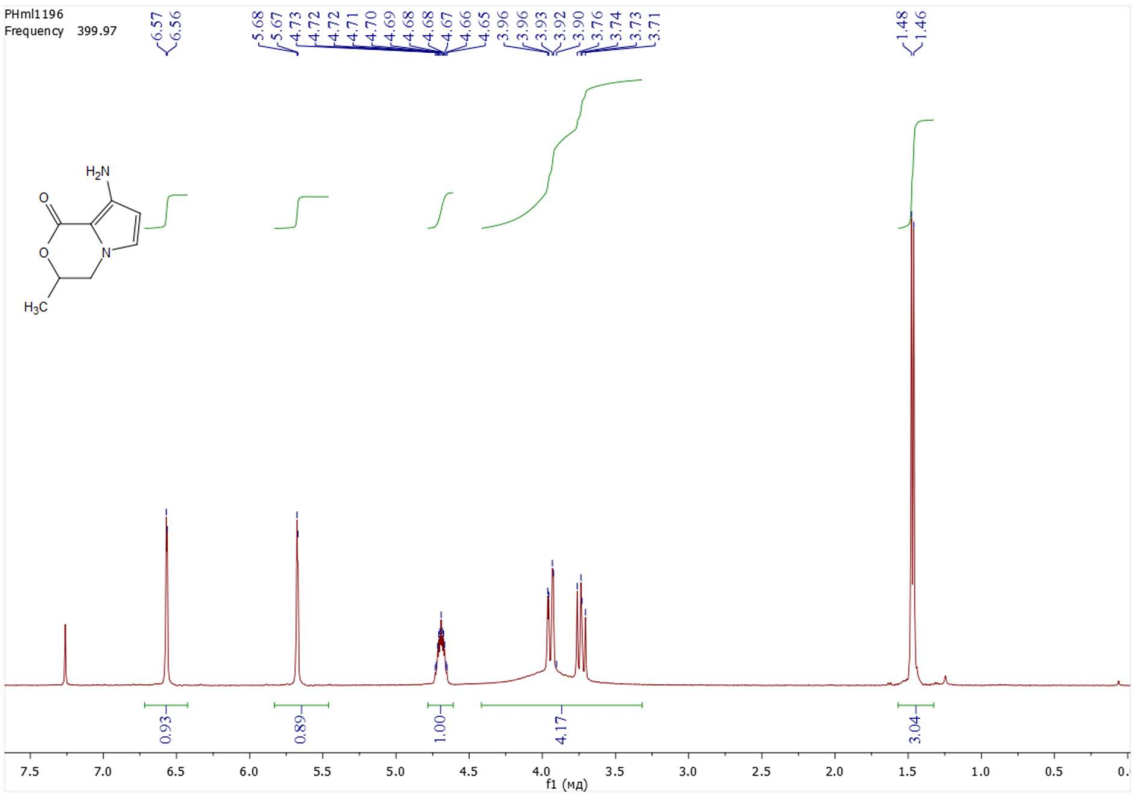

Figure S50. ^{1}H-NMR spectrum of 8-amino-3-methyl-3,4-dihydro-1*H*-pyrrolo[2,1-*c*][1,4]oxazin-1-one (**8a**) in $CDCl_3$

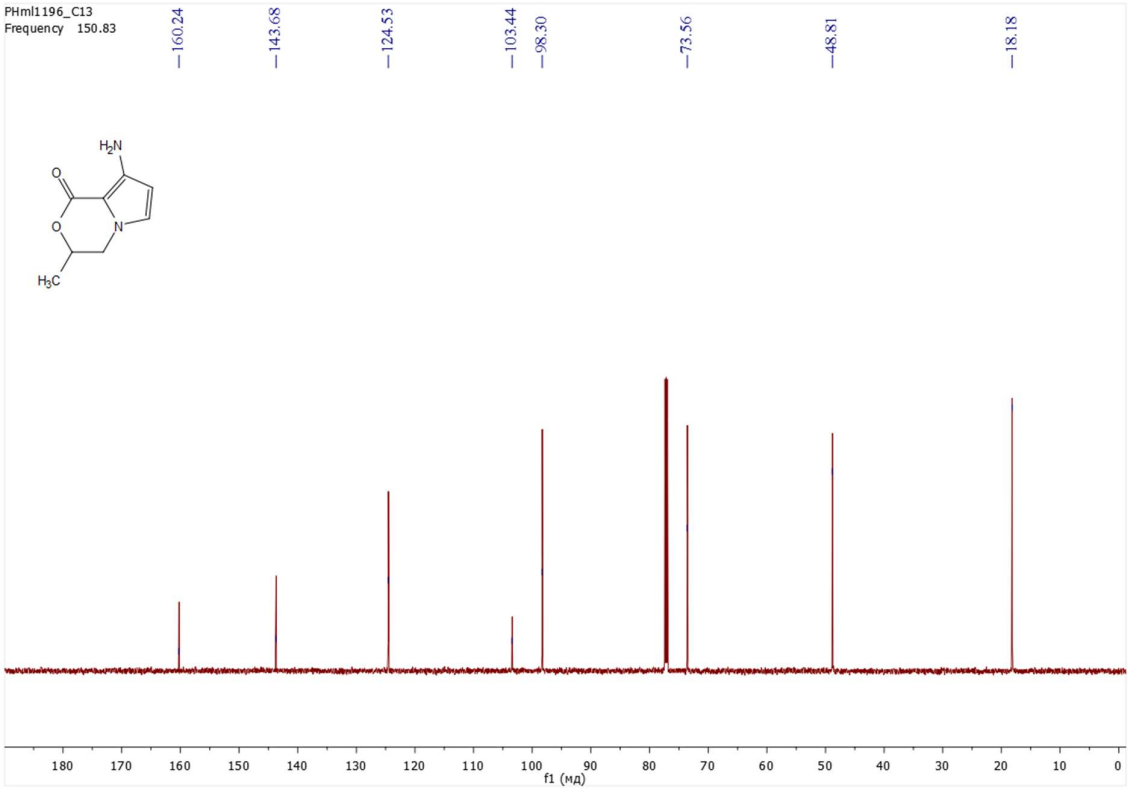

Figure S51. ^{13}C, NMR spectrum of 8-amino-3-methyl-3,4-dihydro-1*H*-pyrrolo[2,1-*c*][1,4]oxazin-1-one (**8a**) in $CDCl_3$

Chemical characterization of 8-amino-4,4-dimethyl-3,4-dihydro-1H-pyrrolo[2,1-c][1,4]oxazin-1-one (**8b**). Beige solid, mp 79-80°C; yield 83%. ^{1}H-NMR (400 MHz, $CDCl_3$): δ 1.45 (s, 6H, $2CH_3$), 4.16 (s, 2H, C^3H_2), 4.52 (s, 2H, NH_2), 5.69 (d, $^3J_{HH}$ = 2.9 Hz, 1H, C^7H), 6.67 (d, $^3J_{HH}$ = 2.9 Hz, 1H, C^6H). ^{13}C, NMR (126 MHz, $CDCl_3$): δ = 24.18, 53.03, 75.57, 98.35, 102.79, 121.14, 144.43, 159.93. MS: m/z 181 (M + H). Anal. Calcd. for $C_9H_{12}N_2O_2$ (%): C, 59.99; H, 6.71; N, 15.55. Found: C, 60.17; H, 6.68; N, 15.63.

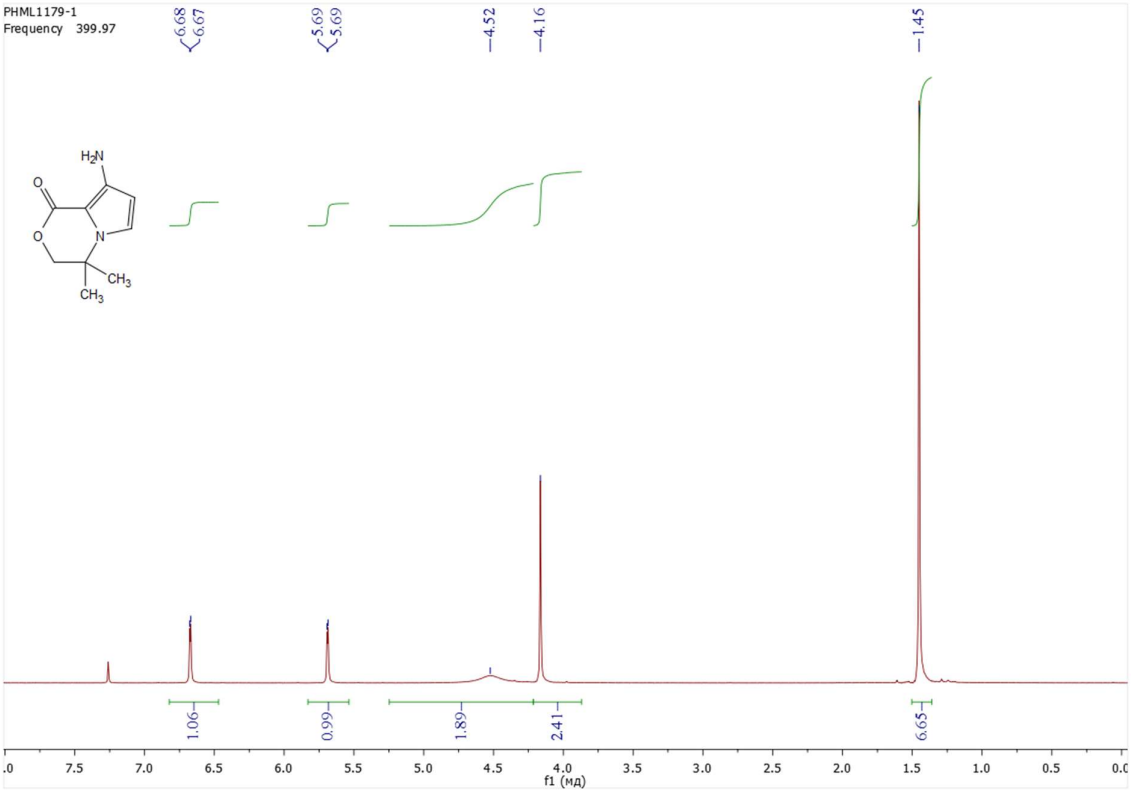

Figure S52. ^{1}H-NMR spectrum of 8-amino-4,4-dimethyl-3,4-dihydro-1*H*-pyrrolo[2,1-*c*][1,4]oxazin-1-one (**8b**) in $CDCl_3$

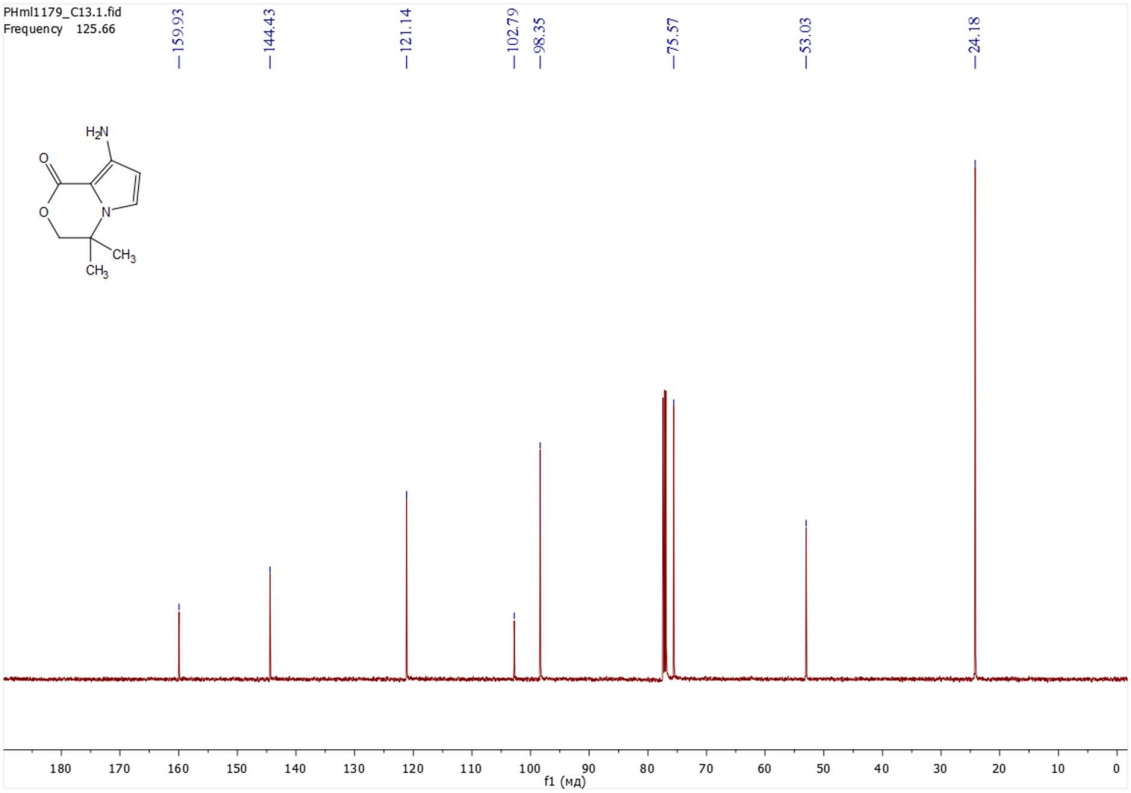

Figure S53. ^{13}C, NMR spectrum of 8-amino-4,4-dimethyl-3,4-dihydro-1*H*-pyrrolo[2,1-*c*][1,4]oxazin-1-one (**8b**) in $CDCl_3$

Chemical characterization of (4S)-8-amino-4-(1-methylethyl)-3,4-dihydro-1H-pyrrolo[2,1-c][1,4]oxazin-1-one (**8c**). Yellow solid, mp 129-130°C; yield 76%. ^{1}H-NMR (400 MHz, $CDCl_3$): δ 0.90 (d, $^3J_{HH}$ = 6.8 Hz, 3H, CH_3), 1.02 (d, $^3J_{HH}$ = 6.7 Hz, 3H, CH_3), 2.10-2.23 (m, 1H, C<u>H</u>$(CH_3)_2$), 3.63-3.66 (m, 1H, C^{4}H), 4.46 (dd, $^2J_{HH}$ = 11.7 Hz, $^3J_{HH}$ = 3.4 Hz, 1H, C^{3}H), 4.48 (s, 2H, NH_2) 4.51 (dd, $^2J_{HH}$ = 11.6 Hz, $^3J_{HH}$ = 2.7 Hz, 1H, C^{3}H), 5.67 (d, $^3J_{HH}$ = 2.1 Hz, 1H, C^{7}H), 6.62 (d, $^3J_{HH}$ = 2.2 Hz, 1H, C^{6}H). ^{13}C, NMR (126 MHz, $CDCl_3$): δ = 19.25, 19.61, 30.21, 59.38, 67.89, 97.80, 103.47, 124.75, 143.74, 160.25. MS: m/z 195 (M + H). Anal. Calcd. for $C_{10}H_{14}N_2O_2$ (%): C, 61.84; H, 7.27; N, 14.42. Found: C, 62.01; H, 7.30; N, 14.30.

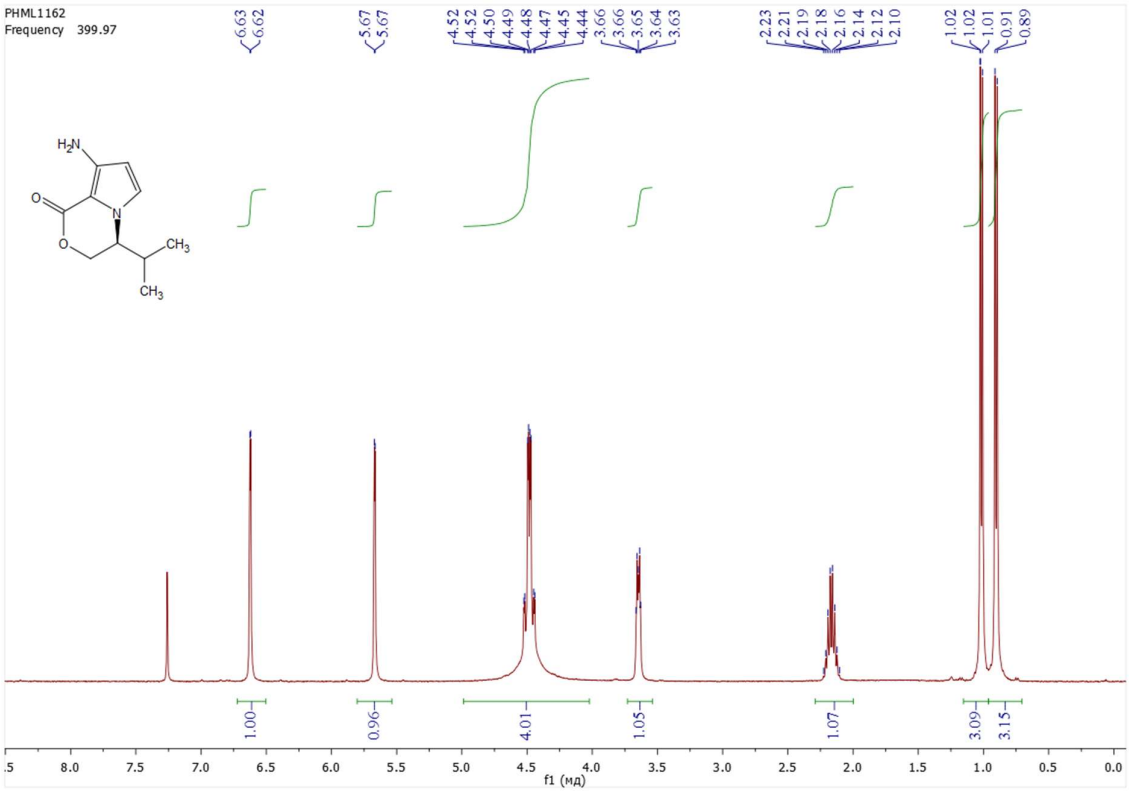

Figure S54. ^{1}H-NMR spectrum of (4*S*)-8-amino-4-(1-methylethyl)-3,4-dihydro-1*H*-pyrrolo[2,1-*c*][1,4]oxazin-1-one (**8c**) in $CDCl_3$

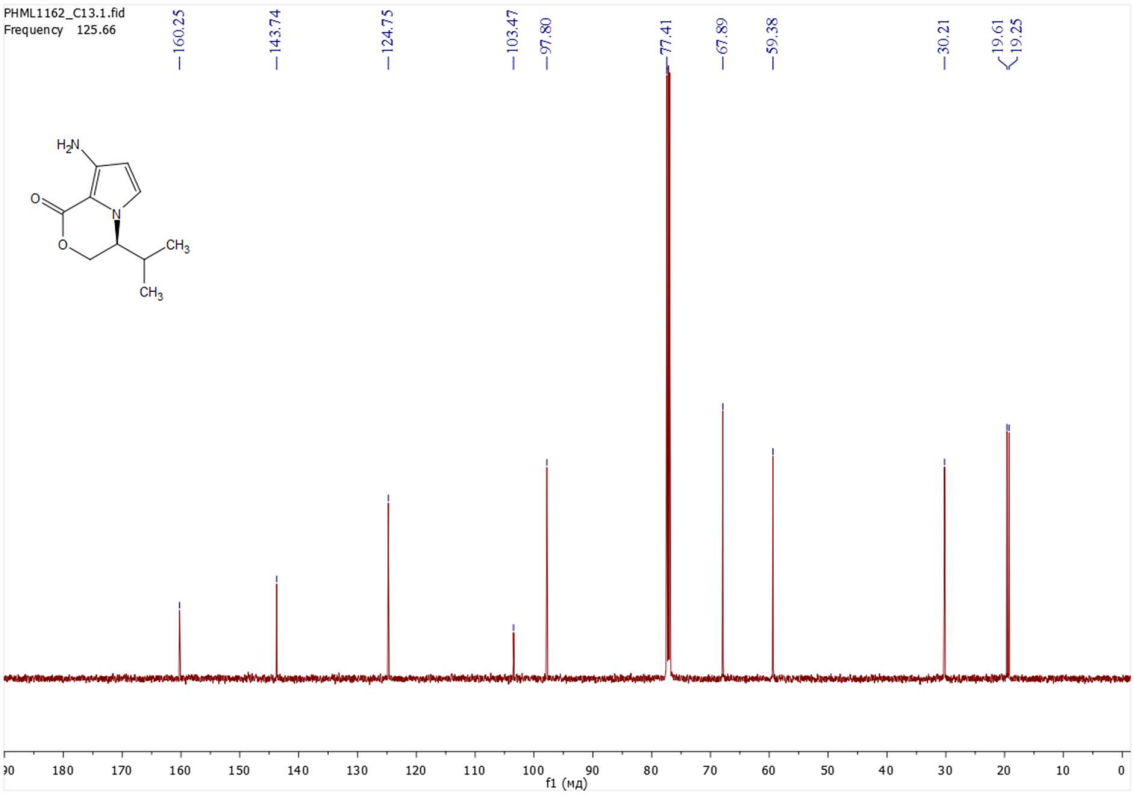

Figure S55. ^{13}C, NMR spectrum of (4*S*)-8-amino-4-(1-methylethyl)-3,4-dihydro-1*H*-pyrrolo[2,1-*c*][1,4]oxazin-1-one (**8c**) in $CDCl_3$

Chemical characterization of 8-amino-3-phenyl-3,4-dihydro-1H-pyrrolo[2,1-c][1,4]oxazin-1-one (**8d**). Beige solid, mp 139-140°C; yield 80%. ^{1}H-NMR (400 MHz, $CDCl_3$): δ 4.03 (dd, $^{2}J_{HH}$ = 12.9, $^{3}J_{HH}$ = 10.5 Hz, 1H, C^{4}H), 4.12 (dd, $^{2}J_{HH}$ = 12.9, $^{3}J_{HH}$ = 3.4 Hz, 1H, C^{4}H), 4.54 (s, 2H, NH_2), 5.58 (dd, $^{3}J_{HH}$ = 10.4, $^{3}J_{HH}$ = 3.2 Hz, 1H, C^{3}H), 5.72 (d, $^{3}J_{HH}$ = 2.8 Hz, 1H, C^{7}H), 6.62 (d, $^{3}J_{HH}$ = 2.7 Hz, 1H, C^{6}H), 7.37–7.47 (m, 5H, $5H_{Ar}$). ^{13}C, NMR (126 MHz, $CDCl_3$): δ = 49.43, 78.75, 98.56, 103.66, 124.69, 126.43, 128.88, 129.12, 136.11, 144.12, 160.03. MS: m/z 229 (M + H). Anal. Calcd. for $C_{13}H_{12}N_2O_2$ (%): C, 68.41; H, 5.30; N, 12.27. Found: C, 68.20; H, 5.28; N, 12.36.

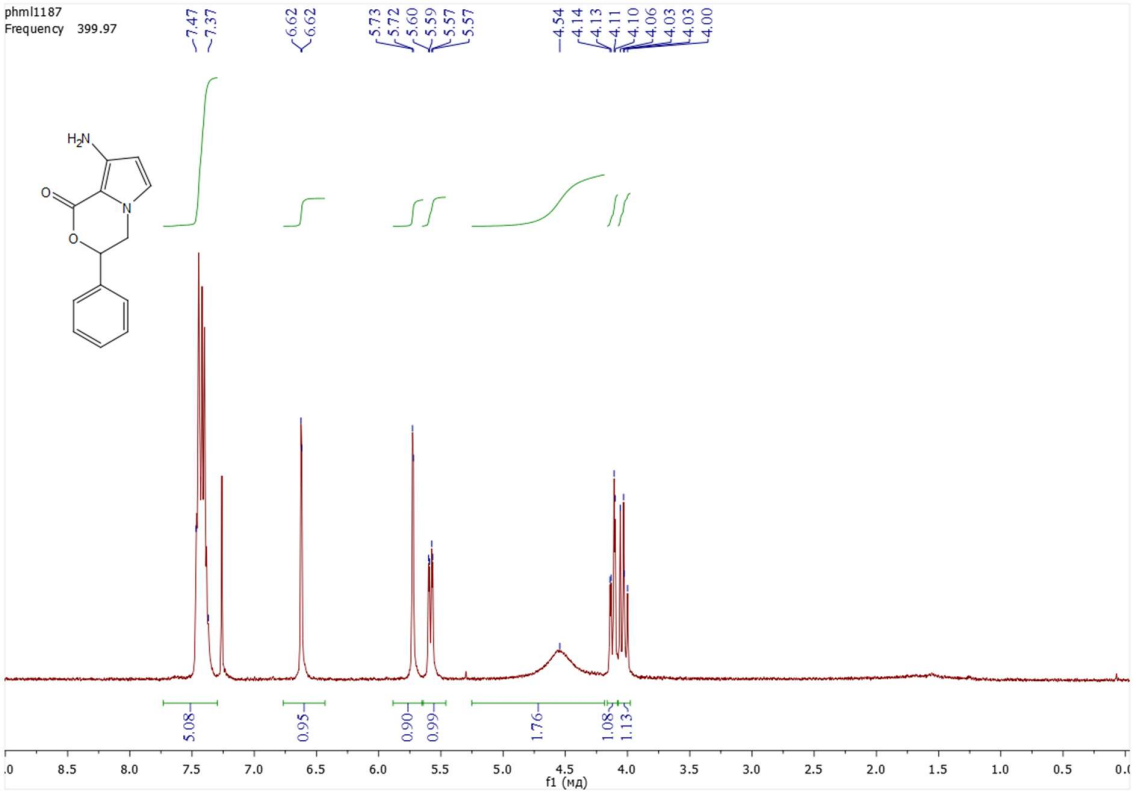

Figure S56. ^{1}H-NMR spectrum of 8-amino-3-phenyl-3,4-dihydro-1*H*-pyrrolo[2,1-*c*][1,4]oxazin-1-one (**8d**) in $CDCl_3$

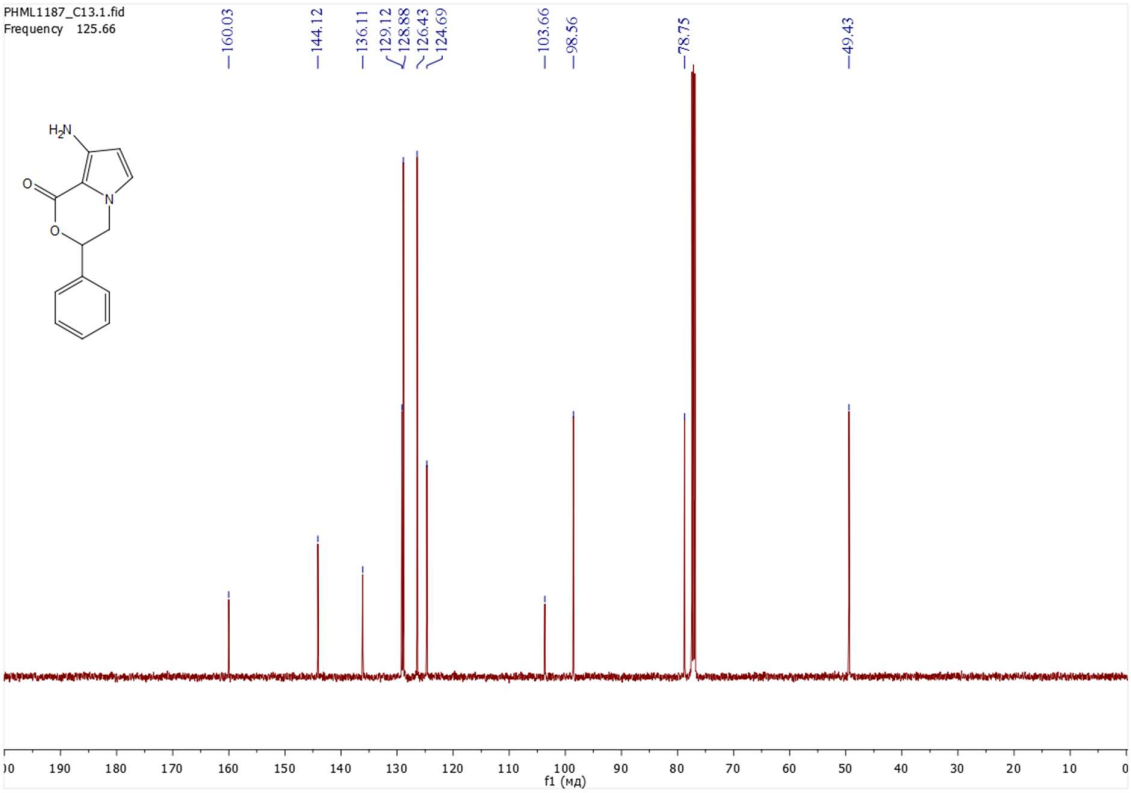

Figure S57. ^{13}C, NMR spectrum of 8-amino-3-phenyl-3,4-dihydro-1*H*-pyrrolo[2,1-*c*][1,4]oxazin-1-one (**8d**) in $CDCl_3$

Chemical characterization of (5aS,9aS)-3-amino-5a,6,7,8,9,9a-hexahydro-4H-pyrrolo[2,1-c][1,4]benzoxazin-4-one (**8e**). Beige solid, mp 158-159°C; yield 84%. ^{1}H-NMR (400 MHz, $CDCl_3$): δ 1.37-1.54 (m, 3H), 1.61-1.71 (m, 1H), 1.89-1.92 (m, 2H), 2.21-2.25 (m, 1H), 2.46-2.51 (m, 1H), 3.65 (td, $^3J_{HH}$ = 10.4, $^3J_{HH}$ = 4.3 Hz, 1H, C^{9a}H), 4.13 (td, $^3J_{HH}$ = 10.7, $^3J_{HH}$ = 4.3 Hz, 1H, C^{5a}H), 4.50 (s, 2H, NH_2), 5.68 (d, $^3J_{HH}$ = 2.8 Hz, 1H, C^{2}H), 6.65 (d, $^3J_{HH}$ = 2.8 Hz, 1H, C^{1}H). ^{13}C, NMR (126 MHz, $CDCl_3$): δ = 23.43, 23.69, 27.32, 29.87, 56.31, 80.62, 98.24, 104.49, 121.14, 144.14, 160.41. MS: m/z 207 (M + H). Anal. Calcd. for $C_{11}H_{14}N_2O_2$ (%): C, 64.06; H, 6.84; N, 13.58. Found: C, 63.89; H, 6.87; N, 13.51.

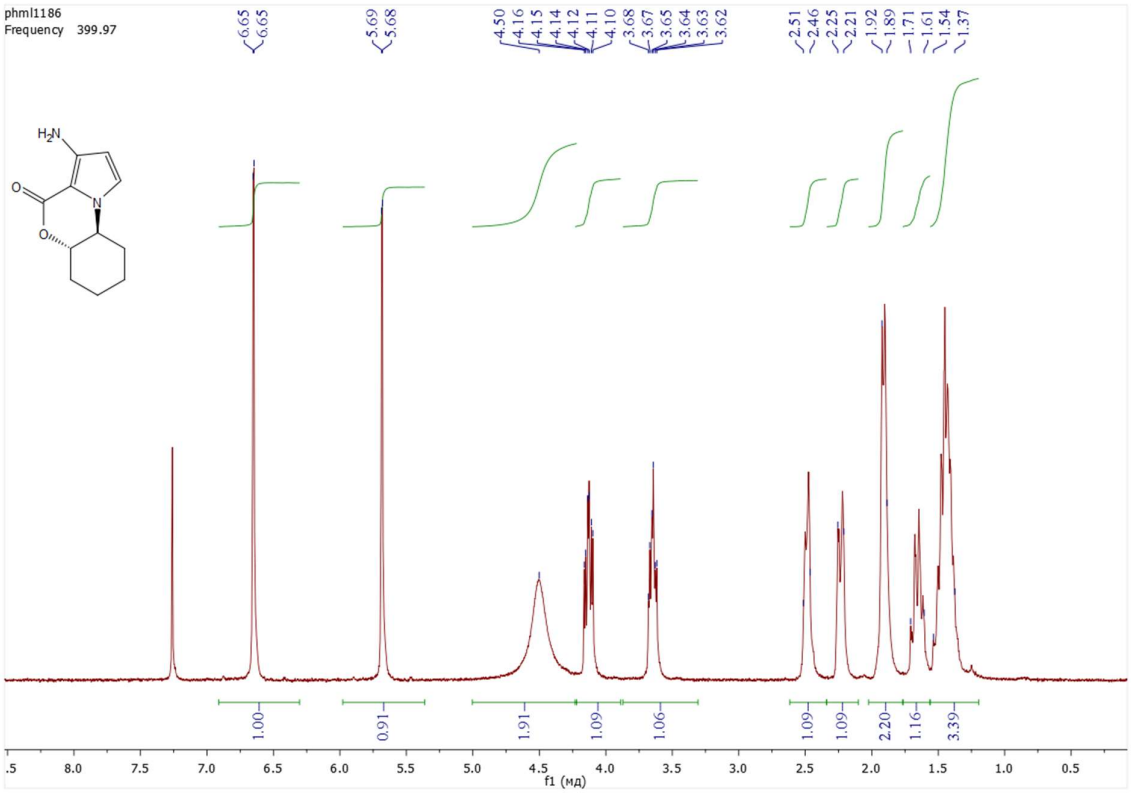

Figure S58. ^{1}H-NMR spectrum of (5*aS*,9*aS*)-3-amino-5*a*,6,7,8,9,9*a*-hexahydro-4*H*-pyrrolo[2,1-*c*][1,4]benzoxazin-4-one (**8e**) in $CDCl_3$

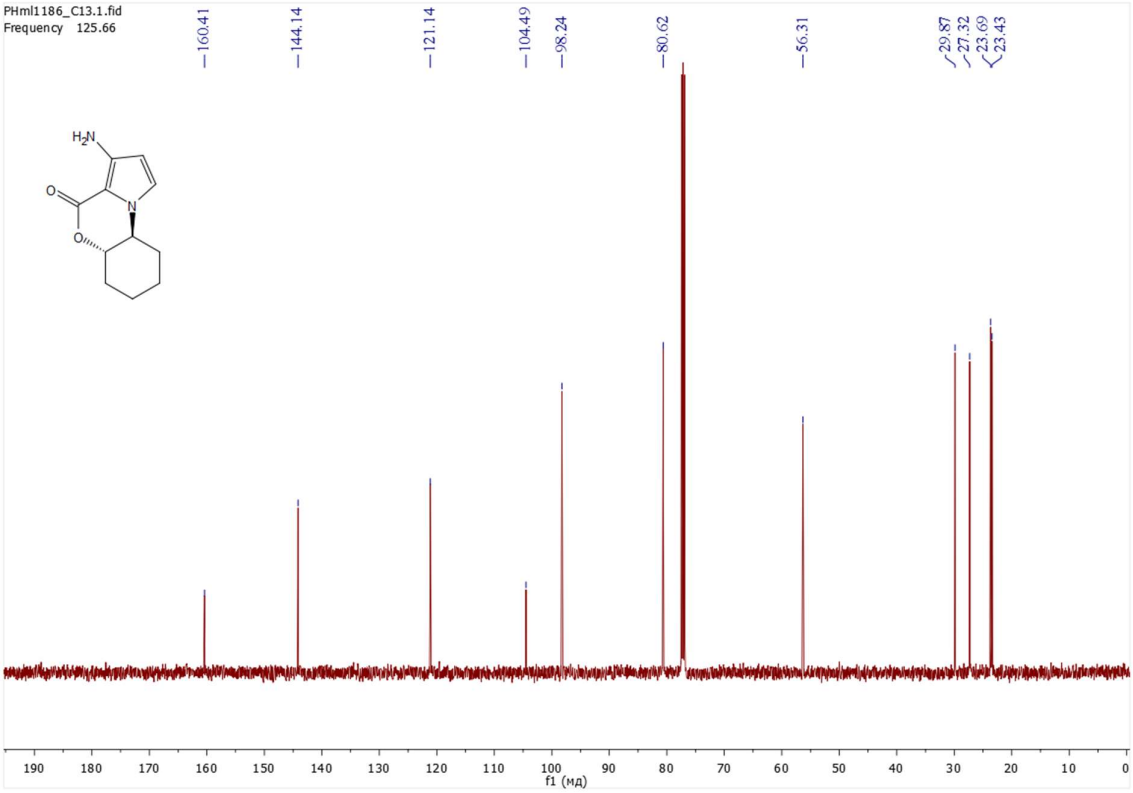

Figure S59. ^{13}C, NMR spectrum of (5*aS*,9*aS*)-3-amino-5*a*,6,7,8,9,9*a*-hexahydro-4*H*-pyrrolo[2,1-*c*][1,4]benzoxazin-4-one (**8e**) in $CDCl_3$

Chemical characterization of 3-amino-4H-pyrrolo[2,1-c][1,4]benzoxazin-4-one (**9a**). Yellow solid, mp 161-162°C; yield 69%. ^{1}H-NMR (400 MHz, DMSO-d_6): δ 5.68 (s, 2H, NH_2), 6.05 (d, $^{3}J_{HH}$ = 2.9 Hz, 1H, C^{2}H), 7.01–7.34 (m, 3H, 3H_{Ar}), 7.82 (d, $^{3}J_{HH}$ = 8.2 Hz, 1H, 1H_{Ar}), 7.89 (d, $^{3}J_{HH}$ = 2.9 Hz, 1H, C^{1}H). ^{13}C, NMR (151 MHz, $CDCl_3$): δ = 101.49, 101.89, 113.12, 118.09, 118.24, 123.30, 124.55, 125.02, 143.03, 143.49, 155.56. MS: m/z 201 (M + H). Anal. Calcd. for $C_{11}H_8N_2O_2$ (%): C, 66.00; H, 4.03; N, 13.99. Found: C, 65.78; H, 4.00; N, 14.06.

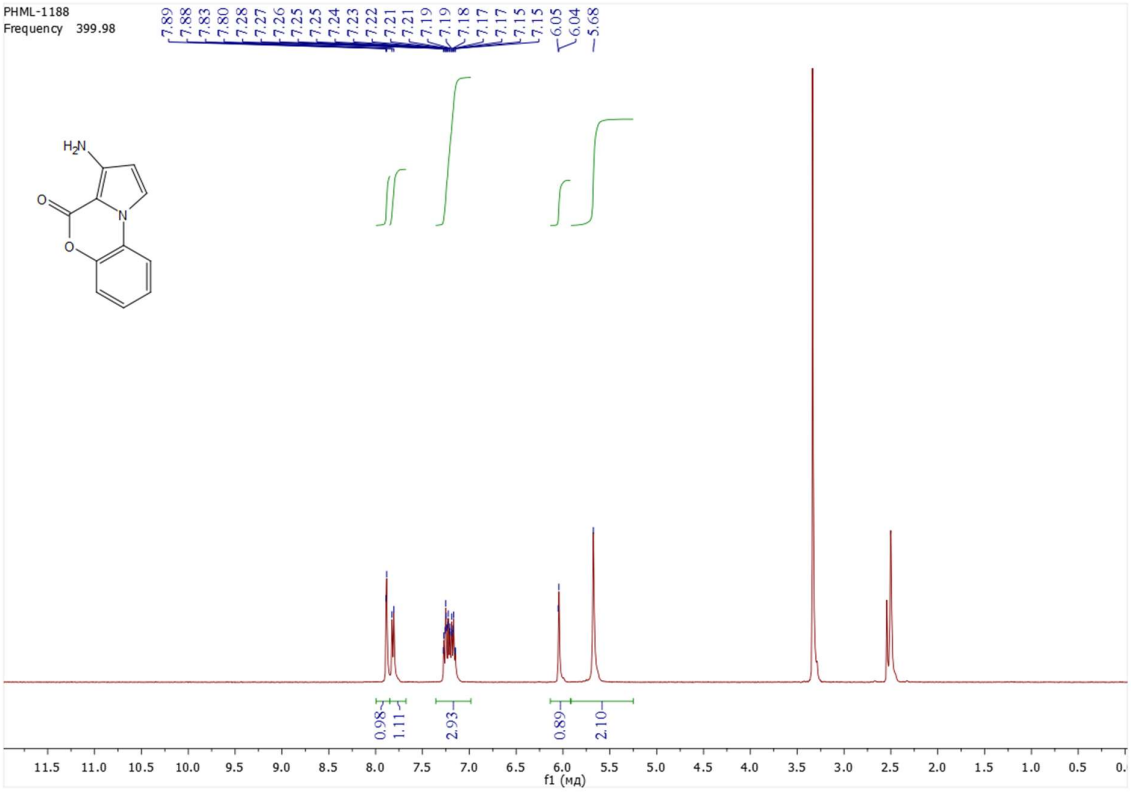

Figure S60. ^{1}H-NMR spectrum of 3-amino-4*H*-pyrrolo[2,1-*c*][1,4]benzoxazin-4-one (**9a**) in DMSO-d_6

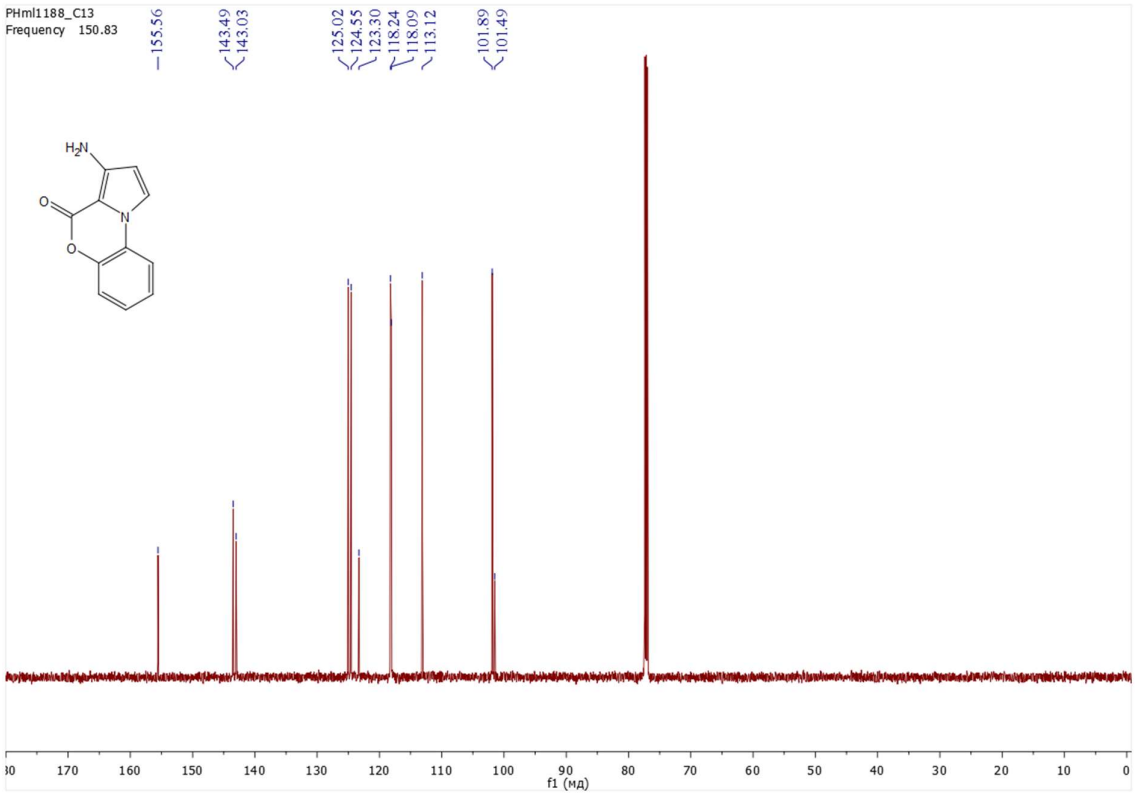

Figure S61. ^{13}C, NMR spectrum of 3-amino-4*H*-pyrrolo[2,1-*c*][1,4]benzoxazin-4-one (**9a**) in $CDCl_3$

Chemical characterization of 3-amino-9-methyl-4H-pyrrolo[2,1-c][1,4]benzoxazin-4-one (**9b**). Brown solid, mp 194-195°C; yield 67%. ^{1}H-NMR (302 MHz, $CDCl_3$): δ 2.64 (s, 3H, CH_3), 4.59 (s, 2H, NH_2), 6.02 (d, $^3J_{HH}$ = 3.1 Hz, 1H, C^{2}H), 6.91–7.06 (m, 2H, 2H$_{Ar}$), 7.11 (d, $^3J_{HH}$ = 7.9 Hz, 1H, 1H$_{Ar}$), 7.60 (d, $^3J_{HH}$ = 3.1 Hz, 1H, C^{1}H). ^{13}C, NMR (76 MHz, $CDCl_3$): δ = 22.88, 101.52, 102.45, 116.69, 123.04, 123.45, 124.43, 125.42, 128.39, 143.19, 144.04, 155.80. MS: m/z 215 (M + H). Anal. Calcd. for $C_{12}H_{10}N_2O_2$ (%): C, 67.28; H, 4.71; N, 13.08. Found: C, 67.46; H, 4.68; N, 13.00.

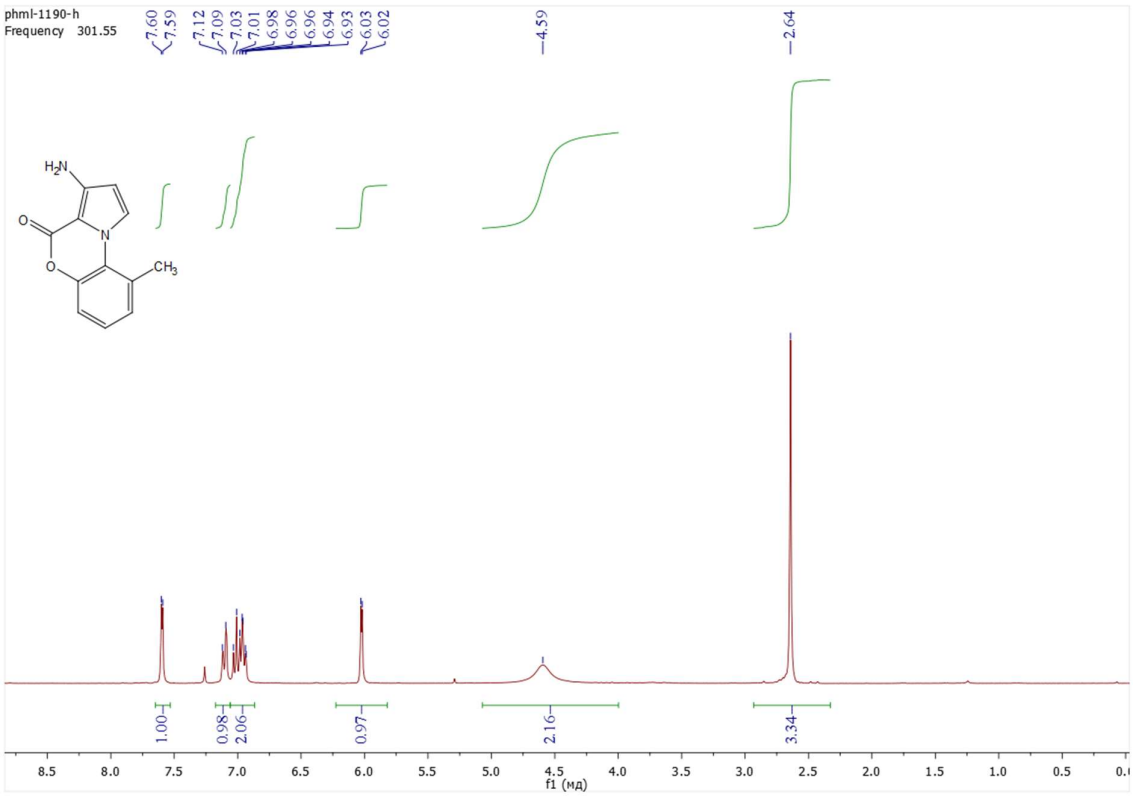

Figure S62. ^{1}H-NMR spectrum of 3-amino-9-methyl-4*H*-pyrrolo[2,1-*c*][1,4]benzoxazin-4-one (**9b**) in $CDCl_3$

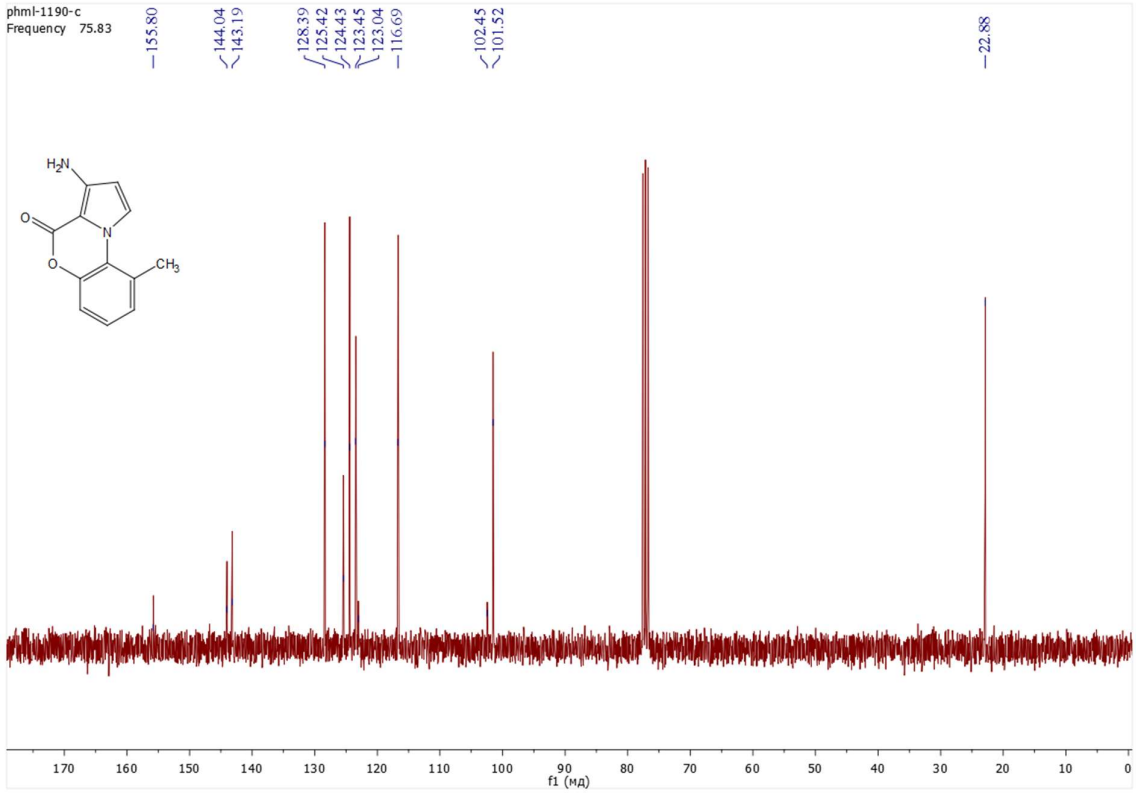

Figure S63. ^{13}C, NMR spectrum of 3-amino-9-methyl-4*H*-pyrrolo[2,1-*c*][1,4]benzoxazin-4-one (**9b**) in $CDCl_3$

Chemical characterization of 3-amino-8-chloro-4H-pyrrolo[2,1-c][1,4]benzoxazin-4-one (**9c**). Brown solid, mp 243-244°C; yield 53%. ^{1}H-NMR (302 MHz, DMSO-d_6): δ = 5.75 (s, 2H, NH_2), 6.06 (d, $^{3}J_{HH}$ = 3.0 Hz, 1H, C^{2}H), 7.19 (dd, $^{3}J_{HH}$ = 8.7 Hz, $^{4}J_{HH}$ = 2.3 Hz, 1H, 1H_{Ar}), 7.28 (d, $^{3}J_{HH}$ = 8.7 Hz, 1H, 1H_{Ar}), 7.95 (d, $^{3}J_{HH}$ = 3.1 Hz, 1H, C^{1}H), 8.02 (d, $^{4}J_{HH}$ = 2.3 Hz, 1H, 1H_{Ar}). ^{13}C, NMR (76 MHz, DMSO-d_6): δ = 98.63, 102.16, 113.99, 119.03, 121.19, 124.17, 124.37, 128.48, 141.18, 145.31, 153.86. MS: m/z 235 (M + H). Anal. Calcd. for $C_{11}H_7ClN_2O_2$ (%): C, 56.31; H, 3.01; N, 11.94. Found: C, 56.10; H, 2.98; N, 12.03.

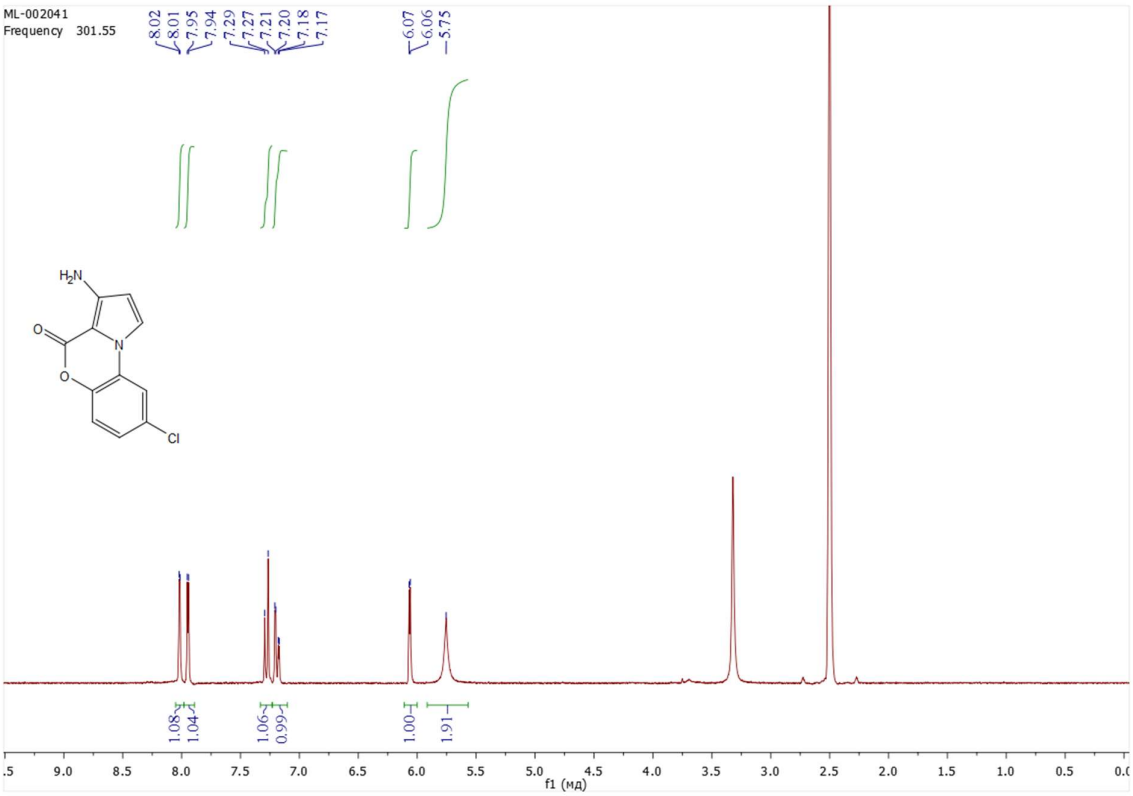

Figure S64. ^{1}H-NMR spectrum of 3-amino-8-chloro-4*H*-pyrrolo[2,1-*c*][1,4]benzoxazin-4-one (**9c**) in DMSO-d_6

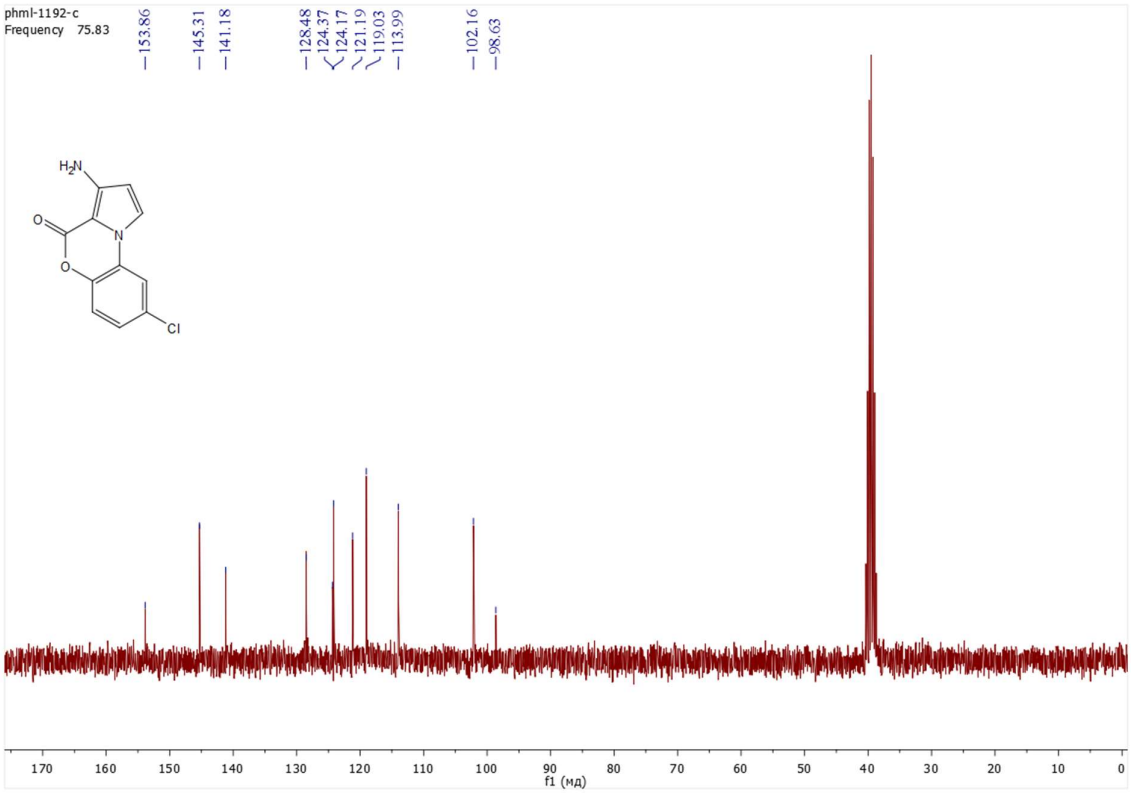

Figure S65. ^{13}C, NMR spectrum of 3-amino-8-chloro-4*H*-pyrrolo[2,1-*c*][1,4]benzoxazin-4-one (**9c**) in DMSO-d_6

Chemical characterization of 3-amino-8-tert-butyl-4H-pyrrolo[2,1-c][1,4]benzoxazin-4-one (**9d**). Brown solid, mp 148-149°C; yield 82%. ^1H-NMR (302 MHz, DMSO-d_6): δ 1.32 (s, 9H, $3CH_3$), 5.65 (s, 2H, NH_2), 6.03 (d, $^3J_{HH}$ = 2.9 Hz, 1H, C^2H), 7.17 (s, 2H, $2H_{Ar}$), 7.77 (s, 1H, $1H_{Ar}$), 8.04 (d, $^3J_{HH}$ = 3.0 Hz, 1H, C^1H). ^{13}C, NMR (126 MHz, $CDCl_3$): δ = 31.45, 34.77, 101.69, 101.74, 109.90, 117.76, 117.86, 122.27, 122.67, 140.89, 143.40, 148.08, 155.85. MS: m/z 257 (M + H). Anal. Calcd. for $C_{15}H_{16}N_2O_2$ (%): C, 70.29; H, 6.29; N, 10.93. Found: C, 70.18; H, 6.33; N, 11.02.

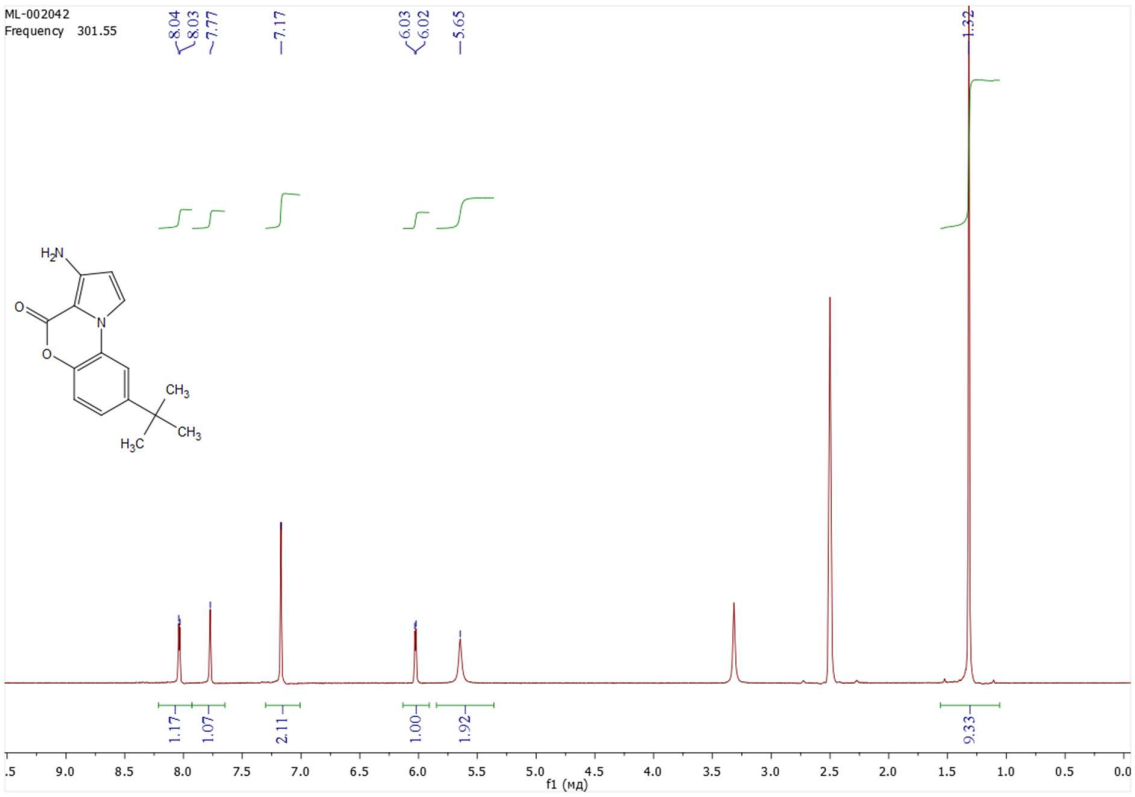

Figure S66 [1]H-NMR spectrum of 3-amino-8-*tert*-butyl-4*H*-pyrrolo[2,1-*c*][1,4]benzoxazin-4-one (**9d**) in DMSO-d_6

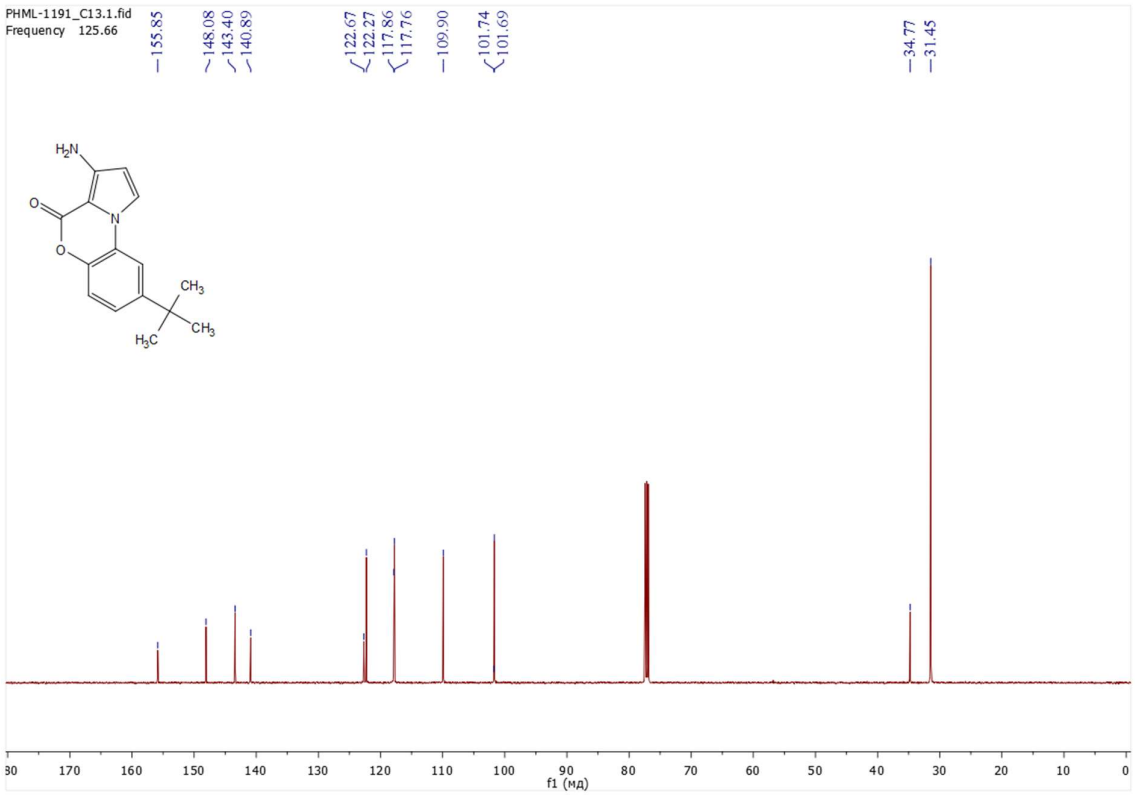

Figure S67. [13]C, NMR spectrum of 3-amino-8-*tert*-butyl-4*H*-pyrrolo[2,1-*c*][1,4]benzoxazin-4-one (**9d**) in $CDCl_3$

Chemical characterization of 3-amino-7-fluoro-4H-pyrrolo[2,1-c][1,4]benzoxazin-4-one (**9e**). Beige solid, mp 214-215°C; yield 73%. ^{1}H-NMR (400 MHz, DMSO-d_6): δ 5.69 (s, 2H, NH_2), 6.03 (d, $^{3}J_{HH}$ = 2.9 Hz, 1H, C^{2}H), 7.10-7.15 (m, 1H, 1H$_{Ar}$), 7.20–7.32 (m, 1H, 1H$_{Ar}$), 7.74–7.94 (m, 2H, H$_{Ar}$+ C^{1}H). ^{13}C, NMR (126 MHz, $CDCl_3$): δ = 98.63, 101.15, 105.06 (d, $^{2}J_{CF}$ = 26.8 Hz, C^{6}), 111.19 (d, $^{2}J_{CF}$ = 23.2 Hz, C^{8}), 115.04 (d, $^{3}J_{CF}$ = 9.4 Hz, C^{9}), 120.16, 120.69, 142.95 (d, $^{3}J_{CF}$ = 12.7 Hz, C^{5a}), 145.07, 153.69, 158.43 (d, $^{1}J_{CF}$ = 242.0 Hz, C^{7}). ^{19}F, NMR (376 MHz, DMSO-d_6) δ -117.32. MS: m/z 219 (M + H). Anal. Calcd. for $C_{11}H_7FN_2O_2$ (%): C, 60.55; H, 3.23; N, 12.84. Found: C, 60.72; H, 3.20; N, 12.91.

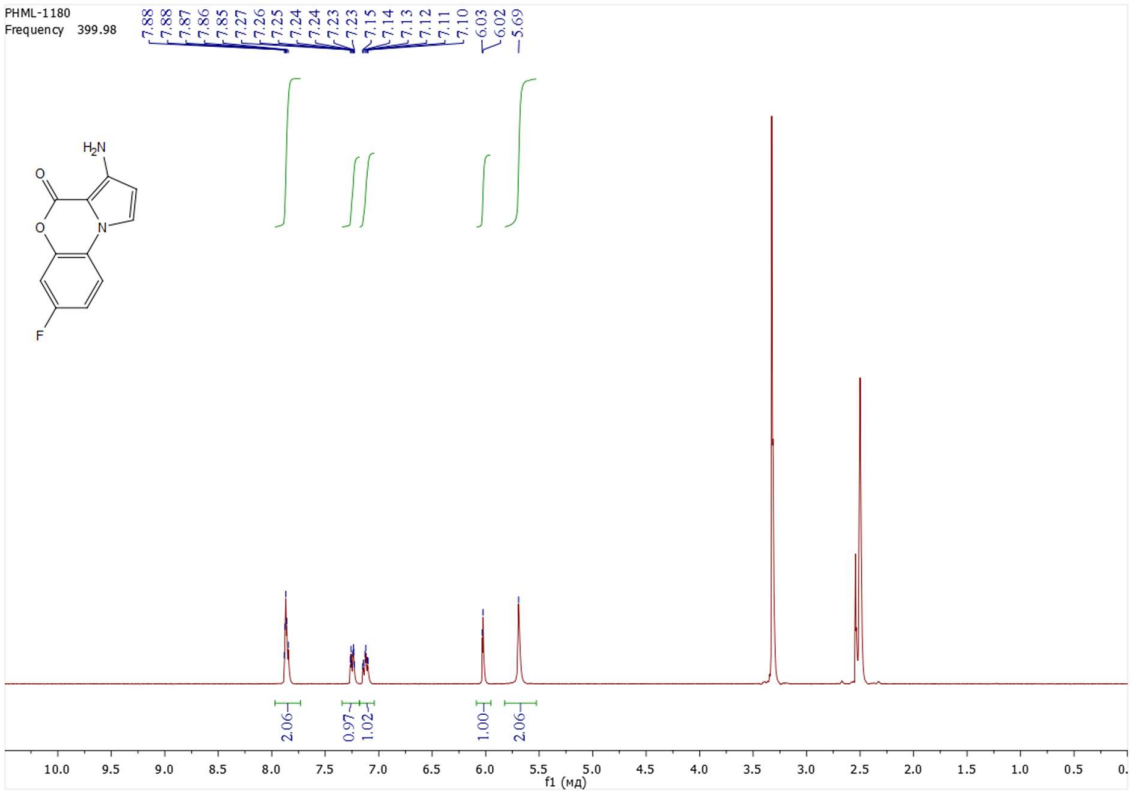

Figure S68. ^{1}H-NMR spectrum of 3-amino-7-fluoro-4*H*-pyrrolo[2,1-*c*][1,4]benzoxazin-4-one (**9e**) in DMSO-d_6

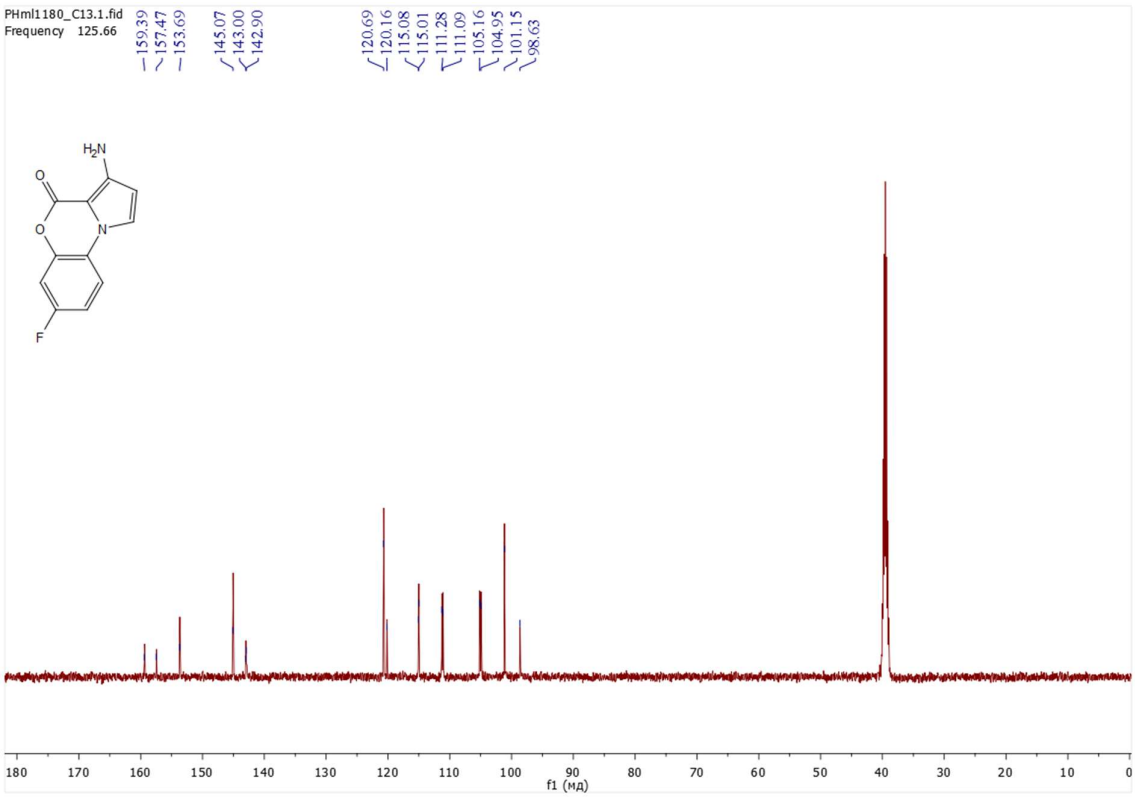

Figure S69. ^{13}C, NMR spectrum of 3-amino-7-fluoro-4*H*-pyrrolo[2,1-*c*][1,4]benzoxazin-4-one (**9e**) in DMSO-d_6

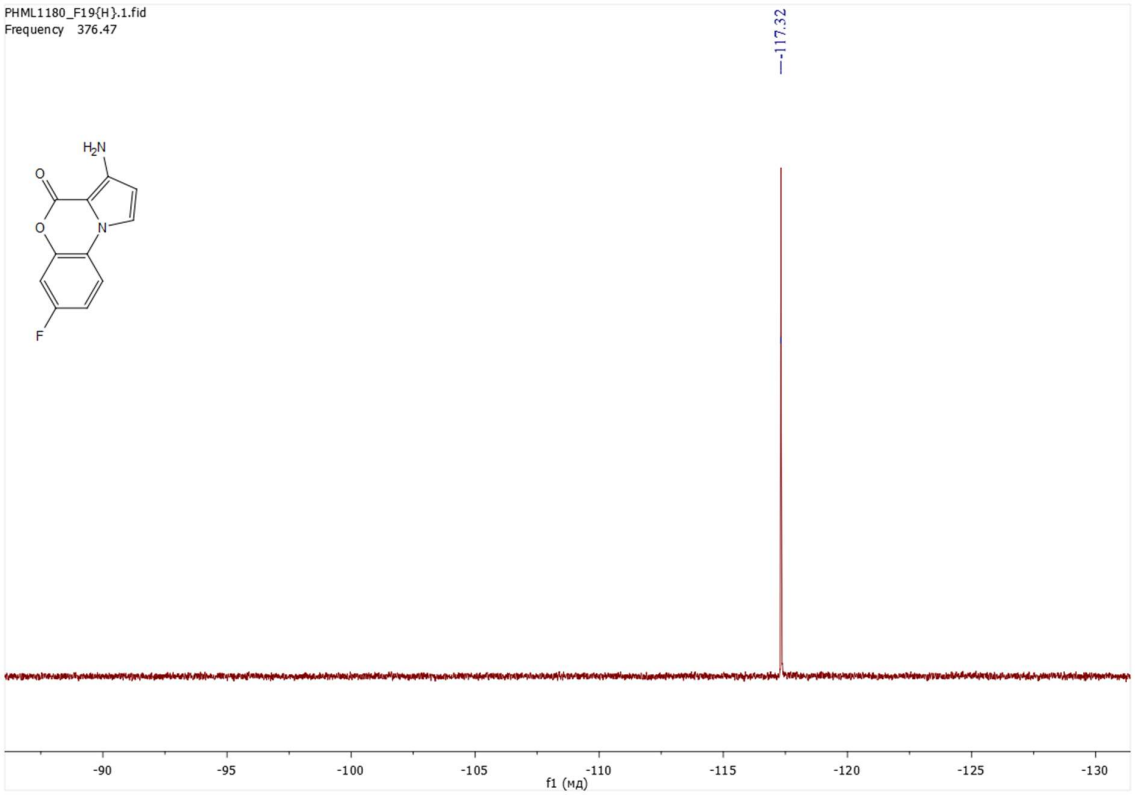

Figure S70. ^{19}F, NMR spectrum of 3-amino-7-fluoro-4*H*-pyrrolo[2,1-*c*][1,4]benzoxazin-4-one (**9e**) in DMSO-d_6

Chemical characterization of 3-amino-6-bromo-4H-pyrrolo[2,1-c][1,4]benzoxazin-4-one (**9f**). Brown solid, mp 224-225°C; yield 80%. ^{1}H-NMR (400 MHz, DMSO-d_6): δ 5.75 (s, 2H, NH_2), 6.09 (d, $^{3}J_{HH}$ = 3.1 Hz, 1H, C^{2}H), 7.15 (t, $^{3}J_{HH}$ = 8.1 Hz, 1H, 1H$_{Ar}$), 7.43 (d, $^{3}J_{HH}$ = 8.1 Hz, 1H, 1H$_{Ar}$), 7.81 (d, $^{3}J_{HH}$ = 8.2 Hz, 1H, 1H$_{Ar}$), 7.90 (d, $^{3}J_{HH}$ = 3.1 Hz, 1H, C^{1}H). ^{13}C, NMR (126 MHz, DMSO-d_6): δ = 98.61, 102.06, 110.17, 113.41, 121.17, 124.53, 125.24, 127.79, 139.56, 145.39, 153.19. MS: m/z 279, 281 (M + H). Anal. Calcd. for $C_{11}H_7BrN_2O_2$ (%): C, 47.34; H, 2.53; N, 10.04. Found: C, 47.17; H, 2.51; N, 10.14.

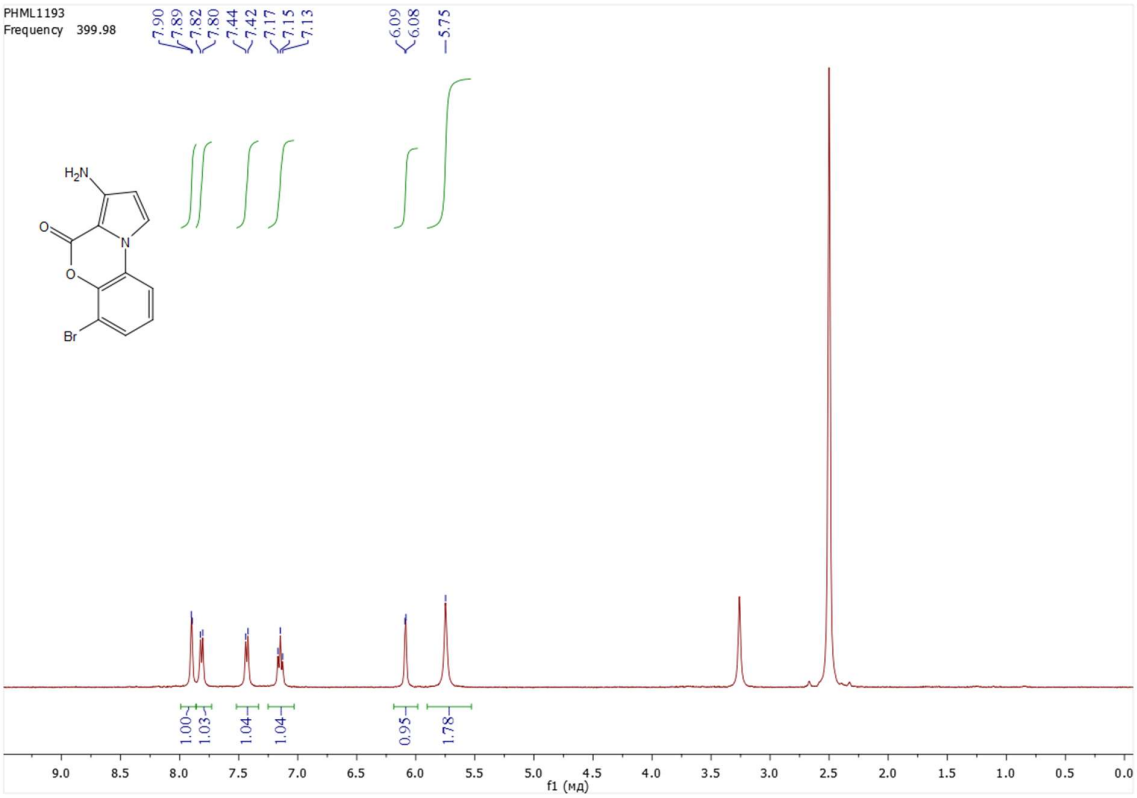

Figure S71. ^{1}H-NMR spectrum of 3-amino-6-bromo-4*H*-pyrrolo[2,1-*c*][1,4]benzoxazin-4-one (**9f**) in DMSO-d_6

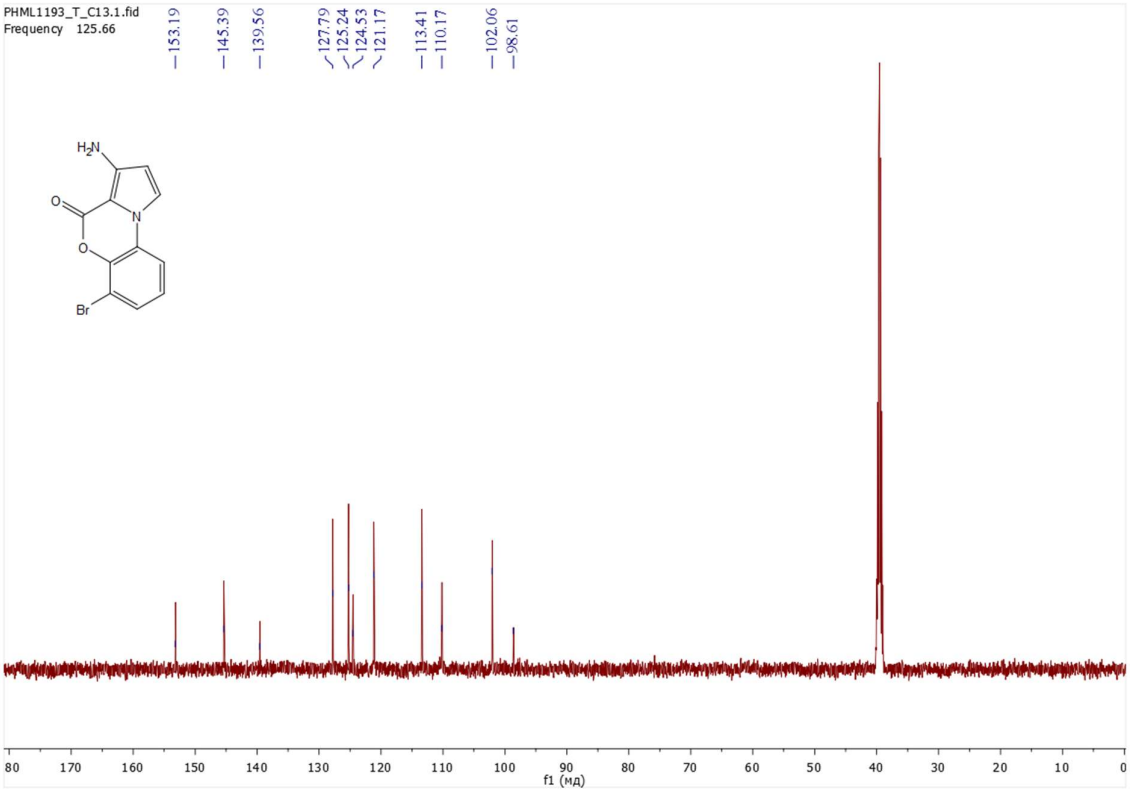

Figure S72. ^{13}C, NMR spectrum of 3-amino-6-bromo-4*H*-pyrrolo[2,1-*c*][1,4]benzoxazin-4-one (**9f**) in DMSO-d_6

Synthesis and spectra characteristics of compounds 11a-i and 12a-d

General procedure for the synthesis of N-alkyl(aryl)-1-oxo-3,4-dihydro-1H-pyrrolo[2,1-c][1,4]oxazine-8-carboxamide ***11a-i*** *and N-alkyl(aryl)-4-oxo-4H-pyrrolo[2,1-c][1,4]benzoxazine-3-carboxamide* ***12a-d****.* To a solution of (1.17 mmol) 1-oxo-3,4-dihydro-1*H*-pyrrolo[2,1-*c*][1,4]oxazine-8-carboxylic acid **4a-e** or 4-oxo-4*H*-pyrrolo[2,1-*c*][1,4]benzoxazine-3-carboxylic acid **5a,d-f** in 5 cm^3 DMF, 1.17 mmol of corresponding amines **10a-g**, 0.23 g DIPEA (1.75 mmol), and 0.53 g HATU (1.40 mmol) were added. The resulting mixture was stirred at 50°C for 8–25 h. After the reaction was completed, the reaction mixture was cooled and water (5 ml) added, the insoluble materials were filtered off, washed with H_2O (2 × 5 cm^3), hexane (2 × 4 cm^3) and dried under reduced pressure.

Chemical characterization of (5aS,9aS)-N-(1-methylethyl)-4-oxo-5a,6,7,8,9,9a-hexahydro-4H-pyrrolo[2,1-c][1,4]benzoxazine-3-carboxamide (**11a**). White solid, mp 189-190°C; yield 93%. ^{1}H-NMR (302 MHz, DMSO-d_6): δ 1.11-1.18 (m, 6H, 2CH_3), 1.33-1.51 (m, 3H), 1.59-1.71 (m, 1H), 1.80-1.82 (m, 2H), 2.07-2.11 (m, 1H), 2.66-2.73 (m, 1H), 3.94-4.11 (m, 2H, C^{9a}H + C<u>H</u>(CH_3)$_2$), 4.44 (td, $^3J_{HH}$ = 11.0, $^3J_{HH}$ = 4.3 Hz, 1H, C^{5a}H), 6.77 (d, $^3J_{HH}$ = 2.6 Hz, 1H, C^2H), 7.36 (d, $^3J_{HH}$ = 2.8 Hz, 1H, C^1H), 9.56 (d, $^3J_{HH}$ = 7.1 Hz, 1H, NH). ^{13}C, NMR (126 MHz, DMSO-d_6): δ = 22.41, 22.53, 22.75, 22.84, 26.87, 29.05, 40.65, 55.86, 80.27, 113.66, 115.65, 122.12, 128.17, 160.29, 160.43. MS: m/z 277 (M + H). Anal. Calcd. for $C_{15}H_{20}N_2O_3$ (%): C, 65.20; H, 7.30; N, 10.14. Found: C, 65.41; H, 7.26; N, 10.06.

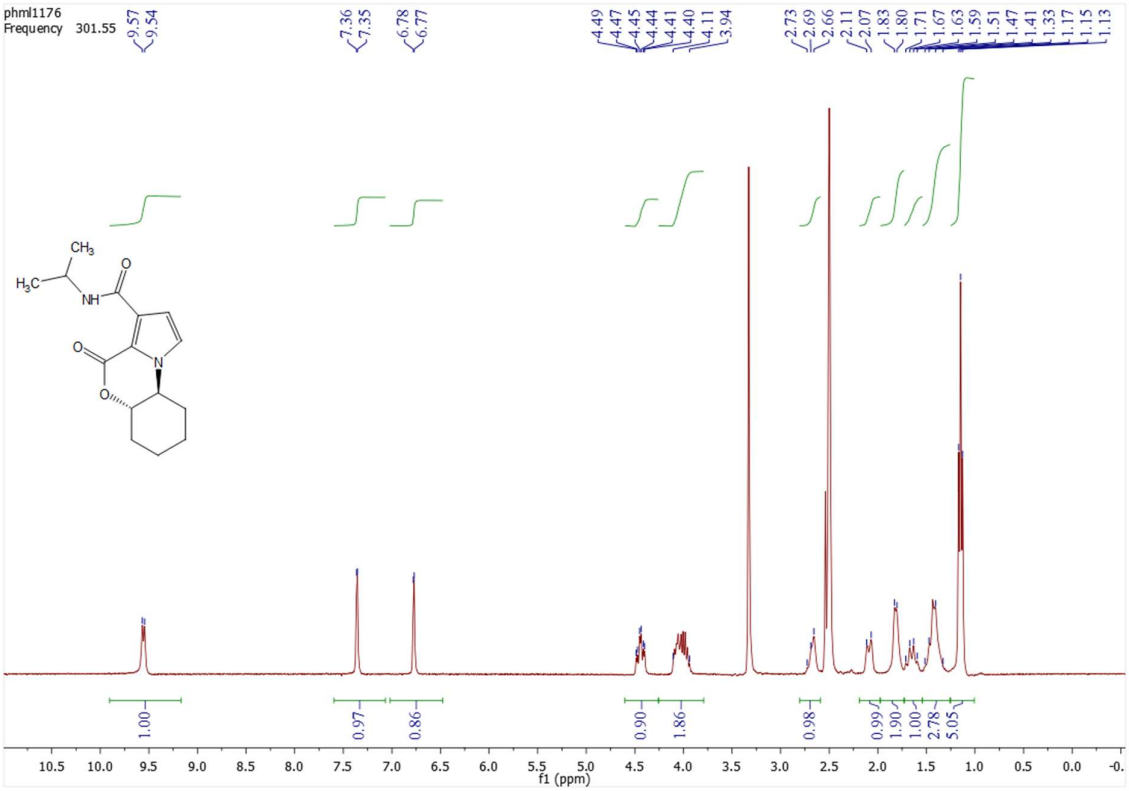

Figure S73. [1]H-NMR spectrum of (5*aS*,9*aS*)-*N*-(1-methylethyl)-4-oxo-5*a*,6,7,8,9,9*a*-hexahydro-4*H*-pyrrolo[2,1-*c*][1,4]benzoxazine-3-carboxamide (**11a**) in DMSO-d_6

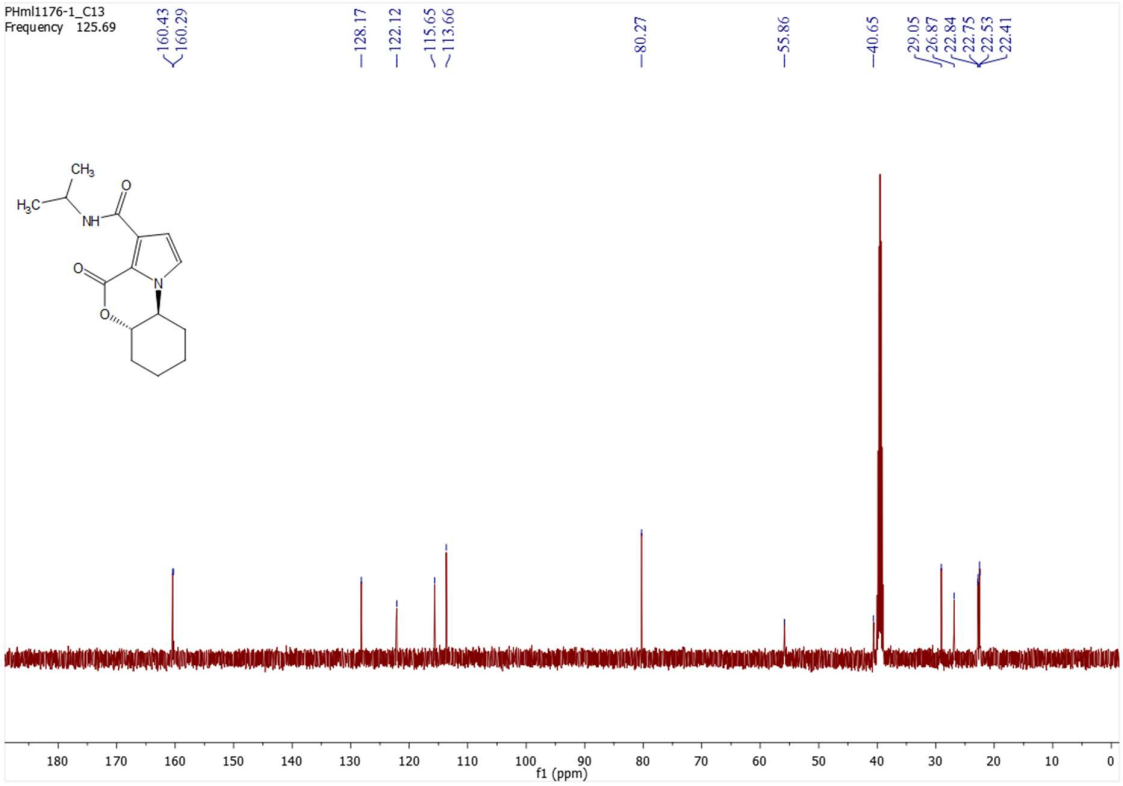

Figure S74. [13]C, NMR spectrum of (5*aS*,9*aS*)-*N*-(1-methylethyl)-4-oxo-5*a*,6,7,8,9,9*a*-hexahydro-4*H*-pyrrolo[2,1-*c*][1,4]benzoxazine-3-carboxamide (**11a**) in DMSO-d_6

Chemical characterization of (4S)-N-(4-bromophenyl)-4-(1-methylethyl)-1-oxo-3,4-dihydro-1H-pyrrolo[2,1-c][1,4]oxazine-8-carboxamide (**11b**). White solid, mp 174-175°C; yield 89%. ^{1}H-NMR (302 MHz, $CDCl_3$): δ 0.97 (d, $^{3}J_{HH}$ = 6.8 Hz, 3H, CH_3), 1.10 (d, $^{3}J_{HH}$ = 6.7 Hz, 3H, CH_3), 2.20–2.32 (m, 1H, C<u>H</u>$(CH_3)_2$), 3.90-3.96 (m, 1H, $C^{4}H$), 4.66 (dd, ^{2}J = 12.0, ^{3}J = 3.3 Hz, $C^{3}H$), 4.72 (dd, ^{2}J = 11.9, ^{3}J = 1.7 Hz, $C^{3}H$), 6.95 (d, $^{3}J_{HH}$ = 2.7 Hz, 1H, $C^{7}H$), 7.15 (d, $^{3}J_{HH}$ = 2.6 Hz, 1H, $C^{6}H$), 7.44 (d, $^{3}J_{HH}$ = 8.8 Hz, 2H, $2H_{Ar}$), 7.70 (d, $^{3}J_{HH}$ = 8.7 Hz, 2H, $2H_{Ar}$), 11.89 (s, 1H, NH). ^{13}C, NMR (126 MHz, $CDCl_3$): δ = 19.37, 19.53, 30.70, 59.94, 68.11, 114.80, 115.20, 116.31, 121.64, 125.41, 129.29, 131.87, 138.09, 159.75, 160.99. MS: m/z 377, 379 (M + H). Anal. Calcd. for $C_{17}H_{17}BrN_2O_3$ (%): C, 54.13; H, 4.54; N, 7.43. Found: C, 53.94; H, 4.56; N, 7.50.

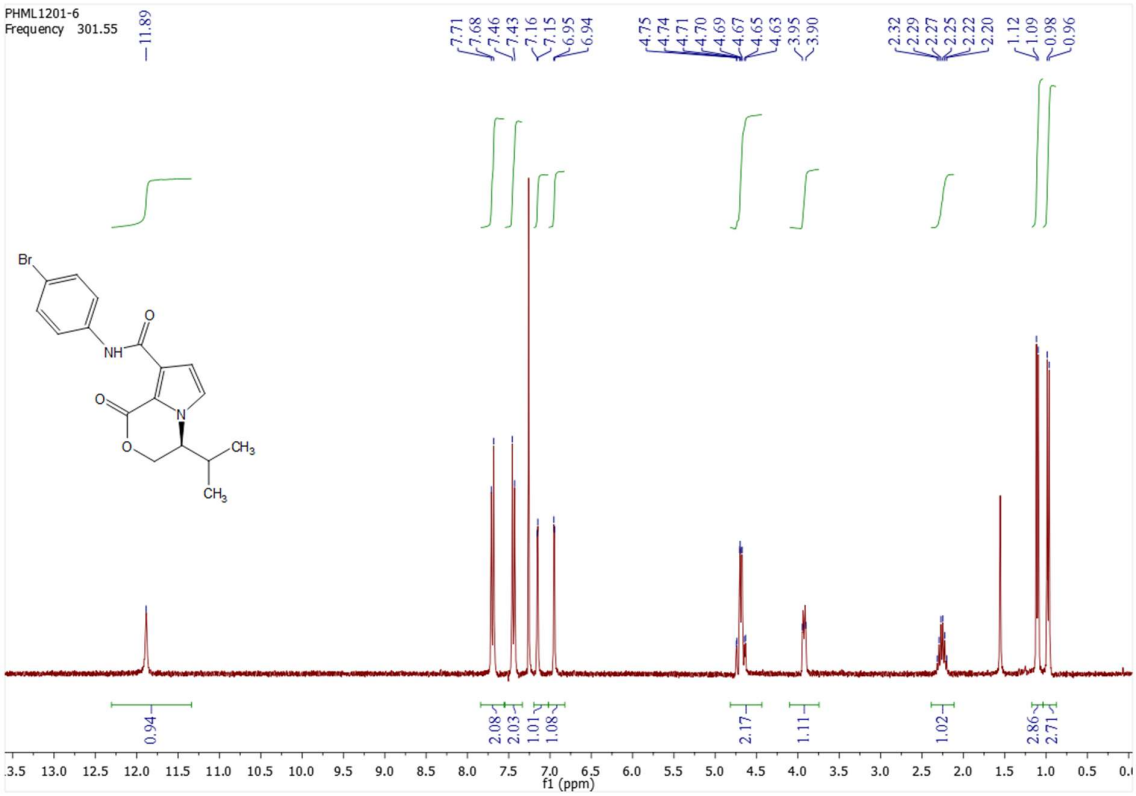

Figure S75. ^{1}H-NMR spectrum of (4*S*)-*N*-(4-bromophenyl)-4-(1-methylethyl)-1-oxo-3,4-dihydro-1*H*-pyrrolo[2,1-*c*][1,4]oxazine-8-carboxamide (**11b**) in $CDCl_3$

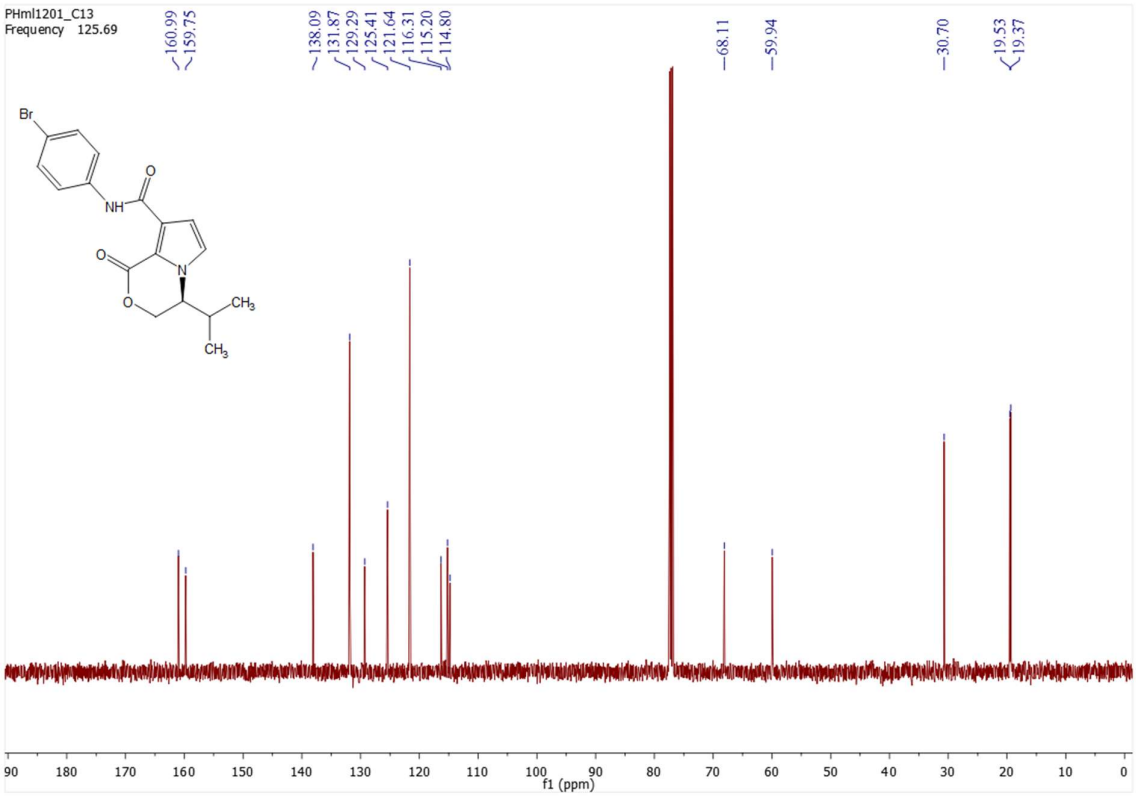

Figure S76. ^{13}C, NMR spectrum of (4*S*)-*N*-(4-bromophenyl)-4-(1-methylethyl)-1-oxo-3,4-dihydro-1*H*-pyrrolo[2,1-*c*][1,4]oxazine-8-carboxamide (**11b**) in $CDCl_3$

X-ray difraction study of (4S)-N-(4-bromophenyl)-4-(1-methylethyl)-1-oxo-3,4-dihydro-1H-pyrrolo[2,1-c][1,4]oxazine-8-carboxamide (**11b**). The colourless crystals of compound **11b** (**(**$C_{17}H_{17}BrN_2O_3$) are tetragonal. At 193 K $a = b = 12.9667(3)$, $c = 19.7357(7)$ Å, V = 3318.27(19) Å^3, M_r = 377.23, Z = 8, space group $P4_12_12$, d_{calc}= 1.510 g/cm^3, μ(MoK_α) = 2.494 mm^{-1}, F(000) = 1536. Intensities of 44737 reflections (2933 independent, R_{int}=0.0778) were measured on the Bruker APEX II diffractometer (graphite monochromated MoK_α radiation, CCD detector, ω-scaning, $2\Theta_{max}$ = 50°). The structure was solved by direct method using SHELXTL package.[56] Absorption correction was performed using the numerical method (T_{min} = 0.488, T_{max} = 1.000). Positions of the hydrogen atoms were located from electron density difference maps and refined using "riding" model with $U_{iso} = nU_{eq}$ of the carrier atom (n = 1.5 for methyl groups and n = 1.2 for other hydrogen atoms). Full-matrix least-squares refinement against F^2 in anisotropic approximation for non-hydrogen atoms using 2933 reflections was converged to $wR_2 = 0.1203$ ($R_1 = 0.0370$ for 2423 reflections with $F>4\sigma(F)$, S = 0.882). The final atomic coordinates, and crystallographic data for molecule **11b** have been deposited to with the Cambridge Crystallographic Data Centre, 12 Union Road, CB2 1EZ, UK (fax: +44-1223-336033; e-mail: deposit@ccdc.cam.ac.uk) and are available on request quoting the deposition numbers CCDC 2373003).

Chemical characterization of N-(4-fluorophenyl)-3-methyl-1-oxo-3,4-dihydro-1H-pyrrolo[2,1-c][1,4]oxazine-8-carboxamide (**11c**). Beige solid, mp 201-202°C; yield 66%. ^{1}H-NMR (302 MHz,

$CDCl_3$): δ 1.54 (d, $^3J_{HH}$ = 6.3 Hz, 3H, CH_3), 4.01 (dd, $^2J_{HH}$ = 13.3, $^3J_{HH}$ = 10.4 Hz, 1H, C^4HH), 4.19 (dd, $^2J_{HH}$ = 13.3, $^3J_{HH}$ = 3.2 Hz, 1H, C^4HH), 4.81–4.92 (m, 1H, C^3H), 6.87 (d, $^3J_{HH}$ = 2.7 Hz, 1H, C^7H), 7.02 (dd, $^3J_{HH}$ = 8.7 Hz, $^3J_{HF}$ = 8.7 Hz, 2H, $2H_{Ar}$), 7.08 (d, $^3J_{HH}$ = 2.7 Hz, 1H, C^6H), 7.73 (dd, $^3J_{HH}$ = 8.8 Hz, $^4J_{HF}$ = 4.9 Hz, 2H, $2H_{Ar}$), 11.84 (s, 1H, NH). ^{13}C, NMR (126 MHz, DMSO-d_6): δ = 17.26, 48.10, 74.68, 113.79, 115.15, 115.53 (d, $^2J_{CF}$ = 22.4 Hz, $2C_{Ar}$), 120.90 (d, $^3J_{CF}$ = 7.9 Hz, $2C_{Ar}$), 125.76, 127.00, 135.21 (d, $^4J_{CF}$ = 2.2 Hz, C_{Ar}), 158.11 (d, $^1J_{CF}$ = 240.0 Hz, C_{Ar}), 159.47, 160.89. ^{19}F, NMR (376 MHz, $CDCl_3$) δ = -119.42. MS: m/z 289 (M + H). Anal. Calcd. for $C_{15}H_{13}FN_2O_3$ (%): C, 62.50; H, 4.55; N, 9.72. Found: C, 62.31; H, 4.53; N, 9.80.

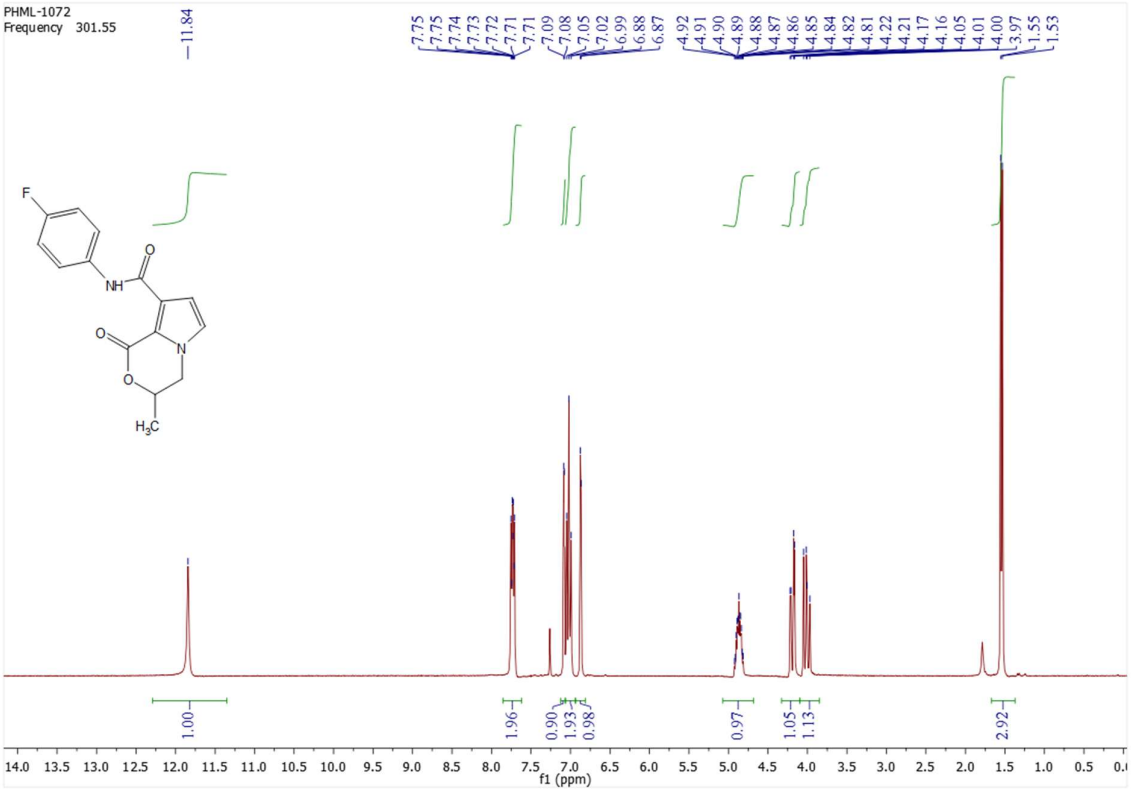

Figure S77. ^{1}H-NMR spectrum of *N*-(4-fluorophenyl)-3-methyl-1-oxo-3,4-dihydro-1*H*-pyrrolo[2,1-*c*][1,4]oxazine-8-carboxamide (**11c**) in $CDCl_3$

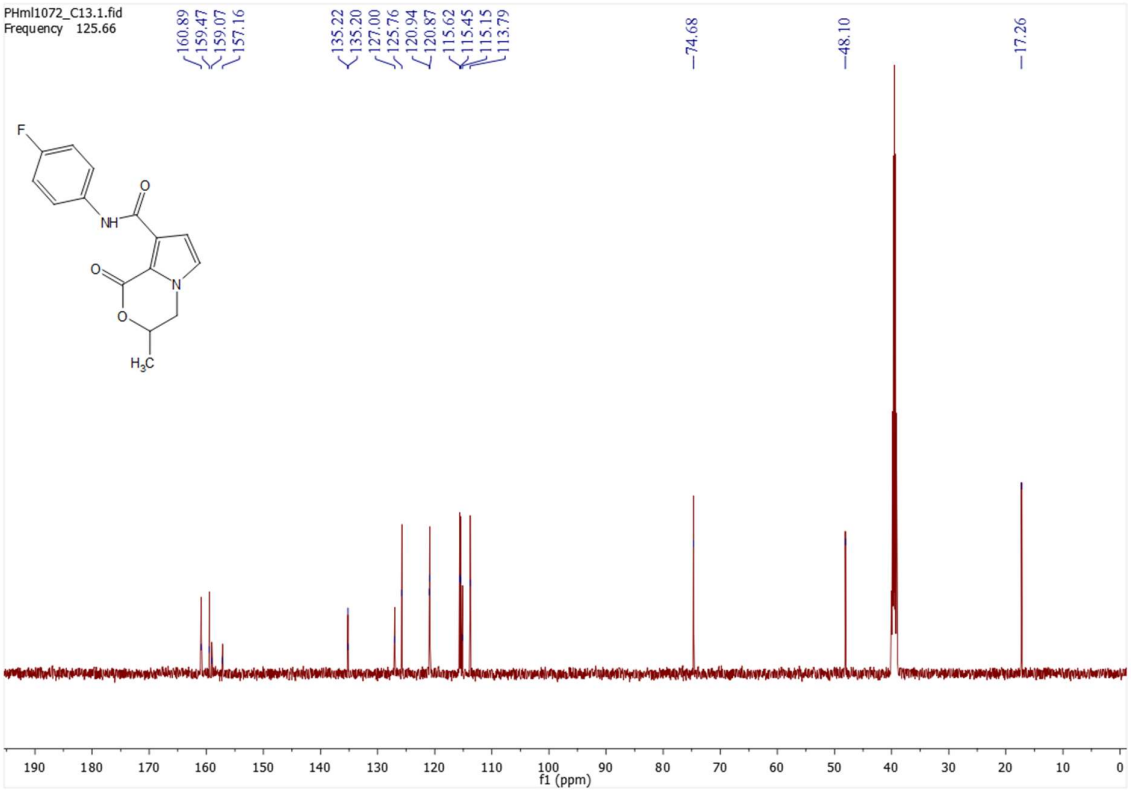

Figure S78. ^{13}C, NMR spectrum of *N*-(4-fluorophenyl)-3-methyl-1-oxo-3,4-dihydro-1*H*-pyrrolo[2,1-*c*][1,4]oxazine-8-carboxamide (**11c**) in DMSO-d_6

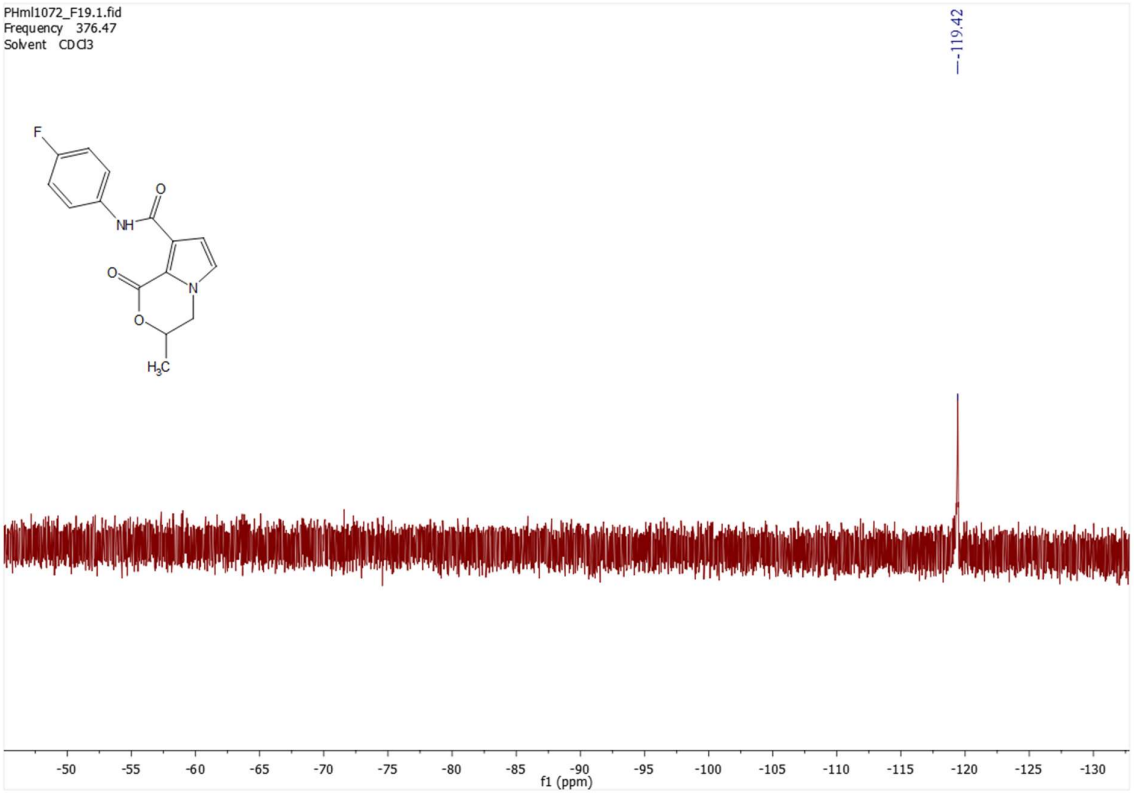

Figure S79. ^{19}F, NMR spectrum of *N*-(4-fluorophenyl)-3-methyl-1-oxo-3,4-dihydro-1*H*-pyrrolo[2,1-*c*][1,4]oxazine-8-carboxamide (**11c**) in $CDCl_3$

Chemical characterization of N-(4-fluorophenyl)-1-oxo-3-phenyl-3,4-dihydro-1H-pyrrolo[2,1-c][1,4]oxazine-8-carboxamide (**11d**). White solid, mp 215-216°C; yield 75%. ^{1}H-NMR (302 MHz, $CDCl_3$): δ 4.20–4.53 (m, 2H, C^{4}H$_2$), 5.77 (dd, $^{3}J_{HH}$ = 9.5, $^{3}J_{HH}$ = 4.8 Hz, 1H, C$_3$H), 6.95 (d, $^{3}J_{HH}$ = 2.7 Hz, 1H, C^{7}H), 7.04 (dd, $^{3}J_{HH}$ = 8.8 Hz, $^{3}J_{HF}$ = 8.8 Hz, 2H, 2H$_{Ar}$), 7.18 (d, $^{3}J_{HH}$ = 2.7 Hz, 1H, C^{6}H), 7.47 (s, 5H, 5H$_{Ar}$), 7.76 (dd, $^{3}J_{HH}$ = 9.0 Hz, $^{4}J_{HF}$ = 4.9 Hz, 2H, 2H$_{Ar}$), 11.84 (s, 1H, NH). ^{13}C, NMR (151 MHz, DMSO-d_6): δ = 48.03, 78.89, 113.99, 115.34, 115.60 (d, $^{2}J_{CF}$ = 22.3 Hz, 2C$_{Ar}$), 120.95 (d, $^{3}J_{CF}$ = 7.9 Hz, 2C$_{Ar}$), 125.90, 126.84, 127.23, 128.73, 129.25, 135.20, 135.22, 158.16 (d, $^{1}J_{CF}$ = 240.2 Hz, C$_{Ar}$–F), 159.48, 160.78. ^{19}F, NMR (376 MHz, $CDCl_3$) δ = -119.29. MS: m/z 351 (M + H). Anal. Calcd. for $C_{20}H_{15}FN_2O_3$ (%): C, 68.57; H, 4.32; N, 8.00. Found: C, 68.38; H, 4.35; N, 8.07.

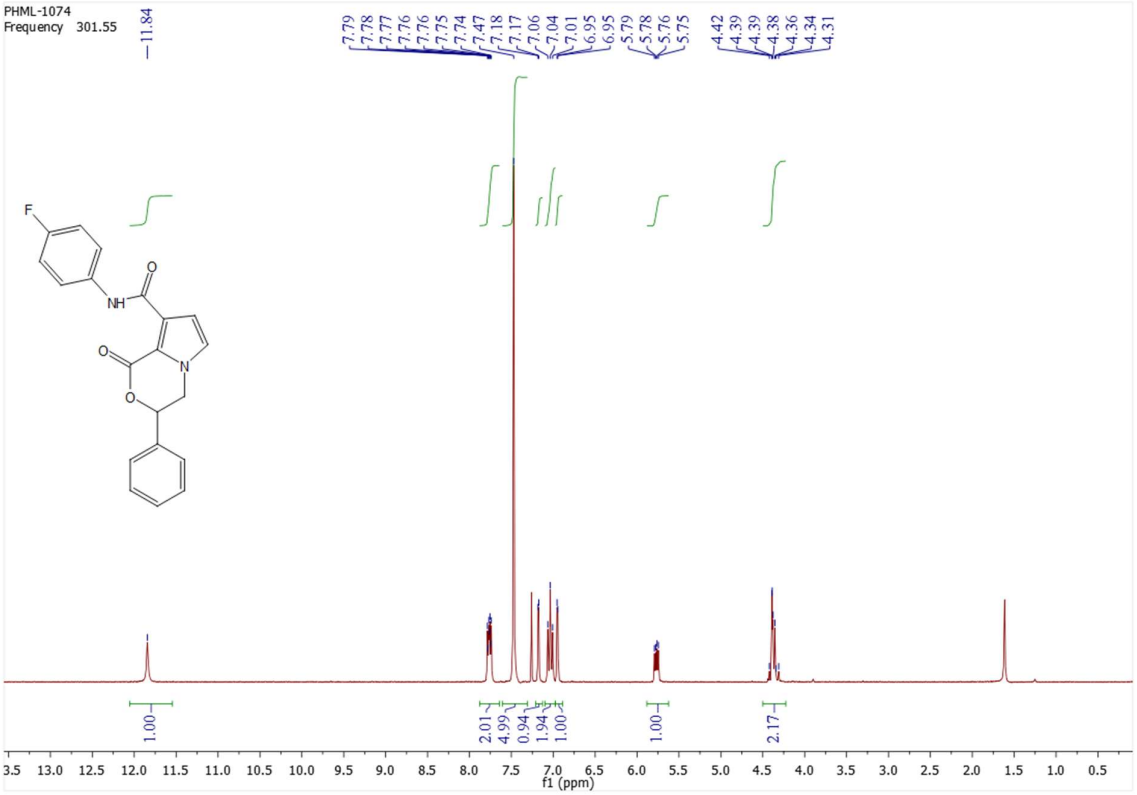

Figure S80. ^{1}H-NMR spectrum of *N*-(4-fluorophenyl)-1-oxo-3-phenyl-3,4-dihydro-1*H*-pyrrolo[2,1-*c*][1,4]oxazine-8-carboxamide (**11d**) in $CDCl_3$

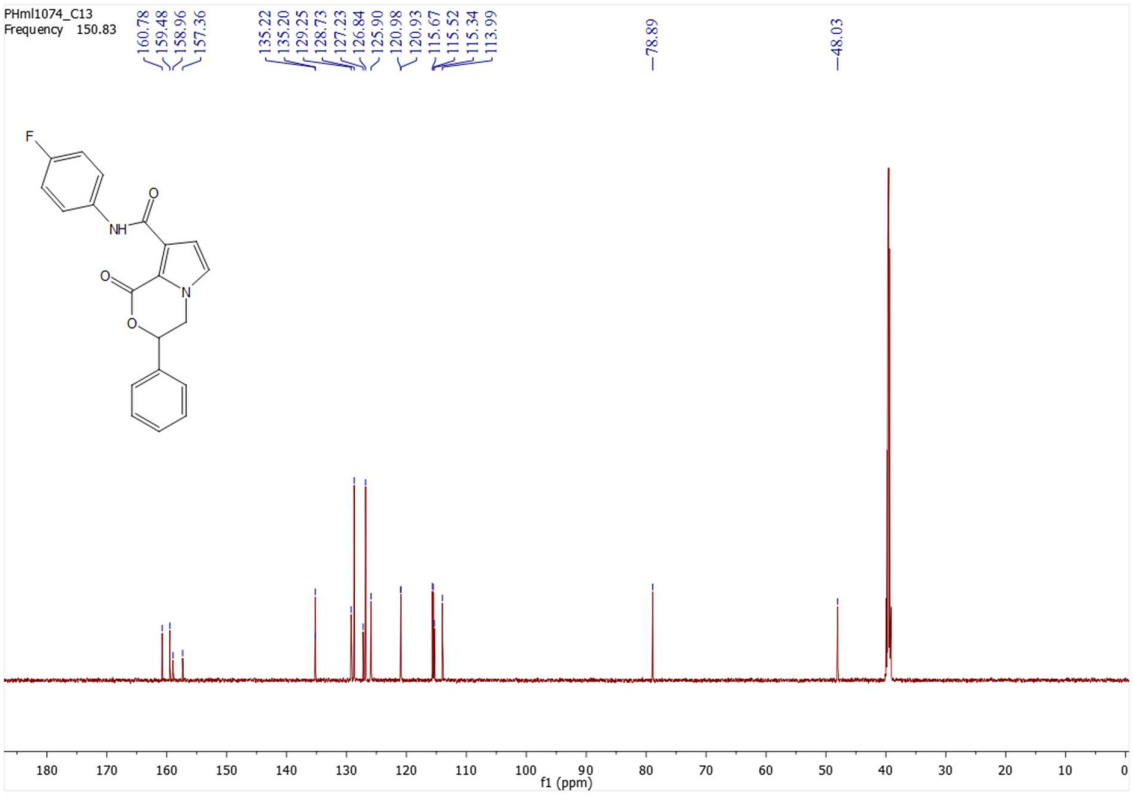

Figure S81. ^{13}C, NMR spectrum of *N*-(4-fluorophenyl)-1-oxo-3-phenyl-3,4-dihydro-1*H*-pyrrolo[2,1-*c*][1,4]oxazine-8-carboxamide (**11d**) in DMSO-d_6

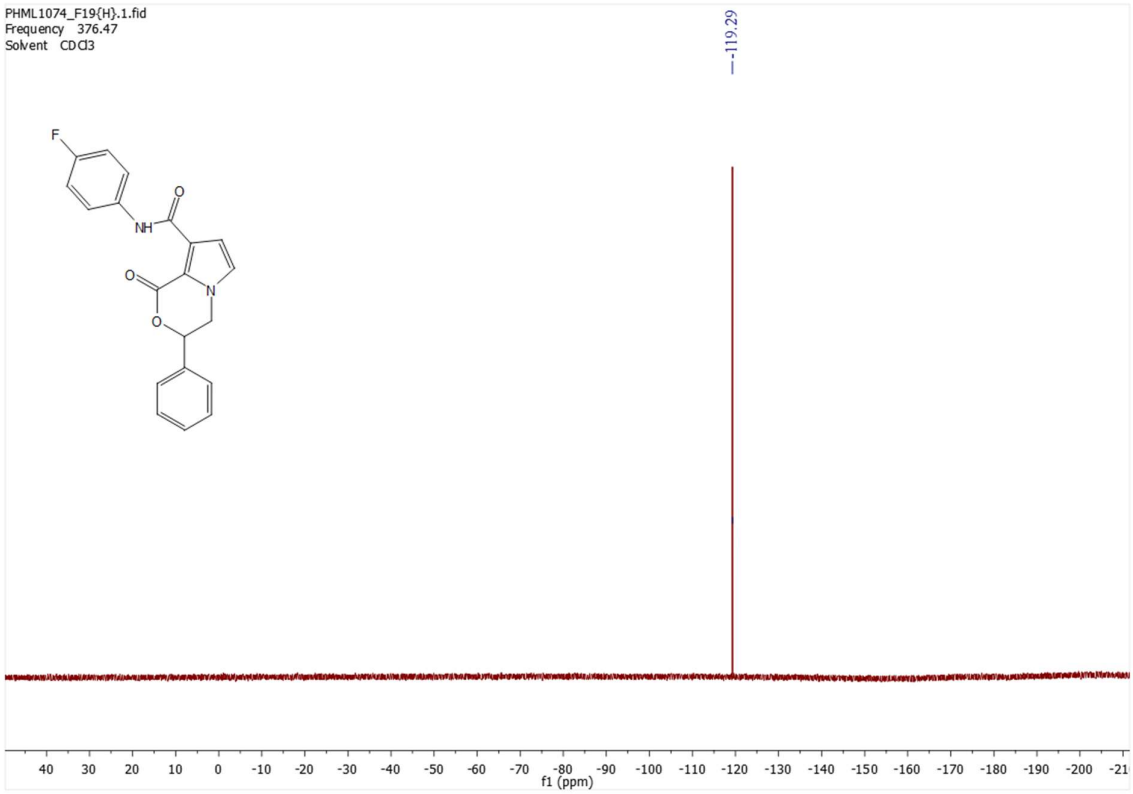

Figure S82. ^{19}F, NMR spectrum of *N*-(4-fluorophenyl)-1-oxo-3-phenyl-3,4-dihydro-1*H*-pyrrolo[2,1-*c*][1,4]oxazine-8-carboxamide (**11d**) in $CDCl_3$

Chemical characterization of 3-methyl-N-(4-methylphenyl)-1-oxo-3,4-dihydro-1H-pyrrolo[2,1-c][1,4]oxazine-8-carboxamide (**11e**). Beige solid, mp 203-204°C; yield 68%. ^{1}H-NMR (400 MHz, DMSO-d_6): δ 1.44 (d, $^{3}J_{HH}$ = 6.4 Hz, 3H, C^{3}-CH$_3$), 2.27 (s, 3H, CH$_3$-Ph), 4.12 (dd, $^{2}J_{HH}$ = 13.4, $^{3}J_{HH}$ = 10.4 Hz, 1H, C^{4}HH), 4.48 (dd, $^{2}J_{HH}$ = 13.6, $^{3}J_{HH}$ = 3.2 Hz, 1H, C^{4}HH), 4.95-5.01 (m, 1H, C^{3}H), 6.87 (d, $^{3}J_{HH}$ = 2.6 Hz, 1H, C^{7}H), 7.16 (d, $^{3}J_{HH}$ = 8.5 Hz, 2H, 2H$_{Ar}$), 7.32 (d, $^{3}J_{HH}$ = 2.6 Hz, 1H, C^{6}H), 7.55 (d, $^{3}J_{HH}$ = 8.5 Hz, 2H, 2H$_{Ar}$), 11.72 (s, 1H, NH). ^{13}C, NMR (151 MHz, DMSO-d_6): δ = 17.35, 20.49, 48.18, 74.76, 113.92, 115.08, 119.23, 125.85, 127.35, 129.43, 132.56, 136.37, 159.39, 161.04. MS: m/z 285 (M + H). Anal. Calcd. for $C_{16}H_{16}N_2O_3$ (%): C, 67.59; H, 5.67; N, 9.85. Found: C, 67.42; H, 5.70; N, 9.91.

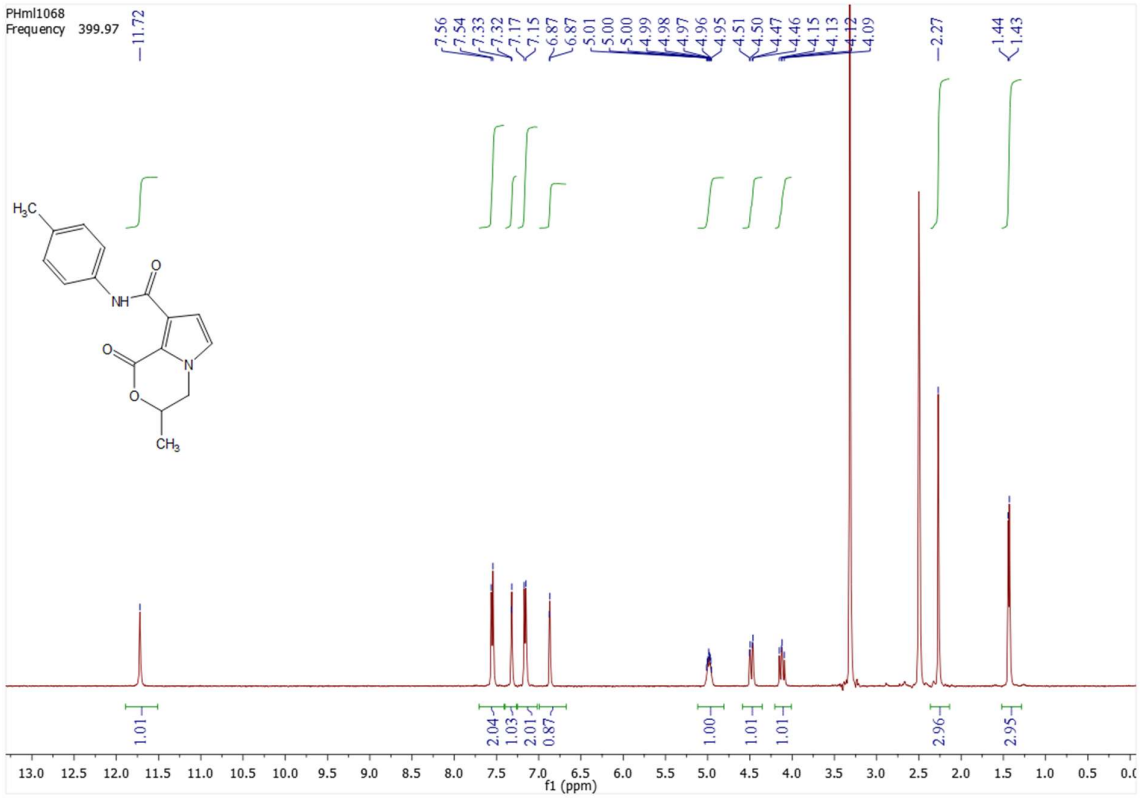

Figure S83. ^{1}H-NMR spectrum of 3-methyl-*N*-(4-methylphenyl)-1-oxo-3,4-dihydro-1*H*-pyrrolo[2,1-*c*][1,4]oxazine-8-carboxamide (**11e**) in DMSO-d_6

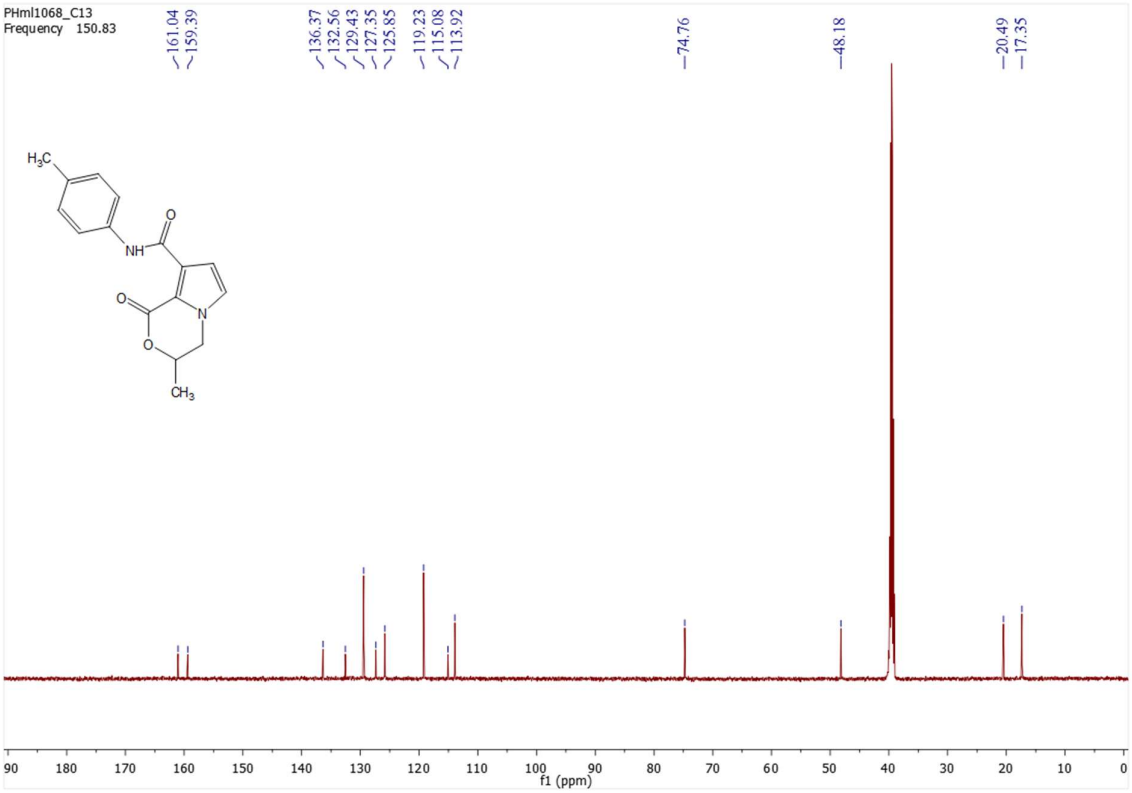

Figure S84. ^{13}C, NMR spectrum of 3-methyl-*N*-(4-methylphenyl)-1-oxo-3,4-dihydro-1*H*-pyrrolo[2,1-*c*][1,4]oxazine-8-carboxamide (**11e**) in DMSO-d_6

Chemical characterization of 4,4-dimethyl-N-(4-methylphenyl)-1-oxo-3,4-dihydro-1H-pyrrolo[2,1-c][1,4]oxazine-8-carboxamide (**11f**). Beige solid, mp 125-126°C; yield 72%. ^{1}H-NMR (302 MHz, DMSO-d_6): δ 1.53 (s, 6H, 2CH$_3$), 2.27 (s, 3H, CH$_3$), 4.50 (s, 2H, C^{3}H), 6.90 (d, $^3J_{HH}$ = 2.7 Hz, 1H, C^{7}H), 7.16 (d, $^3J_{HH}$ = 8.0 Hz, 2H, 2H$_{Ar}$), 7.43–7.62 (m, 3H, 2H$_{Ar}$ + C^{6}H), 11.67 (s, 1H, NH). ^{13}C, NMR (126 MHz, DMSO-d_6): δ = 20.39, 23.67, 54.16, 74.63, 114.25, 114.27, 119.20, 122.53, 128.33, 129.29, 132.45, 136.33, 159.41, 160.50. MS: m/z 299 (M + H). Anal. Calcd. for $C_{17}H_{18}N_2O_3$ (%): C, 68.44; H, 6.08; N, 9.39. Found: C, 68.65; H, 6.05; N, 9.31.

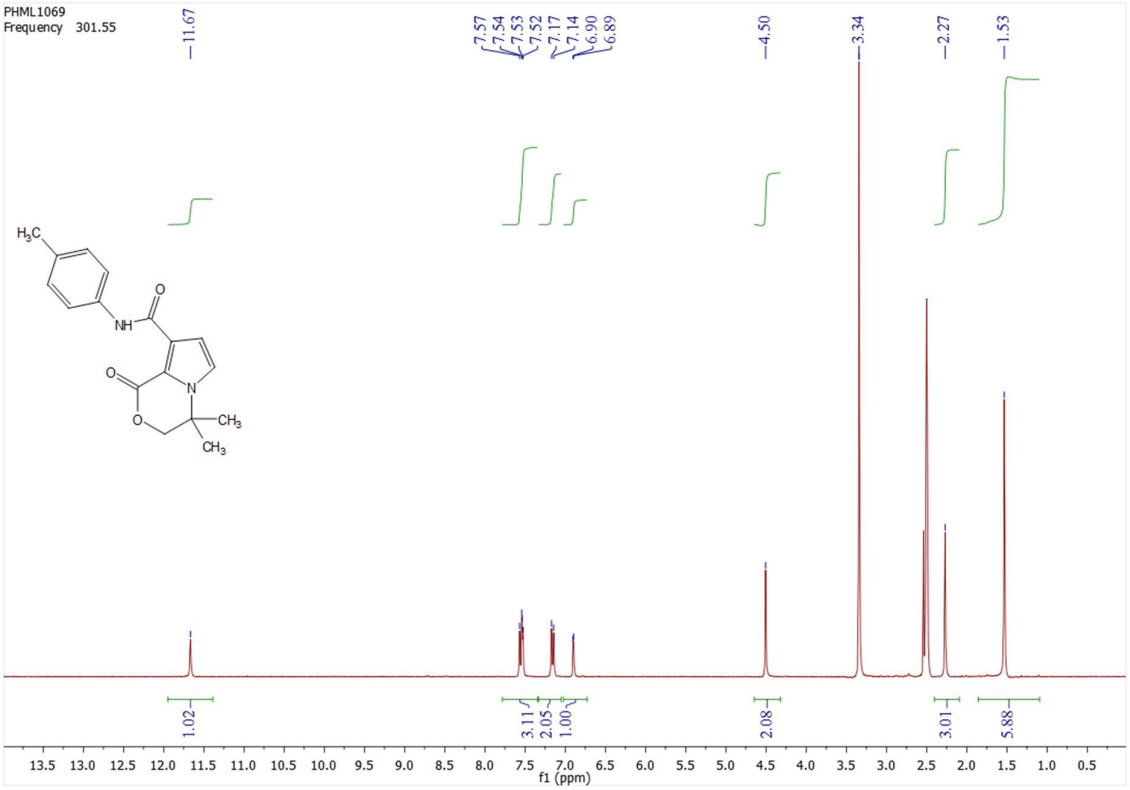

Figure S85. ^{1}H-NMR spectrum of 4,4-dimethyl-*N*-(4-methylphenyl)-1-oxo-3,4-dihydro-1*H*-pyrrolo[2,1-*c*][1,4]oxazine-8-carboxamide (**11f**) in DMSO-d_6

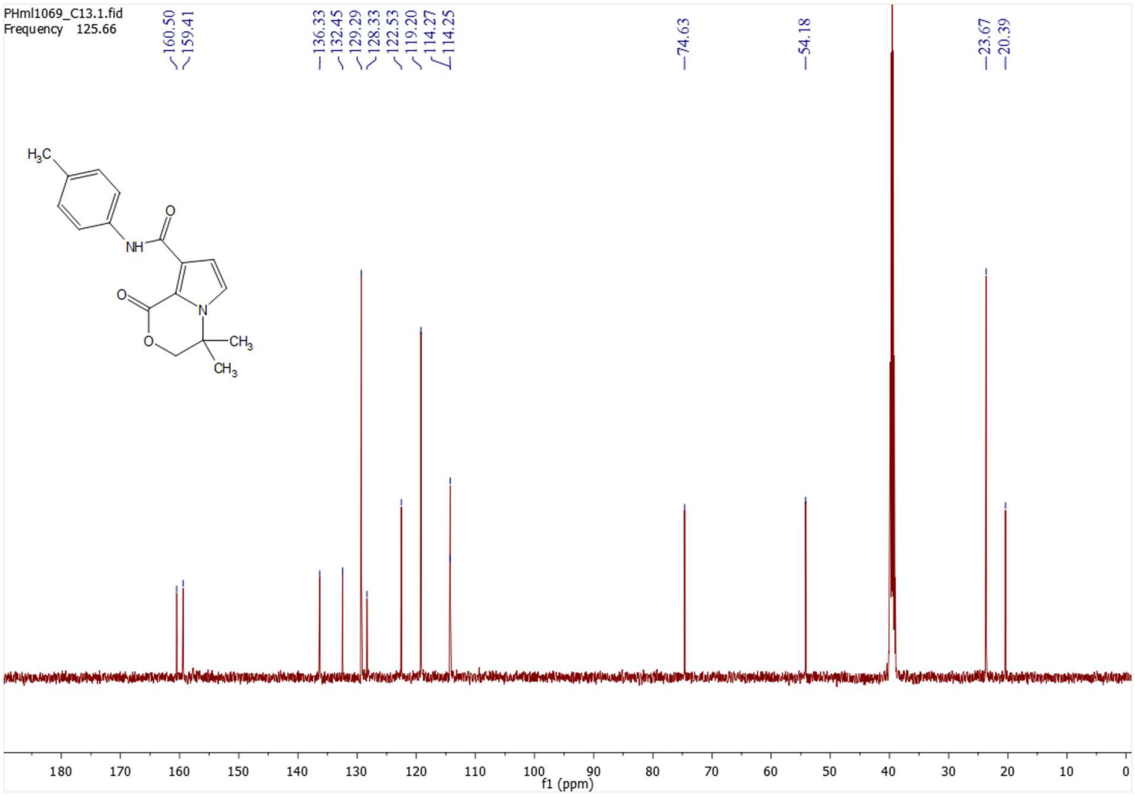

Figure S86. ^{13}C, NMR spectrum of 4,4-dimethyl-*N*-(4-methylphenyl)-1-oxo-3,4-dihydro-1*H*-pyrrolo[2,1-*c*][1,4]oxazine-8-carboxamide (**11f**) in DMSO-d_6

Chemical characterization of N-(4-methylphenyl)-1-oxo-3-phenyl-3,4-dihydro-1H-pyrrolo[2,1-c][1,4]oxazine-8-carboxamide (**11g**). Beige solid, mp 222-223°C; yield 70%. ^{1}H-NMR (400 MHz, DMSO-d_6): δ 2.28 (s, 3H, CH_3), 4.55 (dd, $^{2}J_{HH}$ = 13.6, $^{3}J_{HH}$ = 10.8 Hz, 1H, C^{4}HH), 4.70 (dd, $^{2}J_{HH}$ = 13.6, $^{3}J_{HH}$ = 3.4 Hz, 1H, C^{4}HH), 6.02 (dd, $^{3}J_{HH}$ = 11.1, $^{3}J_{HH}$ = 3.3 Hz, 1H, C^{3}H), 6.92 (d, $^{3}J_{HH}$ = 2.7 Hz, 1H, C^{7}H), 7.17 (d, $^{3}J_{HH}$ = 8.0 Hz, 2H, 2H$_{Ar}$), 7.36 (d, $^{3}J_{HH}$ = 2.6 Hz, 1H, C^{6}H), 7.44-7.51 (m, Hz, 3H, 3H$_{Ar}$), 7.57-7.59 (m, 4H, 4H$_{Ar}$), 11.71 (s, 1H, NH). ^{13}C, NMR (126 MHz, DMSO-d_6): δ = 20.40, 47.98, 78.82, 114.00, 115.17, 119.17, 125.85, 126.79, 127.53, 128.71, 129.20, 129.34, 132.50, 135.22, 136.30, 159.26, 160.80. MS: m/z 347 (M + H). Anal. Calcd. for $C_{21}H_{18}N_2O_3$ (%): C, 72.82; H, 5.24; N, 8.09. Found: C, 73.00; H, 5.21; N, 8.01.

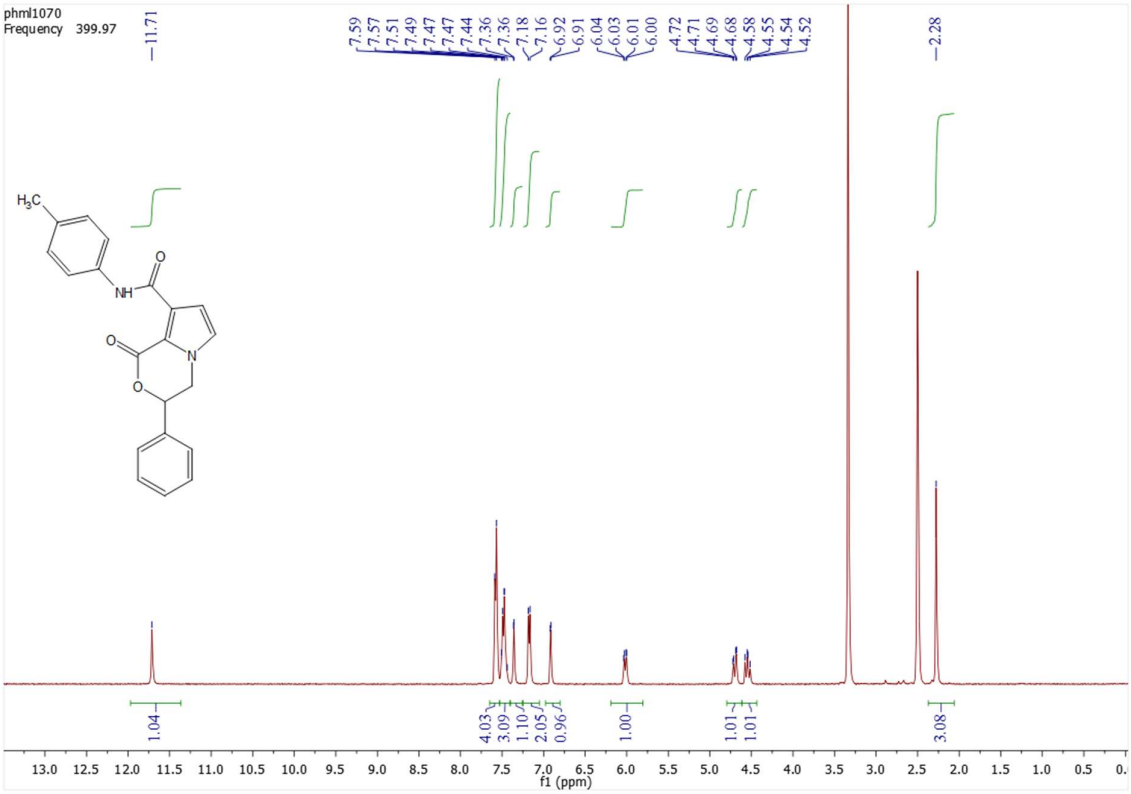

Figure S87. ^{1}H-NMR spectrum of *N*-(4-methylphenyl)-1-oxo-3-phenyl-3,4-dihydro-1*H*-pyrrolo[2,1-*c*][1,4]oxazine-8-carboxamide (**11g**) in DMSO-d_6

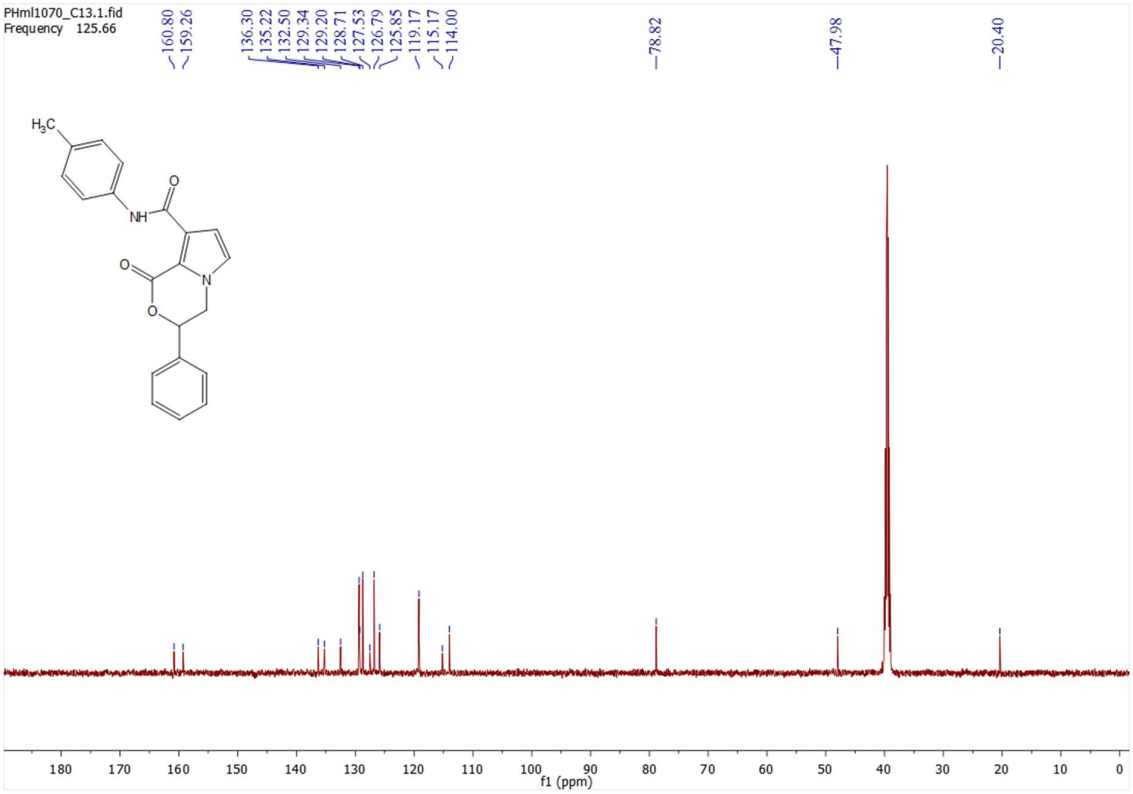

Figure S88. ^{13}C, NMR spectrum of *N*-(4-methylphenyl)-1-oxo-3-phenyl-3,4-dihydro-1*H*-pyrrolo[2,1-*c*][1,4]oxazine-8-carboxamide (**11g**) in DMSO-d_6

Chemical characterization of (5aS,9aS)-N-(3-methoxyphenyl)-4-oxo-5a,6,7,8,9,9a-hexahydro-4H-pyrrolo[2,1-c][1,4]benzoxazine-3-carboxamide (**11h**). White solid, mp 218-219°C; yield 81%. ^{1}H-NMR (302 MHz, DMSO-d_6): δ 1.42-1.54 (m, 3H), 1.62–1.74 (m, 1H), 1.77-1.89 (m, 2H), 2.07-2.18 (m, 1H), 2.61-2.77 (m, 1H), 3.75 (s, 3H, CH_3), 4.09-4.18 (m, 1H), 4.52 (td, $^3J_{HH}$ = 11.1, $^3J_{HH}$ = 4.3 Hz, 1H, C^{5a}H), 6.68 (d, $^3J_{HH}$ = 7.9 Hz, 1H, 1H$_{Ar}$), 6.89 (d, $^3J_{HH}$ = 2.6 Hz, 1H, C^{2}H), 7.10 (d, $^3J_{HH}$ = 8.1 Hz, 1H, 1H$_{Ar}$), 7.26 (t, $^3J_{HH}$ = 8.1 Hz, 1H, 1H$_{Ar}$), 7.42-7.46 (m, 2H, 1H$_{Ar}$ + C^{1}H), 11.77 (s, 1H, NH). ^{13}C, NMR (151 MHz, DMSO-d_6): δ = 22.72, 22.79, 26.82, 28.99, 55.02, 55.95, 80.51, 105.07, 108.94, 111.47, 113.97, 115.98, 122.52, 127.85, 129.78, 140.01, 159.68, 159.70, 160.80. MS: m/z 341 (M + H). Anal. Calcd. for $C_{19}H_{20}N_2O_4$ (%): C, 67.05; H, 5.92; N, 8.23. Found: C, 66.88; H, 5.94; N, 8.31.

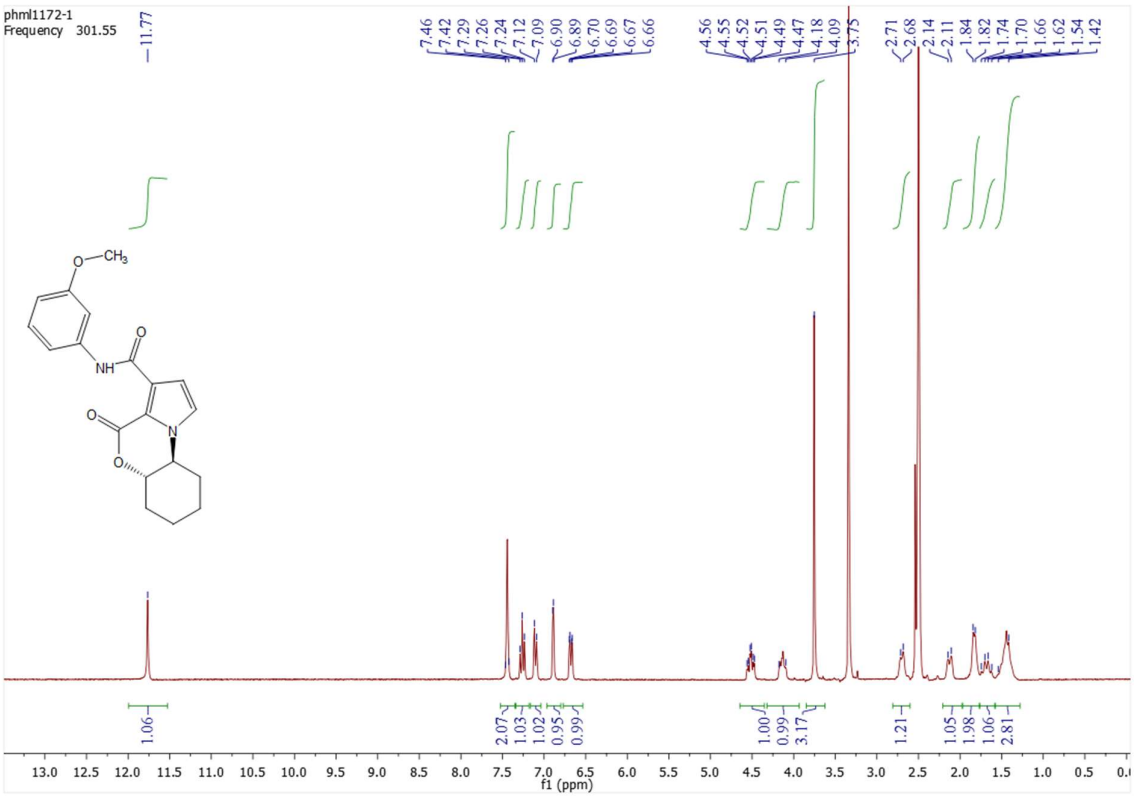

Figure S89. [1]H-NMR spectrum of (5*aS*,9*aS*)-*N*-(3-methoxyphenyl)-4-oxo-5*a*,6,7,8,9,9*a*-hexahydro-4*H*-pyrrolo[2,1-*c*][1,4]benzoxazine-3-carboxamide (**11h**) in DMSO-d_6

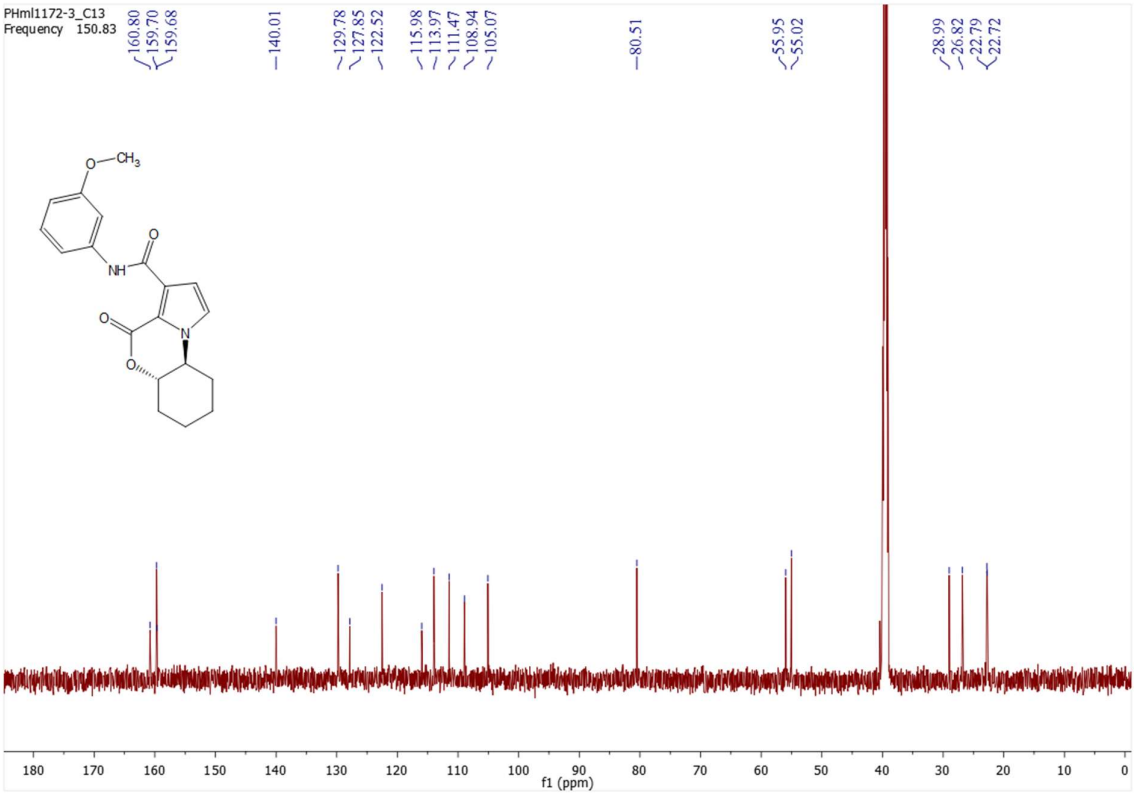

Figure S90. [13]C, NMR spectrum of (5*aS*,9*aS*)-*N*-(3-methoxyphenyl)-4-oxo-5*a*,6,7,8,9,9*a*-hexahydro-4*H*-pyrrolo[2,1-*c*][1,4]benzoxazine-3-carboxamide (**11h**) in DMSO-d_6

Chemical characterization of (4S)-4-(1-methylethyl)-1-oxo-N-[4-(trifluoromethyl)phenyl]-3,4-dihydro-1H-pyrrolo[2,1-c][1,4]oxazine-8-carboxamide (**11i**). Beige solid, mp 145-146°C; yield 79%. ^{1}H-NMR (302 MHz, DMSO-d_6): δ 0.86 (d, $^{3}J_{HH}$ = 6.8 Hz, 3H, CH_3), 0.98 (d, $^{3}J_{HH}$ = 6.7 Hz, 3H, CH_3), 2.07-2.19 (m, 1H, C<u>H</u>$(CH_3)_2$), 4.32-4.34 (m, 1H, C^{4}H), 4.72-4.82 (m, 2H, C$^{3}H_2$), 6.90 (s, 1H, C^{7}H), 7.43 (s, 1H, C^{6}H), 7.73 (d, $^{3}J_{HH}$ = 8.3 Hz, 2H, $2H_{Ar}$), 7.88 (d, $^{3}J_{HH}$ = 8.4 Hz, 2H, $2H_{Ar}$), 11.97 (s, 1H, NH). ^{13}C, NMR (126 MHz, DMSO-d_6): δ = 18.86, 18.93, 30.21, 58.23, 68.24, 113.53, 115.29, 119.16, 123.53 (q, $^{2}J_{CF}$ = 32.2 Hz, C_{Ar}-CF_3), 124.39 (q, $^{1}J_{CF}$ = 271.3 Hz CF_3), 126.35, 126.49, 126.57, 126.79, 142.40, 160.16, 160.84. ^{19}F, NMR (376 MHz, DMSO-d_6) δ -60.79. MS: m/z 367 (M + H). Anal. Calcd. for $C_{18}H_{17}F_3N_2O_3$ (%): C, 59.02; H, 4.68; N, 7.65. Found: C, 58.81; H, 4.72; N, 7.57.

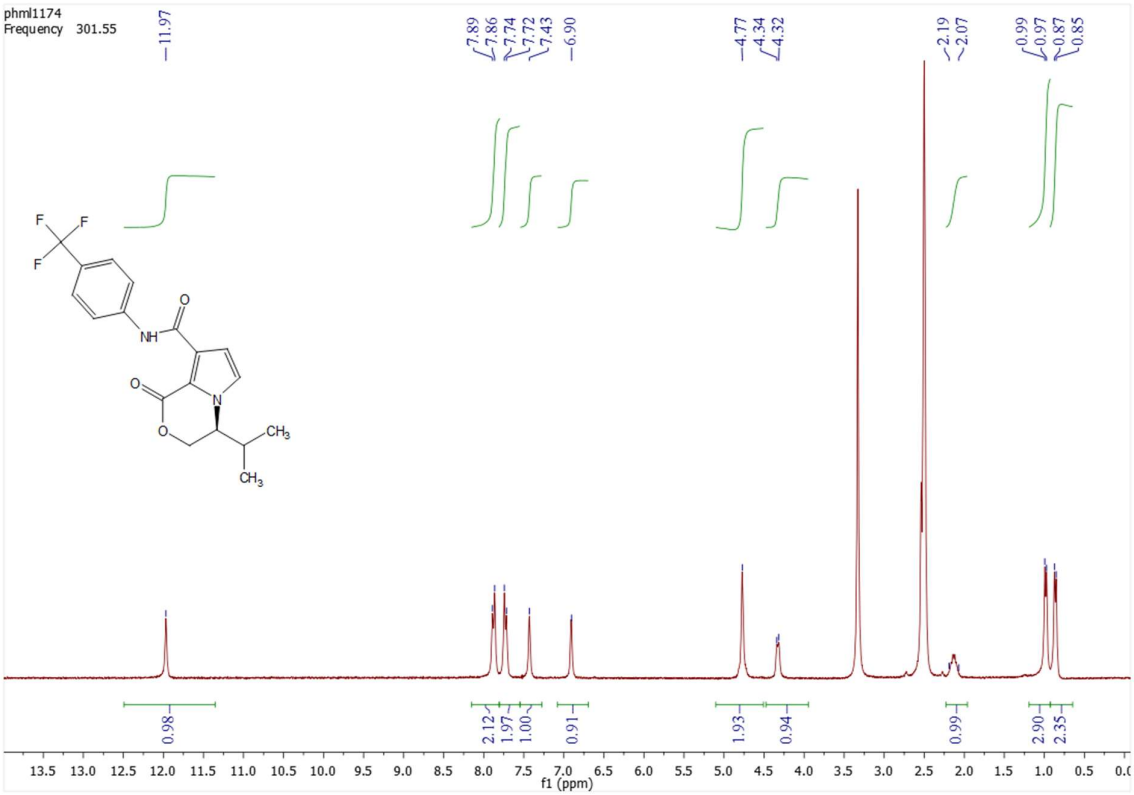

Figure S91. ^{1}H-NMR spectrum of (4*S*)-4-(1-methylethyl)-1-oxo-*N*-[4-(trifluoromethyl)phenyl]-3,4-dihydro-1*H*-pyrrolo[2,1-*c*][1,4]oxazine-8-carboxamide (**11i**) in DMSO-d_6

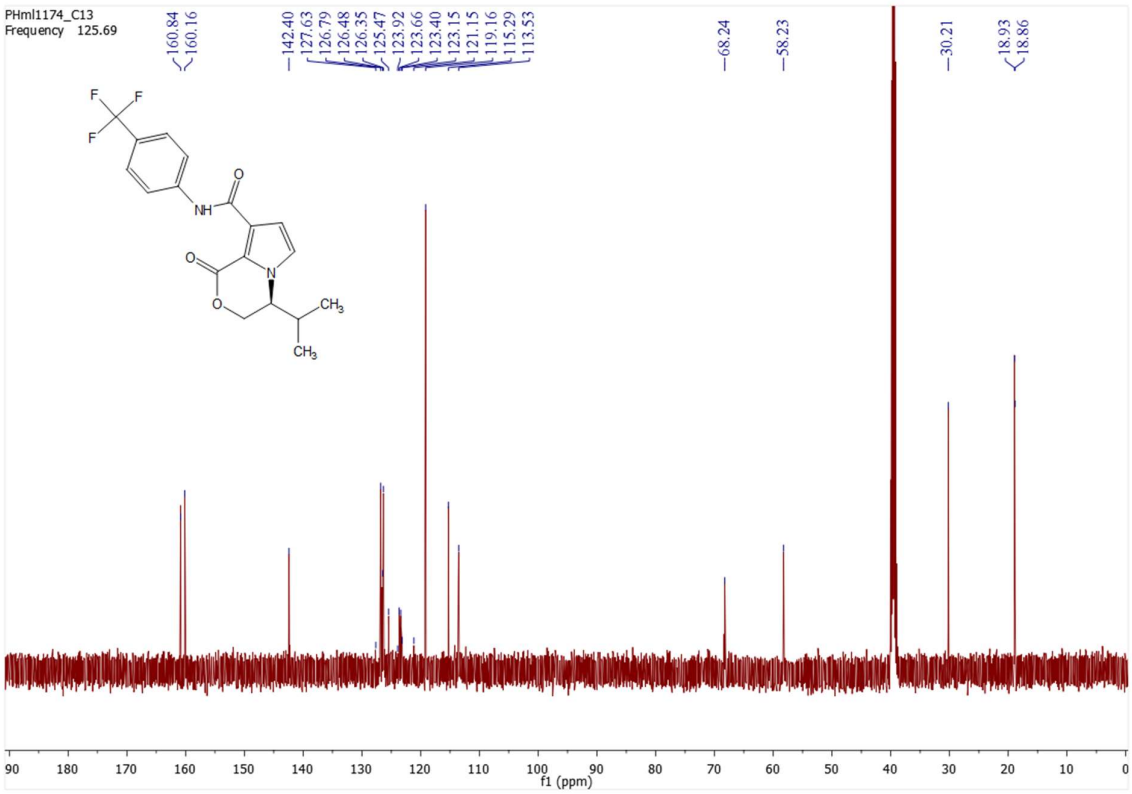

Figure S92. ^{13}C, NMR spectrum of (4*S*)-4-(1-methylethyl)-1-oxo-*N*-[4-(trifluoromethyl)phenyl]-3,4-dihydro-1*H*-pyrrolo[2,1-*c*][1,4]oxazine-8-carboxamide (**11i**) in DMSO-d_6

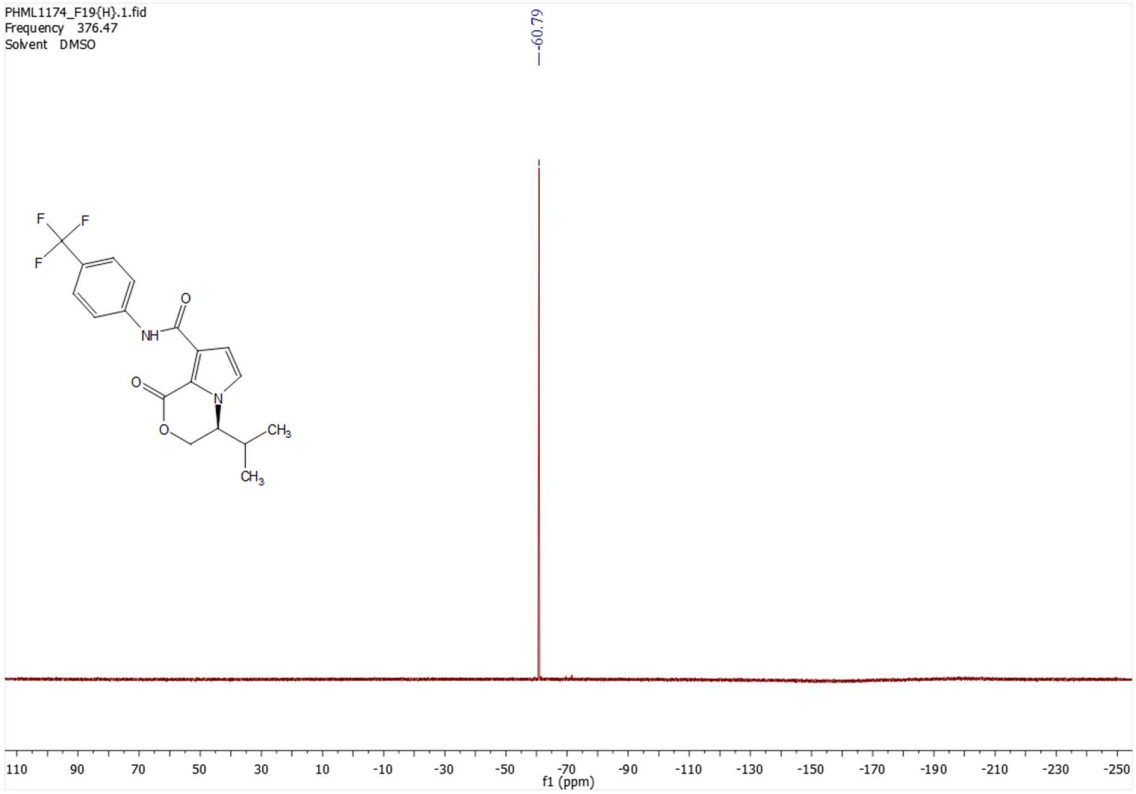

Figure S93. ^{19}F, NMR spectrum of (4*S*)-4-(1-methylethyl)-1-oxo-*N*-[4-(trifluoromethyl)phenyl]-3,4-dihydro-1*H*-pyrrolo[2,1-*c*][1,4]oxazine-8-carboxamide (**11i**) in DMSO-d_6

Chemical characterization of N-(1-methylethyl)-4-oxo-4H-pyrrolo[2,1-c][1,4]benzoxazine-3-carboxamide (**12a**). Beige solid, mp 206-207°C; yield 91%. ^{1}H-NMR (302 MHz, DMSO-d_6): δ 1.19 (s, 3H, CH_3), 1.21 (s, 3H, CH_3), 4.00–4.11 (m, 1H, C<u>H</u>$(CH_3)_2$), 7.19 (d, $^{3}J_{HH}$ = 2.9 Hz, 1H, C^{2}H), 7.41-7.44 (m, 2H, 2 H_{Ar}), 7.49-7.54 (m, 1H, 1H_{Ar}), 8.19 (dd, $^{3}J_{HH}$ = 6.2, $^{3}J_{HH}$ = 3.6 Hz, 1H, 1H_{Ar}), 8.38 (d, $^{3}J_{HH}$ = 2.9 Hz, 1H, C^{1}H), 9.46 (d, $^{3}J_{HH}$ = 7.1 Hz, 1H, NH). ^{13}C, NMR (126 MHz, $CDCl_3$): δ = 22.64, 41.78, 113.14, 114.79, 118.18, 118.51, 122.11, 125.63, 127.28, 129.64, 142.57, 155.78, 160.19. MS: m/z 271 (M + H). Anal. Calcd. for $C_{15}H_{14}N_2O_3$ (%): C, 66.66; H, 5.22; N, 10.36. Found: C, 66.47; H, 5.25; N, 10.45.

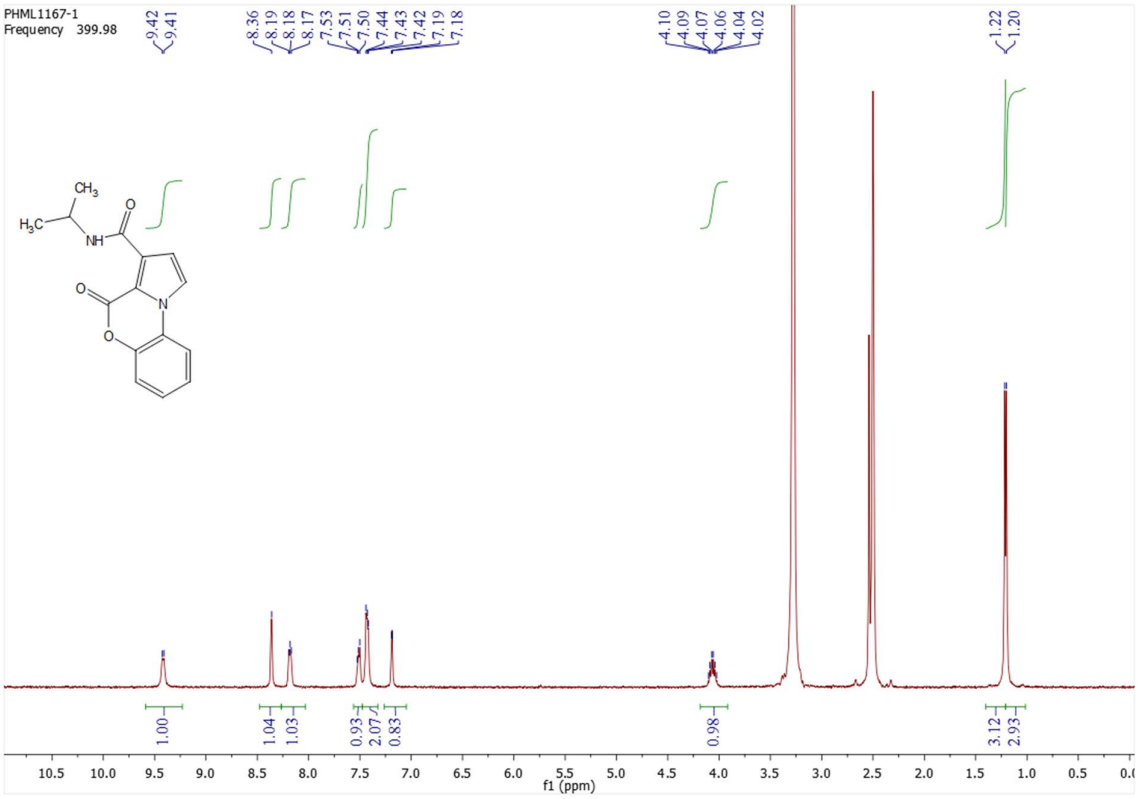

Figure S94. ^{1}H-NMR spectrum of *N*-(1-methylethyl)-4-oxo-4*H*-pyrrolo[2,1-*c*][1,4]benzoxazine-3-carboxamide (**12a**) in DMSO-d_6

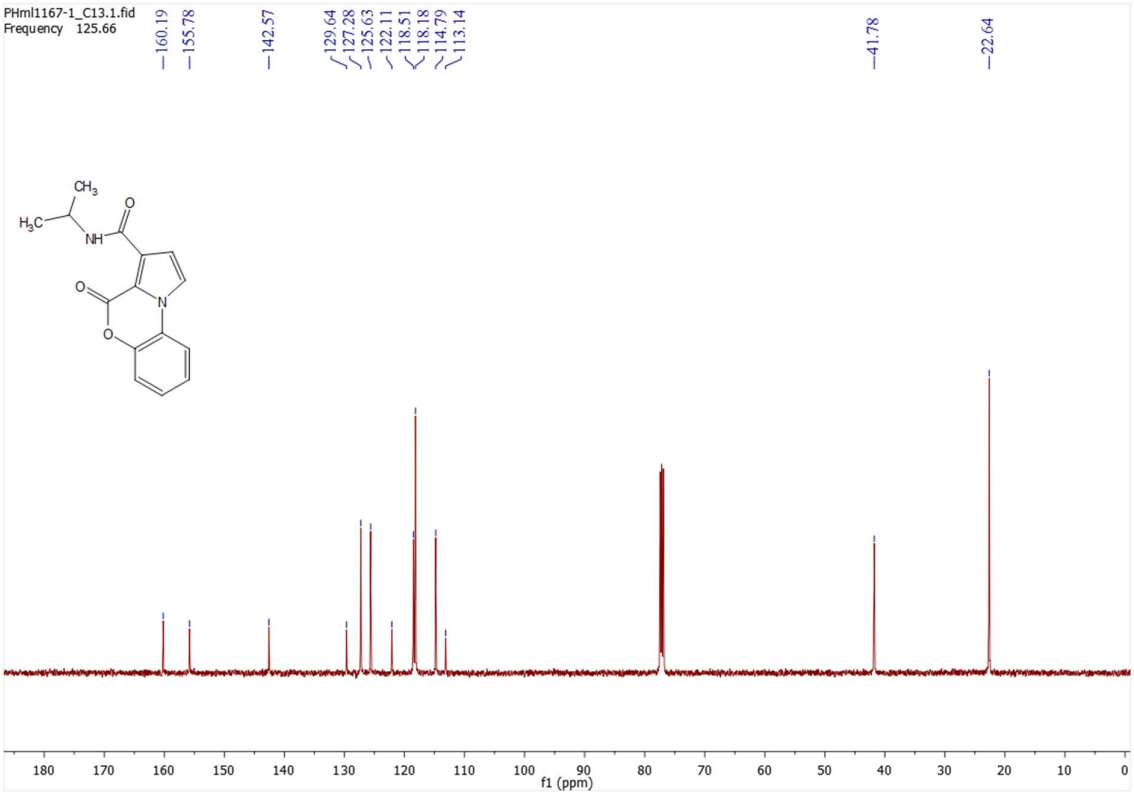

Figure S95. ^{13}C, NMR spectrum of *N*-(1-methylethyl)-4-oxo-4*H*-pyrrolo[2,1-*c*][1,4]benzoxazine-3-carboxamide (**12a**) in $CDCl_3$

Chemical characterization of 6-bromo-N-(3-methoxyphenyl)-4-oxo-4H-pyrrolo[2,1-c][1,4]benzoxazine-3-carboxamide (**12b**). Beige solid, mp 231-232°C; yield 94%. ^{1}H-NMR (400 MHz, DMSO-d_6): δ 3.79 (s, 3H, CH_3), 6.72 (d, $^3J_{HH}$ = 8.2 Hz, 1H, $1H_{Ar}$), 7.20-7.44 (m, 5H, $4H_{Ar}$ + C^2H), 7.75 (d, $^3J_{HH}$ = 8.0 Hz, 1H), 8.23 (d, $^3J_{HH}$ = 8.2 Hz, 1H, $1H_{Ar}$), 8.43 (d, $^3J_{HH}$ = 2.9 Hz, 1H, C^1H), 11.33 (s, 1H, NH). ^{13}C, NMR (101 MHz, CF_3COOD): δ = 57.89, 114.37, 116.70, 117.10, 120.85, 124.01, 124.65, 126.42, 129.81, 132.66, 135.31, 138.22, 142.23, 161.20. MS: m/z 412, 414 (M + H). Anal. Calcd. for $C_{19}H_{13}BrN_2O_4$ (%): C, 55.23; H, 3.17; N, 6.78. Found: C, 55.06; H, 3.15; N, 6.86.

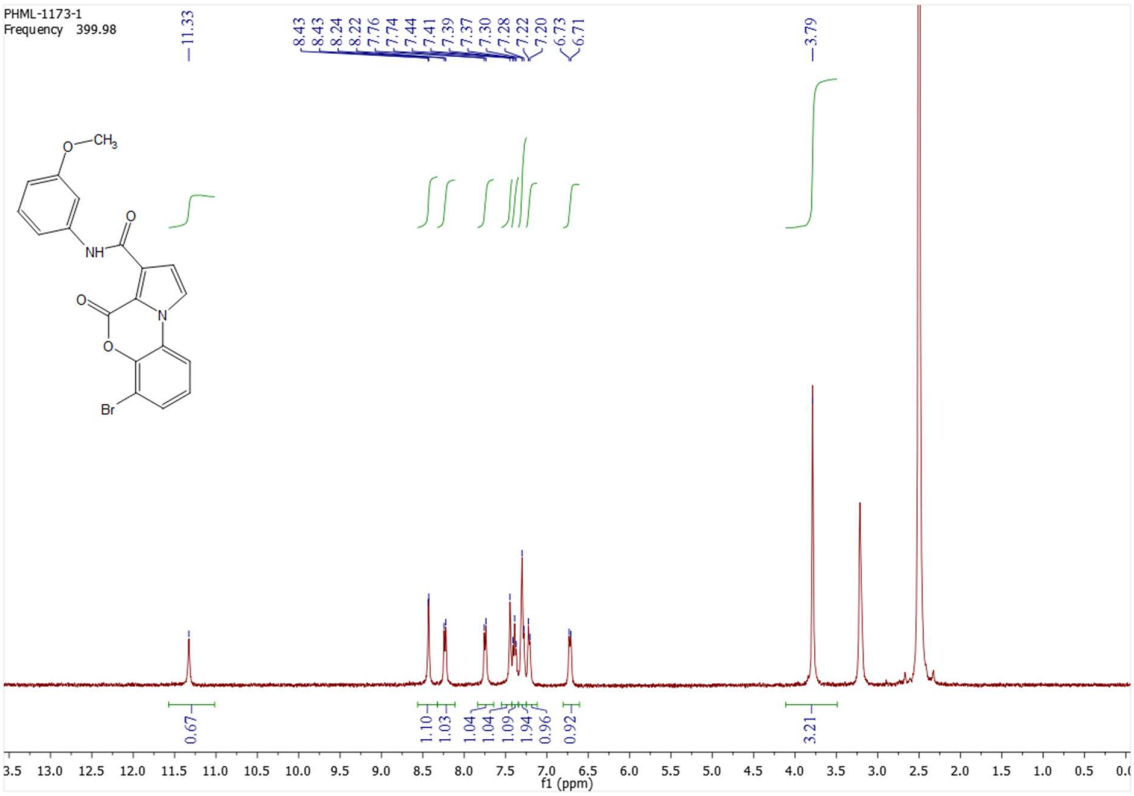

Figure S96. [1]H-NMR spectrum of 6-bromo-*N*-(3-methoxyphenyl)-4-oxo-4*H*-pyrrolo[2,1-*c*][1,4]benzoxazine-3-carboxamide (**12b**) in DMSO-d_6

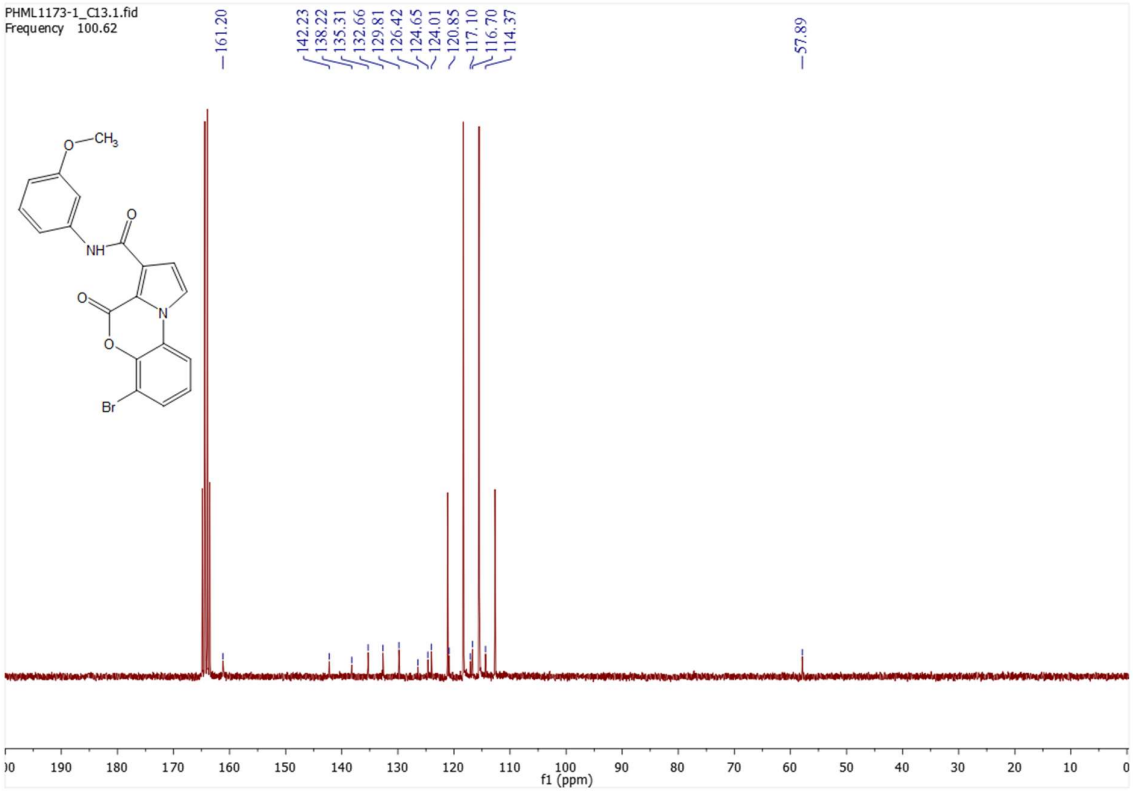

Figure S97. [13]C, NMR spectrum of 6-bromo-*N*-(3-methoxyphenyl)-4-oxo-4*H*-pyrrolo[2,1-*c*][1,4]benzoxazine-3-carboxamide (**12b**) in CF_3COOD

Chemical characterization of 8-tert-butyl-4-oxo-N-[4-(trifluoromethyl)phenyl]-4H-pyrrolo[2,1-c][1,4]benzoxazine-3-carboxamide (**12c**). White solid, mp 242-243°C; yield 90%. ^{1}H-NMR (302 MHz, DMSO-d_6): δ 1.37 (s, 9H), 7.30 (d, $^{3}J_{HH}$ = 2.9 Hz, 1H, C^{2}H), 7.47 (s, 2H, 2H$_{Ar}$), 7.75 (d, $^{3}J_{HH}$ = 8.4 Hz, 2H, 2H$_{Ar}$), 7.91 (d, $^{3}J_{HH}$ = 8.4 Hz, 2H, 2H$_{Ar}$), 8.16 (s, 1H, 1H$_{Ar}$), 8.65 (d, $^{3}J_{HH}$ = 3.0 Hz, 1H, C^{1}H), 11.89 (s, 1H, NH). ^{13}C, NMR (126 MHz, $CDCl_3$): δ = 31.43, 35.14, 111.48, 113.36, 117.92, 118.48, 118.90, 119.73, 121.28, 124.37 (q, $^{1}J_{CF}$ = 271.4 Hz, CF_3), 125.25, 125.66 (q, $^{2}J_{CF}$ = 32.5 Hz, C$_{Ar}$), 126.23 (q, $^{3}J_{CF}$ = 3.3 Hz, C$_{Ar}$), 128.91, 140.39, 141.89, 149.89, 156.74, 159.46. ^{19}F, NMR (376 MHz, $CDCl_3$) δ = -62.48. MS: m/z 427 (M - H). Anal. Calcd. for $C_{23}H_{19}F_3N_2O_3$ (%): C, 64.48; H, 4.47; N, 6.54. Found: C, 64.29; H, 4.49; N, 6.48.

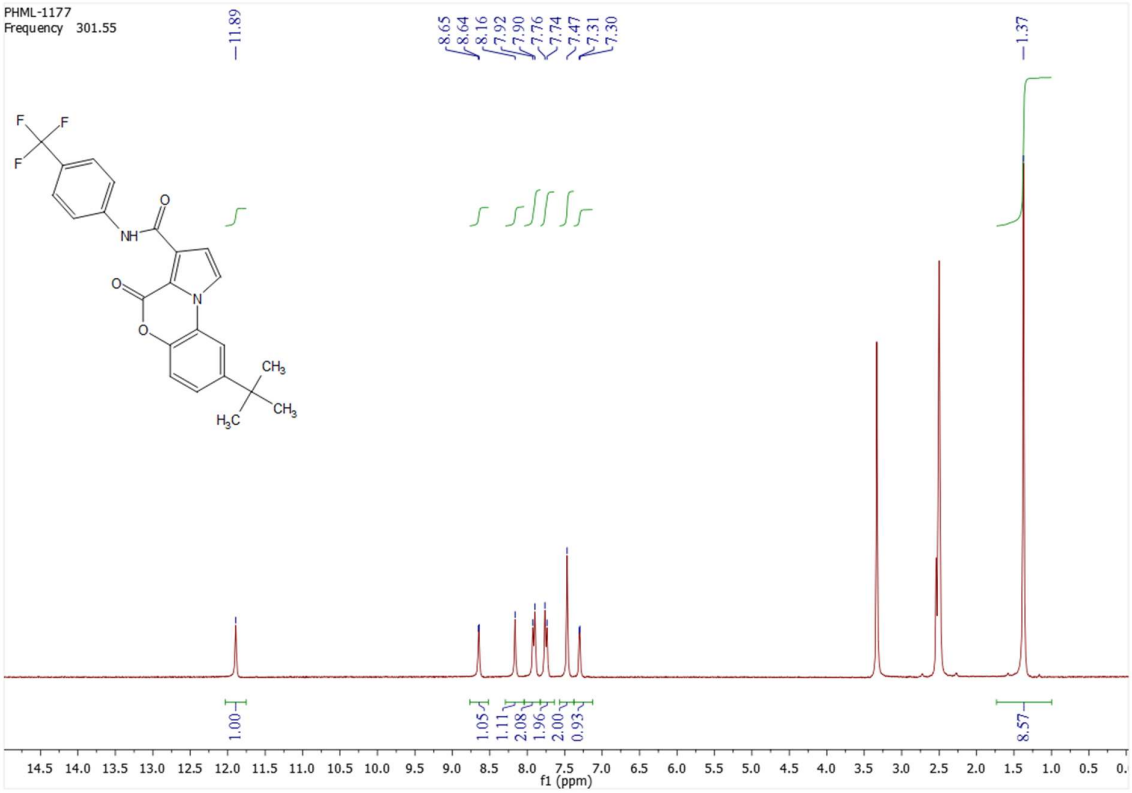

Figure S98. ^{1}H-NMR spectrum of 8-*tert*-butyl-4-oxo-*N*-[4-(trifluoromethyl)phenyl]-4*H*-pyrrolo[2,1-*c*][1,4]benzoxazine-3-carboxamide (**12c**) in DMSO-d_6

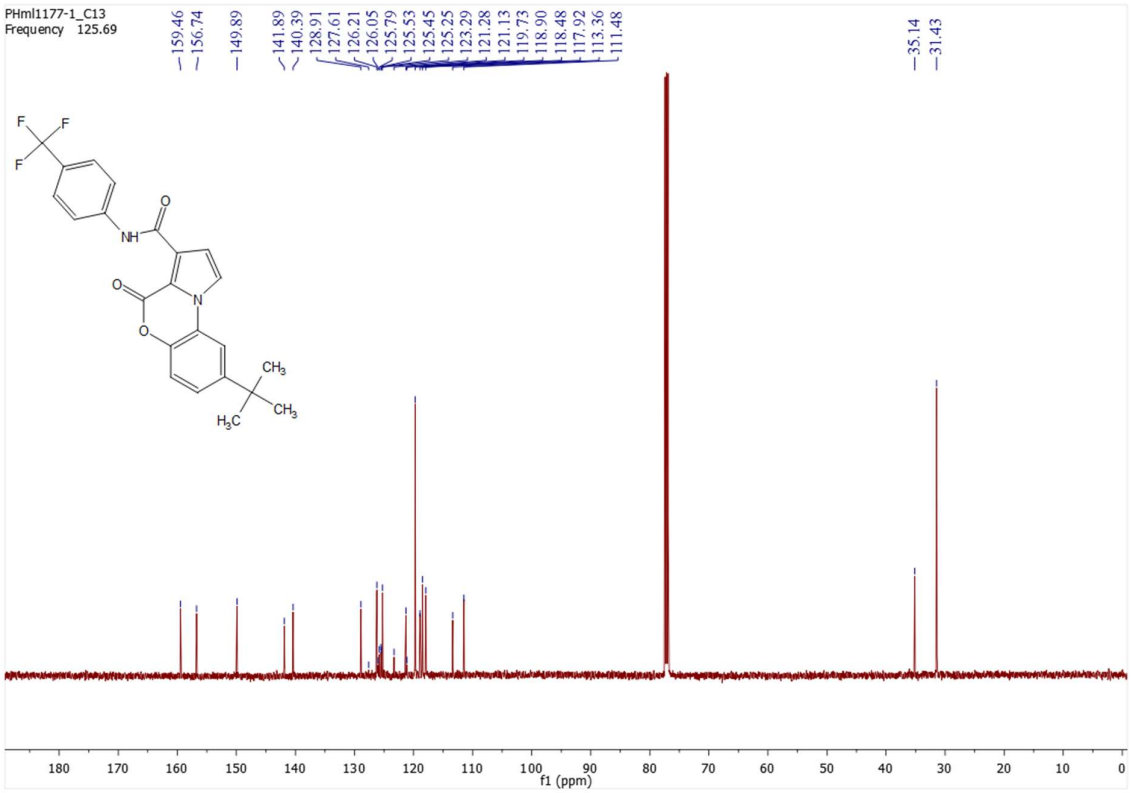

Figure S99. ^{13}C, NMR spectrum of 8-*tert*-butyl-4-oxo-*N*-[4-(trifluoromethyl)phenyl]-4*H*-pyrrolo[2,1-*c*][1,4]benzoxazine-3-carboxamide (**12c**) in $CDCl_3$

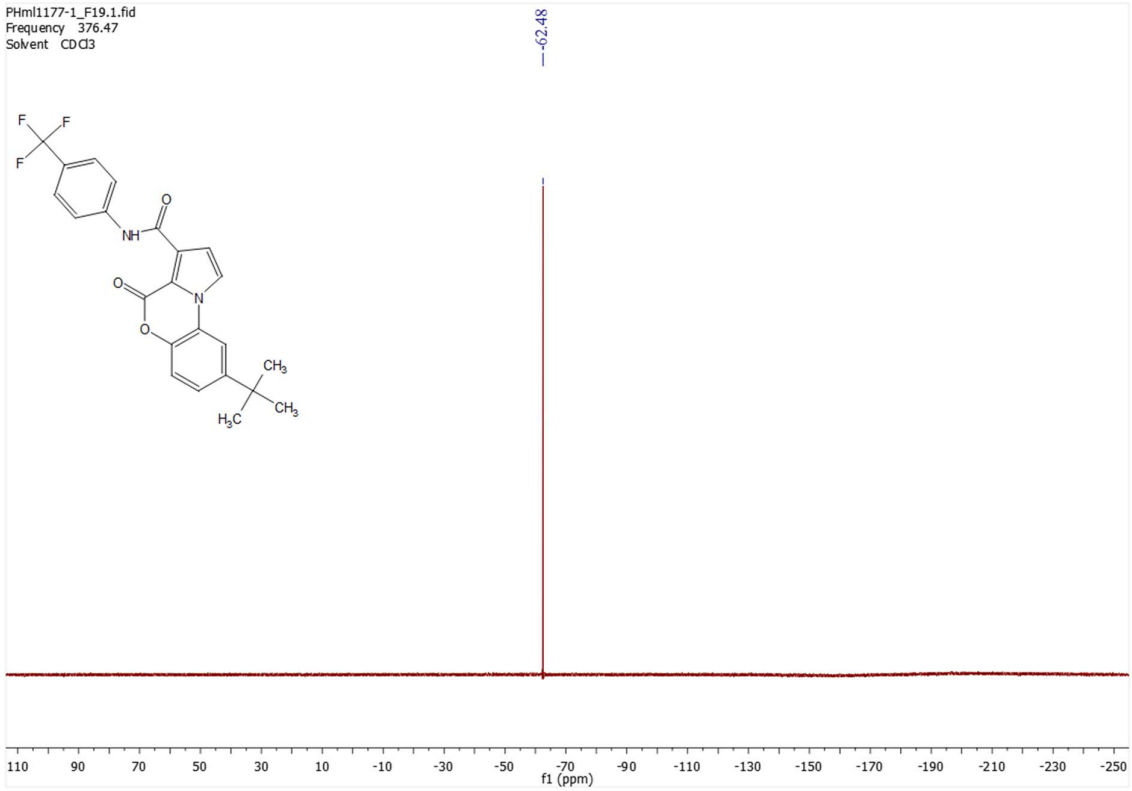

Figure S100. ^{19}F, NMR spectrum of 8-*tert*-butyl-4-oxo-*N*-[4-(trifluoromethyl)phenyl]-4*H*-pyrrolo[2,1-*c*][1,4]benzoxazine-3-carboxamide (**12c**) in $CDCl_3$

Chemical characterization of N-(4-chlorophenyl)-7-fluoro-4-oxo-4H-pyrrolo[2,1-c][1,4]benzoxazine-3-carboxamide (**12d**). Beige solid, mp >250°C; yield 89%. ^{1}H-NMR (400 MHz, DMSO-d_6): δ 7.26 (s, 1H, C^{2}H), 7.35-7.39 (m, 1H, 1H$_{Ar}$), 7.44 (d, $^{3}J_{HH}$ = 8.3 Hz, 2H, 2H$_{Ar}$), 7.59 (d, $^{3}J_{HH}$ = 8.9 Hz, 1H, 1H$_{Ar}$), 7.73 (d, $^{3}J_{HH}$ = 8.4 Hz, 2H, 2H$_{Ar}$), 8.27-8.30 (m, 1H, 1H$_{Ar}$), 8.41 (s, 1H, C^{1}H), 11.45 (s, 1H, NH). ^{19}F, NMR (376 MHz, DMSO-d_6) δ = -113.52. MS: m/z 355 (M - H). Anal. Calcd. for $C_{18}H_{10}ClFN_2O_3$ (%): C, 60.60; H, 2.83; N, 7.85. Found: C, 60.40; H, 2.80; N, 7.93.

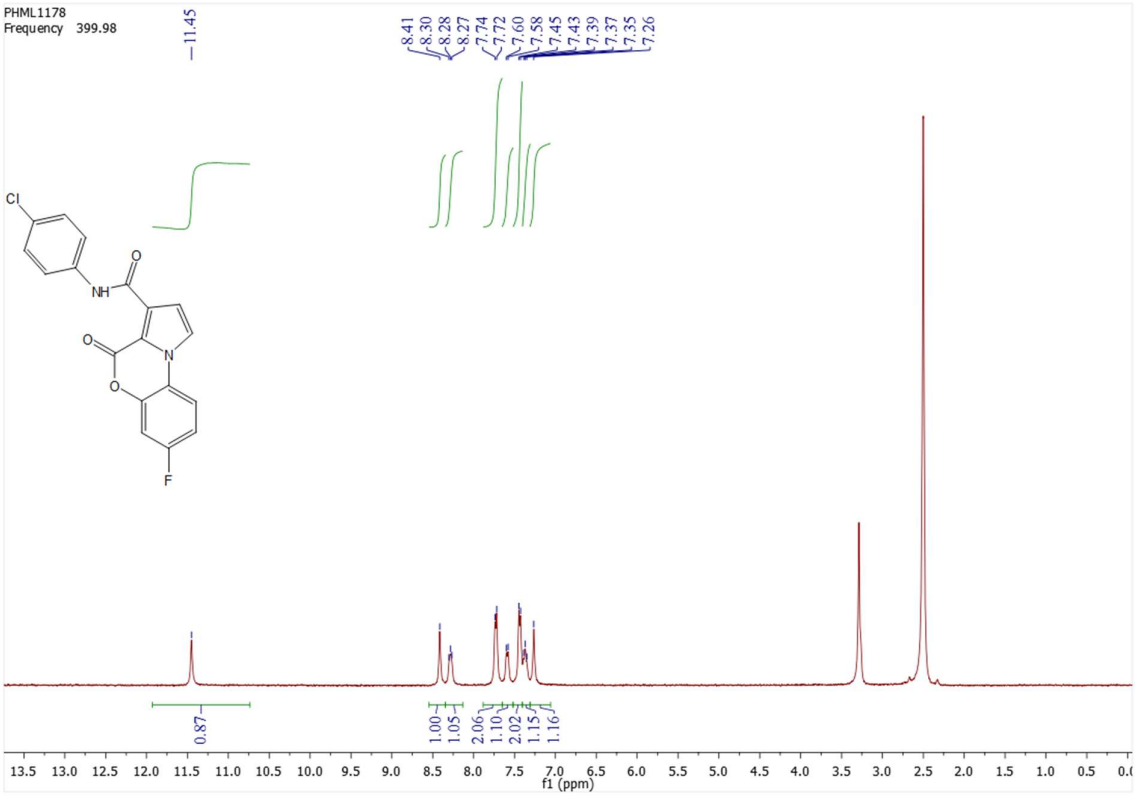

Figure S101. ^{1}H-NMR spectrum of *N*-(4-chlorophenyl)-7-fluoro-4-oxo-4*H*-pyrrolo[2,1-*c*][1,4]benzoxazine-3-carboxamide (**12d**) in DMSO-d_6

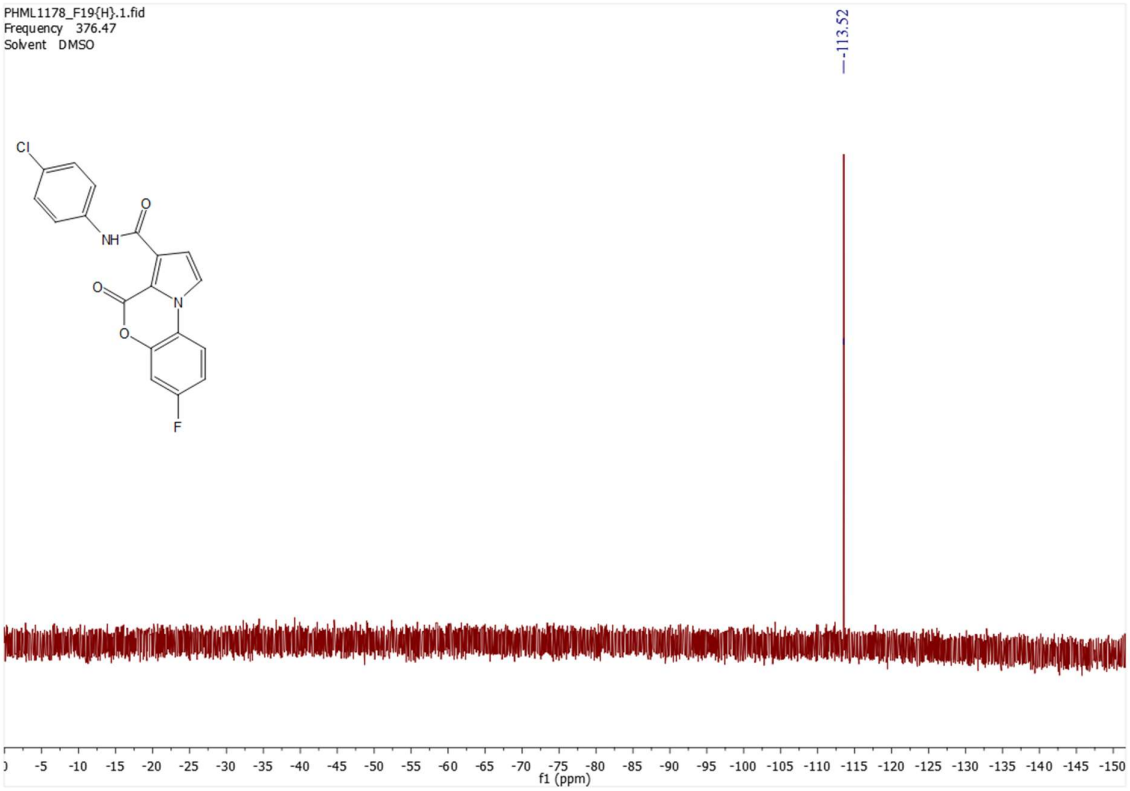

Figure S102. ^{19}F, NMR spectrum of *N*-(4-chlorophenyl)-7-fluoro-4-oxo-4*H*-pyrrolo[2,1-*c*][1,4]benzoxazine-3-carboxamide (**12d**) in DMSO-d_6

Synthesis and spectra characteristics of compounds 13a,b

General procedure for the synthesis of N-(4,4-dimethyl-1-oxo-3,4-dihydro-1H-pyrrolo[2,1-c][1,4]oxazin-8-yl)acetamide ***13a*** *and N-[(4S)-1-oxo-4-(propan-2-yl)-3,4-dihydro-1H-pyrrolo[2,1-c][1,4]oxazin-8-yl]acetamide* ***13b***. To a solution of (1.02 mmol) 8-amino-4,4-dimethyl-3,4-dihydro-1*H*-pyrrolo[2,1-*c*][1,4]oxazin-1-one **8b** or (4*S*)-8-amino-4-(propan-2-yl)-3,4-dihydro-1*H*-pyrrolo[2,1-*c*][1,4]oxazin-1-one **8c** in 5 cm^3 acetonitrile, 0.10 g acetic anhydride (1.02 mmol) was added. The resulting mixture was stirred at 35°C for 3 h. After the reaction was completed, the obtained mixture was evaporated under reduced pressure. The formed precipitate washed with hexane (2 × 4 cm^3), MTBE (1 × 1 cm^3) and dried under reduced pressure.

Chemical characterization of N-(4,4-dimethyl-1-oxo-3,4-dihydro-1H-pyrrolo[2,1-c][1,4]oxazin-8-yl)acetamide (**13a**). Beige solid, mp 149-150°C; yield 86%. ^{1}H-NMR (400 MHz, $CDCl_3$): δ 1.51 (s, 6H, C^4(CH_3)$_2$), 2.19 (s, 3H, CH_3), 4.24 (s, 2H, C^3H_2), 6.84 (d, $^3J_{HH}$ = 2.9 Hz, 1H, C^{7}H), 7.02 (d, $^3J_{HH}$ = 2.9 Hz, 1H, C^{6}H), 9.02 (s, 1H, NH). ^{13}C, NMR (126 MHz, $CDCl_3$): δ = 24.24, 24.39, 53.60, 75.79, 103.13, 104.67, 120.77, 134.14, 159.99, 168.05. MS: m/z 223 (M + H). Anal. Calcd. for $C_{11}H_{14}N_2O_3$ (%): C, 59.45; H, 6.35; N, 12.60. Found: C, 59.64; H, 6.38; N, 12.54.

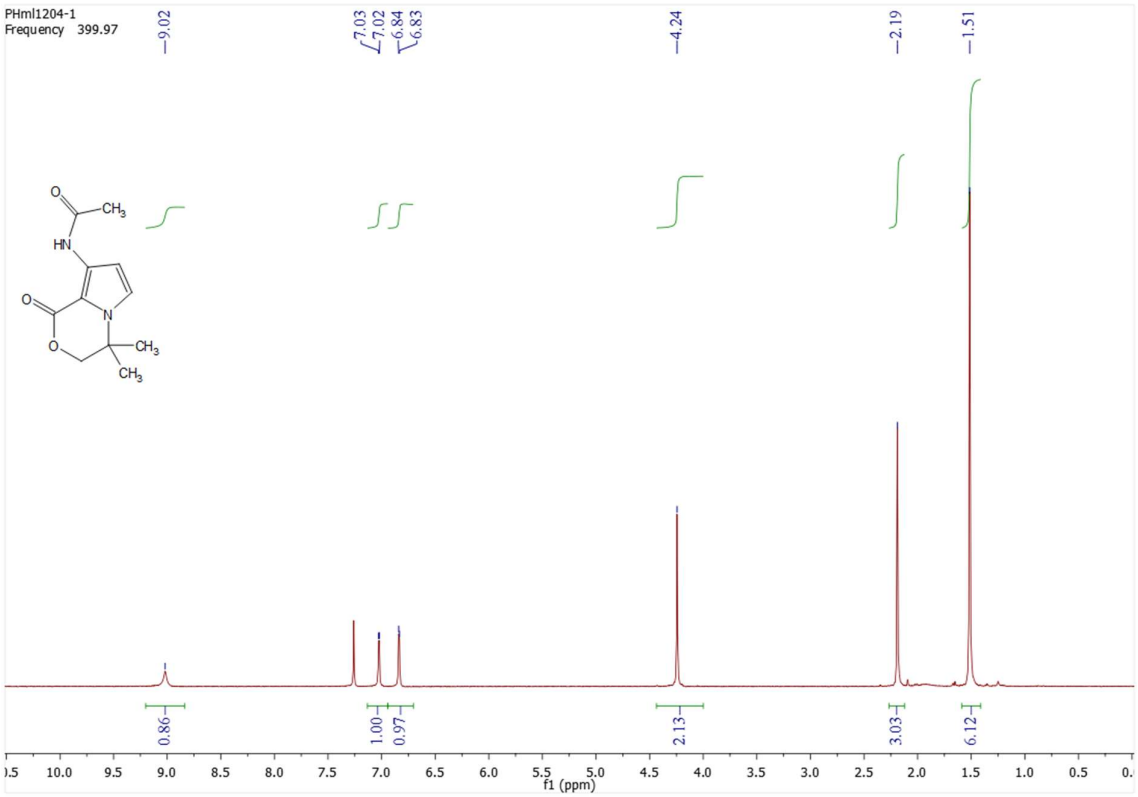

Figure S103. ^{1}H-NMR spectrum of *N*-(4,4-dimethyl-1-oxo-3,4-dihydro-1*H*-pyrrolo[2,1-*c*][1,4]oxazin-8-yl)acetamide (**13a**) in $CDCl_3$

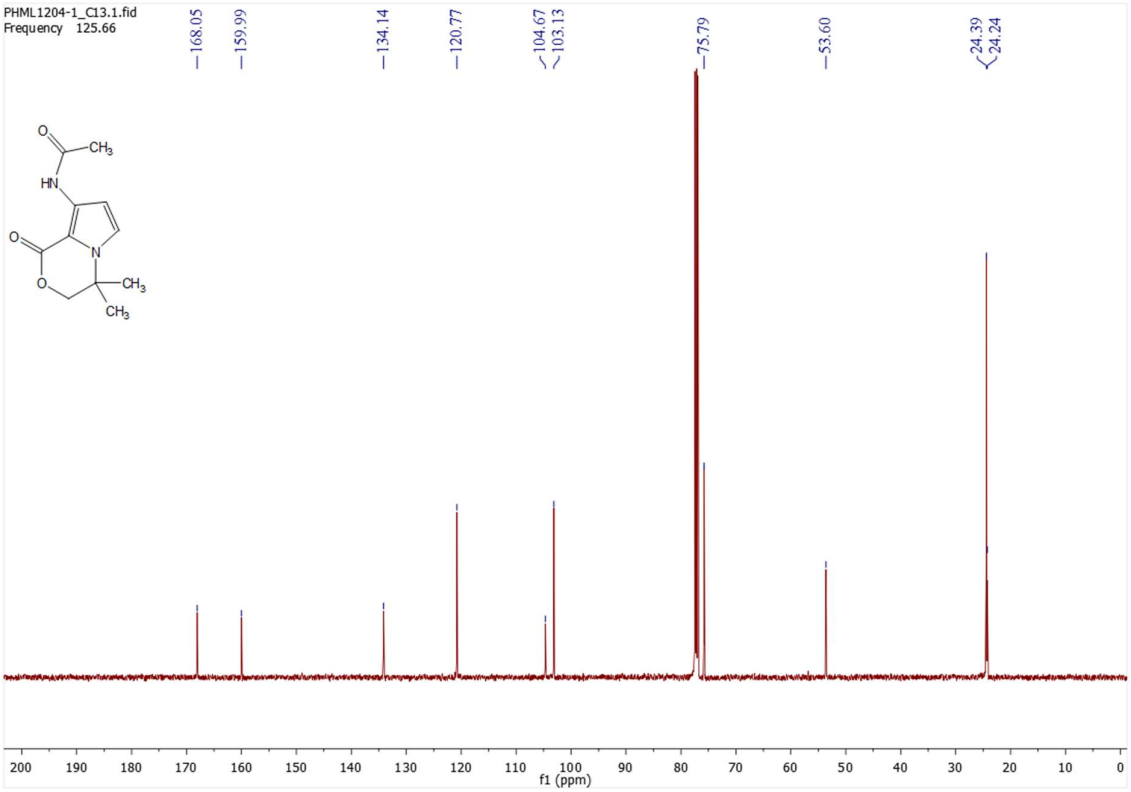

Figure S104. ^{13}C, NMR spectrum of *N*-(4,4-dimethyl-1-oxo-3,4-dihydro-1*H*-pyrrolo[2,1-*c*][1,4]oxazin-8-yl)acetamide (**13a**) in $CDCl_3$

Chemical characterization of N-[(4S)-1-oxo-4-(propan-2-yl)-3,4-dihydro-1H-pyrrolo[2,1-c][1,4]oxazin-8-yl]acetamide (**13b**). Yellow solid, mp 114-115°C; yield 82%. ^{1}H-NMR (400 MHz, $CDCl_3$): δ 0.93 (d, $^{3}J_{HH}$ = 6.8 Hz, 3H, CHC<u>H</u>$_3$), 1.03 (d, $^{3}J_{HH}$ = 6.8 Hz, 3H, CHC<u>H</u>$_3$), 2.15-2.23 (m, 4H, CH_3 + C<u>H</u>CH_3), 3.79 (dt, $^{3}J_{HH}$ = 7.4, $^{3}J_{HH}$ = 3.0 Hz, 1H, C^{4}H), 4.53 (dd, $^{2}J_{HH}$ = 11.9, $^{3}J_{HH}$ = 3.4 Hz, 1H, C^{3}H), 4.59 (dd, $^{2}J_{HH}$ = 11.9, $^{3}J_{HH}$ = 2.8 Hz, 1H, C^{3}H), 6.78 (d, $^{3}J_{HH}$ = 2.8 Hz, 1H, C^{7}H), 7.01 (d, $^{3}J_{HH}$ = 2.8 Hz, 1H, C^{6}H), 8.94 (s, 1H, NH). ^{13}C, NMR (126 MHz, $CDCl_3$): δ = 19.17, 19.44, 24.27, 30.54, 59.24, 68.18, 102.43, 105.14, 124.47, 133.48, 160.19, 168.03. MS: m/z 237 (M + H). Anal. Calcd. for $C_{12}H_{16}N_2O_3$ (%): C, 61.00; H, 6.83; N, 11.86. Found: 60.83; H, 6.80; N, 11.94.

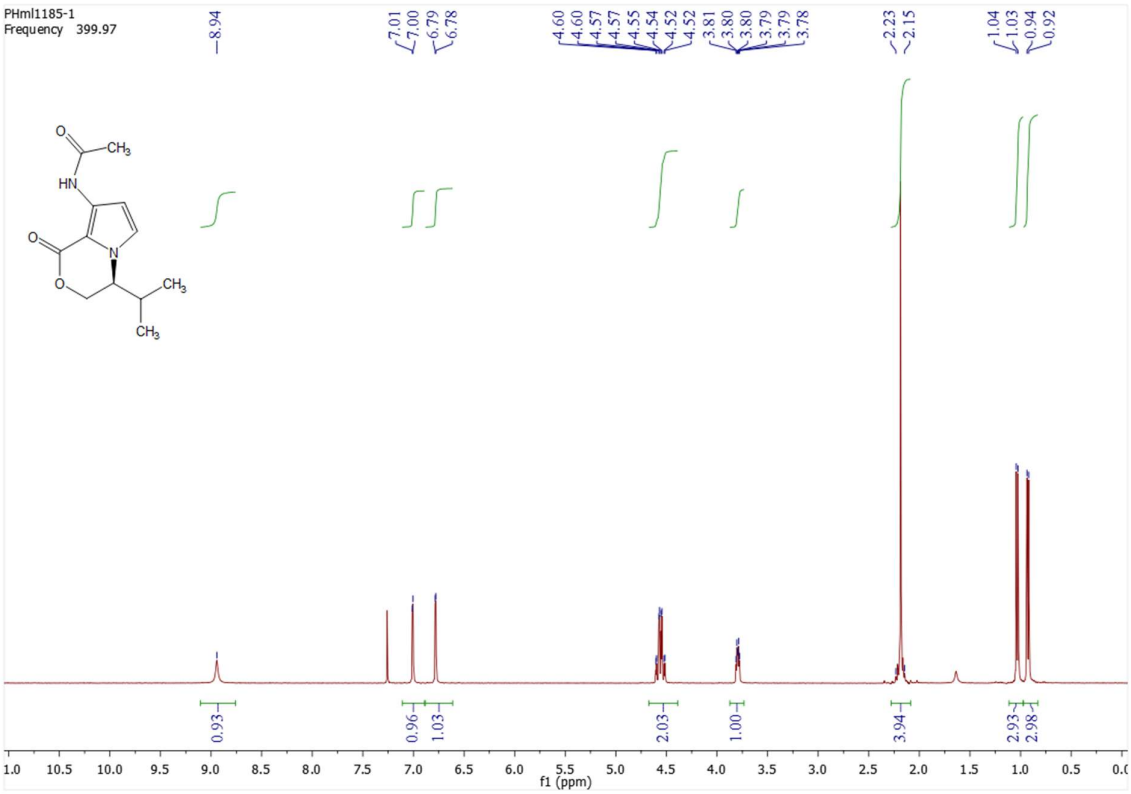

Figure S105. ^{1}H-NMR spectrum of *N*-[(4*S*)-1-oxo-4-(propan-2-yl)-3,4-dihydro-1*H*-pyrrolo[2,1-*c*][1,4]oxazin-8-yl]acetamide (**13b**) in $CDCl_3$

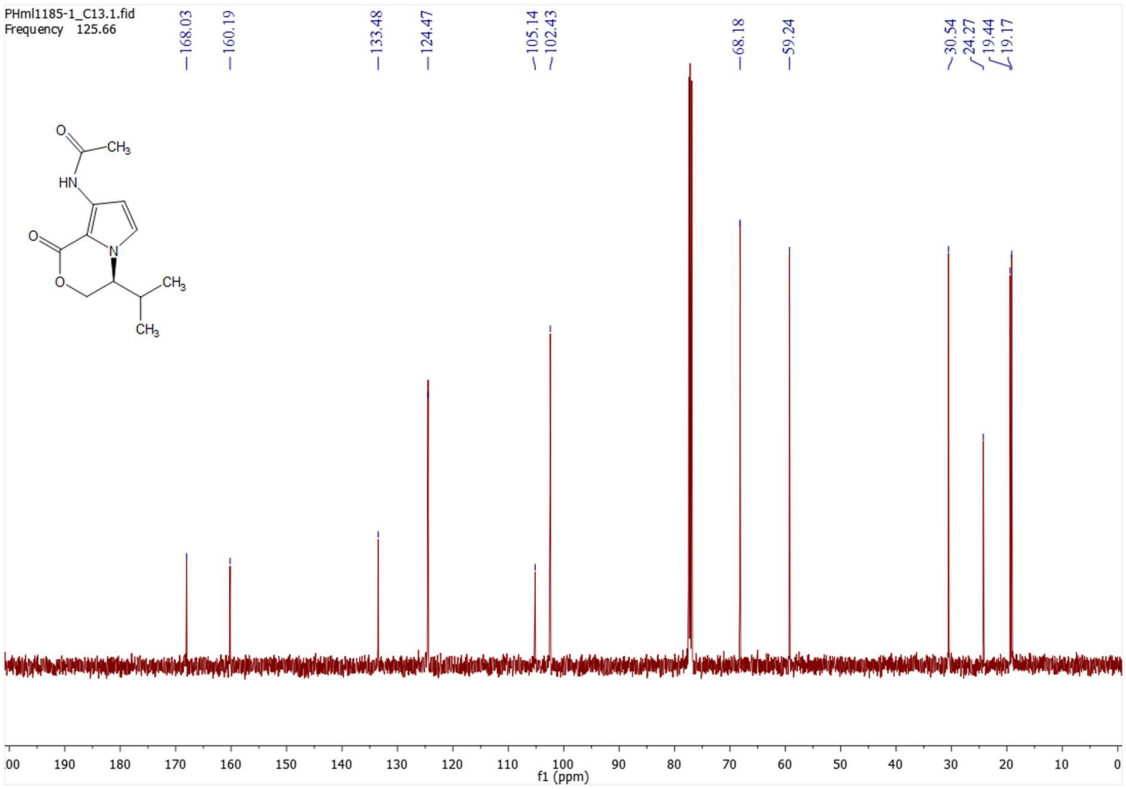

Figure S106. ^{13}C, NMR spectrum of *N*-[(4*S*)-1-oxo-4-(propan-2-yl)-3,4-dihydro-1*H*-pyrrolo[2,1-*c*][1,4]oxazin-8-yl]acetamide (**13b**) in $CDCl_3$

Synthesis and spectra characteristics of compound 14

*General procedure for the synthesis of N-(7-fluoro-4-oxo-4H-pyrrolo[2,1-c][1,4]benzoxazin-3-yl)acetamide **14**.* To a solution of (1.02 mmol) 3-amino-7-fluoro-4*H*-pyrrolo[2,1-*c*][1,4]benzoxazin-4-one **8b** in 20 cm^3 acetonitrile, 0.10 g acetic anhydride (1.02 mmol), and 0.13 g DIPEA (1.02 mmol) were added. The resulting mixture was stirred at 35°C for 8 h. After the reaction was completed, the obtained mixture was evaporated under reduced pressure. The formed precipitate washed with H_2O (2 × 2 cm^3), MTBE (1 × 1 cm^3), hexane (2 × 4 cm^3) and dried under reduced pressure.

Chemical characterization of N-(7-fluoro-4-oxo-4H-pyrrolo[2,1-c][1,4]benzoxazin-3-yl)acetamide (**14**). Beige solid, mp >250°C; yield 95%. ^{1}H-NMR (302 MHz, DMSO-d_6): δ 2.17 (s, 3H, CH_3), 7.20 (d, $^3J_{HH}$ = 2.9 Hz, 1H, C^{2}H), 7.26 (ddd, $^3J_{HH}$ = 8.7, $^3J_{HF}$ = 8.7, $^4J_{HH}$ = 2.7 Hz, 1H, 1H$_{Ar}$), 7.43 (dd, $^3J_{HF}$ = 9.3, $^4J_{HH}$ = 2.7 Hz, 1H, 1H$_{Ar}$), 8.09 (dd, $^3J_{HH}$ = 9.1, $^4J_{HF}$ = 5.3 Hz, 1H, 1H$_{Ar}$), 8.16 (d, $^3J_{HH}$ = 3.0 Hz, 1H, C^{1}H), 9.44 (s, 1H, NH). ^{13}C, NMR (76 MHz, CF_3COOD): δ = 23.88, 106.12, 108.28 (d, $^2J_{CF}$ = 27.4 Hz), 109.70, 115.88 (d, $^2J_{CF}$ = 24.0 Hz), 117.52 (d, $^3J_{CF}$ = 9.5 Hz), 120.91 (d, $^4J_{CF}$ = 3.4 Hz), 122.36, 134.00, 145.12 (d, $^3J_{CF}$ = 12.2 Hz), 160.49, 163.31 (d, $^1J_{CF}$ = 249.2 Hz), 176.47. ^{19}F, NMR (376 MHz, DMSO-d_6): δ = -115.33. MS: m/z 261 (M + H). Anal. Calcd. for $C_{13}H_9FN_2O_3$ (%): C, 60.00; H, 3.49; N, 10.77. Found: C, 59.82; H, 3.52; N, 10.86.

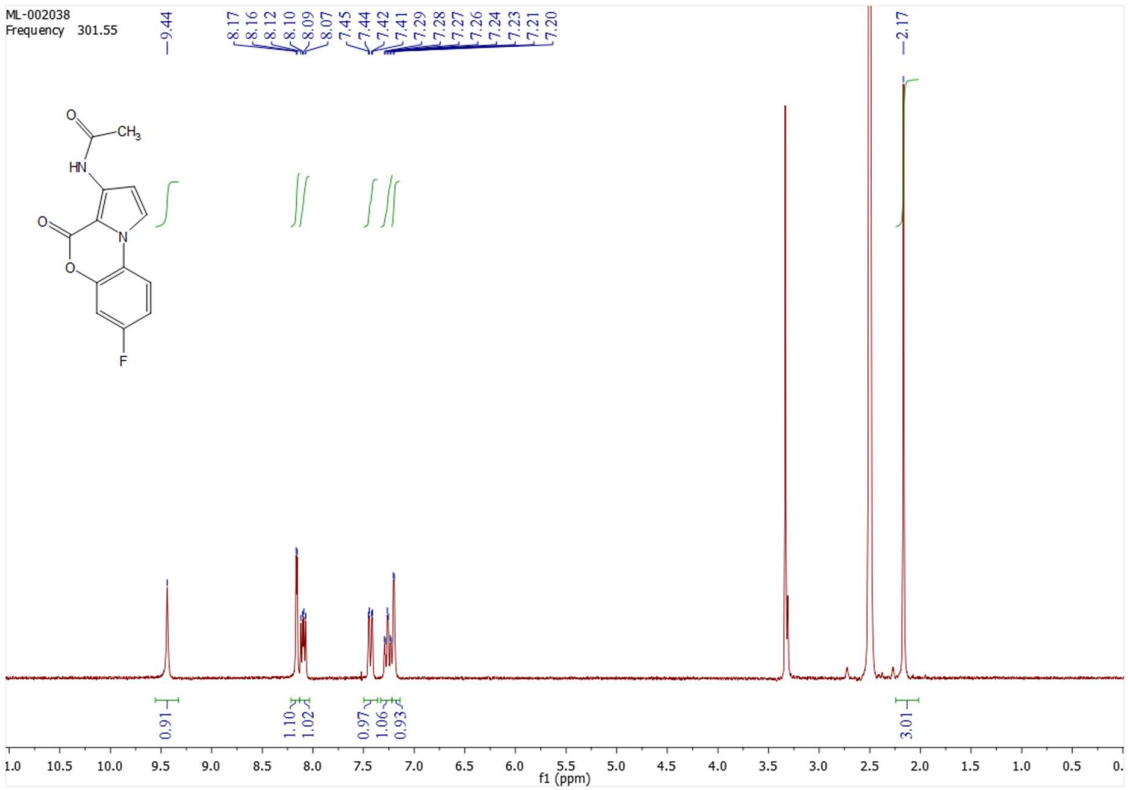

Figure S107. ^{1}H-NMR spectrum of *N*-(7-fluoro-4-oxo-4*H*-pyrrolo[2,1-*c*][1,4]benzoxazin-3-yl)acetamide (**14**) in DMSO-d_6

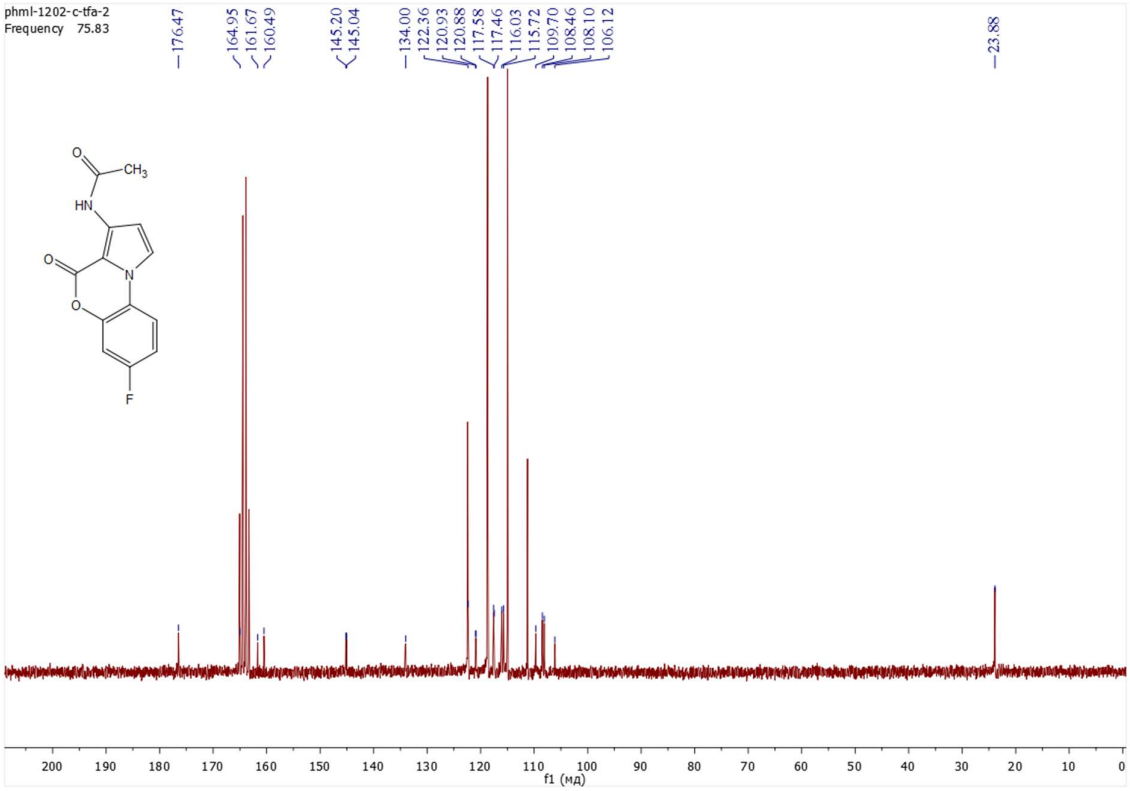

Figure S108. ^{13}C, NMR spectrum of *N*-(7-fluoro-4-oxo-4*H*-pyrrolo[2,1-*c*][1,4]benzoxazin-3-yl)acetamide (**14**) in CF_3COOD

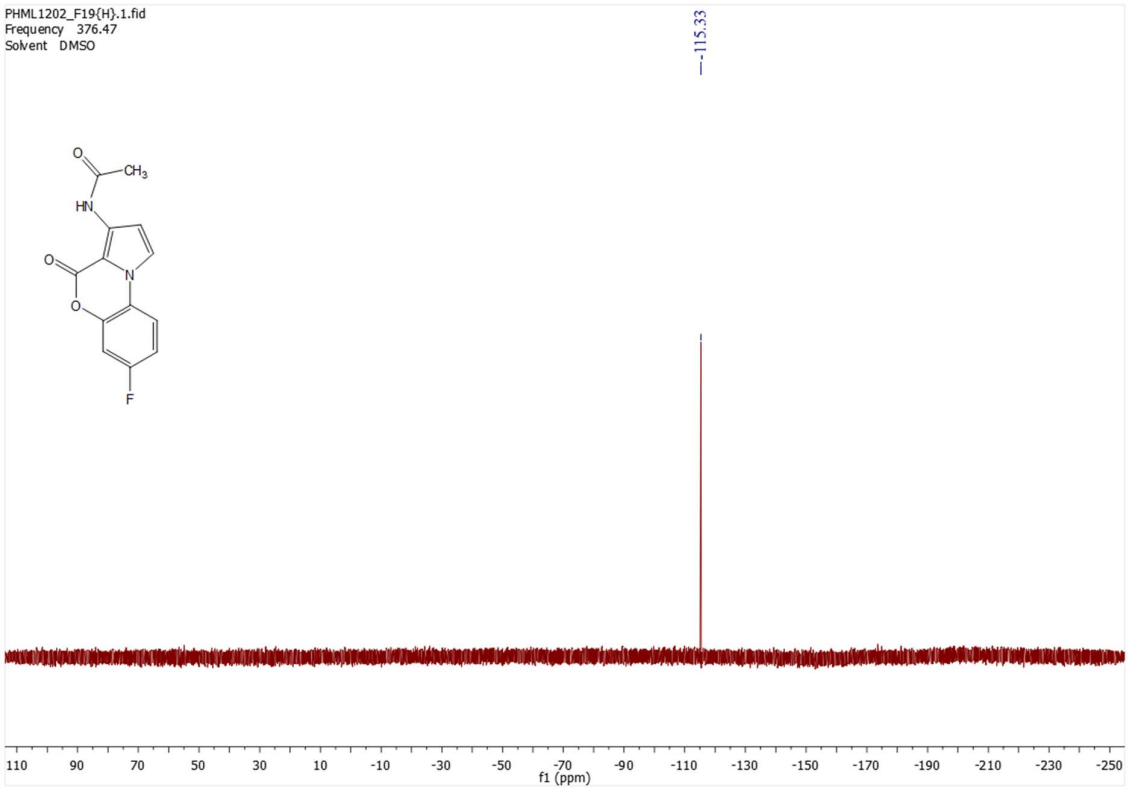

Figure S109. ^{19}F, NMR spectrum of *N*-(7-fluoro-4-oxo-4*H*-pyrrolo[2,1-*c*][1,4]benzoxazin-3-yl)acetamide (**14**) in DMSO-d_6

Synthesis and spectra characteristics of compounds 15, 16

*General procedure for the synthesis of N-(1-oxo-3-phenyl-3,4-dihydro-1H-pyrrolo[2,1-c][1,4]oxazin-8-yl)benzamide **15** and N-(4-oxo-4H-pyrrolo[2,1-c][1,4]benzoxazin-3-yl)benzamide **16**.* To a solution of (1.31 mmol) 8-amino-3-phenyl-3,4-dihydro-1*H*-pyrrolo[2,1-*c*][1,4]oxazin-1-one **8d** or 3-amino-4*H*-pyrrolo[2,1-*c*][1,4]benzoxazin-4-one **9a** in 20 cm^3 CH_2Cl_2, 0.20 g DIPEA (1.58 mmol), 1.45 mmol of benzoyl chloride were added. The resulting mixture was stirred at room temperature for 6–8 h. After the reaction was completed, for the compound **15**, the reaction mixture washed with H_2O (2 × 5 cm^3) and brine (2 × 5 cm^3), the organic phase was dried over Na_2SO_4 and evaporated under reduced pressure. The formed precipitate washed with hexane (2 × 4 cm^3), MTBE (1 × 1 cm^3) and dried under reduced pressure. For the compound **16**, the insoluble materials were filtered off, washed with H_2O (2 × 5 cm^3), hexane (2 × 4 cm^3), and dried under reduced pressure.

Chemical characterization of N-(1-oxo-3-phenyl-3,4-dihydro-1H-pyrrolo[2,1-c][1,4]oxazin-8-yl)benzamide (**15**). White solid, mp 185-186°C; yield 77%. ^{1}H-NMR (302 MHz, $CDCl_3$): δ 4.20 (dd, $^2J_{HH}$ = 13.3, $^3J_{HH}$ = 10.2 Hz, 1H, C^{4}H), 4.28 (dd, $^2J_{HH}$ = 13.2, $^3J_{HH}$ = 3.8 Hz, 1H, C^{4}H), 5.69 (dd, $^3J_{HH}$ = 10.2, $^3J_{HH}$ = 3.8 Hz, 1H, C^{3}H), 6.84 (d, $^3J_{HH}$ = 2.7 Hz, 1H, C^{7}H), 7.21 (d, $^3J_{HH}$ = 2.7 Hz, 1H, C^{6}H), 7.32 – 7.62 (m, 8H, 8H$_{Ar}$), 7.99 (d, $^3J_{HH}$ = 8.0 Hz, 2H, 2H$_{Ar}$), 9.93 (s, 1H, NH). ^{13}C, NMR (126 MHz, $CDCl_3$): δ = 49.19, 79.30, 103.27, 106.10, 124.44, 126.48, 127.39, 128.92, 129.06, 129.51, 132.17, 133.78,

133.91, 135.28, 160.31, 164.74. MS: m/z 333 (M + H). Anal. Calcd. for $C_{20}H_{16}N_2O_3$ (%): C, 72.28; H, 4.85; N, 8.43. Found: C, 72.11; H, 4.87; N, 8.51.

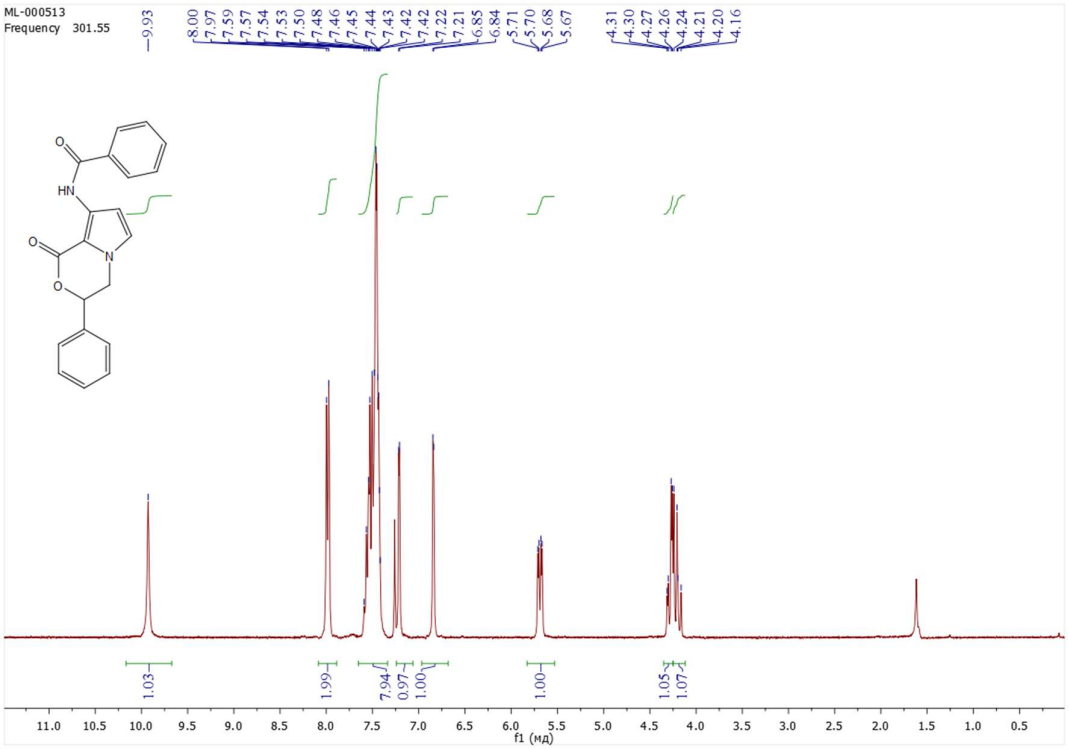

Figure S110. [1]H-NMR spectrum of *N*-(1-oxo-3-phenyl-3,4-dihydro-1*H*-pyrrolo[2,1-*c*][1,4]oxazin-8-yl)benzamide (**15**) in $CDCl_3$

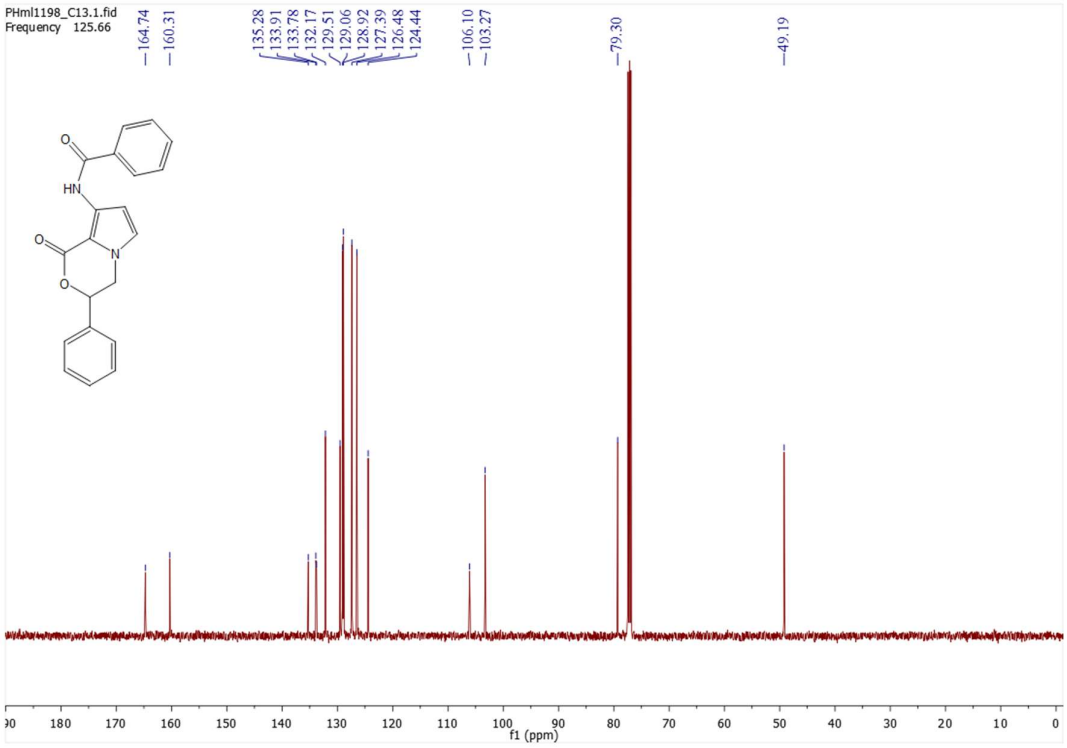

Figure 111. [13]C, NMR spectrum of *N*-(1-oxo-3-phenyl-3,4-dihydro-1*H*-pyrrolo[2,1-*c*][1,4]oxazin-8-yl)benzamide (**15**) in $CDCl_3$

Chemical characterization of N-(4-oxo-4H-pyrrolo[2,1-c][1,4]benzoxazin-3-yl)benzamide (**16**). Yellow solid, mp >250°C; yield 93%. ^{1}H-NMR (400 MHz, DMSO-d_6): δ 7.33 (d, $^{3}J_{HH}$ = 2.9 Hz, 1H, C^{2}H), 7.35-7.40 (m, 2H, 2H$_{Ar}$), 7.43-7.48 (m, 1H, 1H$_{Ar}$), 7.59-7.68 (m, 3H, 3H$_{Ar}$), 7.94 (d, $^{3}J_{HH}$ = 7.4 Hz, 2H, 2H$_{Ar}$), 8.08 (d, $^{3}J_{HH}$ = 6.7 Hz, 1H, 1H$_{Ar}$), 8.25 (d, $^{3}J_{HH}$ = 3.0 Hz, 1H, C^{1}H), 9.96 (s, 1H, NH). ^{13}C, NMR (76 MHz, $CDCl_3$): δ = 106.27, 113.98, 118.04, 118.69, 122.61, 124.07, 125.34, 126.38, 127.45, 129.04, 132.45, 133.50. MS: m/z 305 (M + H). Anal. Calcd. for $C_{18}H_{12}N_2O_3$ (%): C, 71.05; H, 3.97; N, 9.21. Found: C, 70.86; H, 4.01; N, 9.29.

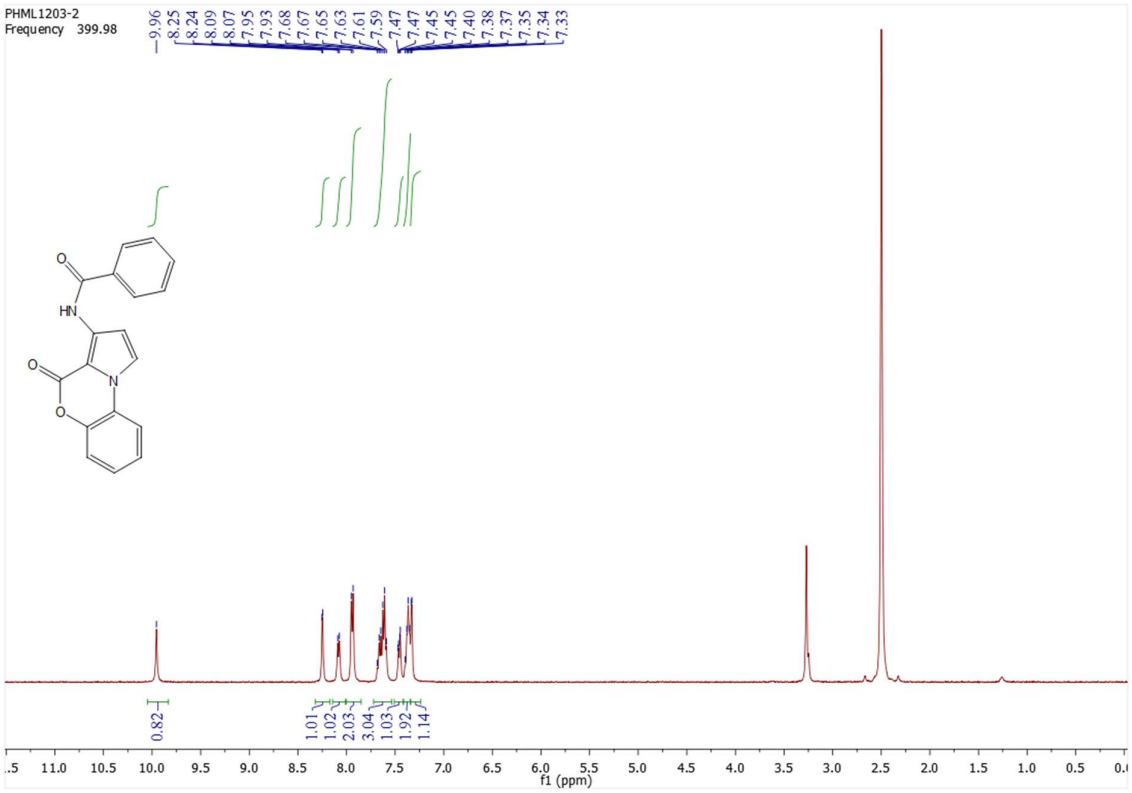

Figure S112. ^{1}H-NMR spectrum of *N*-(4-oxo-4*H*-pyrrolo[2,1-*c*][1,4]benzoxazin-3-yl)benzamide (**16**) in DMSO-d_6

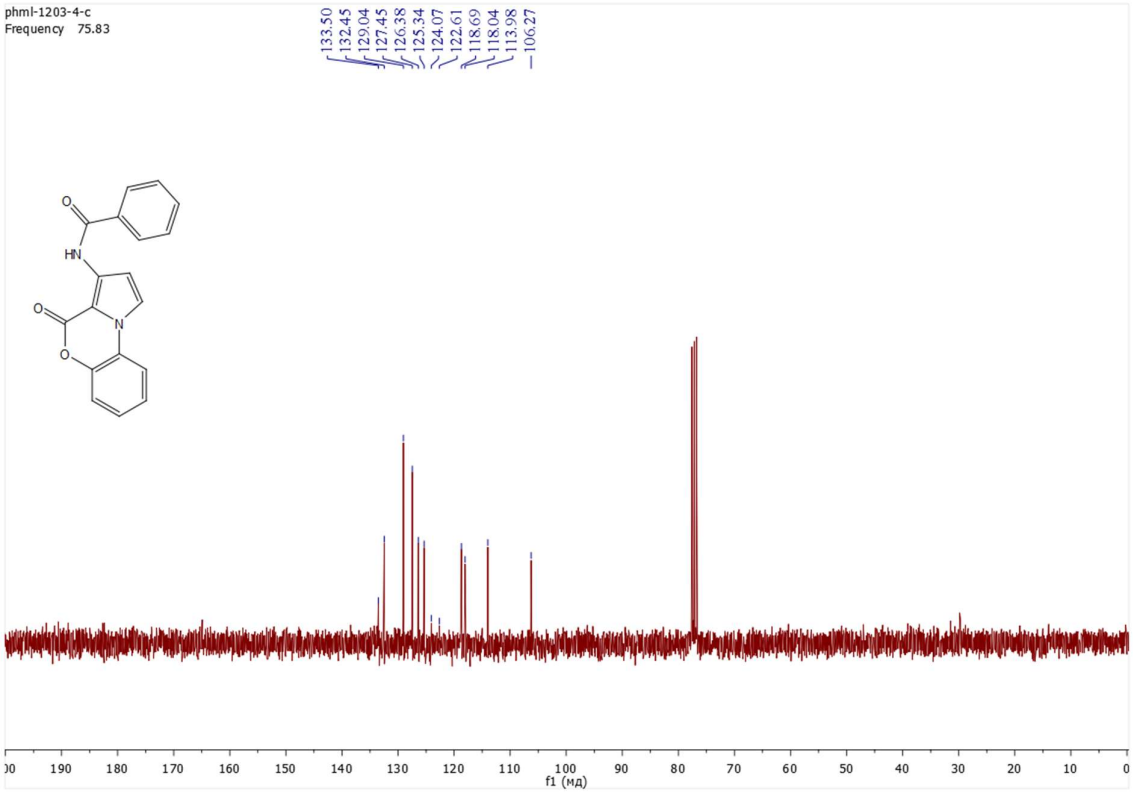

Figure S113. ^{13}C, NMR spectrum of *N*-(4-oxo-4*H*-pyrrolo[2,1-*c*][1,4]benzoxazin-3-yl)benzamide (**16**) in DMSO-d_6

Synthesis and spectra characteristics of compounds 17, 18

*General procedure for the synthesis of N-[(5aS,9aS)-4-oxo-5a,6,7,8,9,9a-hexahydro-4H-pyrrolo[2,1-c][1,4]benzoxazin-3-yl]methanesulfonamide **17** and N-(9-methyl-4-oxo-4H-pyrrolo[2,1-c][1,4]benzoxazin-3-yl)methanesulfonamide **18***. To a solution of (1.07 mmol) (5*aS*,9*aS*)-3-amino-5*a*,6,7,8,9,9*a*-hexahydro-4*H*-pyrrolo[2,1-*c*][1,4]benzoxazin-4-one **8e** or 3-amino-9-methyl-4*H*-pyrrolo[2,1-*c*][1,4]benzoxazin-4-one **9b** in 25 cm^3 CH_2Cl_2, 0.17 g DIPEA (1.28 mmol), 1.17 mmol of methanesulfonyl chloride were added. The resulting mixture was stirred at room temperature for 6 h for the compound **17** or at 40°C for 8 h for the compound **18**. After the reaction was completed, the reaction mixture washed with H_2O (2 × 5 cm^3) and brine (2 × 5 cm^3), the organic phase was dried over Na_2SO_4 and evaporated under reduced pressure. The formed precipitate washed with hexane (2 × 4 cm^3), MTBE (1 × 1 cm^3) and dried under reduced pressure. The formed precipitate was purified by column chromatography on silica gel, eluent $CHCl_3$–MeOH, 100:1 (for compound **17**), $CHCl_3$–MeOH, 50:1 (for compounds **18**).

Chemical characterization of N-[(5aS,9aS)-4-oxo-5a,6,7,8,9,9a-hexahydro-4H-pyrrolo[2,1-c][1,4]benzoxazin-3-yl]methanesulfonamide (**17**). Beige solid, mp 195-196°C; yield 65%. ^{1}H-NMR (400 MHz, $CDCl_3$): δ 1.41-1.68 (m, 3H), 1.64–1.78 (m, 1H), 1.97-1.98 (m, 2H), 2.26–2.30 (m, 1H), 2.55–2.58 (m, 1H), 3.03 (s, 3H, CH_3), 3.80 (td, $^3J_{HH}$ = 10.5, $^3J_{HH}$ = 4.1 Hz, 1H, C^{9a}H), 4.24 (td, $^3J_{HH}$ =

10.9, $^{3}J_{HH}$ = 4.3 Hz, 1H, C^{5a}H), 6.41 (d, $^{3}J_{HH}$ = 2.9 Hz, 1H, C^{2}H), 6.82 (d, $^{3}J_{HH}$ = 2.9 Hz, 1H, C^{1}H), 8.03 (s, 1H, NH). ^{13}C, NMR (126 MHz, $CDCl_3$): δ = 23.42, 23.62, 27.33, 29.81, 39.57, 56.75, 81.37, 101.40, 107.19, 121.00, 132.63, 160.16. MS: m/z 285 (M + H). Anal. Calcd. for $C_{12}H_{16}N_2O_4S$ (%): C, 50.69; H, 5.67; N, 9.85. Found: C, 50.88; H, 5.70; N, 9.77.

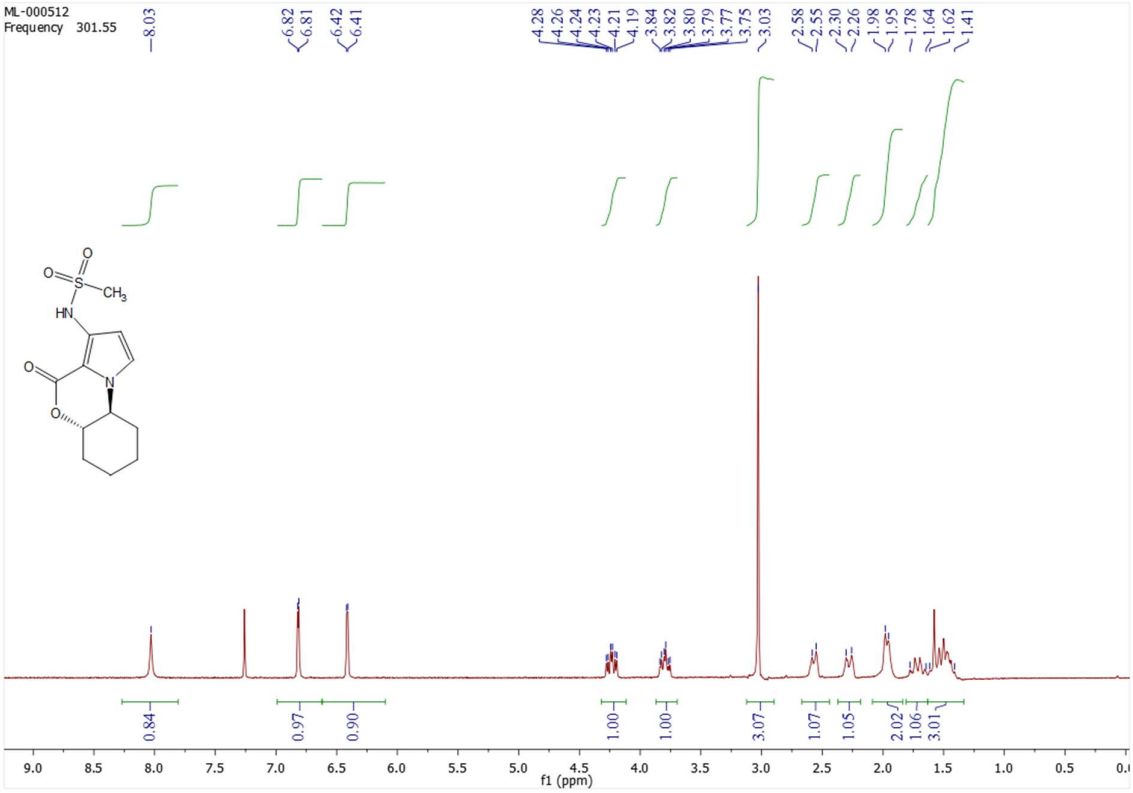

Figure S114. ^{1}H-NMR spectrum of *N*-[(5*aS*,9*aS*)-4-oxo-5*a*,6,7,8,9,9*a*-hexahydro-4*H*-pyrrolo[2,1-*c*][1,4]benzoxazin-3-yl]methanesulfonamide (**17**) in $CDCl_3$

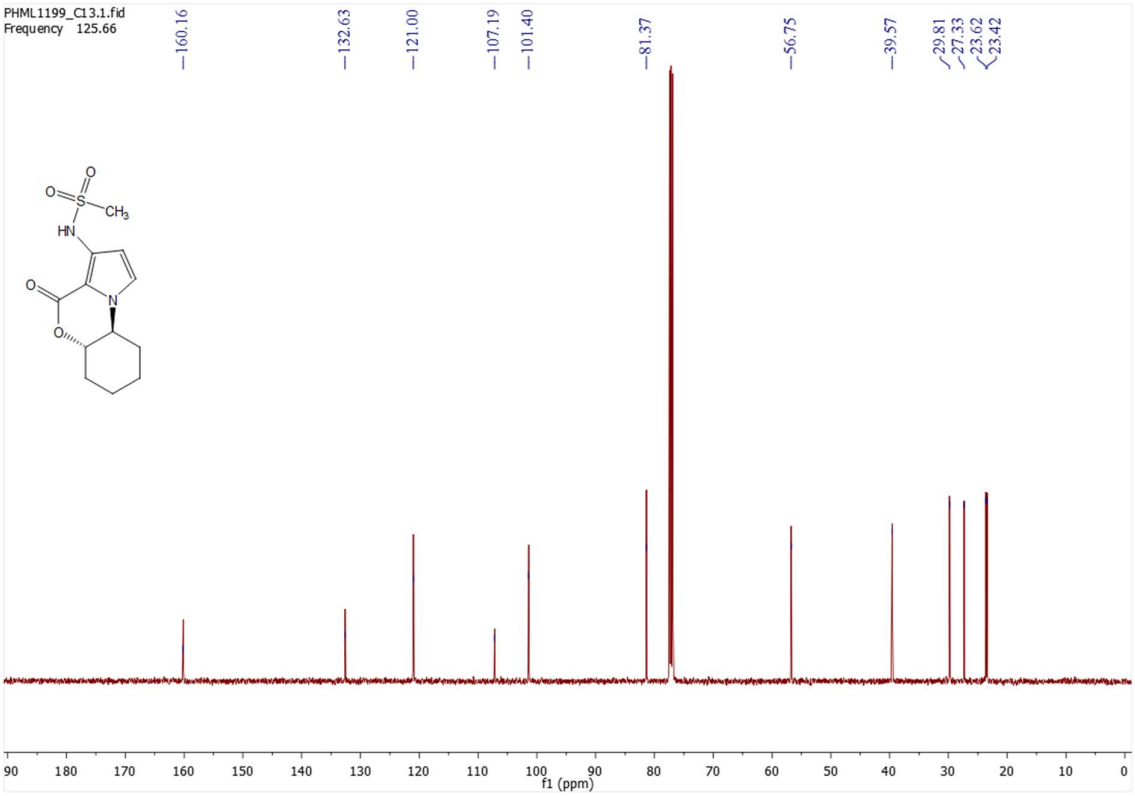

Figure S115. ^{13}C, NMR spectrum of *N*-[(5*aS*,9*aS*)-4-oxo-5*a*,6,7,8,9,9*a*-hexahydro-4*H*-pyrrolo[2,1-*c*][1,4]benzoxazin-3-yl]methanesulfonamide (**17**) in $CDCl_3$

Chemical characterization of N-(9-methyl-4-oxo-4H-pyrrolo[2,1-c][1,4]benzoxazin-3-yl)methanesulfonamide (**18**). Yellow solid, mp 230-231°C; yield 58%. ^{1}H-NMR (302 MHz, $CDCl_3$): δ 2.76 (s, 3H, CH_3), 3.08 (s, 3H, CH_3), 6.81 (d, $^3J_{HH}$ = 3.1 Hz, 1H, C^{2}H), 7.09-7.23 (m, 3H, 3H$_{Ar}$), 7.84 (d, $^3J_{HH}$ = 3.2 Hz, 1H, C^{1}H), 8.32 (s, 1H, NH). ^{13}C, NMR (126 MHz, DMSO-d_6): δ = 22.05, 39.68, 105.34, 105.79, 116.04, 121.65, 124.13, 125.61, 126.64, 128.73, 131.15, 143.13, 153.46. MS: m/z 293 (M + H). Anal. Calcd. for $C_{13}H_{12}N_2O_4S$ (%): C, 53.42; H, 4.14; N, 9.58. Found: C, 53.59; H, 4.11; N, 9.52.

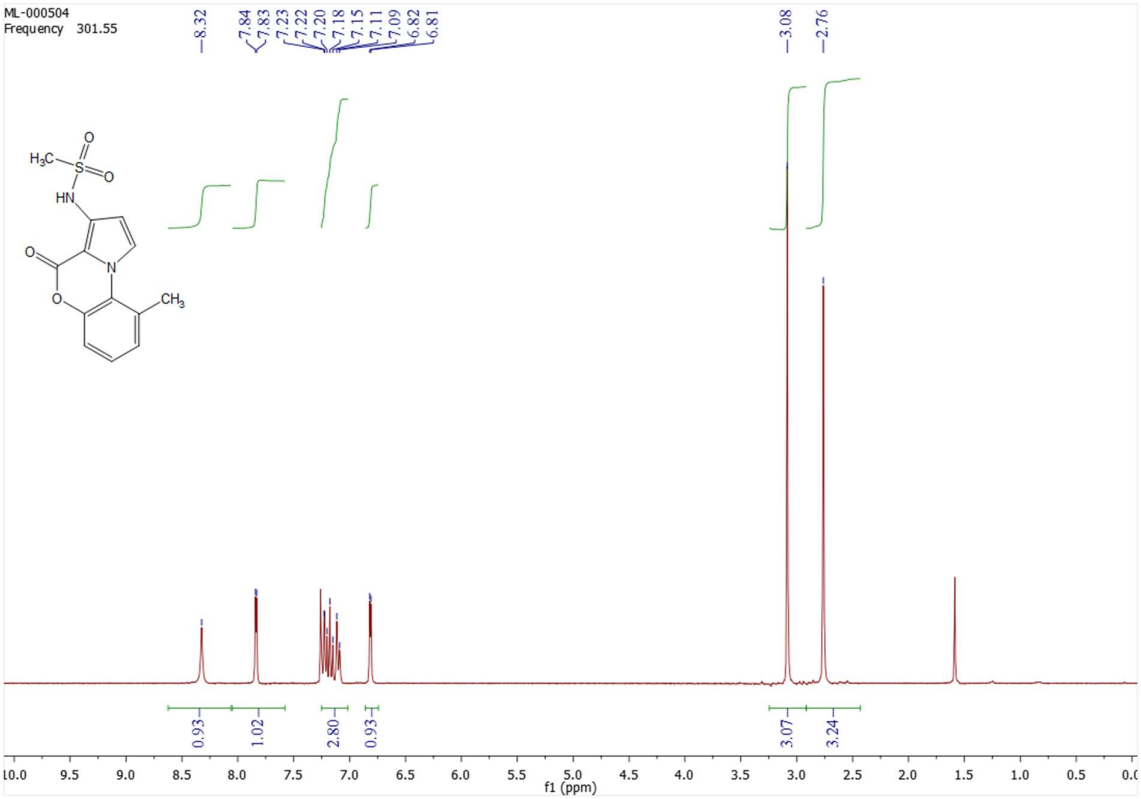

Figure S116. ^{1}H-NMR spectrum of *N*-(9-methyl-4-oxo-4*H*-pyrrolo[2,1-*c*][1,4]benzoxazin-3-yl)methanesulfonamide (**18**) in $CDCl_3$

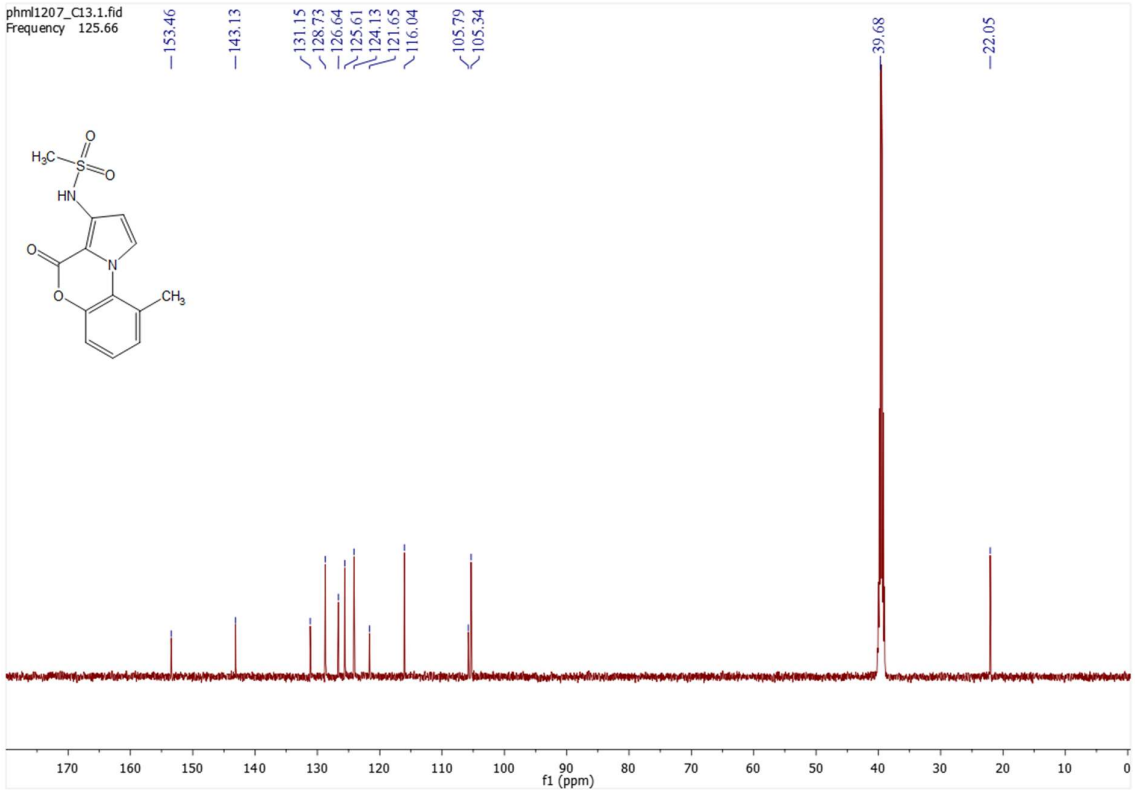

Figure S117. ^{13}C, NMR spectrum of *N*-(9-methyl-4-oxo-4*H*-pyrrolo[2,1-*c*][1,4]benzoxazin-3-yl)methanesulfonamide (**18**) in DMSO-d_6

Synthesis and spectra characteristics of compounds 19, 20

General procedure for the synthesis of N-(8-tert-butyl-4-oxo-4H-pyrrolo[2,1-c][1,4]benzoxazin-3-yl)-4-methylbenzenesulfonamide ***19*** *and 4-methyl-N-(3-methyl-1-oxo-3,4-dihydro-1H-pyrrolo[2,1-c][1,4]oxazin-8-yl)benzenesulfonamide* ***20***. To a solution of (1.08 mmol) 3-amino-8-*tert*-butyl-4*H*-pyrrolo[2,1-*c*][1,4]benzoxazin-4-one **9d** or 8-amino-3-methyl-3,4-dihydro-1*H*-pyrrolo[2,1-*c*][1,4]oxazin-1-one **8a** in 35 cm^3 pyridine, 1.14 mmol of 4-methylbenzenesulfonyl chloride was added. The resulting mixture was stirred at 55°C for 10-12 h. After the reaction was completed, the reaction mixture washed with H_2O (2 × 5 cm^3) and brine (2 × 5 cm^3), the organic phase was dried over Na_2SO_4 and evaporated under reduced pressure. The formed precipitate was purified by column chromatography on silica gel, $CHCl_3$–MeOH, 50:1.

Chemical characterization of 4-methyl-N-(8-tert-butyl-4-oxo-4H-pyrrolo[2,1-c][1,4]benzoxazin-3-yl)benzenesulfonamide (**19**). Yellow solid, mp 161-162°C; yield 60%. ^{1}H-NMR (302 MHz, $CDCl_3$): δ 1.34 (s, 9H, $3CH_3$), 2.34 (s, CH_3), 6.83 (d, $^3J_{HH}$ = 3.0 Hz, 1H, C^2H), 7.11–7.32 (m, 5H, $5H_{Ar}$), 7.44 (d, $^4J_{HH}$ = 2.1 Hz, 1H, H_{Ar}), 7.46 (d, $^3J_{HH}$ = 3.0 Hz, 1H, C^1H), 7.75 (d, $^3J_{HH}$ = 8.3 Hz, 2H, $2H_{Ar}$), 8.30 (s, 1H, NH). ^{13}C, NMR (126 MHz, $CDCl_3$): δ = 21.67, 31.42, 34.92, 104.76, 105.01, 110.49, 117.63, 118.06, 121.73, 123.76, 127.24, 129.85, 131.94, 136.07, 140.49, 144.25, 148.99, 155.38. MS: m/z 411 (M + H). Anal. Calcd. for $C_{22}H_{22}N_2O_4S$ (%): C, 64.37; H, 5.40; N, 6.82. Found: C, 64.18; H, 5.37; N, 6.90.

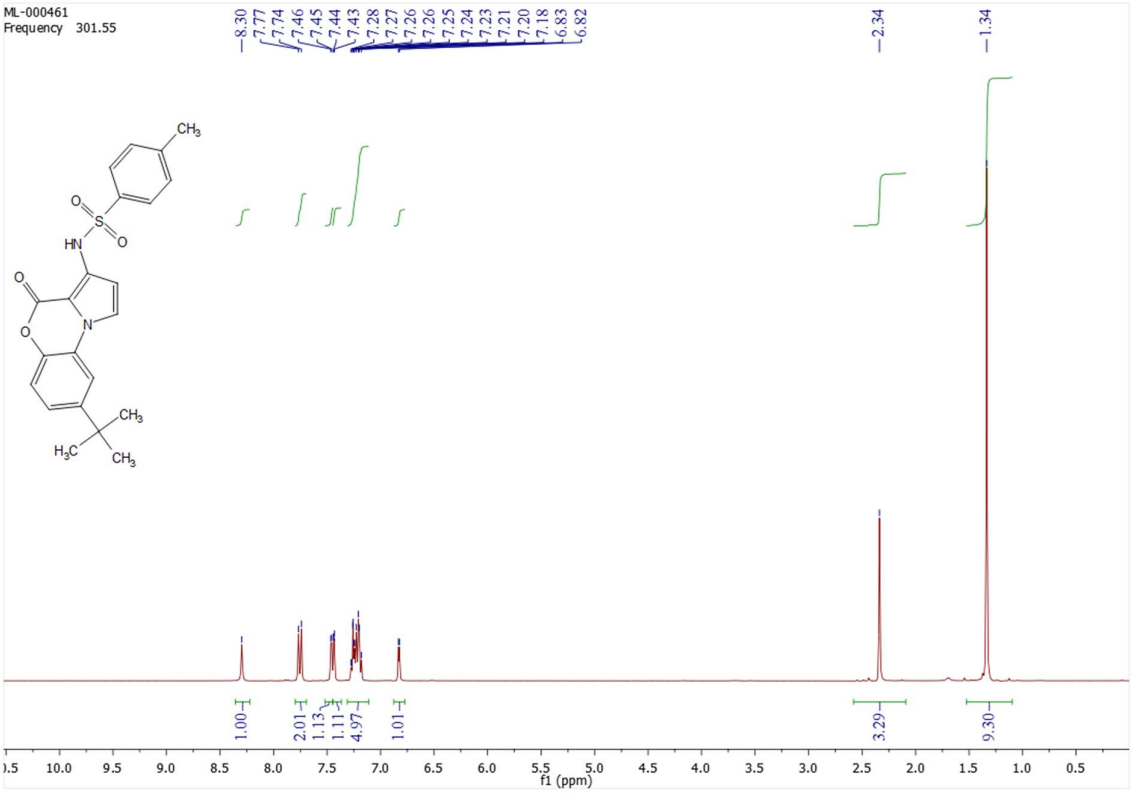

Figure S118. ^{1}H-NMR spectrum of 4-methyl-*N*-(8-*tert*-butyl-4-oxo-4*H*-pyrrolo[2,1-*c*][1,4]benzoxazin-3-yl)benzenesulfonamide (**19**) in $CDCl_3$

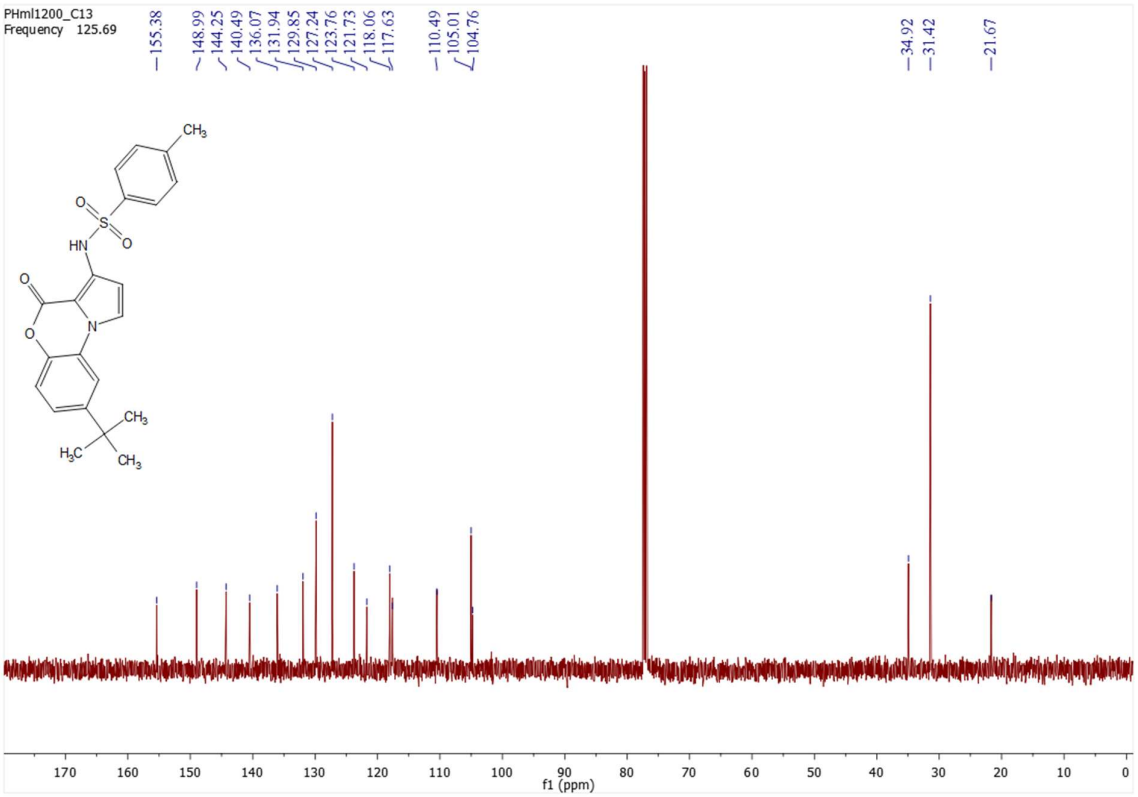

Figure S119. ^{13}C, NMR spectrum of 4-methyl-*N*-(8-*tert*-butyl-4-oxo-4*H*-pyrrolo[2,1-*c*][1,4]benzoxazin-3-yl)benzenesulfonamide (**19**) in $CDCl_3$

Chemical characterization of 4-methyl-N-(3-methyl-1-oxo-3,4-dihydro-1H-pyrrolo[2,1-c][1,4]oxazin-8-yl)benzenesulfonamide (**20**). White solid, mp 169-170°C; yield 55%. ^{1}H-NMR (302 MHz, $CDCl_3$): δ 1.44 (d, $^3J_{HH}$ = 6.5 Hz, 3H, C^3-CH_3), 2.37 (s, 3H, CH_3), 3.76 (dd, $^2J_{HH}$ = 13.0, $^3J_{HH}$ = 10.2 Hz, 1H, C^{4}H), 3.99 (dd, $^2J_{HH}$ = 13.0, $^3J_{HH}$ = 3.2 Hz, 1H, C^{4}H), 4.61-4.72 (m, 1H, C^{3}H), 6.41 (d, $^3J_{HH}$ = 2.8 Hz, 1H, C^{7}H), 6.65 (d, $^3J_{HH}$ = 2.8 Hz, 1H, C^{6}H), 7.22 (d, $^3J_{HH}$ = 8.1 Hz, 2H, 2H$_{Ar}$), 7.73 (d, $^3J_{HH}$ = 8.2 Hz, 2H, 2H$_{Ar}$), 8.18 (s, 1H, NH). ^{13}C, NMR (126 MHz, $CDCl_3$): δ = 18.01, 21.64, 48.66, 74.24, 101.83, 106.21, 124.11, 127.22, 129.70, 131.94, 136.21, 143.99, 159.85. MS: m/z 321 (M + H). Anal. Calcd. for $C_{15}H_{16}N_2O_4S$ (%): C, 56.24; H, 5.03; N, 8.74. Found: C, 56.42; H, 4.99; N, 8.83.

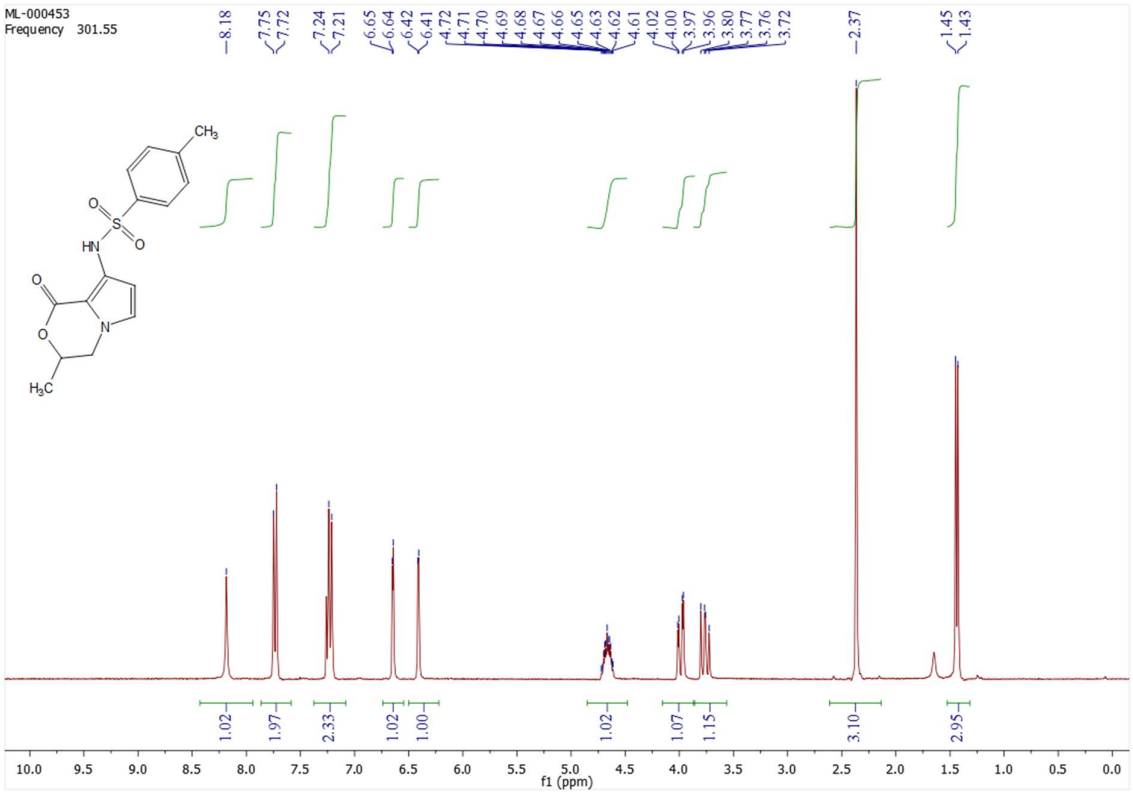

Figure S120. ^{1}H-NMR spectrum of 4-methyl-*N*-(3-methyl-1-oxo-3,4-dihydro-1*H*-pyrrolo[2,1-*c*][1,4]oxazin-8-yl)benzenesulfonamide (**20**) in $CDCl_3$

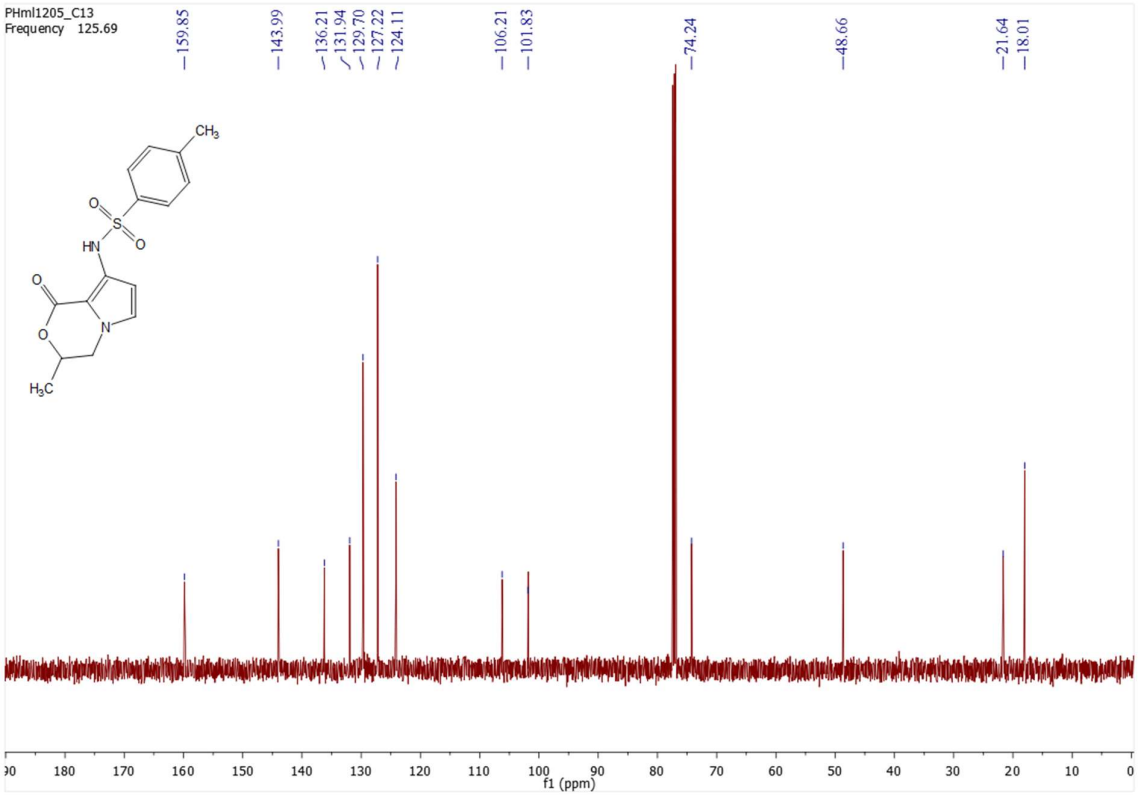

Figure S121. ^{13}C, NMR spectrum of 4-methyl-*N*-(3-methyl-1-oxo-3,4-dihydro-1*H*-pyrrolo[2,1-*c*][1,4]oxazin-8-yl)benzenesulfonamide (**20**) in $CDCl_3$