Synthesis of sulfamoyl-triazolyl-carboxamides as pharmacological myeloperoxidase inhibitors

Allya Larroza,^a Roberta Krüger,^a Mariana G. Fronza,^b Ana Paula Pesarico,^b Daniela H. de Oliveira,^a Lucielli Savegnago^b and Diego Alves^a*

- ^a Laboratório de Síntese Orgânica Limpa LASOL, CCQFA, Universidade Federal de Pelotas UFPel, P. O. Box 354, 96010-900, Pelotas, RS, Brazil.
- ^b Grupo de Pesquisa em Neurobiotecnologia GPN, CDTec, Universidade Federal de Pelotas UFPel, Pelotas, RS, Brazil.

Corresponding author e-mail: diego.alves@ufpel.edu.br

General Information: The reactions were monitored by TLC carried out on Merck silica gel (60 F_{254}) by using UV light as visualizant agent and 5% vanillin in 10% H_2SO_4 and heat as developing agents. Baker silica gel (particle size 0.040-0.063 mm) was used for flash chromatography. Hydrogen nuclear magnetic resonance (¹H NMR) spectra were obtained on a Bruker Avance III HD 400 spectrometer at 400 MHz. The spectra were recorded in DMSO-*d*₆ solutions. The chemical shifts are reported in ppm, referenced to tetramethylsilane as the internal reference. Coupling constants (*J*) are reported in hertz. Abbreviations to denote the multiplicity of a particular signal are s (singlet), d (doublet), dd (double doublet), t (triplet), td (triple triplet), q (quartet), and m (multiplet). ¹³C NMR spectra were obtained on a Bruker Avance III HD 400 spectrometer at 101 MHz. The chemical shifts are reported in ppm, referenced to the solvent peak of DMSO-*d*₆. Low-resolution mass spectra were obtained with a Shimadzu GC-MS-QP2010 mass spectrometer. High resolution mass spectra (HRMS) were recorded on a Bruker Micro TOF-QII spectrometer 10416.

General procedure for the synthesis of sulfamoyl-triazolyl-carboxamides 3a-r: To a 3 mL roundbottomed flask containing an appropriate *N*-(4-sulfamoylphenyl)butanamide 1a-c (0.20 mmol) and DBU (0.04 mmol, 20 mol%) was added the corresponding aryl azide 2a-f (0.25 mmol) solubilized in DMSO (0.5 mL). The homogeneous reaction mixture was stirred at 70 °C for 24 hours. After this time, the solution was cooled to room temperature and transferred directly to a Beaker containing distilled H_2O (5 mL). The obtained crystals were removed by vacuum filtration, washed with diethyl ether and dried under vacuum.

1-(4-Methoxyphenyl)-5-methyl-*N***-(4-sulfamoylphenyl)-1***H***-1,2,3-triazole-4-carboxamide** (3a). Yield: 0.066 g (85%); beige solid; mp 257-259 °C. ¹H NMR (400 MHz, DMSO- d_6) δ : 10.82 (s, 1H); 8.05 (d, *J* = 8.8 Hz, 2H); 7.79 (d, *J* = 8.8 Hz, 2H); 7.57 (d, *J* = 8.9 Hz, 2H); 7.28 (s, 2H); 7.18 (d, *J* = 8.9 Hz, 2H); 3.86 (s, 3H); 2.54 (s, 3H). ¹³C {¹H} NMR (101 MHz, DMSO- d_6) δ : 160.3, 160.0, 141.7, 138.8, 138.3, 137.8, 128.0, 127.0 (2C); 126.5 (2C); 120.0 (2C); 114.8 (2C); 55.7, 9.5. MS (relative intensity) *m/z*: 387(31), 316 (3), 188 (100), 160 (46), 123 (16). HRMS calculated mass for C₁₇H₁₇N₅O₄S: [M+H]⁺ 388.1074, found: 388.1072.

5-Methyl-*N***-(4-sulfamoylphenyl)-1-**(*p***-tolyl)-1***H***-1,2,3-triazole-4-carboxamide (3b).** Yield: 0.050 g (68%); beige solid; mp 242-244 °C; ¹H NMR (400 MHz, DMSO- d_6) δ = 10.84 (s, 1H), 8.05 (d, *J* = 8.8 Hz, 2H), 7.79 (d, *J* = 8.8 Hz, 2H), 7.54 (d, *J* = 8.3 Hz, 2H), 7.46 (d, *J* = 8.3 Hz, 2H), 7.28 (s, 2H), 2.56 (s, 3H), 2.43 (s, 3H). ¹³C {¹H} NMR (101 MHz, DMSO- d_6) δ = 159. 9, 141.6, 140.0, 138.8, 138.1, 137.9, 132.8, 130.2 (2C), 126.5 (2C), 125.3 (2C), 120.0 (2C), 20.8, 9.5. MS (relative intensity)

m/z: 371(47), 248(9), 172(100), 144(61), 91(91) HRMS calculated mass for C₁₇H₁₇N₅O₃S [M+H]⁺: 372.1125, found: 372.1113.

1-(4-Fluorophenyl)-5-methyl-*N***-(4-sulfamoylphenyl)-1***H***-1,2,3-triazole-4-carboxamide** (3c). Yield: 0,026 g (35%); beige solid; mp 214-216 °C; ¹H NMR (400 MHz, DMSO- d_6) δ = 10.86 (s, 1H), 8.06 - 8.05 (m, 2H), 7.81 - 7.74 (m, 4H), 7.54 - 7.50 (m, 2H), 7.28 (s, 2H), 2.57 (s, 3H). ¹³C {¹H} NMR (101 MHz, DMSO- d_6) δ = 163.8, 162.6 (d, *J* = 247 Hz), 141.6, 138.8, 138.5, 137.9, 131.6 (d, *J* = 3 Hz), 128.1 (d, *J* = 9 Hz), 126.5 (2C), 120.0 (2C), 116.7 (d, *J* = 24 Hz), 9.4. MS (relative intensity) *m/z*: 375(70), 237(12), 176(100), 136(53), 95(85) HRMS calculated mass for C₁₆H₁₄FN₅O₃S [M+H]⁺: 376.0874, found: 376.0859.

1-(2-Fluorophenyl)-5-methyl-*N***-(4-sulfamoylphenyl)-1***H***-1,2,3-triazole-4-carboxamide** (3d). Yield: 0.034 g (45%); beige solid; mp 223-225 °C. ¹H NMR (400 MHz, DMSO- d_6) δ = 10.91 (s, 1H), 8.06 (d, *J* = 8.8 Hz, 2H), 7.82 – 7.74 (m, 4H), 7.64 (t, *J* = 8.8 Hz, 1H), 7.53 (t, *J* = 7.8 Hz, 1H), 7.29 (s, 2H), 3.34 (s, 3H). ¹³C {¹H} NMR (101 MHz, DMSO- d_6) δ = 159.6, 155.9 (d, *J* = 251 Hz), 141.5, 139.6, 138.9, 137.7, 133.3 (d, *J* = 8 Hz), 129.1, 126.5 (2C), 125.7 (d, *J* = 3 Hz), 122.6 (d, *J* = 12 Hz), 120.0 (2C), 117.1 (d, *J* = 19 Hz), 8.8. MS (relative intensity) *m/z*: 375(100), 237(18), 176(87), 136(86), 111(78) HRMS calculated mass for C₁₆H₁₄FN₅O₃S [M+H]⁺: 376.0874, found: 376.0873.

5-Methyl-1-(4-nitrophenyl)-*N*-(**4-sulfamoylphenyl)**-1*H*-1,2,3-triazole-4-carboxamide (3e). Yield: 0.046 g (57%); beige solid; ¹H NMR (400 MHz, DMSO- d_6) δ = 10.87 (s, 1H), 8.49 (d, J = 8.9 Hz, 2H), 8.30 (d, J = 8.8 Hz, 2H), 8.00 (d, J = 8.9 Hz, 2H), 7.80 (d, J = 8.8 Hz, 2H), 7.30 (s, 2H), 2.66 (s, 3H). ¹³C {¹H} NMR (101 MHz, DMSO- d_6) δ = 159.8, 148.1, 141.7, 140.1, 139.3, 138.9, 138.5, 126.7 (2C), 126.7 (2C), 125.3 (2C), 120.3 (2C), 9.8. MS (relative intensity) *m/z*: 402(94), 236(30), 203(63), 164(100), 157(69) HRMS calculated mass for C₁₆H₁₄N₆O₅S [M+H]⁺: 403.0825, found: 404.0831.

1-(4-Methoxyphenyl)-N-(4-sulfamoylphenyl)-5-(trifluoromethyl)-1H-1,2,3-triazole-4-

carboxamide (3g). Yield: 0.067 g (76%); pink solid; mp 236-238 °C; ¹H NMR (400 MHz, DMSO- d_6) δ = 11.27 (s, 1H), 8.00 (d, J = 8.7 Hz, 2H), 7.84 (d, J = 8.8 Hz, 2H), 7.64 (d, J = 8.9 Hz, 2H), 7.32 (s, 2H), 7.19 (d, J = 9.0 Hz, 2H), 3.88 (s, 3H). ¹³C {¹H} NMR (101 MHz, DMSO- d_6) δ = 161.6, 157.6, 142.3, 141.5, 140.0, 137.9, 128.2 (2C), 128.0 (q, J = 42 Hz), 127.1 (2C), 120.6 (2C), 119.4 (q, J = 270 Hz), 115.1 (2C), 56.2. MS (relative intensity) *m/z*: 441(34), 344(19), 242(100), 200(25), 92(18) HRMS calculated mass for C₁₇H₁₄F₃N₅O₄S [M+H]⁺: 442.0791, found: 442.0776.

N-(4-Sulfamoylphenyl)-1-(*p*-tolyl)-5-(trifluoromethyl)-1*H*-1,2,3-triazole-4-carboxamide (3h). Yield: 0.052 g (61%); beige solid; mp 263-265 °C; ¹H NMR (400 MHz, DMSO- d_6) δ = 11.29 (s, 1H), 8.00 (d, J = 8.8 Hz, 2H), 7.84 (d, J = 8.8 Hz, 2H), 7.58 (d, J = 8.2 Hz, 2H), 7.48 (d, J = 8.2 Hz, 2H), 7.32 (s, 2H), 2.45 (s, 3H). ¹³C {¹H} NMR (101 MHz, DMSO- d_6) $\delta = 157.1$, 142.0, 141.5, 141.0, 139.6, 132.8, 130.0 (2C), 128.4, 127.8 (q, J = 42 Hz), 127.2, 126.7 (2C), 126.0 (2C), 122.9, 120.2, 120.1 (2C), 118. 9 (q, J = 270 Hz), 20.8. MS (relative intensity) m/z: 425(100), 328(30), 226(79), 172(18), 91(37) HRMS calculated mass for C₁₇H₁₄F₃N₅O₃S [M+H]⁺: 448.0662, found: 448.0677.

1-(4-Fluorophenyl)-N-(4-sulfamoylphenyl)-5-(trifluoromethyl)-1H-1,2,3-triazole-4-

carboxamide (3i). Yield: 0.026 g (30%); beige solid; mp 241-243 °C; ¹H NMR (400 MHz, DMSO d_6) δ = 11.30 (s, 1H), 8.01 (d, J = 8.8 Hz, 2H), 7.83 (dd, J = 8.8, 4.6 Hz, 4H), 7.55 (t, J = 8.7 Hz, 2H), 7.32 (s, 2H). ¹³C {¹H} NMR (101 MHz, DMSO- d_6) δ = 164.5, 163.3 (d, J = 249 Hz), 141.9, 141.0, 139.6, 131.6, 129.0 (d, J = 9 Hz), 128.9 (q, J = 42 Hz), 126.6 (2C), 120.2 (2C), 118.8 (q, J = 277 Hz), 116.7 (d, J = 23 Hz). MS (relative intensity) m/z: 429(100), 332(32), 230(73), 172(28), 95(76) HRMS calculated mass for C₁₆H₁₁F₄N₅O₃S [M+H]⁺: 430.0591, found: 430.0587.

1-(2-Fluorophenyl)-N-(4-sulfamoylphenyl)-5-(trifluoromethyl)-1H-1,2,3-triazole-4-

carboxamide (3j). Yield: 0.033 g (39%); beige solid; mp 198-200 °C; ¹H NMR (400 MHz, DMSOd₆) δ = 11.35 (s, 1H), 8.01 (d, *J* = 8.7 Hz, 2H), 7.93 (td, *J* = 7.8, 1.4 Hz, 1H), 7.86 – 7.79 (m, 3H), 7.67 (t, *J* = 9.0 Hz, 1H), 7.55 (t, *J* = 7.7 Hz, 1H), 7.33 (s, 2H), 2.54 (s, 1H). ¹³C {¹H} NMR (101 MHz, DMSO-*d*₆) δ = 157.0, 155.8 (d, *J* = 250 Hz), 142.0, 140.9, 139.7, 134.3 (d, *J* = 8 Hz), 129.2, 128.9 (q, *J* = 42 Hz), 126.7 (2C), 125.7 (d, *J* = 3 Hz), 122.8 (d, *J* = 12), 120.2 (2C), 118.7 (q, *J* = 270 Hz), 116. 8 (d, *J* = 18 Hz). MS (relative intensity) *m/z*: 429(100), 332(8), 230(5), 190(8), 95(48) HRMS calculated mass for C₁₆H₁₁F₄N₅O₃S [M+H]⁺: 430.0591, found: 430.0577.

1-(4-Nitrophenyl)-*N*-(**4-sulfamoylphenyl**)-**5-(trifluoromethyl**)-1*H*-1,2,3-triazole-4-carboxamide (**3k**). Yield: 0.047 g (52%); beige solid; mp 167-169 °C; ¹H NMR (400 MHz, DMSO-*d*₆) δ = 11.33 (s, 1H), 8.52 (d, *J* = 8.9 Hz, 2H), 8.07 (d, *J* = 8.8 Hz, 2H), 8.02 (d, *J* = 8.7 Hz, 2H), 7.84 (d, *J* = 8.8 Hz, 2H), 7.33 (s, 2H). ¹³C {¹H} NMR (101 MHz, DMSO-*d*₆) δ = 156.8, 149.1, 142.2, 141.0, 139.9, 139.6, 128.5 (q, *J* = 42 Hz), 128.1 (2C), 126. 7 (2C), 125.0 (2C), 120.3 (2C), 118.8 (q, *J* = 270 Hz). MS (relative intensity) *m/z*: 456(100), 230(14), 211(34), 183(17), 92(18) HRMS calculated mass for C₁₆H₁₁F₃N₆O₅S [M+H]⁺: 457.0536, found: 457.0540.

1-(3-Nitrophenyl)-*N*-(**4-sulfamoylphenyl)**-**5-(trifluoromethyl)**-1*H*-1,2,3-triazole-4-carboxamide (**3**). Yield: 0.042 g (47%); pink solid; mp 229-231 °C; ¹H NMR (400 MHz, DMSO- d_6) δ = 11.33 (s, 1H), 8.74 (s, 1H), 8.57 (d, *J* = 9.7 Hz, 1H), 8.26 – 8.24 (m, 1H), 8.05 – 7.97 (m, 3H), 7.85 (d, *J* = 8.8 Hz, 2H), 7.33 (s, 2H). ¹³C {¹H} NMR (101 MHz, DMSO- d_6) δ = 156.8, 148.0, 141.8, 141.0, 139.6, 136.0, 133.0, 131.3, 128. 9 (q, *J* = 42 Hz), 126.6 (2C), 126.3, 122.0, 120.3 (2C), 118.8 (q, *J* = 270)

Hz). MS (relative intensity) *m/z*: 456(100), 246(3), 183(21), 122(14), 92(14) HRMS calculated mass for C₁₆H₁₁F₃N₆O₅S [M+H]⁺: 457.0536, found: 457.0546.

1-(4-Methoxyphenyl)-5-phenyl-*N***-(4-sulfamoylphenyl)-1***H***-1,2,3-triazole-4-carboxamide (3m).** Yield: 0.082 g (92%); beige solid; mp 285-287 °C; ¹H NMR (400 MHz, DMSO- d_6) δ = 10.93 (s, 1H), 7.99 (d, *J* = 8.8 Hz, 2H), 7.77 (d, *J* = 8.7 Hz, 2H), 7.39 – 7.33 (m, 7H), 7.26 (s, 2H), 7.01 (d, *J* = 8.9 Hz, 2H), 3.78 (s, 3H). ¹³C {¹H} NMR (101 MHz, DMSO- d_6) δ = 160.4, 159.4, 142.1, 140.4, 139.3, 138.9, 130.9 (2C), 130.0, 128.8, 128.5 (2C), 127.9 (2C), 126.9 (2C), 126.3, 120.4 (2C), 114.9 (2C), 56.0. MS (relative intensity) *m/z*: 449(11), 341(5), 250(100), 222(63), 89(53) HRMS calculated mass for C₂₂H₁₉N₅O₄S [M+H]⁺: 450.1231, found: 450.1246.

5-Phenyl-*N***-(4-sulfamoylphenyl)-1-***(p***-tolyl)-1***H***-1,2,3-triazole-4-carboxamide (3n).** Yield: 0.058 g (67%); beige solid; mp 273-275 °C; ¹H NMR (400 MHz, DMSO- d_6) δ = 10.94 (s, 1H), 7.99 (d, *J* = 8.9 Hz, 2H), 7.77 (d, *J* = 8.8 Hz, 2H), 7.41 – 7.38 (m, 5H), 7.29 – 7.27 (m, 6H), 3.33 (s, 3H). ¹³C {¹H} NMR (101 MHz, DMSO- d_6) δ = 158.9, 141.6, 139.8, 139.7, 138.8, 138.6, 133.1 (2C), 130.4 (2C), 129.8, 129.5 (2C), 128.1(2C), 126.4 (2C), 125.7 (2C), 119.9 (2C), 20.7. MS (relative intensity) *m/z*: 433(23), 325(4), 234(100), 206(43), 89(57) HRMS calculated mass for C₂₂H₁₉N₅O₃S [M+H]⁺: 434.1281, found: 434.1302.

1-(4-Fluorophenyl)-5-phenyl-*N***-(4-sulfamoylphenyl)-1***H***-1,2,3-triazole-4-carboxamide** (30). Yield: 0.031 g (36%); beige solid; mp 290-292 °C; ¹H NMR (400 MHz, DMSO- d_6) δ = 10.97 (s, 1H), 8.00 (d, *J* = 8.8 Hz, 2H), 7.77 (d, *J* = 8.8 Hz, 2H), 7.50 (dd, *J* = 8.9, 4.9 Hz, 2H), 7.39 (q, *J* = 10.0, 8.7 Hz, 9H). ¹³C {¹H} NMR (101 MHz, DMSO- d_6) δ = 163.5, 162.3 (d, *J* = 247 Hz), 141.5, 140.1, 138.8, 138.5, 131.9 (d, *J* = 3 Hz), 130.4, 129.6, 128.5 (d, *J* = 8 Hz), 128.1 (2C), 126.4 (2C), 125.5, 119.9 (2C), 116.4 (d, *J* = 22 Hz). MS (relative intensity) *m/z*: 437(19), 329(4), 238(95), 210(45), 89(100) HRMS calculated mass for C₂₁H₁₆FN₅O₃S [M+Na]⁺: 460.0850, found: 460.0862.

1-(2-Fluorophenyl)-5-phenyl-*N***-(4-sulfamoylphenyl)-1***H***-1,2,3-triazole-4-carboxamide** (3p). Yield: 0.037 g (43%); beige solid; mp 277-279 °C; ¹H NMR (400 MHz, DMSO- d_6) δ = 11.00 (s, 1H), 7.99 (d, *J* = 8.6 Hz, 2H), 7.78 (d, *J* = 8.7 Hz, 3H), 7.41 – 7.35 (m, 8H), 7.27 (s, 2H). ¹³C {¹H} NMR (101 MHz, DMSO- d_6) δ = 158.5, 155.5 (d, *J* = 252 Hz), 141.3, 141.1, 138.7, 138.1, 132.9 (d, *J* = 8 Hz), 129.7, 129.6 (2C), 129.5, 127.9 (2C), 126.2 (2C), 125.3 (d, *J* = 3 Hz), 124.8, 123.0 (d, *J* = 12 Hz), 119.8 (2C), 116.5 (d, *J* = 19 Hz). MS (relative intensity) *m/z*: 437(25), 238(92), 210(41), 198(29), 89(100) HRMS calculated mass for C₂₁H₁₆FN₅O₃S [M+Na]⁺: 460.0850, found: 460.0866.

 1-(4-Nitrophenyl)-5-phenyl-N-(4-sulfamoylphenyl)-1H-1,2,3-triazole-4-carboxamide
 (3q).

 Yield 0.045 g (48%); beige solid; mp 108-110 °C; ¹H NMR (400 MHz, DMSO- d_6) δ= 10.98 (s, 1H),

8.33 (d, J = 9.0 Hz, 2H), 7.99 (d, J = 8.8 Hz, 2H), 7.78 (d, J = 8.8 Hz, 2H), 7.69 (d, J = 9.0 Hz, 2H), 7.43 (d, J = 7.4 Hz, 3H), 7.40 (d, J = 7.4 Hz, 2H), 7.28 (s, 2H). ¹³C {¹H} NMR (101 MHz, DMSO- d_6) $\delta = 158.6, 147. 8, 141.5, 140.3, 140.2, 139.0, 138.9, 130.5$ (2C), 130.0, 128.3 (2C), 127.1 (2C), 126.5 (2C), 125.2, 124.9 (2C), 120.1 (2C). MS (relative intensity) m/z: 465(36), 265(100), 237(39), 225(23), 89(88) HRMS calculated mass for C₂₁H₁₇N₆O₅S [M+H]⁺: 465.0981, found: 465.0983.

1-(3-Nitrophenyl)-5-phenyl-*N***-(4-sulfamoylphenyl)-1***H***-1,2,3-triazole-4-carboxamide** (3r). Yield 0.050 g (54%); beige solid; mp 272-274 °C; ¹H NMR (400 MHz, DMSO- d_6) δ = 11.02 (s, 1H), 8.35 (m, 2H), 8.02 (d, *J* = 8,7 Hz, 2H), 7.80 (m, 4H), 7.44 (m, 5H), 7,28 (s, 2H). ¹³C {¹H} NMR (101 MHz, DMSO- d_6) δ = 158.6, 147.9, 141.5, 140.3, 138.9, 138.8, 136.2, 132.2, 131.0, 130.6 (2C). 129.9, 128.2 (2C), 126.4 (2C), 125.2, 124.7, 121.0, 120.0 (2C). MS (relative intensity) *m/z*: 464(1), 282(40), 238(29), 190(32), 145(52), 89(100). HRMS calculated mass for C₂₁H₁₆N₆O₅SNa: [M + Na]⁺ 487.0795, found: 487.0798.

SELECTED SPECTRA



Figure 1. ¹H NMR (400 MHz) spectrum for compound **3a** in DMSO-*d*₆.





Figure 2. ¹³C NMR (101 MHz) spectrum for compound 3a in DMSO- d_6 .

Figure 3. ¹H NMR (400 MHz) spectrum for compound 3b in DMSO-*d*₆.



Figure 4. ¹³C NMR (101 MHz) spectrum for compound **3b** in DMSO-*d*₆.





Figure 5. ¹H NMR (400 MHz) spectrum for compound 3c in DMSO- d_6 .

Figure 6. ¹³C NMR (101 MHz) spectrum for compound 3c in DMSO- d_6 .



Figure 7. ¹H NMR (400 MHz) spectrum for compound 3d in DMSO-*d*₆.





Figure 8. ¹³C NMR (101 MHz) spectrum for compound 3d in DMSO- d_6 .

Figure 9. ¹H NMR (400 MHz) spectrum for compound 3e in DMSO- d_6 .



Figure 10. ¹³C NMR (101 MHz) spectrum for compound 3e in DMSO- d_6 .





Figure 11. ¹H NMR (400 MHz) spectrum for compound 3g in DMSO- d_6 .

Figure 12. ¹³C NMR (101 MHz) spectrum for compound 3g in DMSO- d_6 .



Figure 13. ¹H NMR (400 MHz) spectrum for compound **3h** in DMSO- d_6 .





Figure 14. ¹³C NMR (101 MHz) spectrum for compound **3h** in DMSO- d_6 .

Figure 15. ¹H NMR (400 MHz) spectrum for compound 3i in DMSO-*d*₆.



Figure 16. ¹³C NMR (101 MHz) spectrum for compound 3i in DMSO- d_6 .





Figure 17. ¹H NMR (400 MHz) spectrum for compound 3j in DMSO- d_6 .

Figure 18. ¹³C NMR (101 MHz) spectrum for compound 3j in DMSO- d_6 .



Figure 19. ¹H NMR (400 MHz) spectrum for compound 3k in DMSO-*d*₆.



Figure 20. ¹³C NMR (101 MHz) spectrum for compound 3k in DMSO-*d*₆.



Figure 21. ¹H NMR (400 MHz) spectrum for compound 3l in DMSO-*d*₆.





Figure 22. ¹³C NMR (101 MHz) spectrum for compound 31 in DMSO- d_6 .

Figure 23. ¹H NMR (400 MHz) spectrum for compound **3m** in DMSO-*d*₆.





Figure 24. ¹³C NMR (101 MHz) spectrum for compound 3m in DMSO- d_6 .





Figure 25. ¹H NMR (400 MHz) spectrum for compound 3n in DMSO- d_6 .

Figure 26. ¹³C NMR (101 MHz) spectrum for compound 3n in DMSO- d_6 .



Figure 27. ¹H NMR (400 MHz) spectrum for compound **30** in DMSO-*d*₆.





Figure 28. ¹³C NMR (101 MHz) spectrum for compound 30 in DMSO- d_6 .

Figure 29. ¹H NMR (400 MHz) spectrum for compound 3p in DMSO-*d*₆.



Figure 30. ¹³C NMR (101 MHz) spectrum for compound 3p in DMSO-*d*₆.



Figure 31. ¹H NMR (400 MHz) spectrum for compound 3q in DMSO-*d*₆.



Figure 32. ¹³C NMR (101 MHz) spectrum for compound 3q in DMSO- d_6 .





Figure 33. ¹H NMR (400 MHz) spectrum for compound 3r in DMSO- d_6 .

Figure 34. ¹³C NMR (101 MHz) spectrum for compound 3r in DMSO- d_6 .