Supplementary Information

Rhodium-Catalyzed Synthesis of Multi-substituted Furans from N-sulfonyl-1,2,3-triazoles Bearing Tethered Carbonyl Group

Wen-Biao Zhang, Shi-Dong Xiu and Chuan-Ying Li*

Department of Chemistry, Zhejiang Sci-Tech University, Xiasha West Higher Education District, Hangzhou 310018, China.

E-mail: licy@zstu.edu.cn

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1. General information

Analytical thin layer chromatography (TLC) was performed using Silica Gel HSGF254 pre-coated plates. Flash column chromatography was performed using 200 - 300 Mesh Silica Gel. Proton nuclear magnetic resonance (1H-NMR) spectra were recorded using Brucker Avance II DMX 400MHz spectrometers. Chemical shift (δ) is reported in parts per million (ppm) downfield relative to tetramethylsilane (TMS, 0.0 ppm) or CDCl3 (7.26 ppm). Coupling constants (J) are reported in Hz. Multiplicities are reported using the following abbreviations: s, singlet; d, doublet; t, triplet; q, quartet; m, multiplet; br, broad; Carbon-13 nuclear magnetic resonance (13C-NMR) spectra were recorded using a Brucker Avance II DMX 400 spectrometer at 100 MHz. Chemical shift is reported in ppm relative to the carbon resonance of CDCl3 (77.00 ppm). High resolution mass spectra (HRMS) were obtained by Mass Spectrometry Core Laboratory of Zhejiang University, and are reported as m/e (relative ratio). Accurate masses are reported for the molecular ion (M+) or a suitable fragment ion.

2. Procedures and spectra data of N-sulfonyl-1,2,3-triazoles

Compounds 1a-1n were synthesized by the same procedures as shown in Scheme S1.

Scheme S1

\[
\begin{align*}
\text{R}^1\text{C}=\text{O} & \xrightarrow{\text{Br} & \text{NaOEt}} \text{R}^1\text{C}=\text{O} \xrightarrow{\text{NaOH, RT-60 \degree C}} \text{R}^1\text{C}=\text{O} \\
\text{R}^2 & \xrightarrow{\text{N}_3-\text{R}^4} \xrightarrow{\text{CuTc, toluene}} \xrightarrow{\text{HCl, pH = 4}} \end{align*}
\]

In a mixture of ketone ester (30 mmol) and 50 mL of anhydrous ethanol 0.76 g (33 mmol) of sodium was dissolved. Propargyl bromide (3.76 mL, 80 wt% solution in toluene, 33 mmol) was added dropwise at 0 °C within 20 min. The mixture was stirred at ambient temperature for 24 h. Then the sodium bromide was filtered off, and the solvent removed under vacuum in a rotatory
evaporator. To the residue was added 12 mL (30 mmol) of 10% aq. sodium hydroxide, and the mixture was stirred at ambient temperature for 2 h and at 60 °C for 3 h. The mixture was cooled to ambient temperature, acidified with conc. hydrochloric acid to a pH of 4 and extracted with diethyl ether (3×30 mL). The organic phase was washed with 50 mL each of saturated sodium hydrogen carbonate solution and water, and then dried over MgSO₄. The ether was distilled off in a rotatory evaporator. The obtained crude product was purified by SiO₂-column chromatography (PE: EA = 40:1) to give the alkyne [1].

A flask was charged with copper (I) thiophene-2-carboxylate (CuTC, 0.095 g, 0.5 mmol, 0.1 equiv in regards to alkyne), toluene (20 mL), and the alkyne (5.0 mmol, 1 equiv). The reaction mixture was cooled in an ice-water bath. Subsequently, the sulfonyl azide (5.0 mmol, 1 equiv) was added slowly as the limiting reagent to avoid a run-away exotherm, and the reaction mixture allowed to warm to room temperature and stirred overnight. The mixture was filtered rapidly through a funnel with a thin layer of silica gel and eluted with ethyl acetate, and the solvent was removed in vacuo. The obtained crude product was purified by SiO₂-column chromatography (PE: EA = 3:1) to give the desired product [2].

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\text{1a}
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1-(1-tosyl-1H-1,2,3-triazol-4-yl)hexan-3-one (1a): White solid, mp 56.8 – 57.6 °C; ¹H NMR (400 MHz, Chloroform-d) δ 7.90 (d, J = 8.4 Hz, 2H), 7.82 (s, 1H), 7.30 (d, J = 8.4 Hz, 2H), 2.90 (t, J = 7.0 Hz, 2H), 2.76 (t, J = 7.0 Hz, 2H), 2.38 (s, 3H), 2.30 (t, J = 7.2 Hz, 2H), 1.61 – 1.37 (m, 3H), 0.80 (t, J = 7.4 Hz, 3H); ¹³C NMR (100 MHz, Chloroform-d) δ 209.3, 147.1, 146.7, 133.2, 130.3, 128.5, 121.1, 44.7, 41.1, 21.8, 19.2, 17.2, 13.6; HRMS (EI) calculated for C₁₅H₁₉N₃O₃S (M⁺): 321.1147, found: 321.1141.

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\text{1b}
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1-(1-((4-bromophenyl)sulfonyl)-1H-1,2,3-triazol-4-yl)hexan-3-one (1b): White solid, mp 85.6 – 87.4 °C; ¹H NMR (400 MHz, Chloroform-d) δ 8.03 – 7.87 (m, 3H), 7.73 (d, J = 8.8 Hz, 2H),
2.98 (t, J = 6.8 Hz, 2H), 2.84 (t, J = 6.8 Hz, 2H), 2.38 (t, J = 7.4 Hz, 2H), 1.62 – 1.52 (m, 2H), 0.86 (t, J = 7.4 Hz, 3H); 
$^{13}$C NMR (100 MHz, Chloroform-d) δ 209.1, 146.9, 135.1, 133.1, 131.2, 129.8, 121.2, 44.6, 40.9, 19.1, 17.1, 13.5; HRMS (El) calculated for C$_{14}$H$_{16}$BrN$_{3}$O$_{3}$S (M$^+$): 385.0096, found: 385.0089.

$^{13}$C NMR (100 MHz, Chloroform-d) δ 209.2, 165.2, 146.5, 131.0, 127.1, 120.9, 114.9, 55.9, 44.6, 41.0, 19.2, 17.1, 13.6; HRMS (El) calculated for C$_{15}$H$_{19}$N$_{3}$O$_{4}$S (M$^+$): 337.1096, found: 337.1092.

1-(1-((4-methoxyphenyl)sulfonyl)-1H-1,2,3-triazol-4-yl)hexan-3-one (1c): White solid, mp 74.2 – 75.7°C; 
$^1$H NMR (400 MHz, Chloroform-d) δ 8.02 (d, J = 9.0 Hz, 2H), 7.88 (s, 1H), 7.02 (d, J = 9.0 Hz, 2H), 3.88 (s, 3H), 2.97 (t, J = 6.9 Hz, 2H), 2.83 (t, J = 6.9 Hz, 2H), 2.37 (t, J = 7.3 Hz, 2H), 1.69 – 1.47 (m, 2H), 0.87 (t, J = 7.4 Hz, 3H); 
$^{13}$C NMR (100 MHz, Chloroform-d) δ 209.2, 165.2, 146.5, 131.0, 127.1, 120.9, 114.9, 55.9, 44.6, 41.0, 19.2, 17.1, 13.6; HRMS (El) calculated for C$_{15}$H$_{19}$N$_{3}$O$_{4}$S (M$^+$): 337.1096, found: 337.1092.

1-(1-(naphthalen-2-ylsulfonyl)-1H-1,2,3-triazol-4-yl)hexan-3-one (1d): White solid, mp 85.1 – 86.8 °C; 
$^1$H NMR (400 MHz, Chloroform-d) δ 8.63 (s, 1H), 8.00 – 7.76 (m, 5H), 7.65 – 7.55 (m, 2H), 2.89 (t, J = 6.9 Hz, 2H), 2.73 (t, J = 6.9 Hz, 2H), 2.26 (t, J = 7.3 Hz, 2H), 1.62 – 1.48 (m, 2H), 0.75 (t, J = 7.4 Hz, 3H); 
$^{13}$C NMR (100 MHz, Chloroform-d) δ 209.3, 135.9, 132.9, 131.8, 131.0, 130.4, 130.2, 129.7, 128.2, 128.0, 122.1, 121.3, 44.6, 41.0, 19.2, 17.2, 13.6; HRMS (El) calculated for C$_{18}$H$_{19}$N$_{3}$O$_{3}$S (M$^+$): 357.1147, found: 357.1151.
1-(1-((2-(trimethylsilyl)ethyl)sulfonyl)-1H-1,2,3-triazol-4-yl)hexan-3-one (1e): White solid, mp 78.5 - 79.7 °C; $^1$H NMR (400 MHz, Chloroform-d) $\delta$ 7.88 (s, 1H), 3.56 – 3.42 (m, 2H), 3.05 (t, $J$ = 6.9 Hz, 2H), 2.90 (t, $J$ = 6.9 Hz, 2H), 2.41 (t, $J$ = 7.3 Hz, 2H), 1.65 – 1.58 (m, 2H), 1.02 – 0.84 (m, 5H), 0.05 (s, 9H); $^{13}$C NMR (100 MHz, Chloroform-d) $\delta$ 209.2, 146.5, 122.0, 52.5, 44.7, 41.0, 19.2, 17.2, 13.6, 9.6, -2.2; HRMS (EI) calculated for C$_{13}$H$_{25}$N$_3$O$_3$SSi (M$^+$): 331.1386, found: 331.1382.

1-(1-((2,4,6-triisopropylphenyl)sulfonyl)-1H-1,2,3-triazol-4-yl)hexan-3-one (1f): White solid, mp 93.4 – 95.6 °C; $^1$H NMR (400 MHz, Chloroform-d) $\delta$ 7.96 (s, 1H), 7.22 (s, 2H), 4.15 – 4.08 (m, 2H), 3.01 (t, $J$ = 6.9 Hz, 2H), 2.96 – 2.88 (m, 1H), 2.85 (t, $J$ = 6.9 Hz, 2H), 2.38 (t, $J$ = 7.3 Hz, 2H), 1.61 – 1.55 (m, 2H), 1.25 (d, $J$ = 6.8 Hz, 6H), 1.19 (d, $J$ = 6.8 Hz, 12H), 0.89 (t, $J$ = 7.4 Hz, 3H); $^{13}$C NMR (100 MHz, Chloroform-d) $\delta$ 209.1, 156.0, 152.8, 146.2, 129.0, 124.6, 120.2, 44.7, 41.2, 34.3, 29.9, 24.5, 23.3, 19.2, 17.2, 13.6; HRMS (EI) calculated for C$_{23}$H$_{35}$N$_3$O$_3$S (M$^+$): 433.2399, found: 433.2394.

4-(1-tosyl-1H-1,2,3-triazol-4-yl)butan-2-one (1g): White solid, mp 45.4 – 46.7 °C; $^1$H NMR (400 MHz, Chloroform-d) $\delta$ 7.97 (d, $J$ = 8.4 Hz, 2H), 7.91 (s, 1H), 7.38 (d, $J$ = 8.4 Hz, 2H), 2.96 (t, $J$ = 6.9 Hz, 2H), 2.87 (t, $J$ = 6.9 Hz, 2H), 2.45 (s, 3H), 2.15 (s, 3H); $^{13}$C NMR (100 MHz, Chloroform-d) $\delta$ 206.8, 147.1, 146.5, 133.1, 130.3, 128.6, 121.1, 41.9, 29.9, 21.8, 19.2; HRMS (EI) calculated for C$_{13}$H$_{15}$N$_3$O$_3$S (M$^+$): 293.0834, found: 293.0827.
4-methyl-1-(1-tosyl-1H-1,2,3-triazol-4-yl)pentan-3-one (1h): White solid, mp 52.1 – 54.2 °C; \(^1\)H NMR (400 MHz, Chloroform-d) \(\delta\) 7.96 (d, \(J = 8.4\) Hz, 2H), 7.89 (s, 1H), 7.37 (d, \(J = 8.4\) Hz, 2H), 2.97 (t, \(J = 6.8\) Hz, 2H), 2.88 (t, \(J = 6.8\) Hz, 2H), 2.61 – 2.54 (m, 1H) 2.44 (s, 3H), 1.05 (d, \(J = 9.2\) Hz, 6H); \(^{13}\)C NMR (100 MHz, Chloroform-d) \(\delta\) 212.9, 147.1, 146.7, 133.2, 130.3, 128.5, 121.1, 40.8, 38.8, 21.7, 19.3, 18.1; HRMS (EI) calculated for C\(_{15}\)H\(_{16}\)N\(_3\)O\(_3\)S (M\(^+\)): 321.1147, found: 321.1154.

1-phenyl-3-(1-tosyl-1H-1,2,3-triazol-4-yl)propan-1-one (1i): White solid, mp 103.7– 104.5 °C; \(^1\)H NMR (400 MHz, Chloroform-d) \(\delta\) 7.99 – 7.79 (m, 5H), 7.57 – 7.25 (m, 5H), 3.34 (t, \(J = 7.0\) Hz, 2H), 3.09 (t, \(J = 7.0\) Hz, 2H), 2.36 (s, 3H); \(^{13}\)C NMR (100 MHz, Chloroform-d) \(\delta\) 198.3, 147.1, 146.7, 136.5, 133.3, 130.4, 128.7, 128.6, 128.0, 121.3, 37.4, 21.8, 19.6; HRMS (EI) calculated for C\(_{18}\)H\(_{17}\)N\(_3\)O\(_3\)S (M\(^+\)): 355.0991, found: 355.0988.

1-(4-methoxyphenyl)-3-(1-tosyl-1H-1,2,3-triazol-4-yl)propan-1-one (1j): White solid, mp 128.1 – 129.7 °C; \(^1\)H NMR (400 MHz, Chloroform-d) \(\delta\) 8.04 – 7.81 (m, 5H), 7.36 (d, \(J = 8.3\) Hz, 2H), 6.91 (d, \(J = 8.8\) Hz, 2H), 3.86 (s, 3H), 3.35 (t, \(J = 7.0\) Hz, 2H), 3.14 (t, \(J = 7.0\) Hz, 2H), 2.43 (s, 3H); \(^{13}\)C NMR (100 MHz, Chloroform-d) \(\delta\) 196.8, 163.6, 147.0, 146.9, 133.2, 130.3, 129.6, 128.5, 126.4, 121.3, 113.7, 55.4, 37.0, 21.7, 19.7; HRMS (EI) calculated for C\(_{19}\)H\(_{19}\)N\(_3\)O\(_4\)S (M\(^+\)): 385.1096, found: 385.1091.
1-(4-bromophenyl)-3-(1-tosyl-1H-1,2,3-triazol-4-yl)propan-1-one (1k): White solid, mp 129.6 – 130.8 ºC; 1H NMR (400 MHz, Chloroform-d) δ 7.98 – 7.96 (m, 3H), 7.80 (d, J = 8.6 Hz, 2H), 7.59 (d, J = 8.6 Hz, 2H), 7.37 (d, J = 8.2 Hz, 2H), 3.38 (t, J = 6.9 Hz, 2H), 3.15 (t, J = 6.9 Hz, 2H), 2.44 (s, 3H); 13C NMR (100 MHz, Chloroform-d) δ 197.3, 135.2, 133.1, 131.9, 130.4, 129.7, 129.5, 128.6, 128.5, 126.4, 121.3, 37.3, 21.8, 19.5; HRMS (EI) calculated for C18H15BrN3O3S (M⁺): 433.0096, found: 433.0091.

1-(thiophen-2-yl)-3-(1-tosyl-1H-1,2,3-triazol-4-yl)propan-1-one (1l): Pale yellow solid, mp 120.4 – 122.0 ºC; 1H NMR (400 MHz, Chloroform-d) δ 7.98 – 7.96 (m, 3H), 7.70 (d, J = 3.8 Hz, 1H), 7.63 (d, J = 4.9 Hz, 1H), 7.37 (d, J = 8.2 Hz, 2H), 7.18 – 6.97 (m, 1H), 3.35 (t, J = 7.0 Hz, 2H), 3.16 (t, J = 7.0 Hz, 2H), 2.44 (s, 3H); 13C NMR (100 MHz, Chloroform-d) δ 191.2, 147.1, 146.4, 143.6, 133.8, 133.1, 132.1, 130.4, 128.6, 128.2, 121.3, 37.9, 21.8, 19.7; HRMS (EI) calculated for C16H15N3O3S2 (M⁺): 361.0555, found: 361.0558.

3-methyl-4-(1-tosyl-1H-1,2,3-triazol-4-yl)butan-2-one (1m): colorless oil; 1H NMR (400 MHz, Chloroform-d) δ 7.96 (d, J = 8.4 Hz, 2H), 7.91 (s, 1H), 7.38 (d, J = 8.4 Hz, 2H), 3.27 – 2.91 (m, 2H), 2.85 – 2.59 (m, 1H), 2.44 (s, 3H), 2.14 (s, 3H), 1.15 (d, J = 7.2 Hz, 3H); 13C NMR (100 MHz, Chloroform-d) δ 210.8, 147.1, 145.5, 133.0, 130.3, 128.4, 121.4, 46.1, 28.3, 27.6, 21.6, 16.5; HRMS (EI) calculated for C14H17N3O3S (M⁺): 307.0991, found: 307.0999.
1n

3-benzyl-4-(1-tosyl-1H-1,2,3-triazol-4-yl)butan-2-one (1n): colorless oil; $^1$H NMR (400 MHz, Chloroform-d) $\delta$ 7.94 (d, $J = 8.3$ Hz, 2H), 7.79 (s, 1H), 7.46 – 7.01 (m, 7H), 3.37 – 3.18 (m, 1H), 3.10 – 2.84 (m, 2H), 2.84 – 2.58 (m, 2H), 2.43 (s, 3H), 1.93 (s, 3H); $^{13}$C NMR (100 MHz, Chloroform-d) $\delta$ 210.9, 147.1, 145.2, 138.3, 133.1, 130.3, 128.8, 128.6, 128.5, 126.7, 121.3, 53.1, 38.1, 30.6, 26.4, 21.7; HRMS (EI) calculated for C$_{20}$H$_{21}$N$_3$O$_3$S (M$^+$): 383.1304, found: 383.1312.

Compound 1o was synthesized by the procedures as shown in Scheme S2.

Scheme S2

To a solution of diisopropylamine (2.8 mL, 20 mmol) in THF (30 mL) cooled to -78 °C was added $n$-BuLi (12.5 mL, 1.6 M solution in hexanes, 20 mmol) under argon. The solution was warmed to 0 °C and stirred at this temperature for 30 min. After cooling to -78 °C, cyclohexanone (2.1 mL, 20 mmol) was added slowly and stirred 1 h. HMPA (0.4 mL) was then added to the solution and stirring was continued for 10 min. Propargyl bromide (2.28 mL, 80 wt% solution in toluene, 20 mmol) that has been dried over MgSO$_4$ was then added slowly. After 2 h at this temperature, the reaction was warmed to 0 °C and stirred an additional 2 h. The crude reaction mixture was then quenched with aqueous NH$_4$Cl and extracted with ether. The organic fractions were dried over MgSO$_4$, and the solvent was removed in vacuo.$^{[3]}$ The crude product was distilled (64 °C at 1 mmHg) to yield 1.36 g (51%) of 2-prop-2-ynyl-cyclohexanone.

A 100-mL Erlenmeyer flask was charged with CuTC (0.19 g, 1 mmol) and dry toluene (50 mL). Subsequently, alkyne (1.36 g, 10 mmol) then tosyl azide (1.55 mL, 10 mmol) were added
and the reaction mixture allowed to warm to room temperature and stirred overnight. The mixture was filtered rapidly through a funnel with a thin layer of silica gel and eluted with ethyl acetate, and the solvent was removed in vacuo. The obtained crude product was purified by SiO$_2$-column chromatography (PE: EA = 4:1) to give 10 (2.67 g, 83% yield) as a pale yellow oil.

2-((1-tosyl-1H-1,2,3-triazol-4-yl)methyl)cyclohexanone (10): pale yellow oil; $^1$H NMR (400 MHz, Chloroform-d) $\delta$ 7.98 (d, $J$ = 8.3 Hz, 2H), 7.93 (s, 1H), 7.37 (d, $J$ = 8.3 Hz, 2H), 3.13 (dd, $J$ = 5.8, 14.8 Hz, 1H), 2.78 – 2.69 (m, 1H), 2.62 (dd, $J$ = 5.8, 14.8 Hz, 1H), 2.45 (s, 3H), 2.36 – 2.03 (m, 4H), 1.93 – 1.58 (m, 2H), 1.42– 1.26 (m, 2H); $^{13}$C NMR (100 MHz, Chloroform-d) $\delta$ 211.7, 147.0, 146.0, 133.2, 130.3, 128.6, 121.9, 50.3, 42.1, 34.1, 28.0, 25.4, 25.1, 21.8; HRMS (EI) calculated for C$_{16}$H$_{19}$N$_3$O$_3$S (M$^+$): 333.1147, found: 333.1142.

Compound 1p was synthesized by the procedures as shown in Scheme S3.

Scheme S3 Synthesis of compound 1p

A mixture of Co(OAc)$_2$·4H$_2$O (185 mg, 0.75 mmol), dppe (300 mg, 0.75 mmol), Zn powder (98 mg, 1.5 mmol), enone (3.0 mmol), and (triisopropylsilyl)acetylene (1.35 mL, 6.0 mmol) in DMSO (10 mL) was stirred at 80 °C for 20 h under N$_2$. The mixture was passed through a short column of silica gel with diethyl ether as eluent. After evaporation of the solvent, the obtained crude product was purified by SiO$_2$-column chromatography (PE: EA = 100:1) to give the alkyne $^{[4]}$. To a solution of the alkyne (0.82 g, 2.5 mmol) in THF (40 mL) was added tetrabutylammonium fluoride solution (3.0 mL, 1.0 M in THF) at 0 °C, and the mixture was stirred at room temperature for 2 h. The mixture was quenched with H$_2$O and extracted with ethyl
acetate. The combined organic layer was washed with brine, dried over MgSO₄, filtered, and concentrated on a rotary evaporator. The residue was subjected to a column chromatography on silica gel (PE: EA = 80:1) to give 3-methyl-1-phenylpent-4-yn-1-one.

A flask was charged with copper (I) thiophene-2-carboxylate (CuTC, 38mg, 0.2 mmol, 0.1 equiv in regards to alkyne), toluene (10 mL), and the alkyne (2.0 mmol, 1 equiv). The reaction mixture was cooled in an ice-water bath. Subsequently, the sulfonyl azide (2.0 mmol, 1 equiv) was added slowly as the limiting reagent to avoid a run-away exotherm, and the reaction mixture allowed to warm to room temperature and stirred overnight. The mixture was filtered rapidly through a funnel with a thin layer of silica gel and eluted with ethyl acetate, and the solvent was removed in vacuo. The obtained crude product was purified by SiO₂-column chromatography (PE: EA = 3:1) to give the desired product.

\[ \text{1p: colorless oil, } ^1\text{H NMR (400 MHz, Chloroform-d)} \delta 7.97 - 7.91 \text{ (m, 5H), 7.55 -7.52 \text{ (m, 1H), 7.42 (t, } J = 8.0 \text{ Hz, 2H), 7.35 (d, } J = 8.0 \text{ Hz, 2H), 3.73 - 3.68 \text{ (m, 1H), 3.55 (dd, } J = 6.4, 17.6 \text{ Hz, 1H), 3.19 (dd, } J = 6.4, 17.6 \text{ Hz, 1H), 2.42 (s, 3H), 1.39 (d, } J = 6.8 \text{ Hz, 3H); } ^{13}\text{C NMR (100 MHz, Chloroform-d)} \delta 198.0, 151.7, 147.0, 136.6, 133.1, 130.3, 128.5, 127.8, 120.2, 44.6, 26.5, 21.7, 19.9; \text{ HRMS (EI) calculated for } C_{19}H_{19}N_{3}O_{3}S(M^+) : 369.1147, \text{ found: 369.1142.} \]

3. Synthesis of furans

3.1. Synthesis of compounds 2a-2d and 2f-2n

A mixture of N-sulfonyl-1,2,3-triazoles (0.2 mmol), Rh₂(esp)₂ (1.5 mg, 1 mol %) and DCE (2 mL) was stirred under a nitrogen atmosphere at 100 ºC. After completion of the reaction (monitored by TLC), the resulting mixture was filtered rapidly through a funnel with a thin layer of silica gel and eluted with ethyl acetate. The filtrate was concentrated and the residue was purified by chromatography on silica gel (PE: EA = 5:1) to afford the desired products.
Synthesis of compounds 2e and 2o

A mixture of N-sulfonyl-1,2,3-triazoles (0.2 mmol), Rh$_2$(OAc)$_4$ (0.9 mg, 1 mol %) and DCE (2 mL) was stirred under a nitrogen atmosphere at 100 °C. After completion of the reaction (monitored by TLC), the resulting mixture was filtered rapidly through a funnel with a thin layer of silica gel and eluted with ethyl acetate. The filtrate was concentrated and the residue was purified by chromatography on silica gel (PE: EA = 4:1) to afford the desired products.

**2a**

4-methyl-N-((5-propylfuran-2-yl)methyl)benzenesulfonamide (2a): White solid, yield: 89%; mp 82.5 – 83.6 °C; $^1$H NMR (400 MHz, Chloroform-d) $\delta$ 7.71 (d, $J = 8.3$ Hz, 2H), 7.26 (d, $J = 8.3$ Hz, 2H), 5.96 (d, $J = 3.0$ Hz, 1H), 5.78 (d, $J = 3.0$ Hz, 1H), 4.92 (t, $J = 5.8$ Hz, 1H), 4.12 (d, $J = 5.8$ Hz, 2H), 2.60 – 2.28 (m, 5H), 1.73 – 1.37 (m, 2H), 0.90 (t, $J = 7.4$ Hz, 3H); $^{13}$C NMR (100 MHz, Chloroform-d) $\delta$ 156.5, 147.4, 143.2, 137.0, 129.5, 127.1, 108.8, 105.4, 40.2, 29.8, 21.4, 21.1, 13.6; HRMS (EI) calculated for C$_{15}$H$_{19}$NO$_3$S (M$^+$): 293.1086, found: 293.1088.

**2b**

4-bromo-N-((5-propylfuran-2-yl)methyl)benzenesulfonamide (2b): White solid, yield: 92%; mp 82.7 – 83.8 °C; $^1$H NMR (400 MHz, Chloroform-d) $\delta$ 7.66 (d, $J = 8.7$ Hz, 2H), 7.58 (d, $J = 8.7$ Hz, 2H), 5.97 (d, $J = 2.9$ Hz, 1H), 5.75 (d, $J = 2.9$ Hz, 1H), 5.08 (t, $J = 5.8$ Hz, 1H), 4.16 (d, $J = 5.8$ Hz, 2H), 2.38 (t, $J = 7.5$ Hz, 2H), 1.55 – 1.48 (m, 2H), 0.90 (t, $J = 7.4$ Hz, 3H); $^{13}$C NMR (100 MHz, Chloroform-d) $\delta$ 156.5, 147.0, 139.3, 132.1, 128.6, 127.3, 109.2, 105.3, 40.2, 29.8, 21.1, 13.7; HRMS (EI) calculated for C$_{14}$H$_{18}$BrNO$_3$S (M$^+$): 357.0034, found: 357.0032.

**2c**

4-methoxy-N-((5-propylfuran-2-yl)methyl)benzenesulfonamide (2c): White solid, yield: 73%; mp 92.1 – 93.4 °C; $^1$H NMR (400 MHz, Chloroform-d) $\delta$ 7.76 (d, $J = 8.9$ Hz, 2H), 6.93 (d, $J =
8.9 Hz, 2H), 5.96 (d, J = 2.9 Hz, 1H), 5.78 (d, J = 2.9 Hz, 1H), 4.88 (t, J = 5.8 Hz, 1H), 4.11 (d, J = 5.8 Hz, 2H), 3.85 (s, 3H), 2.42 (t, J = 7.5 Hz, 2H), 1.57 – 1.51 (m, 2H), 0.90 (t, J = 7.4 Hz, 3H); \(^{13}\)C NMR (100 MHz, Chloroform-d) \(\delta\) 162.8, 156.5, 147.4, 131.8, 129.2, 114.0, 108.7, 105.4, 55.5, 40.2, 29.8, 21.1, 13.6; HRMS (EI) calculated for C\(_{15}\)H\(_{19}\)NO\(_4\)S (M\(^+\)): 309.1035, found: 309.1035.

![2d](attachment:image)

\(N\)-((5-propylfuran-2-yl)methyl)naphthalene-2-sulfonamide (2d): colorless oil, 67%; \(^1\)H NMR (400 MHz, Chloroform-d) \(\delta\) 8.39 (s, 1H), 7.94 – 7.87 (m, 3H), 7.79 (d, J = 7.3 Hz, 1H), 7.65 – 7.57 (m, 2H), 5.95 (d, J = 2.9 Hz, 1H), 5.67 (d, J = 2.9 Hz, 1H), 4.97 (t, J = 5.8 Hz, 1H), 4.19 (d, J = 5.8 Hz, 2H), 2.22 (t, J = 7.5 Hz, 2H), 1.40 – 1.34 (m, 2H), 0.79 (t, J = 7.4 Hz, 3H); \(^{13}\)C NMR (100 MHz, Chloroform-d) \(\delta\) 156.6, 147.2, 136.9, 134.8, 132.1, 129.2, 128.7, 128.5, 127.8, 127.4, 122.3, 109.0, 105.3, 40.3, 29.7, 21.0, 13.6; HRMS (EI) calculated for C\(_{18}\)H\(_{19}\)NO\(_3\)S (M\(^+\)): 329.1086, found: 329.1089.

![2e](attachment:image)

\(N\)-((5-propylfuran-2-yl)methyl)-2-(trimethylsilyl)ethanesulfonamide (2e): colorless oil, yield: 72%; \(^1\)H NMR (400 MHz, Chloroform-d) \(\delta\) 6.22 (d, J = 2.9 Hz, 1H), 5.98 (d, J = 2.9 Hz, 1H), 4.82 (t, J = 5.8 Hz, 1H), 4.31 (d, J = 5.8 Hz, 2H), 2.98 – 2.83 (m, 2H), 2.62 (t, J = 7.5 Hz, 2H), 1.73 – 1.68 (m, 2H), 1.07 – 0.88 (m, 5H), 0.05 (s, 9H); \(^{13}\)C NMR (100 MHz, Chloroform-d) \(\delta\) 156.8, 148.4, 108.9, 105.6, 49.5, 40.0, 30.0, 21.3, 13.7, 10.3, -2.1; HRMS (EI) calculated for C\(_{13}\)H\(_{25}\)NO\(_3\)SSi (M\(^+\)): 303.1324, found: 303.1328.
2,4,6-triisopropyl-N-((5-propylfuran-2-yl)methyl)benzenesulfonamide (2f): colorless oil, yield: 69%; \(^1\)H NMR (400 MHz, Chloroform-d) \(\delta\) 7.15 (s, 2H), 5.93 (d, \(J = 2.9\) Hz, 1H), 5.78 (d, \(J = 2.9\) Hz, 1H), 4.66 (t, \(J = 5.8\) Hz, 1H), 4.27 – 4.02 (m, 4H), 2.99 – 2.77 (m, 1H), 2.41 (t, \(J = 7.5\) Hz, 2H), 1.56 – 1.51 (m, 2H), 1.25 (d, \(J = 6.9\) Hz, 18H), 0.89 (t, \(J = 7.4\) Hz, 3H); \(^{13}\)C NMR (101 MHz, Chloroform-d) \(\delta\) 156.5, 152.6, 150.2, 147.6, 132.4, 123.7, 108.8, 105.5, 40.0, 34.1, 29.9, 29.6, 24.7, 23.5, 21.1, 13.6; HRMS (EI) calculated for C\(_{23}\)H\(_{35}\)NO\(_3\)S (M\(^+\)): 405.2338, found: 405.2340.

\[\begin{align*}
\text{2f} & \hspace{1cm} \text{O} \\
\text{N} & \\
\text{T}\text{s} & \\
\text{2h} & \\
\end{align*}\]

4-methyl-N-((5-methylfuran-2-yl)methyl)benzenesulfonamide (2g): White solid, yield: 78%; \(^1\)H NMR (400 MHz, Chloroform-d) \(\delta\) 7.71 (d, \(J = 8.2\) Hz, 2H), 7.27 (d, \(J = 8.2\) Hz, 2H), 5.96 (d, \(J = 2.7\) Hz, 1H), 5.77 (d, \(J = 2.7\) Hz, 1H), 4.82 (t, \(J = 5.8\) Hz, 1H), 4.11 (d, \(J = 5.8\) Hz, 2H), 2.41 (s, 3H), 2.13 (s, 3H); \(^{13}\)C NMR (100 MHz, Chloroform-d) \(\delta\) 152.2, 147.5, 143.3, 137.0, 129.5, 127.1, 109.0, 106.1, 40.2, 21.5, 13.3.

\[\begin{align*}
\text{2g} & \hspace{1cm} \text{O} \\
\text{N} & \\
\text{T}\text{s} & \\
\text{2i} & \\
\end{align*}\]

N-((5-isopropylfuran-2-yl)methyl)-4-methylbenzenesulfonamide (2h): White solid, yield: 77%; mp 98.1 – 100.4 \(^\circ\)C; \(^1\)H NMR (400 MHz, Chloroform-d) \(\delta\) 7.71 (d, \(J = 8.2\) Hz, 2H), 7.26 (d, \(J = 8.2\) Hz, 2H), 5.96 (d, \(J = 2.9\) Hz, 1H), 5.75 (d, \(J = 2.9\) Hz, 1H), 4.94 (t, \(J = 5.8\) Hz, 1H), 4.13 (d, \(J = 5.8\) Hz, 2H), 2.87 – 2.62 (m, 1H), 2.40 (s, 3H), 1.13 (d, \(J = 6.9\) Hz, 6H); \(^{13}\)C NMR (100 MHz, Chloroform-d) \(\delta\) 161.9, 147.3, 143.2, 137.1, 129.5, 127.1, 108.6, 103.3, 40.3, 27.6, 21.4, 20.9; HRMS (EI) calculated for C\(_{15}\)H\(_{19}\)NO\(_3\)S (M\(^+\)): 293.1086, found: 293.1083.

\[\begin{align*}
\text{2h} & \hspace{1cm} \text{O} \\
\text{N} & \\
\text{T}\text{s} & \\
\text{2i} & \\
\end{align*}\]

4-methyl-N-((5-phenylfuran-2-yl)methyl)benzenesulfonamide (2i): White solid, yield: 60%;
mp 132.3 – 133.5 °C; \(^1\)H NMR (400 MHz, Chloroform-d) \(\delta\) 7.70 (d, \(J = 8.2\) Hz, 2H), 7.46 (d, \(J = 7.4\) Hz, 2H), 7.35 – 7.31 (m, 2H), 7.26 – 7.18 (m, 3H), 6.43 (d, \(J = 3.2\) Hz, 1H), 6.17(d, \(J = 3.2\) Hz, 1H), 5.05 (t, \(J = 6.1\) Hz, 1H), 4.24 (d, \(J = 6.1\) Hz, 2H), 2.29 (s, 3H); \(^1^3\)C NMR (100 MHz, Chloroform-d) \(\delta\) 153.9, 149.0, 143.4, 137.0, 130.3, 129.5, 128.5, 127.4, 127.0, 123.6, 110.4, 105.5, 40.3, 21.3; HRMS (EI) calculated for C\(_{18}\)H\(_{17}\)NO\(_3\)S (M\(^+\)): 327.0929, found: 327.0926.

\(N\)-((5-(4-methoxyphenyl)furan-2-yl)methyl)-4-methylbenzenesulfonamide (2j): White solid, yield: 54%; mp 115.4 – 116.7 °C; \(^1\)H NMR (400 MHz, Chloroform-d) \(\delta\) 7.71 (d, \(J = 8.2\) Hz, 2H), 7.40 (d, \(J = 8.8\) Hz, 2H), 7.21 (d, \(J = 8.2\) Hz, 2H), 6.87 (d, \(J = 8.8\) Hz, 2H), 6.29 (d, \(J = 3.2\) Hz, 1H), 6.13 (d, \(J = 3.2\) Hz, 1H), 4.96 (t, \(J = 6.0\) Hz, 1H), 4.23 (d, \(J = 6.0\) Hz, 2H), 3.82 (s, 3H), 2.32 (s, 3H); \(^1^3\)C NMR (100 MHz, Chloroform-d) \(\delta\) 159.1, 154.0, 148.2, 143.4, 137.0, 129.6, 127.0, 125.1, 123.4, 114.0, 110.3, 103.9, 55.3, 40.3, 21.4; HRMS (EI) calculated for C\(_{19}\)H\(_{19}\)NO\(_4\)S (M\(^+\)): 357.1035, found: 357.1031.

\(N\)-((5-(4-bromophenyl)furan-2-yl)methyl)-4-methylbenzenesulfonamide (2k): White solid, yield: 61%; mp 165.1 – 166.3 °C; \(^1\)H NMR (400 MHz, Chloroform-d) \(\delta\) 7.70 (d, \(J = 8.0\) Hz, 2H), 7.45 (d, \(J = 8.4\) Hz, 2H), 7.33 (d, \(J = 8.4\) Hz, 2H), 7.20 (d, \(J = 8.0\) Hz, 2H), 6.44 (d, \(J = 2.9\) Hz, 1H), 6.18 (d, \(J = 2.9\) Hz, 1H), 5.01 (t, \(J = 6.0\) Hz, 1H), 4.24 (d, \(J = 6.0\) Hz, 2H), 2.31 (s, 3H); \(^1^3\)C NMR (100 MHz, Chloroform-d) \(\delta\) 152.9, 149.5, 143.4, 137.0, 131.7, 132.2, 129.6, 127.0, 125.1, 121.2, 110.5, 106.1, 40.3, 21.4; HRMS (EI) calculated for C\(_{18}\)H\(_{16}\)BrNO\(_3\)S (M\(^+\)): 405.0034, found: 405.0033.
4-methyl-N-((5-(thiophen-2-yl)furan-2-yl)methyl)benzenesulfonamide (2l): Pale yellow solid, yield: 50%; mp 104.5 – 105.8 °C; $^1$H NMR (400 MHz, Chloroform-d) $\delta$ 7.70 (d, $J = 8.1$ Hz, 2H), 7.25 – 7.17 (m, 3H), 7.11 – 7.08 (m, 1H), 7.03 – 6.96 (m, 1H), 6.28 (d, $J = 3.0$ Hz, 1H), 6.13 (d, $J = 3.0$ Hz, 1H), 4.88 (t, $J = 6.0$ Hz, 1H), 4.22 (d, $J = 6.0$ Hz, 2H), 2.33 (s, 3H); $^{13}$C NMR (100 MHz, Chloroform-d) $\delta$ 149.4, 148.6, 143.4, 136.9, 133.1, 129.6, 127.5, 127.0, 124.3, 122.7, 110.4, 105.5, 40.2, 21.4; HRMS (EI) calculated for C$_{16}$H$_{15}$NO$_3$S$_2$ (M$^+$): 333.0493, found: 333.0493.

N-((4,5-dimethylfuran-2-yl)methyl)-4-methylbenzenesulfonamide (2m): White solid, yield: 66%; mp 74.2 – 75.7 °C; $^1$H NMR (400 MHz, Chloroform-d) $\delta$ 7.70 (d, $J = 8.1$ Hz, 2H), 7.26 (d, $J = 8.1$ Hz, 2H), 5.83 (s, 1H), 4.78 (t, $J = 6.4$ Hz, 1H), 4.06 (d, $J = 6.4$ Hz, 2H), 2.41 (s, 3H), 2.03 (s, 3H), 1.80 (s, 3H); $^{13}$C NMR (100 MHz, Chloroform-d) $\delta$ 147.3, 146.2, 143.2, 137.0, 129.4, 127.2, 114.5, 111.5, 40.2, 21.4, 11.1, 9.6; HRMS (EI) calculated for C$_{14}$H$_{17}$NO$_3$S (M$^+$): 279.0929, found: 279.0927.

N-((4-benzyl-5-methylfuran-2-yl)methyl)-4-methylbenzenesulfonamide (2n): Colorless oil, yield: 61%; $^1$H NMR (400 MHz, Chloroform-d) $\delta$ 7.68 (d, $J = 8.2$ Hz, 2H), 7.40 – 6.99 (m, 7H), 5.82 (s, 1H), 4.71 (t, $J = 6.0$ Hz, 1H), 4.06 (d, $J = 6.0$ Hz, 2H), 3.55 (s, 2H), 2.39 (s, 3H), 2.09 (s, 3H); $^{13}$C NMR (100 MHz, Chloroform-d) $\delta$ 147.7, 146.7, 143.2, 140.5, 137.0, 129.5, 128.4, 128.2, 127.1, 126.1, 118.6, 110.6, 40.3, 31.0, 21.5, 11.3; HRMS (EI) calculated for C$_{20}$H$_{21}$NO$_3$S (M$^+$): 355.1242, found: 355.1246.
4-methyl-N-((4,5,6,7-tetrahydrobenzofuran-2-yl)methyl)benzenesulfonamide (2o): colorless oil, yield: 81%; \(^1\)H NMR (400 MHz, Chloroform-d) \(\delta\) 7.69 (d, \(J = 8.0\) Hz, 2H), 7.24 (d, \(J = 8.0\) Hz, 2H), 5.86 (s, 1H), 5.01 (t, \(J = 6.0\) Hz, 1H), 4.09 (d, \(J = 6.0\) Hz, 2H), 2.40 (s, 3H), 2.36 (t, \(J = 5.7\) Hz, 2H), 2.26 (t, \(J = 5.7\) Hz, 2H), 1.79 – 1.69 (m, 2H), 1.67 – 1.55 (m, 2H); \(^1^3\)C NMR (100 MHz, Chloroform-d) \(\delta\) 150.6, 146.8, 143.0, 137.0, 129.3, 127.1, 117.3, 109.3, 40.3, 22.9, 22.8, 21.8, 21.4; HRMS (EI) calculated for C\(_{16}\)H\(_{19}\)NO\(_3\)S (M\(^+\)): 305.1086, found: 305.1093.

Synthesis of compounds 2p’ and 2p

Scheme S4

A mixture of 1p (74 mg, 0.2 mmol), Rh\(_2\)(esp)\(_2\) (1.5 mg, 1 mol %) and DCE (2 mL) was stirred under a nitrogen atmosphere at reflux. After completion of the reaction (monitored by TLC), the resulting mixture was filtered rapidly through a funnel with a thin layer of silica gel and eluted with ethyl acetate. The filtrate was concentrated and the residue was purified by chromatography on silica gel (PE: EA = 5:1) to afford 2p’ (40.7 mg, 60% yield).

2p’ (40.7 mg, 0.12 mmol) was dissolved in MeOH (1 mL), then sodium borohydride (9.1 mg, 0.24 mmol) and MeOH (1 mL) were added at 0°C and stirred for 2h at rt. The resulting mixture was filtered rapidly through a funnel with a thin layer of silica gel and eluted with ethyl acetate. The filtrate was concentrated and the residue was purified by column chromatography (PE: EA = 5:1) to give 2p (37 mg, 90% yield) \[^6\].

4-methyl-N-((3-methyl-5-phenylfuran-2-yl)methylene)benzenesulfonamide (2p’): Pale yellow solid, mp 145.6 – 146.8 °C; \(^1\)H NMR (400 MHz, Chloroform-d) \(\delta\) 8.85 (s, 1H), 7.89 (d, \(J = 8.0\) Hz,
2H), 7.77 (d, \( J = 8.0 \text{ Hz}, 2H \)), 7.47 (t, \( J = 7.6 \text{ Hz}, 1H \)), 7.41 (d, \( J = 8.0 \text{ Hz}, 2H \)), 7.33 (d, \( J = 8.0 \text{ Hz}, 2H \)), 6.75 (s, 1H), 2.42 (s, 3H), 2.40 (s, 3H); \(^{13}\)C NMR (100 MHz, Chloroform-d) \( \delta \) 160.5, 144.7, 143.9, 136.1, 133.6, 130.1, 129.6, 128.9, 128.4, 127.7, 125.4, 111.5, 108.0, 21.6, 11.3; HRMS (EI) calculated for C\(_{19}\)H\(_{17}\)NO\(_3\)S (M\(^{+}\)): 339.0929, found: 339.0925.

4-methyl-N-((3-methyl-5-phenylfuran-2-yl)methyl)benzenesulfonamide (2p): Pale yellow solid, mp 141.5 – 142.7 °C; \(^1\)H NMR (400 MHz, Chloroform-d) \( \delta \) 7.67 (d, \( J = 8.0 \text{ Hz}, 2H \)), 7.43 (d, \( J = 8.0 \text{ Hz}, 2H \)), 7.32 (t, \( J = 7.6 \text{ Hz}, 2H \)), 7.27 – 7.20 (m, 1H), 7.16 (d, \( J = 8.0 \text{ Hz}, 2H \)), 6.29 (s, 1H), 4.95 (br, 1H), 4.20 (d, \( J = 6.0 \text{ Hz}, 2H \)), 2.27 (s, 3H), 1.92 (s, 3H); \(^{13}\)C NMR (100 MHz, Chloroform-d) \( \delta \) 152.8, 144.2, 143.3, 137.0, 133.9, 129.5, 128.5, 127.4, 126.9, 123.6, 120.2, 108.1, 38.2, 21.4, 9.7; HRMS (EI) calculated for C\(_{19}\)H\(_{19}\)NO\(_3\)S (M\(^{+}\)): 341.1086, found: 341.1084.

4. Synthetic derivatization of products

Synthesis of Compound 3a and 4a

**Scheme S5**

The furan 2a (0.59 g, 2 mmol) was dissolved in acetone (10 mL). K\(_2\)CO\(_3\) (0.83 g, 6 mmol) and propargyl bromide (0.68 ml, 80% solution in toluene, 6 mmol) were added and the mixture was stirred overnight at room temperature. Then the solvent was removed under vacuum, the residue was taken up in water and dichloromethane and the aqueous phase was extracted with two additional portions of dichloromethane. The combined organic phases were dried with Mg\(_2\)SO\(_4\), filtered and concentrated under reduced pressure. The crude product was purified by column
chromatography (PE:EA=5:1) to give 3a (0.53 g, 80% yield).

In a flask 3a (66 mg, 0.2 mmol) was dissolved in dry CHCl₃ (1 mL) under nitrogen. The AuCl₃ (3.0 mg, 5 mol %) was then added and the reaction mixture was stirred at room temperature for 1h (monitored by TLC). Afterward the solvent was removed under vacuum, the crude product was purified by column chromatography (PE:EA=3:1) to give 4a (58 mg, 87% yield)[7].

![3a](image)

4-methyl-N-(prop-2-yn-1-yl)-N-((5-propylfuran-2-yl)methyl)benzenesulfonamide (3a): White solid, yield: 80%; mp 68.7 – 70.2 °C; ¹H NMR (400 MHz, Chloroform-d) δ 7.74 (d, J = 8.2 Hz, 2H), 7.28 (d, J = 8.2 Hz, 2H), 6.17 (d, J = 2.9 Hz, 1H), 5.87 (d, J = 2.9 Hz, 1H), 4.39 (s, 2H), 4.01 (d, J = 2.4 Hz, 2H), 2.49 (t, J = 7.5 Hz, 2H), 2.42 (s, 3H), 2.06 (t, J = 2.4 Hz, 1H), 1.61 – 1.56 (m, 2H), 0.92 (t, J = 7.4 Hz, 3H); ¹³C NMR (100 MHz, Chloroform-d) δ 157.0, 146.3, 143.4, 136.1, 129.4, 127.7, 110.7, 105.5, 73.7, 42.9, 36.0, 29.9, 21.5, 21.2, 13.6; HRMS (EI) calculated for C₁₈H₂₁NO₃S (M⁺): 331.1242, found: 331.1244.

![4a](image)

5-propyl-2-tosylisodolin-4-ol (4a): White solid, yield: 87%; mp 147.6 – 149.4 °C; ¹H NMR (400 MHz, Chloroform-d) δ 7.77 (d, J = 8.2 Hz, 2H), 7.30 (d, J = 8.2 Hz, 2H), 6.98 (d, J = 7.7 Hz, 1H), 6.66 (d, J = 7.7 Hz, 1H), 5.15 (br, 1H), 4.62 (s, 2H), 4.59 (s, 2H), 2.51 (t, J = 7.6 Hz, 2H), 2.40 (s, 3H), 1.60 – 1.55 (m, 2H), 0.94 (t, J = 7.3 Hz, 3H); ¹³C NMR (100 MHz, Chloroform-d) δ 148.7, 143.6, 135.6, 133.7, 130.0, 129.8, 127.6, 127.4, 122.8, 114.4, 54.0, 51.6, 31.4, 23.0, 21.5, 13.9; HRMS (EI) calculated for C₁₈H₂₁NO₃S (M⁺): 331.1242, found: 331.1245.
5. References


6. $^1$H and $^{13}$C NMR spectra for new compounds