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Synthesis of β-azolyl- and β-azolylcarbonylenamines and their reactions with aromatic azides

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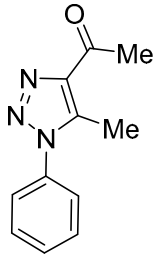
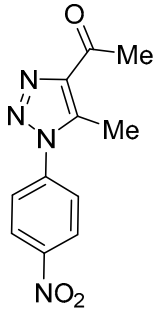
SUPPLEMENTARY INFORMATION

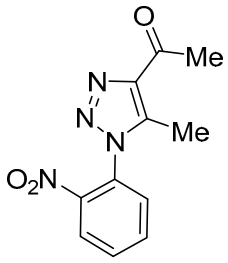
Synthesis of ketones 1b, 1c, 1d, 1m, 1o, 1r and 1s.



1-(5-Methyl-1-phenyl-1*H*-1,2,3-triazol-4-yl)ethanone (**1b**). To solution of azide **2a** (1192 mg,10.00 mmol) and acetylacetone (1517 mg, 15.00 mmol) of in 4 ml of $CHCl_3$ was added Et_3N (1,013 g 9.99 mmol) of and DBU (261 mg,1.69 mmol) of. The solution was kept at room temperature for 24 h. Volatiles were evaporated to dryness, the solid residue were treated twice with dilute HCl, and with H_2O, then dried in desiccator and crystallized from PhH–PE mixture. Yield 1.875 g (93%), colorless powder, m. p. 101–102 °C (PhH–PE) (lit.:118–120 °C (EtOH)[2]). NMR ^{1}H (DMSO-d_6), δ, ppm (*J*, Hz): 2.60 (s, 3H, Me); 2.77 (s, 3H, Me); 7.46 (dd, *J* = 7.7, 2.0, 2H, H Ar); 7.59 (dd, *J* = 4.8, 2.5, 3H, H Ar). NMR ^{1}H ($CDCl_3$), δ, ppm (*J*, Hz): 2.60 (s, 3H, Me); 2.77 (s, 3H, Me); 7.46 (dd, *J* = 7.7, 2.0, 2H, H Ar); 7.59 (dd, *J* = 4.8, 2.5, 3H, H Ar). Found, %: C 66.05; H 5.15; N 20.69. $C_{11}H_{11}N_3O$. Calcd, %: C 65.66; H 5.51; N 20.88.



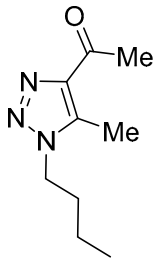
1-[5-Methyl-1-(4-nitrophenyl)-1*H*-1,2,3-triazole-4-yl]ethanone (1c). To solution of azide **2b** (246 mg, 1.50 mmol) of and acetylacetone (193 mg,1.92 mmol) in CH_2Cl_2 (5 ml) was added DIPEA (221 mg, 1.71 mmol) and DBU (114 mg,0.75 mmol) of. Reaction mixture was kept at room temperature for 0.5 h. Volatiles were evaporated to dryness, the residue was treated with hot hexanes and PE. Yield 353 mg (96%), light-beige crystals, m. p. 143–145 °C (lit.: m. p. 145–146 °C (EtOH)[2]). NMR ^{1}H ($CDCl_3$), δ, ppm (*J*, Hz): 2.67 (s, 3H, Me); 2.74 (s, 3H, Me); 7.72 (d, *J* = 9.0, 2H, H Ar); 8.46 (d, *J* = 9.0, 2H, H Ar). Found, %: C 53.39; H 3.74; N 22.44. $C_{11}H_{10}N_4O_3$. Calcd, %: C 53.66; H 4.09; N 22.75.



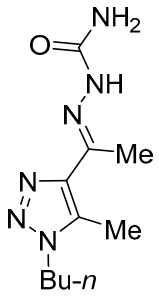
1-[5-Methyl-1-(2-nitrophenyl)-1*H*-1,2,3-triazole-4-yl]ethan-1-one (**1d**).

To solution of azide **2c** (246 mg, 1.50 mmol) of and acetylacetone (191 mg, 1.91 mmol) in CH_2Cl_2 (3 ml) was added DBU (36 mg, 0.237 mmol) of. Reaction mixture was stirred at room temperature for 24 h. Volatiles were evaporated to dryness, the residue was treated with small amount of PE. The residue (dark oil) chromatographed on silica gel with CH_2Cl_2, then CH_2Cl_2–EtOAc, 1:1 and CH_2Cl_2–EtOAc,1:4 as eluents. Fraction containing the product was

evaporated to dryness and solidified with PE. Yield 332 mg (90%), light beige crystals, m. p. 118–119 °C (lit.: m. p. 118–119 °C (EtOH)[3]). NMR ^{1}H ($CDCl_3$), δ, ppm (*J*, Hz): 2.48 (3H, s, Me); 2.73 (3H, s, Me); 7.50 (1H, dd, *J* = 7.7, 1.5, H Ar); 7.83 (2H, dt, *J* = 24.9, 7.7, 1.5, H Ar); 8.22 (1H, dd, *J* = 8.0, 1.5, H Ar). NMR ^{13}C ($CDCl_3$), δ, ppm: 9.5; 27.8; 126.0; 128.5; 129.6; 132.0; 134.4; 139.4; 143.3; 145.3; 194.0. Found, %: C 53.95; H 4.44; N 23.01. $C_{11}H_{10}N_4O_3$. Calcd, %: C 53.66; H 4.09; N 22.75.

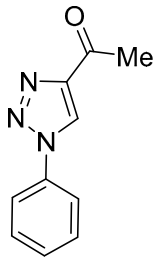


1-(1-Butyl-5-methyl-1*H*-1,2,3-triazol-4-yl)ethan-1-one (**1m**).[2,4] To solution of diazoacetylacetone (1,261 g, 10.00 mmol) in 2 ml of EtOH was added Et_3N (1,011 g, 10.00 mmol)and *n*-butylamine (731 mg, 10.00 mmol). Reaction mixture was stirred at room temperature for 24 h. Volatiles were evaporated to dryness, the residue was extracted with PE, the solution evaporated to dryness. Yield of raw ketone 663 mg (37%), colorless oil that can be used further without purufucation. Pure sample of this compound was obtained by conversion to corresponding semicarbazone **1m'** followed by treatment with HCl. NMR ^{1}H ($CDCl_3$), δ, м. д. (*J*, Гц): 4.25 (2H, t, *J* = 7.3, $C\underline{H_2}CH_2CH_2CH_3$); 2.66 (3H, s, Me); 2.55 (3H, s, Me); 1.76–1.90 (2H, m, $CH_2C\underline{H_2}CH_2CH_3$); 1.35 (2H, dd, *J* = 15.1, 7.5, $CH_2CH_2C\underline{H_2}CH_3$); 0.95 (3H, t, *J* = 7.4, $CH_2CH_2CH_2C\underline{H_3}$). MS-EI, *m/z* (*I*, %): 181 $[M]^+$ (30), 166 (55), 138 (100), 110 (94). Found, %: C 59.59; H 8.13; N 23.56. $C_9H_{15}N_3O$. Calcd, %: C 59.64; H 8.34; N 23.19.

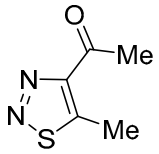


2-[1-(1-Butyl-5-methyl-1*H*-1,2,3-triazol-4-yl)ethylidene)hydrazinecarboxamide (**1m′**). To a solution of ketone **1m** (453 mg, 2.50 mmol) in EtOH (4 ml) semicarbazide hydrochloride (304 mg, 2.73 mmol) was added, followed by Et_3N (331 mg, 3.27 mmol). The volatiles were evaporated to dryness. EtOH (2 ml) and conc. HCl (1 drop) were added to the residue, the suspension formed was triturated and left to stay overnight. The precipitate was separated, washed with H_2O twice and dried. Yield 218 mg (36%), colourless powder, m. p. 268–272 °C. NMR ^{1}H ($CDCl_3$), δ, ppm (*J*, Hz): 0.96 (3H, t, *J* = 7.4, $CH_2CH_2CH_2C\underline{H_3}$); 1.37 (2H, dd, *J* = 15.1, 7.5, $CH_2CH_2C\underline{H_2}CH_3$); 1.83 (2H, dd, *J* = 14.9, 7.5, $CH_2C\underline{H_2}CH_2CH_3$); 2.42 (3H, s, Me); 2.50 (3H, s, Me); 4.27 (2H,t, *J* = 7.3, $C\underline{H_2}CH_2CH_2CH_3$); 5.63 (2H, br. s, NH_2); 8.40 (1H, s,NH). NMR ^{13}C ($CDCl_3$), δ, ppm: 10.1; 13.4; 13.5; 19.7; 47.6; 31.8; 130.6; 142.5; 143.2; 157.9. MS-EI, *m/z* (%): 238 $[M]^+$ (15); 221 (2); 195 (12), 138 (100). Found, %: C 50.06; H 7.97; N 35.02. $C_{10}H_{18}N_6O$. Calculated, %: C 50.40; H 7.61; N 35.27.

Decomposition of semicarbazone 1m′ into ketone 1m. The suspension of semicarbazone **1m′** (358 mg, 1.50 mmol) in a mixture of *i*-PrOH (15 ml) of and 10N HCl (1 ml) was stirred at 90°C during 1.5 h. The solution was evaporated to dryness and re-evaporated with PhH twice. The residue was extracted with hot PE, the extract was evaporated to dryness to afford ketone **1m**. Yield 250 mg (92%), colorless oil.

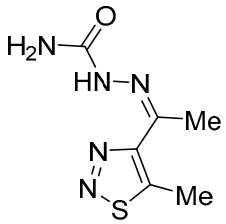


1-(1-Phenyl-1*H*-1,2,3-triazol-4-yl)ethanone (**1o**). Solution of (E)-4-(dimethylamino)but-3-en-2-one (1.131 g, 10.00 mmol) and phenylazide (1.191 g, 10.00 mmol) in PhMe (4 ml) was stirred at 100 °C for 11 h. After cooling, the volatile components are evaporated, the residue is separated on a column with silica gel (eluent $CHCl_3$). Portions containing the product are combined, evaporated to dryness, the residue is crystallized from petroleum ether.Yield 842 mg (45%), light-beige powder, m. p. 99–102 °C (m. p. 108–109 °C).[5] ^{1}H NMR (400 MHz, $CDCl_3$), δ, ppm (*J*, Hz): 2.74 (s, 3H, Me); 7.62–7.43 (m, 3H, H Ar); 7.75 (dd, *J* = 8.3, 1.0, 2H, H Ar); 8.49 (s, 1H, CH-triaz.). MS-EI, *m/z* (*I*, %): 187 $[M]^+$ (11), 159 $[M\text{-}N_2]^+$ (4), 144 (84), 130 (9), 117 (82), 77 (100). Found, %: C 64.43; H 4.72; N 22.48. $C_{10}H_9N_3O$ Calcd, %: C 64.16; H 4.85; N 22.45.



1-(5-Methyl-1,2,3-thiadiazol-4-yl)ethanone (1s).[6,7] Solution of diazoacetylacetone (1.887 g, 15.00 mmol) and Et_3N (3.055 mg, 30.20 mmol) in 5 ml of EtOH at 0 °C was saturated with dry H_2S for 2 h. Reaction mixture was kept for 24 h in closed flask, then evaporated to dryness. The residue was washed with Et_2O (2 × 15 ml) and extract was evaporated. To the residue hexane was added and kept for 24 h at –5 °C. Solvent was decanted, the residue dried under reduced pressure. Yield 1.726 g (81%), colorless oil. NMR ^{1}H ($CDCl_3$), δ, ppm (*J*, Hz): 2.90 (s, 3H, Me); 2.91 (s, 3H, Me). NMR ^{13}C ($CDCl_3$), δ, м. д.: 11.2; 30.0; 156.3; 159.4; 193.6. MS-EI, *m/z* (*I*, %): 114 $[M\text{-}N_2]^+$ (30), 72 (38), 43 (100). Found, %: C 42.09; H 4.04; N 19.93. $C_5H_6N_2OS$. Calcd, %: C 42.24; H 4.25; N 19.70.

Pure sample was obtained similarly to that of **1m**.



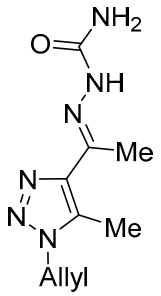
2-[1-(5-Methyl-1,2,3-thiadiazol-4-yl)ethylidene]hydrazine carboxamide (**1s′**). To a solution of ketone **1s** (2.135 g, 15.0 mmol) in EtOH (6 ml) semicarbazide hydrochloride (1.368 g, 12.3 mmol) and Et_3N (1.862 g, 18.40 mmol) were added. The reaction mixture was stirred at rt for 1 h, then concentrated to a half of initial volume. Conc. HCl (2 drops) was added to the solution

and the suspension was stirred for 2 h. The precipitate was separated, crystallized from MeCN, washed with H_2O and dried. Yield 1.042 г (35%), pale-brown powder, m. p. 228-229 °C. NMR ^1H (DMSO-d_6), δ, ppm (*J*, Hz): 2.51 (3H,s, Me); 2.81 (3H, s, C(5)Me); 6.20 (2H, br. s, NH_2); 9.64 (1H, s, NH). NMR ^{13}C (DMSO-d_6), δ, ppm: 11.5; 15.6; 140.1; 150.4; 156.9; 157.2. MS-EI, *m/z* (%): 199 $[M]^+$ (13); 171 $[M\text{-}N_2]^+$ (24); 154 (4); 138 (11); 128 (13), 87 (100). Found, %: C 35.96; H 4.42; N 35.21. $C_6H_9N_5OS$. Calculated, %: C 36.17; H 4.55; N 35.15.

Decomposition of semicarbazone 1s′ into ketone 1s.

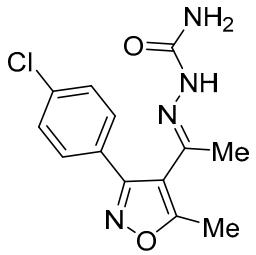
To a solution of semicarbazone **1s' (**299 mg, 1.50 mmol) in *i*-PrOH (1 ml) H_2O (2 ml) and 10N HCl (1.5 ml) were added, the suspension was warmed at 80 °C for 2 h. Volatiles were evaporated to dryness. The residue was extracted with hot PE, the extract was evaporated to dryness to obtain ketone **1s**. Yield 186 mg (87%), pale yellow oil.

Purification of ketones 1n and 1t



2-{1-(5-methyl-1-(prop-2-en-1-yl)-1*H*-1,2,3-triazol-4-yl]ethylidene}hydrazinecarboxamide (**1n′**)To a solution of ketone **1n** (413 mg, 2.50 mmol) and semicarbazide hydrochloride (280 mg, 2.50 mmol) in EtOH (2 ml), Et_3N (289 mg, 2.85 mmol) were added. The solution was evaporated to dryness, EtOH (2 ml) and conc. HCl (1 drop) were added, the residue was triturated and left to stay overnight. The precipitate was separated, washed with EtOH, Et_2O and H_2O, and dried. Yield 353 mg (69%), colourless powder, m. p. 199–200 °C. NMR ^1H (DMSO-d_6), δ, ppm (*J*, Hz): 2.29 (3H, s, Me); 2.45 (3H, s, Me); 4.97 (1H, d, *J* = 10.9, $C\underline{H_2}CH{=}CH_2$); 5.00 (2H, br. s, $CH_2CH{=}C\underline{H_2}$); 5.22 (1H, d, *J* = 10.9 Hz, $C\underline{H_2}CH{=}CH_2$);–5.88-6.09 (1H, m, $CH_2C\underline{H}{=}CH_2$); 6.25 (2H, br. s, NH_2); 9.36 (s, 1H, NH). NMR ^{13}C (DMSO-d_6), δ, ppm: 9.4; 13.8; 49.5; 117.6; 131.3; 132.3; 141.1; 142.3; 157.2. MS-EI, *m/z* (%): 222 $[M]^+$ (15); 205 (2); 179 (12); 150 (4), 122 (100). Found, %: C 48.68; H 6.05; N 38.02. $C_9H_{14}N_6O$. Calculated, % C 48.64; H 6.35; N 37.81.

Decomposition of semicarbazone 1n′ into ketone 1n. To a solution of semicarbazone **1n′ (**333 mg, 1.50 mmol) in *i*-PrOH (1 ml) H_2O (2 ml) and 10N HCl (1.5 ml) were added, the suspension was warmed at 80 °C for 2 h. Volatiles were evaporated to dryness. The residue was extracted with hot PhH, the extract was evaporated to dryness. The new residue was extracted with hot PE, the extract was evaporated to dryness to obtain ketone **1n**. Yield 231 mg (93%), colourless oil.



2-{1-[3-(4-Chlorophenyl)-5-methyl-1,2-oxazol-4-yl]ethylidene}hydrazinecarboxamide (**1t′**). To a solution of ketone **1t** (589 mg, 2.50 mmol) in *i*-PrOH (1 ml), semicarbazide hydrochloride (280 mg, 2.51 mmol) and Et_3N (269 mg, 2.66 mmol) were added. The solution formed was evaporated to dryness, the oily residue was dissolved in *i*-PrOH (1.5 ml), conc. HCl (2 drops) were added, and the suspension was stirred at rt for 12 h. Volatiles were evaporated to dryness. The oil thus formed was treated with H_2O three times. The residue was dissolved in a minimal amount of hot DMF, non-dissolved solid phase was separated. Liquid phase was evaporated to dryness. The oily residue was treated with boiling *i*-PrOH and cooled to rt. The residue formed was separated, washed with H_2O twice and dried. Yield 629 mg (86%), pale beige powder, m. p. 207–208 °C. NMR ^{1}H (DMSO-d_6), δ, ppm (*J*, Hz): 1.88 (3H, s, C(5)Me); 2.51 (3H, s, NMe); 6.17 (2H, br. s, NH_2); 7.55 (4H, q, *J* = 8.7, H Ar); 9.41 (1H, s, NH). NMR ^{13}C (DMSO-d_6), δ, ppm: 11.8; 17.1; 115.2; 128.0; 128.8; 129.8; 134.6; 137.1; 156.9; 159.8; 168.2. MS-EI, m/z (%): 294 $[M+2]^+$ (20); 293 $[M+1]^+$ (12); 292 $[M]^+$ (60); 249 (73); 234 (56); 199 (26), 124 (100). Found, %: C 53.67; H 4.59; N 19.07. $C_{13}H_{13}ClN_4O_2$. Calculated, %: C 53.34; H 4.48; N 19.14.

Decomposition of semicarbazone 1t′ into 1-[3-(4-chlorophenyl)-5-methyl-1,2-oxazol-4-yl]ethan]one (**1t**). The suspension of semicarbazone **1t′** (439 mg, 1.50 mmol) in a mixture of water (3 ml), 10N HCl (1.7 ml) and 1,4-dioxane (7 ml) was warmed (80 °C) at stirring for 6 h. The reaction mixture was concentrated to 1/3 of initial volume, the residue was diluted with two volumes of H_2O, the desired product was extracted with EtOAc, the extract was evaporated to dryness, the residue was triturated with hexanes. Yield 336 mg (95%), colorless powder, m. p. 136–137 °C (m. p. 135–137 °C[1]). NMR ^{1}H ($CDCl_3$), δ, ppm (*J*, Hz): 2.14 (3H, s, COMe); 2.71 (3H, s, Me); 7.46 (4H, s, H Ar). MS-EI, *m/z* (%): 237 $[M+2]^+$ (9); 236 $[M+1]^+$ (7); 235 $[M]^+$ (24), 193 (11), 178 (40), 43 (100). Found, %: C 61.25; H 4.64; N 5.75. $C_{12}H_{10}ClNO_2$. Calculated, %: C 61.16; H 4.28; N 5.94.

References

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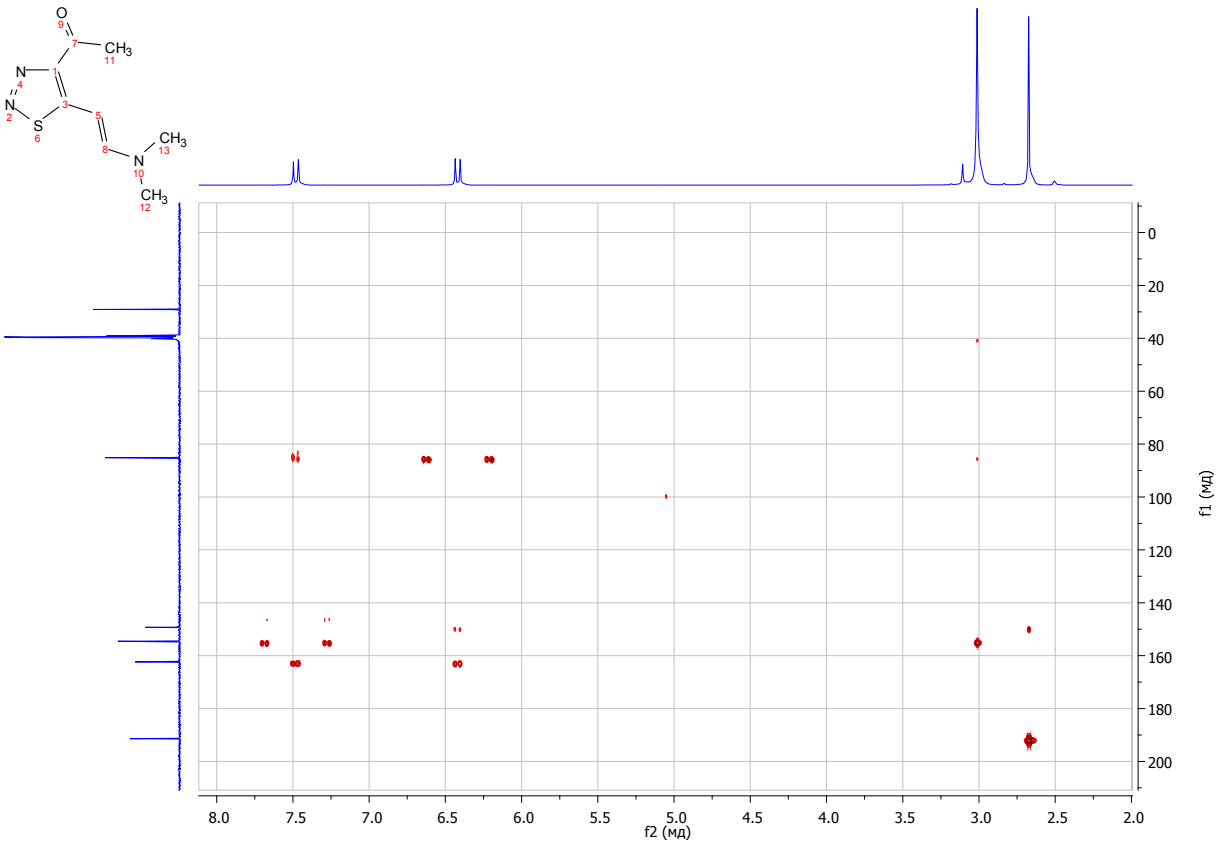
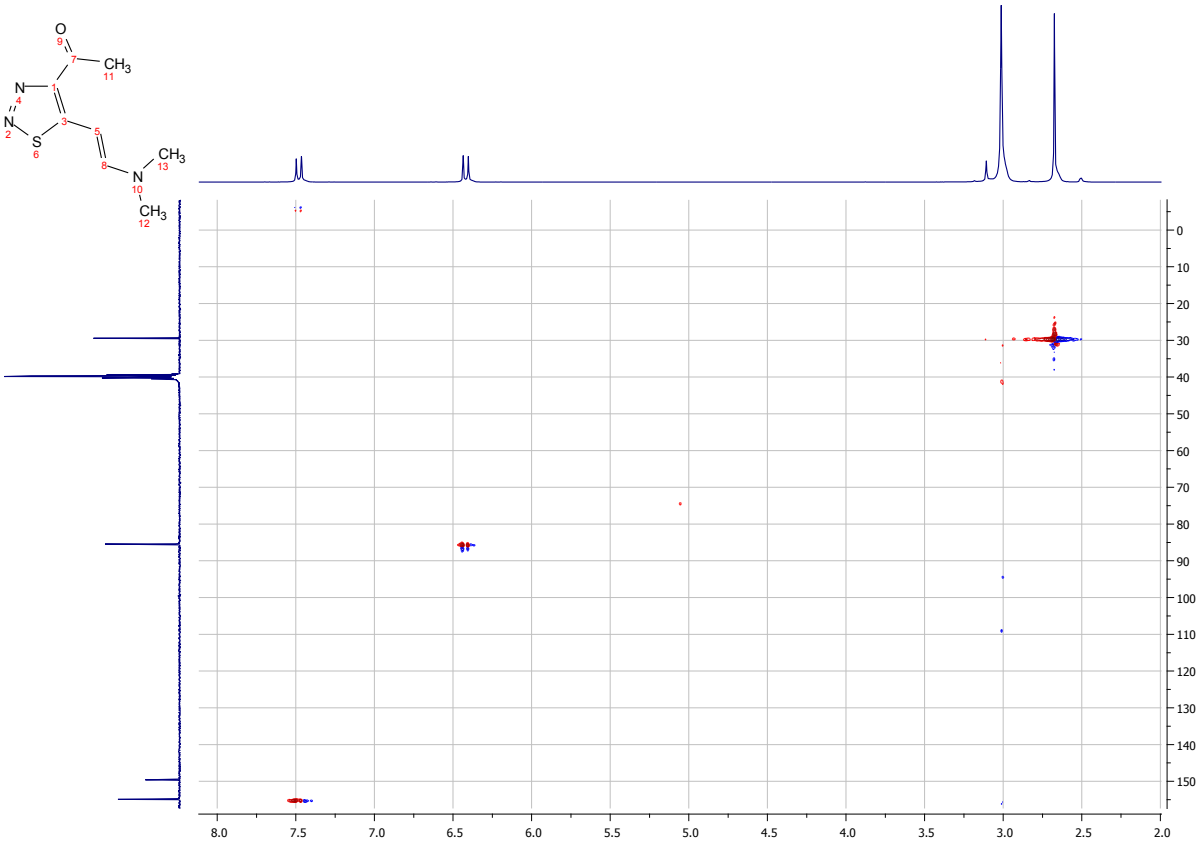
^{1}H and ^{13}C HMBC and HSQC spectra of compound 4s

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