Solvent-Catalyzed Umpolung Carbon–Sulfur Bond-Forming Reactions by Nucleophilic Addition of Thiolate and Sulfinate Ions to in Situ-Derived Nitrosoalkenes in Deep Eutectic Solvents

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ELECTRONIC SUPPLEMENTARY INFORMATION

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1. General Methods

Reactions were carried out using non-conventional solvents (DESs or LTTMs) and under air. Deep eutectic solvents and low melting transition mixtures [choline chloride (ChCl)−glycerol (Gly) (1:2 mol/mol); L-lactic acid−ChCl (2:1 mol/mol); L-tartaric acid−ChCl (1:2 mol/mol); L-lactic acid−L-alanine (9:1 mol/mol), urea–ChCl (2:1)] were prepared by gently heating under stirring at 60–80 °C for 20 min the corresponding individual components until a clear solution was obtained. Reagents and solvents, unless otherwise specified, were purchased from Sigma-Aldrich (Sigma-Aldrich, St. Louis, MO, USA) and used without any further purification. Flash column chromatography was performed on silica gel 60 (230–400 mesh). Analytical thin layer chromatography (TLC) was carried out on precoated 0.25 mm thick plates of Kieselgel 60 with F-254 indicator; visualization was accomplished by UV light (254 nm) or by spraying with a solution of 5 % (w/v) ammonium molybdate and 0.2 % (w/v) cerium(III) sulfate in 100 ml 17.6 % (w/v) aq. sulfuric acid and heating to 473 K until blue spots appear. The ^{1}H and ^{13}C NMR were recorded on a 600 Bruker or on a Varian Inova 400 MHz spectrometer at ambient temperature, with $CDCl_3$ as the solvent and TMS as an internal standard (δ = 7.26 ppm for ^{1}H spectra; δ = 77.0 ppm for ^{13}C spectra). The IR spectra were recorded on a PERKIN-ELMER 283® FT-IR spectrometer. The electrospray ionization (HRMS (ESI)) experiments were carried out in a hybrid Q-TOF mass spectrometer AGILENT 1100 LC/MSD equipped with an ion-spray ionization source. GC-MS spectrometry analyses were performed on a gas chromatograph (HEWLETT-PACKARD 6890C with a dimethylsilicon capillary column, 30 m, 0.25 mm i.d.) equipped with a mass selective detector operating at 70 eV (EI). Reactions run under sonication were performed using an ultrasonic cleaner (CEIA CP104; frequency: 40 kHz; nominal power 50W). Copies of ^{1}H and ^{13}C NMR spectra have been reported for all the new compounds.

2. Synthetic Procedures

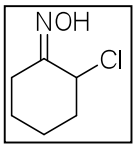
2.1 Preparation of 2-chlorocyclohexanone oxime (1a).

To a solution of sodium acetate (3.40 g, 41.44 mmol) in water (15 mL), hydroxylamine hydrochloride (2.88 g, 41.44 mmol) and 2-chlorocyclohexanone (5.0 g, 37.71 mmol) were added at room temperature and shaken vigorously for 20 min. Then, the mixture was cooled to –20 °C and left at this temperature for 12 h. After this time, the reaction mixture was extracted with CH_2Cl_2 (3 × 5 mL), and the combined organic extracts were washed with brine, dried over Na_2SO_4, and the solvent removed under reduced pressure. The crude product was purified by chromatography over silica gel using 20:80 EtOAc/hexane as the solvent to give the desired oxime **1a** as a white solid in 92% yield.

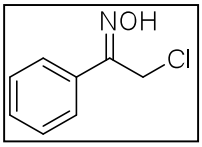
2.2 Preparation of 2-chloro-1-phenylethanone oxime (1b).

A mixture of 2-chloroacetophenone (1.00 g, 6.46 mmol) in methanol (12 mL) and water (1.5 mL) was reacted with hydroxylamine hydrochloride (1.35 g, 19.4 mmol). The resulting homogenous clear solution was stirred for 12 h at room temperature, and then it was concentrated under reduced pressure. The resulting crude was dissolved in water (3 mL) and extracted with CH_2Cl_2 (3 × 5 mL). The organic layer was dried over anhydrous Na_2SO_4 and concentrated under reduced pressure. The crude product was purified by chromatography over silica gel using 20:80 EtOAc/hexane as the solvent to give the desired oxime **1b** as a white solid in 90% yield.

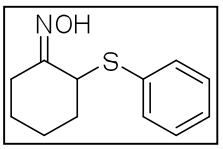
3. Spectroscopic data of α–chlorinated oximes 1a,b, α-sulfenylated oximes 3a,b and 3d.



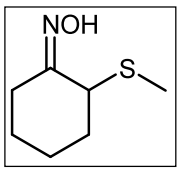
2-Chlorocyclohexanone oxime (1a):[1] white solid, m.p. 79−80 °C, 92% yield. ^{1}H NMR (600 MHz, $CDCl_3$): δ 1.35−1.46 (m, 1 H), 1.61−1.64 (m, 1 H), 1.84−1.96 (m, 3 H), 2.12−2.16 (m, 1 H), 2.23−2.32 (m, 1 H), 3.04−3.09 (m, 1 H), 4.69 (t, *J* = 3.0 Hz, 1 H), 8.94 (br s, 1 H, exchanges with D_2O); ^{13}C NMR (125 MHz, $CDCl_3$): δ 20.1, 20.4, 24.8, 35.5, 58.9, 158.5; FT-IR (film, cm^{-1}): 3229, 2914, 1490, 1330, 1065, 989, 918; GC/MS (70 eV): *m/z* (%) 147 (M^+, 18), 130 (20), 111 (82), 94 (24), 81 (100), 67 (56). HRMS (ESI): calcd for $C_6H_{10}ClNO$ [M + H]$^+$ 148.0524; found: 148.0518.



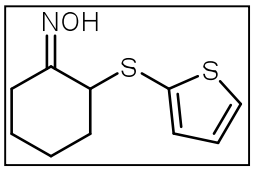
2-Chloroacetophenone oxime (1b):[2] white solid, m.p. 78−79 °C, 90% yield. ^{1}H NMR (600 MHz, $CDCl_3$): δ 4.67 (s, 2 H), 7.41–7.42 (m, 3 H), 7.67–7.69 (2 H, m) 9.26 (br s, 1 H, exchanges with D_2O); ^{13}C-NMR (125 MHz, $CDCl_3$): δ 32.5, 126.1, 128.7, 129.9, 132.9, 154.1; FT-IR (film, cm^{-1}): 3222, 3060, 2914, 1494, 1437, 1326, 1288, 1070, 999, 911; GC/MS (70 eV): *m/z* (%) 169 (M^+, 78), 120 (40), 103 (65), 77 (100), 51. HRMS (ESI): calcd for C_8H_8ClNO [M + H]$^+$ 170.0367; found: 170.0388.



(*Z*)-2-(Phenylthio)cyclohexanone oxime (3a):[1] white solid, m.p. 90–93 °C, >98% yield. ^{1}H-NMR (600 MHz, $CDCl_3$): δ 1.43–1.65 (m, 3 H), 1.82–2.02 (m, 3 H), 2.48–2.53 (m, 1 H), 2.84–2.91 (m, 1 H), 3.97 (t, *J* = 4 Hz, 1 H), 7.24–7.42 (m, 5 H), 7.77 (br s, 1 H, exchanges with D_2O); ^{13}C NMR (125 MHz, $CDCl_3$): δ 21.2, 22.1, 25.5, 33.0, 49.8, 127.2, 128.8, 132.4, 134.4, 159.4; FT-IR (film, cm^{-1}): 3269, 2935, 2859, 1653, 1583, 1480, 1430, 981, 909; GC/MS (70 eV): *m/z* (%) 221 (M^+, 72) 204 (16), 112 (100), 81 (37), 67 (37). HRMS (ESI): calcd for $C_{12}H_{15}NOS$ [M + H]$^+$ 222.0947; found: 222.0979.



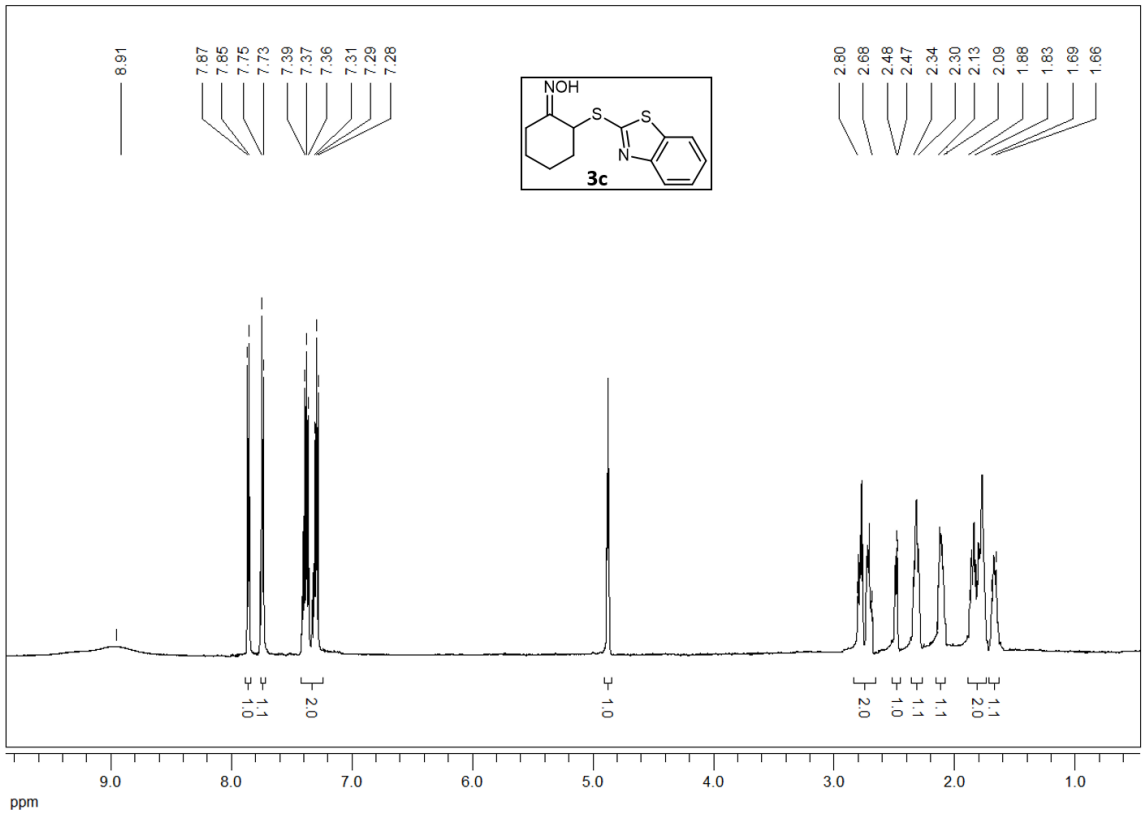
2-(Methylthio)cyclohexanone oxime (3b):[3] white solid, m.p. 76–78 °C, inseparable mixture of diastereoisomers, dr (*E*):(*Z*) = 75/25, 90% yield. ^{1}H NMR (600 MHz, $CDCl_3$): δ 1.41–1.47 [m, 1 H (*Z*) + 1 H (*E*)], 1.57–1.62 [m, 1 H (*Z*) + 1 H (*E*)], 1.74–1.87 [m, 1 H (*Z*) + 1 H (*E*)], 1.93–2.01 [m, 1 H (*Z*) + 1 H (*E*)], 2.02 [s, 3 H (*Z*)], 2.11 [s, 3 H (*E*)], 2.16–2.22 [m, 1 H (*Z*) + 1 H (*E*)], 2.37–2.40 [m, 1 H (*Z*) + 1 H (*E*)], 2.55–2.78 [m, 1 H (*Z*) + 1 H (*E*)], 3.00–3.06 [m, 1 H (*Z*) + 1 H (*E*)], 3.34–3.39 [m, 1 H (*E*)], 4.59–4.62 [m, 1 H (*Z*)], 8.14 (br s, 1 H (*E*), exchanges with D_2O], 8.54 [br s, 1 H (*Z*), exchanges with D_2O]; ^{13}C-NMR (125 MHz, $CDCl_3$): δ 14.5 (*Z*), 14.7 (*E*), 20.6 (*E*), 21.1 (*Z*), 21.7 (*E*), 25.4 (*E*), 26.8 (*Z*), 27.5 (*Z*), 30.9 (*Z*), 32.4 (*E*), 37.4 (*Z*), 47.4 (*E*), 159.5 (*Z*) 159.8 (*E*); FT-IR (film, cm^{-1}): 3419 (OH), 2952, 2259, 2128, 1634, 1451, 1416, 1017; GC/MS (70 eV): *m/z* (%) (*Z*)-**3b** 159 (16) $[M]^+$, 113 (100), 94 (11), 81 (64), 67 (24); (*E*)-**3b** 159 (13) $[M]^+$, 113 (100), 94 (8), 81 (33), 67 (26). HRMS (ESI): calcd for $C_7H_{13}NOS$ $[M + H]^+$ 160.0700; found: 160.0789.



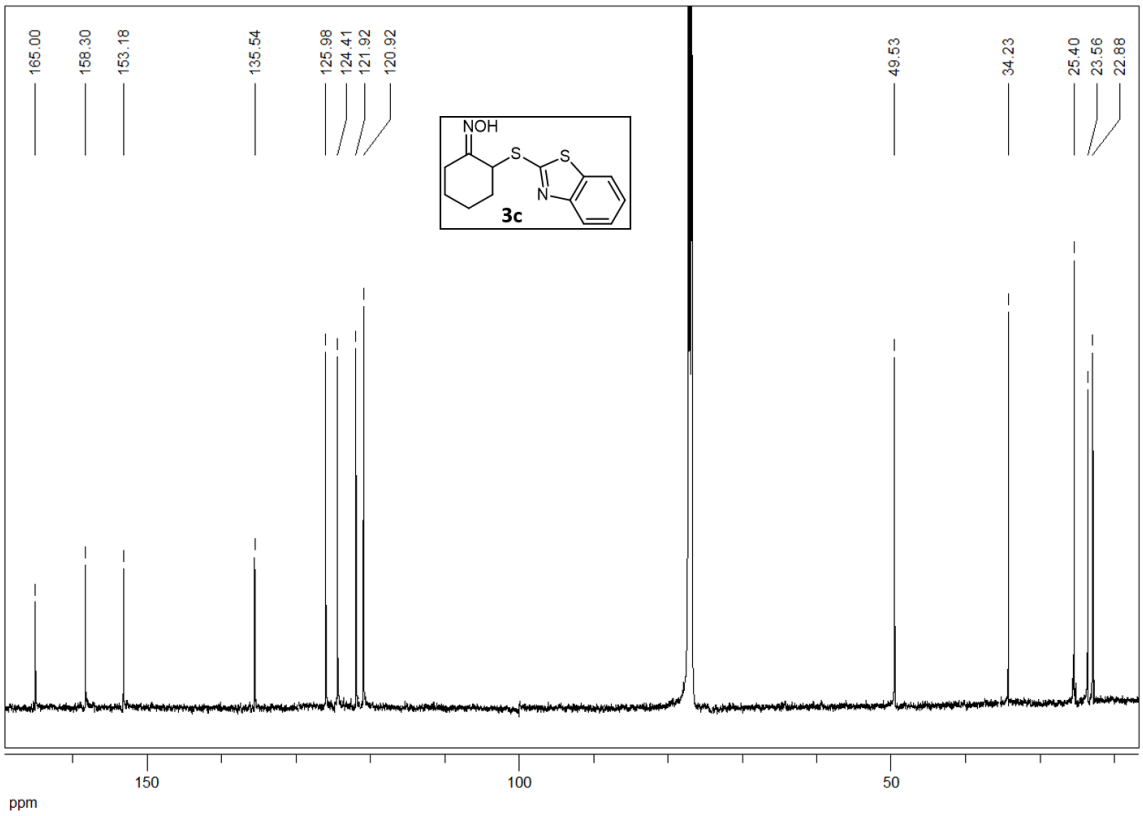
(*Z*)-2-(Thiophen-2-ylthio)cyclohexanone oxime (3d):[1] colourless oil, 63% yield. ^{1}H-NMR (600 MHz, $CDCl_3$): δ 1.42–1.64 (m, 2 H), 1.78–2.04 (m, 4 H), 2.42–2.56 (m, 1 H), 2.82–2.88 (m, 1 H), 3.76 (t, *J* = 4.4 Hz, 1 H), 6.96 (dd, *J* = 4.0, 2.8 Hz, 1 H), 7.10 (dd, *J* = 2.8, 0.8 Hz, 1 H), 7.35 (dd, *J* = 4.0, 0.8 Hz, 1 H), 8.42 (br s, 1 H, exchanges with D_2O); ^{13}C-NMR (125 MHz, $CDCl_3$): δ 21.1, 21.9, 25.3, 32.1, 53.0, 127.6, 130.4, 132.1, 135.5, 158.4; FT-IR (film, cm^{-1}): 3307, 3101, 2986, 2860, 1723, 1651, 1446, 1403, 1217, 981. HRMS (ESI): calcd for $C_{10}H_{13}NOS_2$ $[M + H]^+$ 228.0511; found: 227.0544.
(*E*)-2-(Thiophen-2-ylthio)cyclohexanone oxime: colourless oil, 21% yield. ^{1}H-NMR (600 MHz, $CDCl_3$): δ 1.24–1.27 (m, 1 H), 1.38–1.45 (m, 1 H), 1.61–1.63 (m, 1 H), 1.72–1.78 (m, 1 H), 1.84–1.89 (m, 1 H), 2.02–2.04 (m, 1 H), 2.27–2.45 (m, 1 H), 2.55–2.80 (m, 1 H), 4.90 (t, *J* = 4.0 Hz, 1 H), 6.97 (dd, *J* = 5.2, 3.2 Hz, 1 H), 7.09 (dd, *J* = 3.2, 0.8 Hz, 1 H), 7.36 (dd, *J* = 5.2, 0.8 Hz, 1 H), 7.75 (br s, 1 H, exchanges with D_2O); ^{13}C-NMR (125 MHz, $CDCl_3$): δ 20.7, 26.6, 28.2, 30.3, 43.5, 127.6, 130.4, 132.1, 135.5, 158.4; FT-IR (film, cm^{-1}): 3310, 3109, 2860, 1723, 1651, 1446, 1403, 1217, 988. HRMS (ESI): calcd for $C_{10}H_{13}NOS_2$ $[M + H]^+$ 228.0511; found: 227.0564.

4. ^{1}H and ^{13}C NMR spectra of compounds 3c, 3e–j, 7a,b

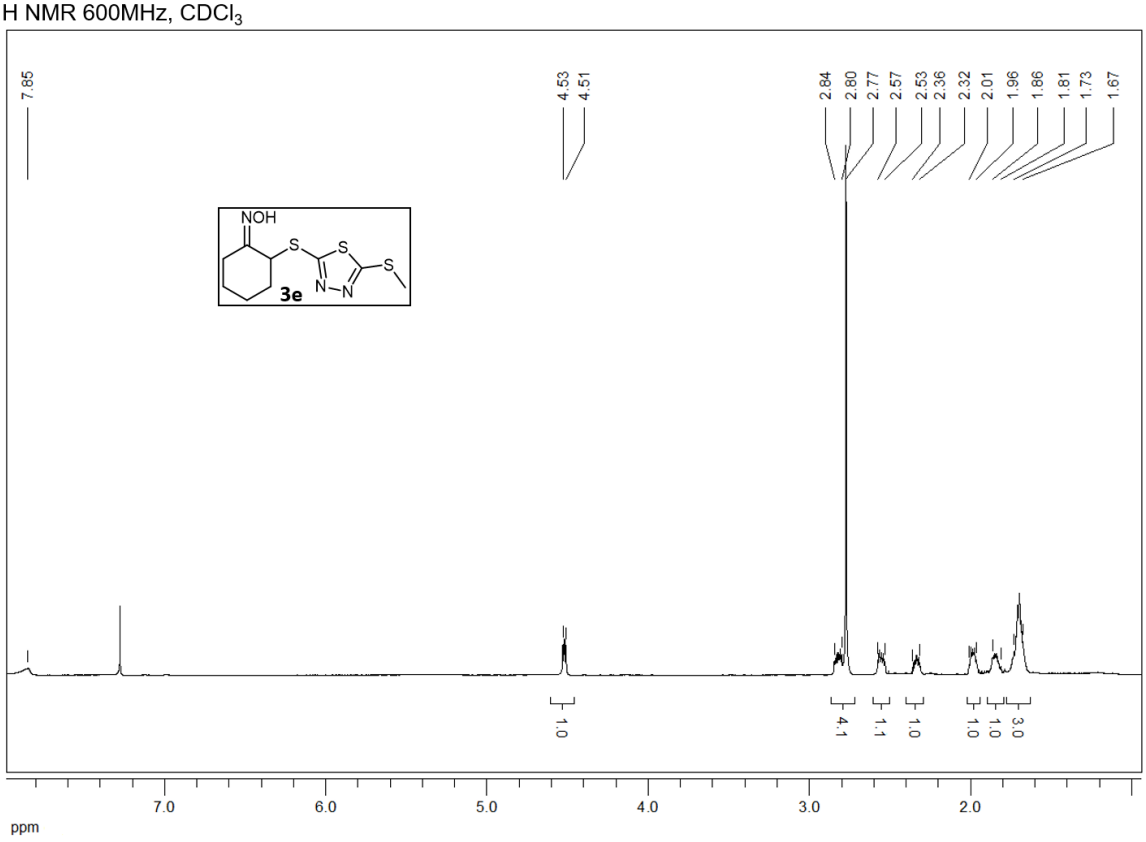
^{1}H NMR 600MHz, $CDCl_3$



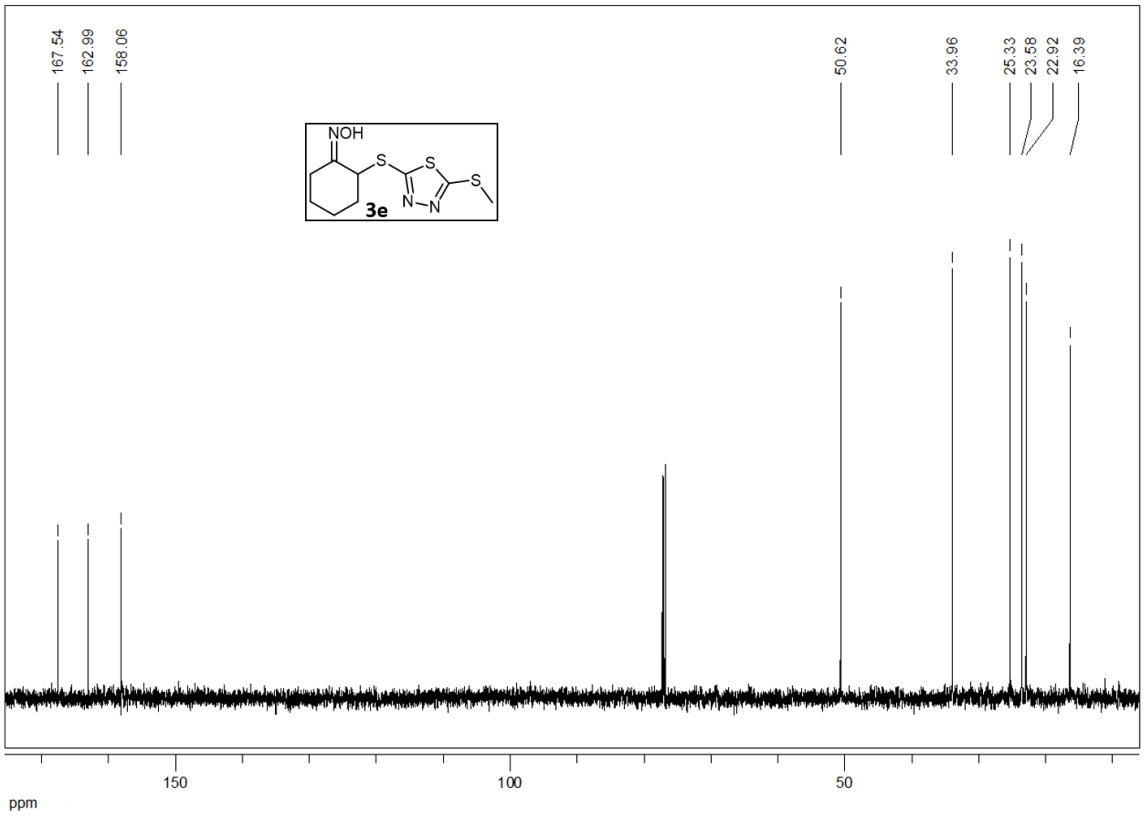
^{13}C NMR 125 MHz, $CDCl_3$



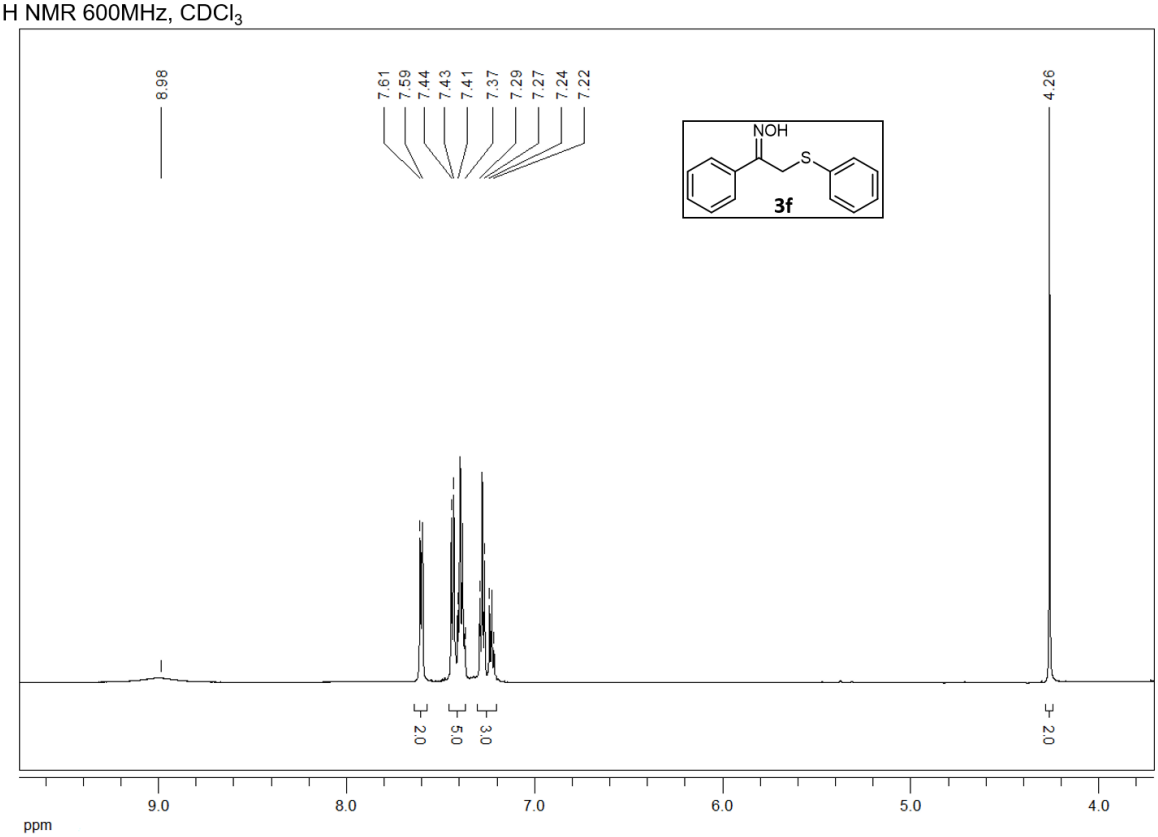
^{1}H NMR 600MHz, $CDCl_3$



^{13}C NMR 125 MHz, $CDCl_3$



^{1}H NMR 600MHz, $CDCl_3$



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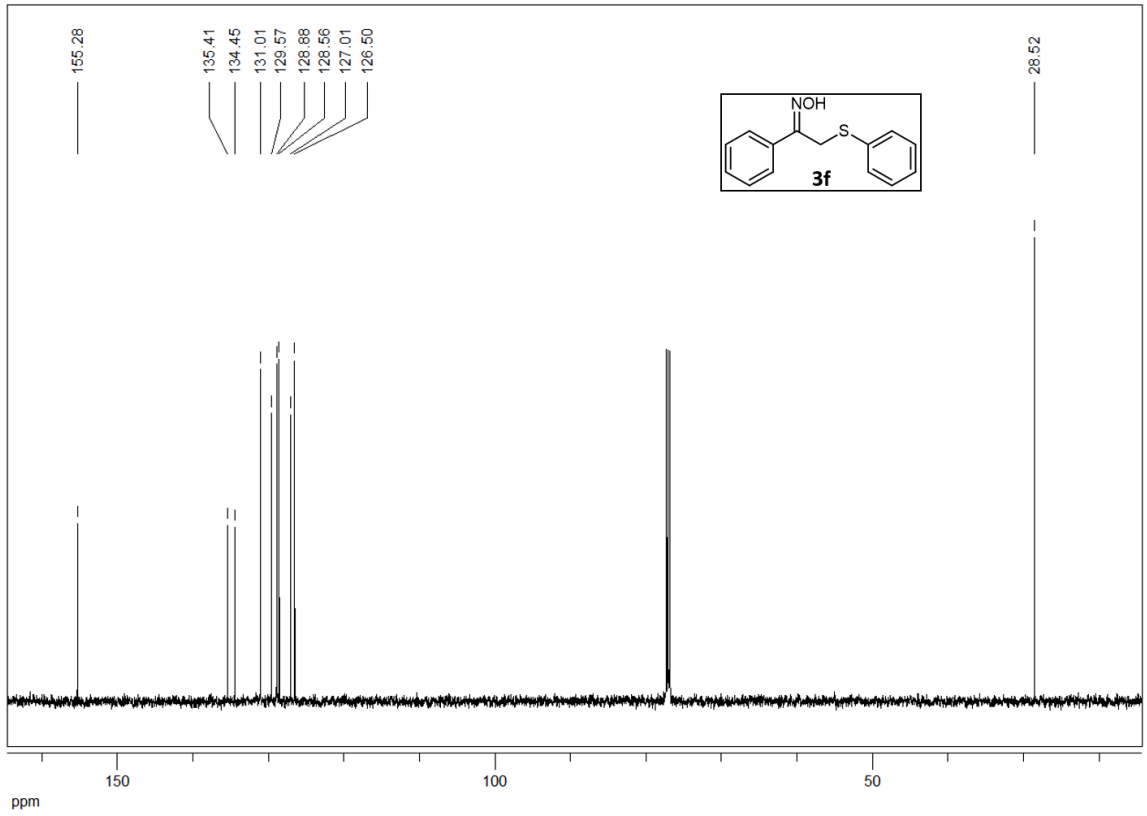

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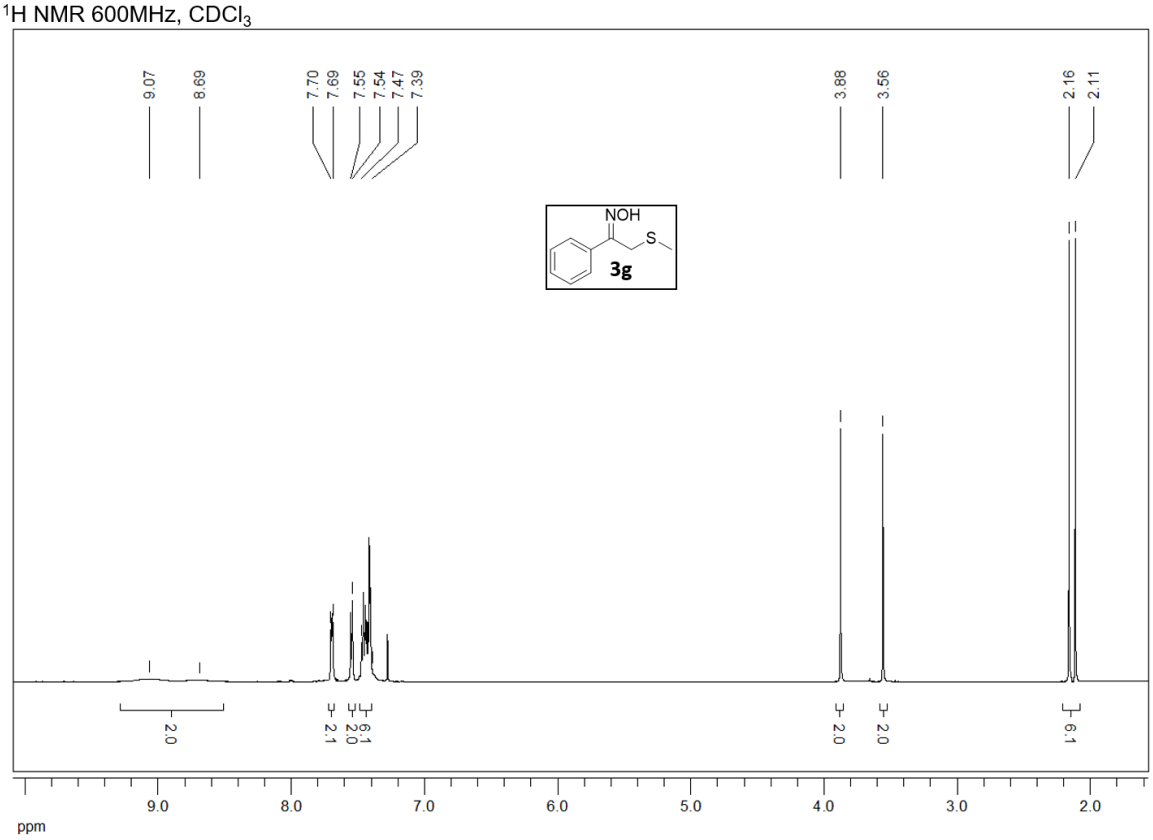

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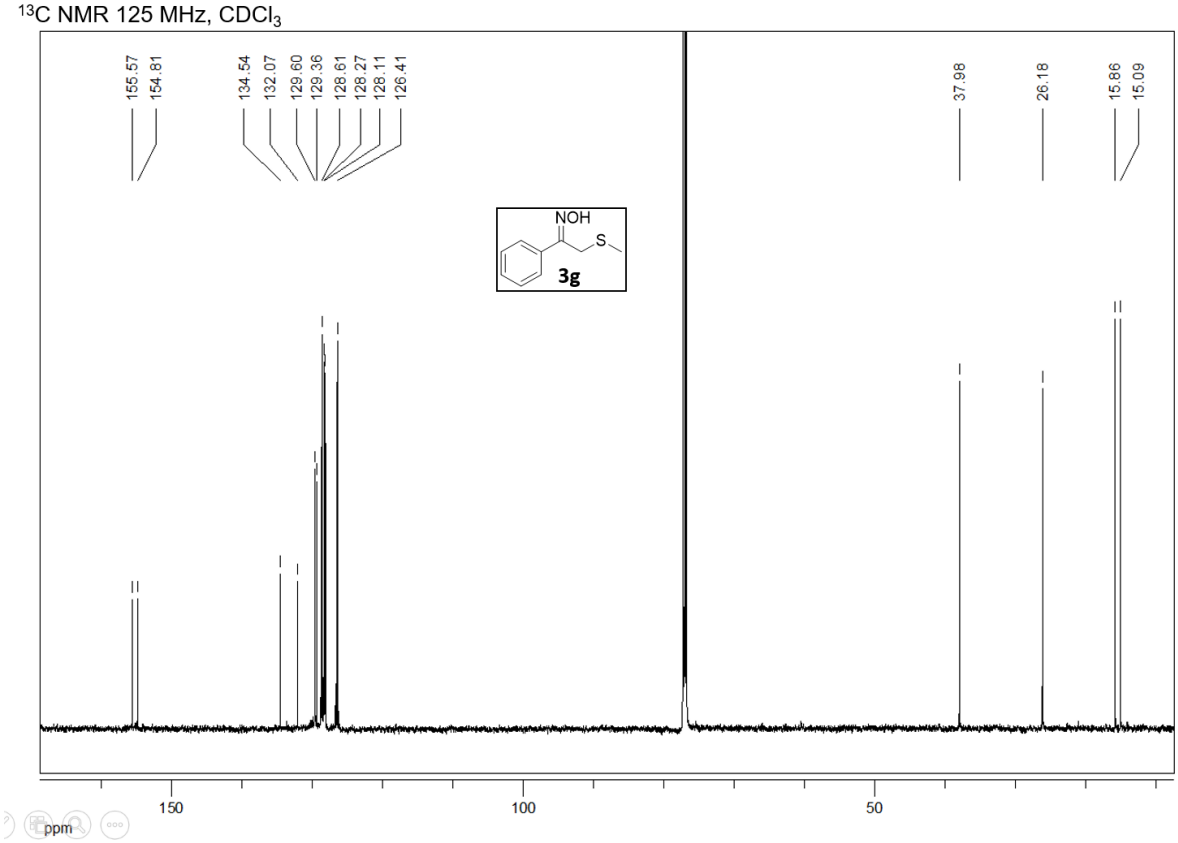

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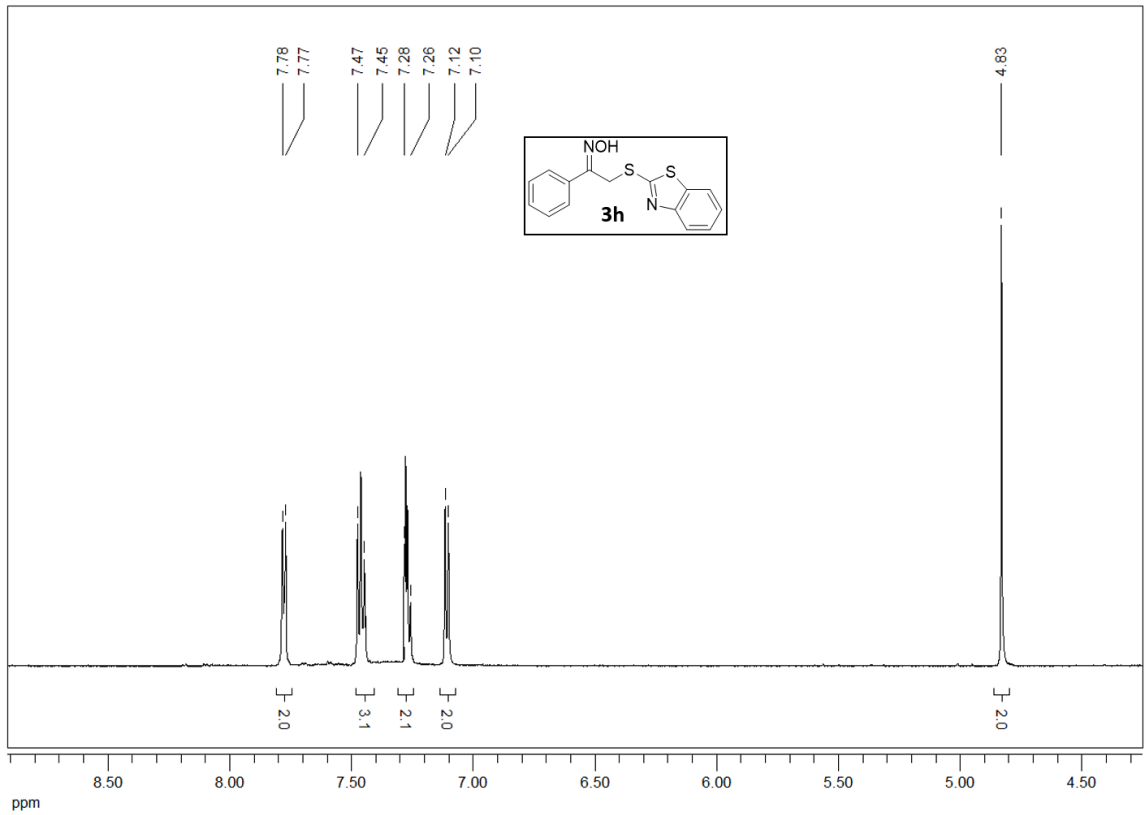

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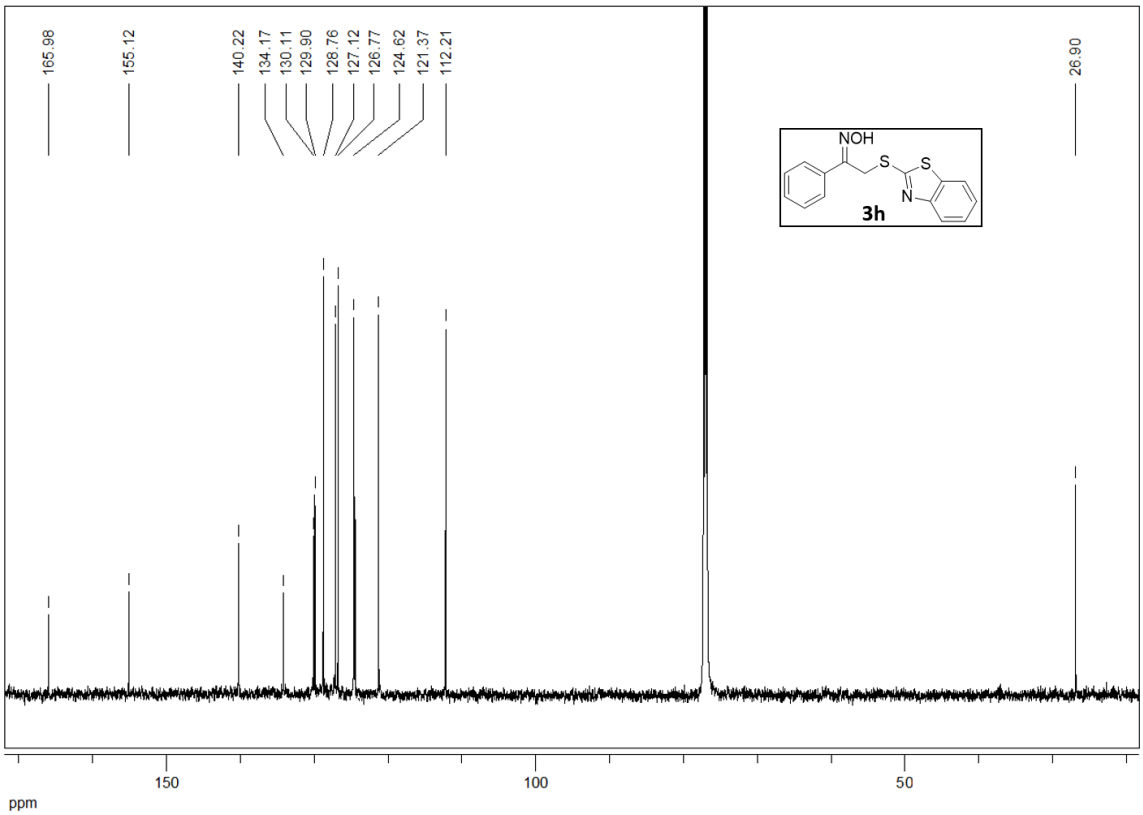

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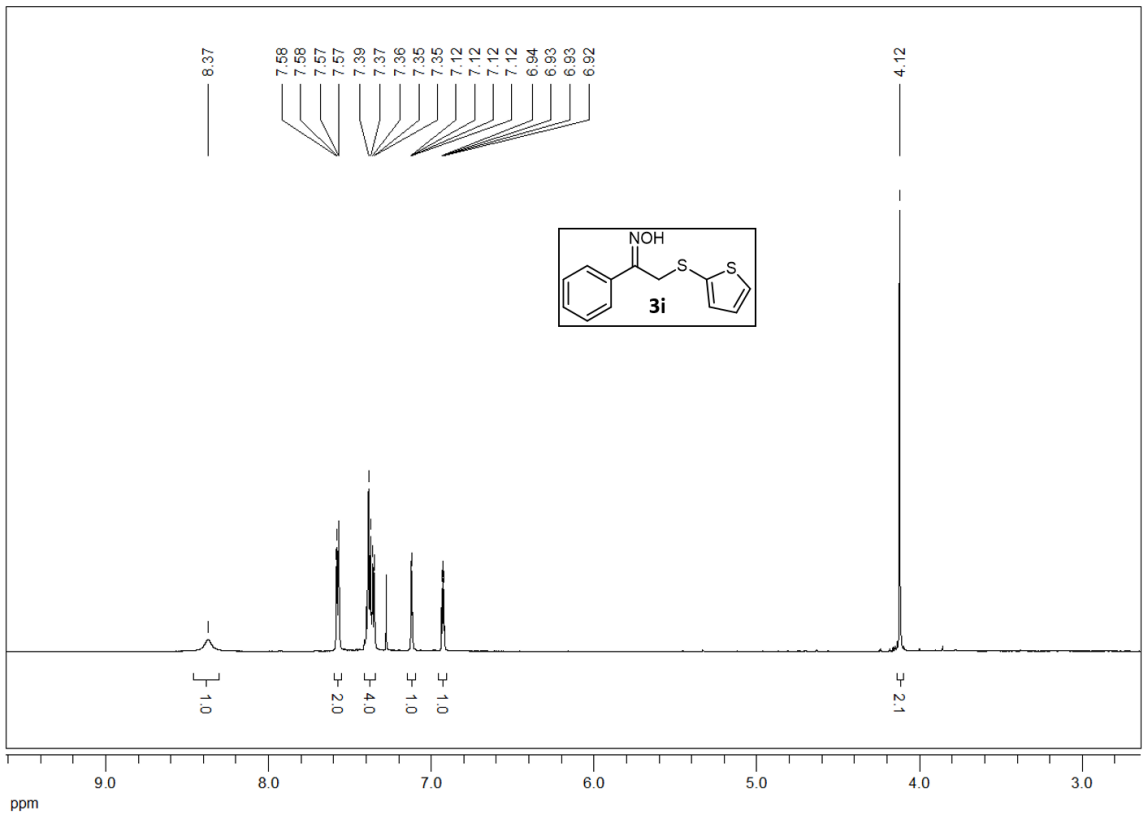

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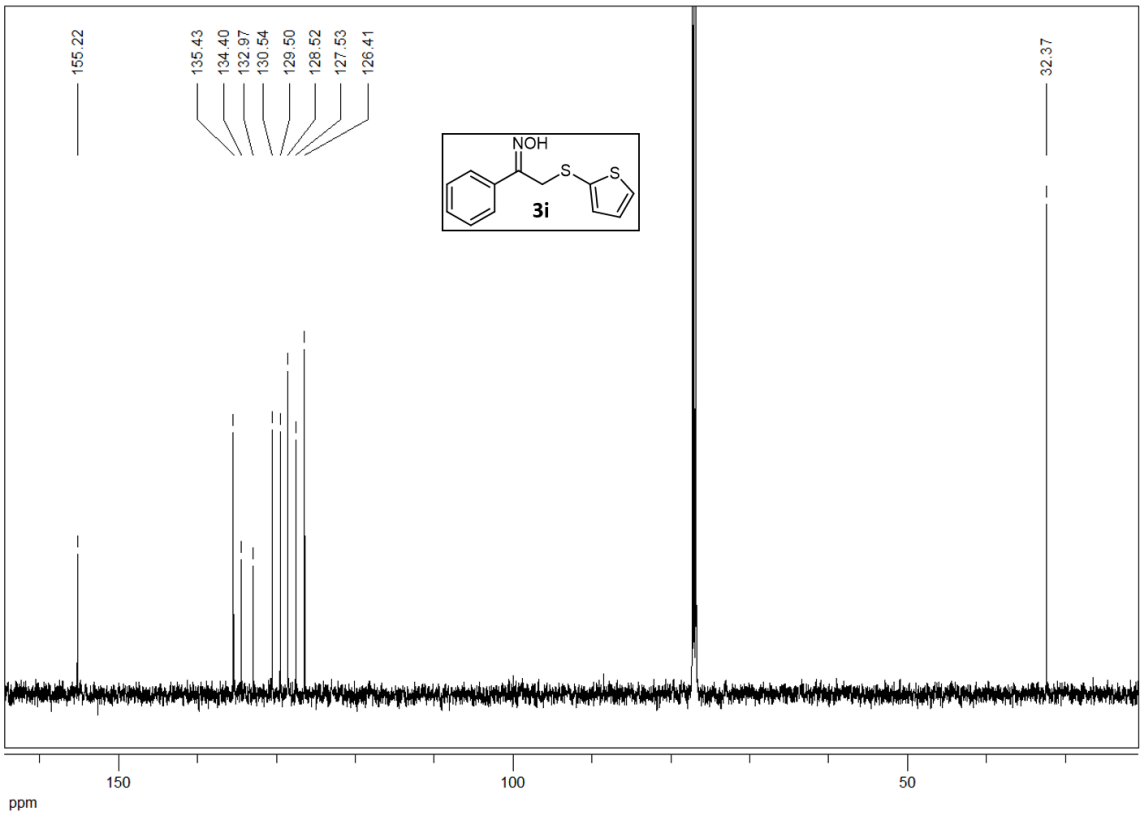

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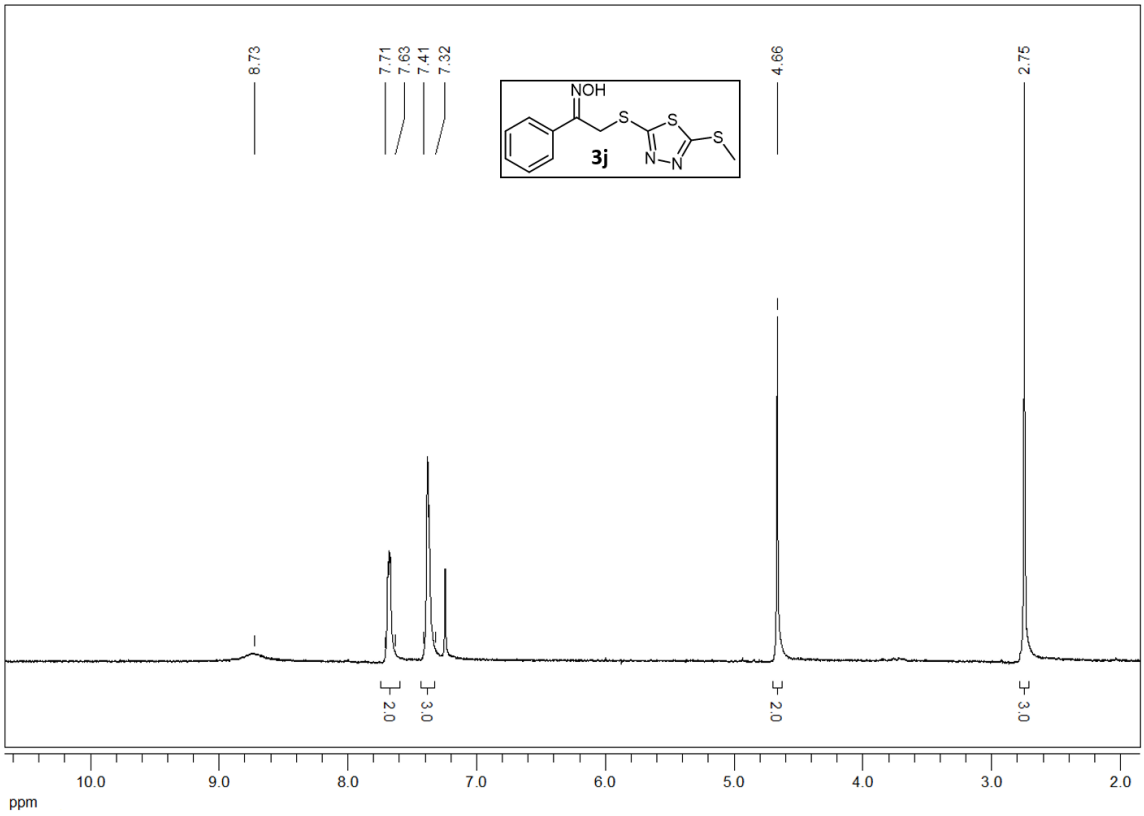

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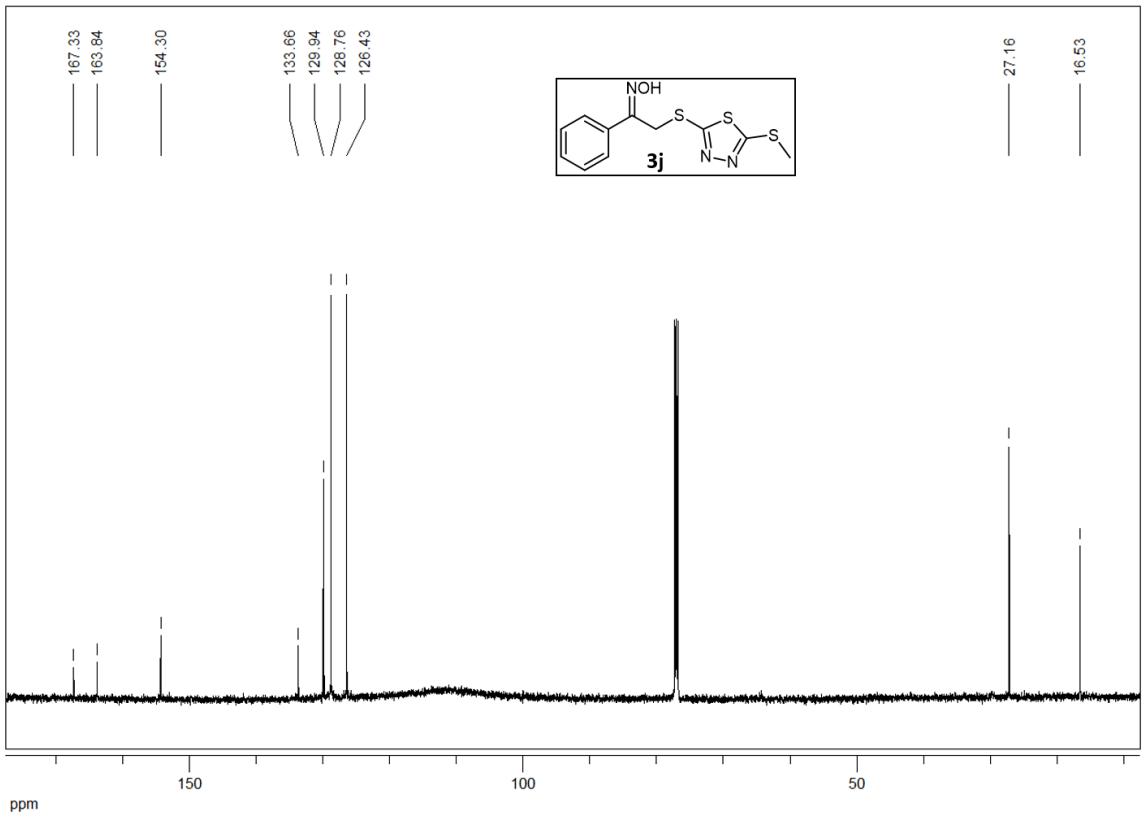

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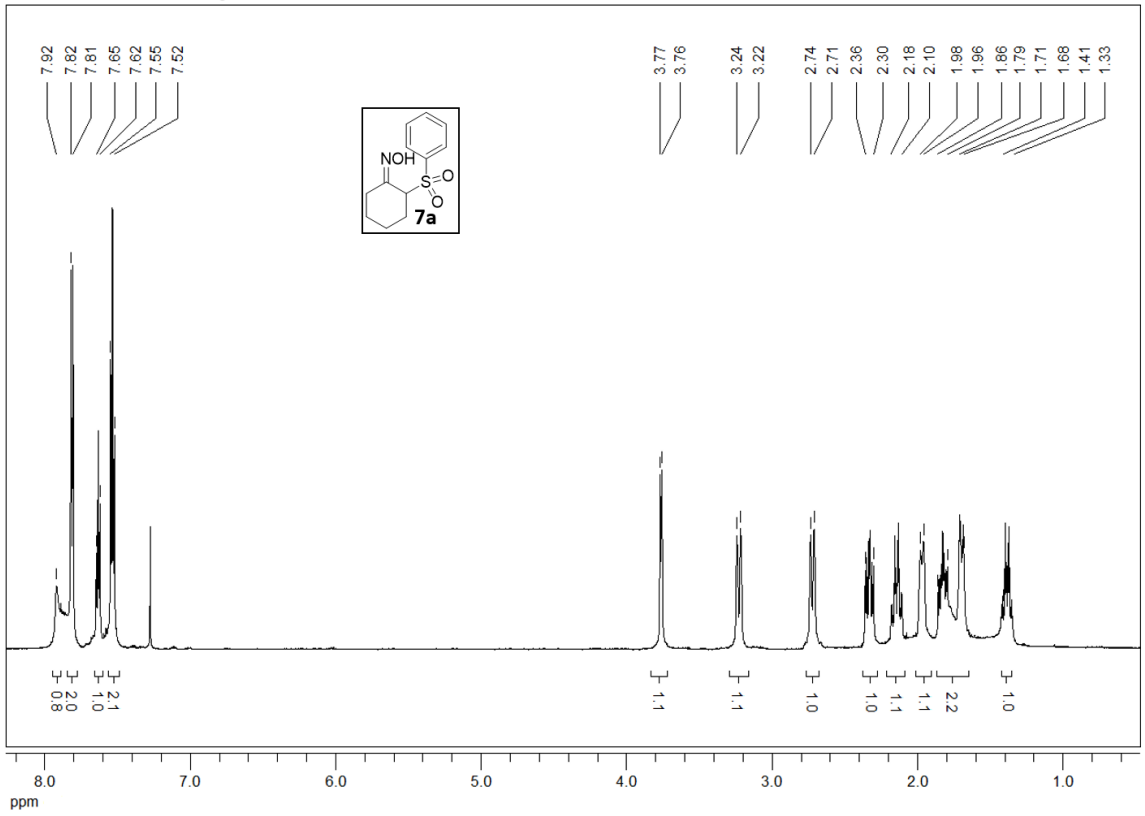

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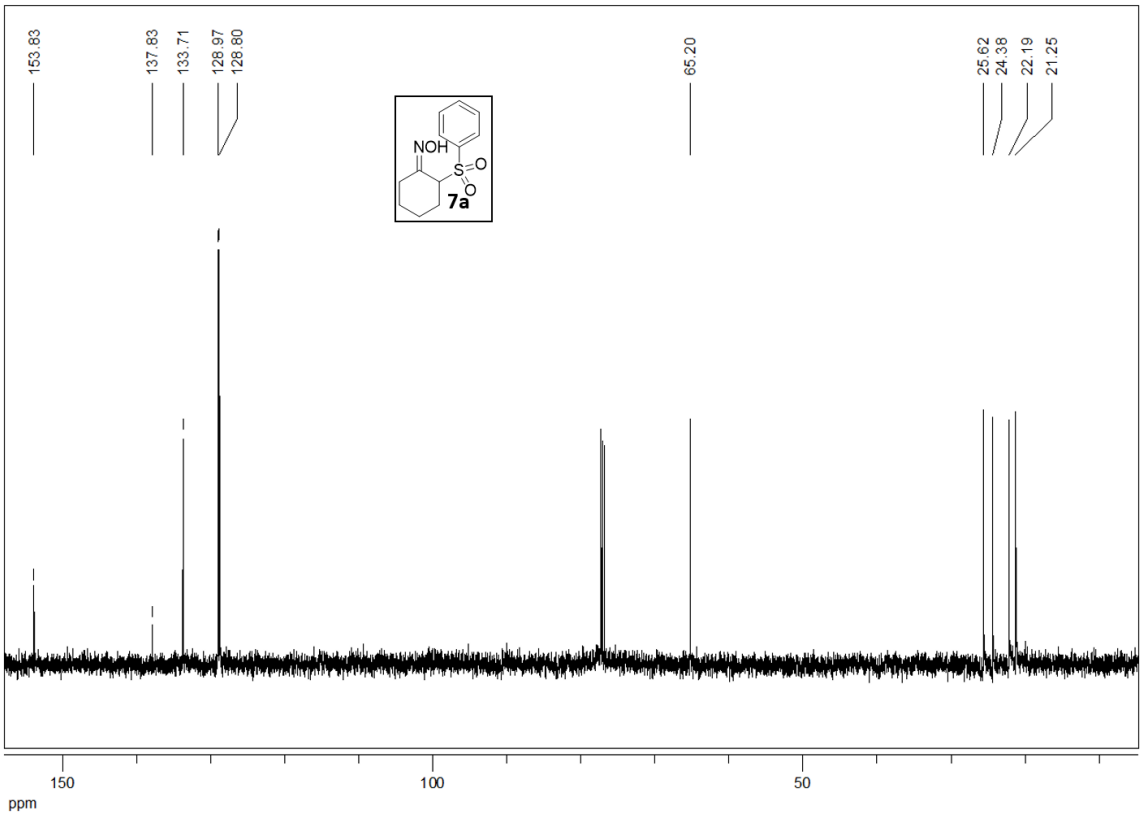

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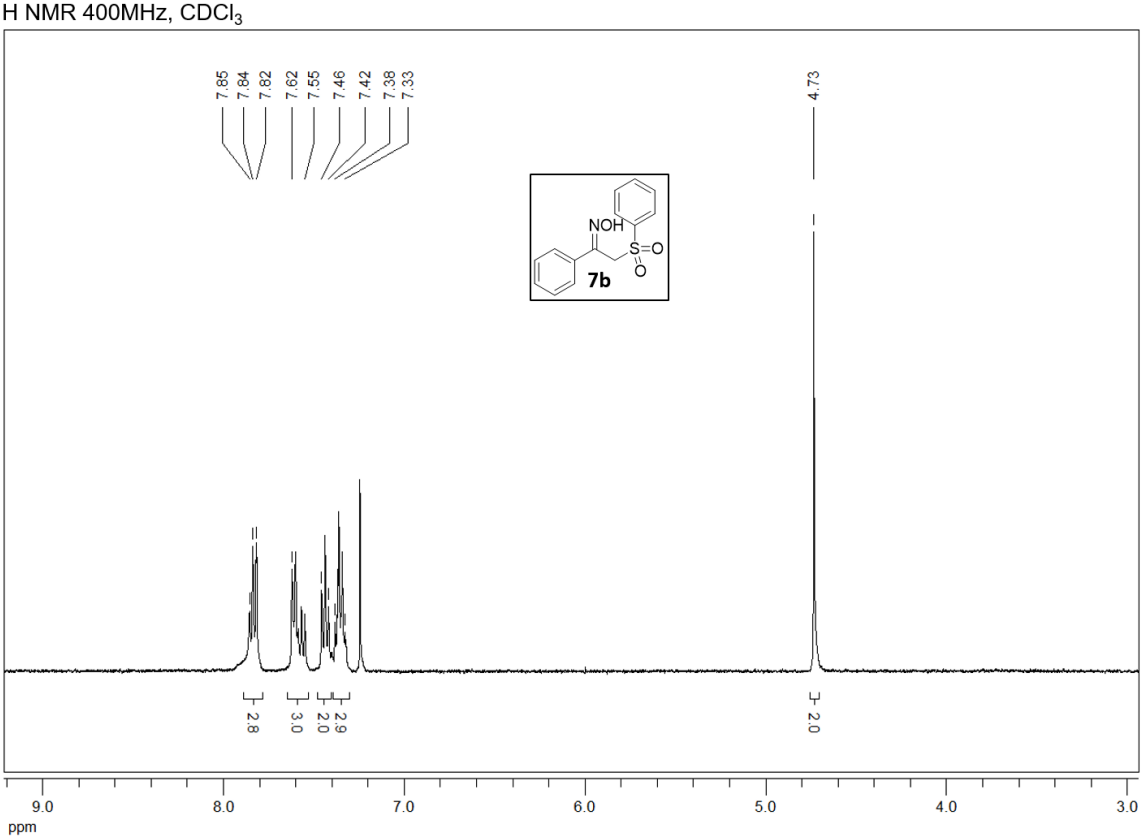

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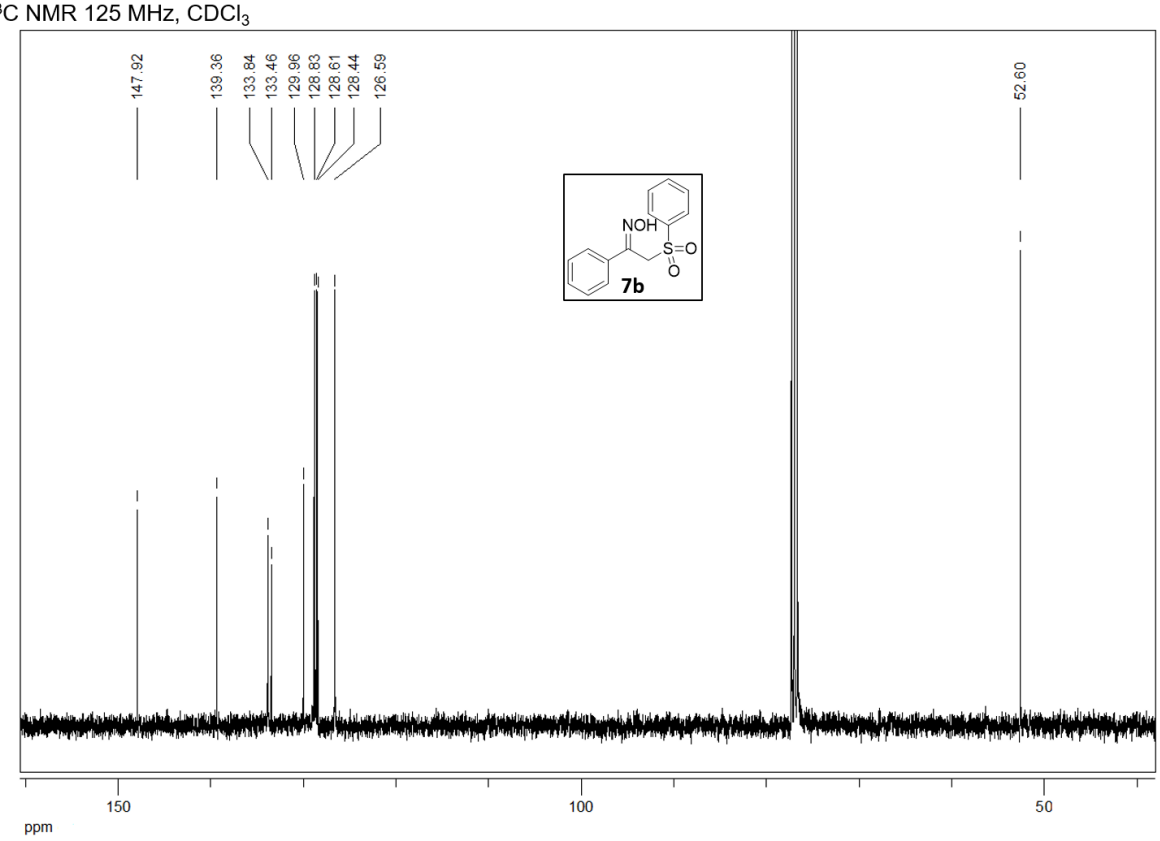

5. References

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