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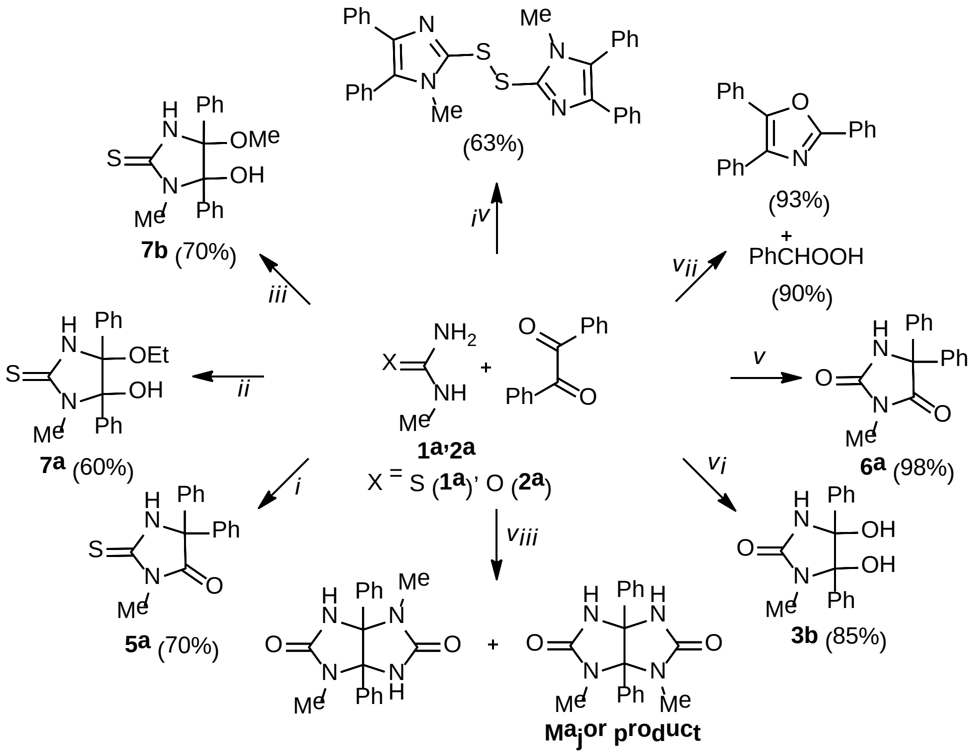
New aspects of reactions of methyl (thio)ureas with benzil

Vladimir V. Baranov, Tatyana N. Vol’khina, Yulia V. Nelyubina
and Angelina N. Kravchenko

General

All reagents (Acros) were used as purchased, unless otherwise indicated. ^{1}H and ^{13}C NMR were recorded at 23 to 28 °C using Bruker AM300 (^{1}H, 300.13 MHz; 13C, 75.5 MHz). Chemical shifts are reported in the δ scale relative to Me4Si as internal standard. High resolution mass spectra (HRMS) were recorded on a Bruker micrOTOF II instrument using the electrospray ionization method (ESI). Melting points were determined in a SMP10 instrument (Stuart).

The synthesis of 1-alkyl thioureas **1b**,**c** was carried out by treatment of ethyl or isobutyl isothiocyanates, respectively, with aqueous ammonia [S1,S2]. 1-Ethyl-, 1-propyl- and 1-butylureas were obtained by the reaction of the corresponding alkylamine hydrochlorides with potassium isocyanate [S3-S5]. Compounds **5a-c**,**6a-d,7a**,**b** were obtained using methods (see Online Supplementary Materials) different from the known ones [S6-S11]. The melting points of the compounds **7a**,**b**, given in the literature [S8], differ from the melting temperatures of these compounds synthesized in this work.



Scheme S1 *Reagents and conditions*: *i*. X = S, EtOH, NaOH, reflux, 3 h; *ii*. X = S, EtOH, NaOH, 30 °C, 30 min; *iii*. X = S, MeOH, NaOH, 30 °C, 30 min; *iv*. X = S, EtOH, HCl, reflux, 3 h; *v*. X = O, dipenten, reflux, 1.5 h; *vi*. 1) Na, Pr^iOH, reflux, 2) 1-methyl ureas 2 equiv, reflux, 30 min; *vii*. 1-methyl ureas 3 equiv 180 °C, $(CH_2OH)_2$, 1 h; *viii*. 1-methyl ureas 2 equiv, TFA, PhH, reflux, 6 h.

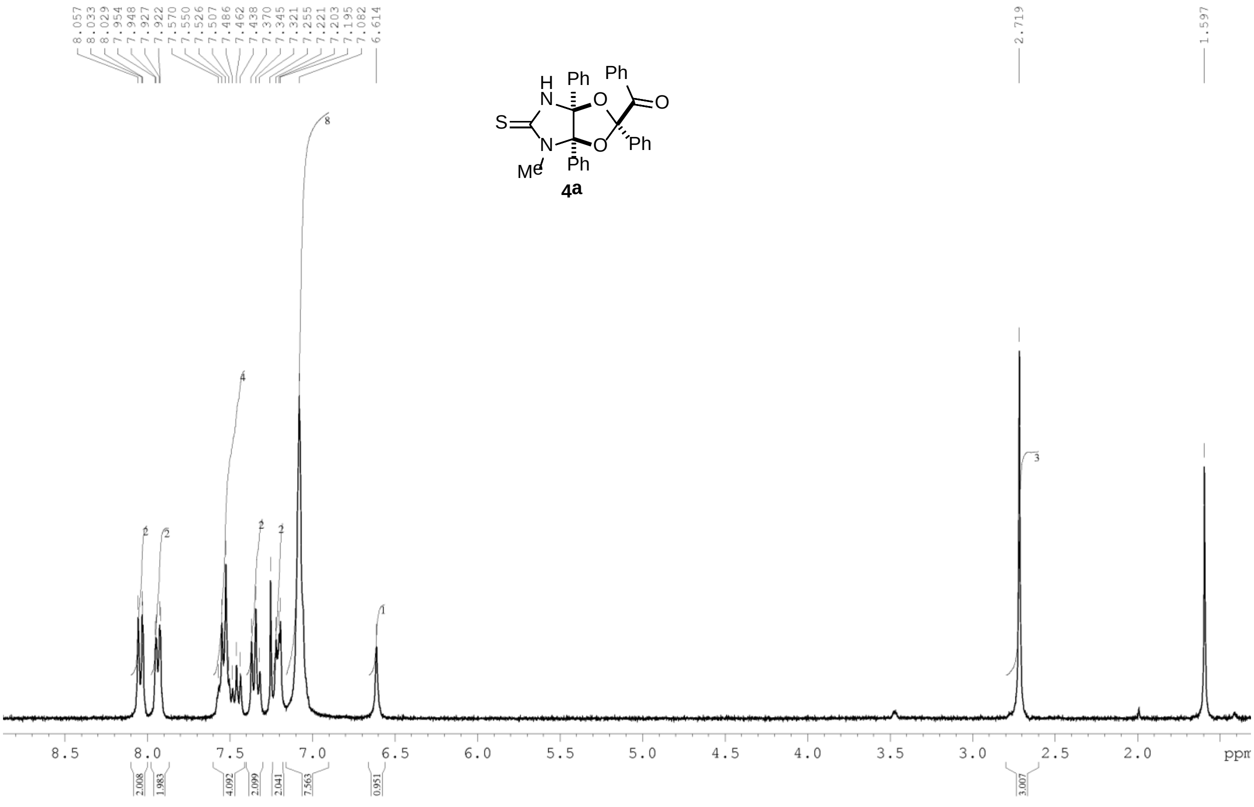


Figure S1. ^{1}H NMR spectrum of compound **4a**.

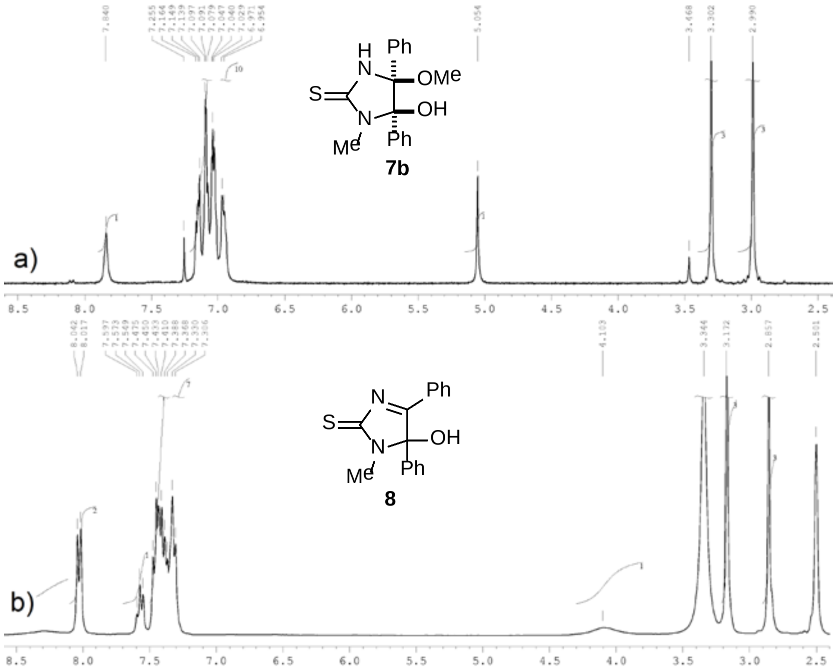


Figure S2 ^{1}H NMR spectra: *a*) compound **7b** ($CDCl_3$), *b*) (**8** + MeOH (DMSO-d_6).

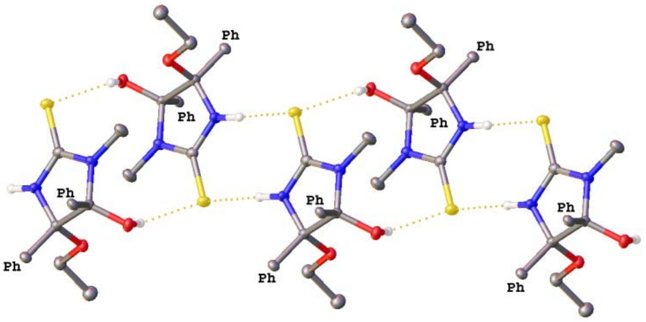


Figure S3 Fragment of the crystal packing in **7a** illustrating the formation of infinite chains from centrosymmetric dimers.

Synthesis of compounds **4a,b** *(general procedure)*: A solution of KOH (16 mg, 0.35 mmol) in water (5 ml) was added to a suspension of benzil (1.05 g, 5 mmol) and 1-methyl(thio)urea (5 mmol) in Pr^iOH. The mixture was stirred at room temperature for 25 min. The precipitate of the product **4a,b** was filtered off and washed with Et_2O. To obtain the crystals, the powders of compounds **4a,4b** were crystallized from MeCN.

rac-(2S,3aR*,6aS*)-4-Methyl-2,3a,6a-triphenyl-5-thioxotetrahydro-3aH-[1,3]dioxolo[4,5-d]imidazol-2-yl)(phenyl)methanone* **4a.** Colorless crystals. Yield 34% (0.42 g), mp 225–227 °C (MeCN). ^{1}H NMR ($CDCl_3$), δ: 2.72 (s, 3H, NMe); 6.61 (s, 1H, NH); 7.00-7.10 (m, 8H, Ph); 7.15-7.24 (m, 2H, Ph); 7.29-7.38 (м, 2H, Ph); 7.42-7.58 (m, 4H, Ph); 7.88-8.00 (m, 2H, Ph); 8.02-8.11 (m, 2H, Ph). ^{13}C NMR ($CDCl_3$), δ: 30.52 (Me), 100.24, 105.80, 109.92 (C-

Ph), 126.07, 126.86, 127.04, 127.93, 128.12, 128.15, 129.12, 130.07, 130.28, 133.11 (CH(Ph)), 133.18, 133.60, 134.99, 135.17 (C(Ph)), 183.48 (C=S), 194.35 (C=O). HRMS, m/z: 493.1581 $[M+H]^+$ (calc. for: $C_{30}H_{24}N_2O_3S+H$, *m/z*: 493.1580).

rac-(2S,3aR*,6aS*)-2-Benzoyl-4-methyl-2,3a,6a-triphenyldihydro-3aH-[1,3]dioxolo[4,5-d]imidazol-5(4H)-one* **4b.** Colorless crystals**.** Yield 37% (0.44 g), mp 200–201 °C (MeCN). ^{1}H NMR (CDCl$_3$), δ: 2.47 (s, 3H, NMe); 5.67 (s, 1 H, NH); 6.97-7.14 (m, 8H, Ph); 7.15-7.24 (m, 2H, Ph); 7.27-7.38 (m, 2H, Ph); 7.39-7.59 (m, 4H, Ph); 7.85-7.98 (m, 2H, Ph); 8.00-8.11 (m, 2H, Ph). ^{13}C NMR (CDCl$_3$), δ:: 26.31 (Me), 98.40, 103.08, 109.89 (C-Ph), 126.06, 127.10, 127.79, 128.01, 128.21, 128.74, 128.82, 129.06, 129.89, 130.30, 132.99 (CH(Ph)), 133.78, 133.99, 135.55, 135.98 (C(Ph)), 158.12 (N-C=O), 196.10 (C=O). HRMS, m/z: 477.1808 $[M+H]^+$ (calc. for: $C_{30}H_{24}N_2O_4+H$, m/z: 477.1809).

Synthesis 5-hydroxy-1-methyl-4,5-diphenyl-1H-imidazole-2(5H)-thione **8.** A solution of bright orange compound **8** was obtained, when ethers **7a,b** were dissolved in DMSO-d$_6$ after heating for 1 min. ^{1}H NMR (DMSO-*d*$_6$), δ: 2.86 (s, 3H, NMe); 3.17 (s, 3H, Me(MeOH)); 4.10 (s, 1H, OH(MeOH)); 7.25-7.50 (m, 7H, Ph); 7.53-7.62 (m, 1H, Ph); 7.98-8.10 (m, 2H, Ph); 8.11-8.60 (br.s, 1H, OH). ^{13}C NMR (DMSO-*d*$_6$), δ: 27.41 (NMe), 48.60 (MeOH) 98.16 (C-Ph), 124.77, 126.67, 128.42, 128.70, 129.31, 133.68, 135.34 (Ph), 183.81, 191.04 (C=S, C=N). HRMS, m/z: 283.0905 $[M+H]^+$ (calc. for: $C_{16}H_{14}N_2OS+H$, m/z: 283.0900).

*Synthesis of compounds **7a**,**b** (general procedure).* A solution of KOH (16 mg, 0.35 mmol) in water (1 ml) was added to a suspension of benzil (2.10 g, 10 mmol) and 1-methylthiourea (0.90 g, 10 mmol) in methanol or ethanol (5 ml). The mixture was stirred at ~20 °C for 25 min. The precipitates of products **7a**,**b** were filtered off and washed with Et_2O.

rac-(4S,5R*)-4-Ethoxy-5-hydroxy-1-methyl-4,5-diphenylimidazolidine-2-thione* **7a.** White powder, yield 60% (1.97 g), mp 174–176 °C (EtOH), (141 °C [S7]). ^{1}H NMR (CDCl$_3$, δ, ppm): 1.29 (t, 3 H, *J* = 7.0 Hz, Me); 2.99 (s, 3 H, NMe); 3.28 – 3.40 m, 1 H, CH$_2$); 3.59 – 3.62 (m, 1 H, CH$_2$); 5.14 (s, 1 H, OH); 6.90-7.20 (m, 10 H, Ph); 7.82 (s, 1 H, NH). ^{13}C NMR (CDCl$_3$, δ, ppm): 15.09 (CMe), 28.77 (NMe), 59.53 (CH$_2$) 94.06, 98.12 (C-Ph), 126.52, 126.90, 127.73, 127.84, 128.27, 128.58 (CH(Ph)), 133.86, 135.22 (C(Ph)), 181.86 (C=S). HRMS, m/z: 283.0905 $[M+H–C_2H_5OH]^+$ (calc. for: $C_{18}H_{20}N_2O_2S+H–C_2H_5OH$, m/z: 283.0900).

rac-(4S,5R*)-5-Hydroxy-4-methoxy-1-methyl-4,5-diphenylimidazolidine-2-thione* **7b**. White powder, yield 73% (2.29 g), mp 178–180 °C (MeOH), (136 °C [S7]). ^{1}H NMR (CDCl$_3$, δ, ppm): 2.99 (s, 3 H, NMe); 3.30 (s, 3 H, OMe); 5.05 (s, 1 H, OH); 6.90-7.20 (m, 10 H, Ph); 7.84 (s, 1 H, NH). ^{13}C NMR (CDCl$_3$, δ, ppm): 28.86 (NMe), 51.17 (OMe) 94.51, 98.34 (C-Ph), 126.63, 127.22, 127.88, 128.03, 128.44, 128.82 (CH(Ph)), 133.14, 135.32 (C(Ph)), 181.99

(C=S). HRMS, m/z: 283.0904 $[M+H–CH_3OH]^+$ (calc. for: $C_{17}H_{18}N_2O_2S$+H–CH_3OH, m/z: 283.0900).

Synthesis of 3-alkyl-5,5-diphenyl-2-thioxoimidazolidin-4-ones ***5a-c*** *and 3-alkyl-5,5-diphenylimidazolidine-2,4-diones* ***6a-d*** *(general procedure).* A solution of KOH (16 mg, 0.35 mmol) in water (1 ml) was added to a suspension of benzil (1.05 g, 5 mmol) and 1-methyl-, 1-ethyl- or 1-isobutylthiourea (5 mmol) **1a-c** or 1-methyl-, 1-ethyl, 1-propyl, or 1-butylurea **2a-d** in Pr^iOH (50 ml). The reaction mixture was stirred at room temperature for 12 h, evaporated to dryness, and the resulting powders were crystallized from MeOH. The precipitate **5a-c**, **6a-d** was filtered off and washed with Et_2O. Yields: **5a**, 92% (70% [S7]); **5b**, 89% (56% [S9]); **5c**, 88% (40% [S10]); **6a**, 91% (98% [S12]); **6b**, 90% (42% [S11]); **6c**, 87% (71% [S11]); **6d**, 90%, (62% [S6]). Physicochemical characteristics of the synthesized thiohydantoines **3a-c** and hydantoines **6a-d** correspond to the literature data [S6,S7,S9-S12].

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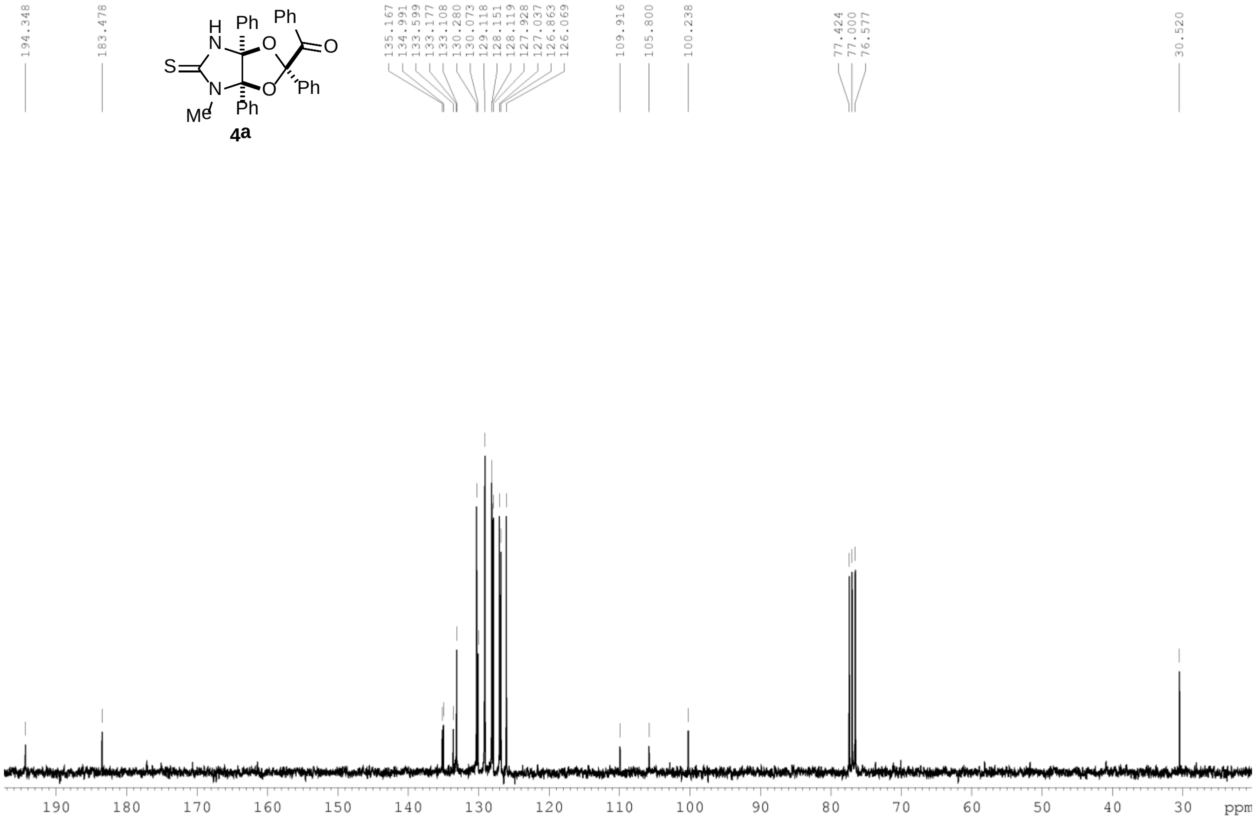

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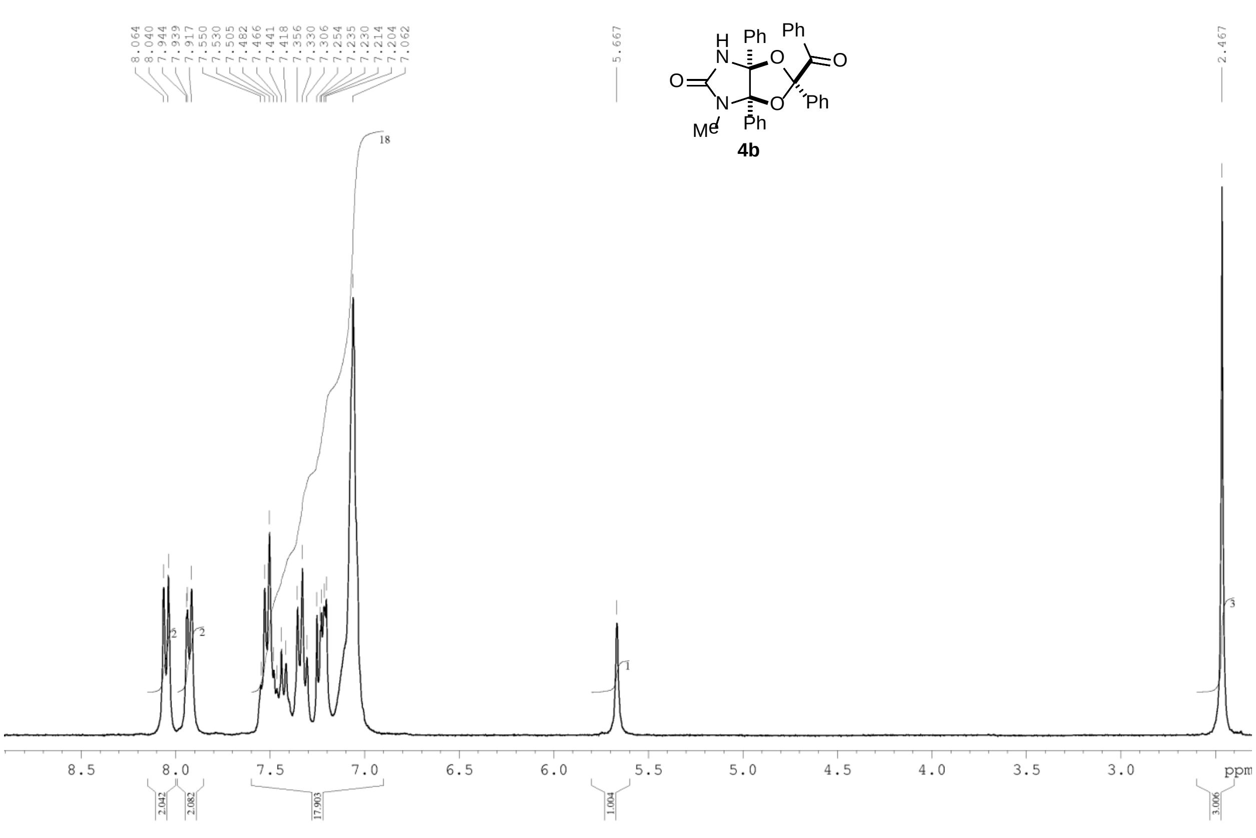

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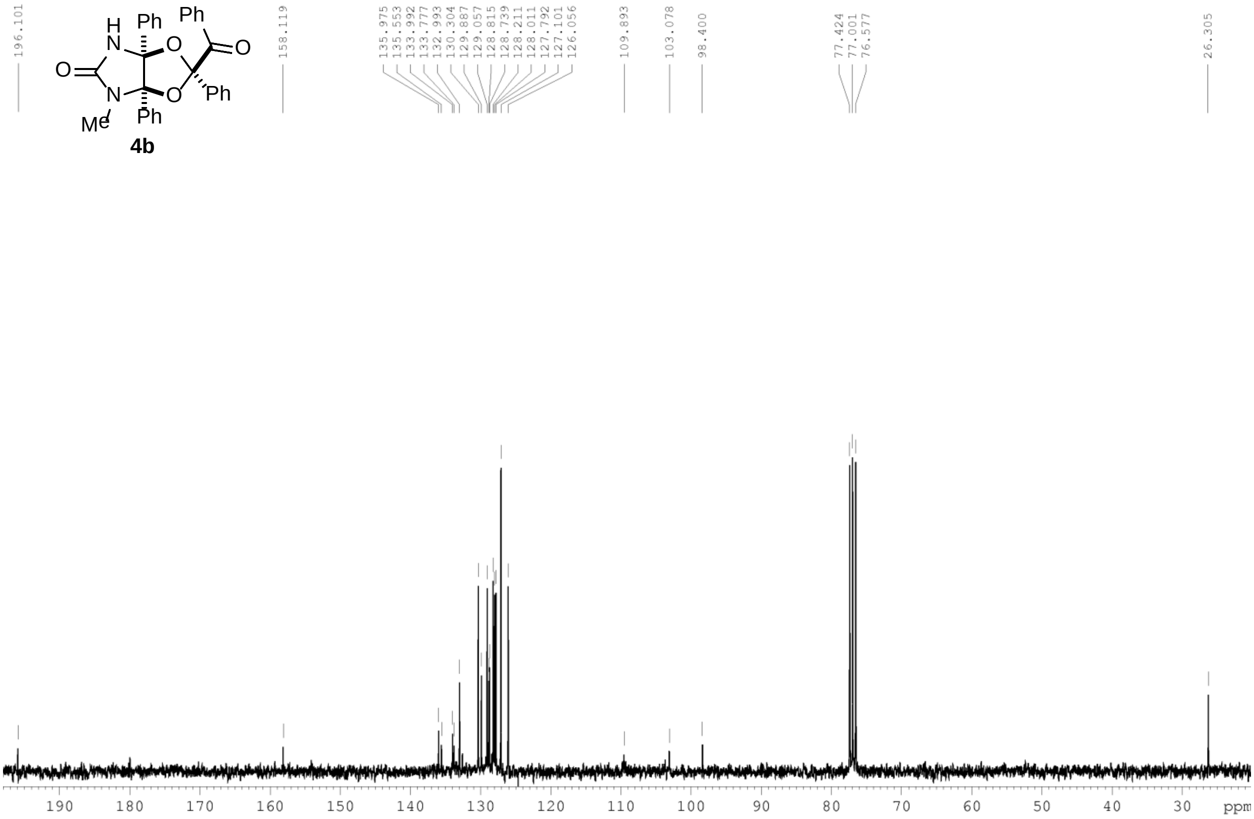
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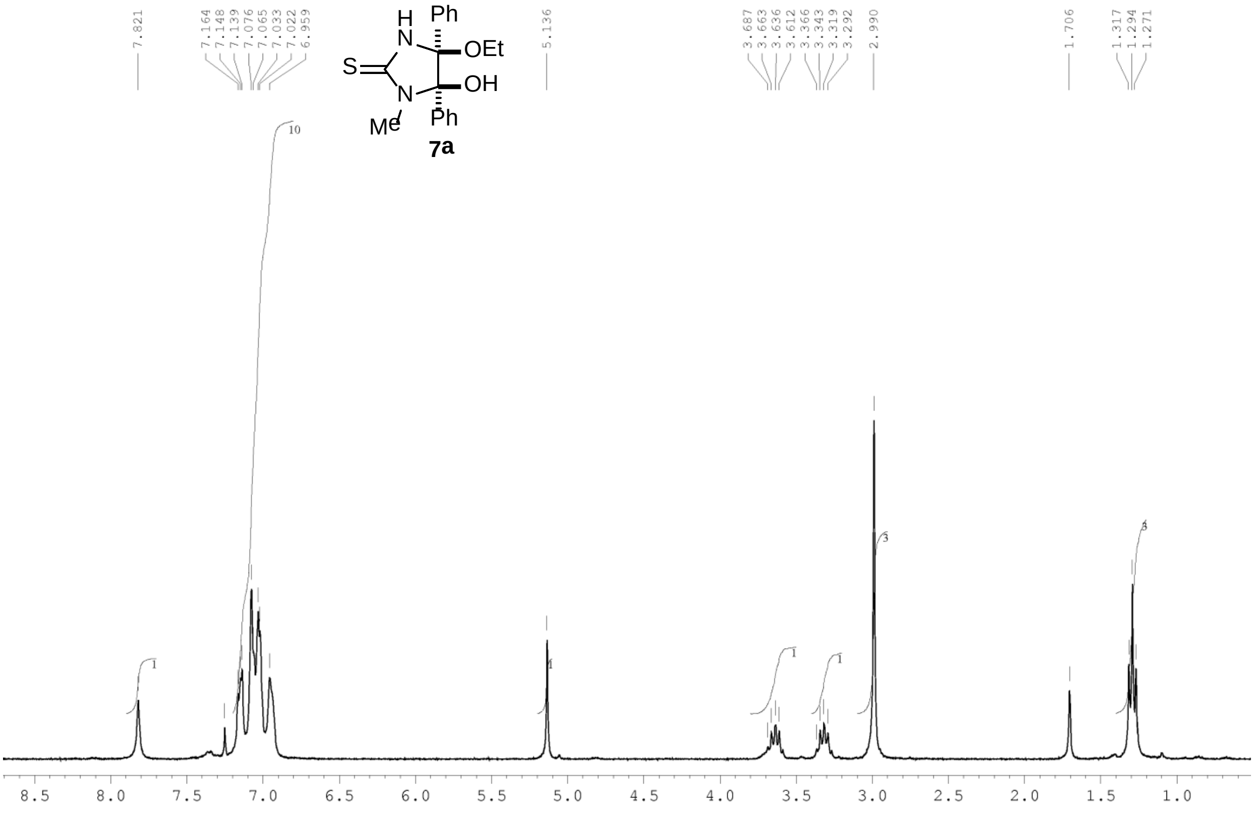
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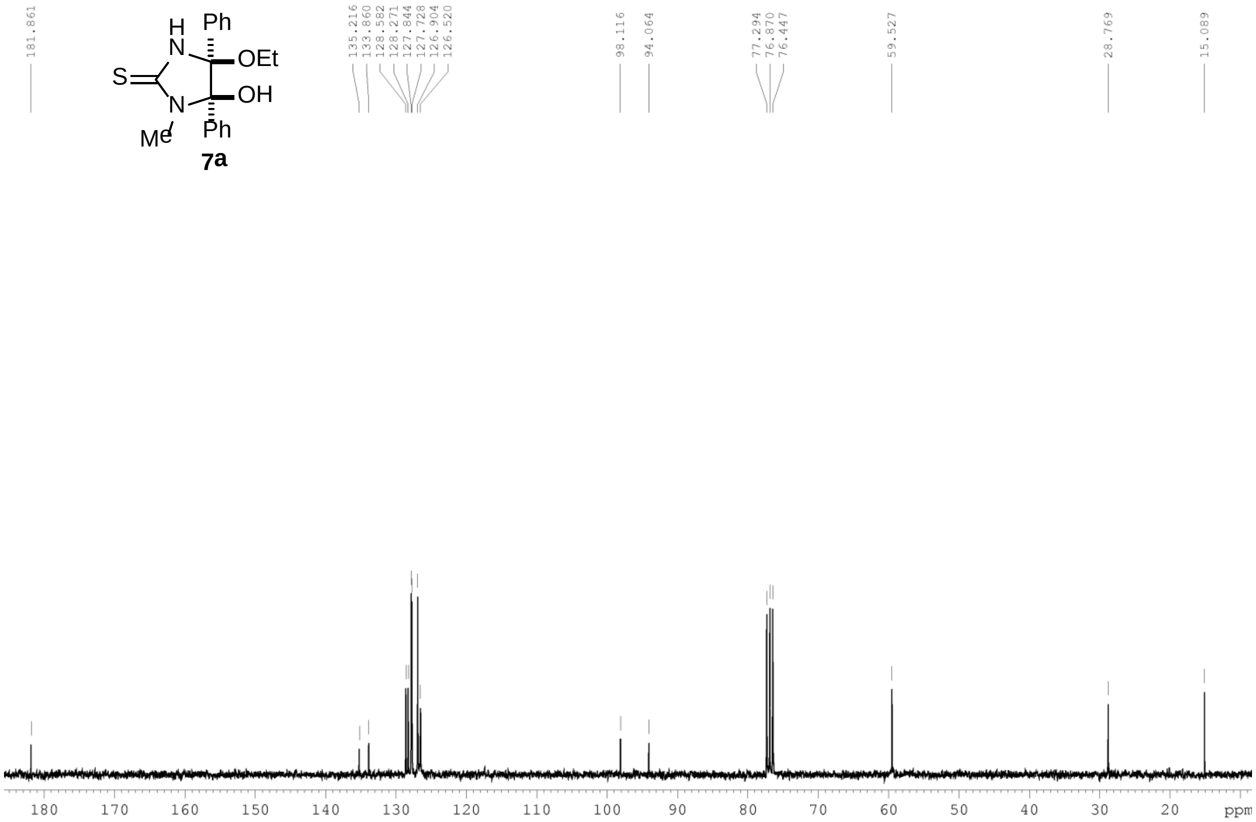
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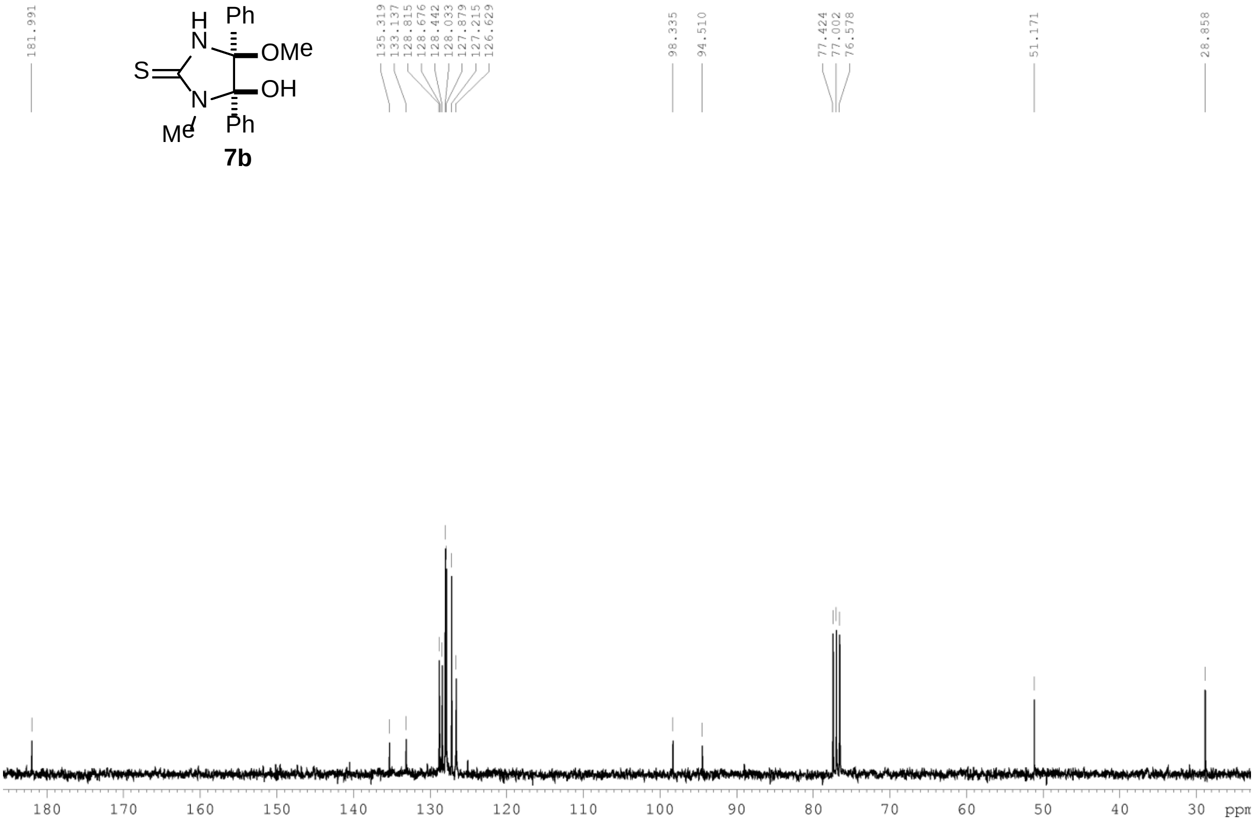
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