A Route to the Heterocyclic Cluster of the E-Series of Thiopeptide Antibiotics

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Supporting Information

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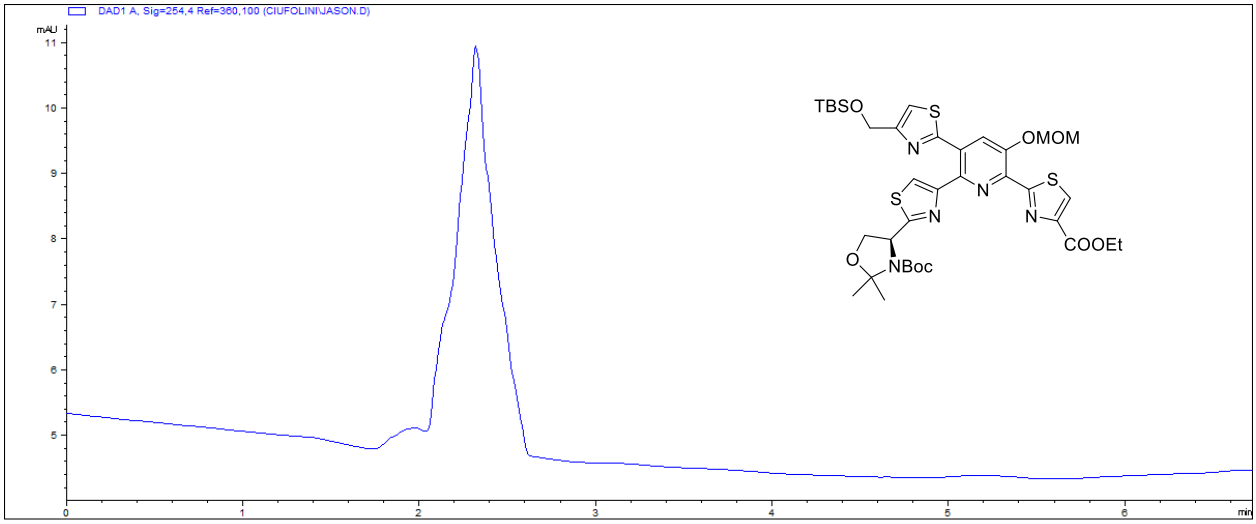
A. Experimental Protocols.

Unless otherwise stated, ^{1}H and ^{13}C NMR spectra were recorded at room temperature at 300 MHz for ^{1}H and 75 MHz for ^{13}C using $CDCl_3$ as the solvent. Chemical shifts are reported in parts per million (ppm) on the δ scale and coupling constants, J, are in hertz (Hz). Multiplicities are reported as "s" (singlet), "d" (doublet), "t" (triplet), "q" (quartet), "dd" (doublet of doublets), "m" (multiplet), "br" (broad). Infrared (IR) spectra (cm^{-1}) were recorded on a Fourier transform spectrophotometer on a Universal Sampling Accessories while optical rotations were measured at the sodium D line (589 nm). Unless otherwise stated, low-resolution mass spectra (m/z) were obtained in the electrospray (ESI) mode. High-resolution mass spectra (m/z, TOF analyzer) were recorded in the electrospray (ESI) mode. Melting points are uncorrected. All reagents and solvents were commercial products and used without further purification except THF (freshly distilled from Na/benzophenone under nitrogen), THP (freshly distilled from Na), and CH_2Cl_2 (freshly distilled from CaH_2 under nitrogen). Commercial n-BuLi, and t-BuLi were titrated against N-benzylbenzamide in THF at -40 °C until persistence of a blue color was observed. Flash chromatography was performed on 230-400 mesh silica gel. Analytic and preparative TLC was carried out using plates doped with fluorescent indicator. Spots were visualized with UV light. Unless otherwise stated, reactions were performed under dry argon in flame- or oven-dried flasks equipped with Teflon™ stirbars. All flasks were fitted with rubber septa for the introduction of substrates, reagents and solvents via syringe. Solvents, pure liquid reagents or reagents in solution, and solids were added in one portion unless otherwise stated.

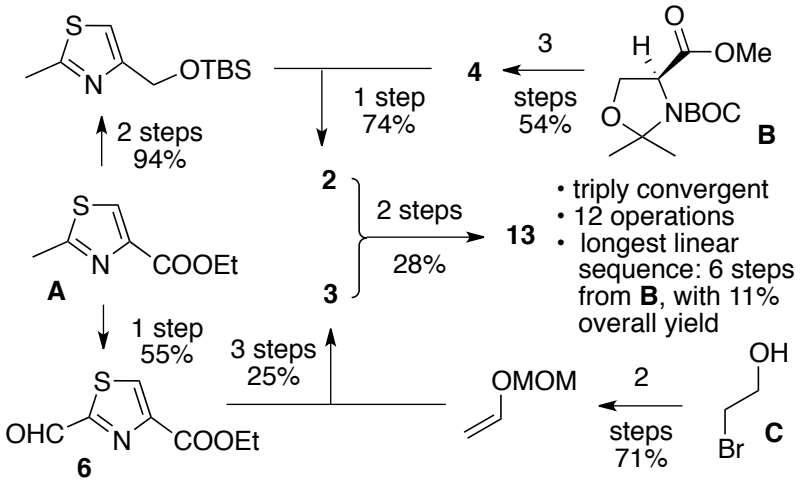
B. HPLC Trace of Pyridine 13

Column: Reverse-phase C18, 5µm, 4.6mm x 150mm
Solvent: MeOH (5%), H_2O (95%)
Flow rate: 0.7mL/min
Detection: UV, 254nm

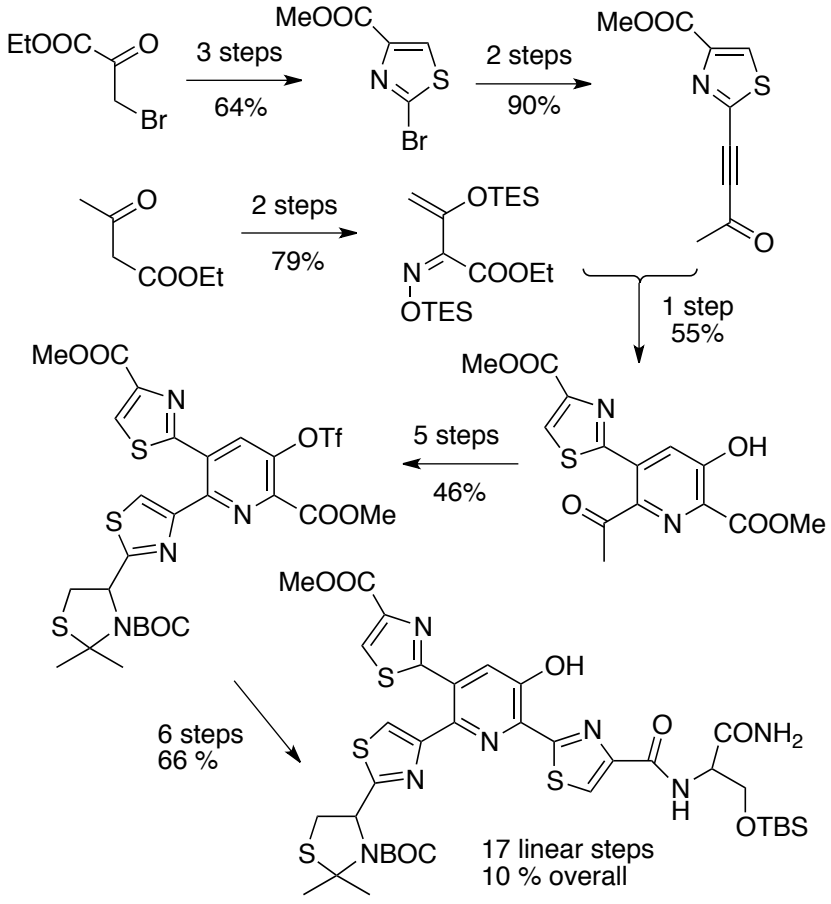


C. Comparison of present route vs. alternatives

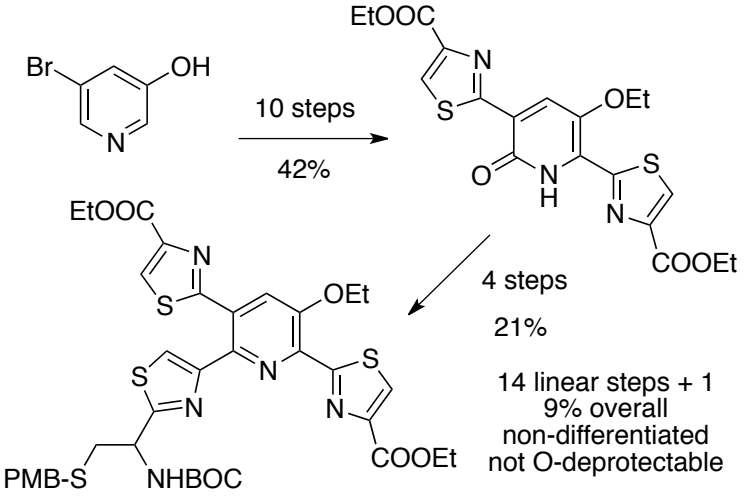
a. Present route:



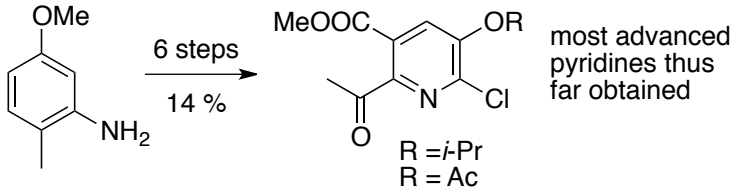
b. Arndt: (a) Lu, J.-Y.; Arndt, H.-D. *J. Org. Chem.* **2007**, *72*, 4205.
(b) Lu, J.-Y.; Riedrich, M.; Mikyna, M.; Arndt, H.-D. *Angew. Chem. Int. Ed.* **2009**, *48*, 8137.
(c) Lu, J.-Y.; Riedrich, M.; Mikyna, M.; Arndt, H.-D. *Angew. Chem. Int. Ed.* **2009**, *48*, 9211 (erratum).



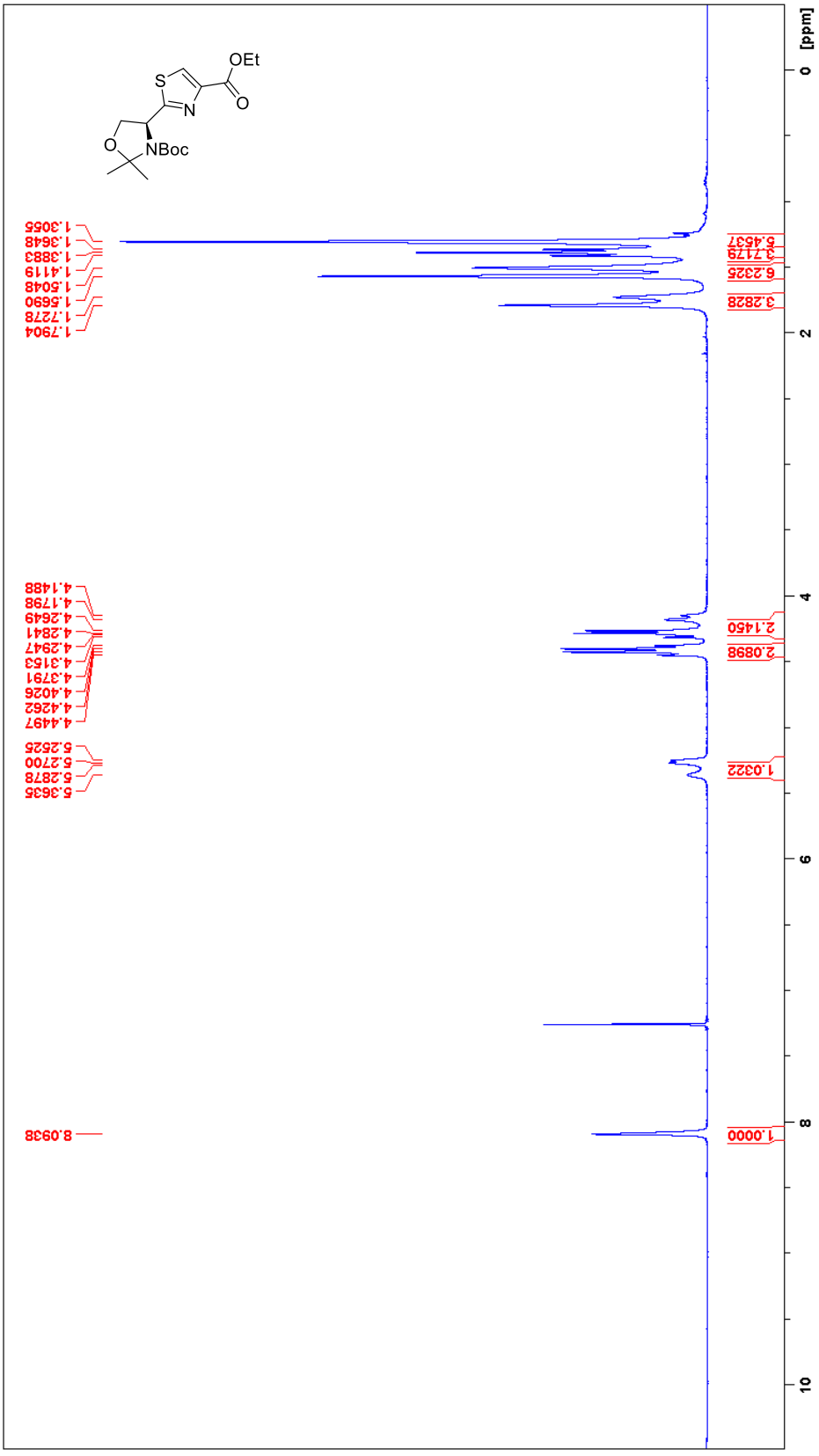
c. Shin: (a) Umemura, K.; Noda, H.; Yoshimura, J.; Konn, A.; Yonezawa, Y.; Shin, C.-G. *Tetrahedron Lett.* **1997**, *38*, 3539.
(b) Umemura, K.; Noda, H.; Yoshimura, J.; Konn, A.; Yonezawa, Y.; Shin, C.-G. *Bull Chem. Soc. Jpn.* **1998**, *71*, 1391.



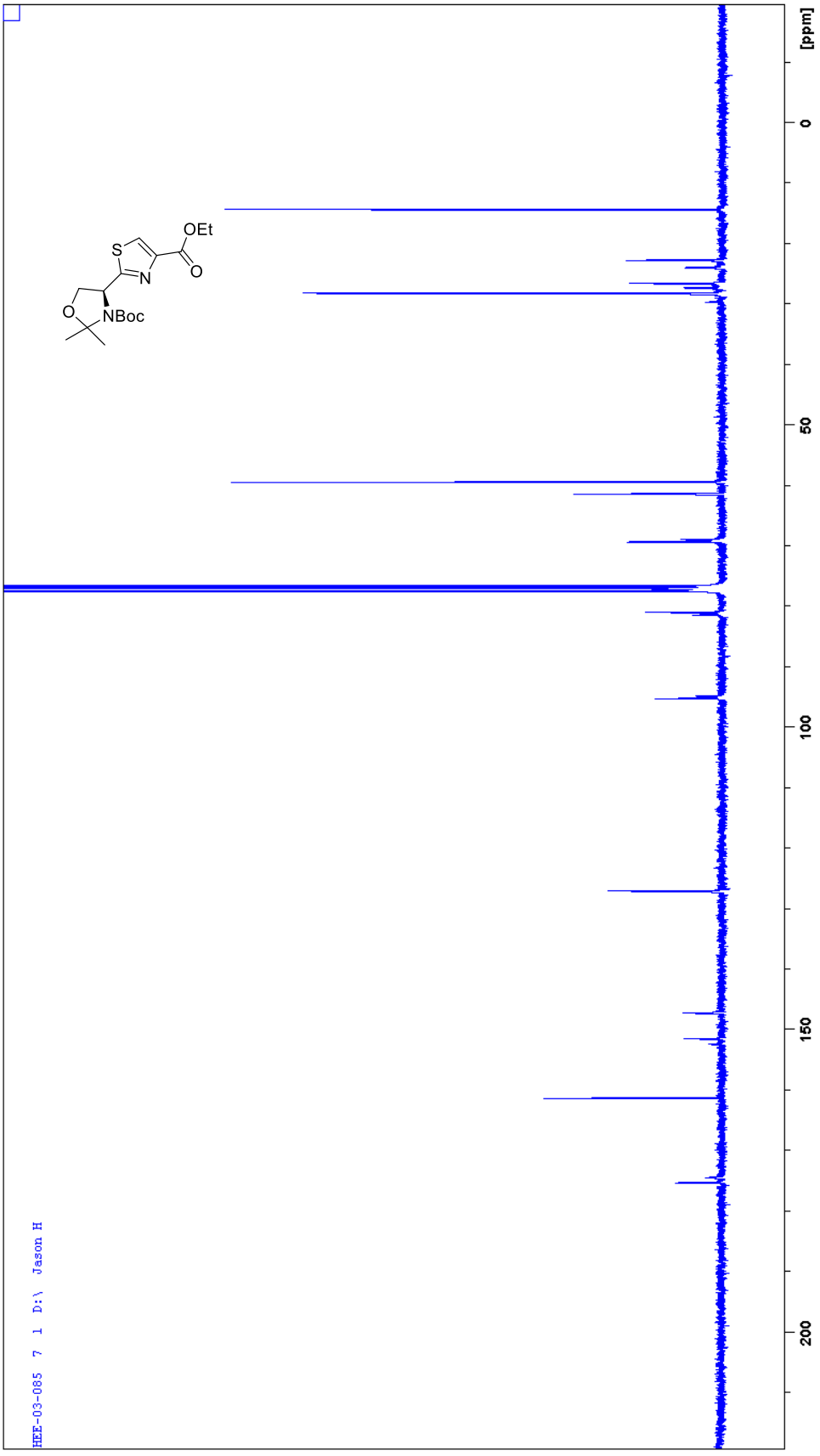
d. Moody: (a) Taddei, D.; Poriel, C.; Moody, C. J. *ARKIVOC* **2007**, 56.
(b) Kimber, M. C.; Moody, C. J. *Chem. Commun.* **2008**, 591.



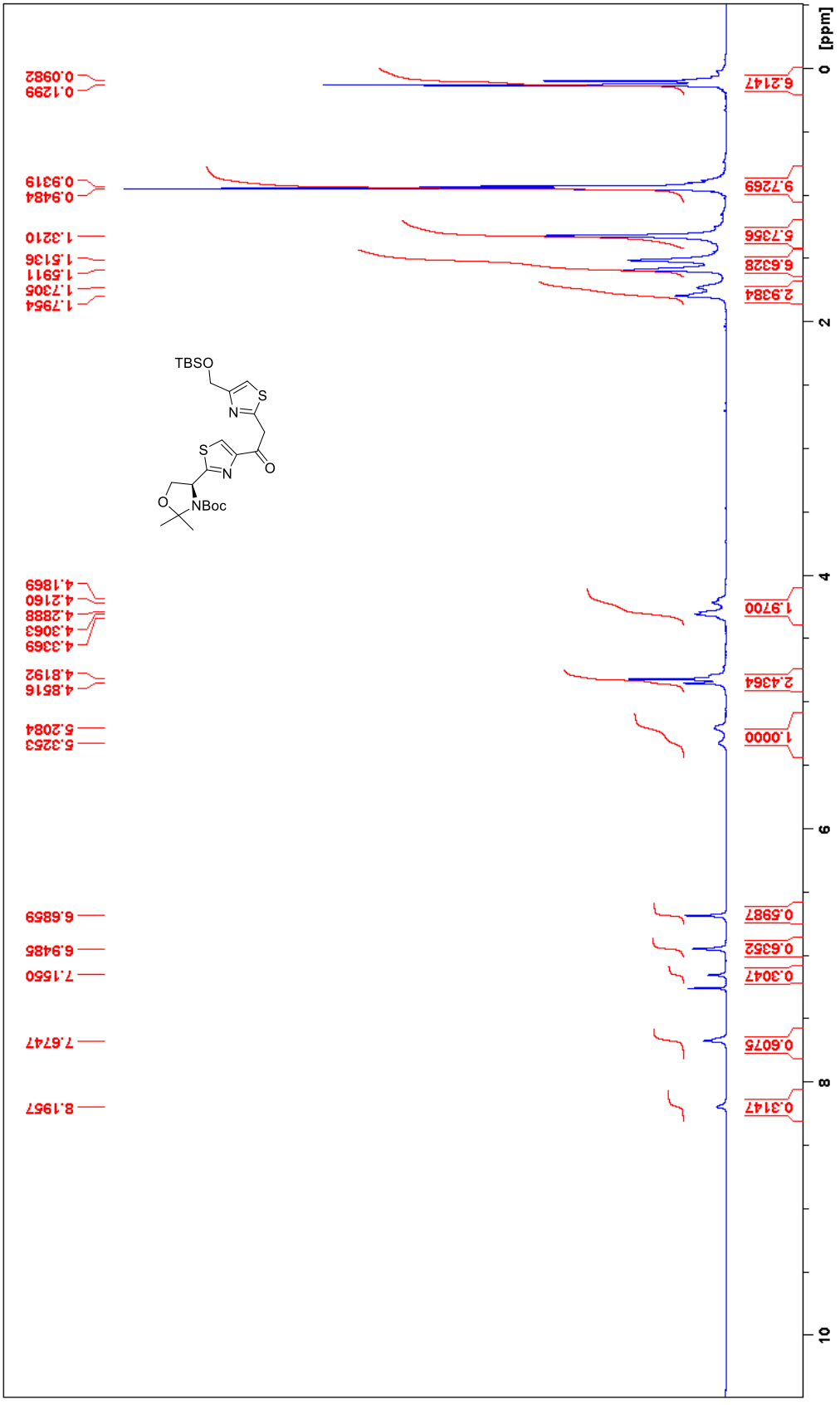
D. ^{1}H and ^{13}C NMR spectra



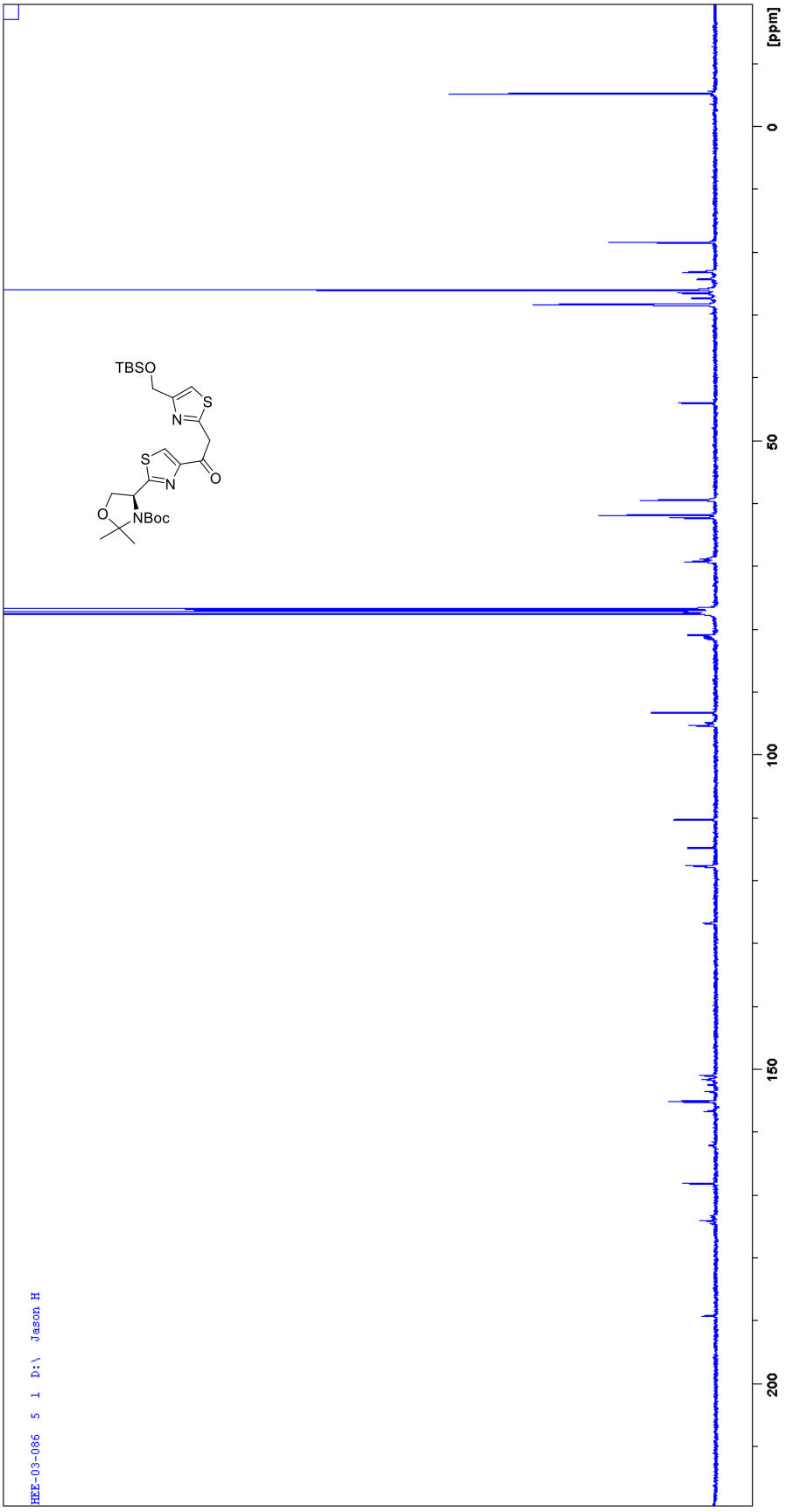
^{1}H NMR Spectrum of compound 4 in $CDCl_3$ at room temperature (BOC rotamers)



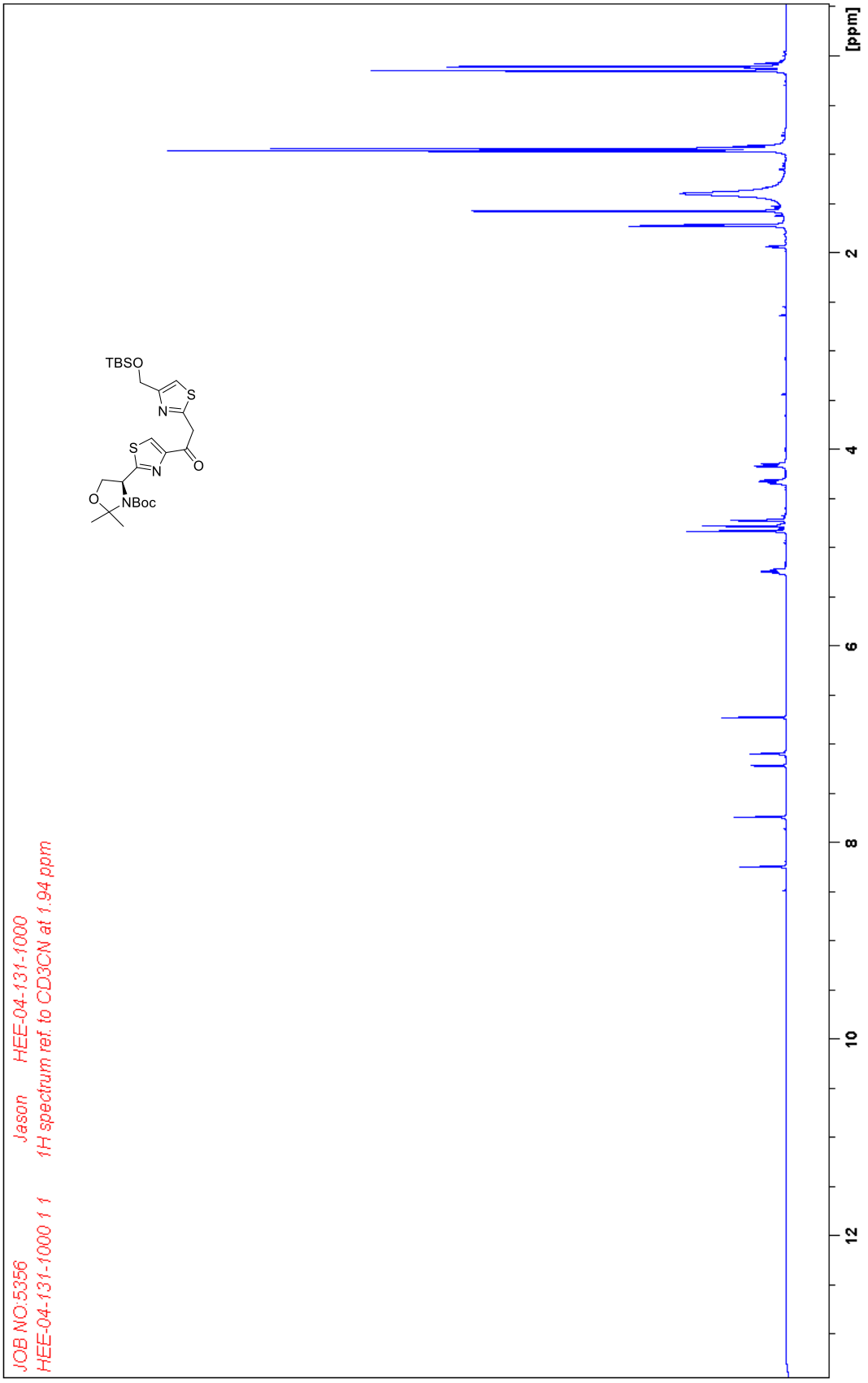
^{13}C NMR Spectrum of compound 4 in $CDCl_3$ at room temperature (BOC rotamers)



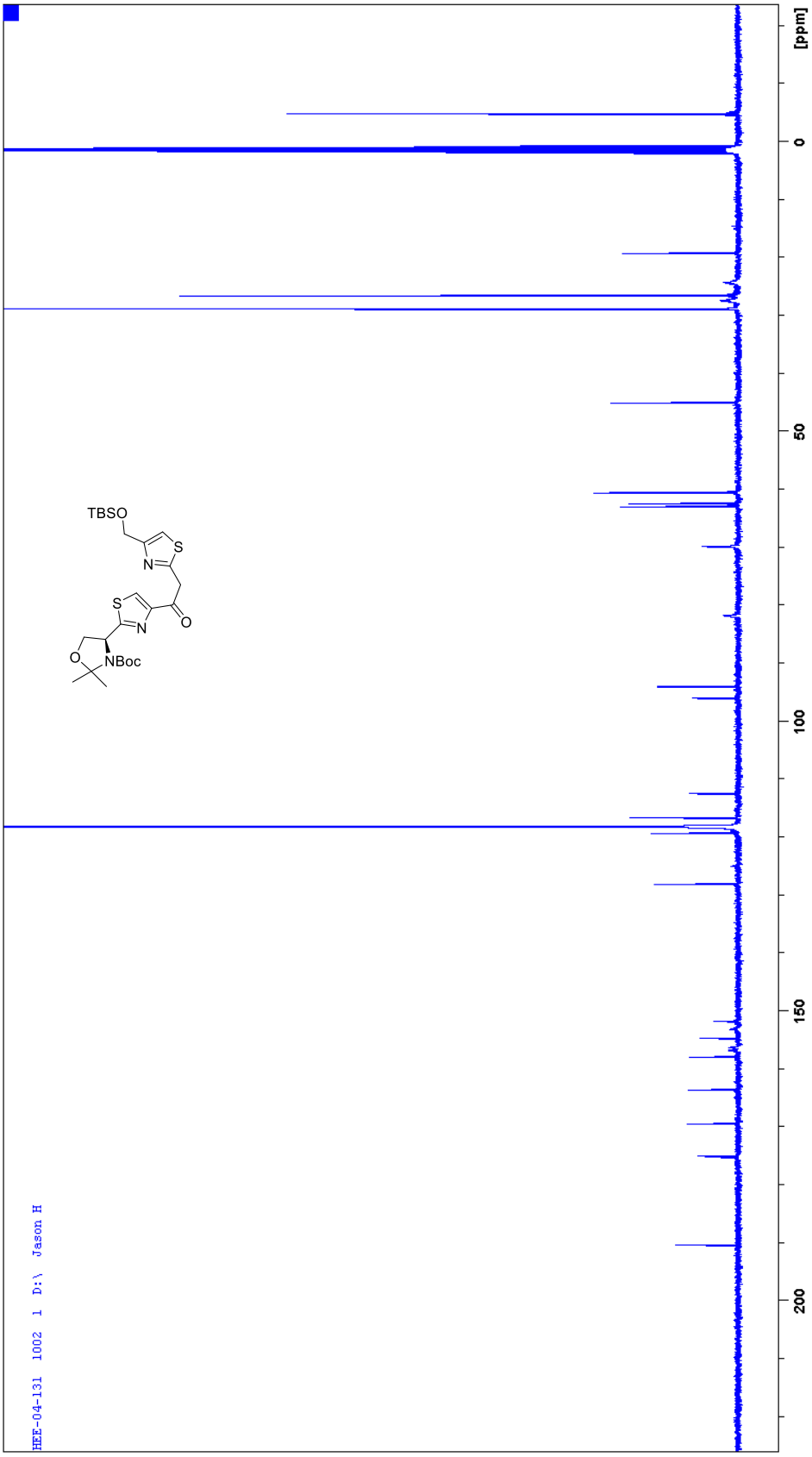
^{1}H NMR Spectrum of compound 2 in $CDCl_3$ at room temperature (BOC rotamers; keto - enol tautomers



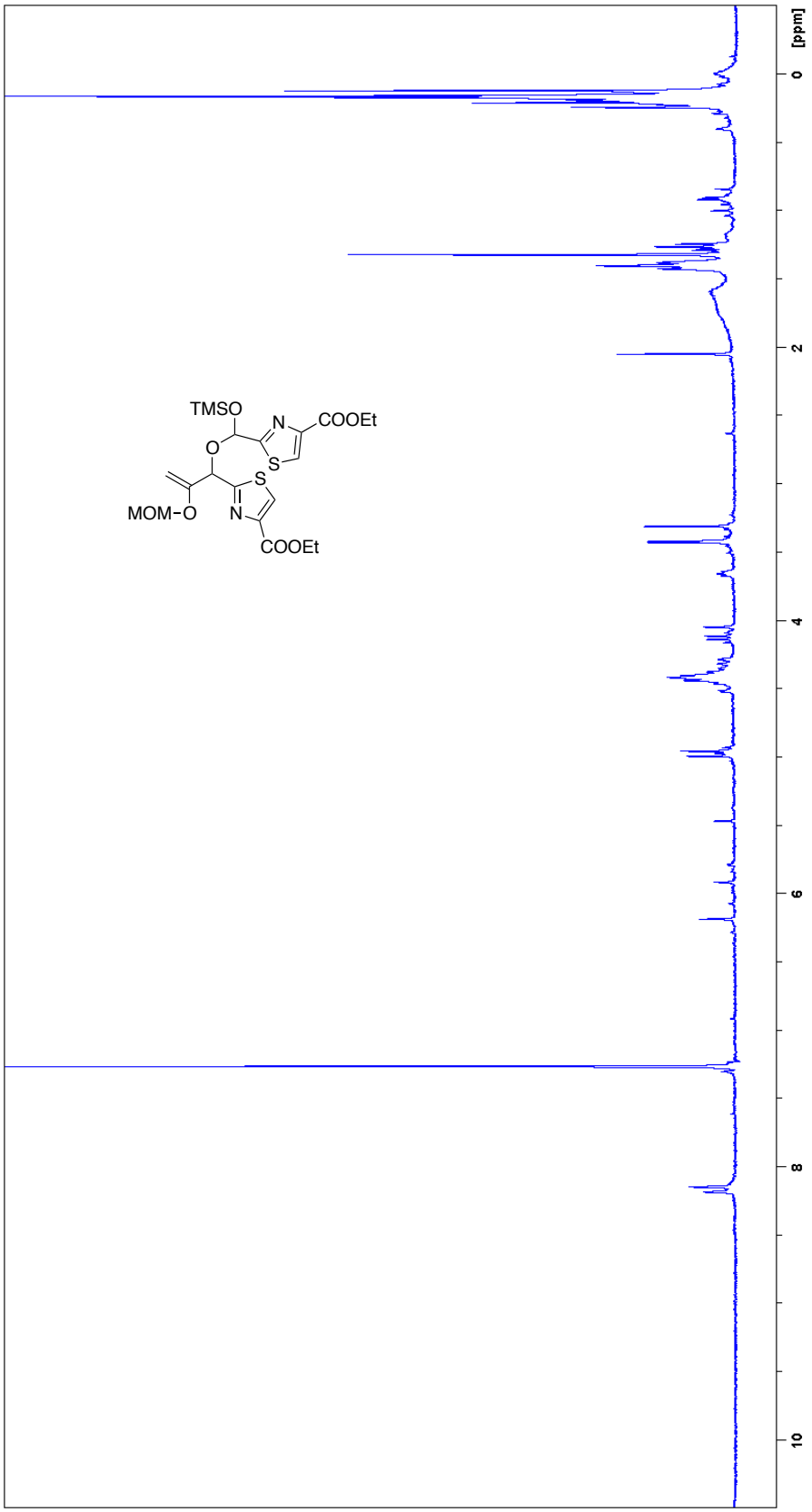
^{13}C NMR Spectrum of compound 2 in $CDCl_3$ at room (BOC rotamers; keto - enol tautomers



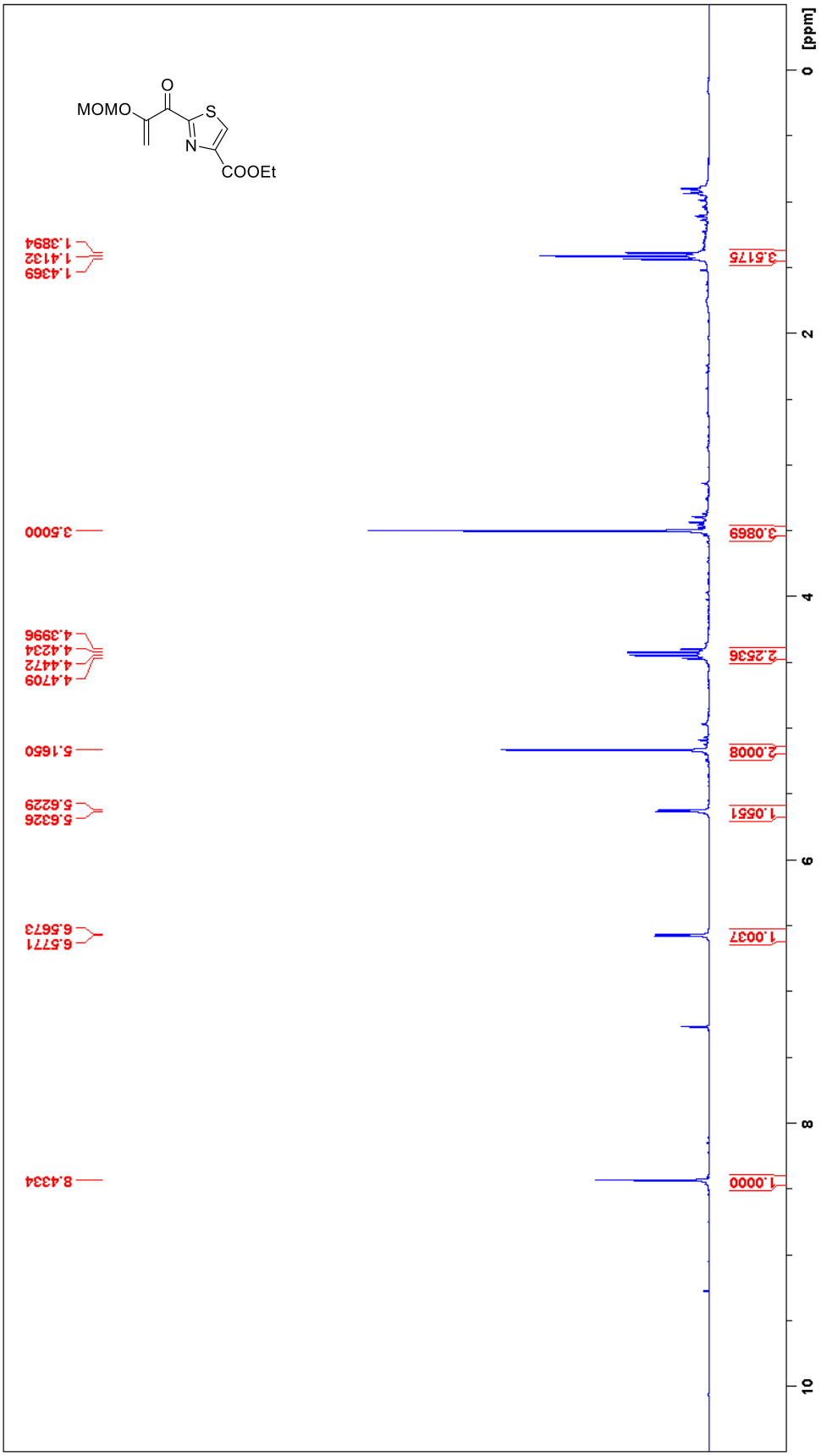
^{1}H NMR Spectrum of compound 2 in CD_3CN at 65 °C (keto - enol tautomers)



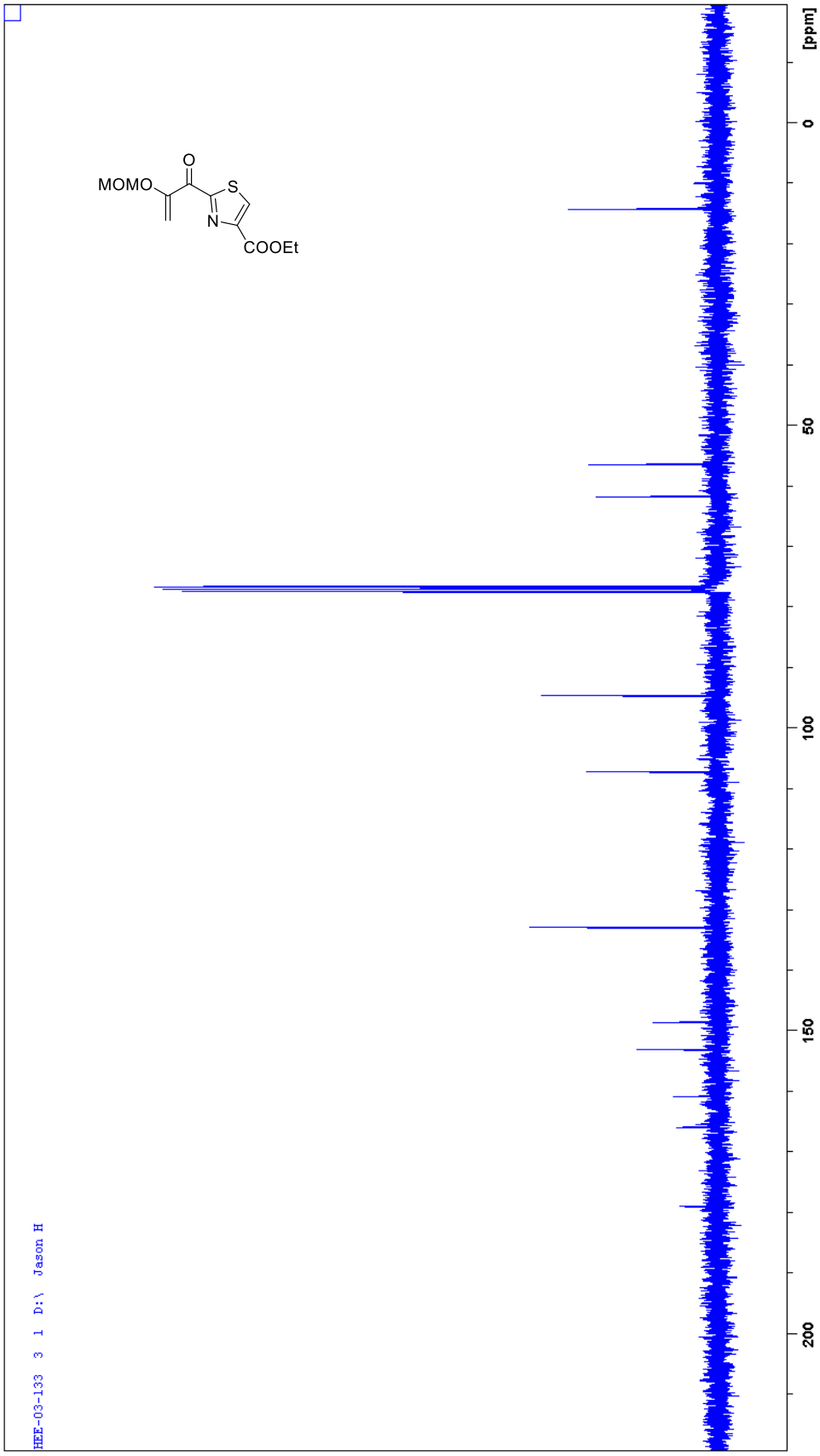
^{13}C NMR Spectrum of compound 2 in CD_3CN at 65^{o}C (keto - enol tautomers)



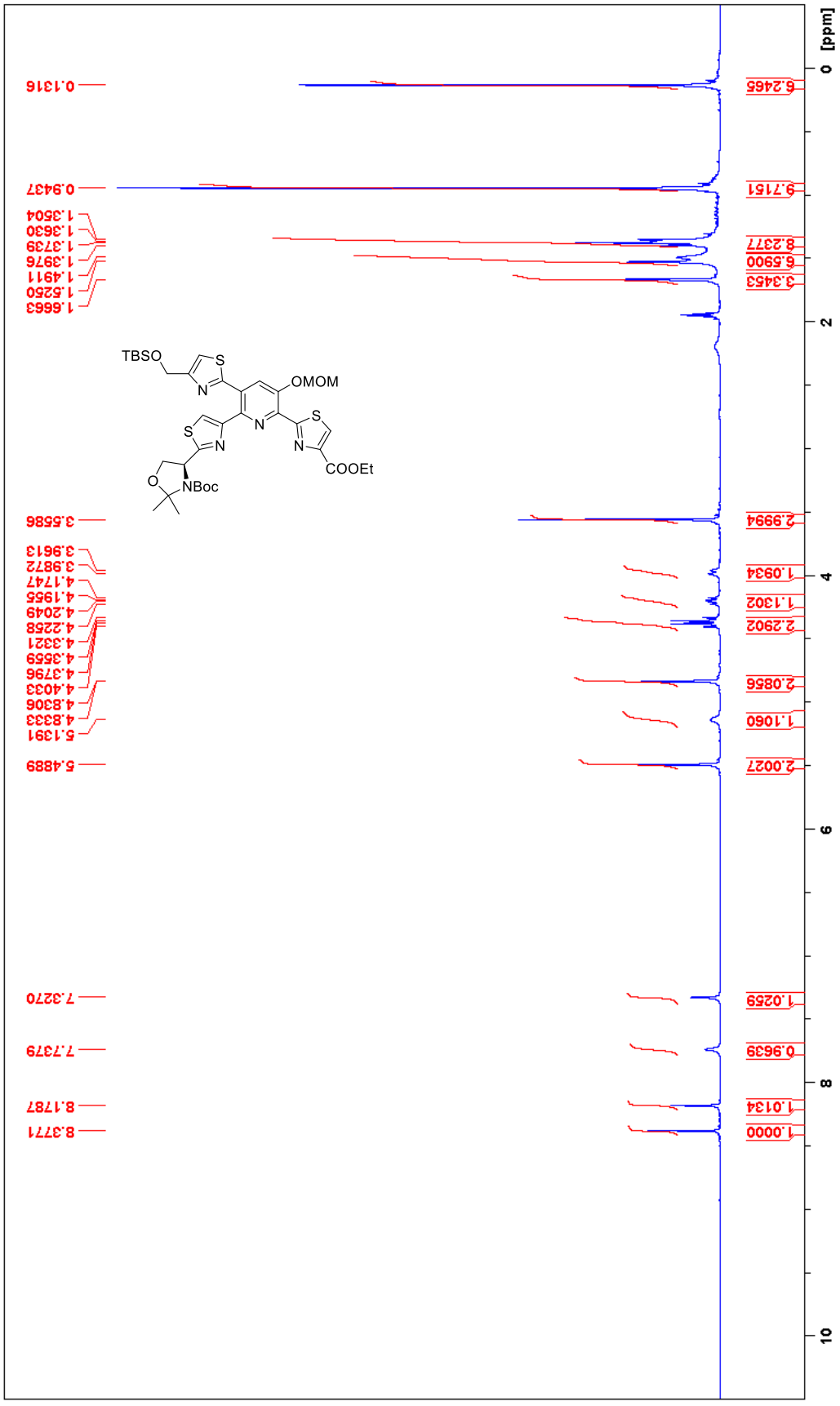
^{1}H NMR Spectrum of crude compound 10 (1:1 mixture of diastereomers) in $CDCl_3$



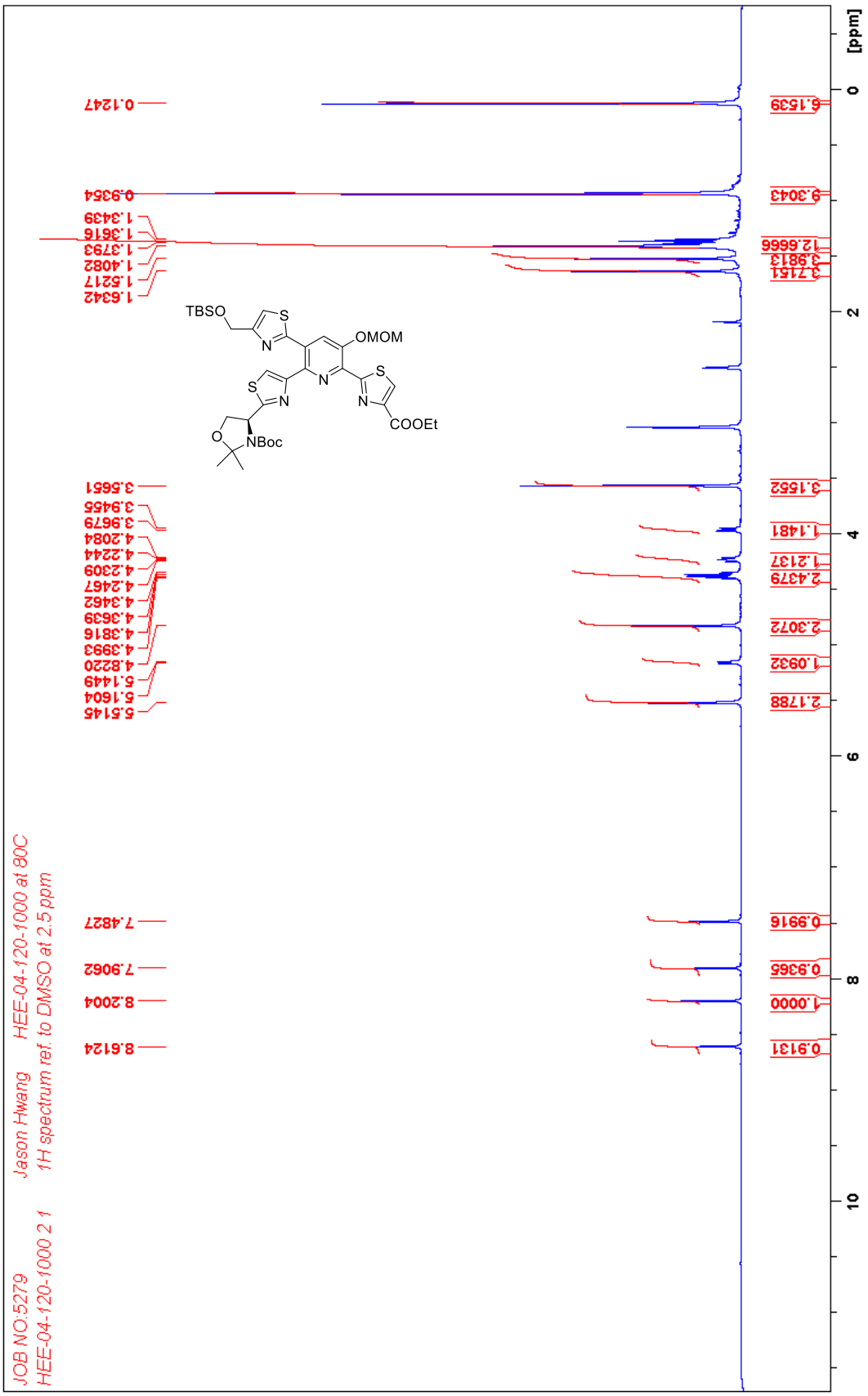
^{1}H NMR Spectrum of partially purified compound 3 in $CDCl_3$



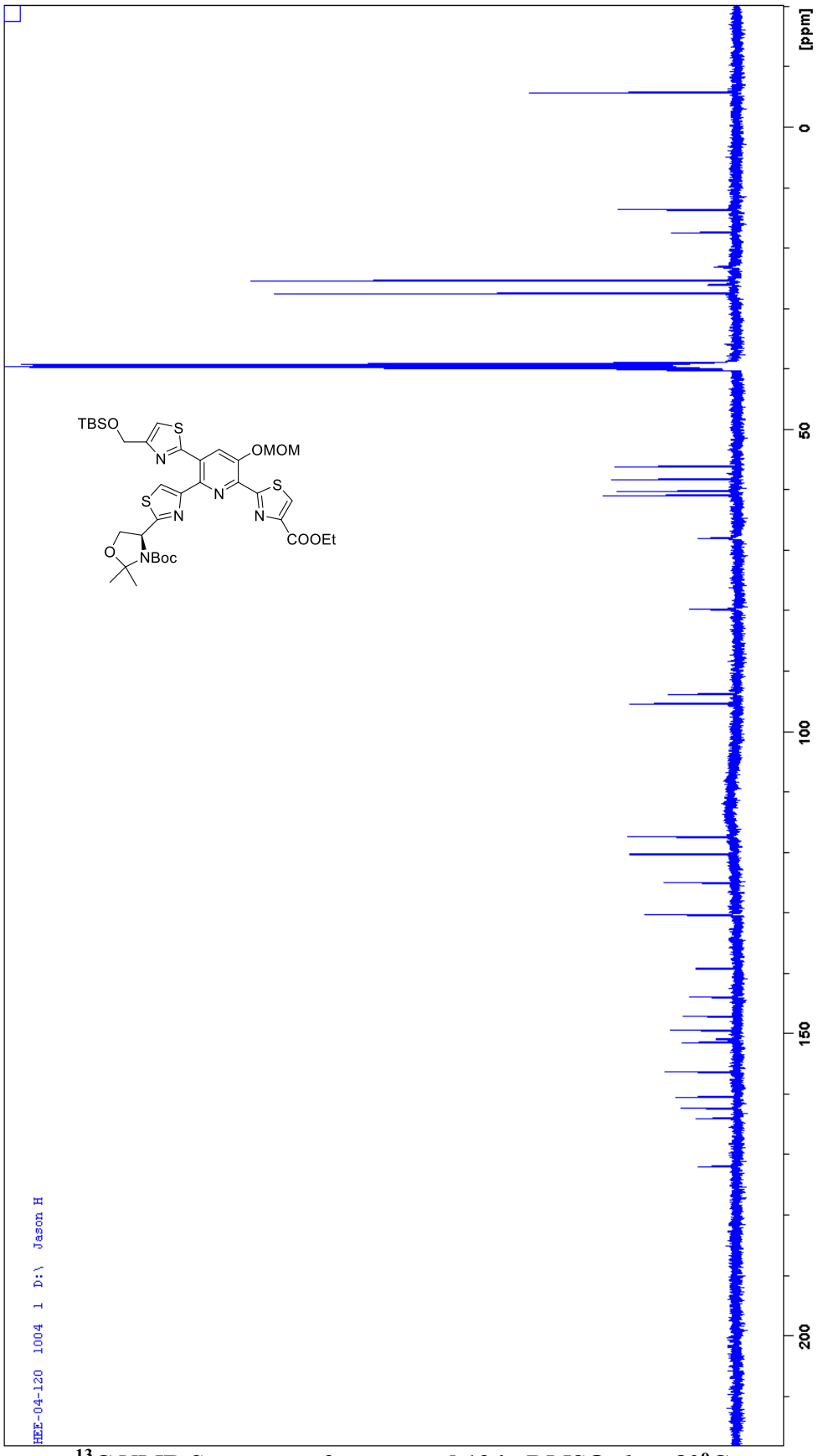
^{13}C NMR Spectrum of partially purified compound 3 in $CDCl_3$



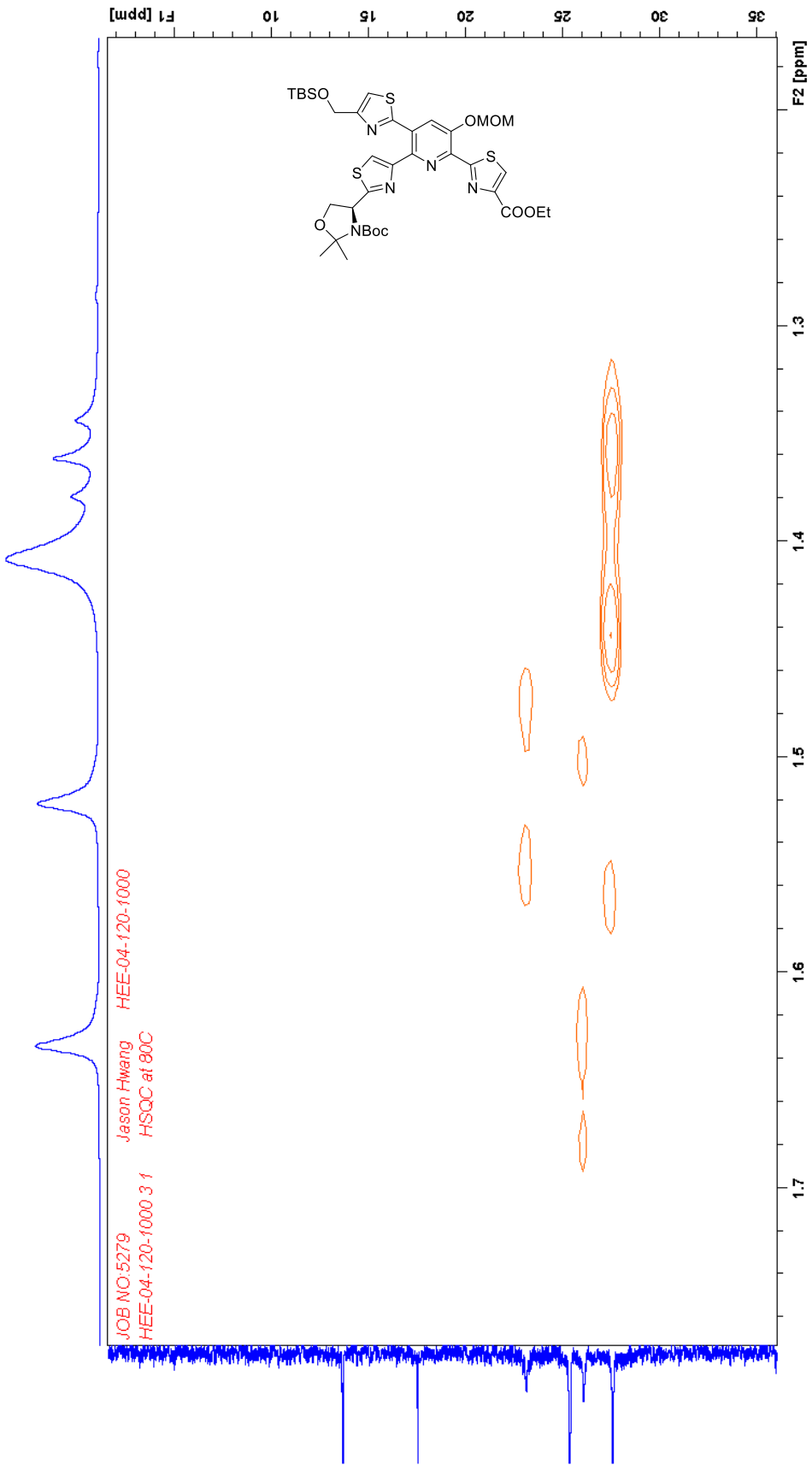
^{1}H NMR Spectrum of compound 13 in CD_3CN at room temperature (line broadening due to slow-interconverting BOC rotamers)



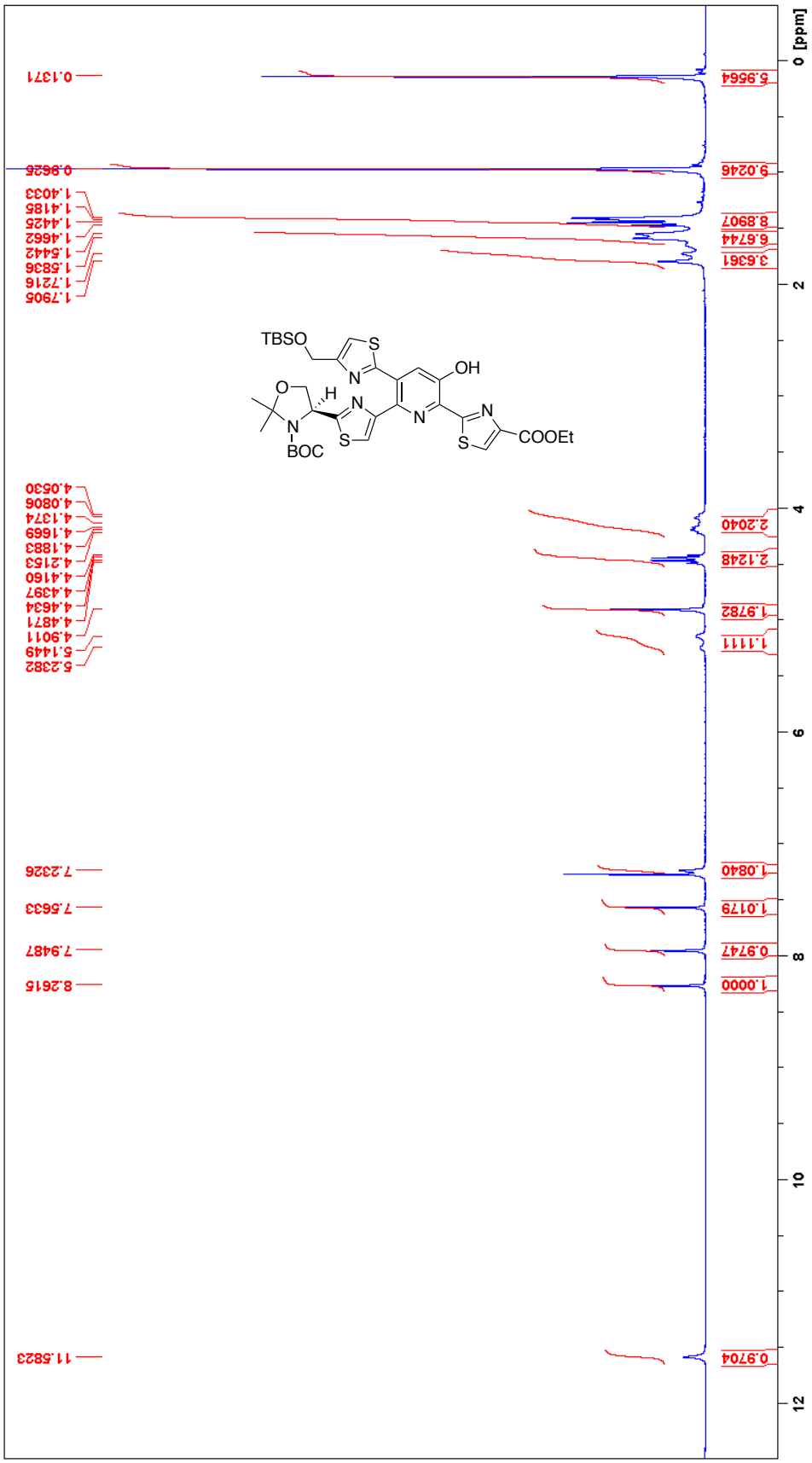
^{1}H NMR Spectrum of compound 13 in DMSO-d_6 at 80^{o}C



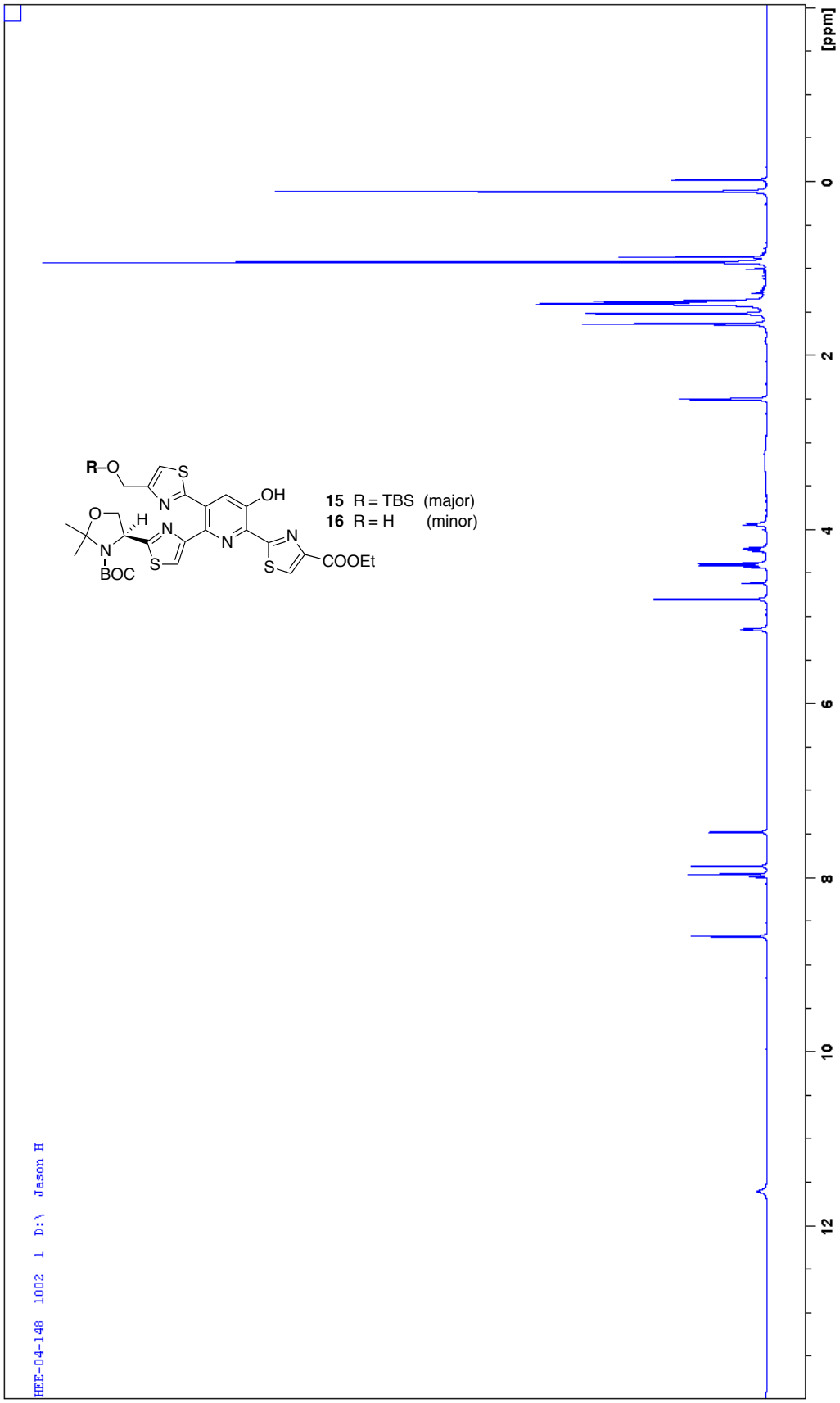
^{13}C NMR Spectrum of compound 13 in DMSO-d_6 at 80^{o}C



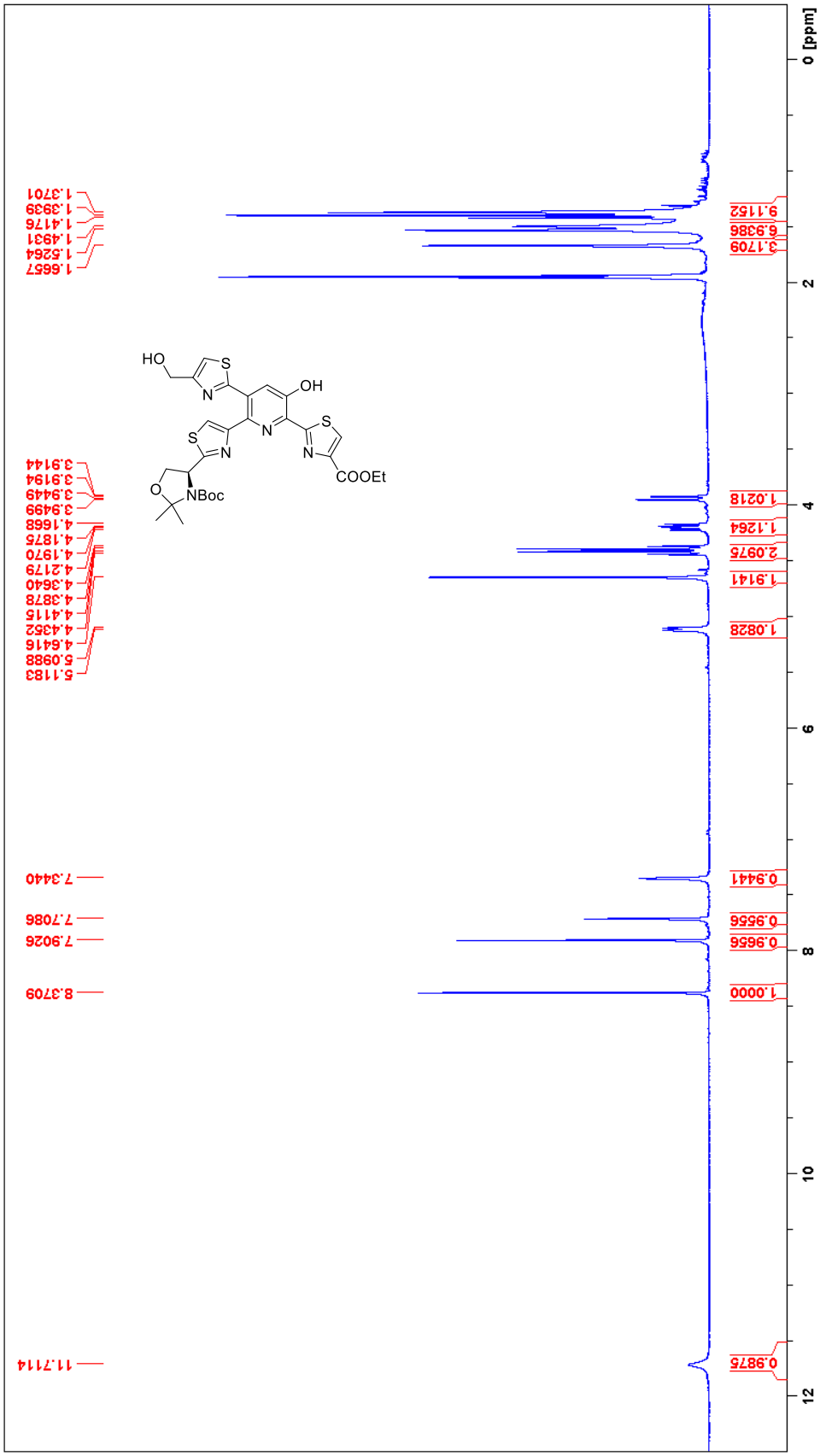
Expanded portion of the HSQC spectrum of compound 13 in DMSO-d_6 at 80°C



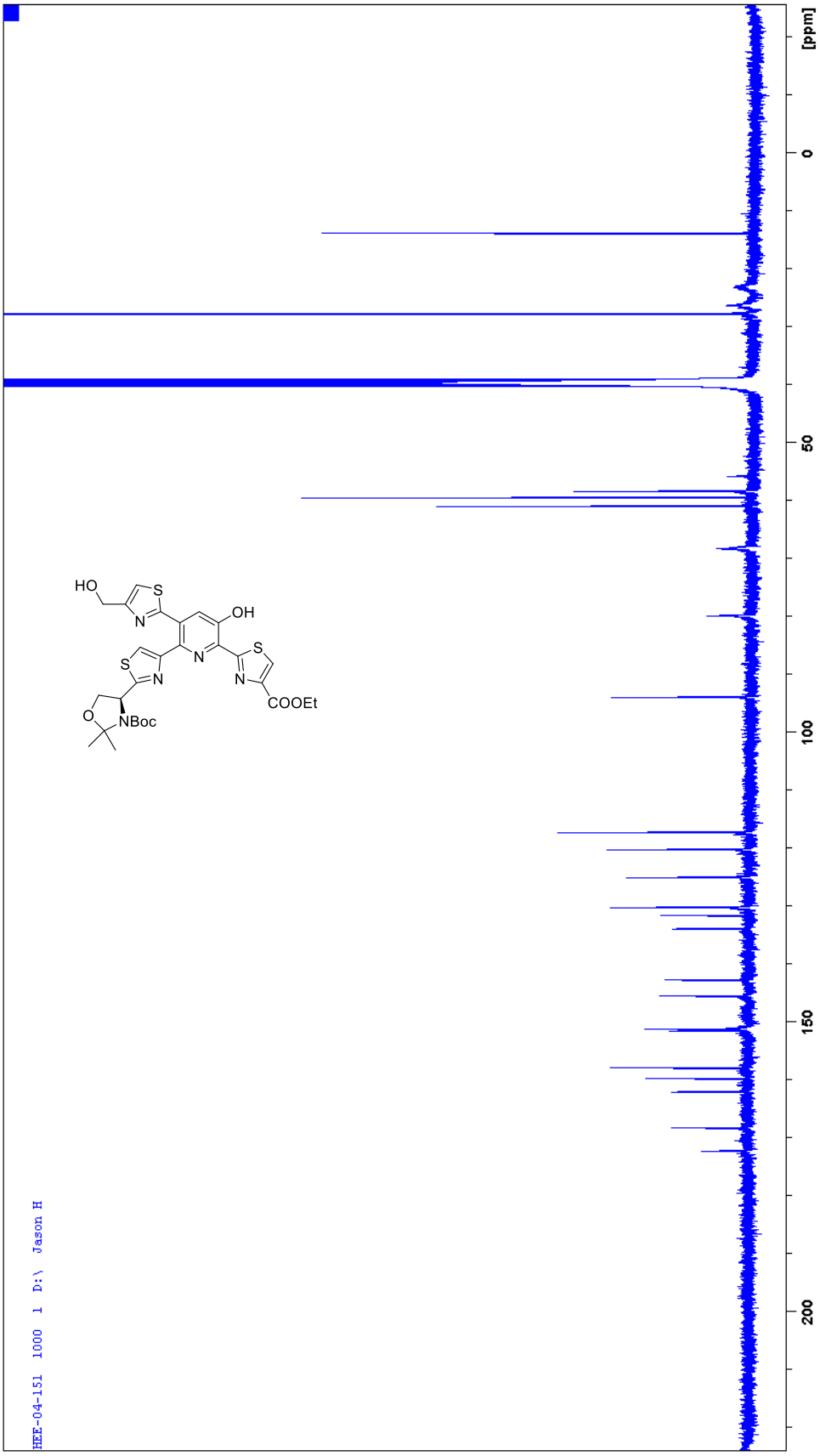
^{1}H NMR Spectrum of compound 15 in $CDCl_3$ (line broadening due to slow-interconverting BOC rotamers)



^{1}H NMR Spectrum of compound 15 (+ 16 formed *in situ*) in DMSO-d_6 at 80 °C (30 min into the experiment; about 20% release of the TBS group)



^{1}H NMR Spectrum of compound 16 in CD_3CN at room temperature (line broadening due to slow-interconverting BOC rotamers)



^{13}C NMR Spectrum of compound 16 in DMSO-d_6 at 65^{o}C