

## Supporting information for:

### **AiZynth Impact on Medicinal Chemistry Practice at AstraZeneca**

Jason D. Shields,\* Rachel Howells, Gillian Lamont, Yin Leilei, Andrew Madin, Christopher E. Reimann, Hadi Rezaei, Tristan Reuillon, Bryony Smith, Clare Thomson, Yuting Zheng, Robert E. Ziegler

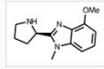
Snapshots of the AiZynth GUI	S2
<sup>1</sup> H NMR spectra of previously unreported compounds	S6

# Snapshots of the AiZynth GUI

← back to AiZynth Finder

## AiZynth Finder Results

Target compound:



Description:

### Results

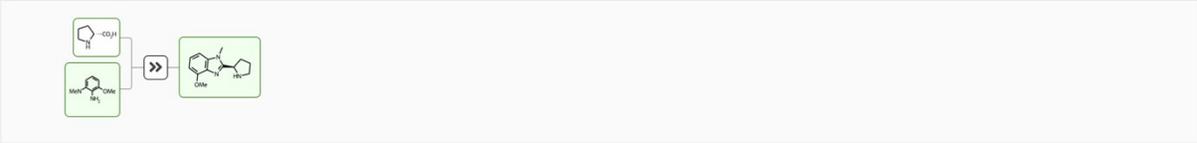
After expanding the target, 14 route(s) were found (grouped in 2 cluster(s)). Click to view the top 10, 25, or all routes at once in the interactive path planner (expect slow rendering times in some cases when clicking 'all').

Ordered by:

Cluster 1 (8 routes)

<< First < Previous Route 1 of 8 Next > Last >>

- State score: 0.098
- Number of reactions: 1
- Number of pre-cursors: 2
- Number of pre-cursors in stock: 2
- Route cost: 500.050
- Sum of prices: 639.960



Cluster 2 (6 routes)

Figure S1. A snapshot of the AiZynthFinder search results for compound **1**. Results are clustered together by similarity and can be viewed individually by the chemist. This example was the highest ranking route and is therefore Cluster 1 Route 1. Compounds have a green border if they are found within our inventory or a commercial catalogue. They have green shading within the boxes if they are reported as products in our internal ELN database.

Cluster 2 (6 routes) [hide](#)

<< First < Previous Route 1 of 6 Next > Last >>

- State score: 0.98
- Number of reactants: 2
- Number of products: 1
- Number of precursors: 0
- Route cost: 104.6
- Sum of prices: 51.26

COc1cccc(N)c1N

Explore as a target

listed in ReactionConnect

available

as of September 28, 2023 01:56 PM

Location	Price per gram	Amount
ACD (MFCD08276903) Sigma-Aldrich Corporation	\$51.26	25 G

Give feedback on this compound

Give feedback on

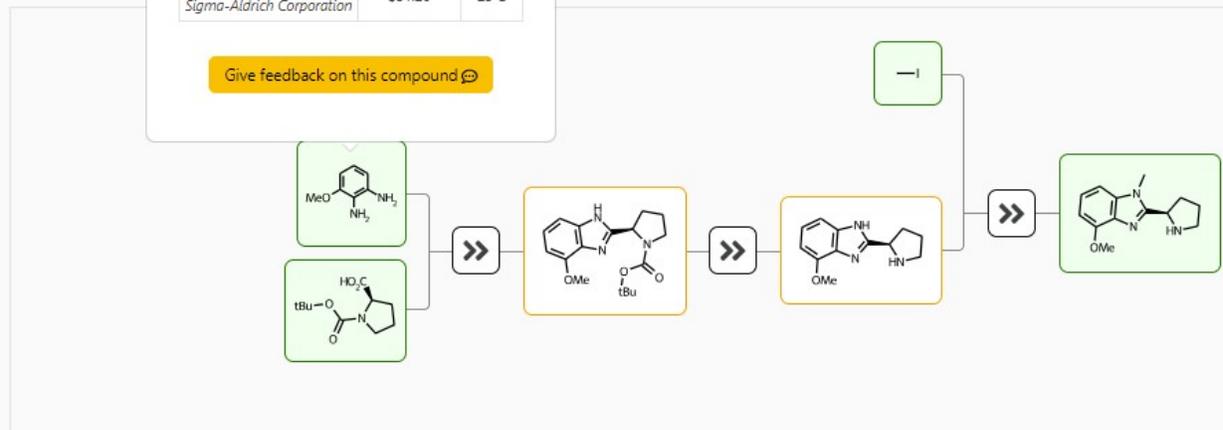


Figure S2. A view of one of the AiZynthFinder routes to compound **1** from Cluster 2. This route is less efficient (and indeed it may suffer from regioselectivity of methylation on the final step) but can still be viewed by the chemist for completeness. Note the mouseover on 3-methoxybenzene-1,2-diamine which provides basic information about commercial availability, including the MFCD number, a unique identifier that can be copy-pasted into online commercial catalogues for easy searching. Note also the feedback buttons that are available for chemists to indicate if a reaction or compound are unsuitable, which can be taken into account in future development of AiZynth.

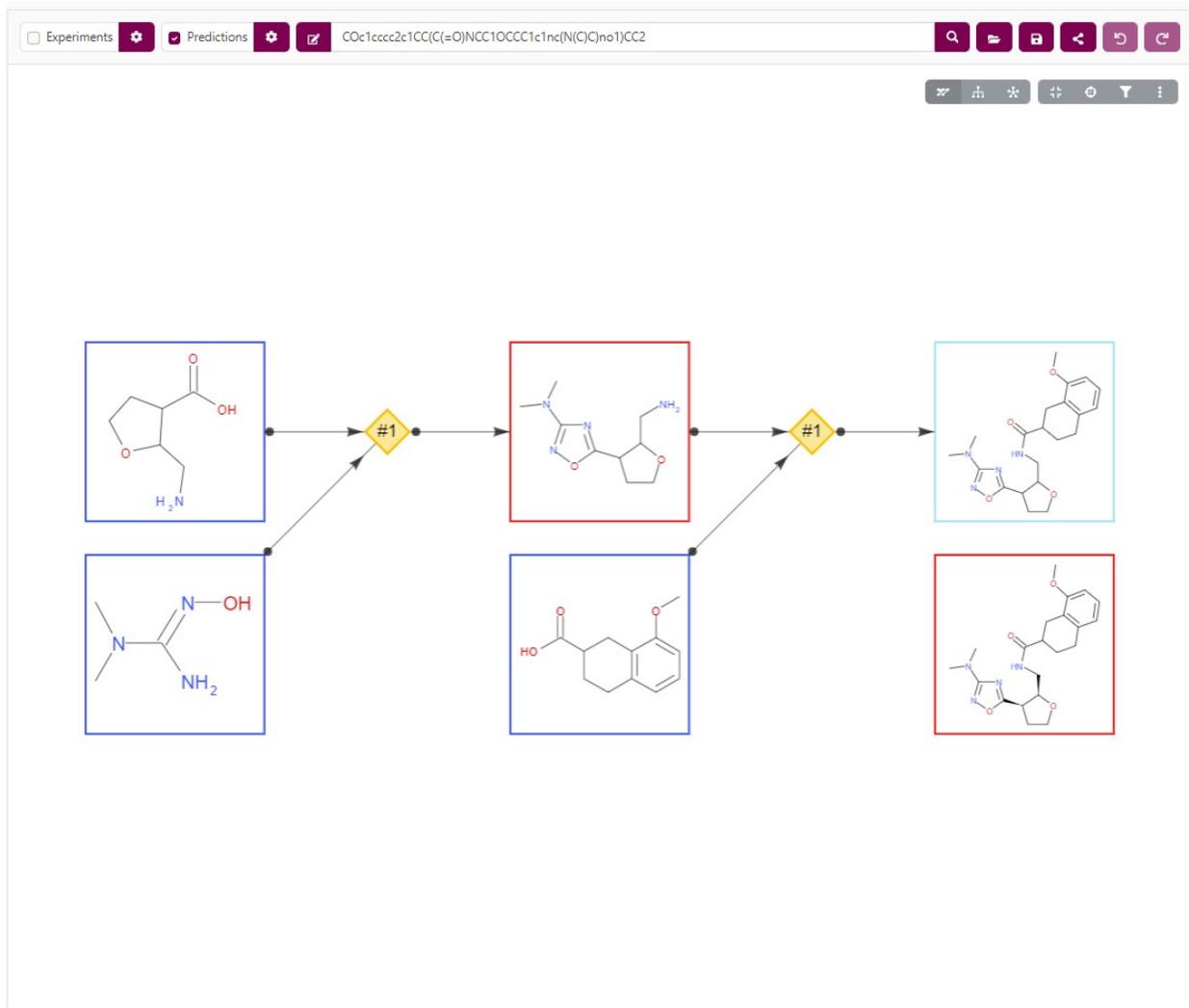
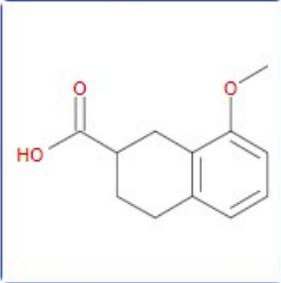


Figure S3. A snapshot of the AiZynth single-step retrosynthesis tool. Here, the view can be changed to read from left-to-right to any desired direction (e.g. for a bottom-to-top view see Figure 7B in the paper). Chemists can hide and add AI suggestions to the reaction network in order to get a sense of multiple alternative routes at once. Additional, unconnected compounds can also be added for the user to refer to visually, e.g. the *cis* isomer at the bottom right. Here, a blue border indicates commercial or inventory availability, while a red border indicates the opposite. The light blue border indicates the target molecule.

Details   Precursors   Experiments   Routes

### Currently selected molecule



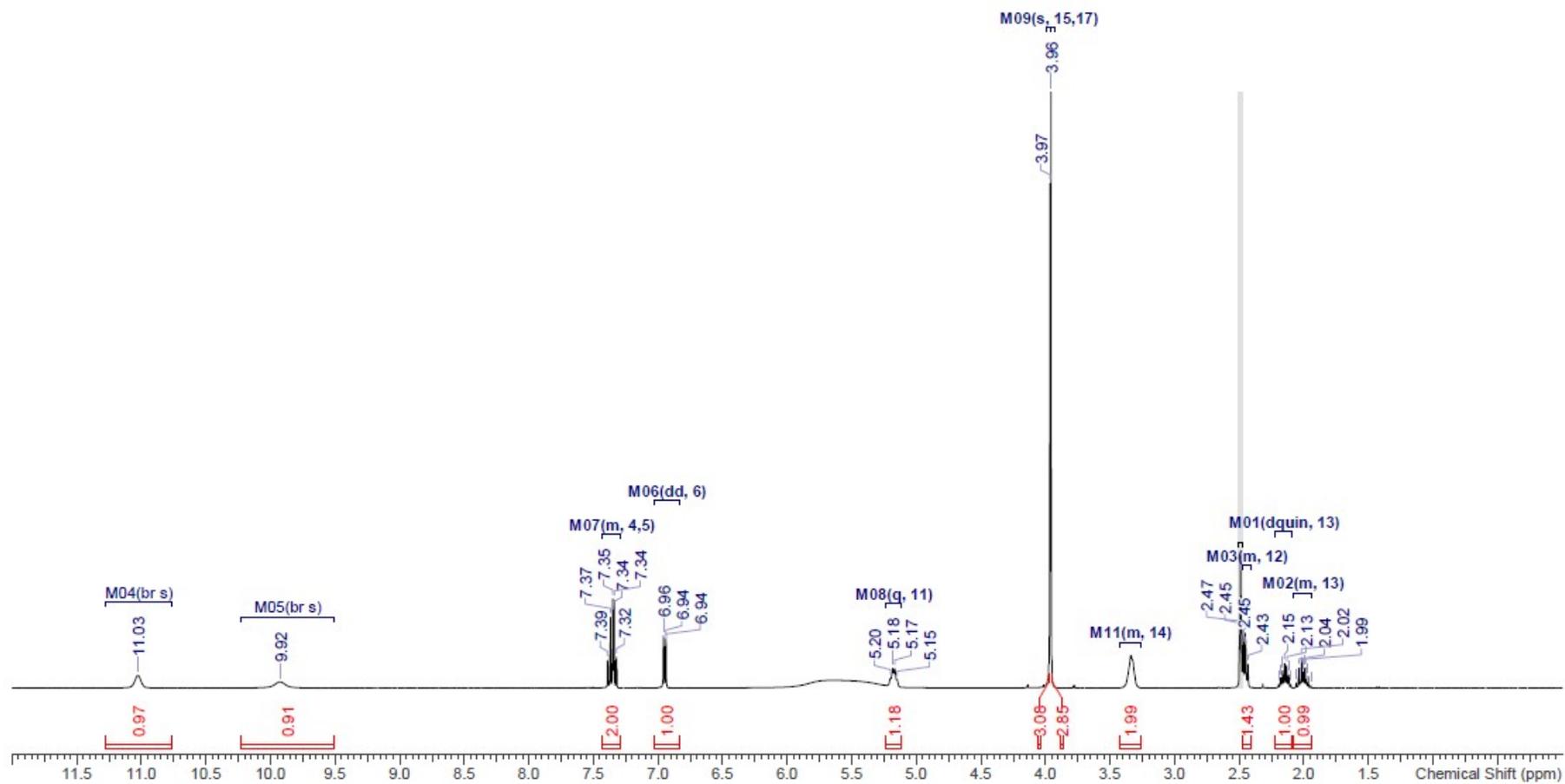
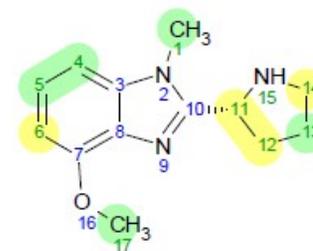
VOAFGTBETRJDPU-UHFFFAOYN  
A-N  
Smiles: COC1=CC=C(C=C1)C2(C)CC(=O)OCC2  
Price (\$/g): 573.6

Give feedback on this compound

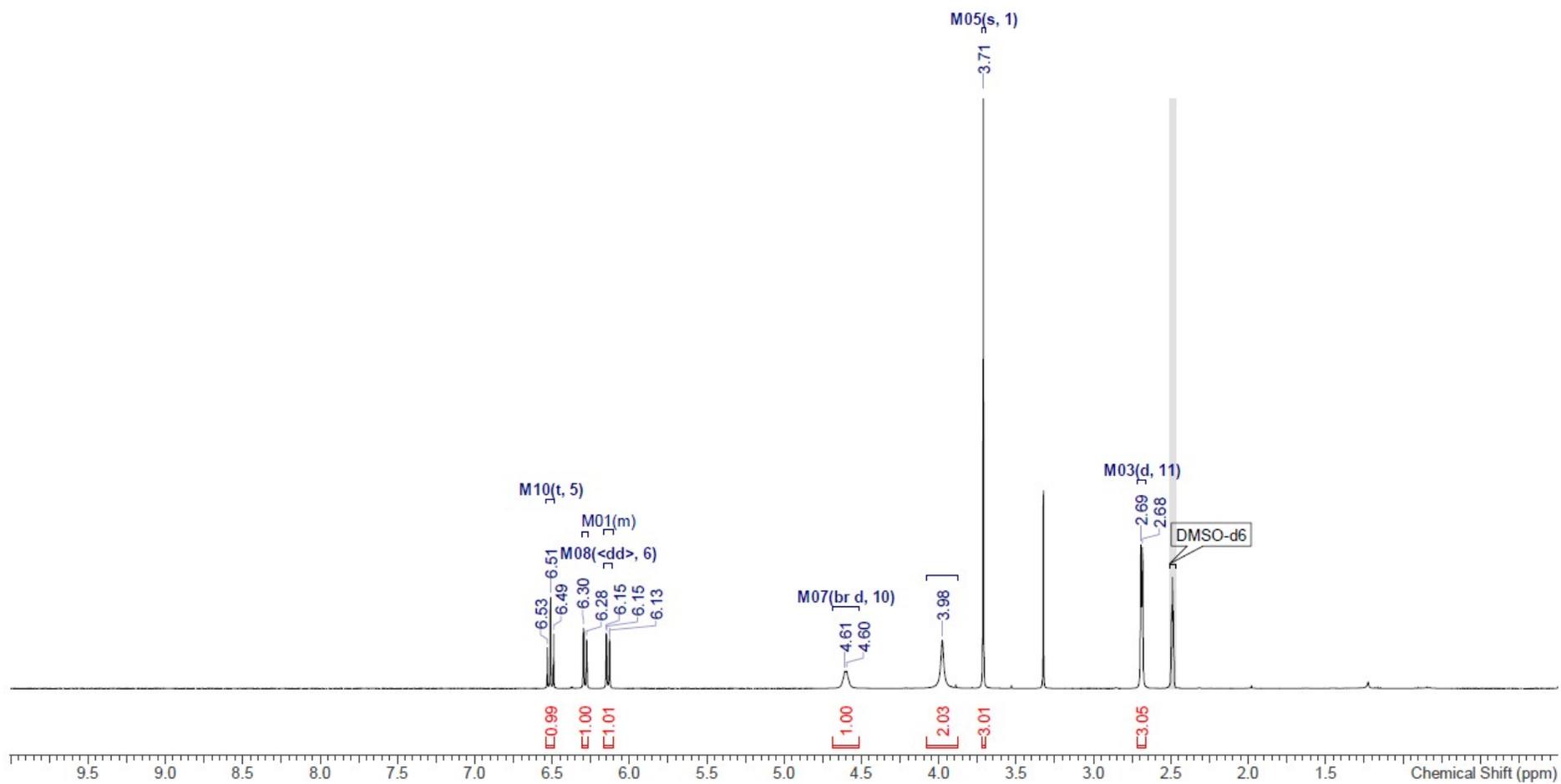
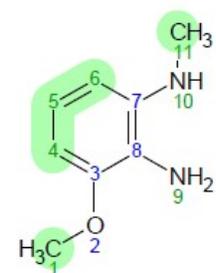
Location	Price per gram	Amount
ACD (MFCD01075657) <i>Sigma-Aldrich Corporation</i>	\$573.6	5 G

Figure S4. A side panel that can be viewed within the AiZynth single-step retrosynthesis interface. Here, a chemist can get a quick sense of the price and scale of the availability of a given molecule.

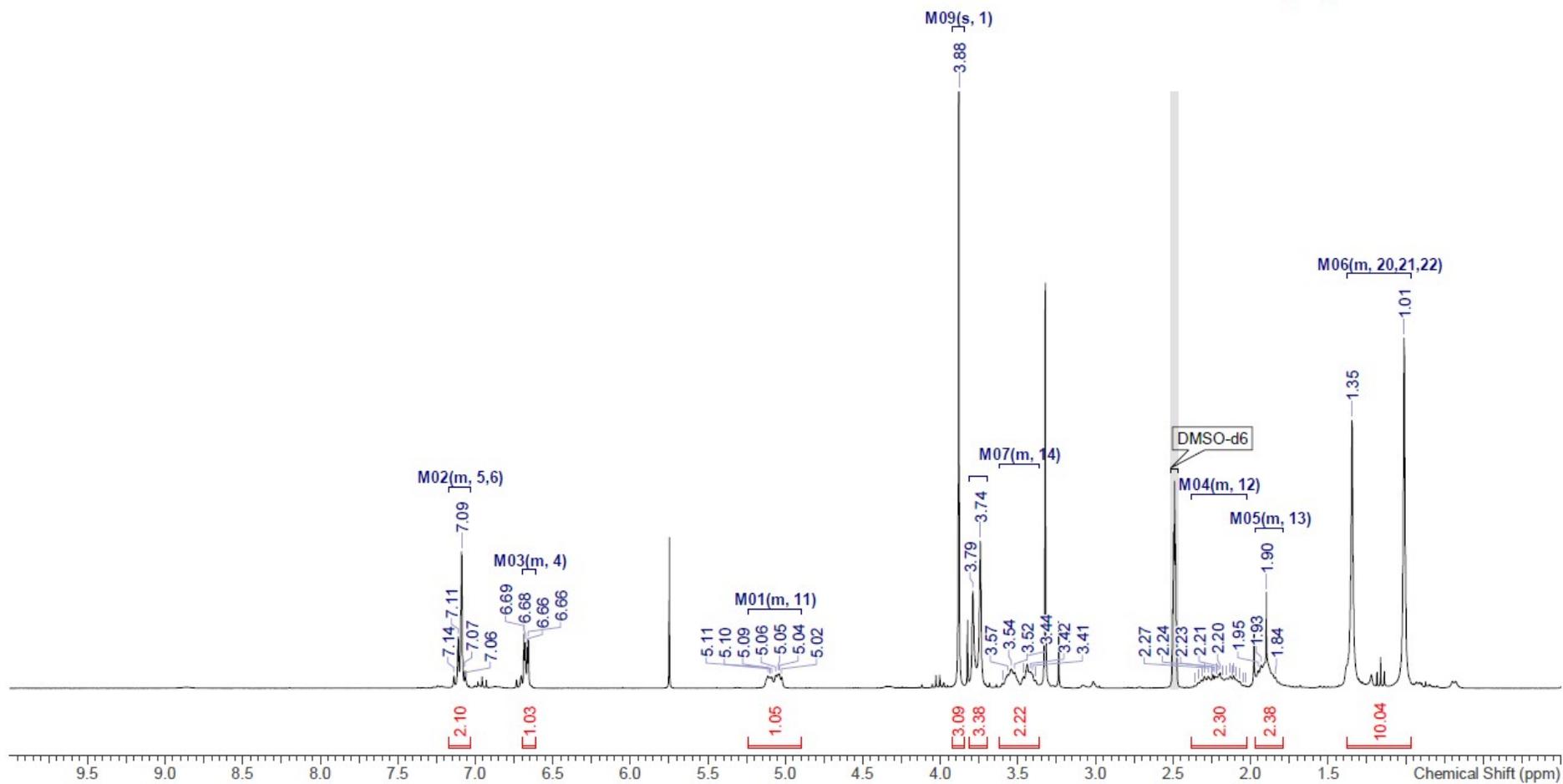
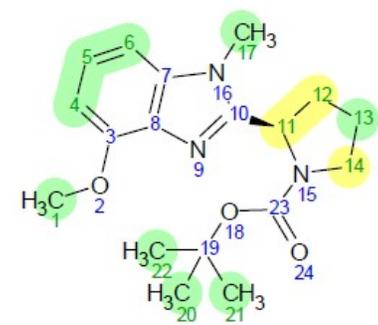
# $^1\text{H}$ NMR spectra of previously unreported compounds



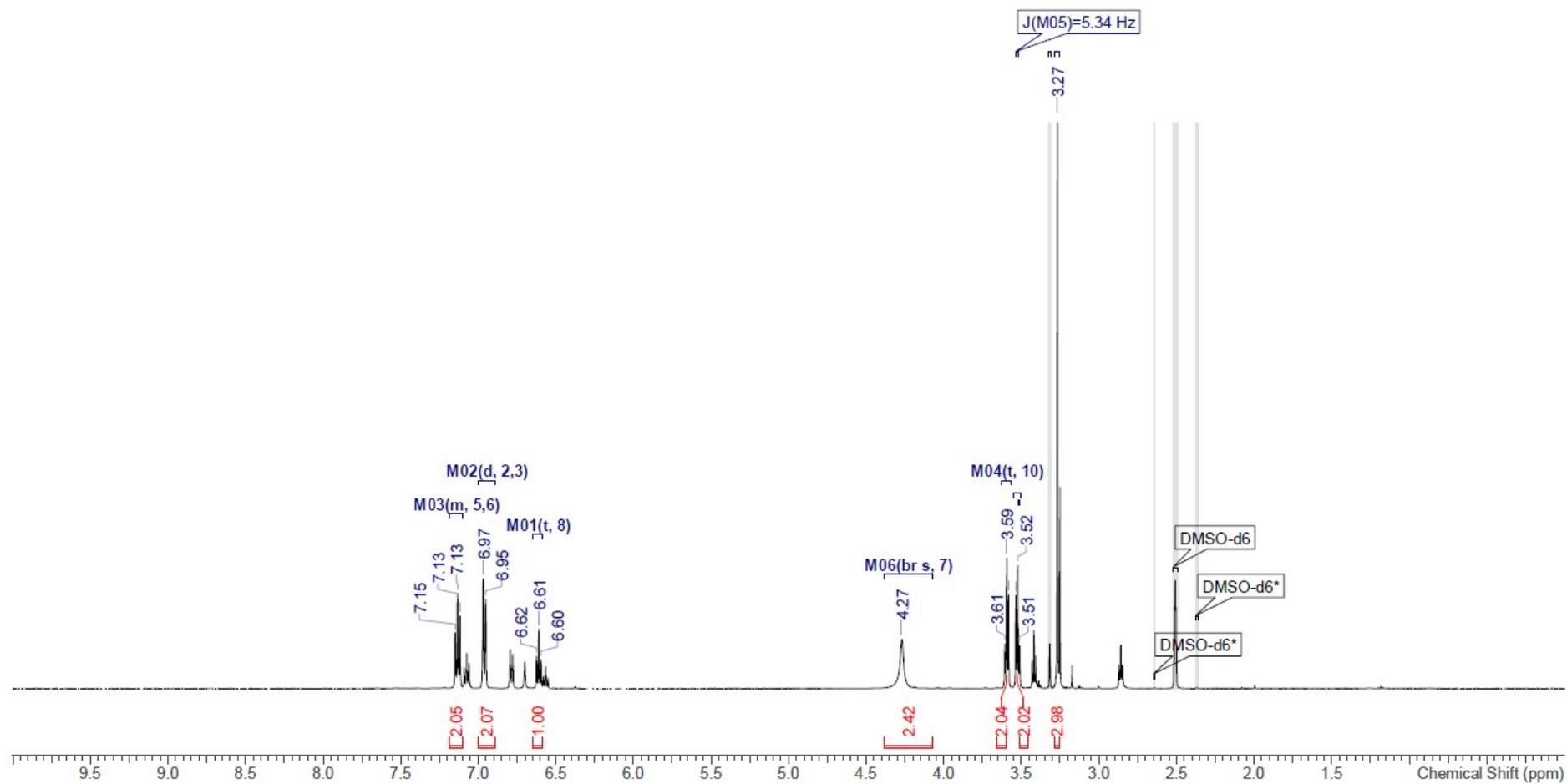
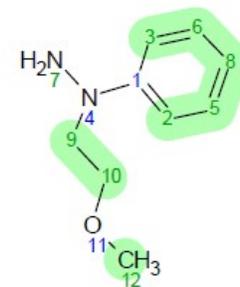
Compound 1  $^1\text{H}$  NMR



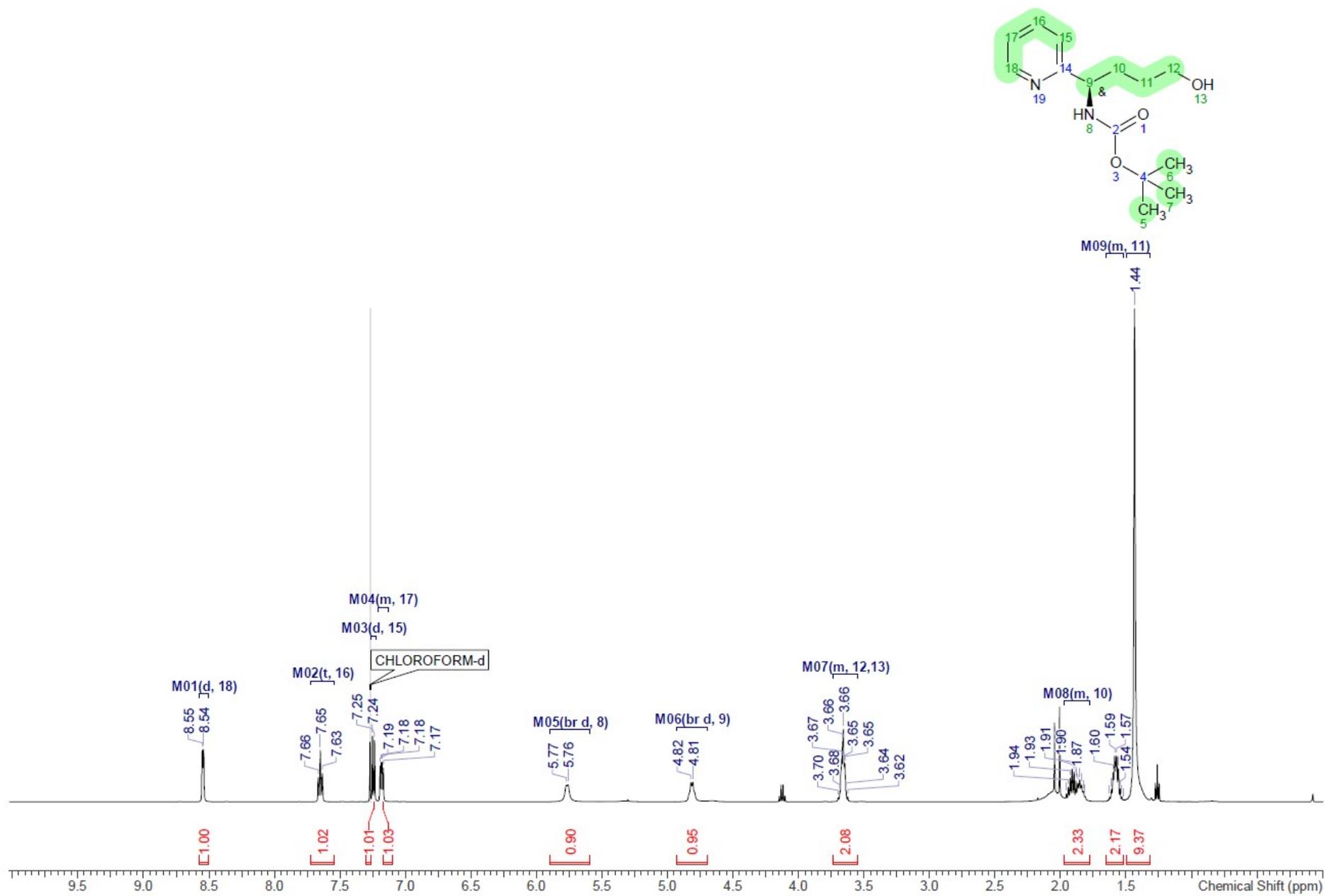
Compound 3 <sup>1</sup>H NMR



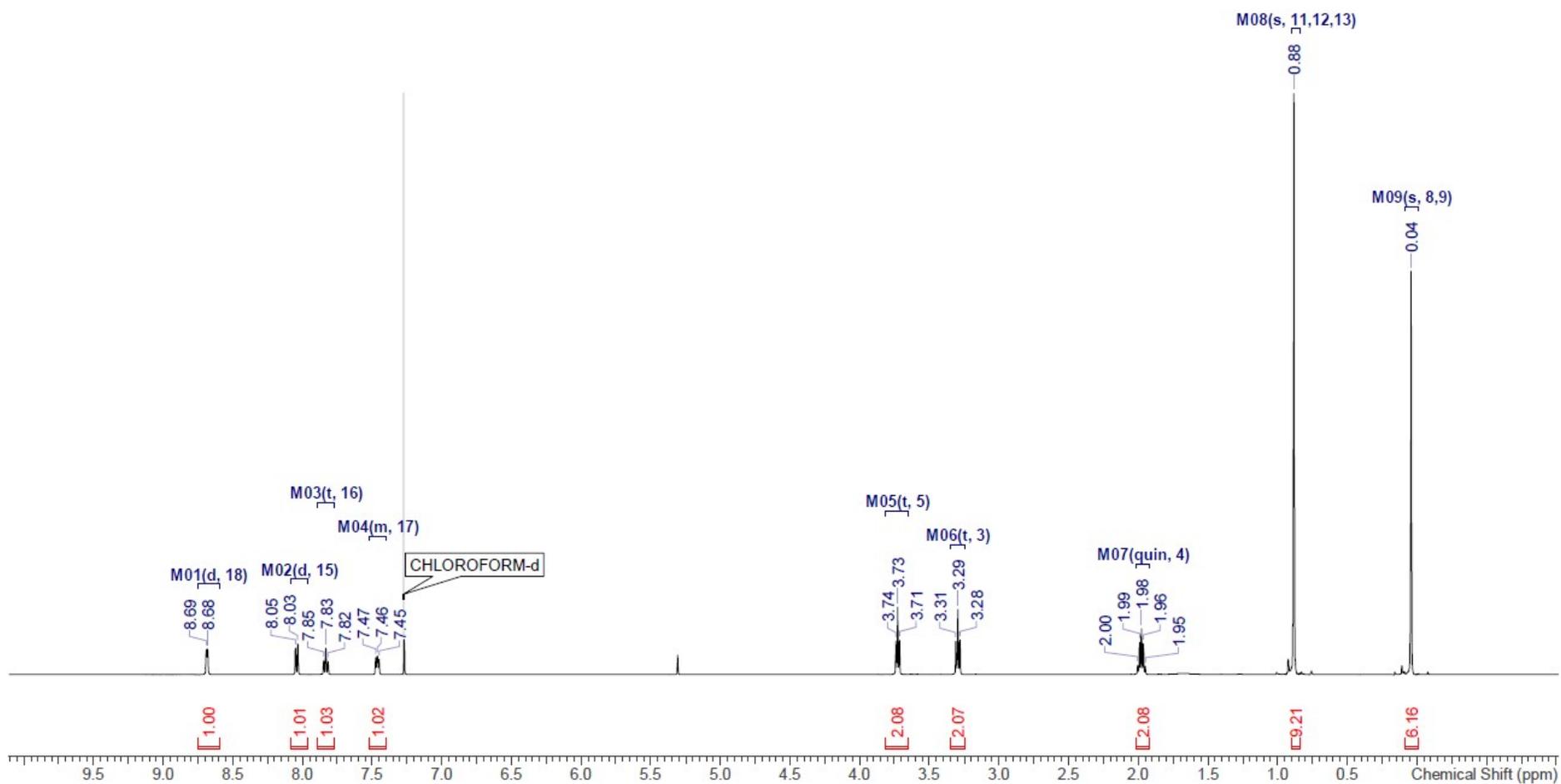
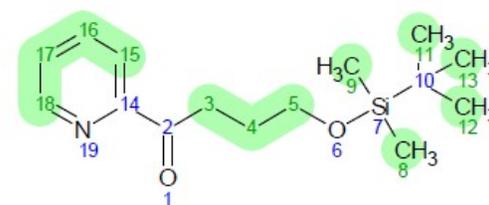
Compound 6 <sup>1</sup>H NMR



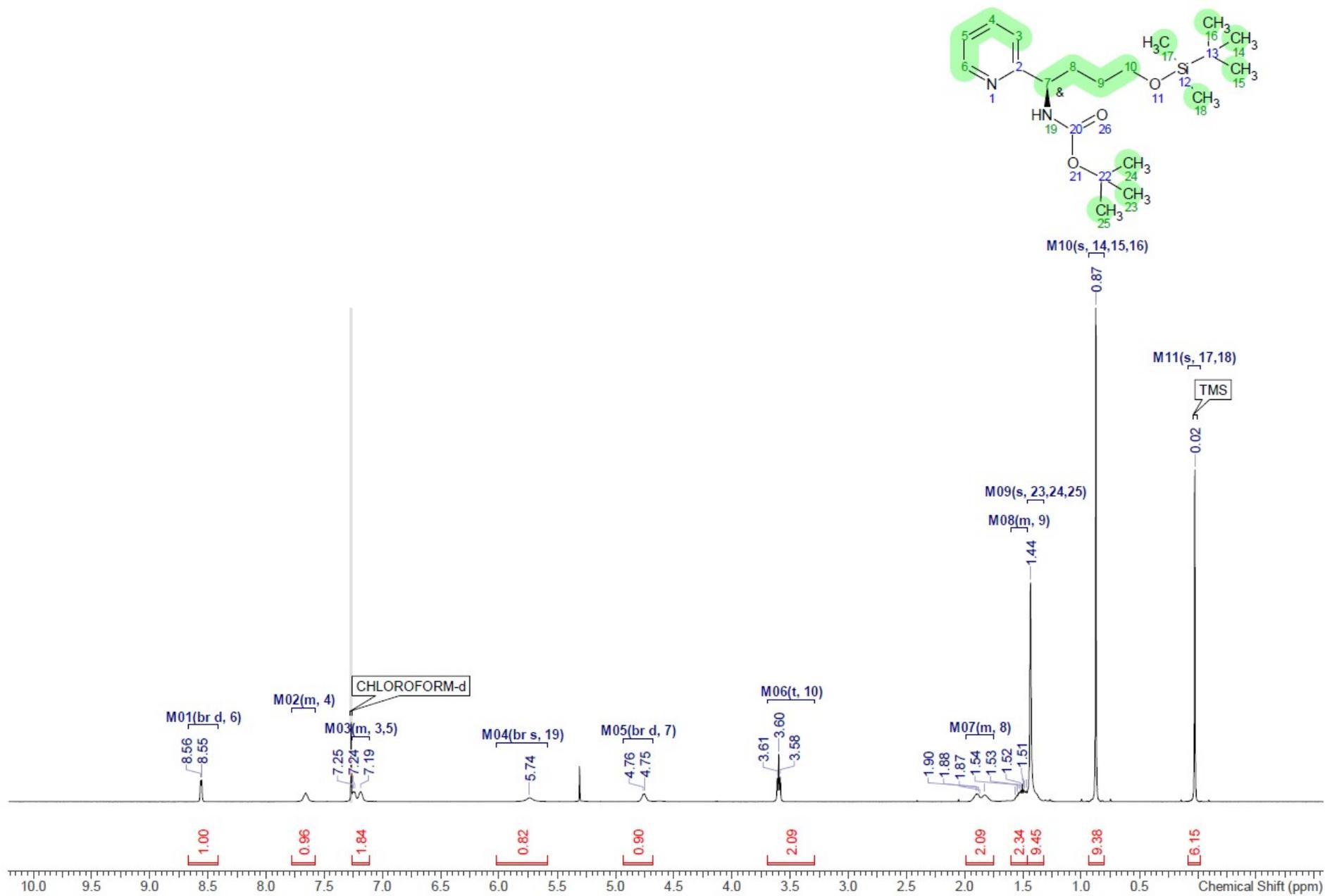
Compound **19**  $^1\text{H}$  NMR.  $\sim$ 3:1 mixture with N2-alkylated regioisomer



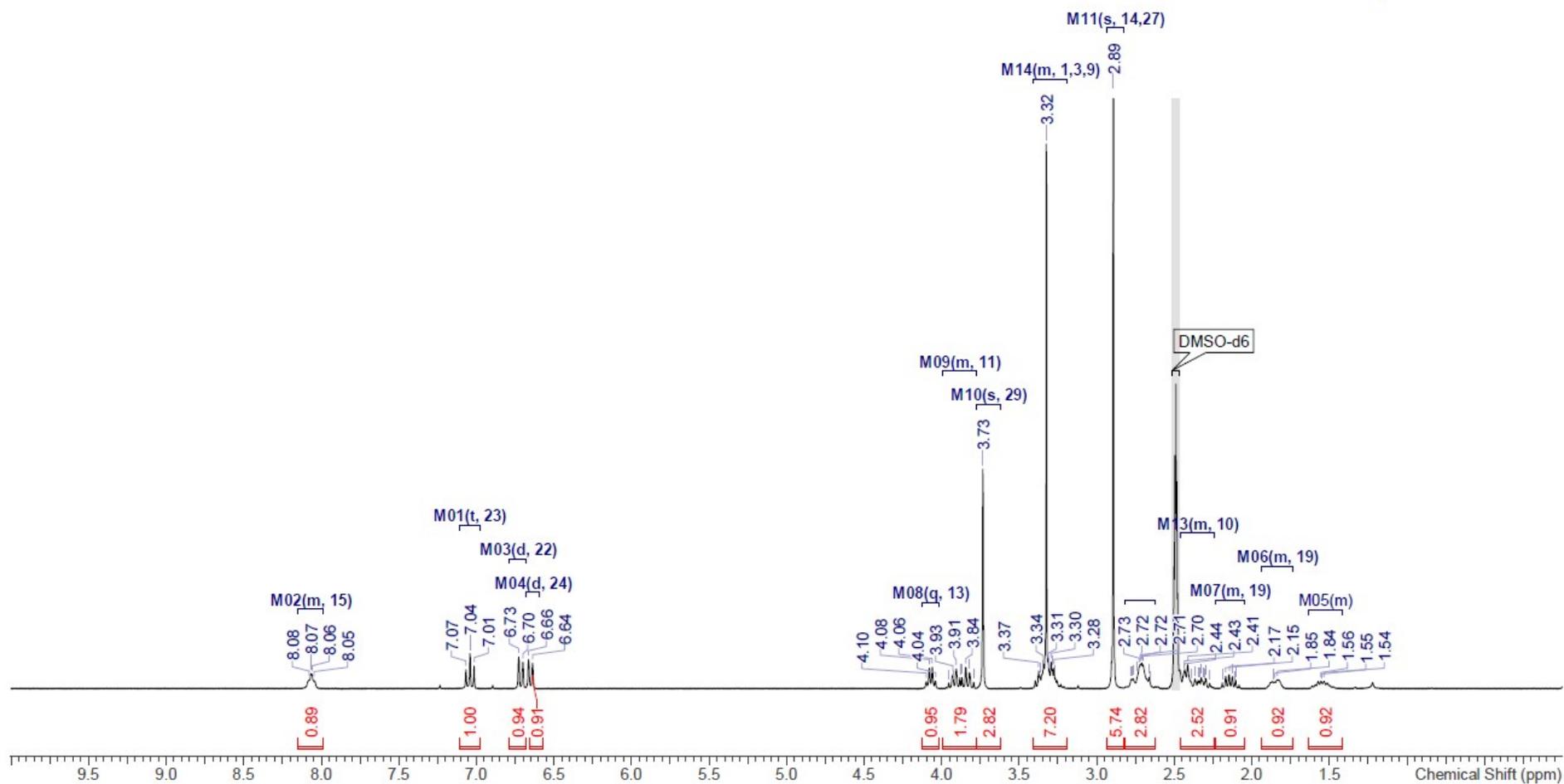
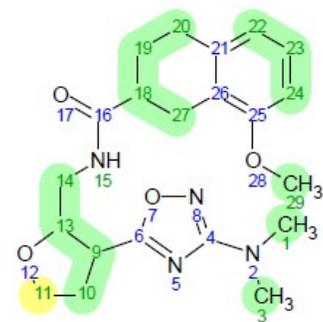
Compound **20** <sup>1</sup>H NMR



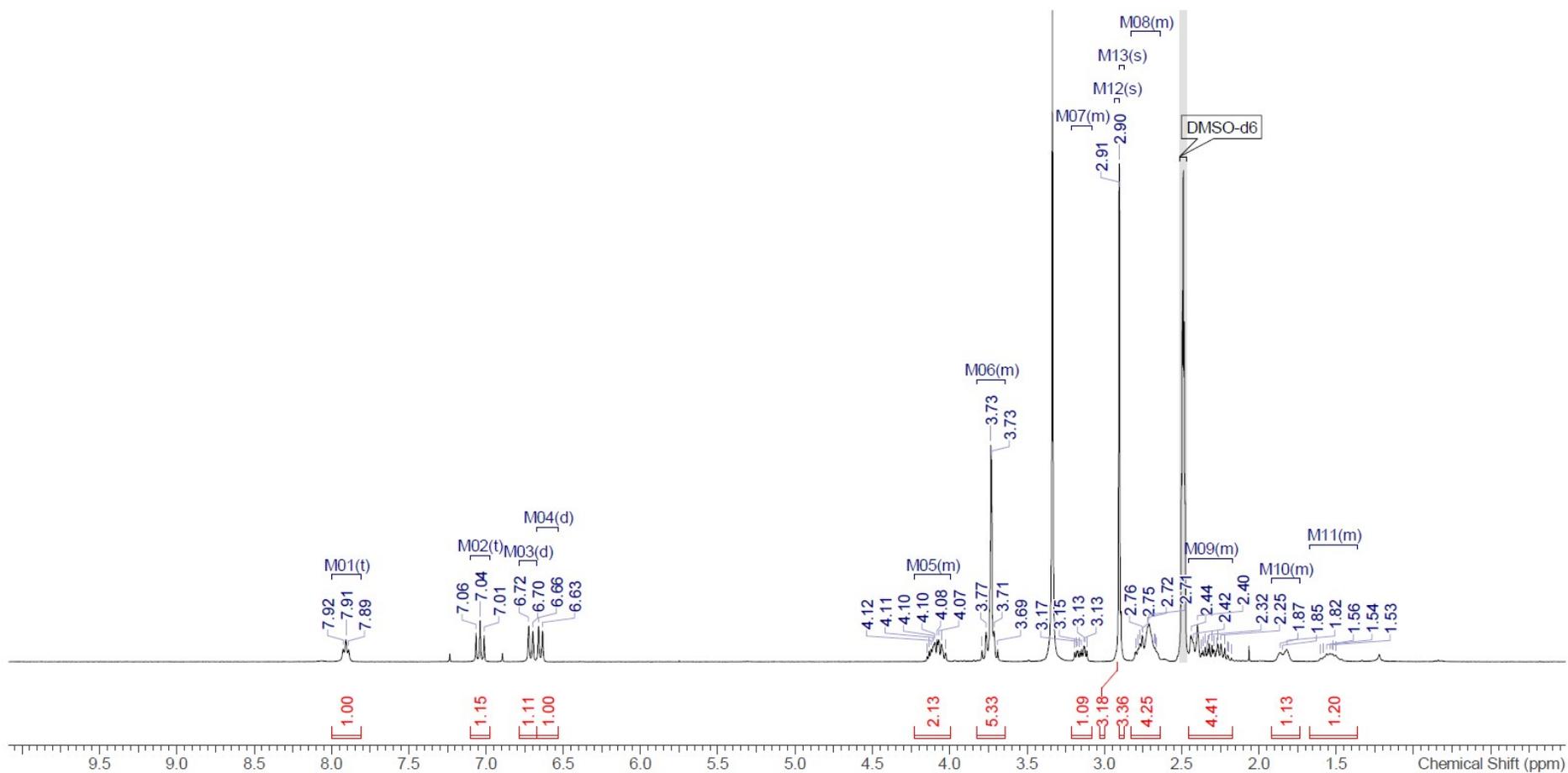
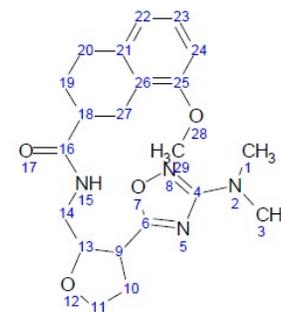
Compound **23**  $^1\text{H}$  NMR



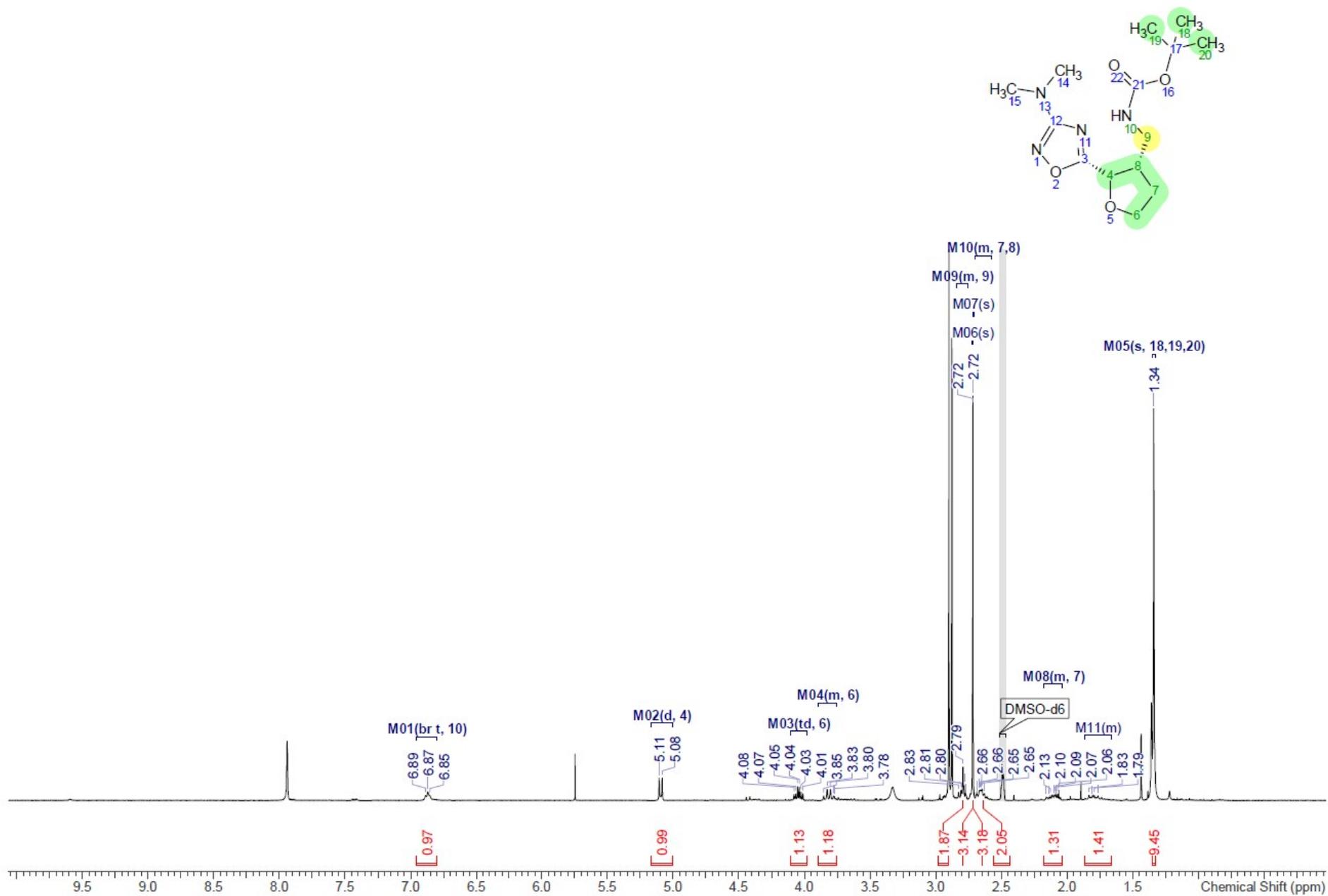
Compound 25 <sup>1</sup>H NMR



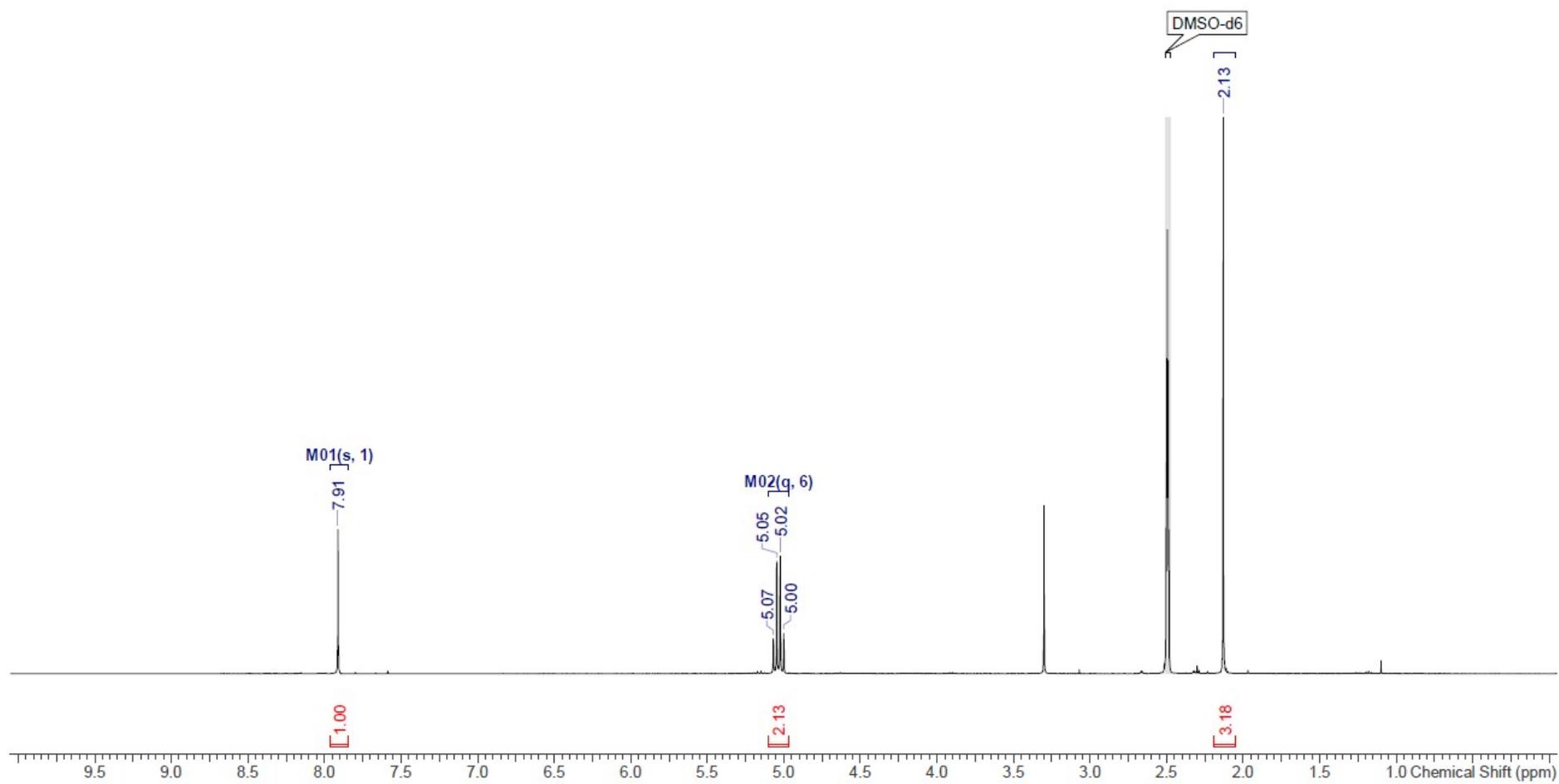
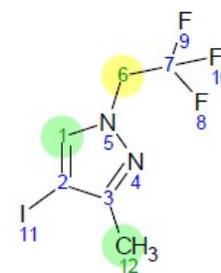
Compound **27** Isomer 1  $^1\text{H}$  NMR



Compound 27 Isomer 2 <sup>1</sup>H NMR



Compound **32** <sup>1</sup>H NMR. Heavily contaminated with DMF



Compound **38** <sup>1</sup>H NMR