Supplementary Material

N2-Alkylation of semicarbazones. A general and efficient protocol for the synthesis of 2-alkylsemicarbazides from semicarbazide

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Email: anatshu@gmail.com

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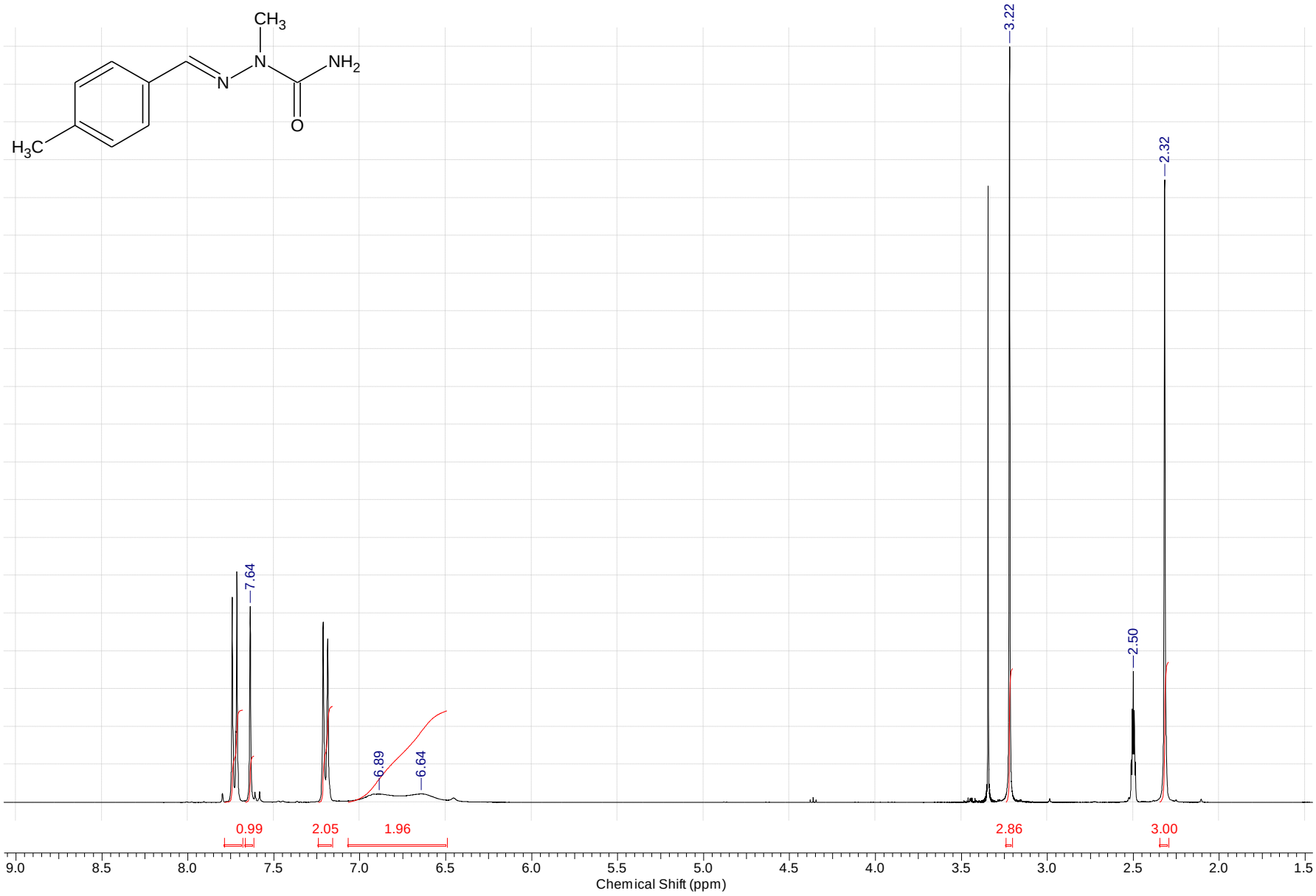
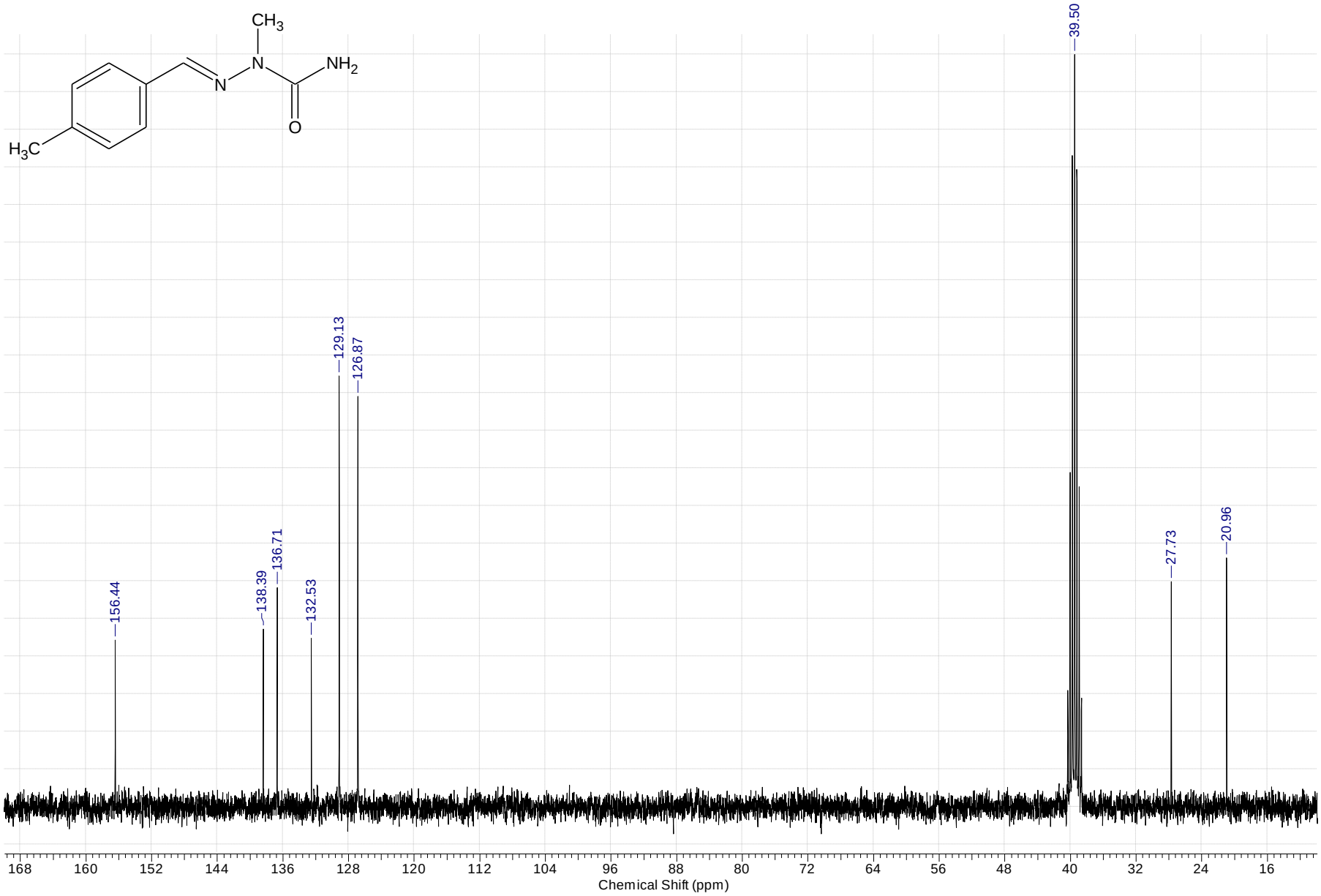
^{1}H NMR spectrum of compound **2b** (DMSO-d_6)



^{13}C NMR spectrum of compound **2b** (DMSO-d_6)



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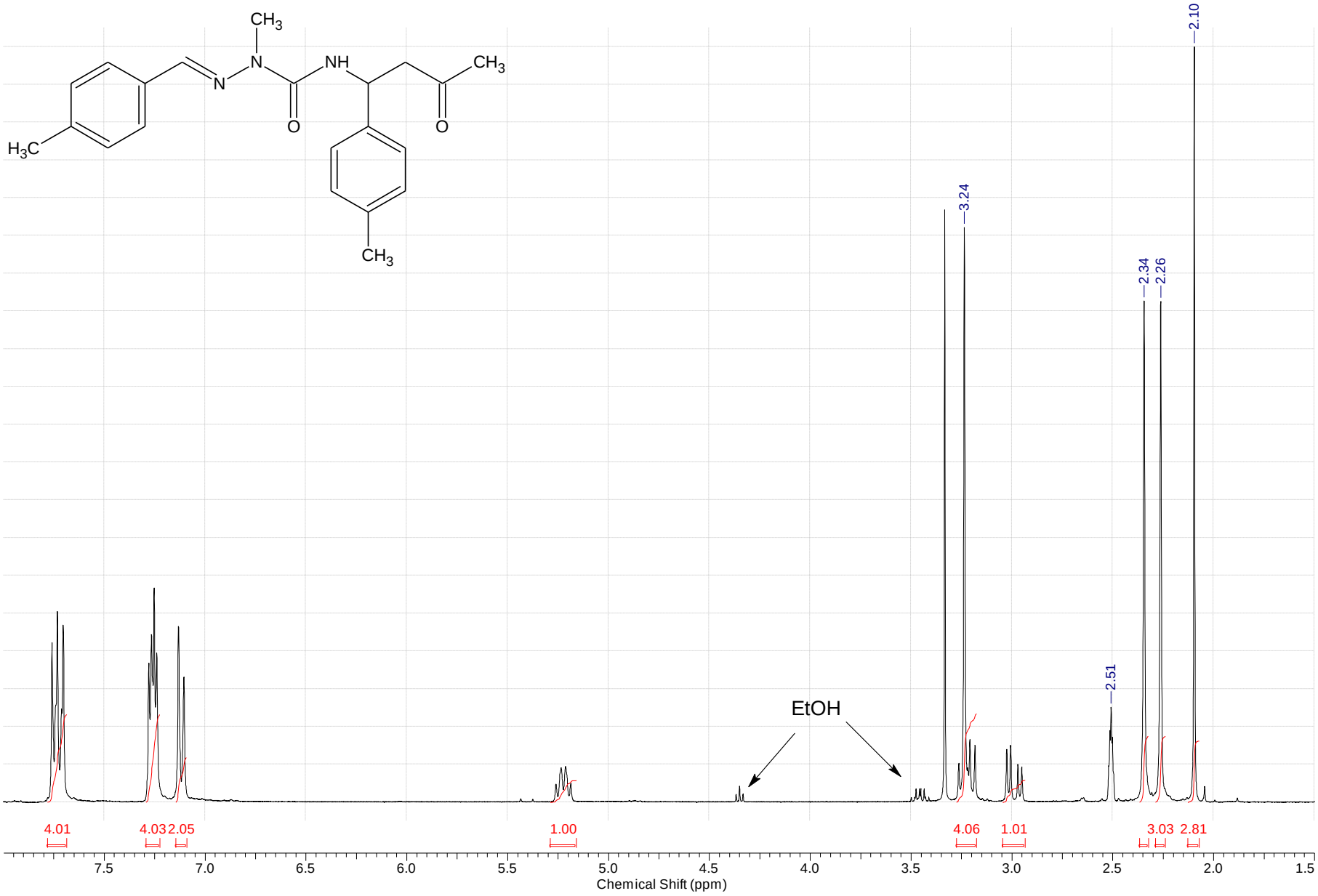

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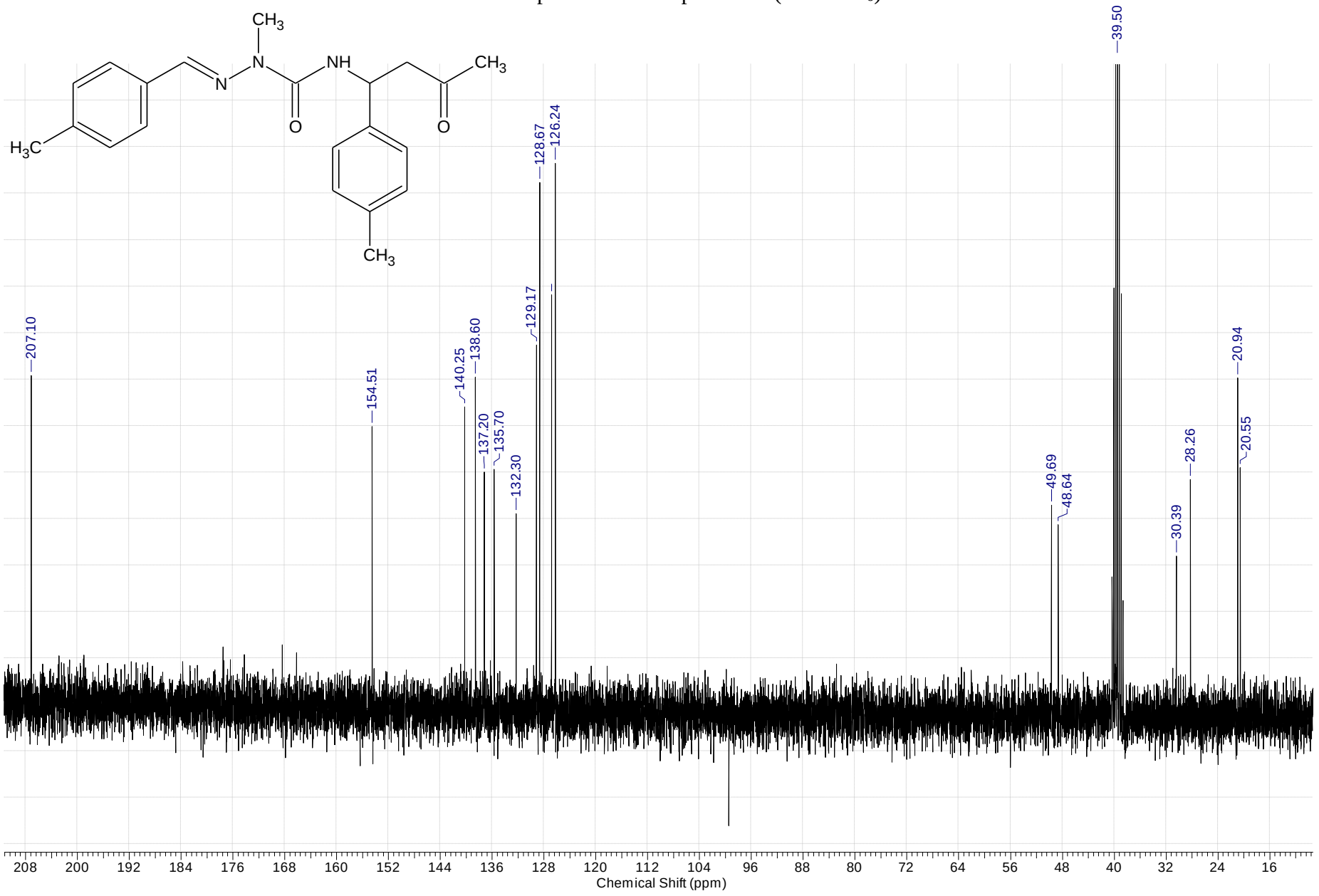

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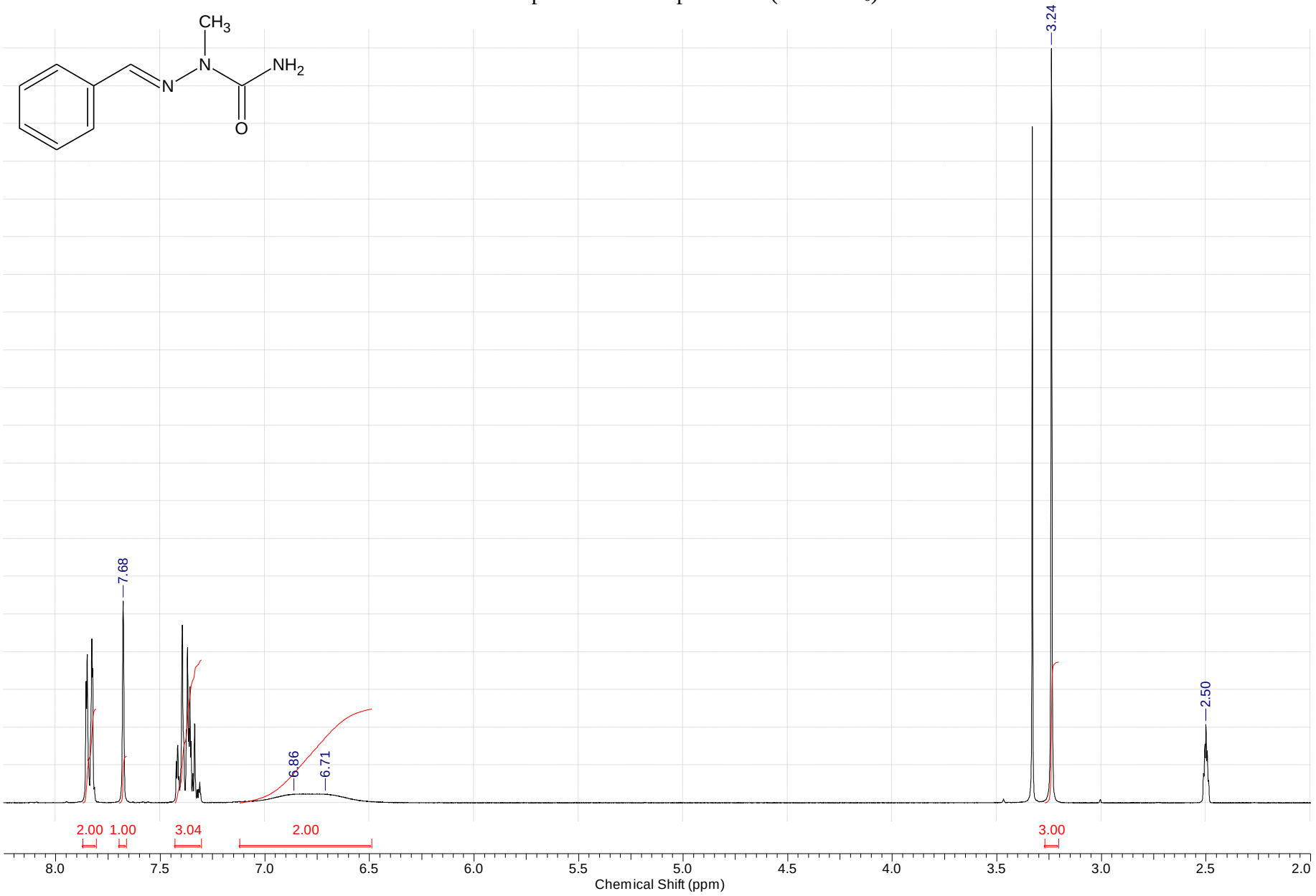

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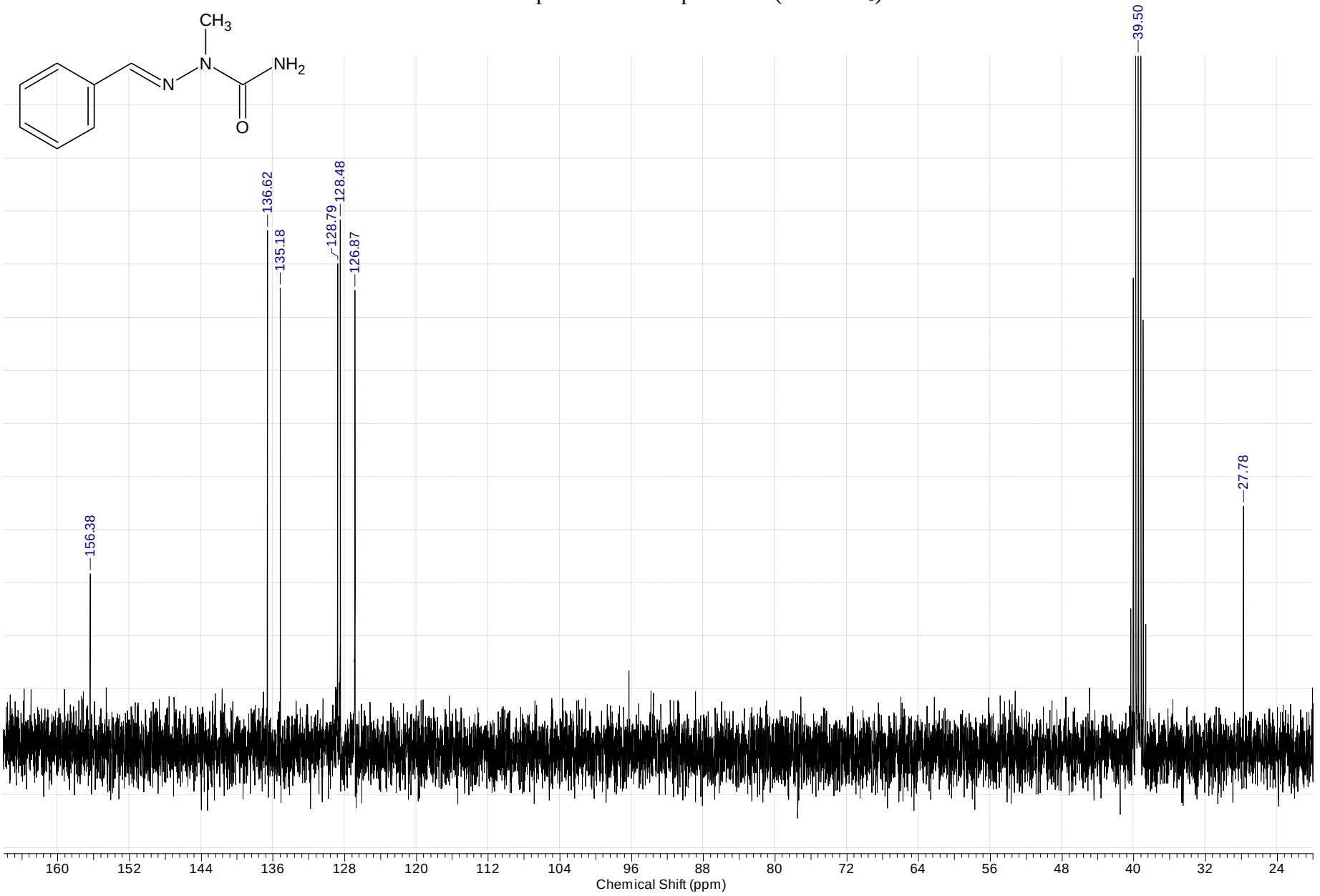

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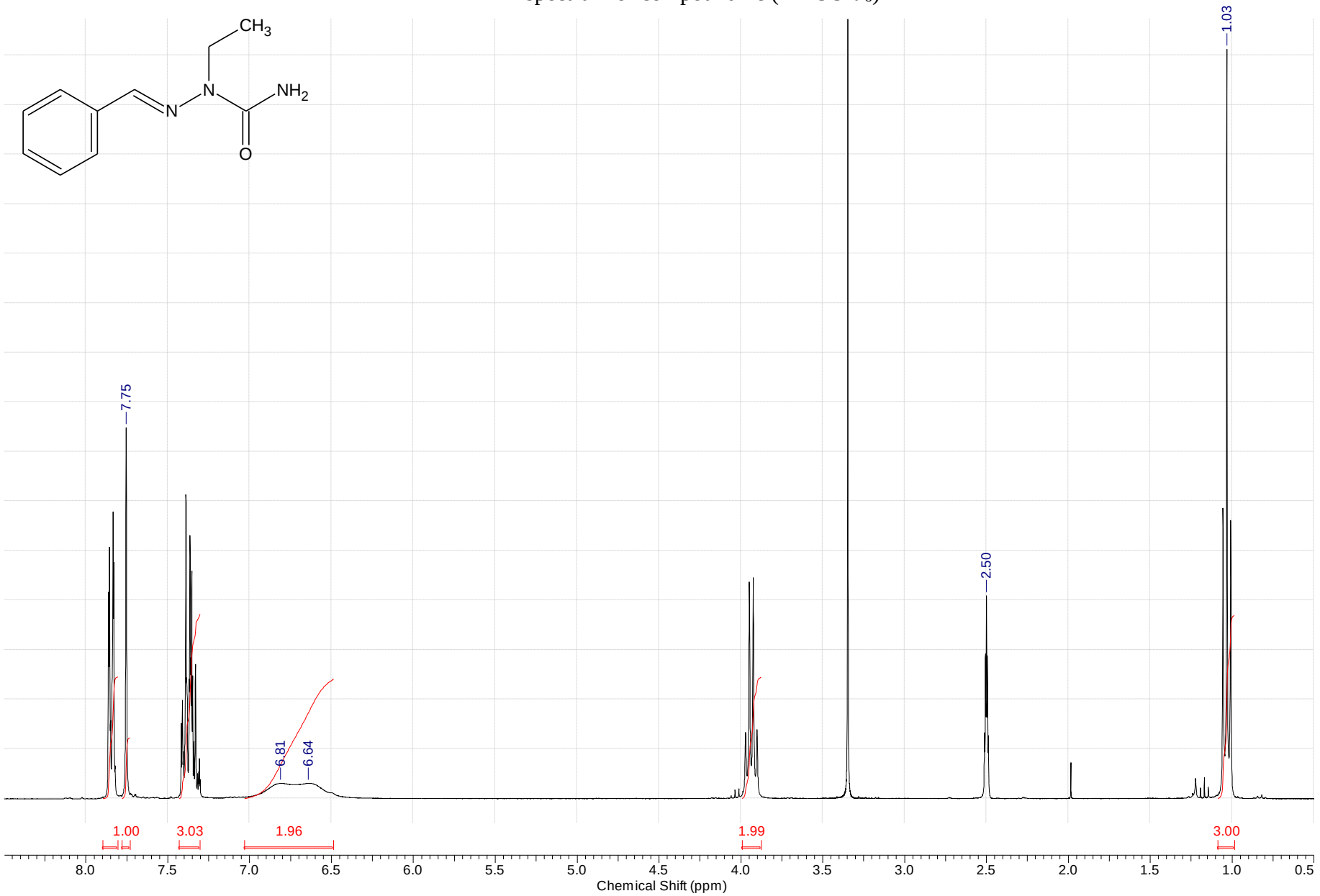

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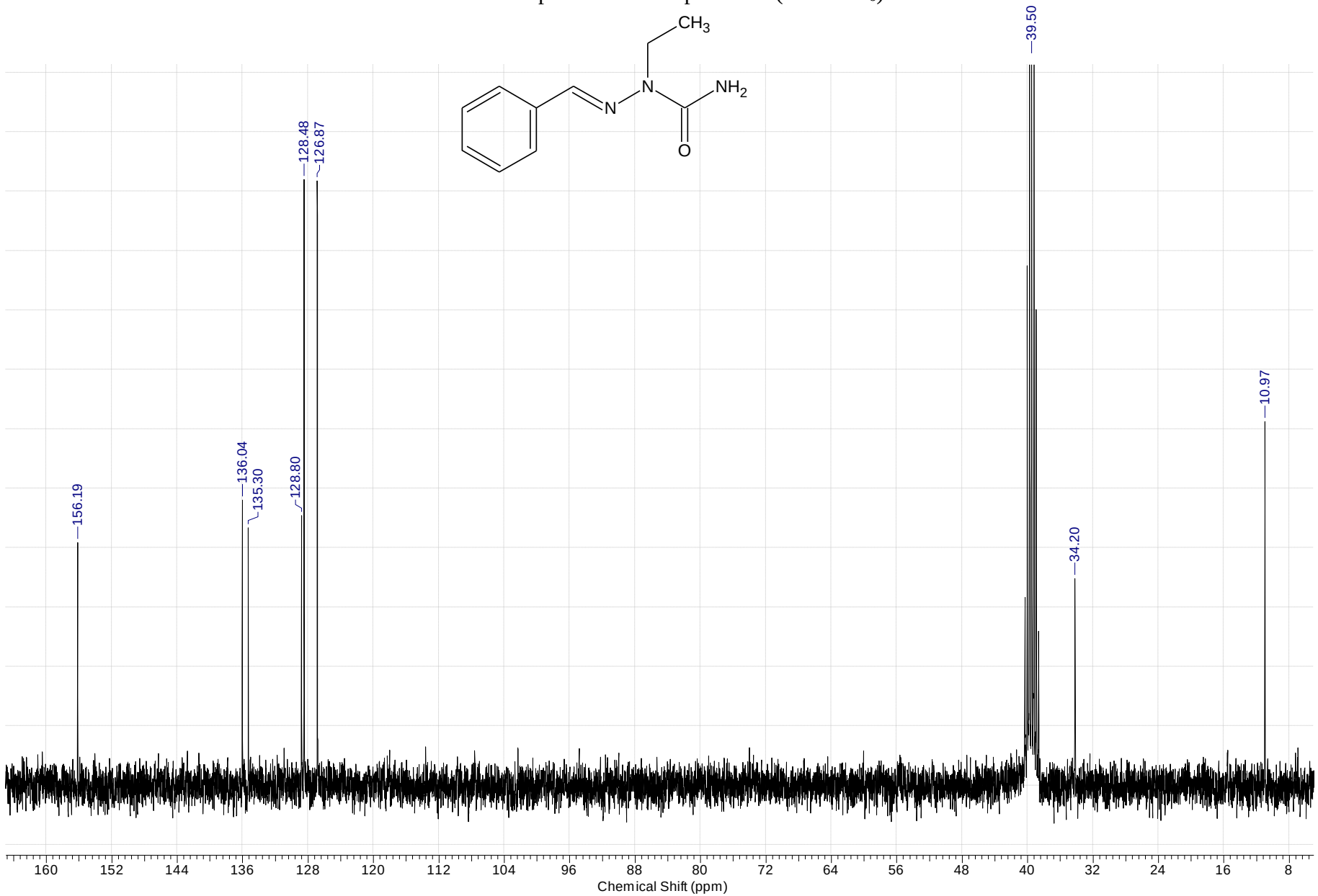

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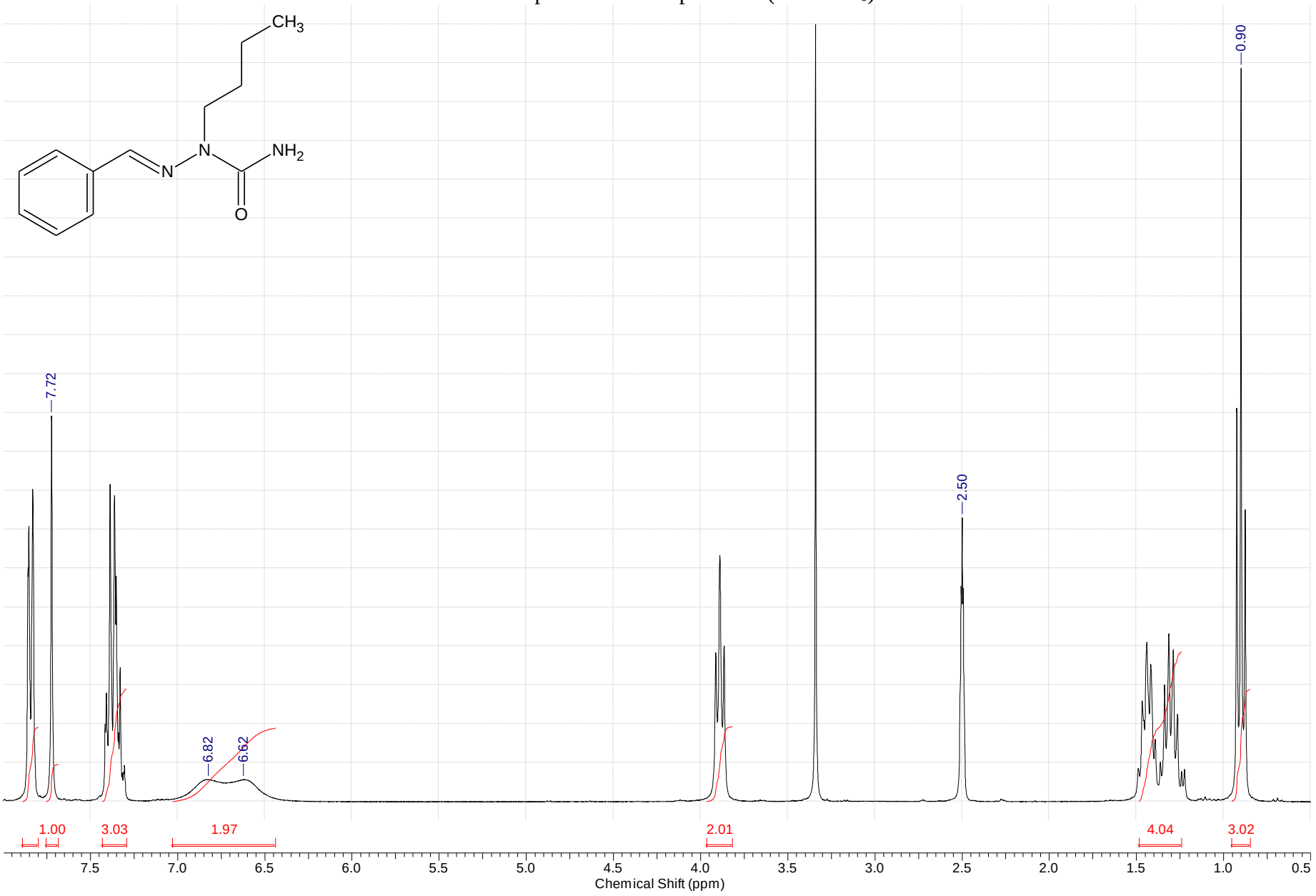

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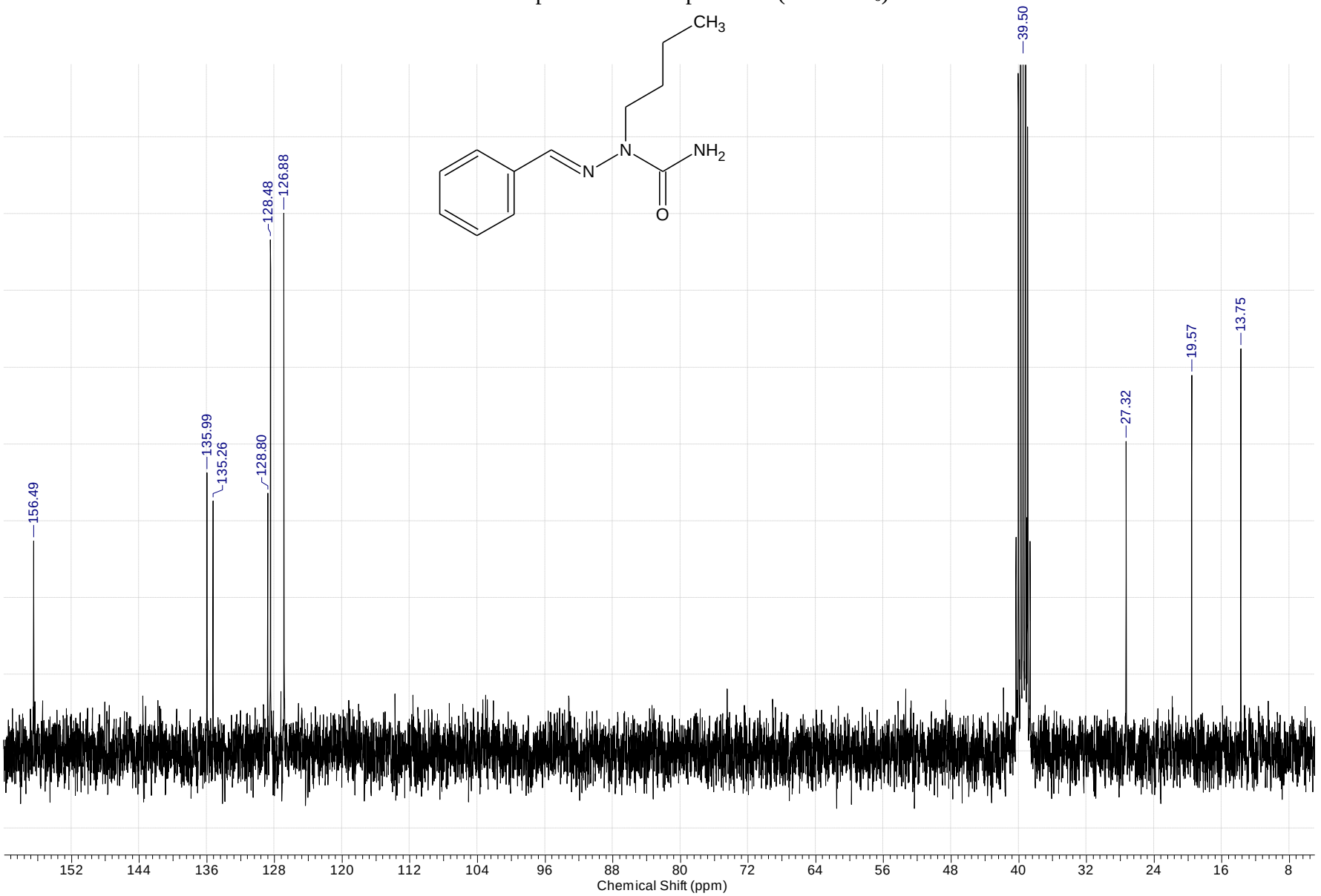

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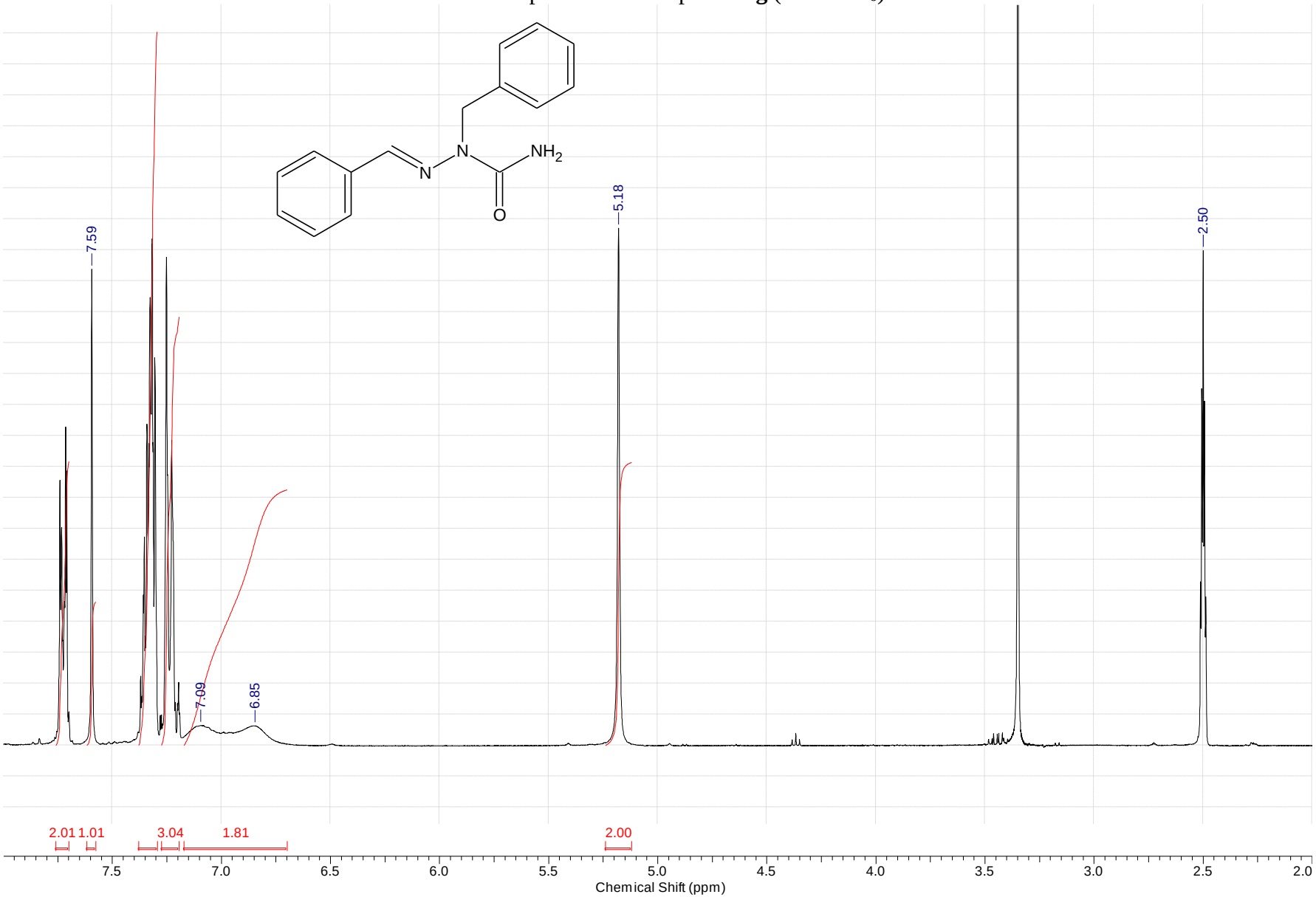

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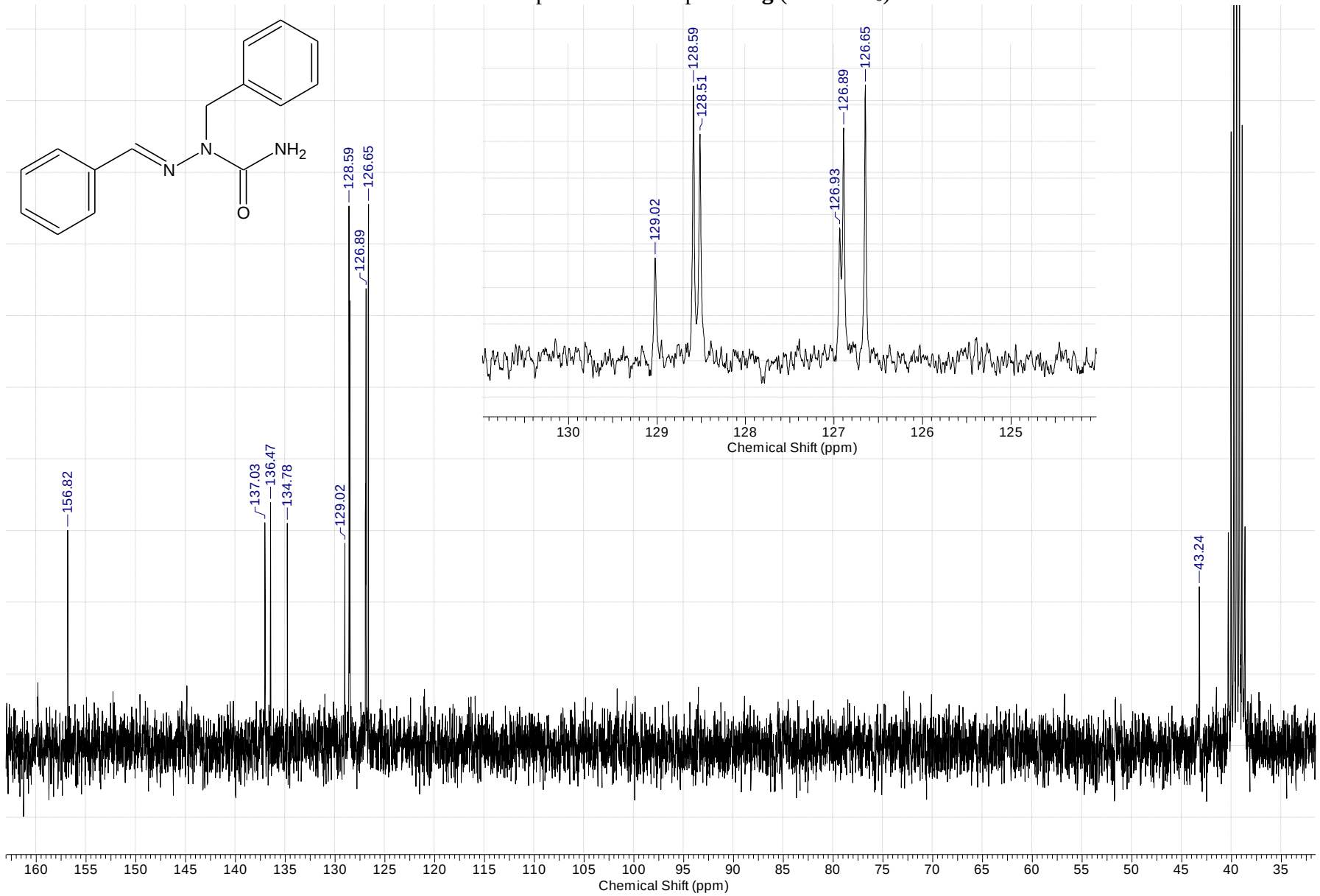

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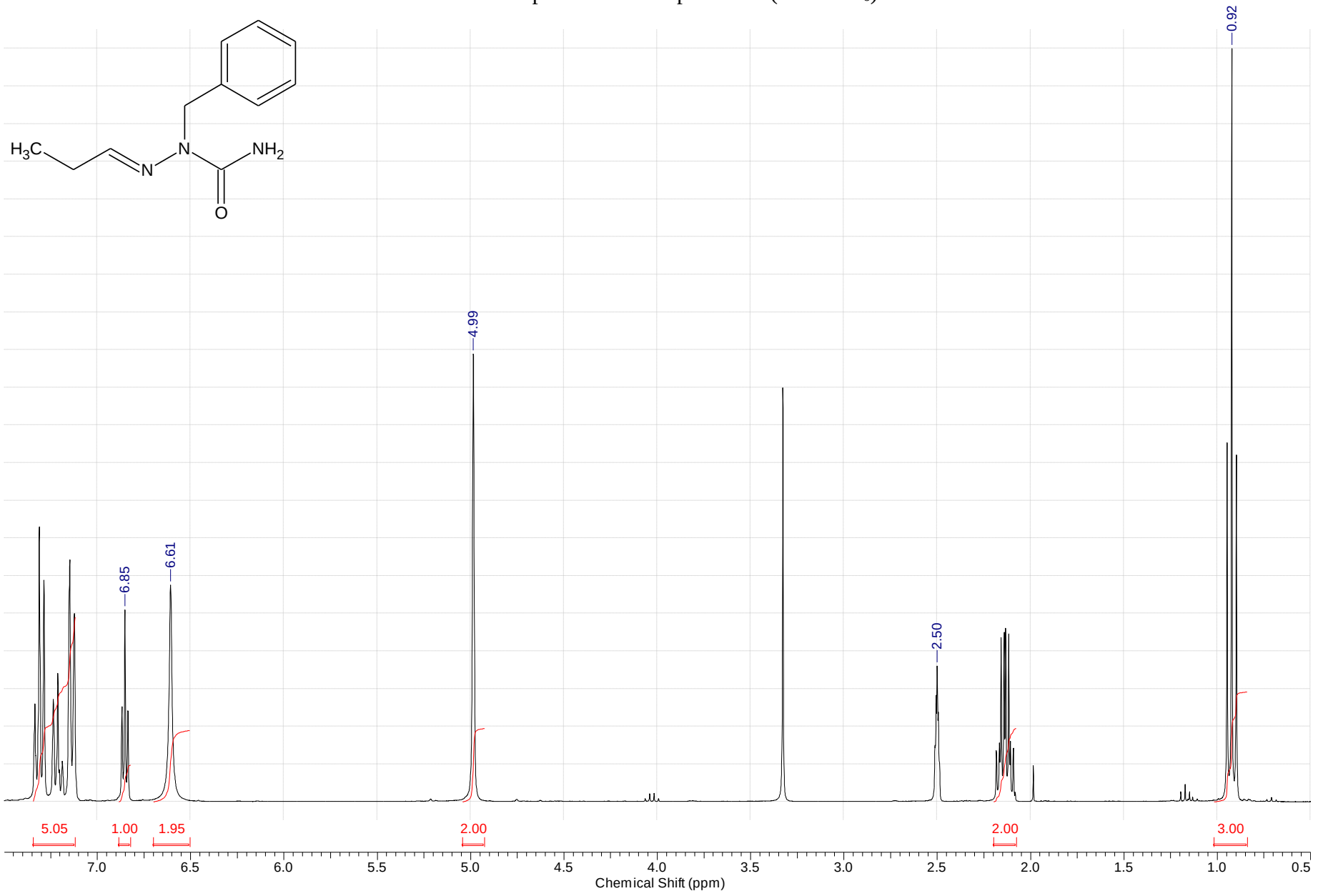

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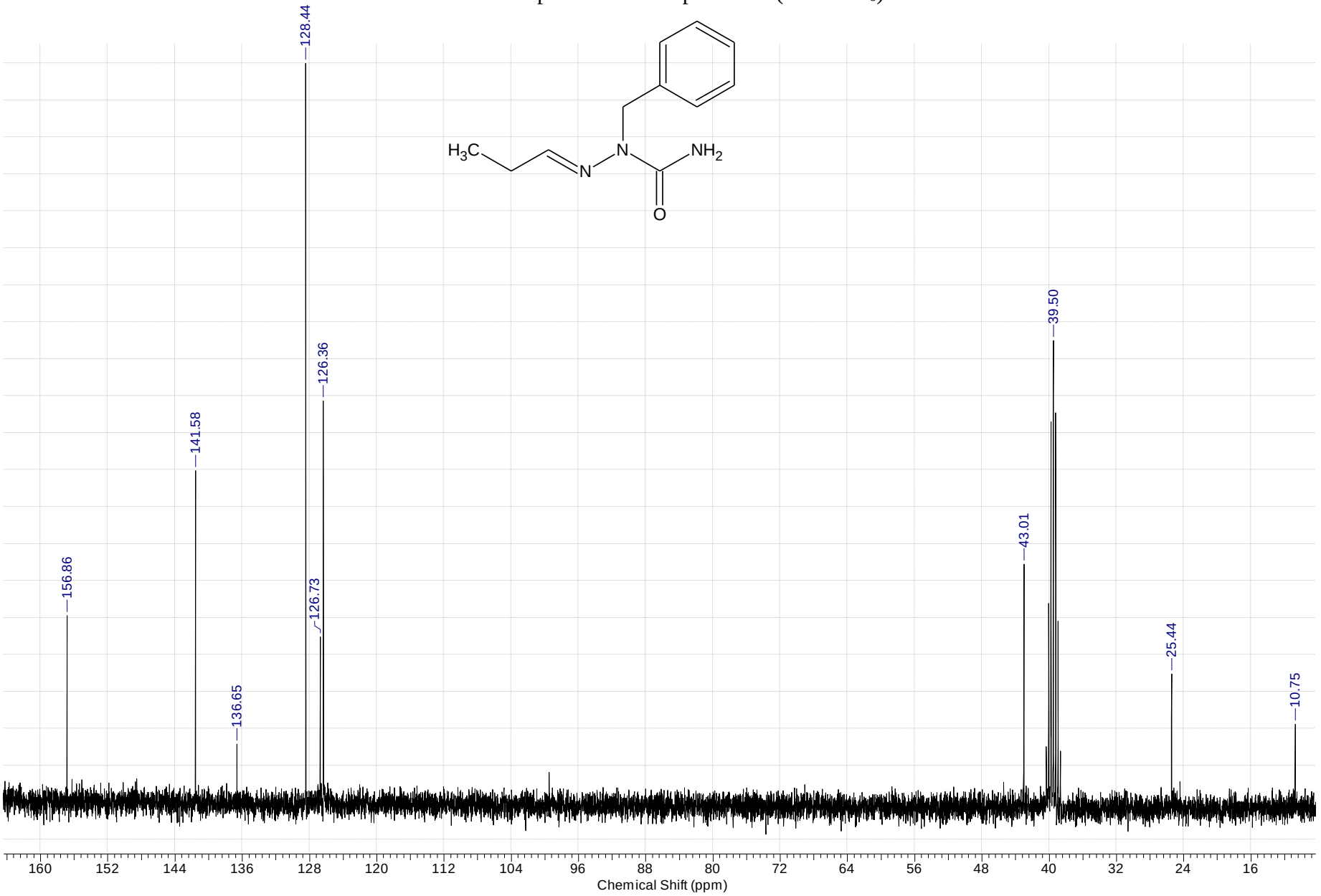

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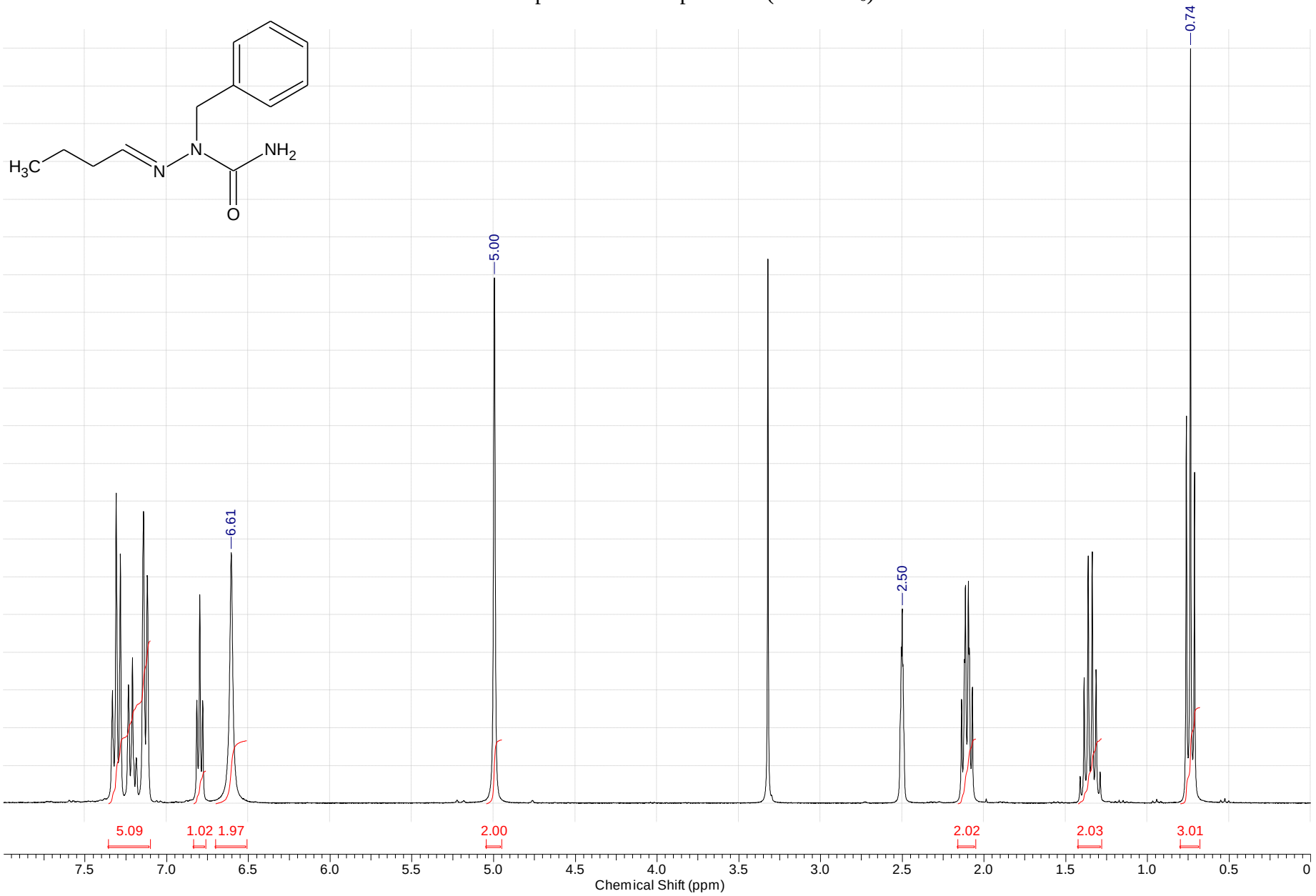

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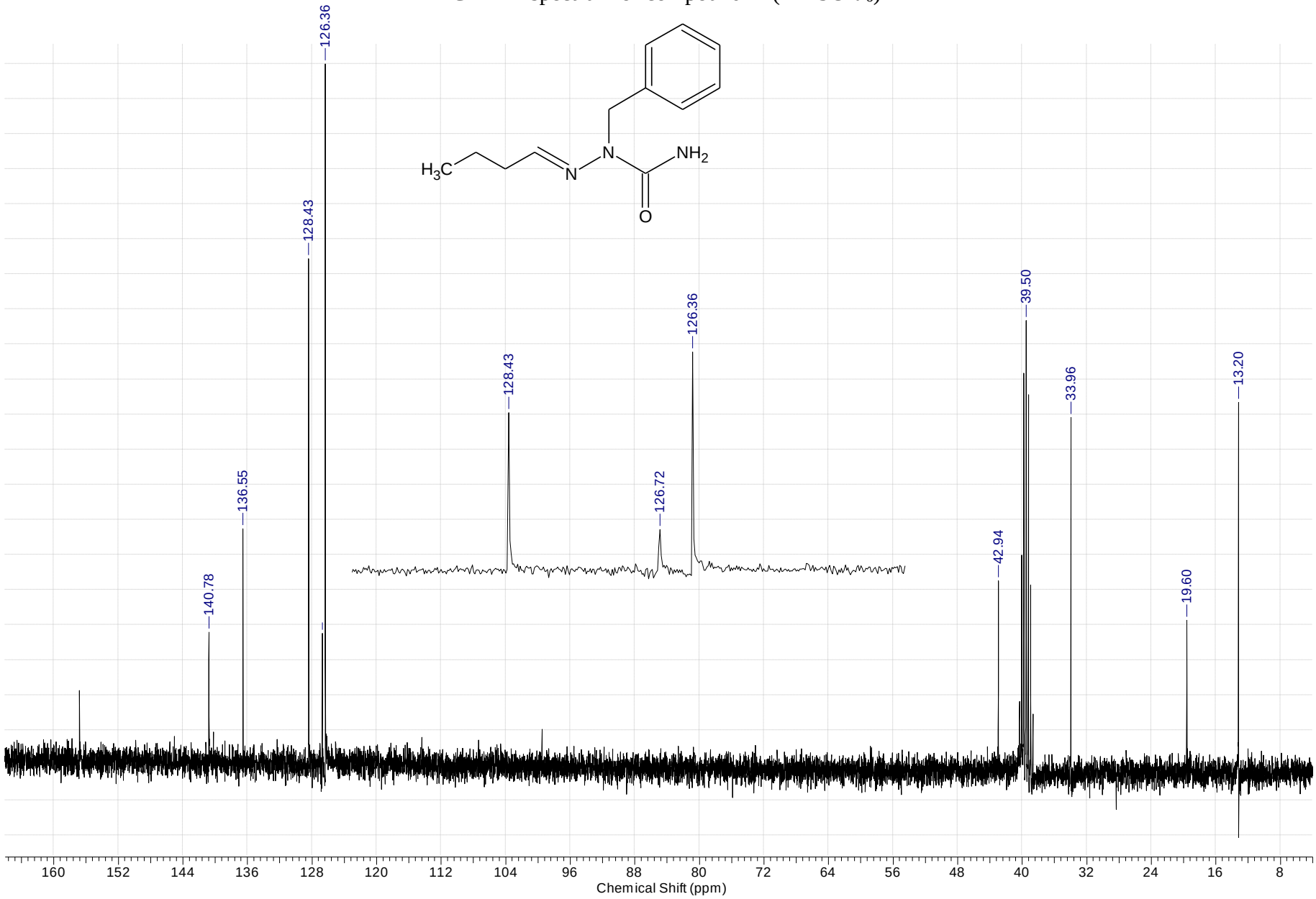

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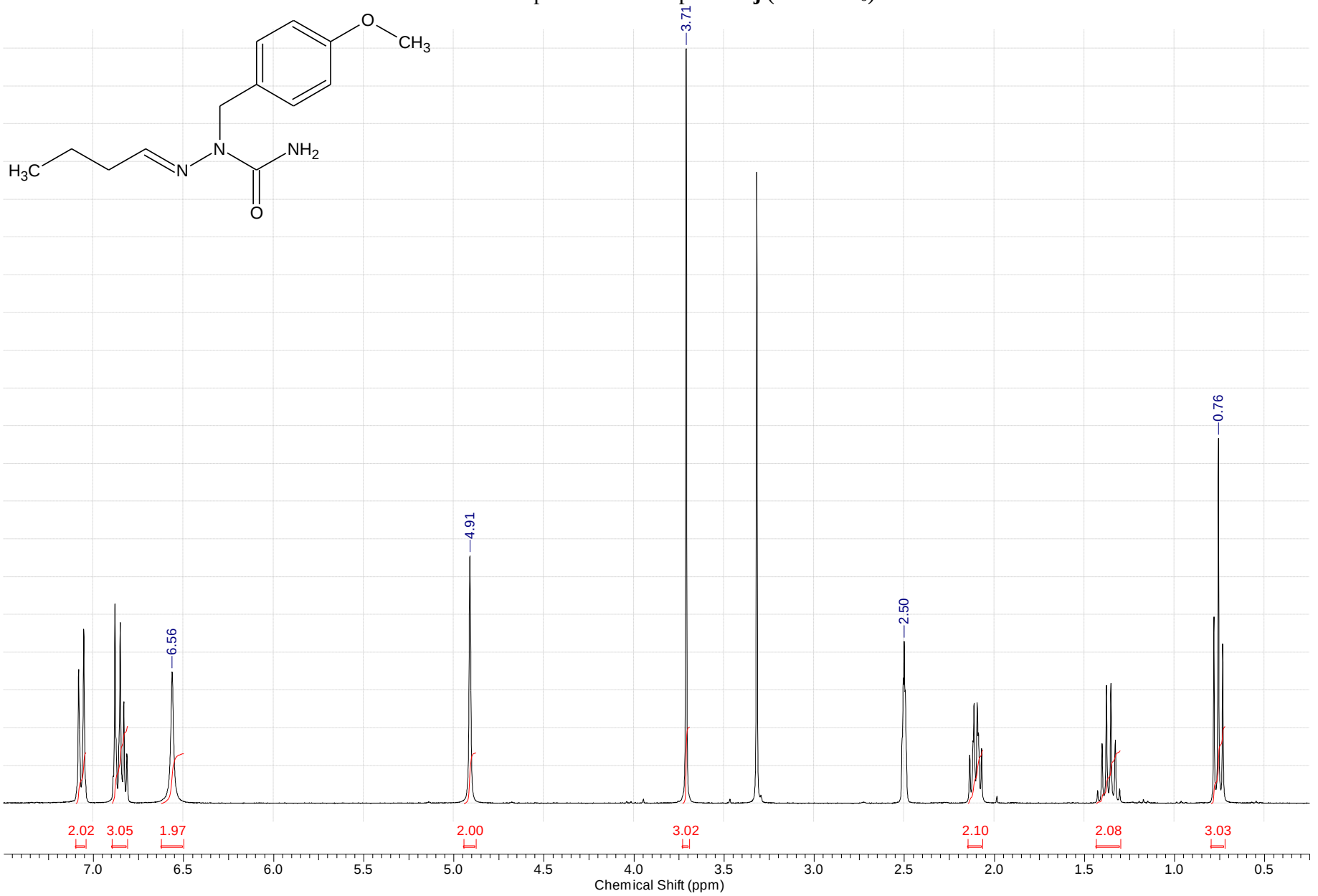

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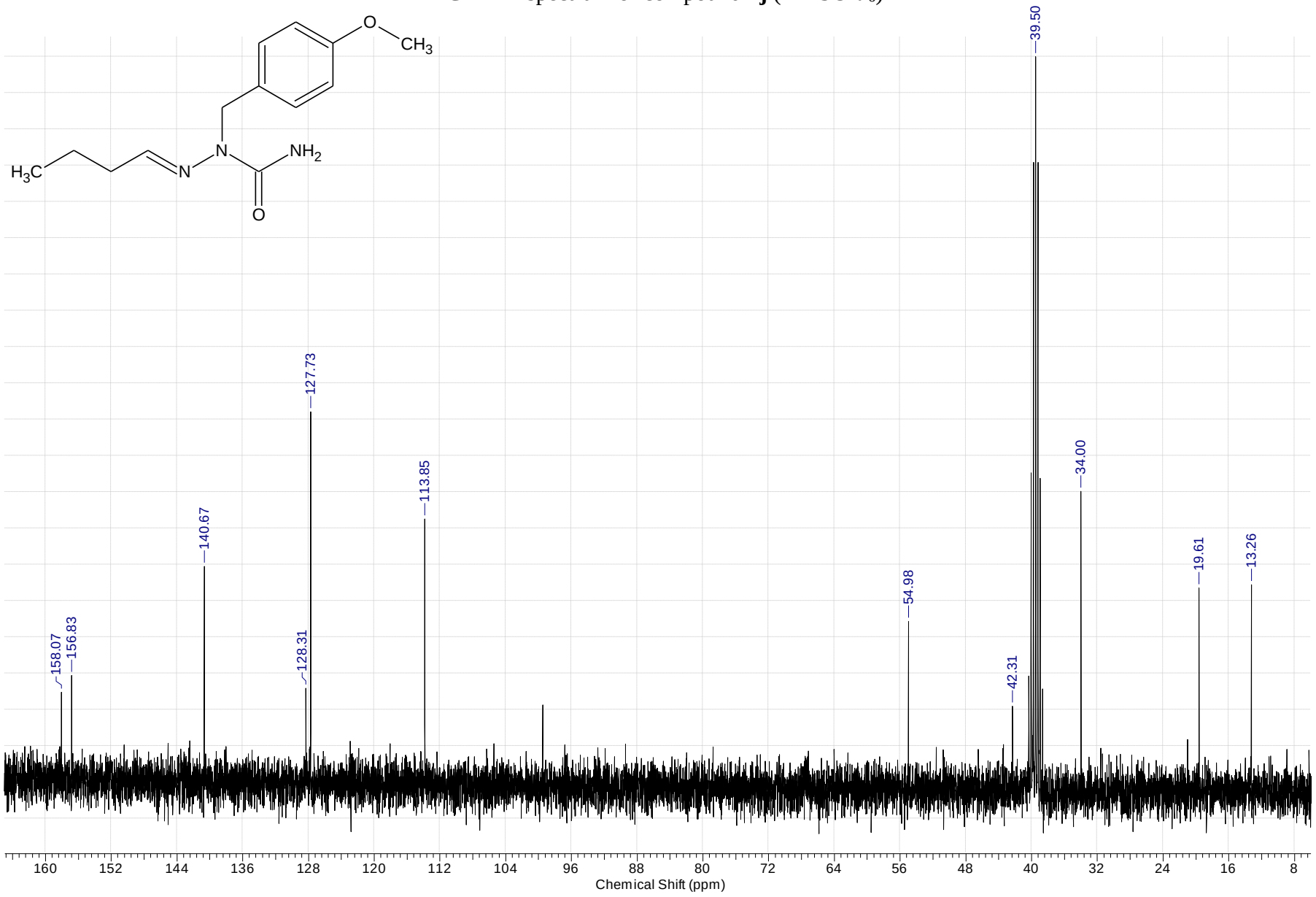

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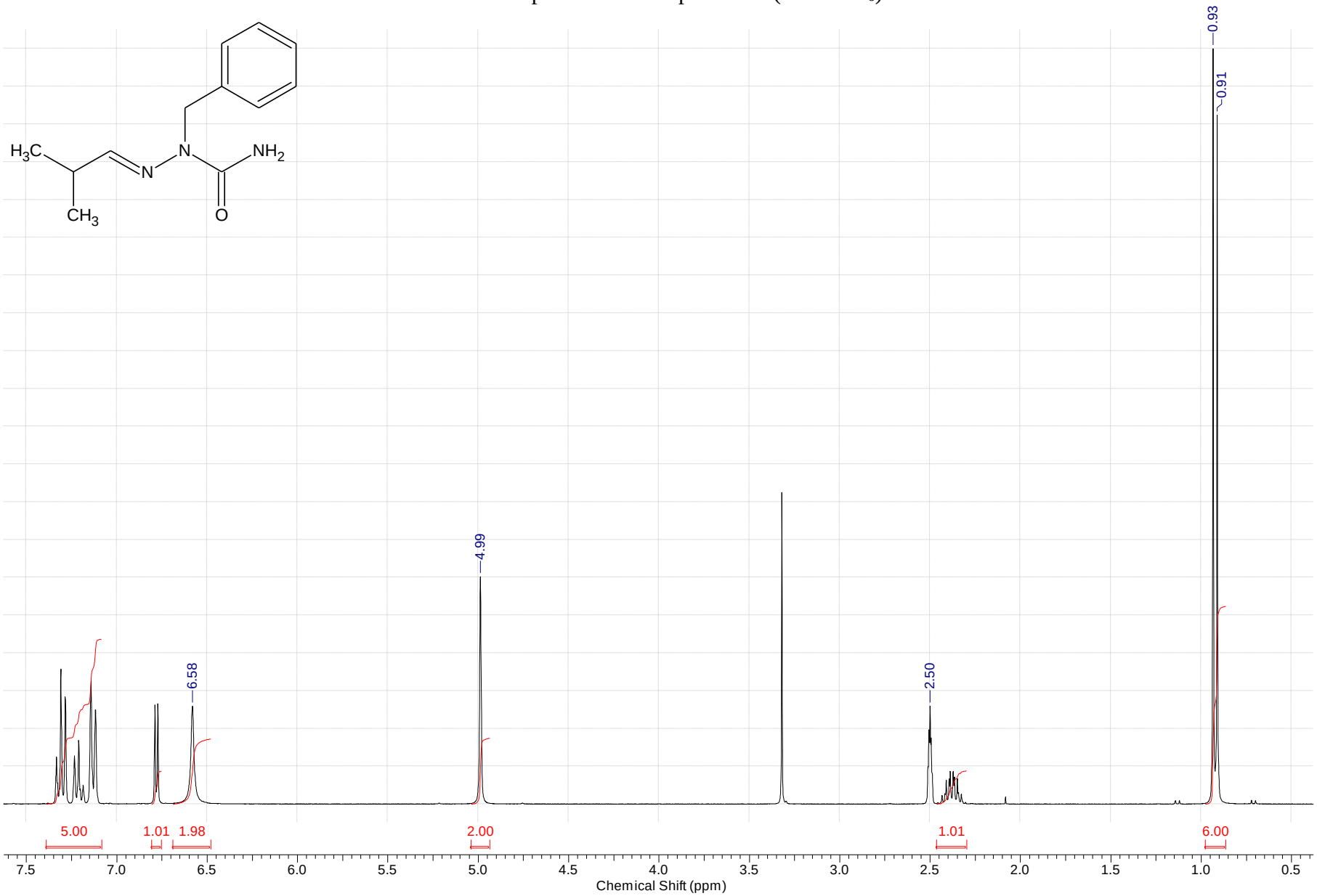

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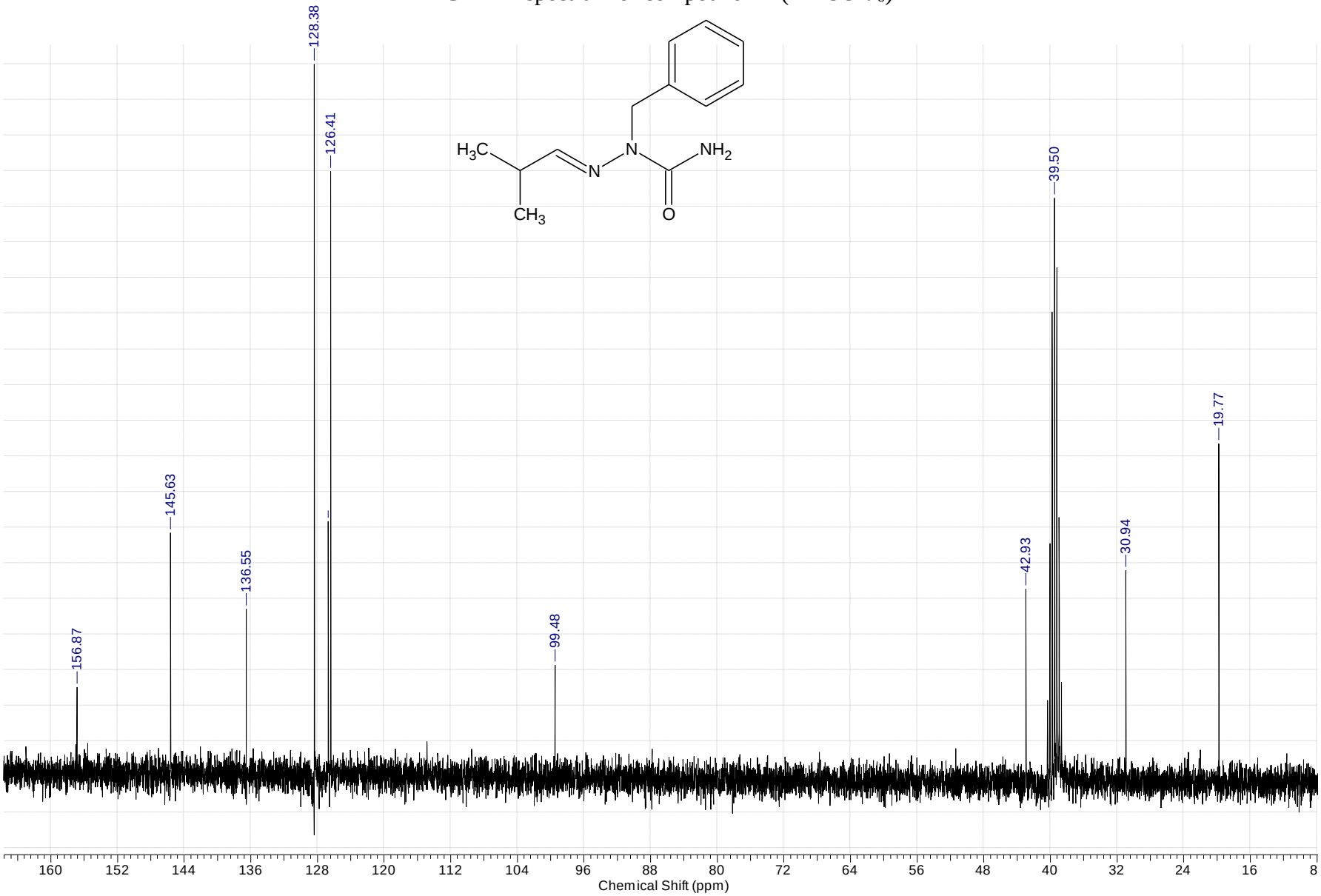

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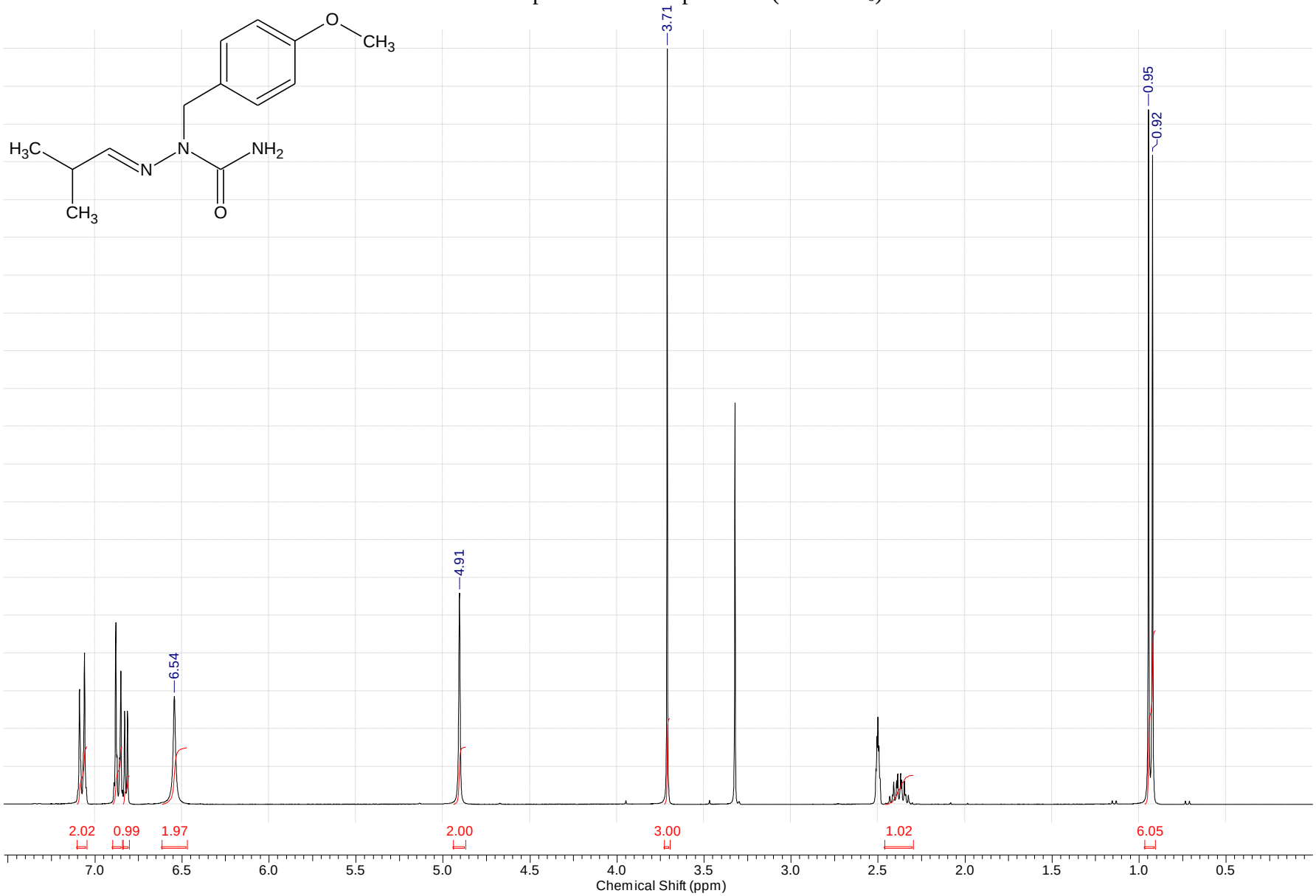

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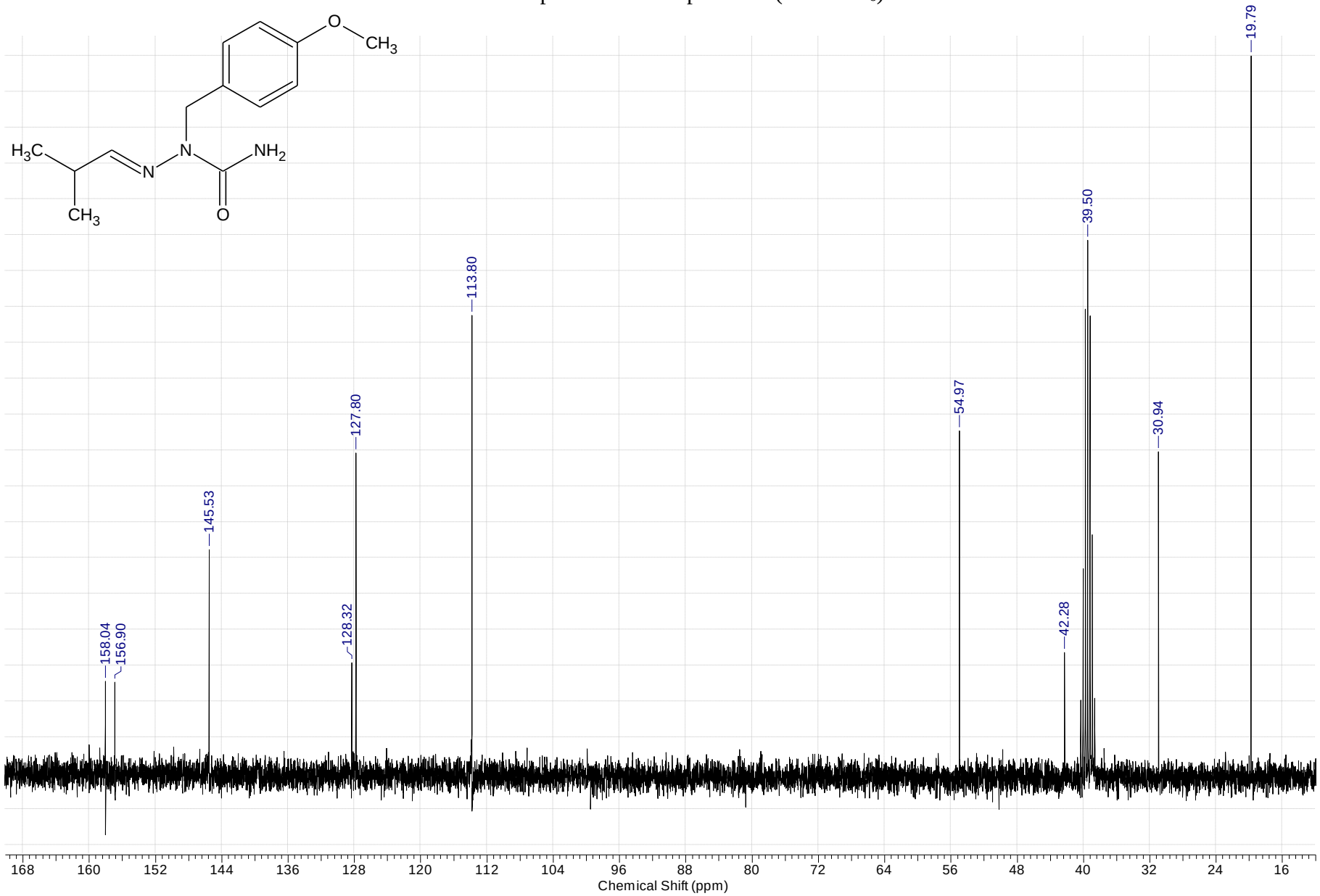

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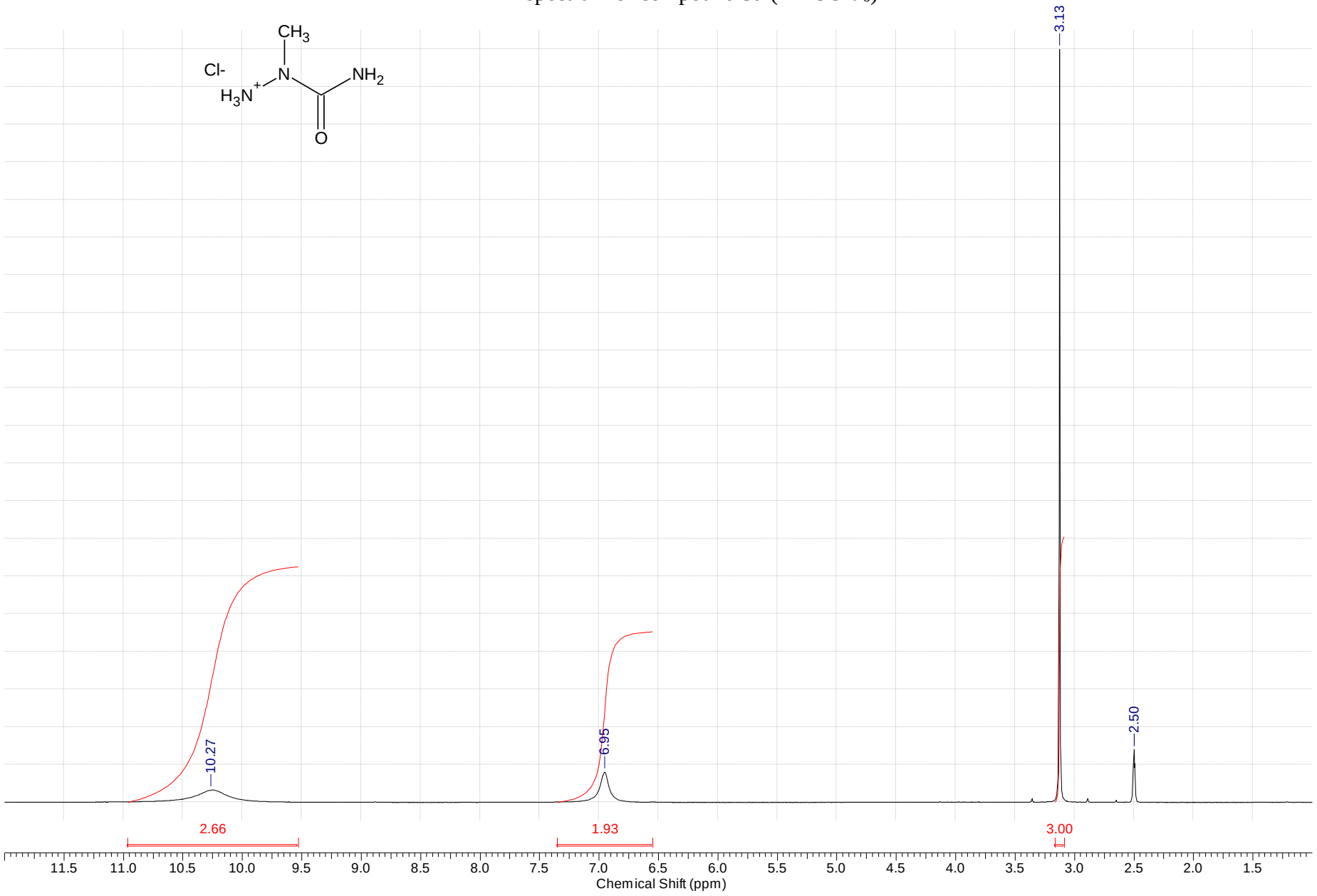
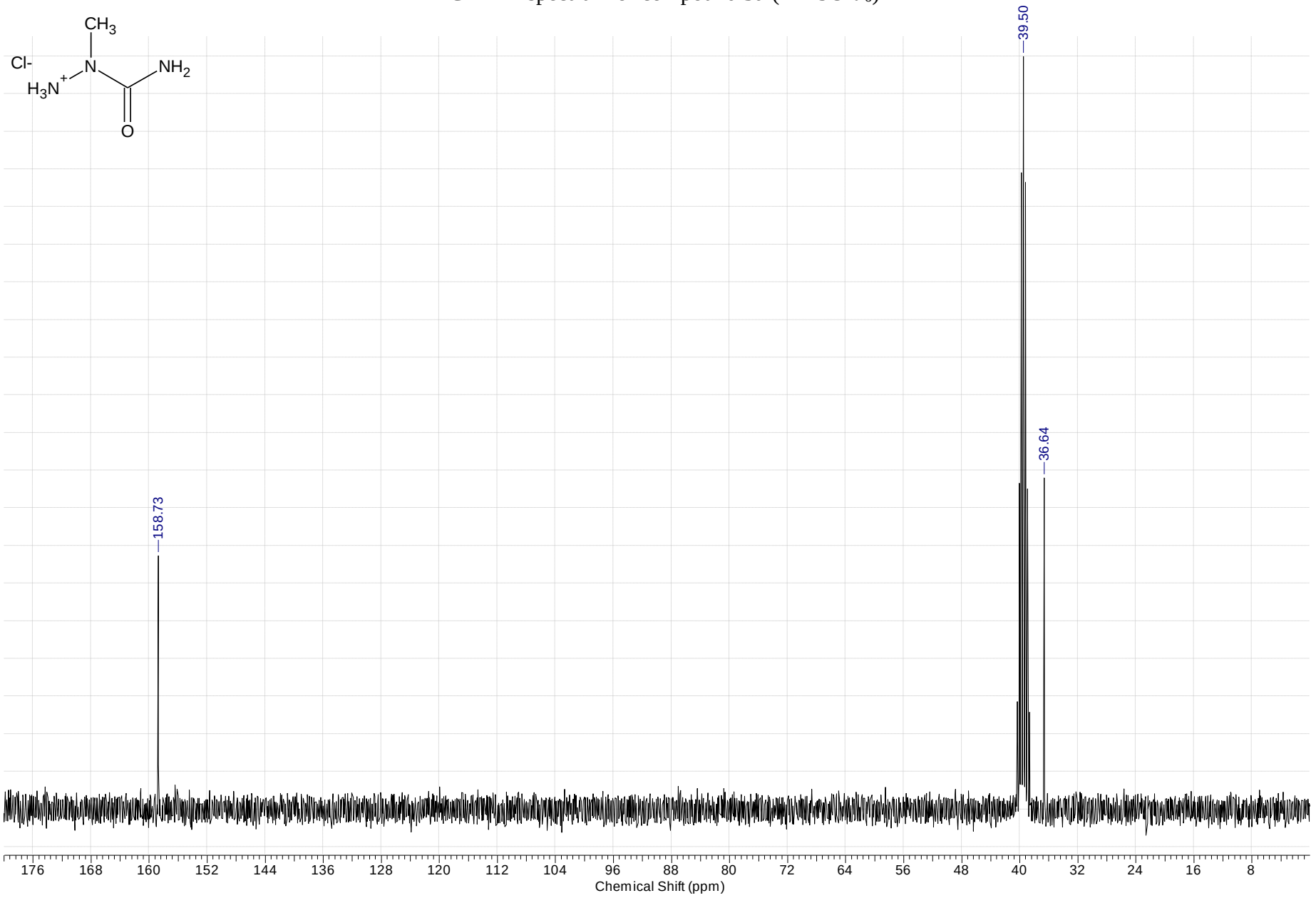


^{13}C NMR spectrum of compound **5a** (DMSO-d_6)



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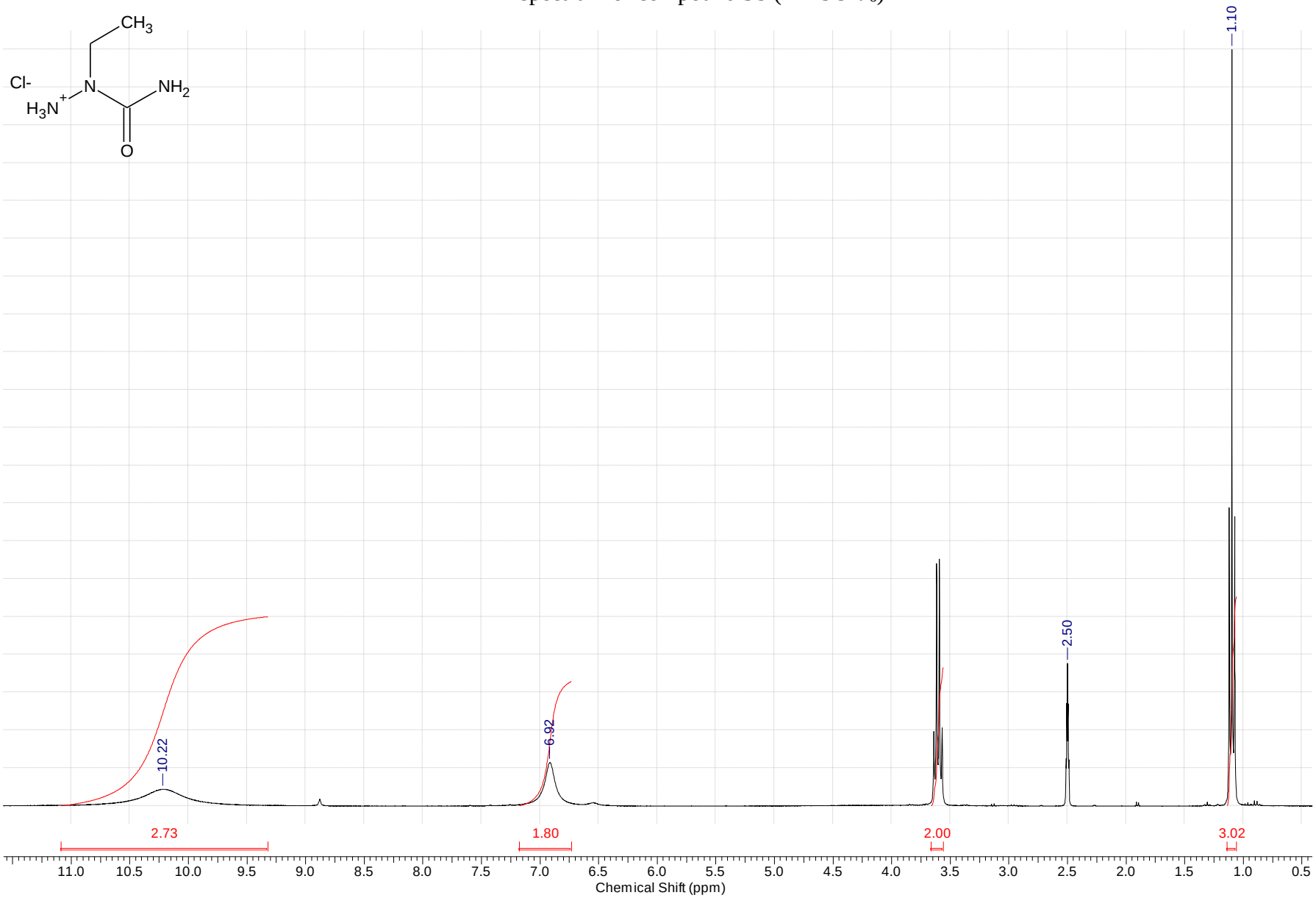

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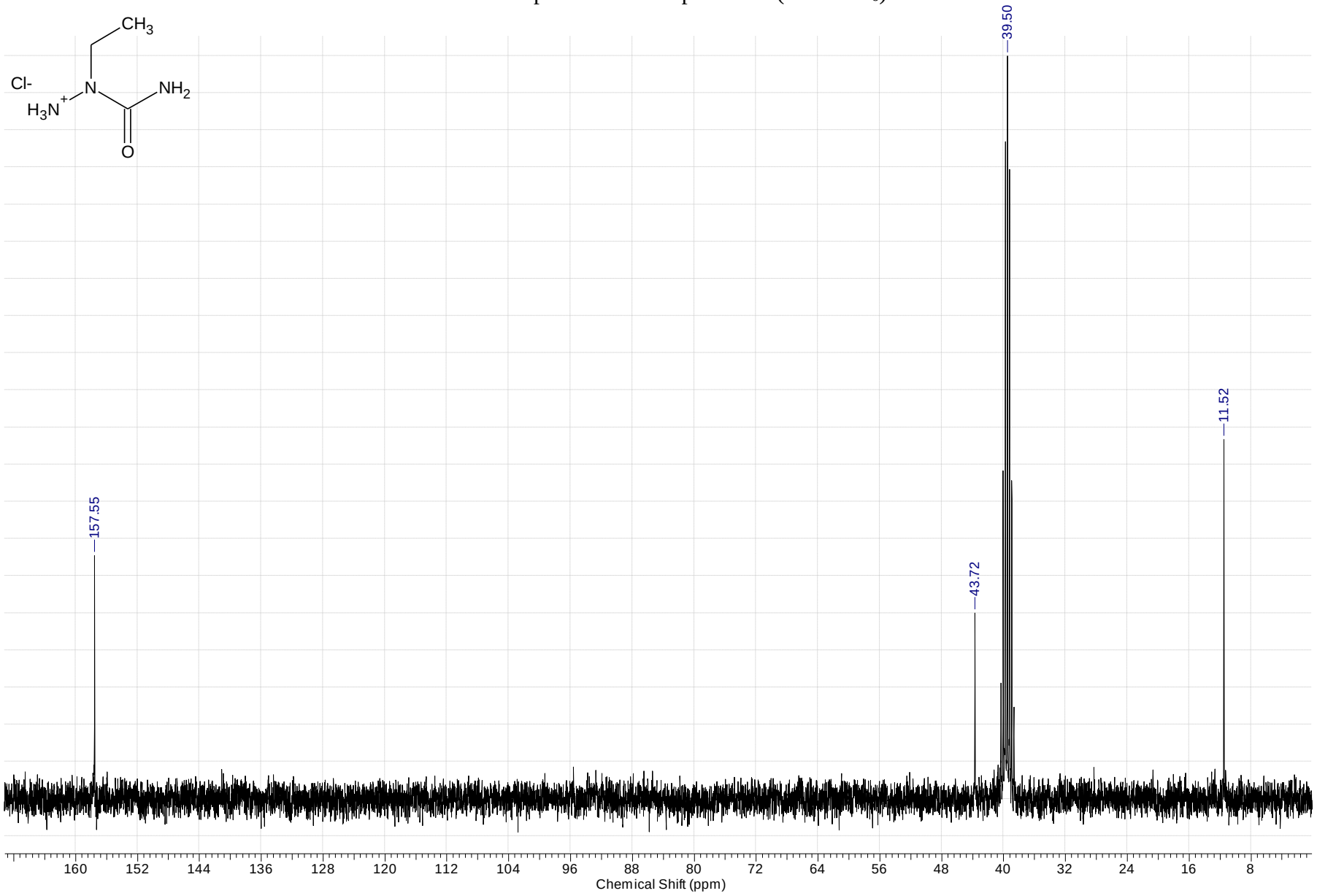

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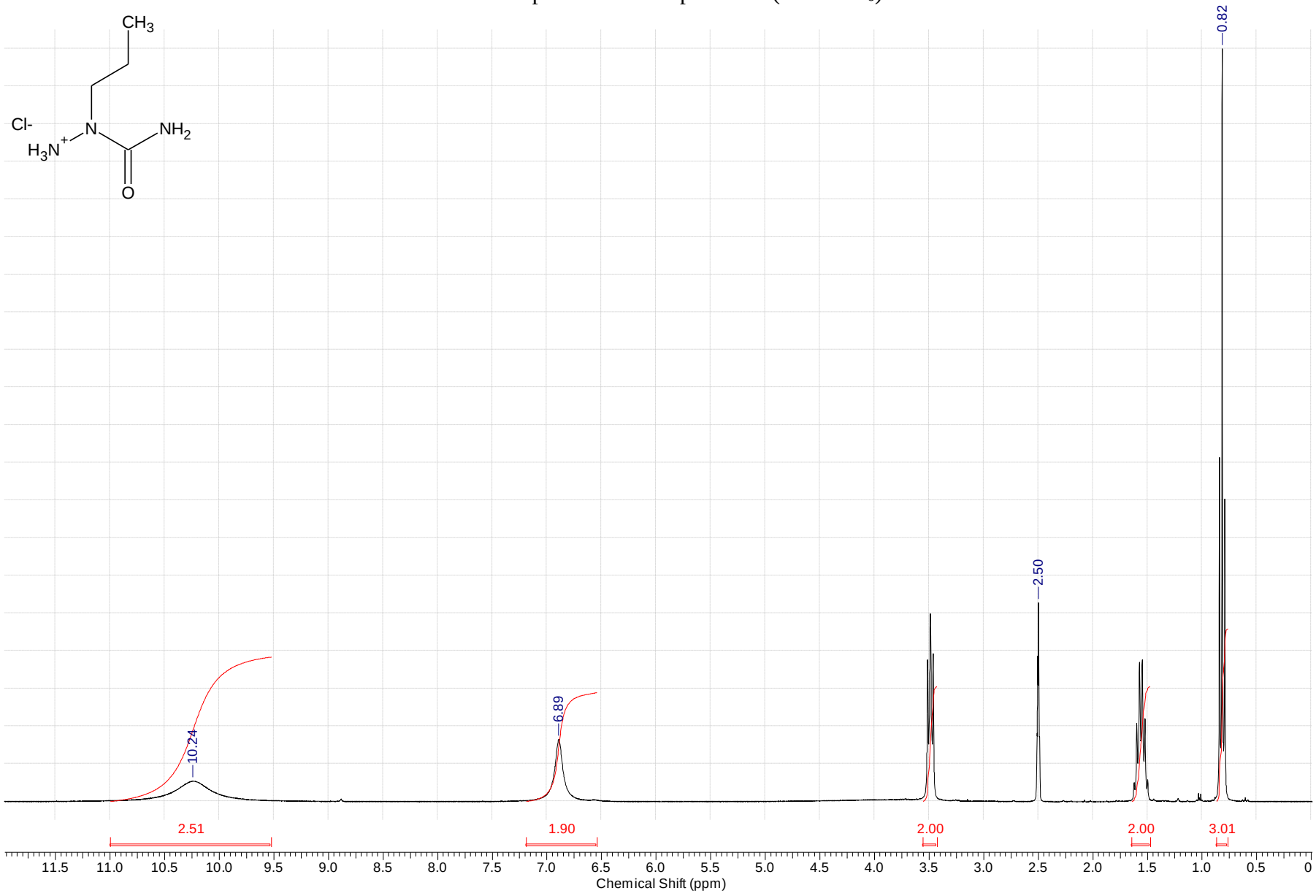

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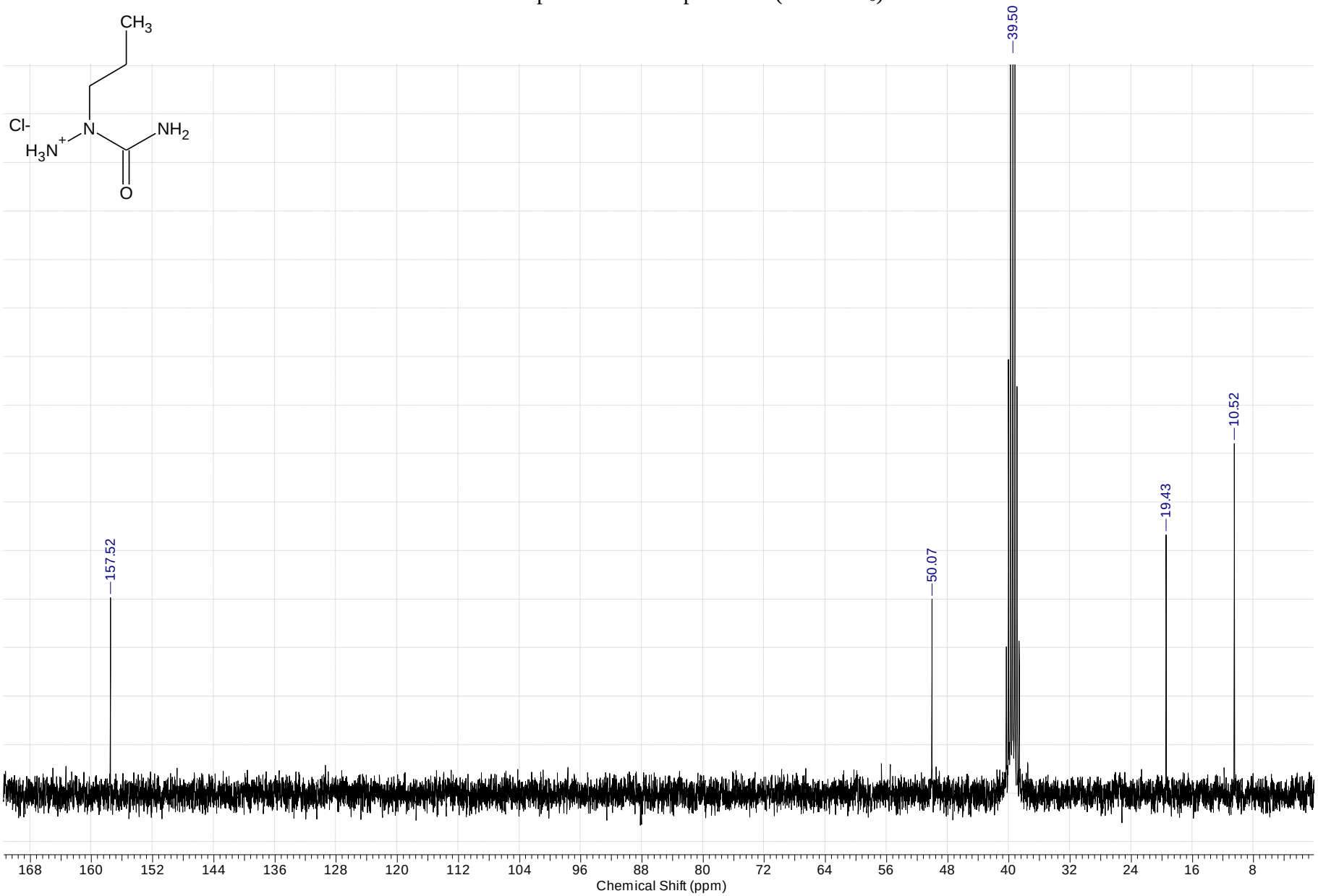

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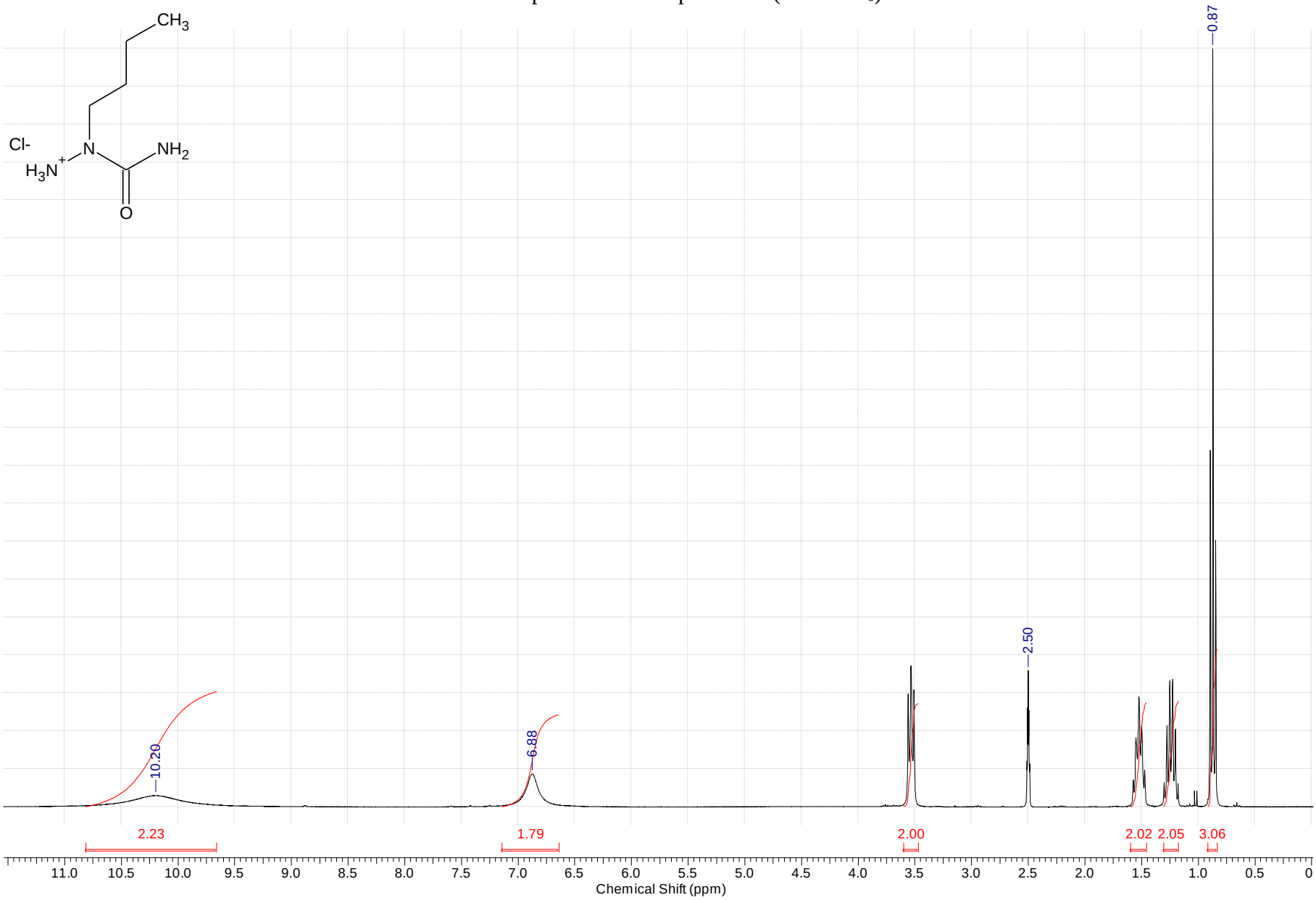

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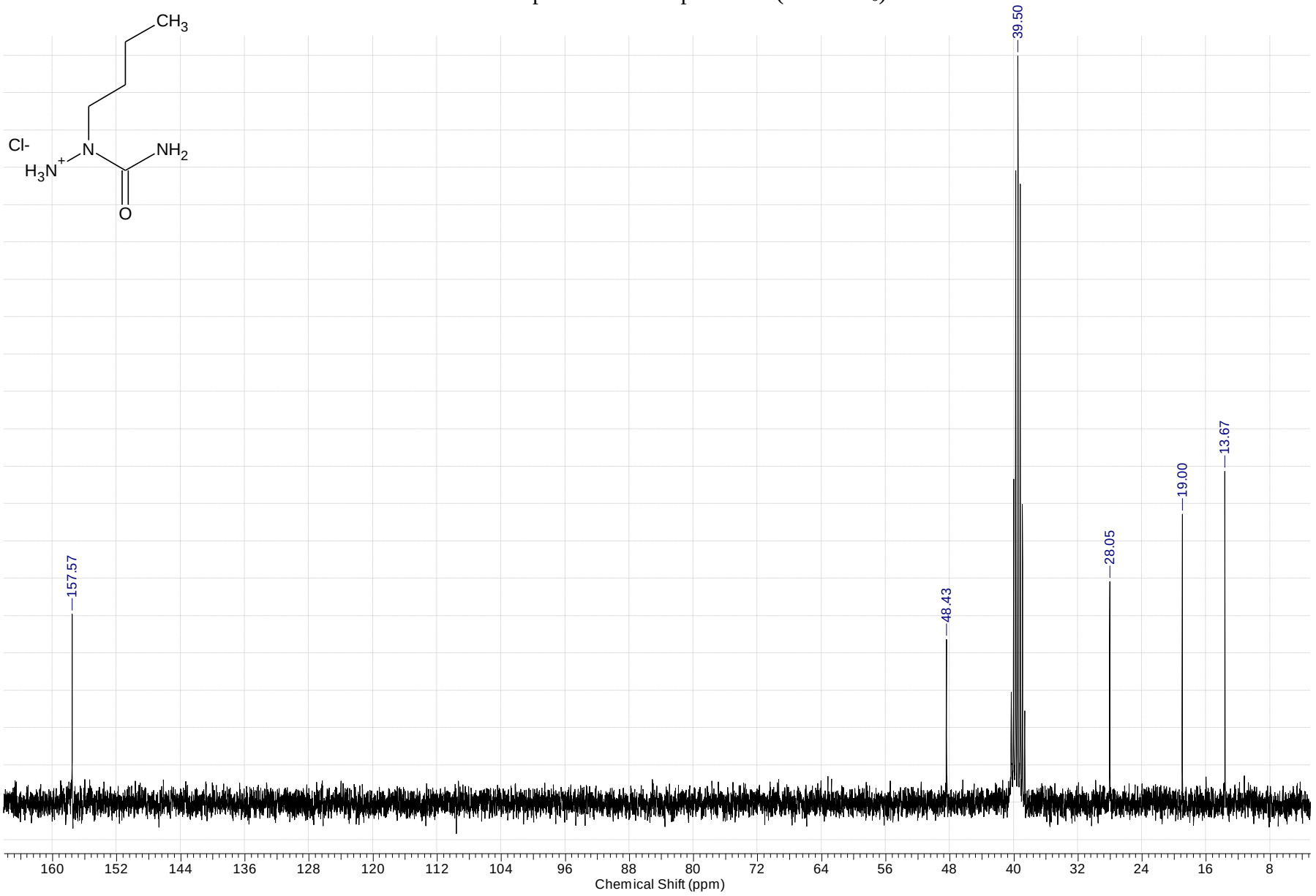

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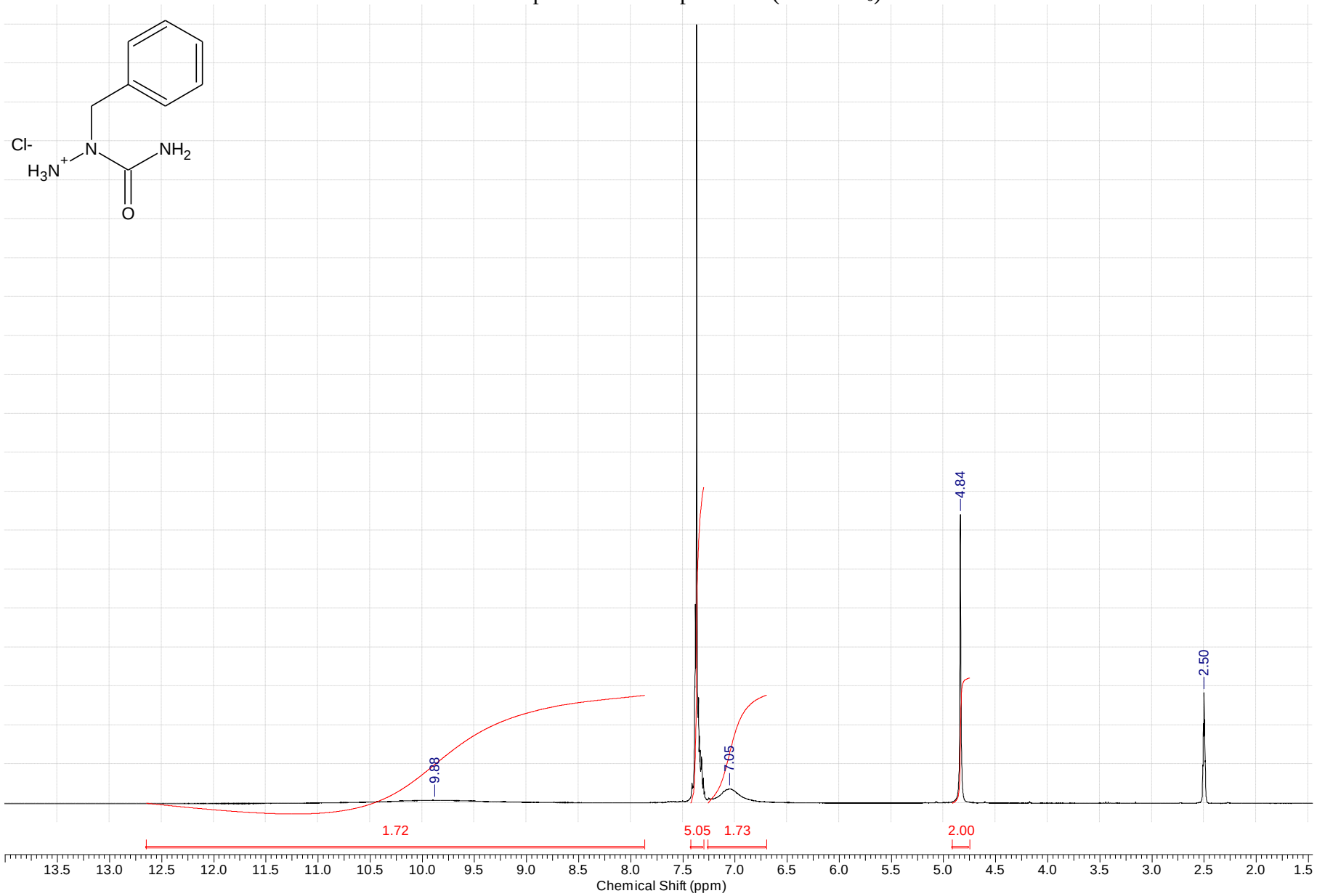

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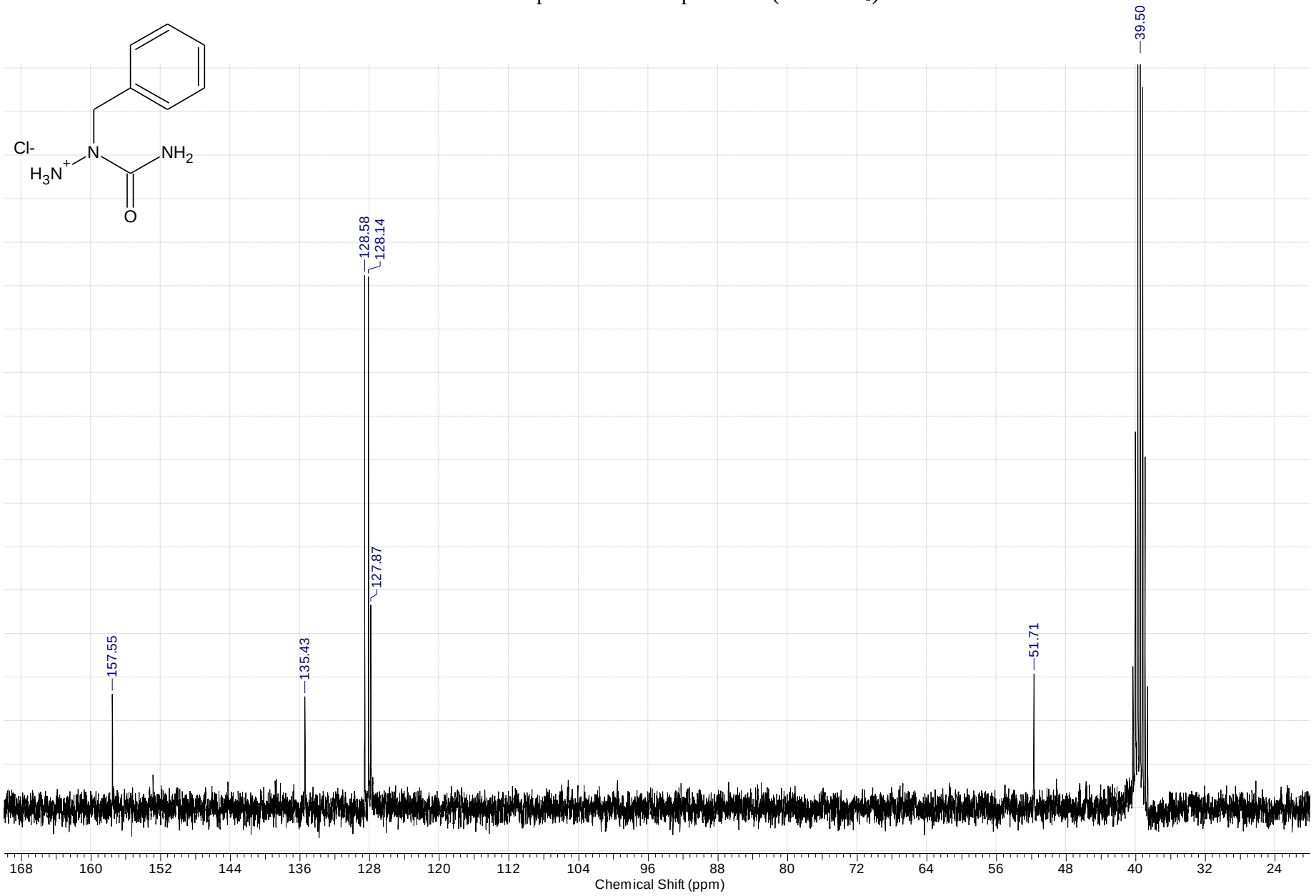

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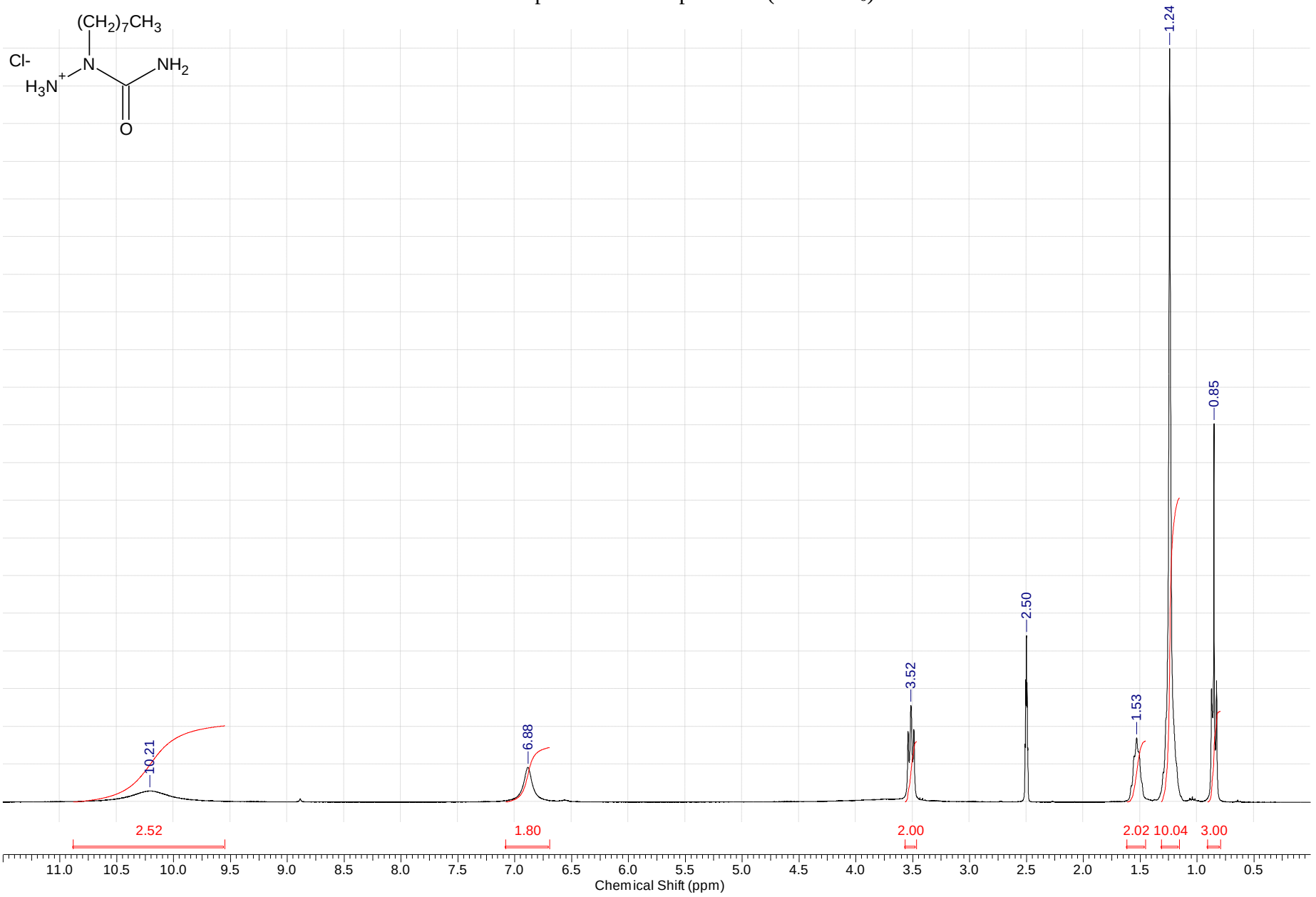

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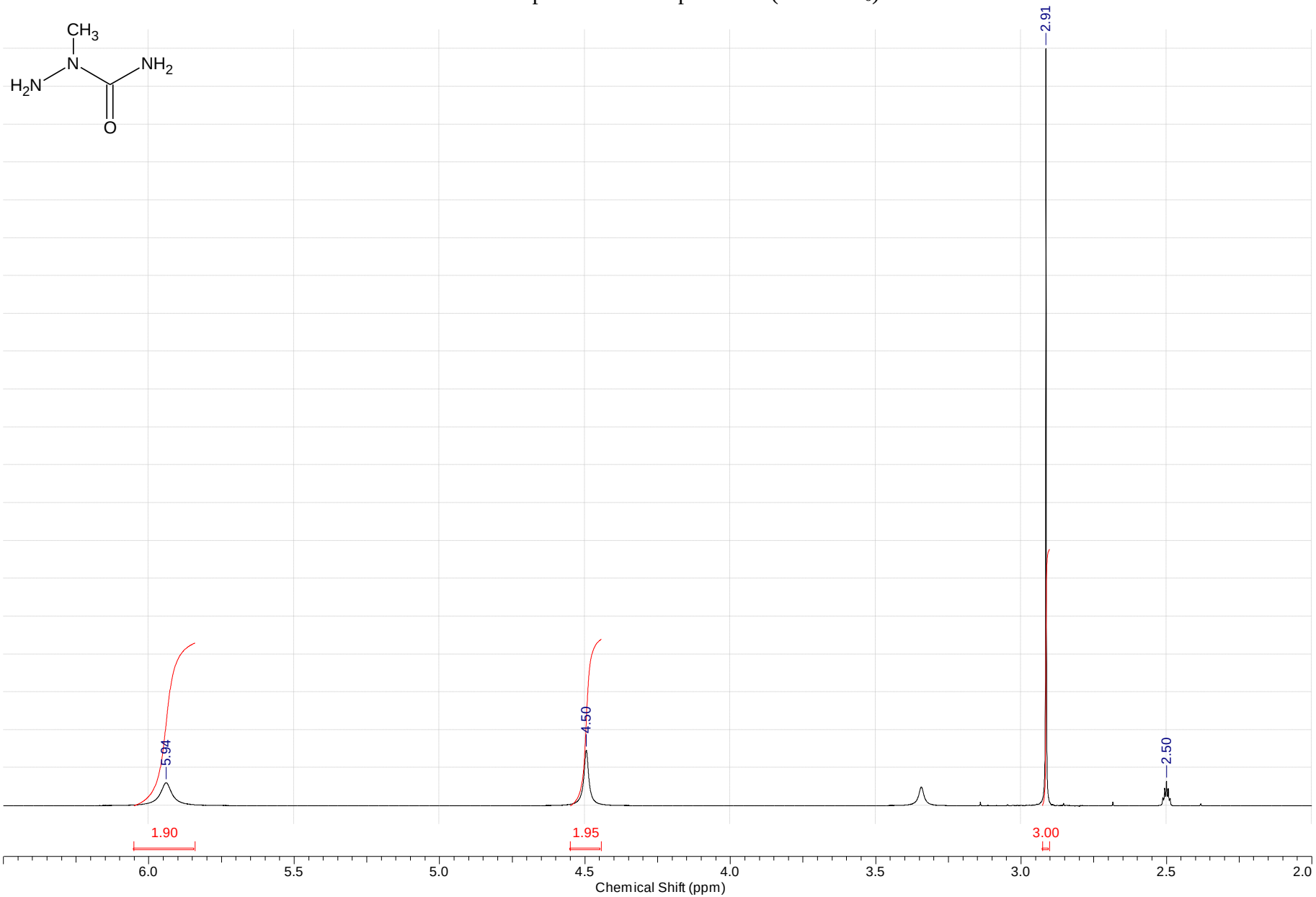

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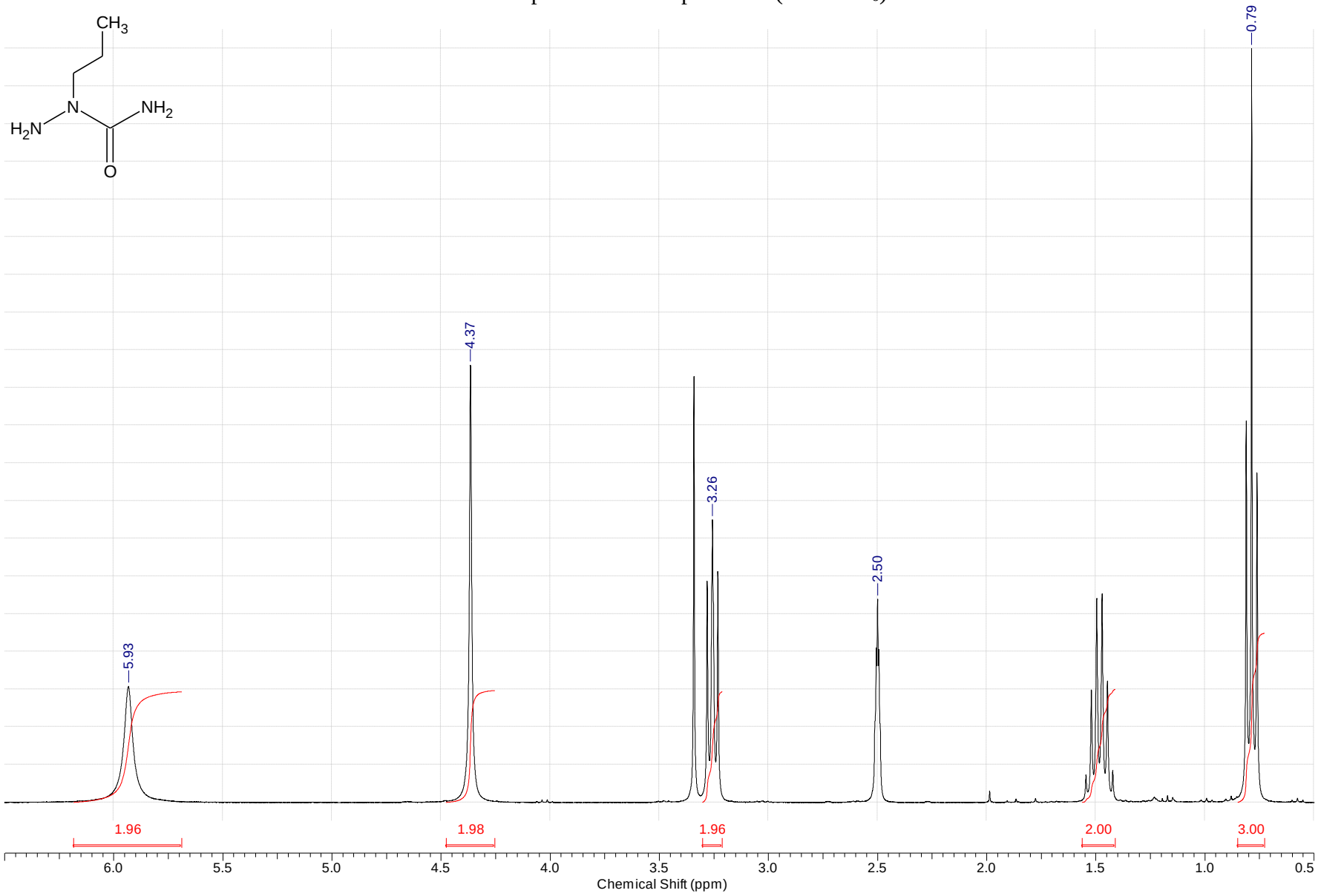

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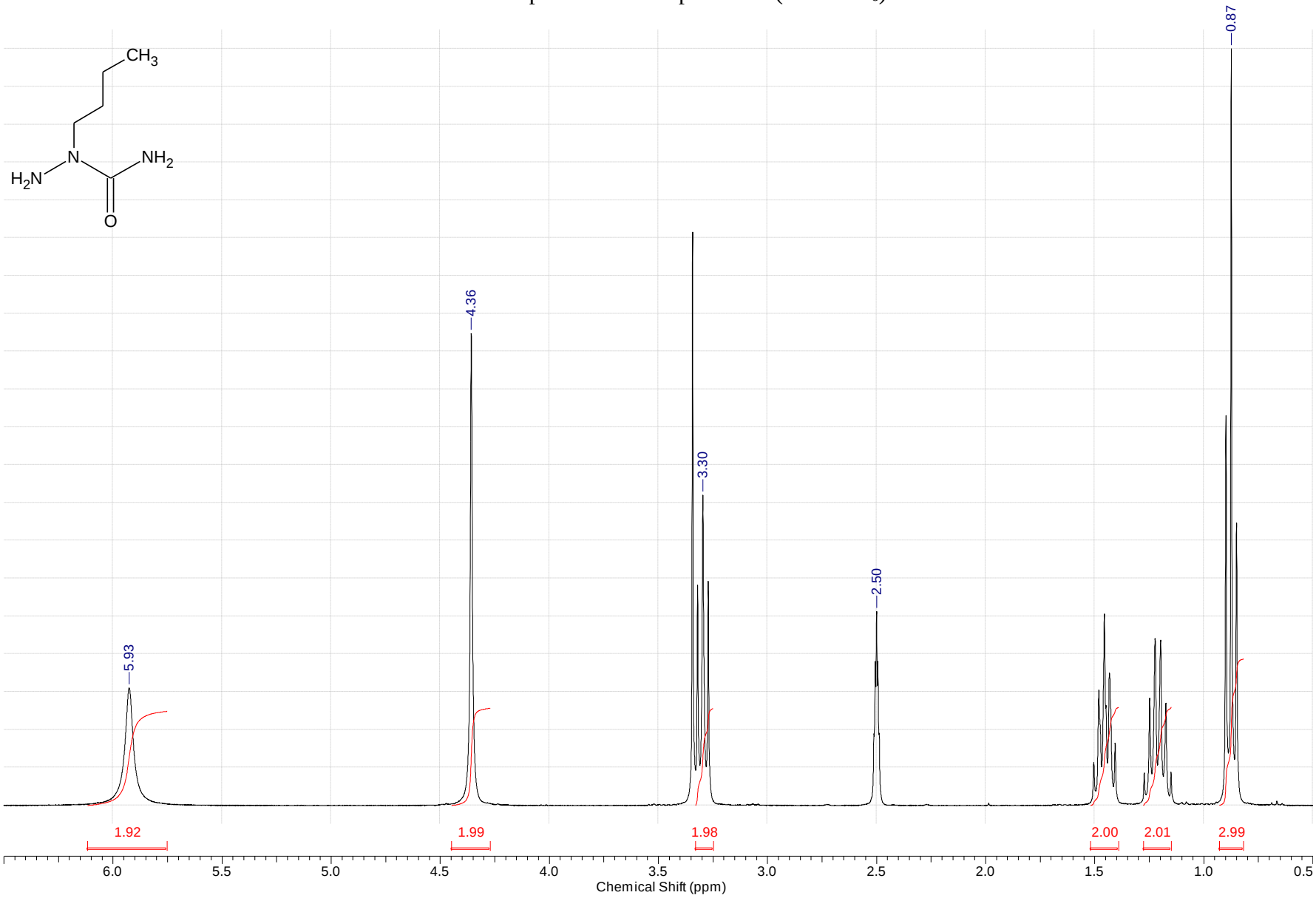

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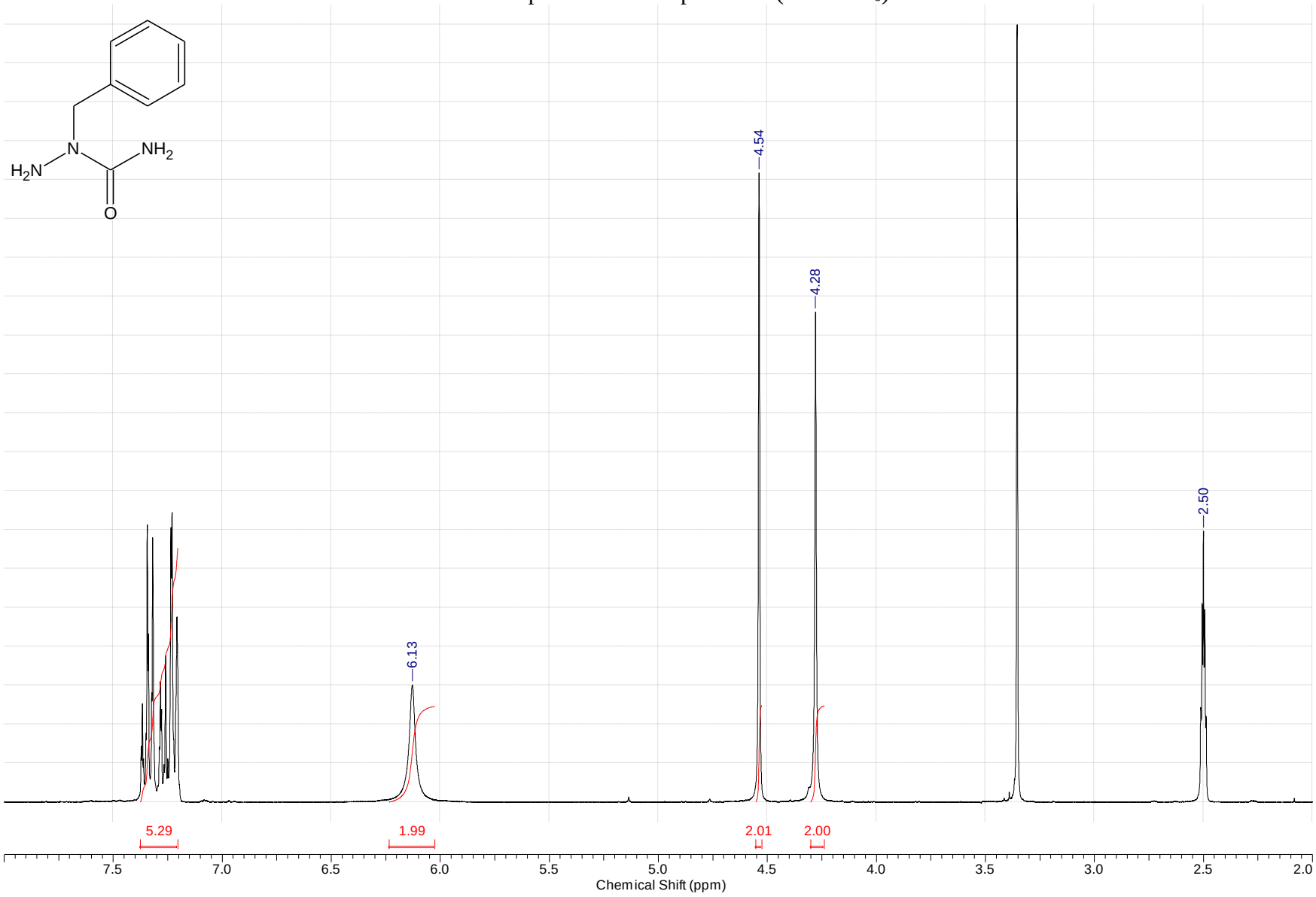

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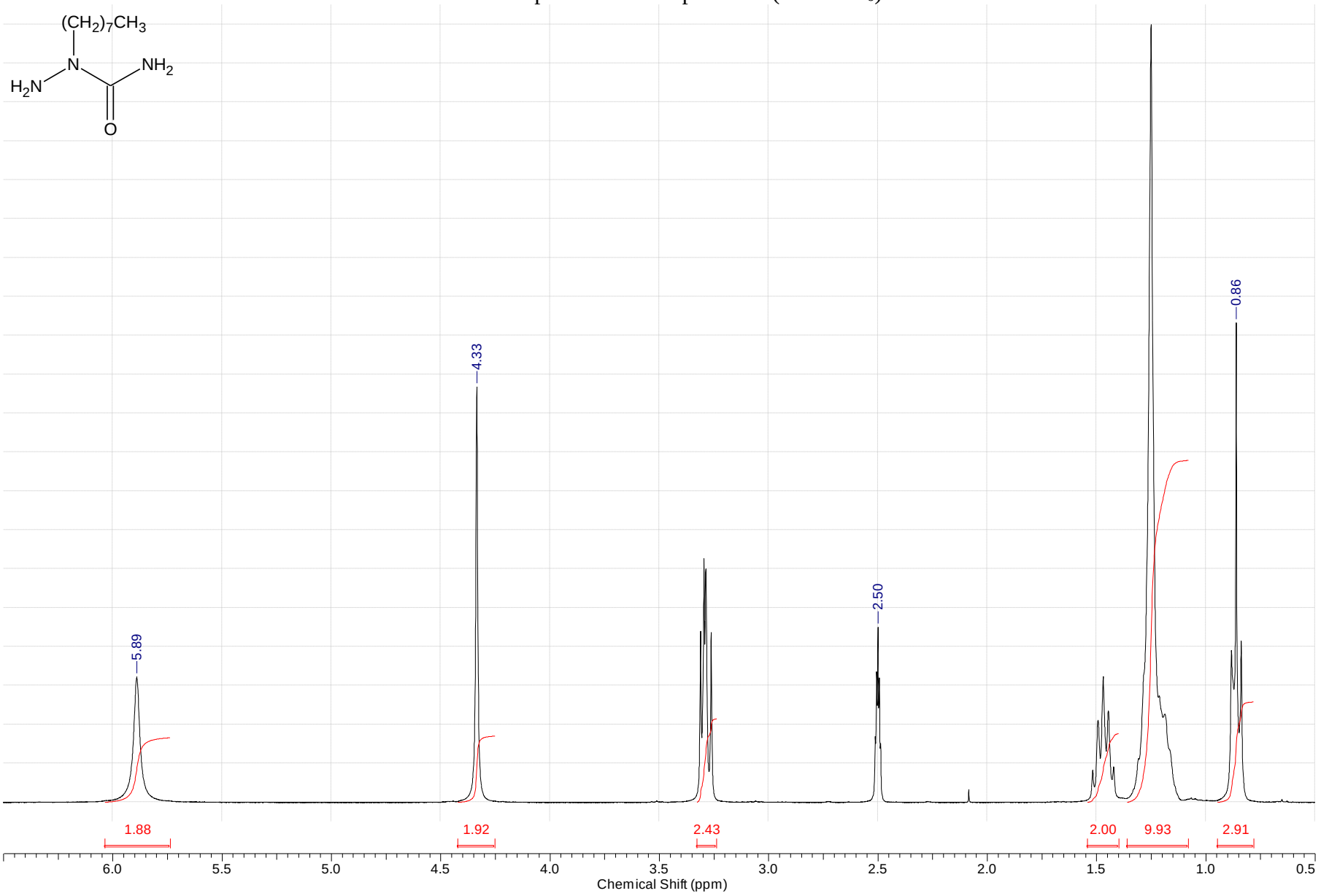

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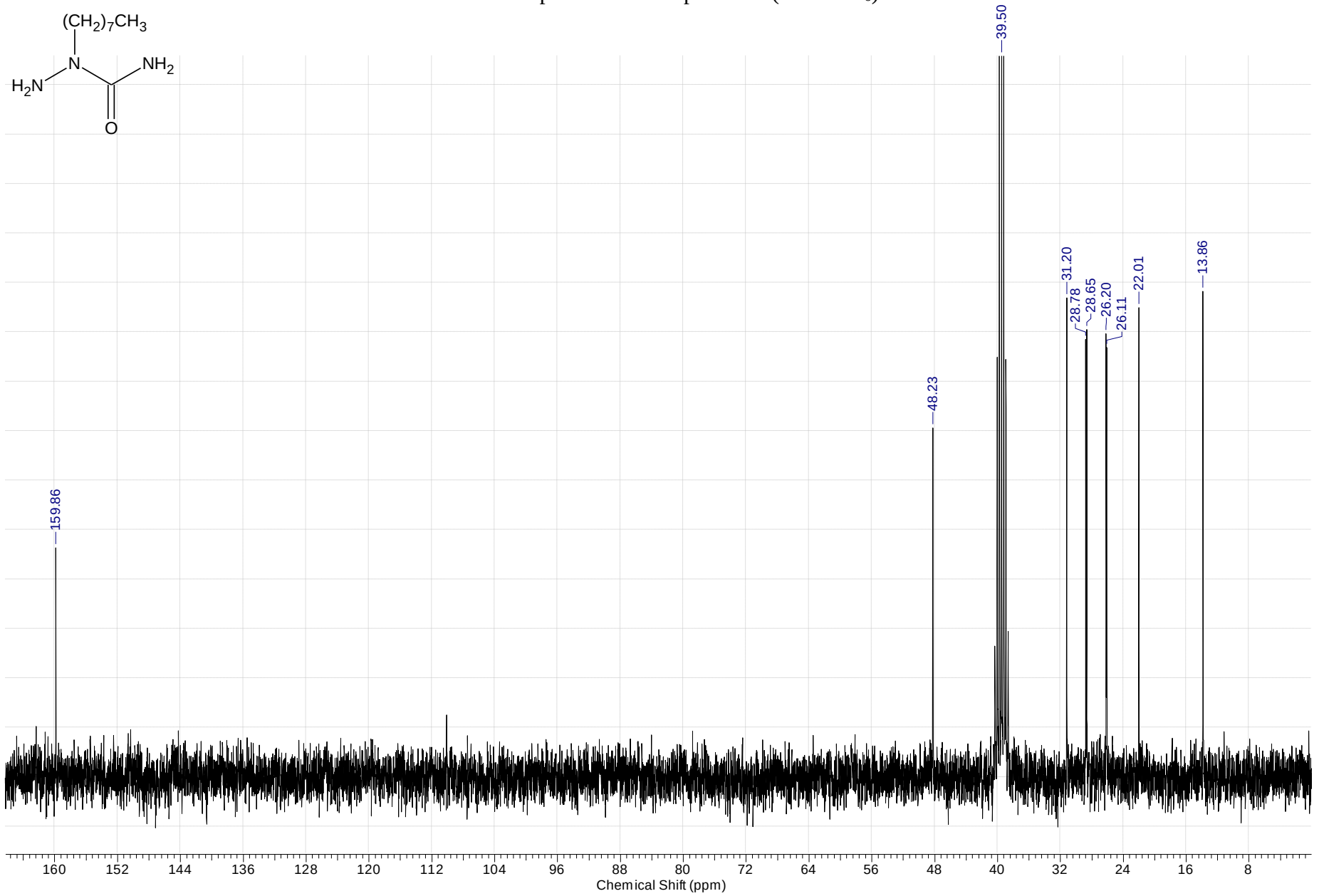

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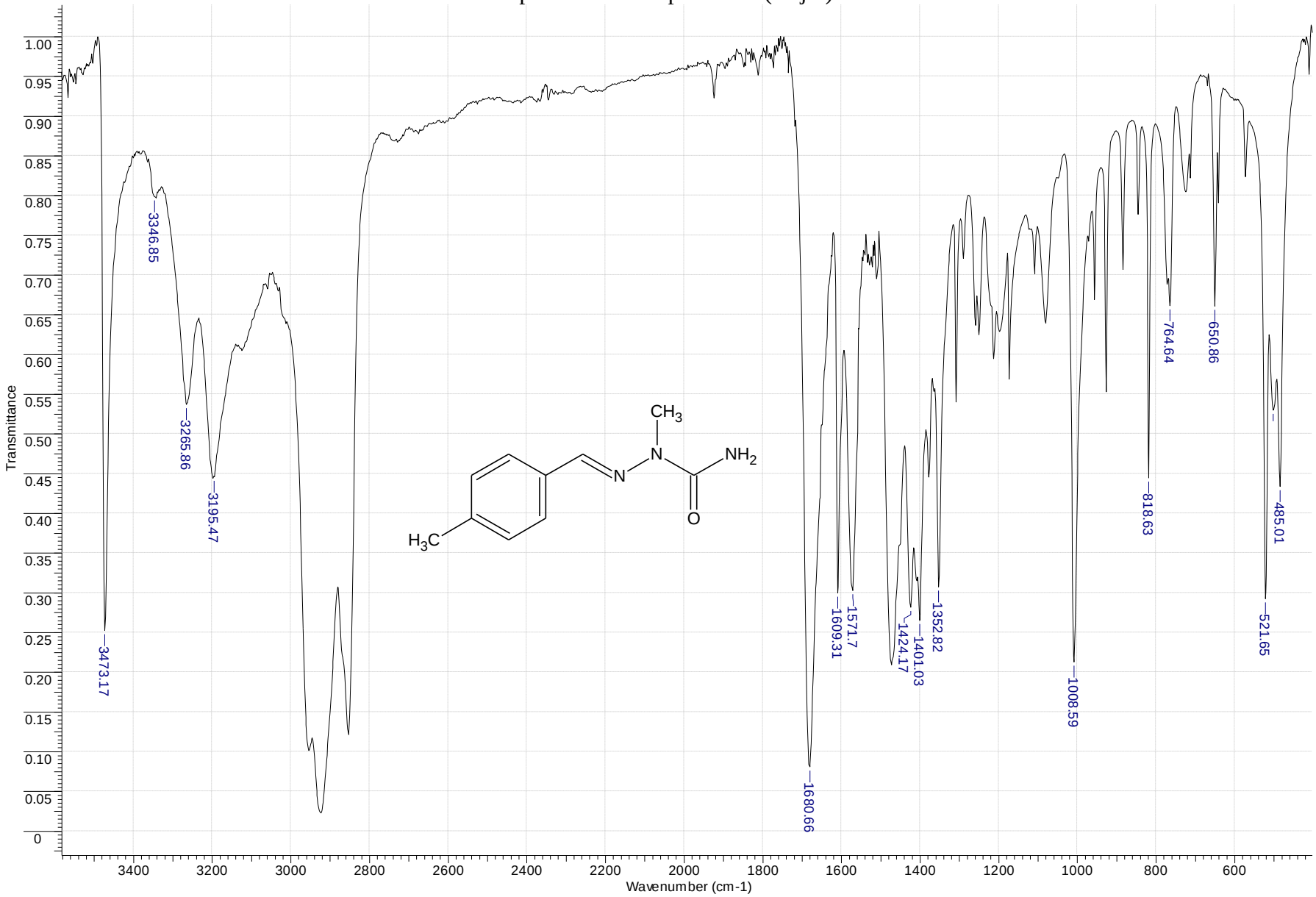

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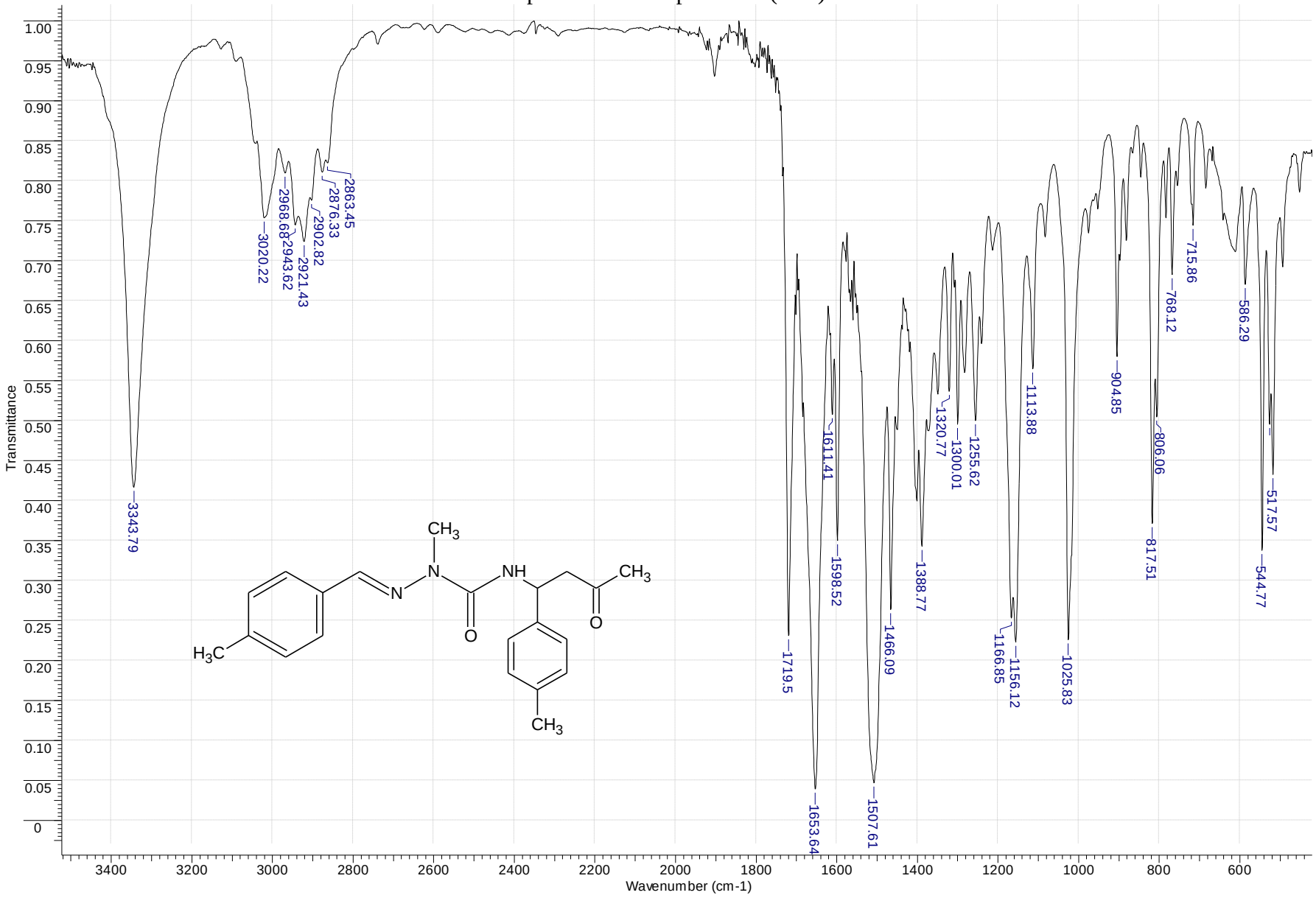
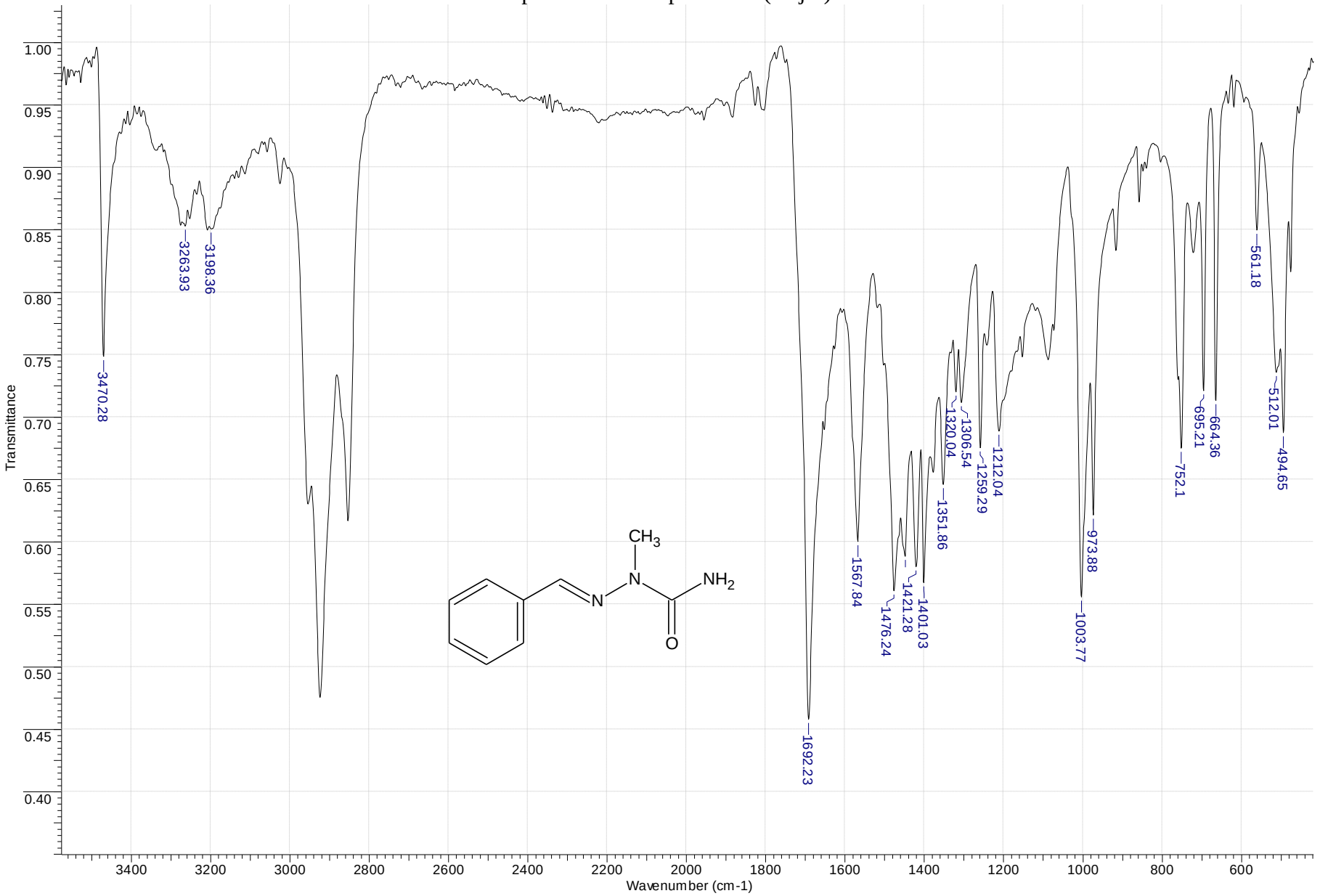


IR spectrum of compound **2d** (Nujol)



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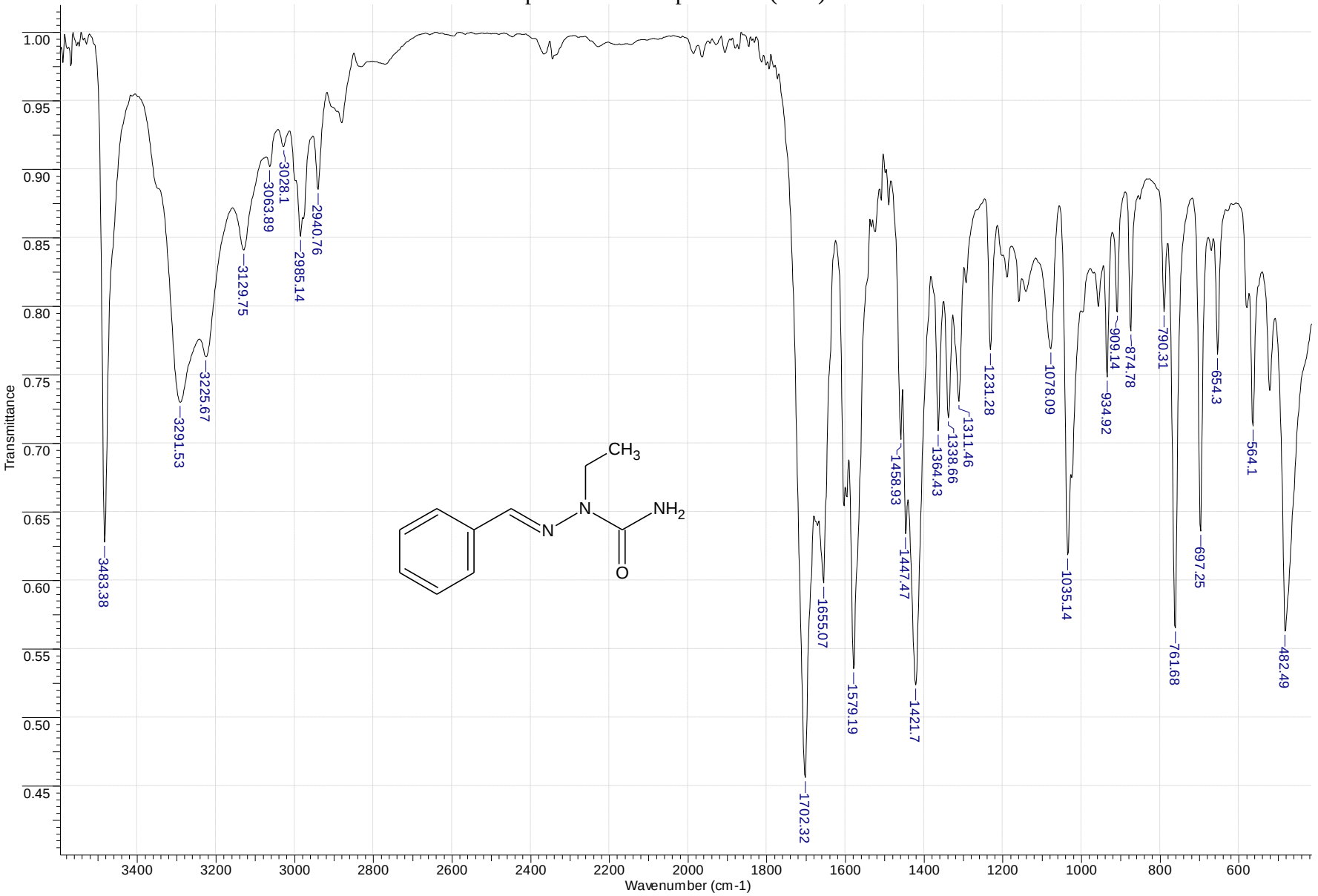

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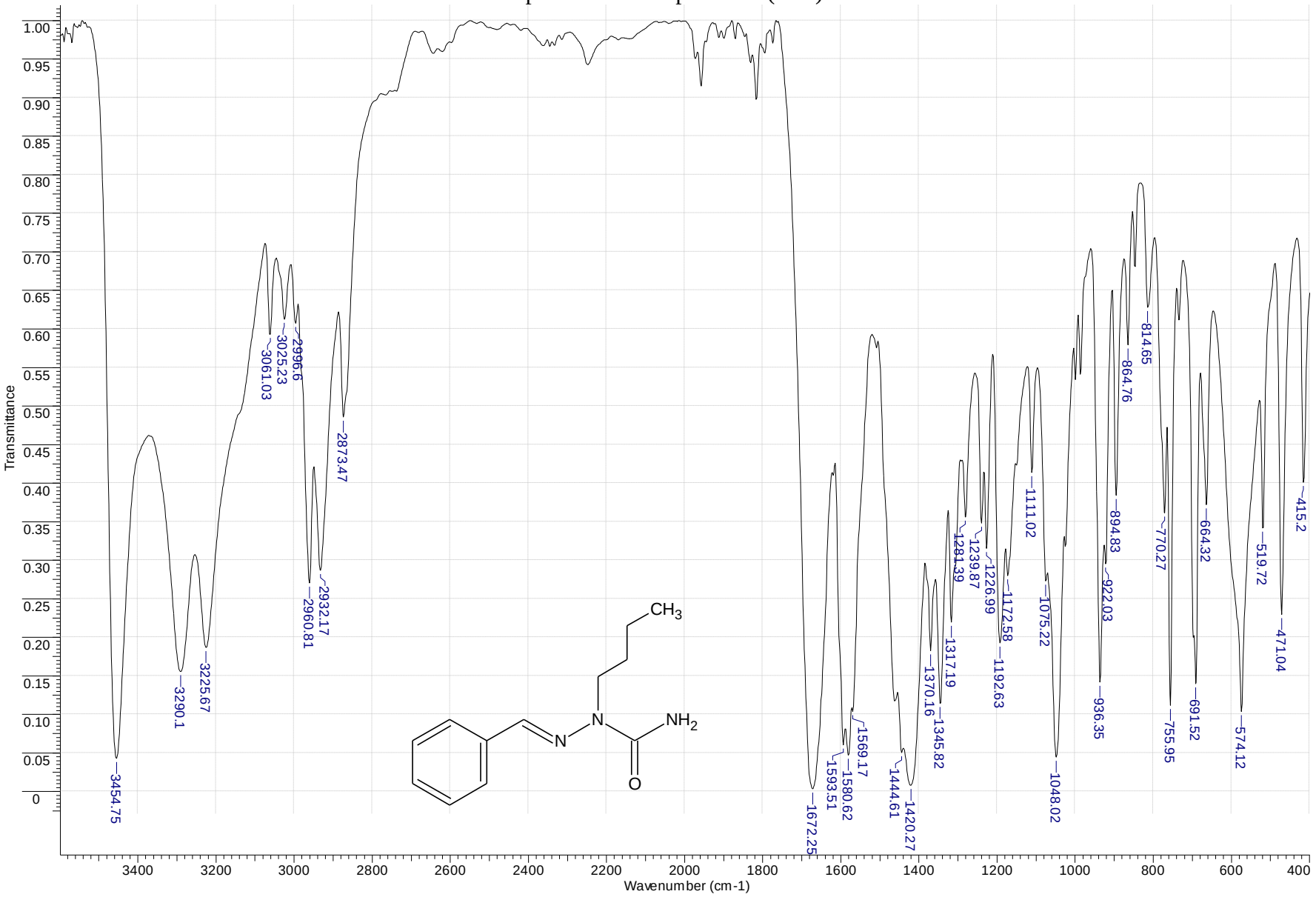

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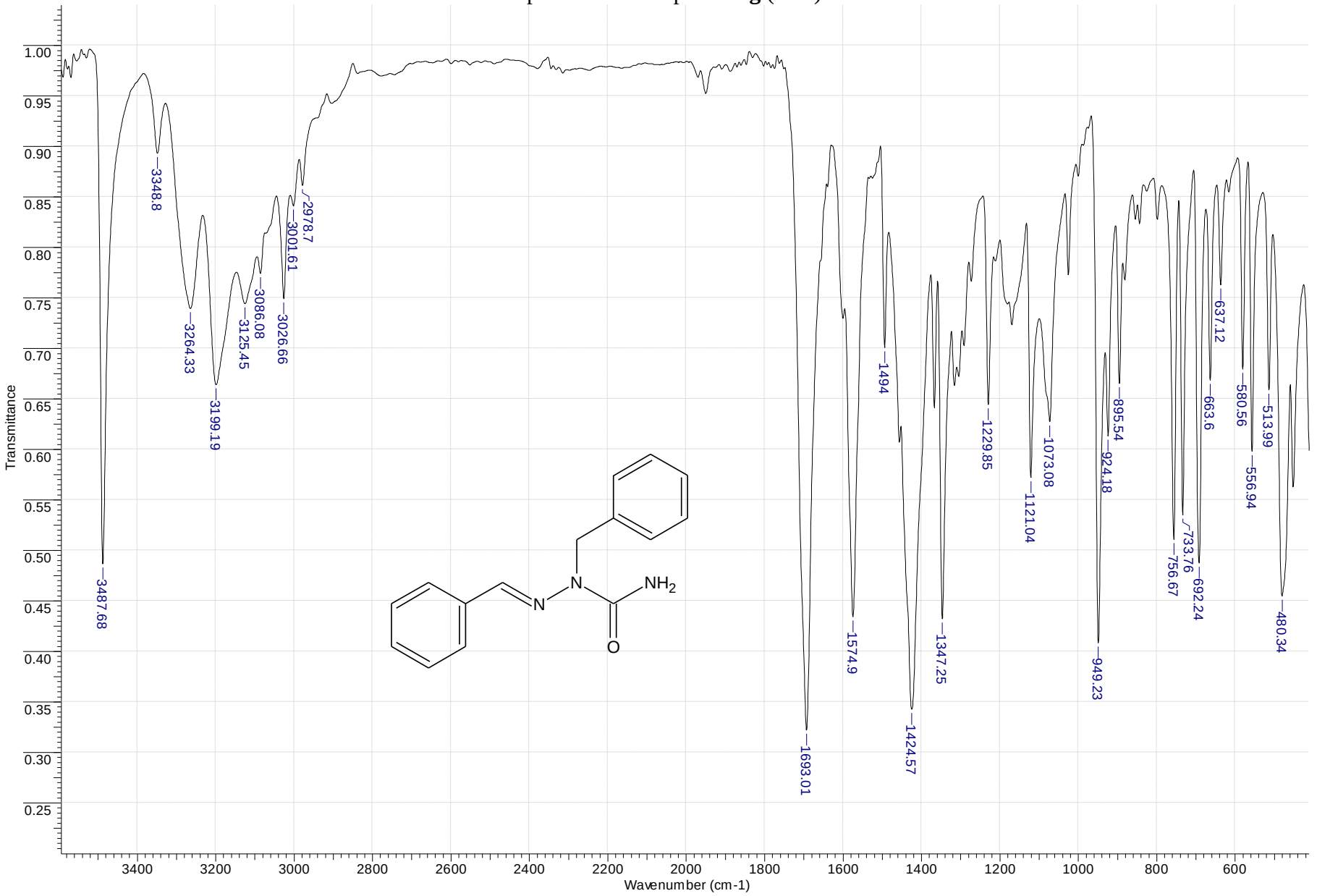

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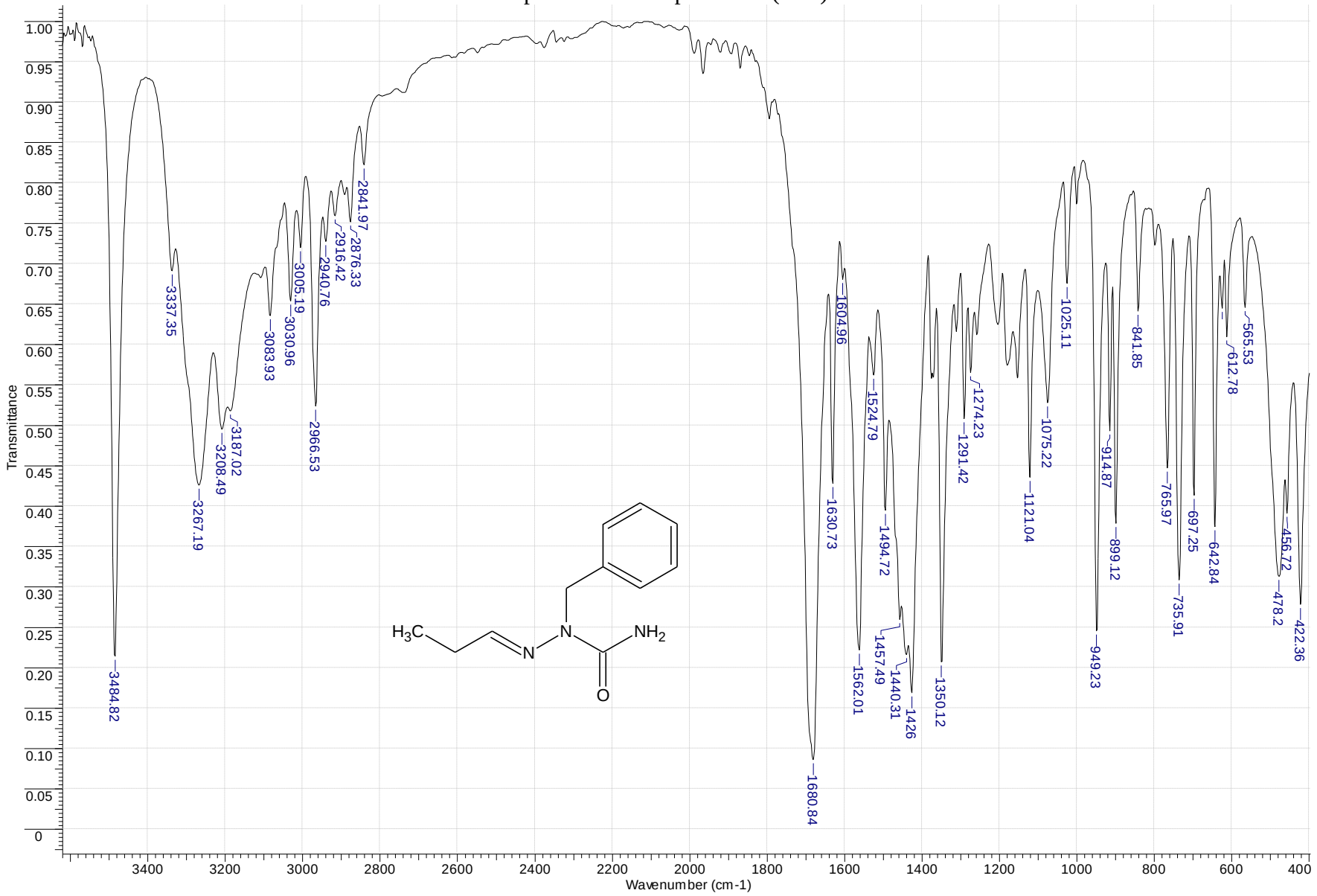
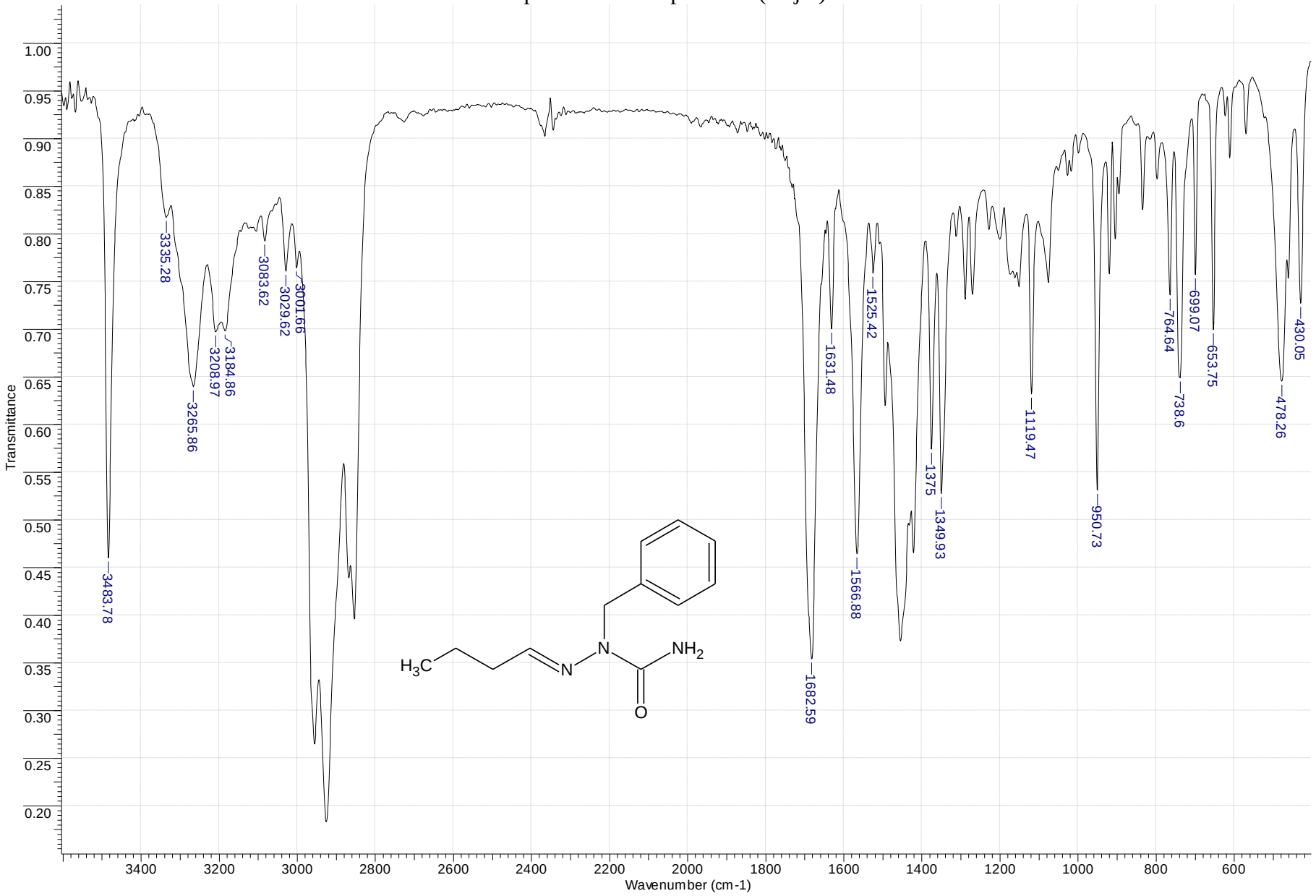


IR spectrum of compound **2i** (Nujol)



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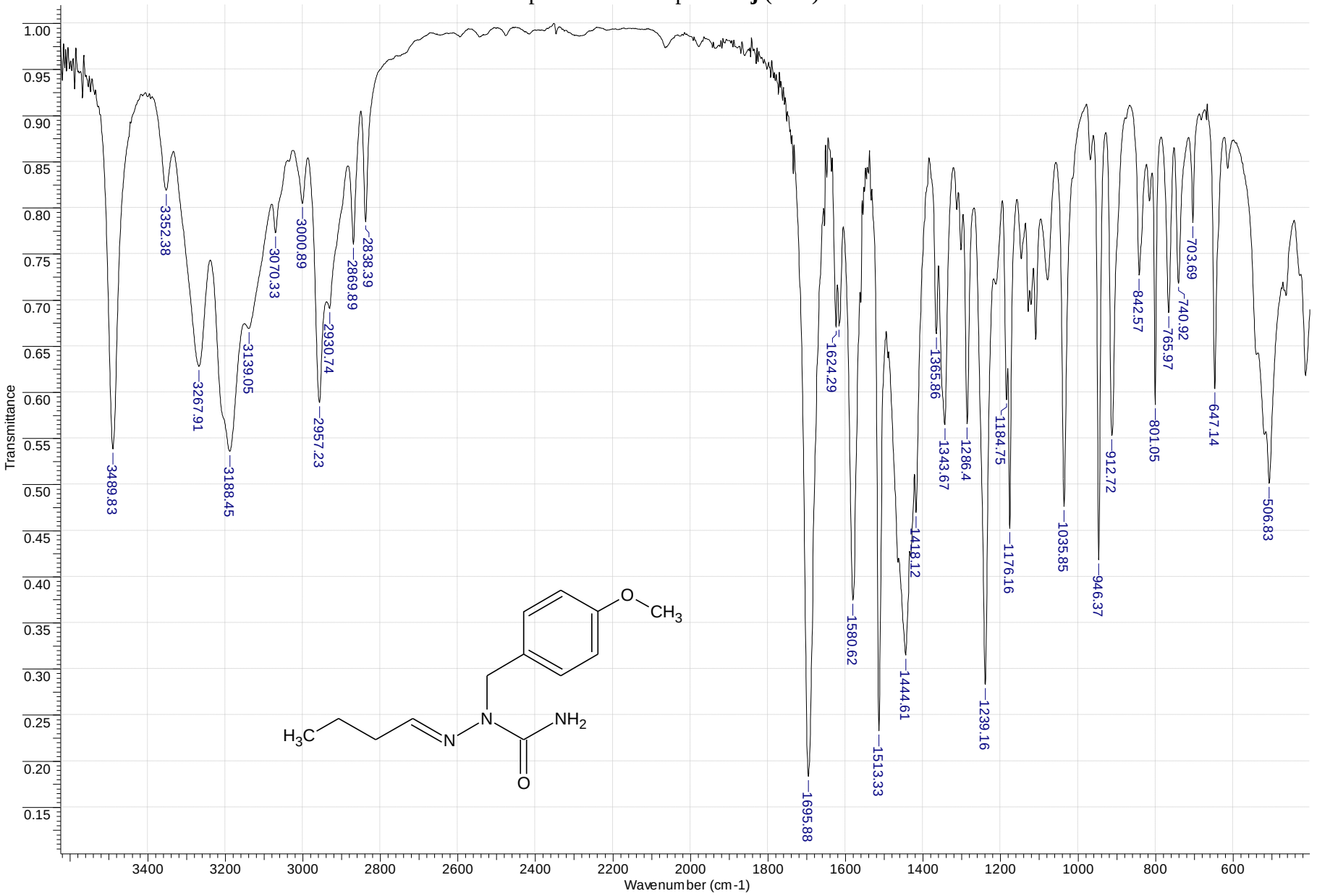

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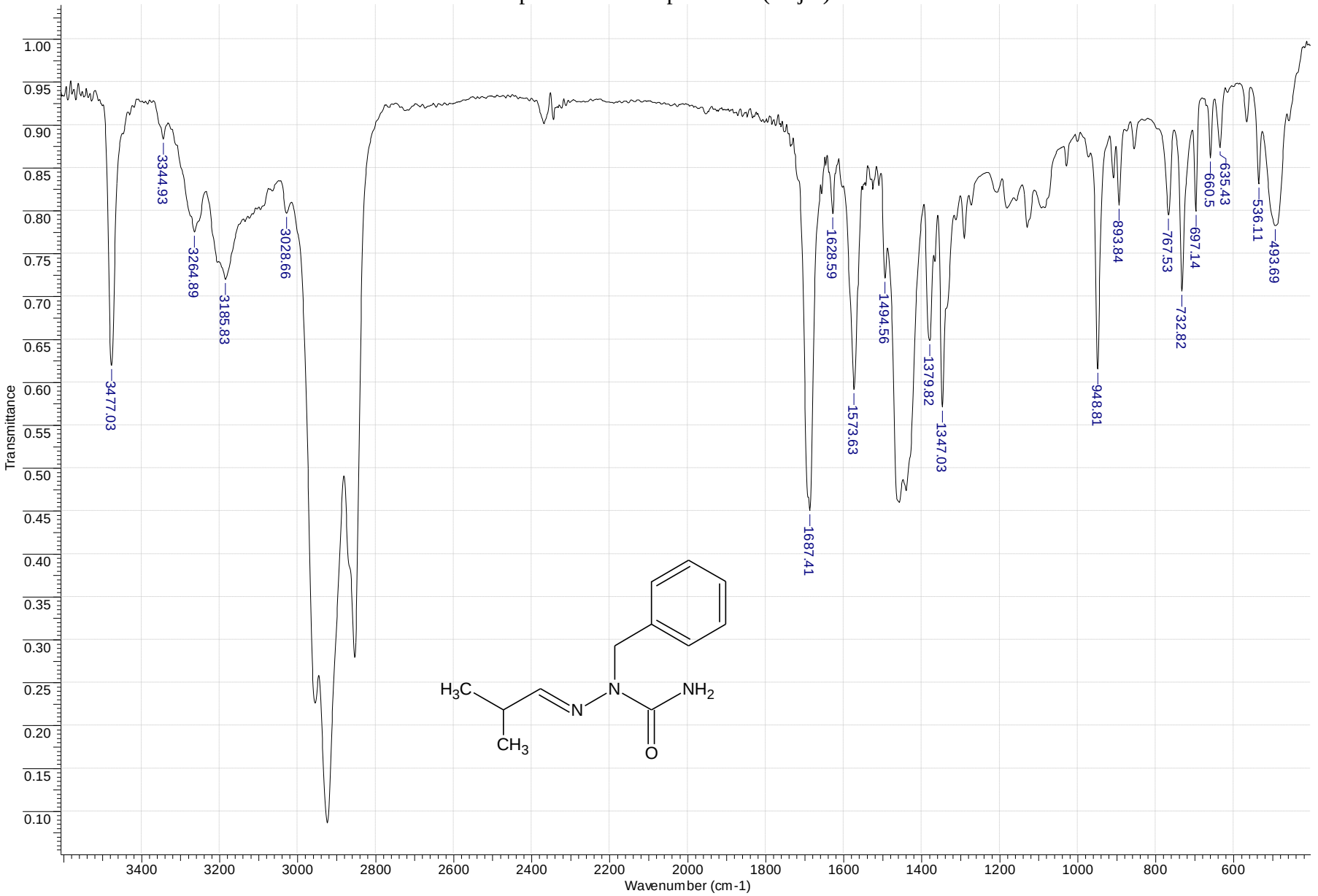
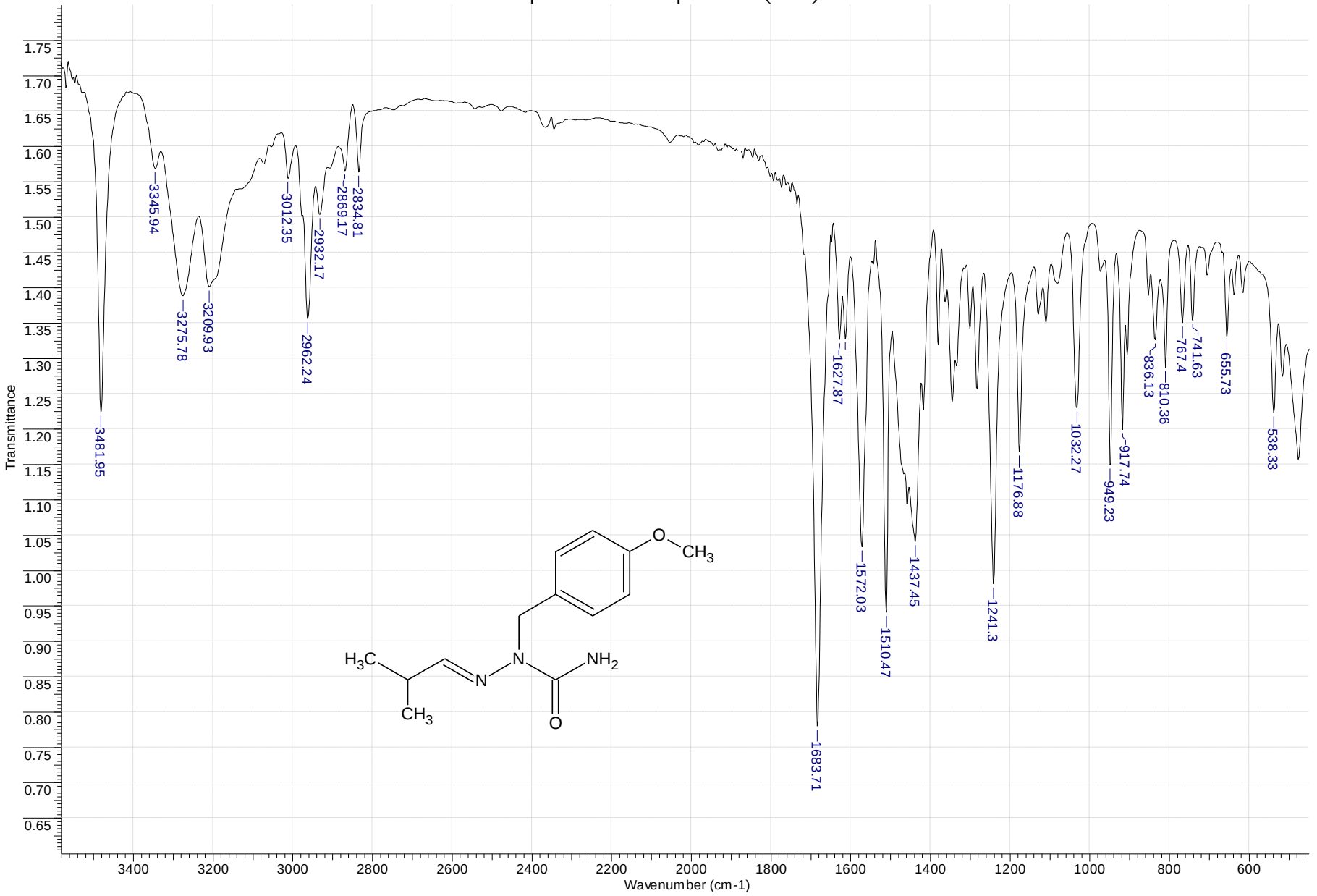
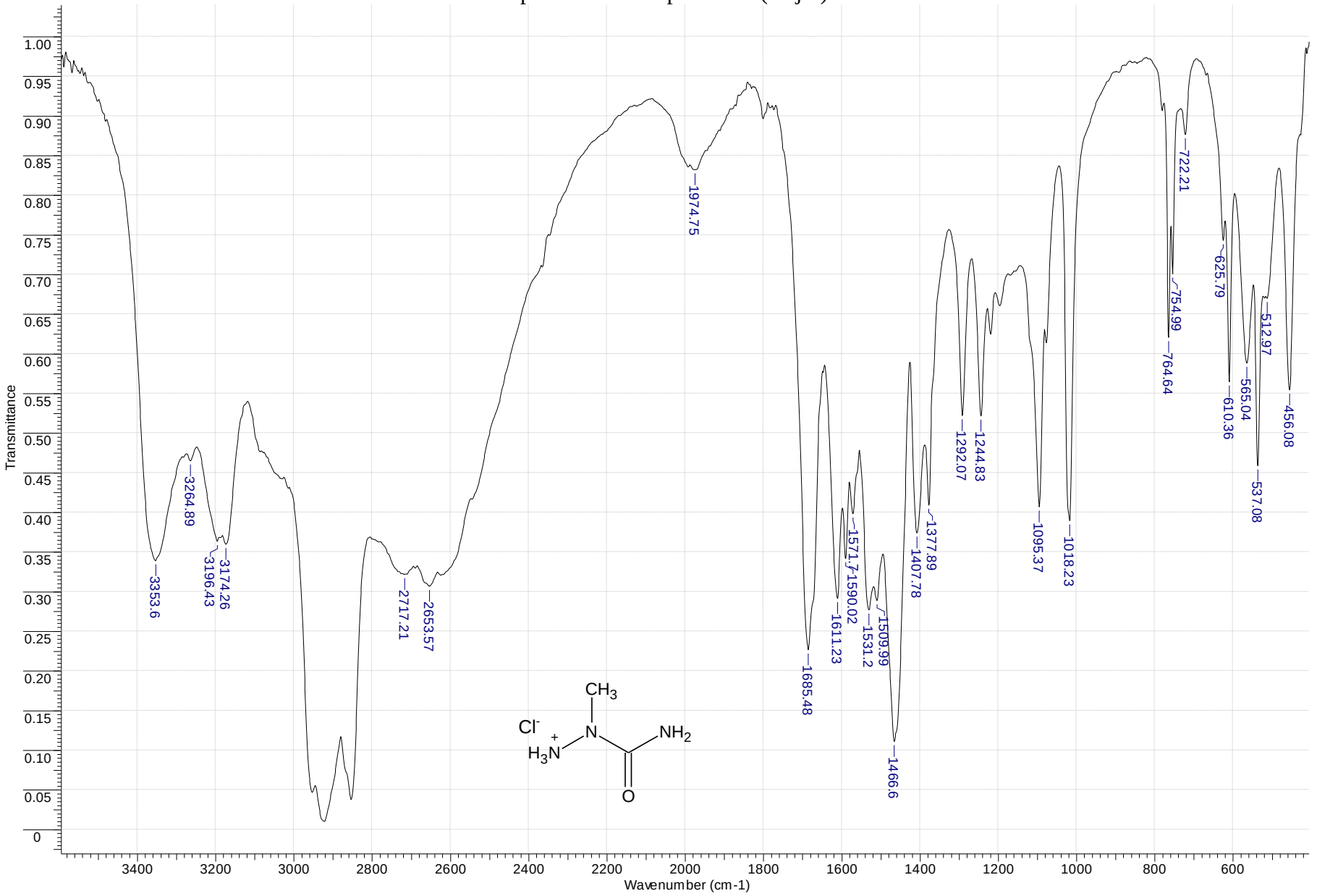


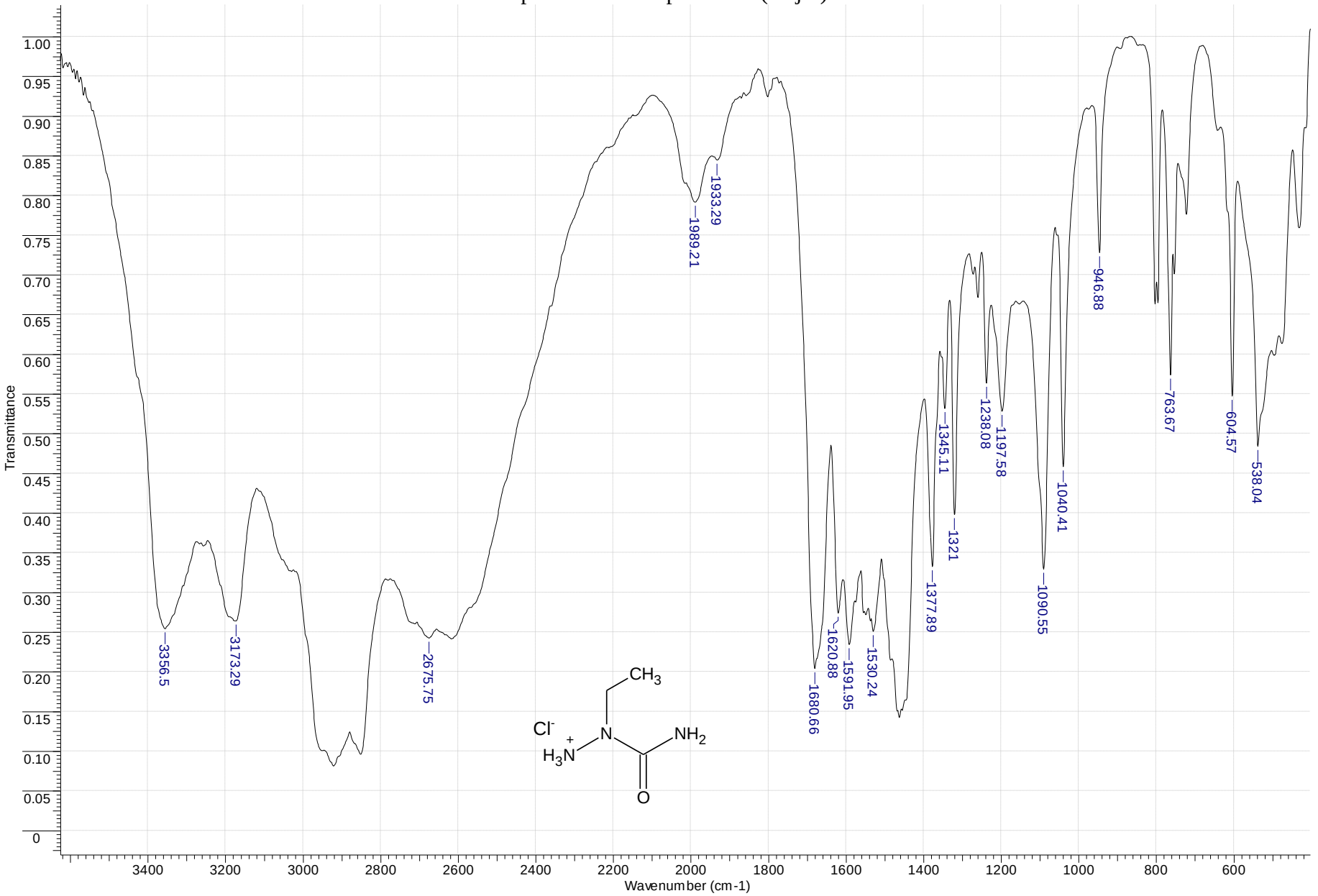
IR spectrum of compound **2l** (KBr)



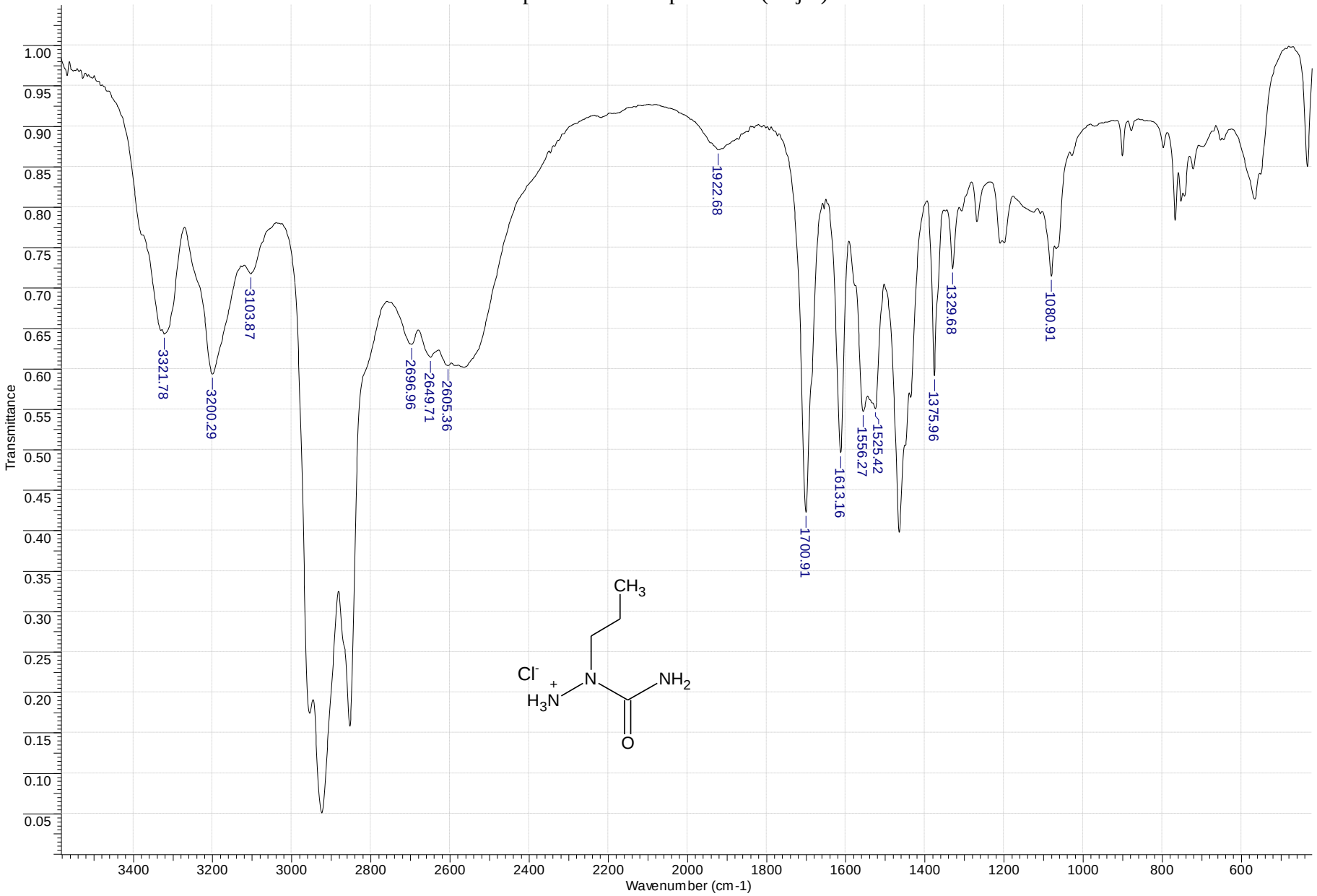
IR spectrum of compound **5a** (Nujol)



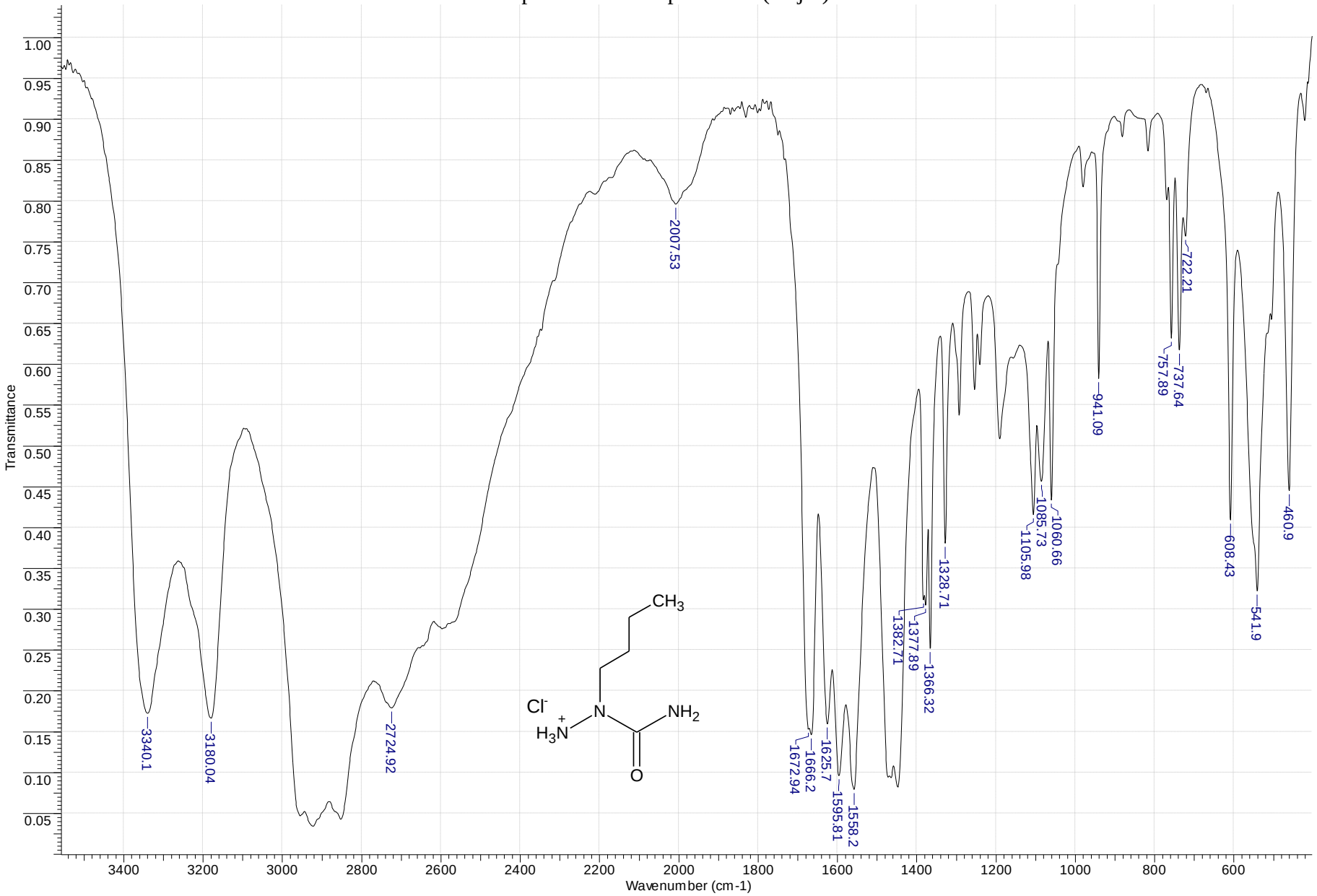
IR spectrum of compound **5b** (Nujol)



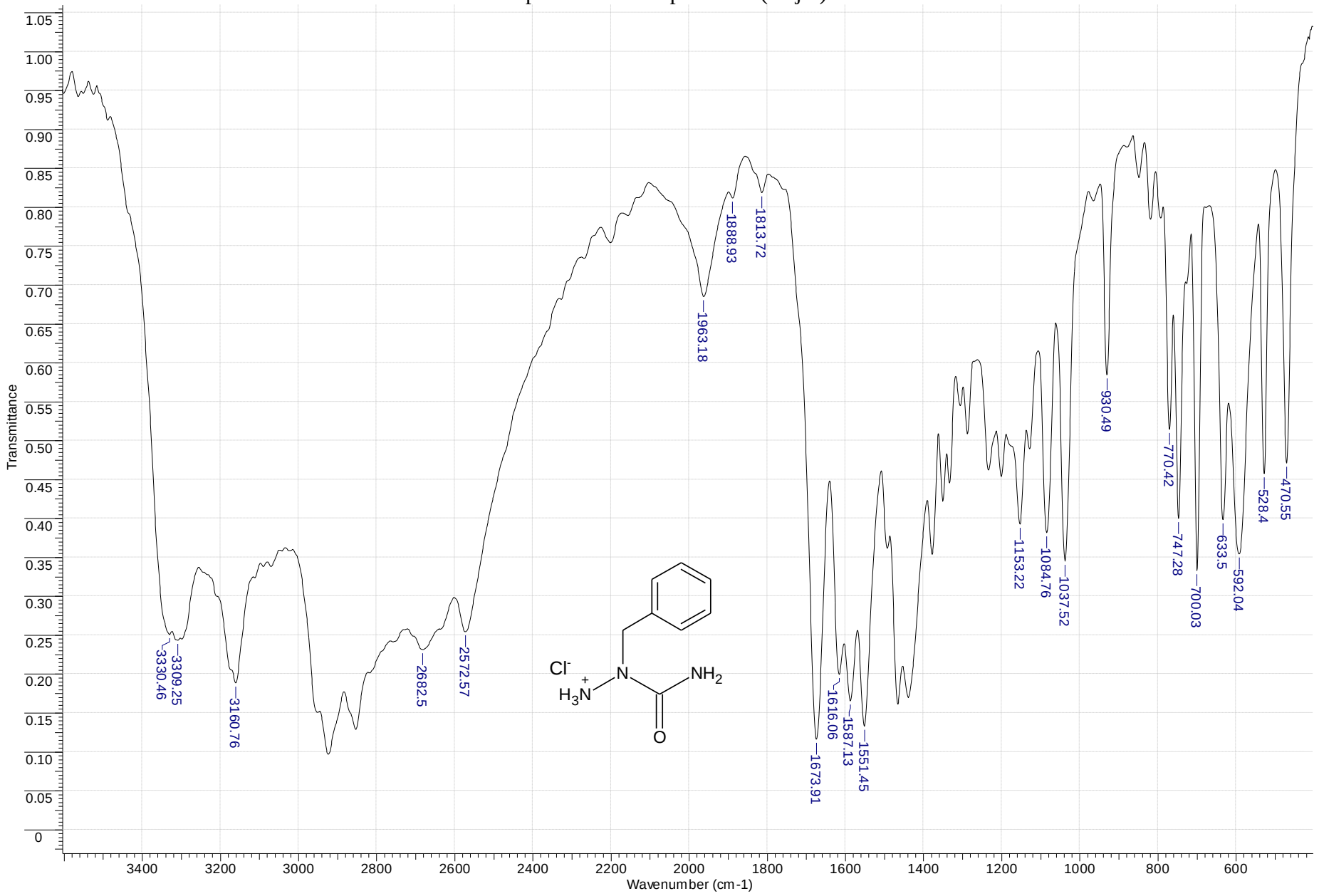
IR spectrum of compound **5c** (Nujol)



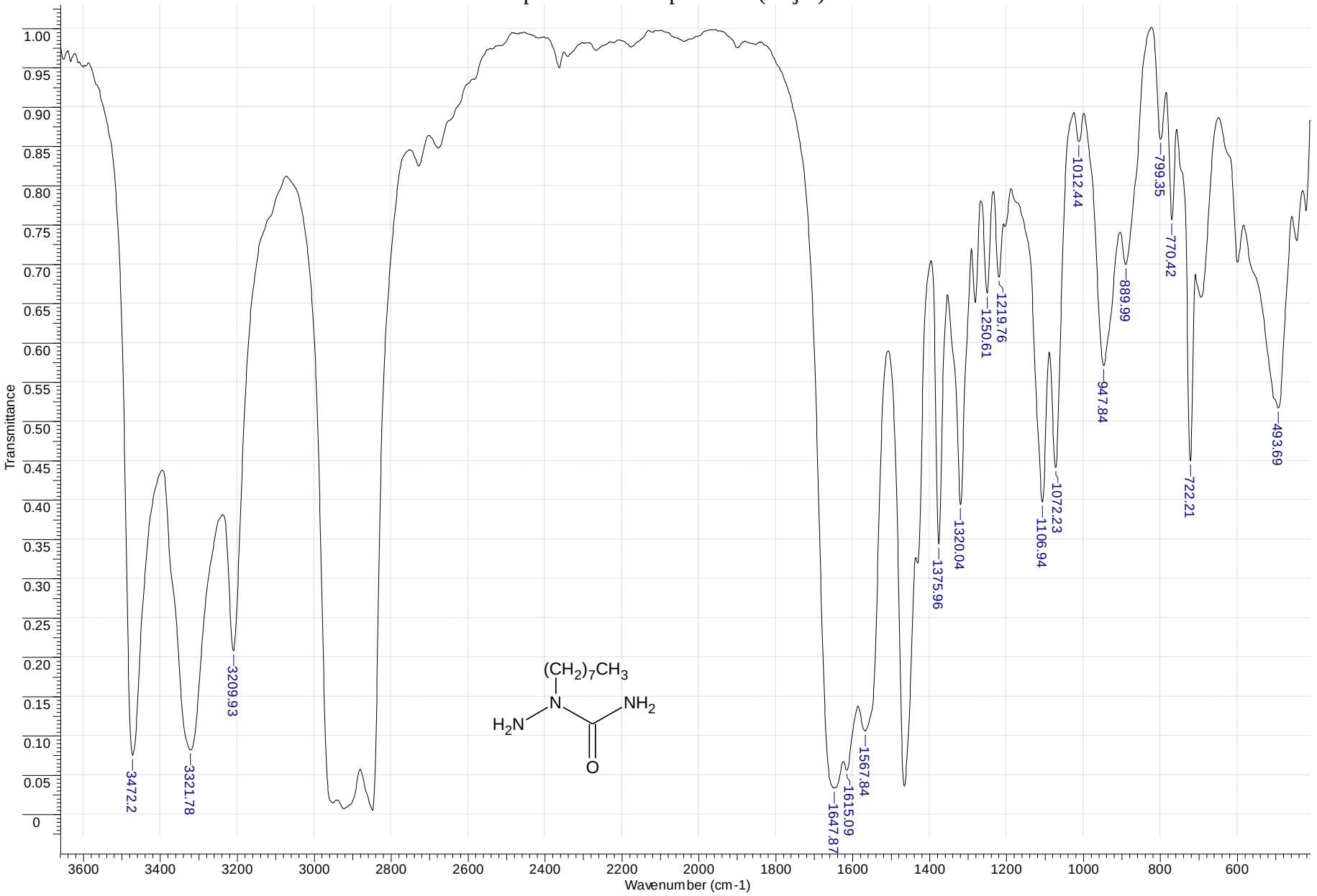
IR spectrum of compound **5d** (Nujol)



IR spectrum of compound **5e** (Nujol)

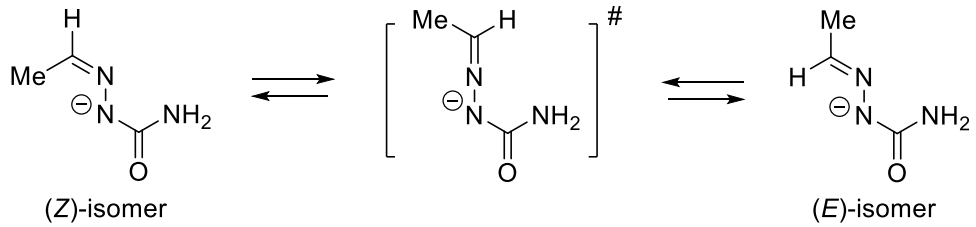


IR spectrum of compound **6f** (Nujol)

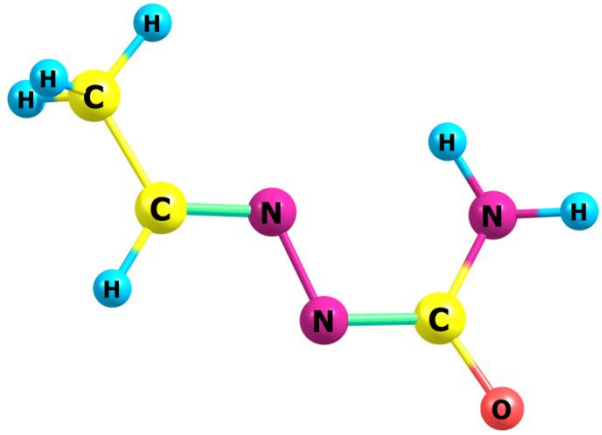


Computational details

The geometry optimizations of all key stationary points were carried out at the B3LYP level of theory using Gaussian 09 suite[1] of quantum chemical programs. Pople's basis sets, 6-311++G(d,p), was employed for geometry optimization. The effect of continuum solvation was incorporated by using the polarizable continuum model (PCM). Enthalpies and Gibbs free energies were obtained by adding unscaled zero-point vibrational energy corrections (ZPVE) and thermal contributions to the energies. All transition states were fully optimized and characterized as a first-order saddle point by harmonic vibrational frequency analysis. One and only one imaginary frequency of the first-order saddle point was subjected to visual inspection to examine whether it represented the desired reaction coordinate. Furthermore, the intrinsic reaction coordinate (IRC) analysis was performed to authenticate that the transition state pertains to the desired reaction coordinate. The IRC calculations were done at the B3LYP/6-311++G(d,p) level of theory.



Data 1: Cartesian coordinates and energies of the optimized geometry for the most stable conformer of (*E*)-isomer of the conjugated base of ethanal semicarbazone (DMSO solution).



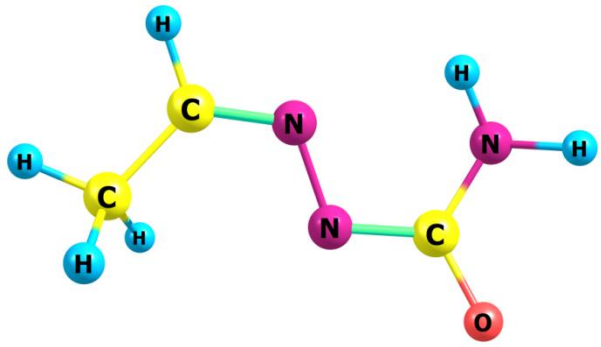
Electronic Energy =	-357.641696796 a.u.
Zero-point correction=	0.098296 (Hartree/Particle)
Thermal correction to Energy=	0.105808
Thermal correction to Enthalpy=	0.106752
Thermal correction to Gibbs Free Energy=	0.066638
Sum of electronic and zero-point Energies=	-357.543400
Sum of electronic and thermal Energies=	-357.535889

Sum of electronic and thermal Enthalpies= -357.534945
Sum of electronic and thermal Free Energies= -357.575058

Standard orientation:

Center Number	Atomic Number	Atomic Type	Coordinates (Angstroms) X	Y	Z
1	6	0	-3.139302	0.290977	0.016573
2	6	0	-1.866689	-0.498270	-0.024449
3	7	0	-0.716332	0.064938	0.023783
4	7	0	0.384784	-0.767860	-0.004246
5	6	0	1.555110	-0.103485	-0.005328
6	8	0	2.662870	-0.705459	0.027715
7	7	0	1.570575	1.297437	-0.100994
8	1	0	2.401885	1.719120	0.286807
9	1	0	0.700110	1.744725	0.155272
10	1	0	-3.758971	-0.000338	0.873391
11	1	0	-3.745017	0.112974	-0.880208
12	1	0	-2.930667	1.360511	0.087582
13	1	0	-1.938197	-1.590252	-0.095138

Data 2: Cartesian coordinates and energies of the optimized geometry for the most stable conformer of (*Z*)-isomer of the conjugated base of ethanal semicarbazone (DMSO solution).



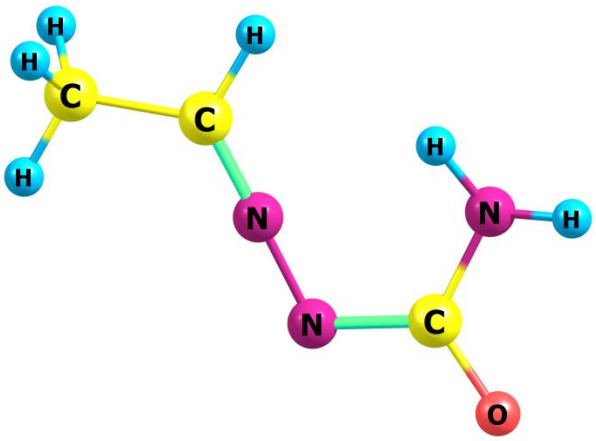
Electronic Energy = -357.640318732 a.u.
Zero-point correction= 0.098553 (Hartree/Particle)
Thermal correction to Energy= 0.106063
Thermal correction to Enthalpy= 0.107007
Thermal correction to Gibbs Free Energy= 0.066382
Sum of electronic and zero-point Energies= -357.541766
Sum of electronic and thermal Energies= -357.534256
Sum of electronic and thermal Enthalpies= -357.533312
Sum of electronic and thermal Free Energies= -357.573937

Standard orientation:

Center Number	Atomic Number	Atomic Type	Coordinates (Angstroms) X	Y	Z

1	6	0	2.732175	-0.641119	0.038473
2	6	0	1.941585	0.635795	-0.029716
3	7	0	0.656683	0.735148	-0.049165
4	7	0	-0.058742	-0.439041	-0.015615
5	6	0	-1.395444	-0.240029	0.005518
6	8	0	-2.209527	-1.200141	-0.029089
7	7	0	-1.908208	1.058237	0.123668
8	1	0	-2.844126	1.164390	-0.238985
9	1	0	-1.255727	1.790663	-0.124500
10	1	0	2.485235	-1.214247	0.939163
11	1	0	3.803808	-0.431967	0.041755
12	1	0	2.505747	-1.294600	-0.811575
13	1	0	2.483259	1.578596	-0.071015

Data 3: Cartesian coordinates, energy, imaginary frequency of the transition state for the transformation of (*Z*)-isomer of the conjugated base of ethanal semicarbazone into (*E*)-isomer (DMSO solution).



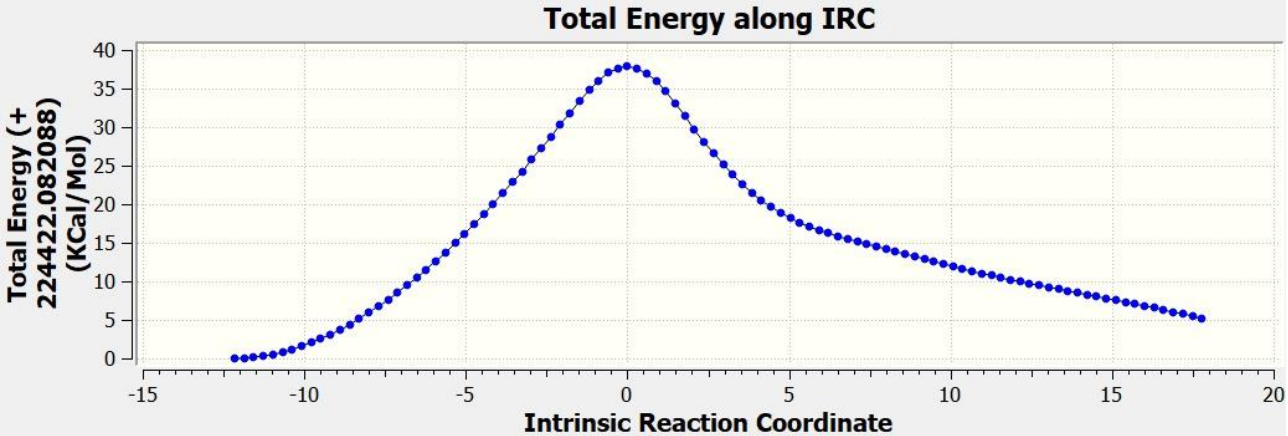
Imaginary Frequency=	-461.3578 cm^{-1}
Electronic Energy =	-357.578981015 a.u.
Zero-point correction=	0.095364 (Hartree/Particle)
Thermal correction to Energy=	0.102798
Thermal correction to Enthalpy=	0.103742
Thermal correction to Gibbs Free Energy=	0.063525
Sum of electronic and zero-point Energies=	-357.483617
Sum of electronic and thermal Energies=	-357.476183
Sum of electronic and thermal Enthalpies=	-357.475239
Sum of electronic and thermal Free Energies=	-357.515456

Standard orientation:

Center Number	Atomic Number	Atomic Type	Coordinates (Angstroms) X	Y	Z

1	6	0	-3.180811	-0.194762	-0.001815
2	6	0	-1.779020	0.411721	0.000880
3	7	0	-0.700695	-0.222473	0.007019
4	7	0	0.442133	-0.919275	0.005678
5	6	0	1.572662	-0.134403	-0.004062
6	8	0	2.714313	-0.644170	0.005791
7	7	0	1.438711	1.248231	-0.073538
8	1	0	2.247211	1.772107	0.225777
9	1	0	0.541751	1.625690	0.195629
10	1	0	-3.134542	-1.286758	-0.004739
11	1	0	-3.747572	0.136477	-0.881824
12	1	0	-3.749296	0.131051	0.879138
13	1	0	-1.810083	1.534088	-0.004435

Data 4: The intrinsic reaction coordinate analysis for the transformation of (*Z*)-isomer of the conjugated base of ethanal semicarbazone into (*E*)-isomer (DMSO solution).



Reference

1. *Gaussian 09, Revision D.01*, M. J. Frisch, G. W. Trucks, H. B. Schlegel, G. E. Scuseria, M. A. Robb, J. R. Cheeseman, G. Scalmani, V. Barone, B. Mennucci, G. A. Petersson, H. Nakatsuji, M. Caricato, X. Li, H. P. Hratchian, A. F. Izmaylov, J. Bloino, G. Zheng, J. L. Sonnenberg, M. Hada, M. Ehara, K. Toyota, R. Fukuda, J. Hasegawa, M. Ishida, T. Nakajima, Y. Honda, O. Kitao, H. Nakai, T. Vreven, J. A. Montgomery, J. E. Peralta, F. Ogliaro, M. Bearpark, J. J. Heyd, E. Brothers, K. N. Kudin, V. N. Staroverov, R. Kobayashi, J. Normand, K. Raghavachari, A. Rendell, J. C. Burant, S. S. Iyengar, J. Tomasi, M. Cossi, N. Rega, N. J. Millam, M. Klene, J. E. Knox, J. B. Cross, V. Bakken, C. Adamo, J. Jaramillo, R. Gomperts, R. E. Stratmann, O. Yazyev, A. J. Austin, R. Cammi, C. Pomelli, J. W. Ochterski, R. L. Martin, K. Morokuma, V. G. Zakrzewski, G. A. Voth, P. Salvador, J. J. Dannenberg, S. Dapprich, A. D. Daniels, Ö. Farkas, J. B. Foresman, J. V. Ortiz, J. Cioslowski and D. J. Fox, Gaussian, Inc., Wallingford CT, 2013.

