N –Heterocyclic Carbene –Catalyzed (NHC) Three-Component Domino Reactions: Highly Stereoselective Synthesis of Functionalized Acylic ε-Ketoester

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General Considerations

All the reactions are conducted under a dry N_2 atmosphere. All the solvent are commercially available and used without further purification. ^{1}H NMR spectra were recorded on a Bruker 400 MHz spectrometer in chloroform-d. Chemical shifts are reported in ppm with the internal TMS signal at 0.0 ppm as a standard. The date is being reported as (s=singlet, d=doublet, t=triplet, m=multiplet or unresolved, brs=broad singlet, coupling constant(s) in Hz, integration). ^{13}C NMR spectra were recorded on a Bruker 100 MHz spectrometer in chloroform-d. Chemical shifts are reported in ppm with the internal chloroform signal at 77.0 ppm as a standard. The date with * indicate peaks of the minor diastereomer. N-heterocyclic carbenes **I**,[1] **II** ,[2] **III**, [3] **IV**, [4] **V**, [5] and **VI** [6]are synthesized according to the reported literatures.

General Procedure for the NHC-catalyzed three-component domino reaction for the synthesis of ε-ketoester: Preparation of ε-ketoester 3g:

To a dry flask filled with nitrogen were added 1,3-dimesityl imidazolium chloride1 **III** (0.3 mmol), cinnamaldehyde **1a** （1.0 mmol), propaygly Alcohol (1.5 mmol), and chalcone **2g** (0.5 mmol) in 3 ml dry CH_2Cl_2 under N_2 atmosphere. After stirring for 5 min, DBU (0.3mmol) was added. This solution was stirred at room temperature until the completed consumption of chalcone as monitored by TLC. After the removal of the solvent, the residue was subjected to chromatography on a silica gel (60-120 mesh) column using 12:1 petroleum ether -ethyl acetate solvent mixture as the eluent to afford **3g** in 93% yield.

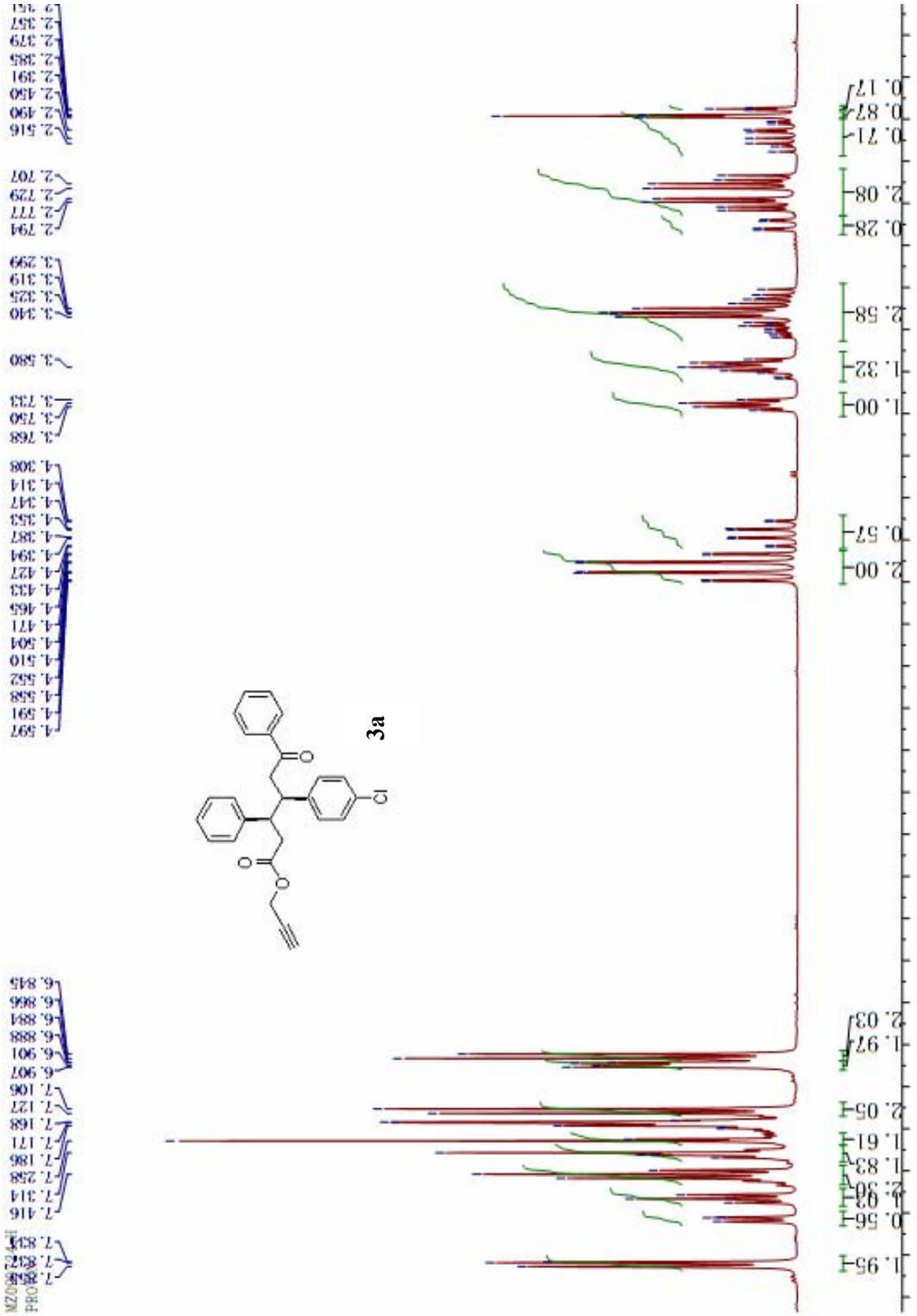
Procedure for the preparation of 4:

CuI (0.1 mmol) was added to the a suspension of the benzyl azides (1.2 mmol) and ε -ketoester **3g** (1.0 mmol) in 2ml *t*-BuOH under N_2 atmosphere. This solution was fluxed until the completed consumption of **3g** as monitored by TLC. After the removal of the solvent, the residue was subjected to chromatography on a silica gel (60-120 mesh) column using 15:1 petroleum ether -ethyl acetate solvent mixture as the eluent to afford **4** as colorless oil in 75% yield.

Reference:

1. J. He, S. Tang, J. Liu, Y. Su, X. Pan and X. She, *Tetrahedron* 2008, **64**, 8797.
2. W. Hinz, R. A. Jones, S. U. Patel and M. –H. Karatza, *Tetrahedron* 1986, **42**, 3753.
3. L. Hintermamn, *Beilstein J. Org. Chem*. 2007, **3**. doi: 10.1186/1860-5397-3-22.
4. J. E. Thomson, C. D. Campbell, C. Concellón, N. Duguet, K. Rix, A. M. Z. Slawin, and A. D. Smith , *J. Org. Chem.* 2008, **73**, 2784–2791.
5. D. Enders, K. Breuer, U. Kallfass, T. Balensiefer, *synthesis* 2003, 1292.
6. B. Bostai, Z. Novák, A. C. Bényei, and A. Kotschy**,** *Org. Lett.*, 2007, ***9***, 3437.

^{1}HNMR of compound 3a



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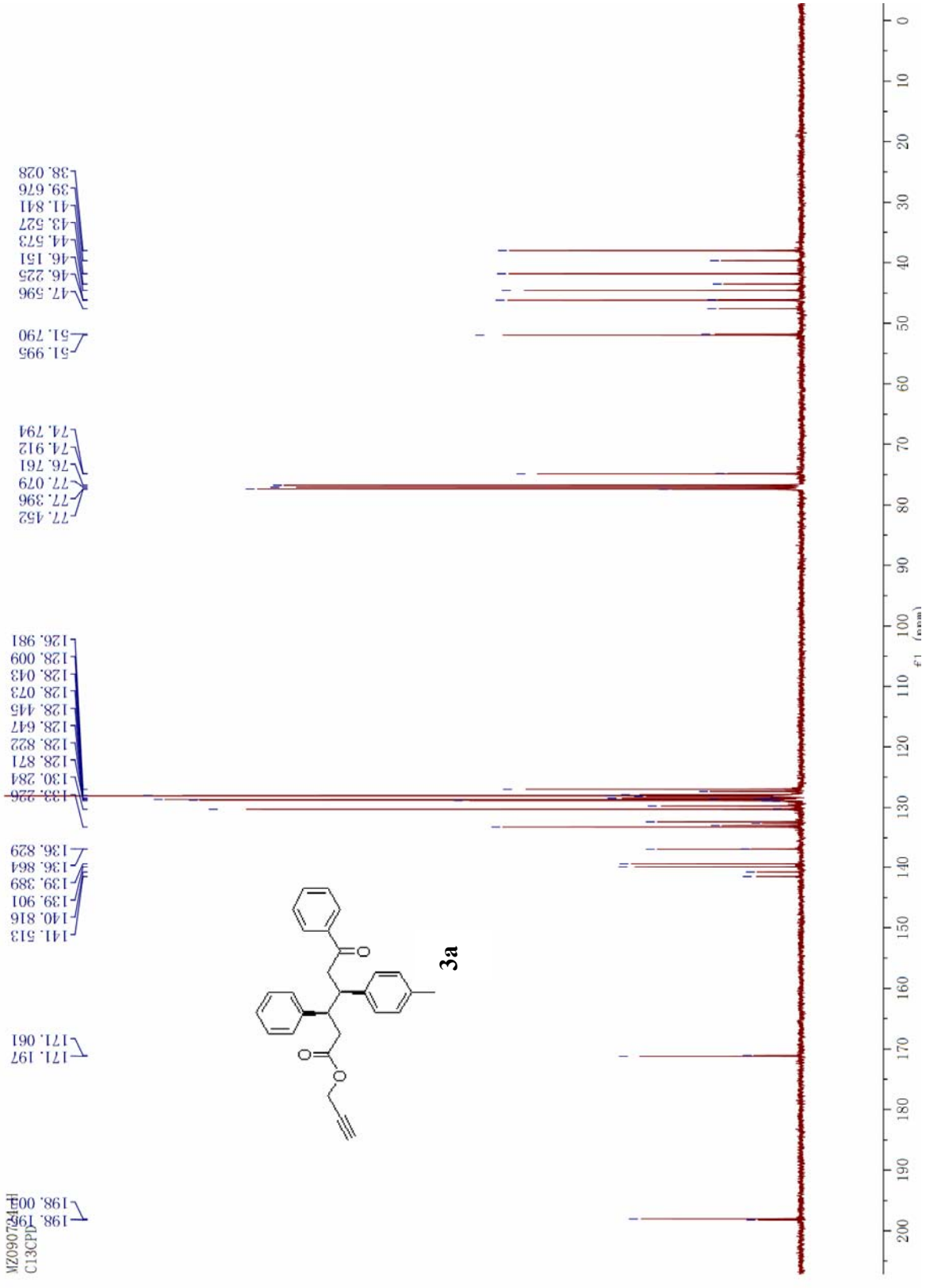

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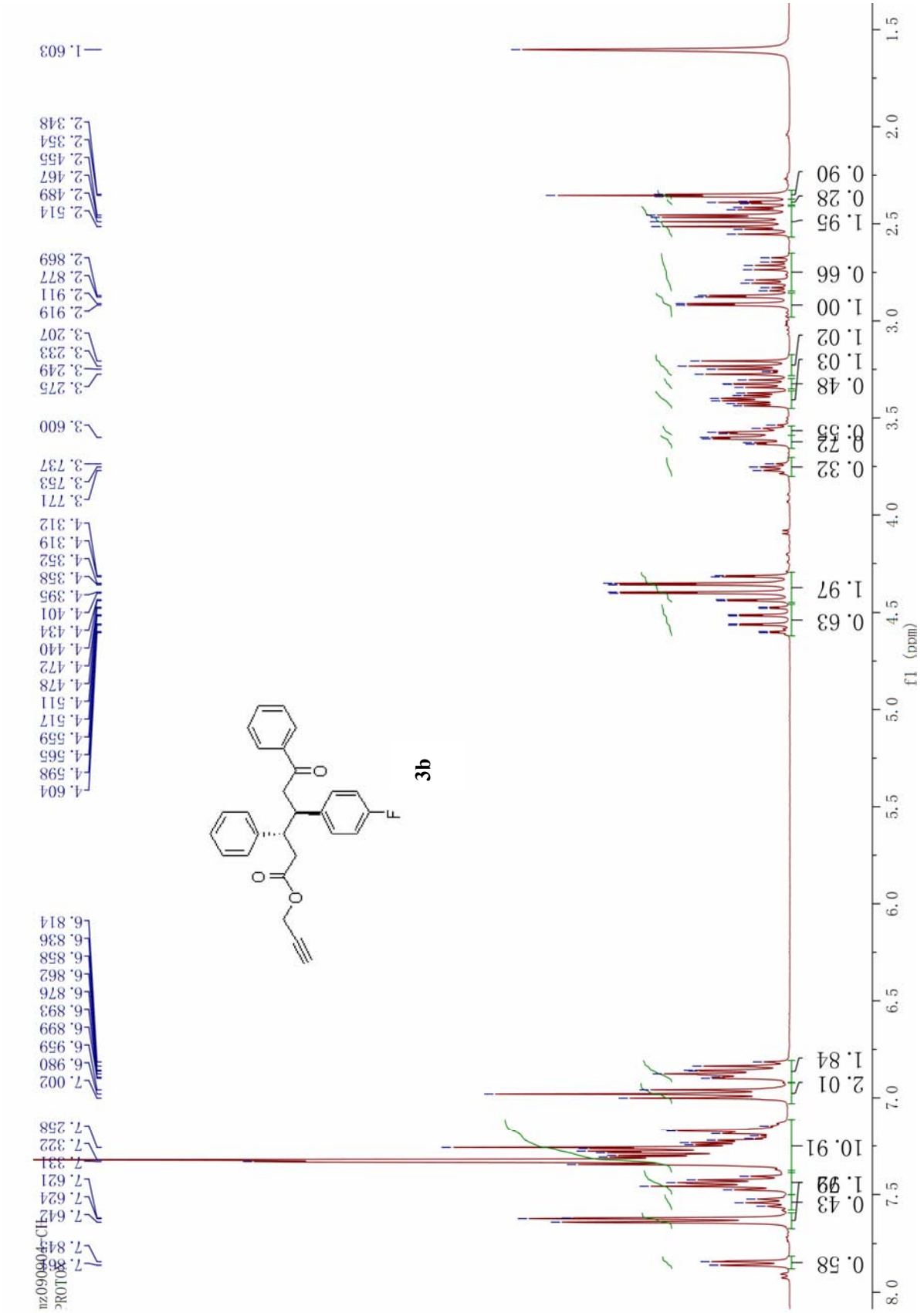

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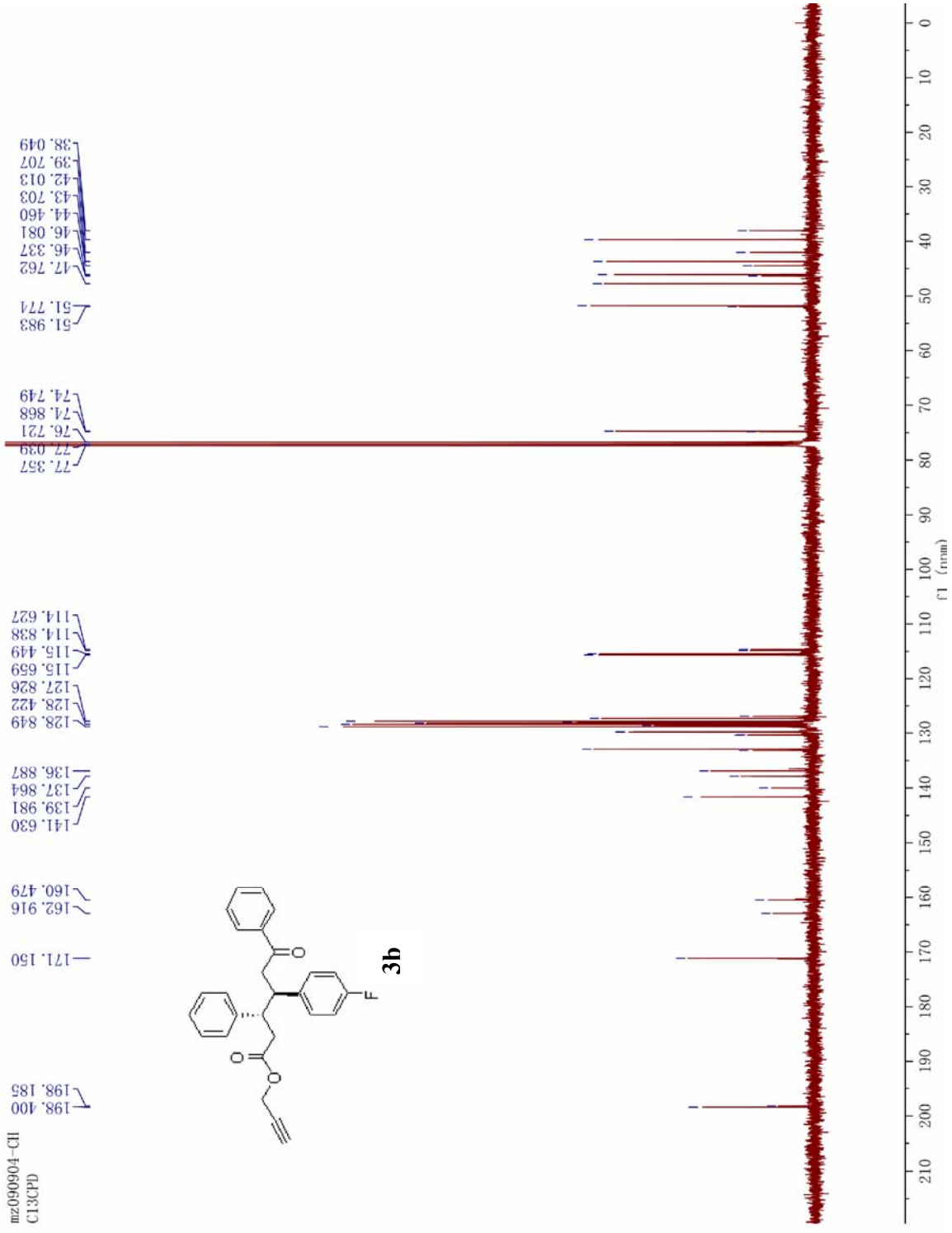

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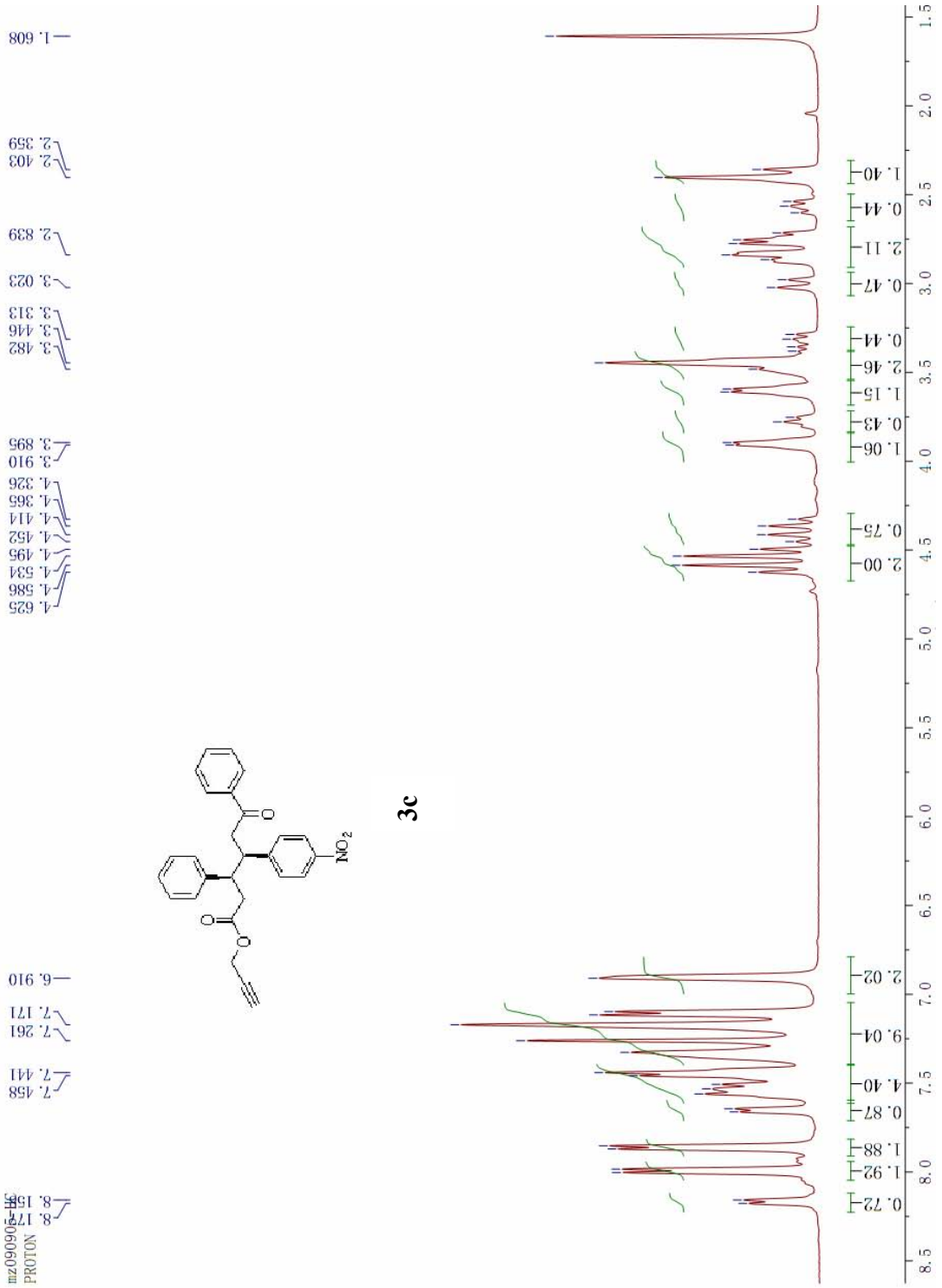

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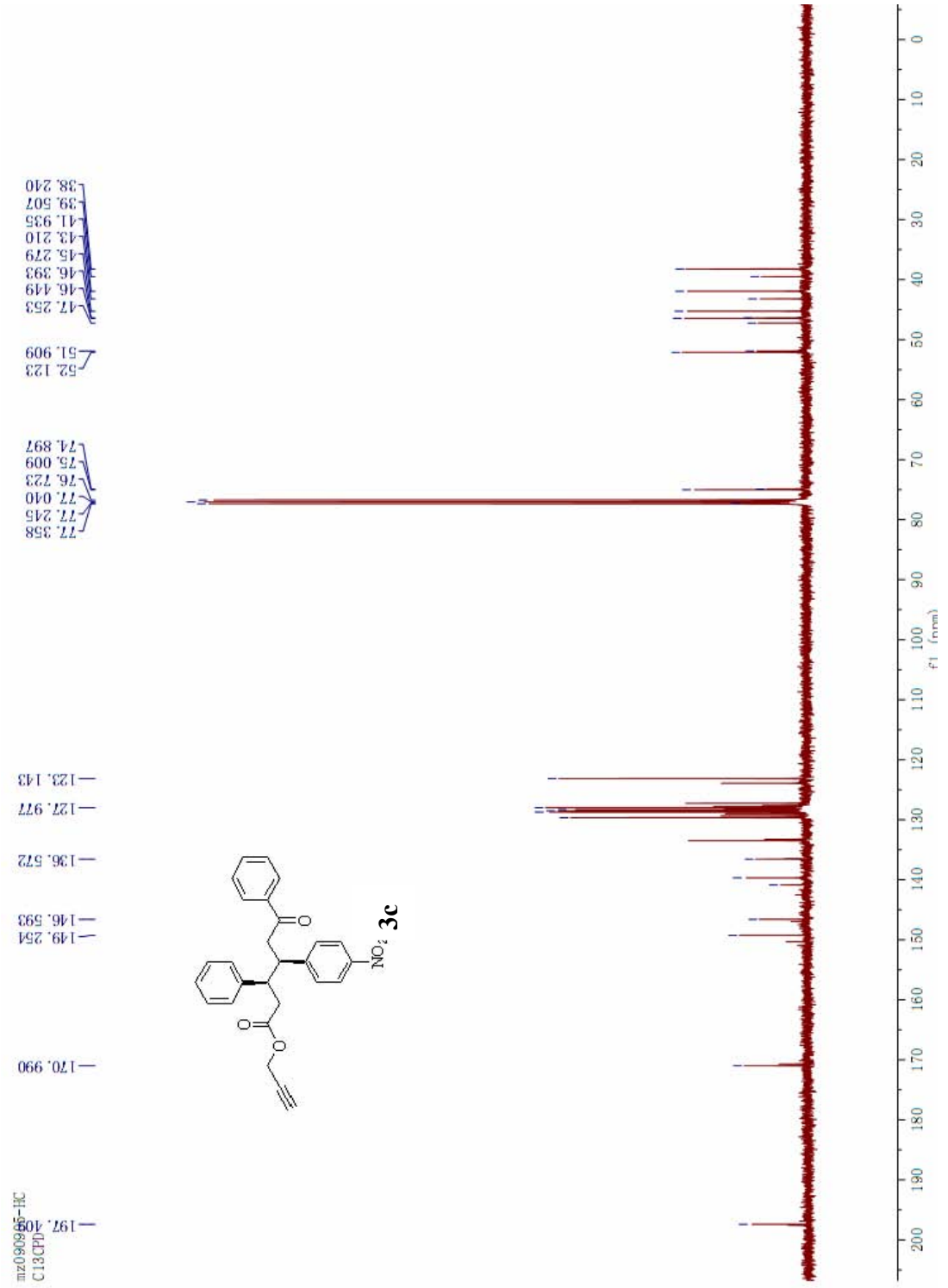

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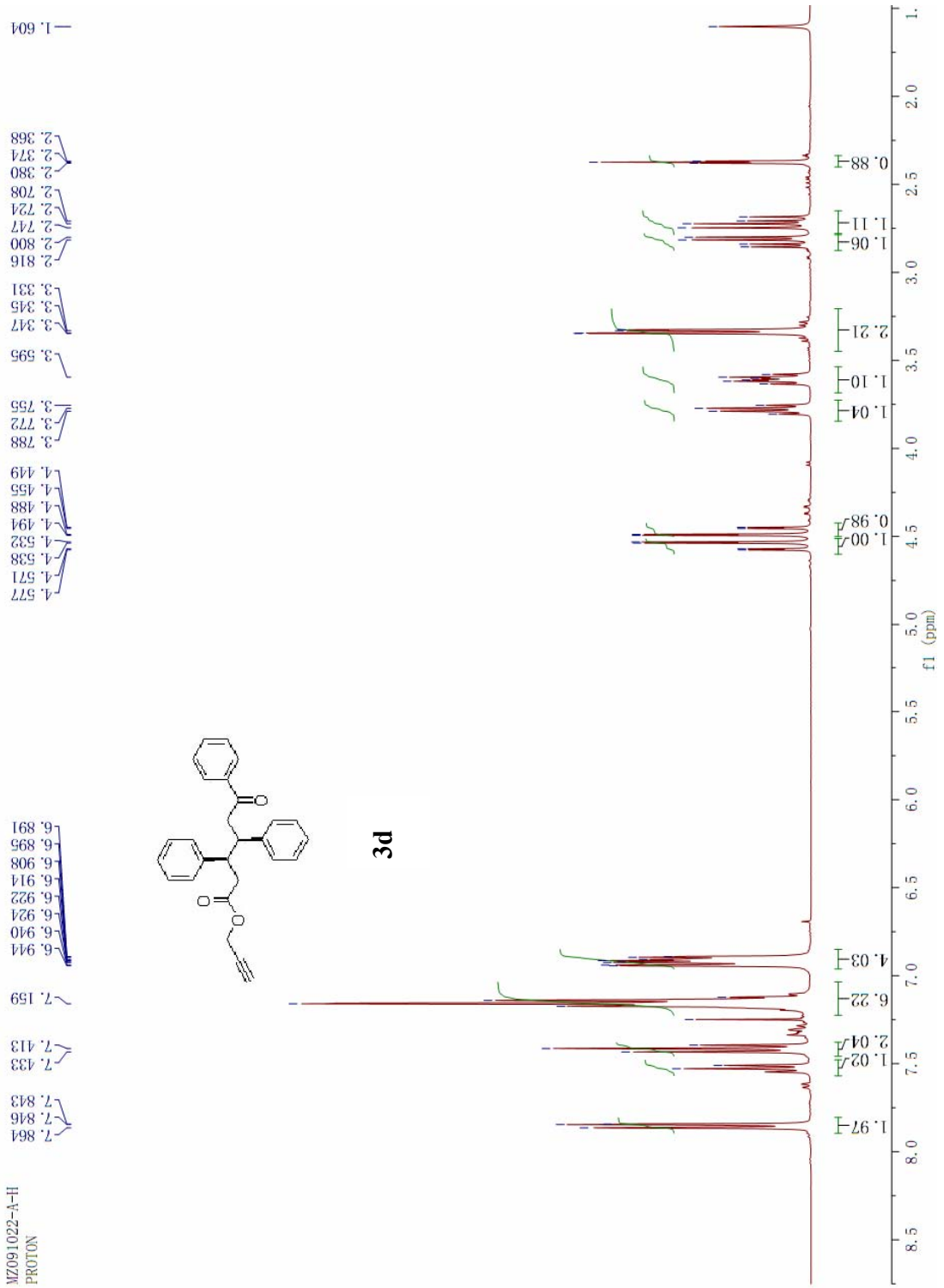

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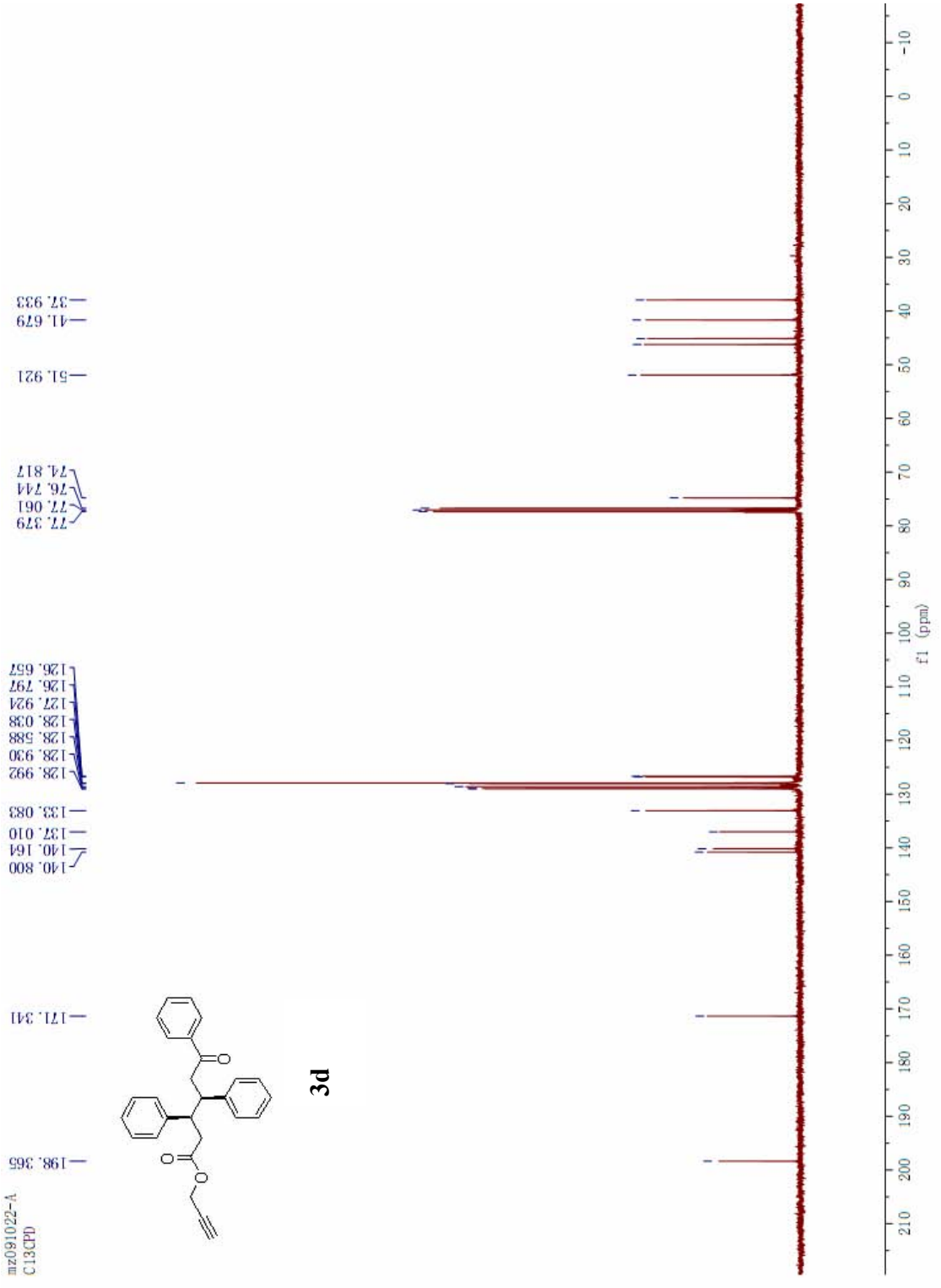

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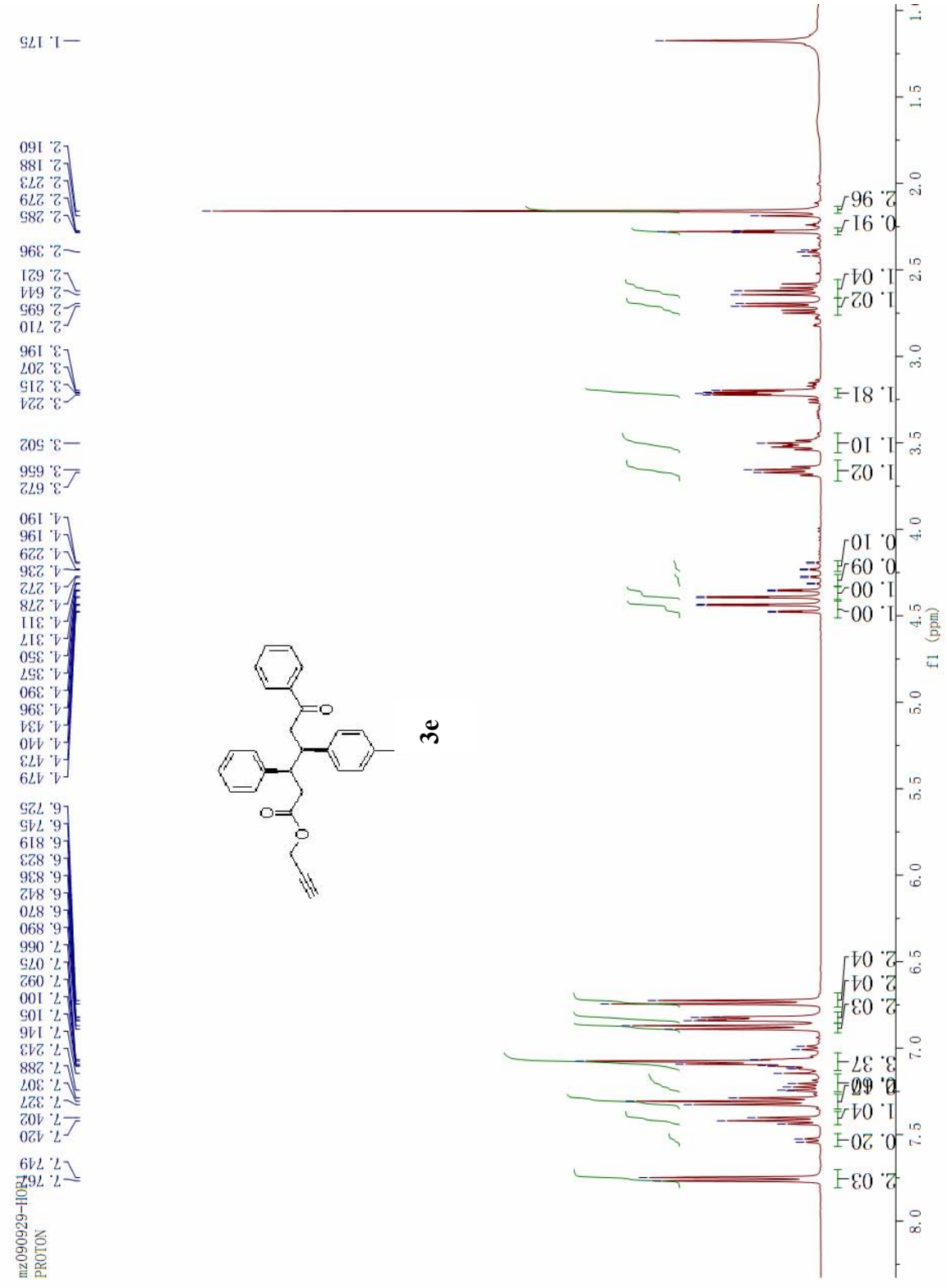

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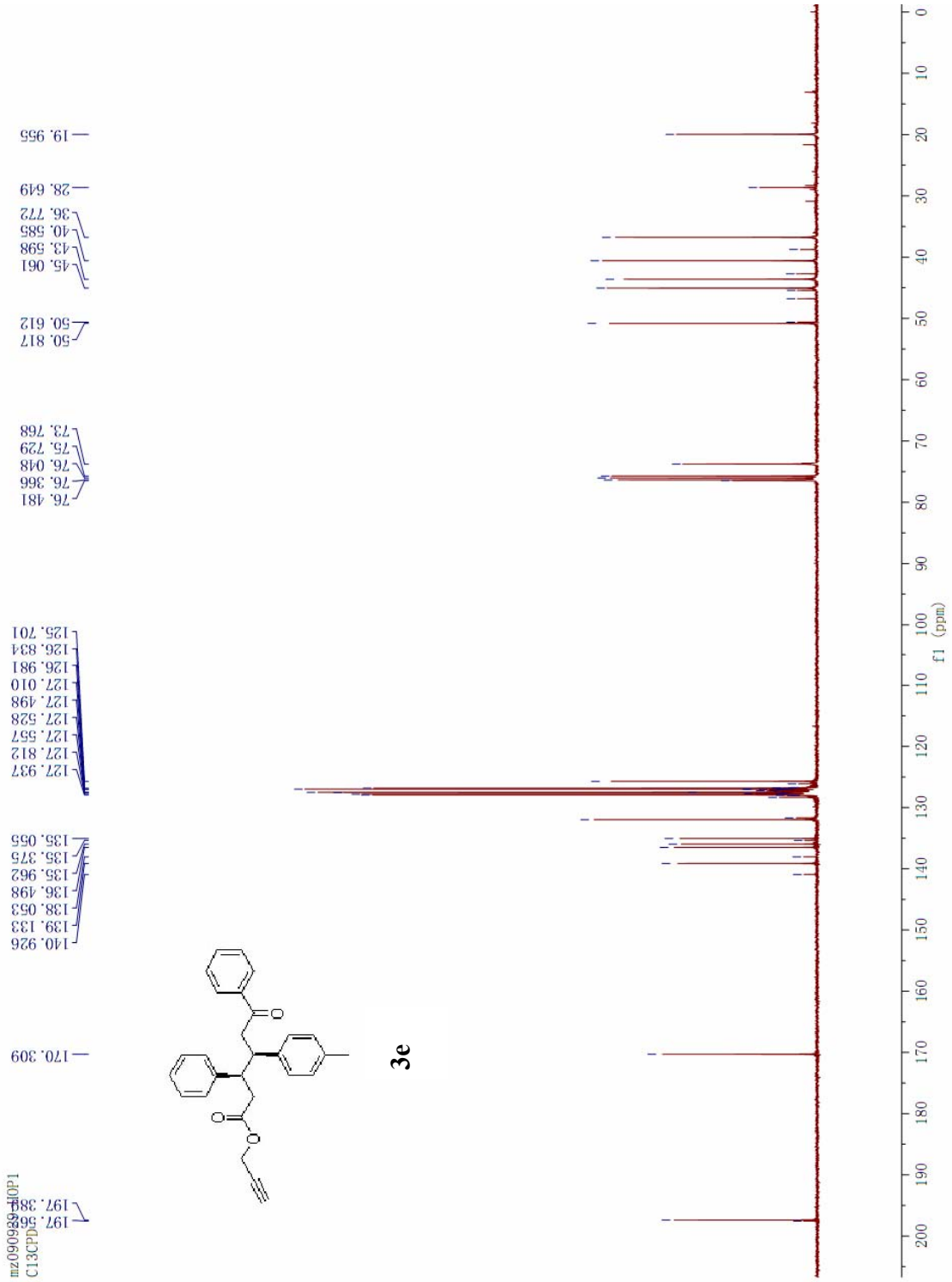

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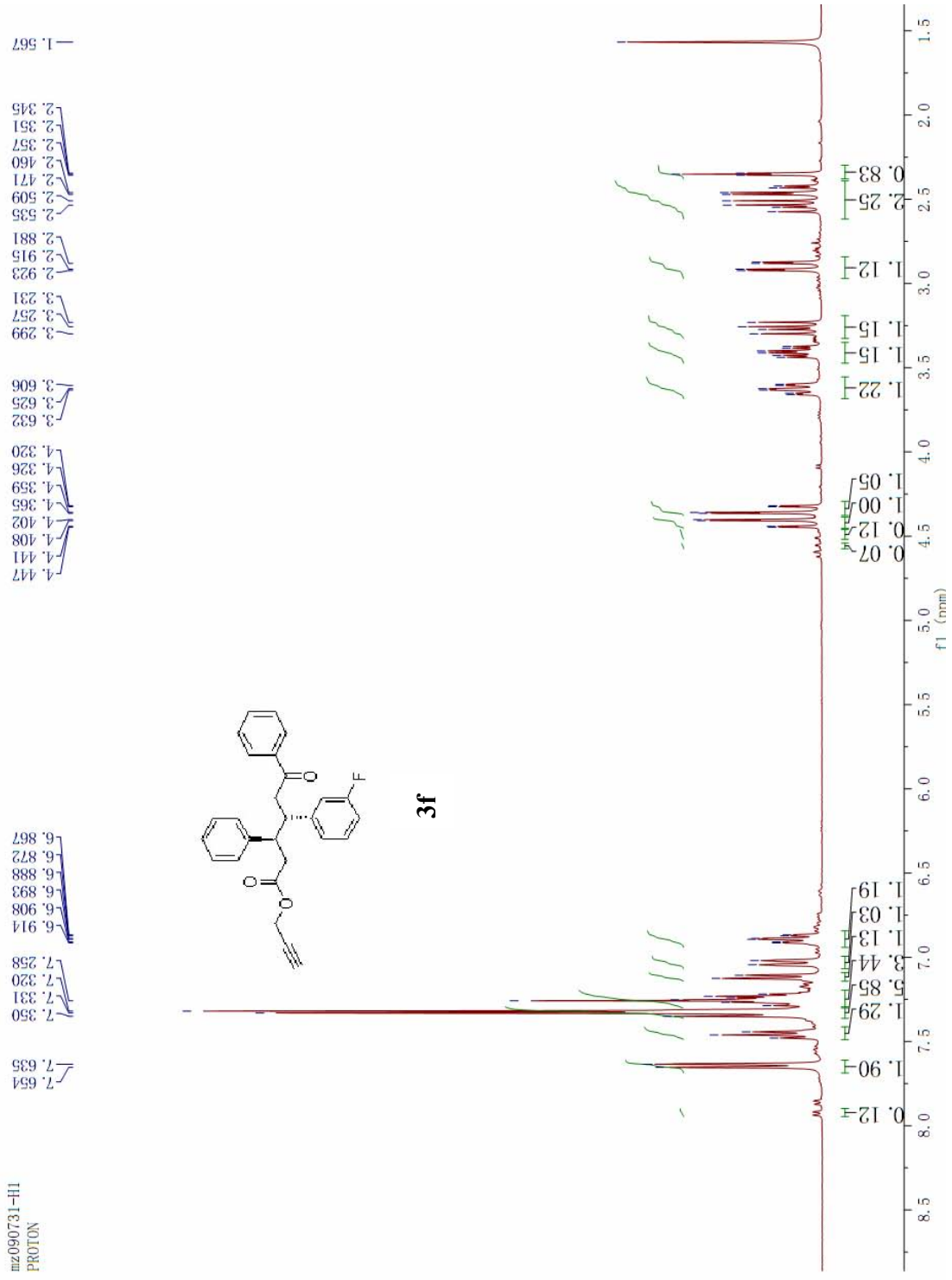

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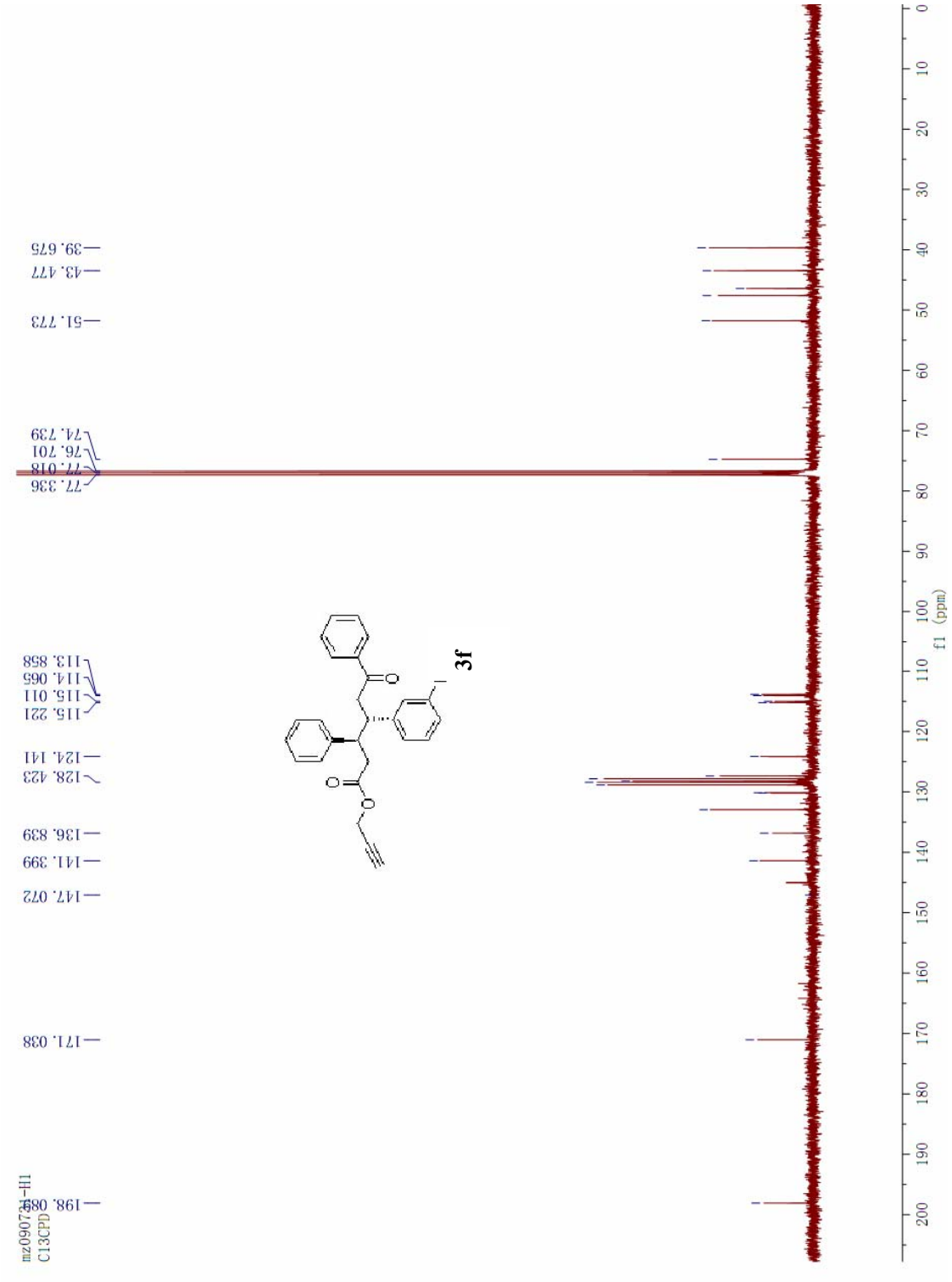

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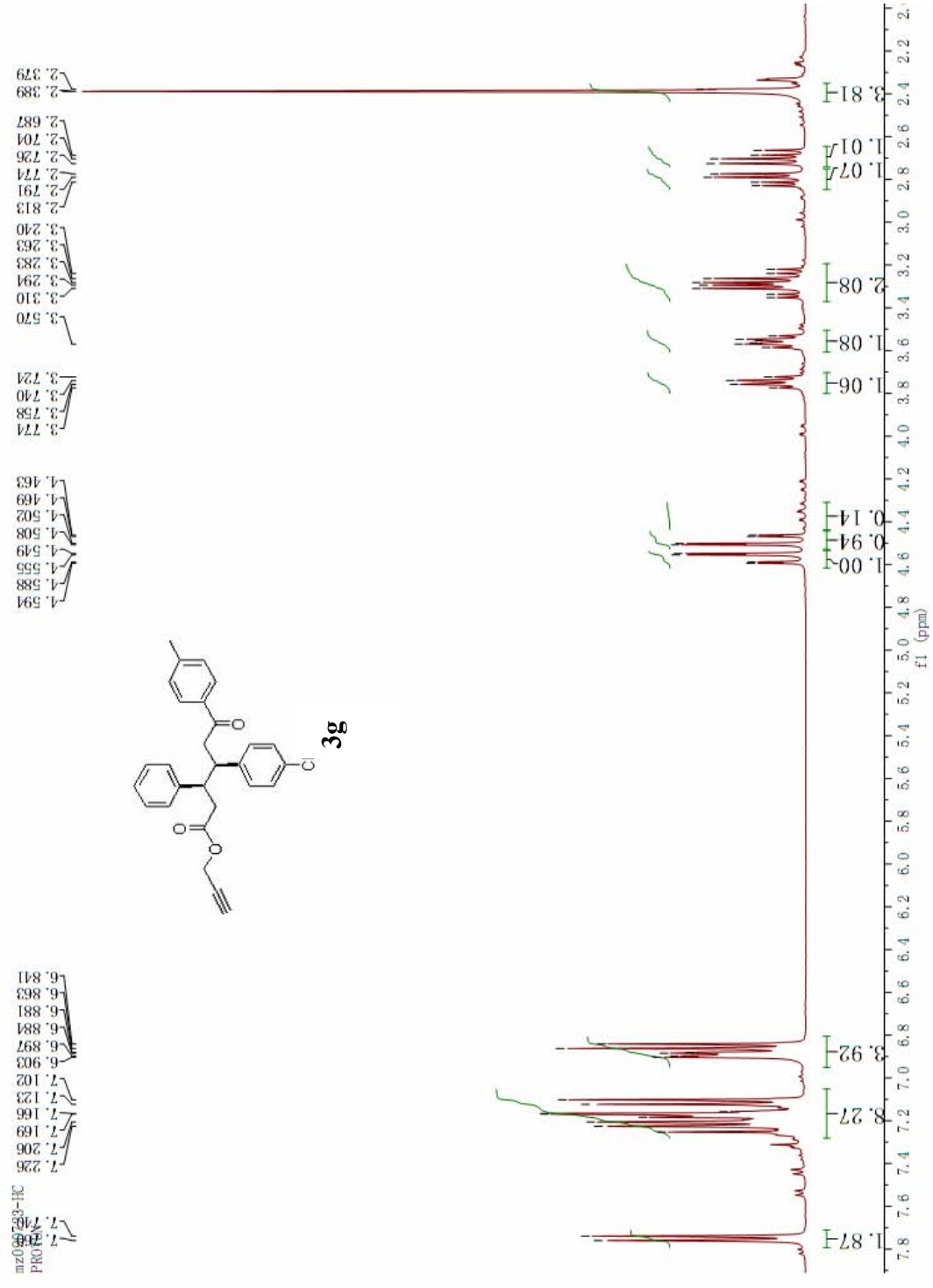

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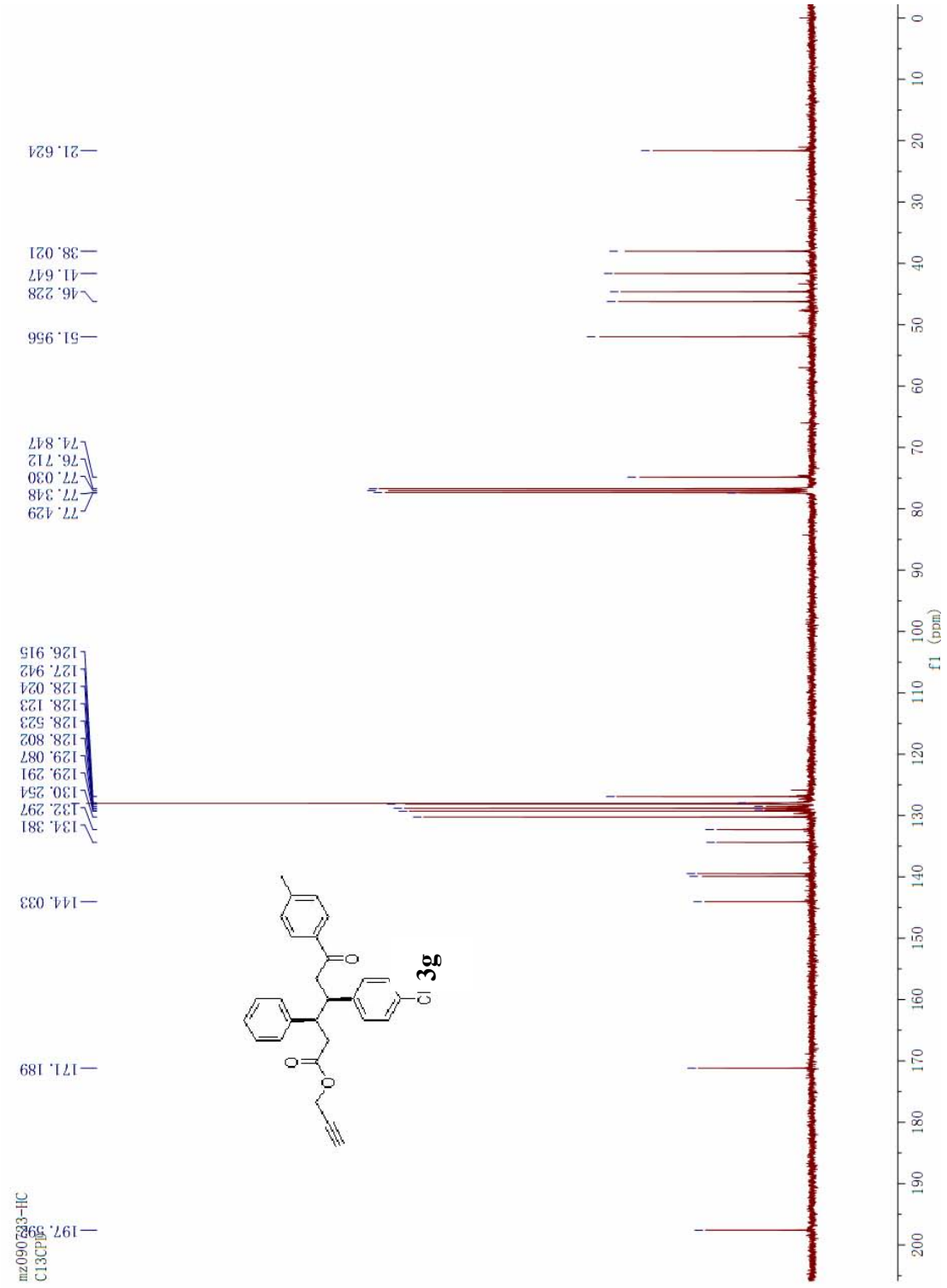

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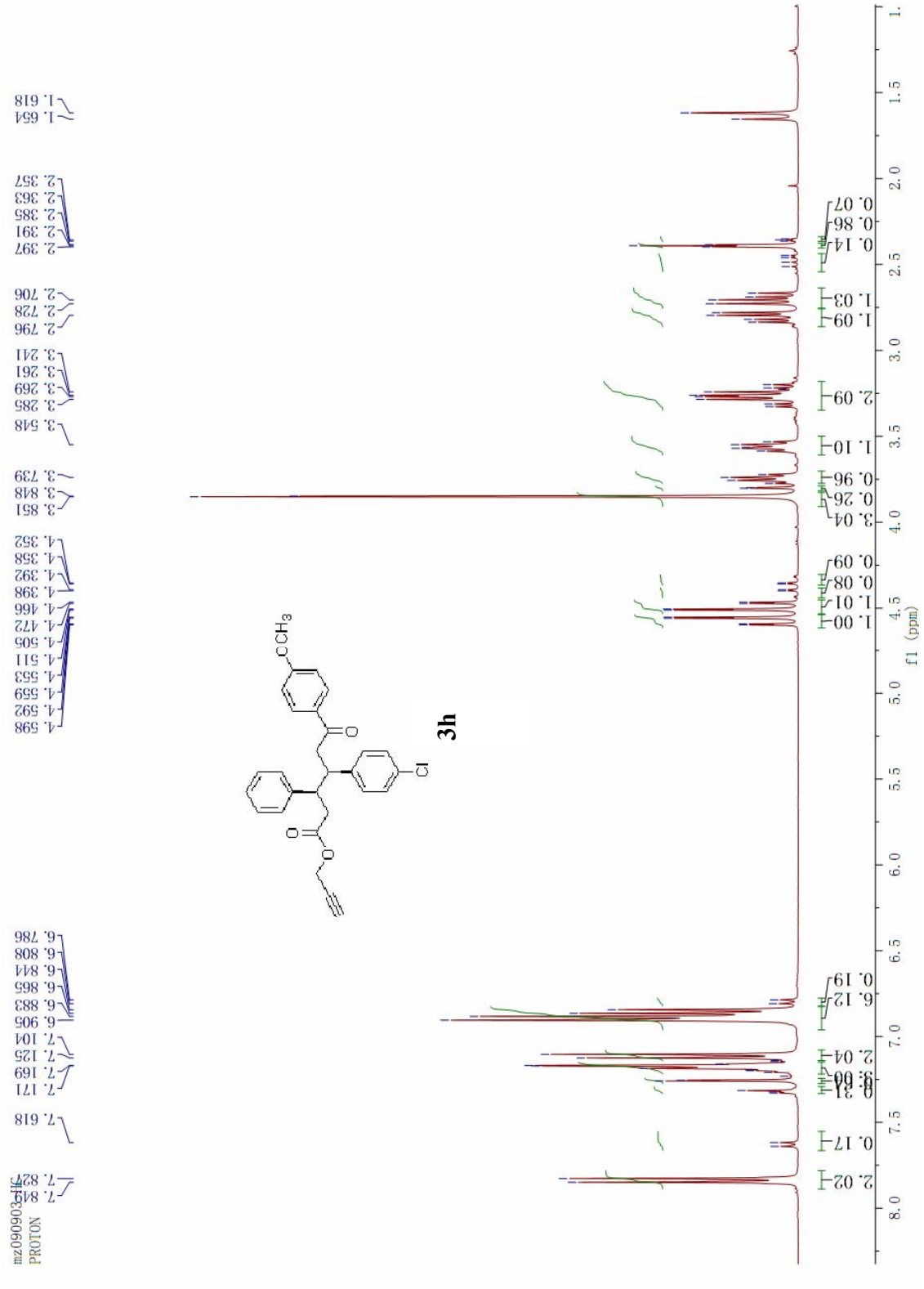

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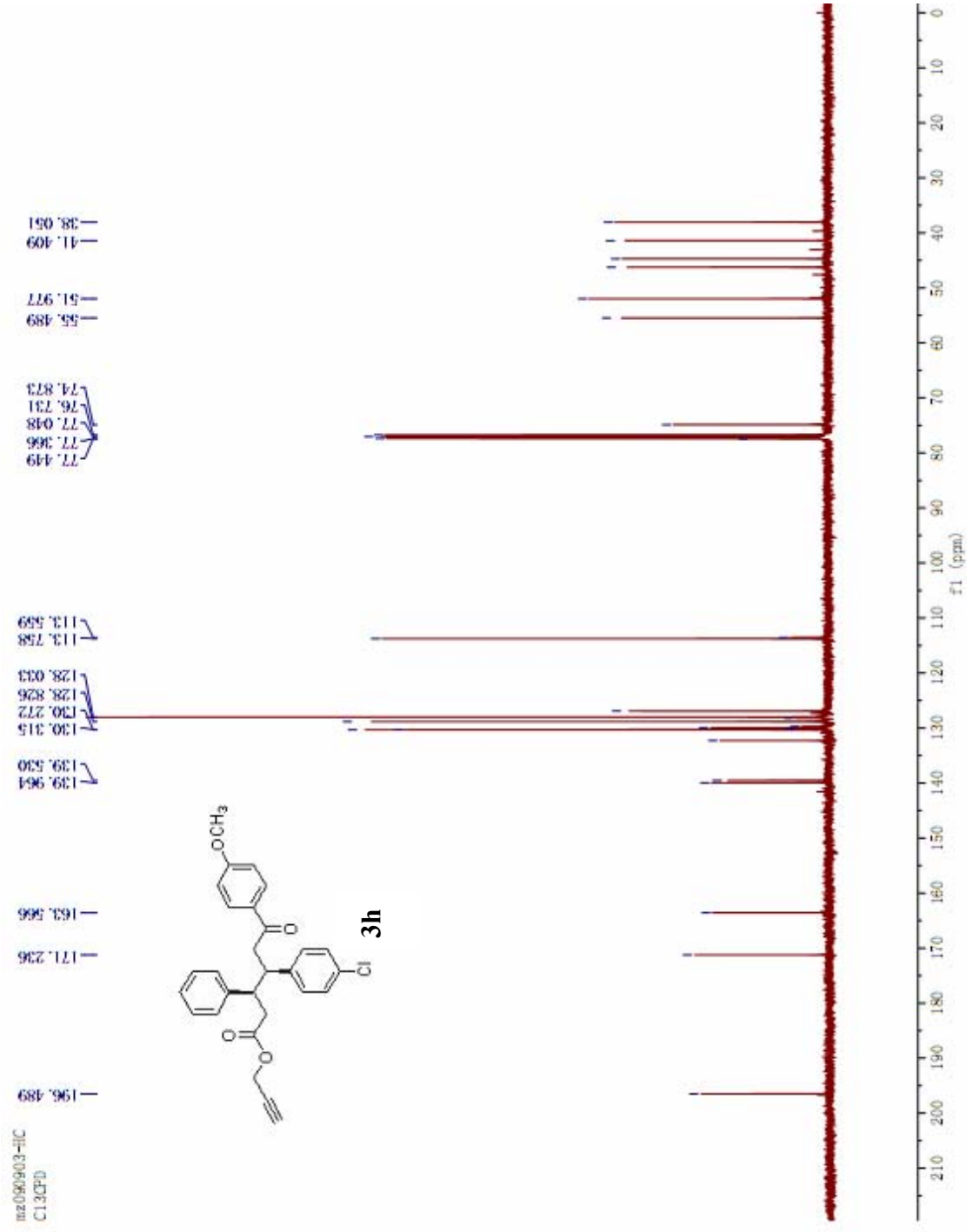

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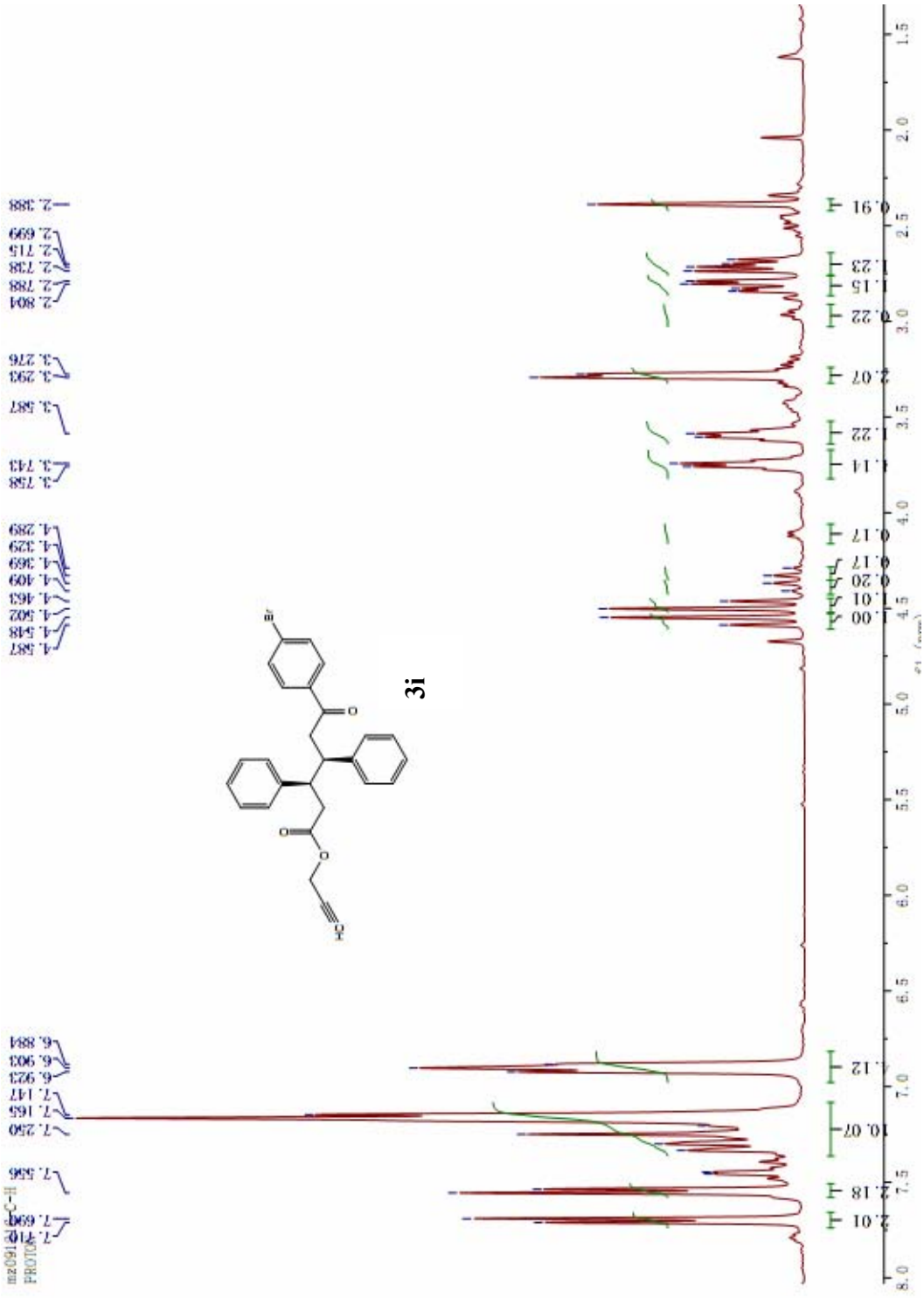

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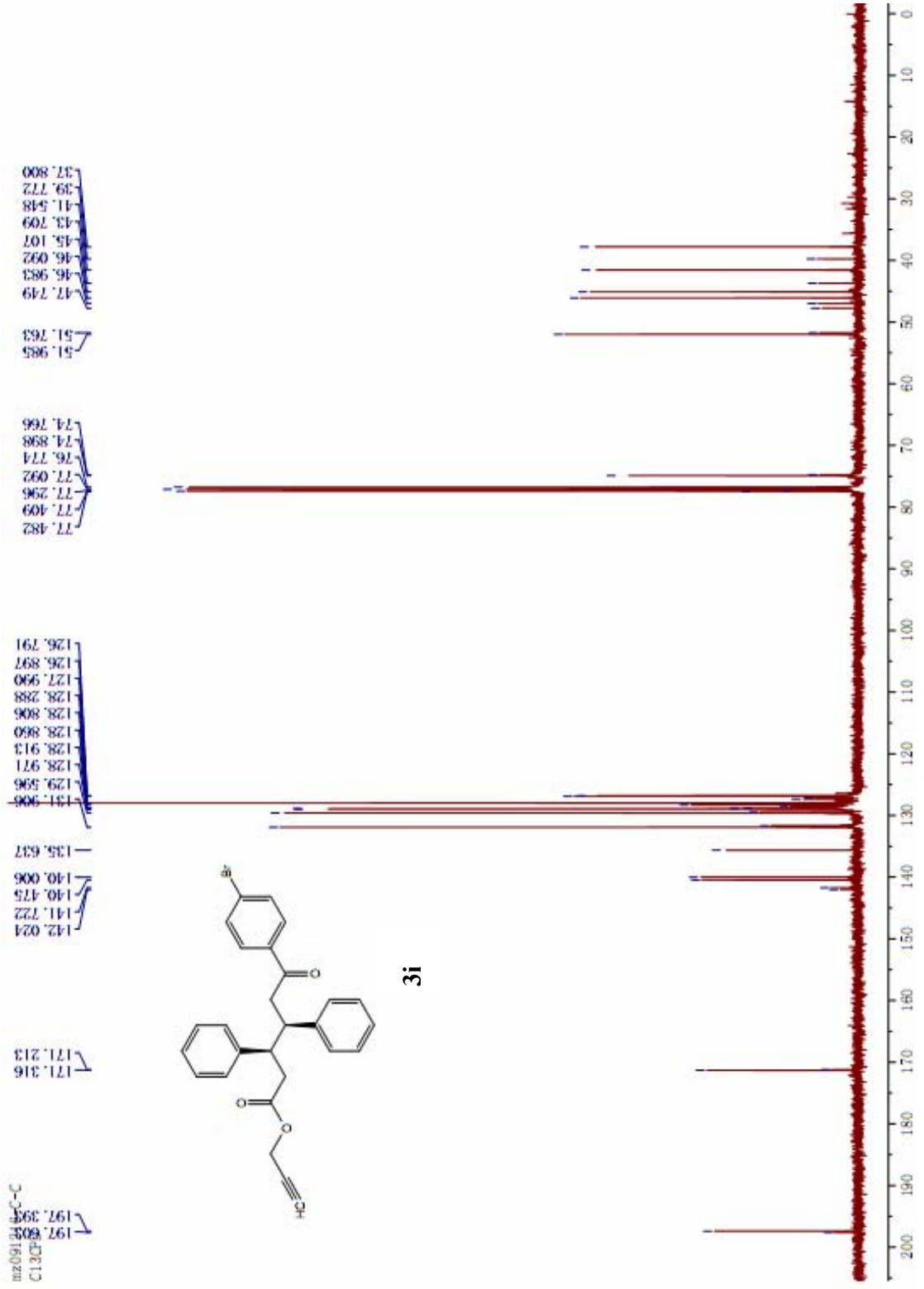

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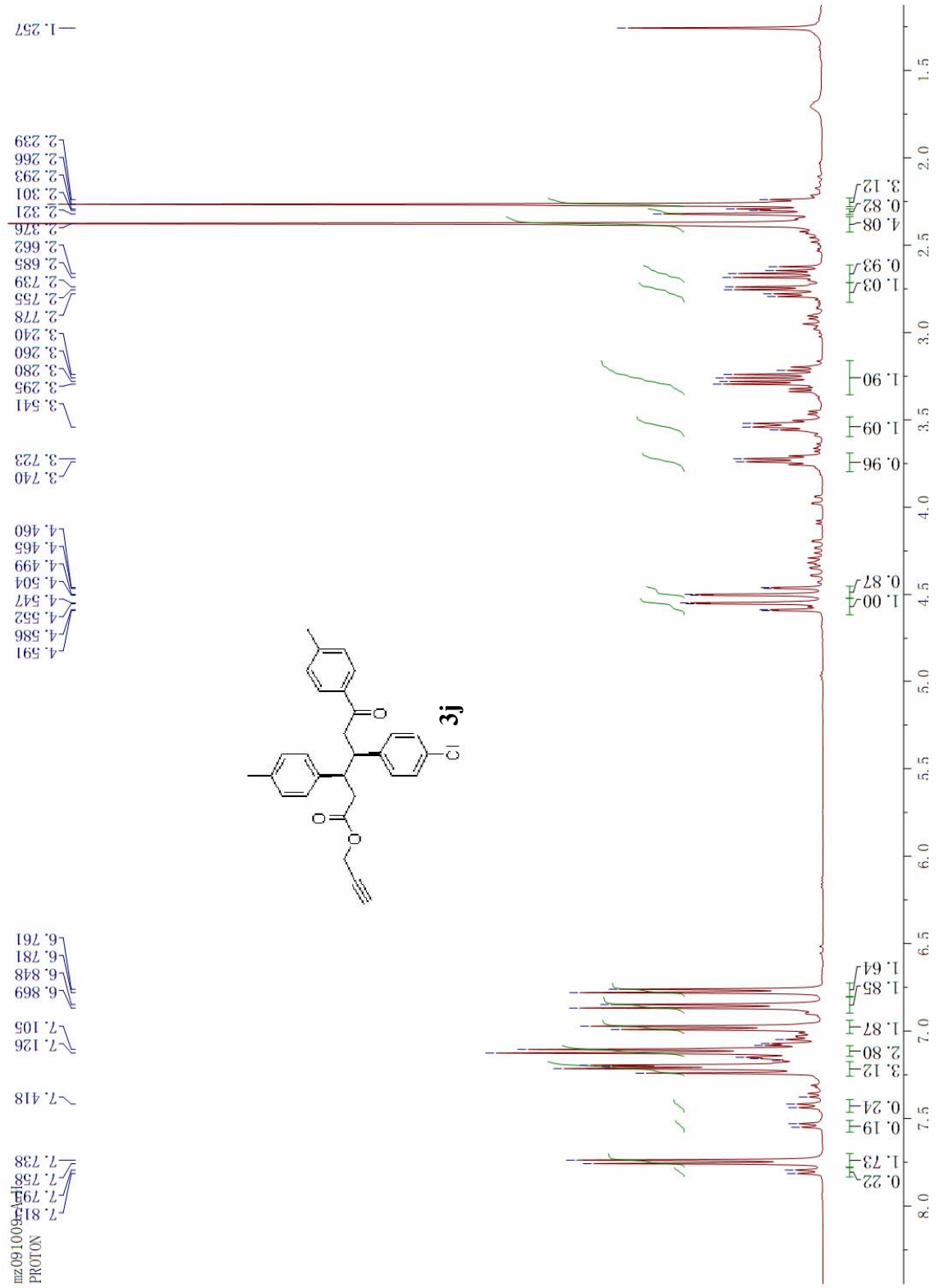

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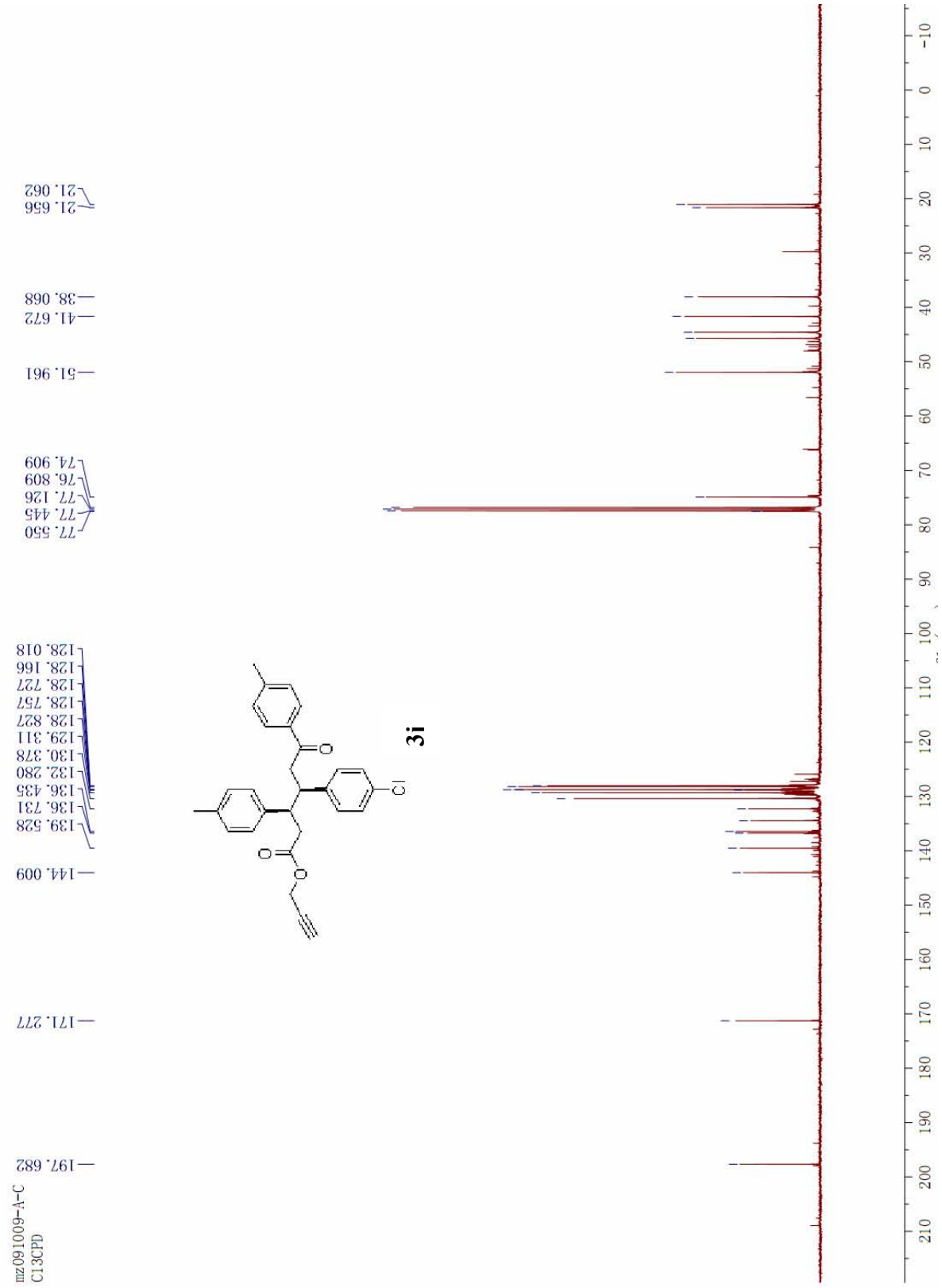

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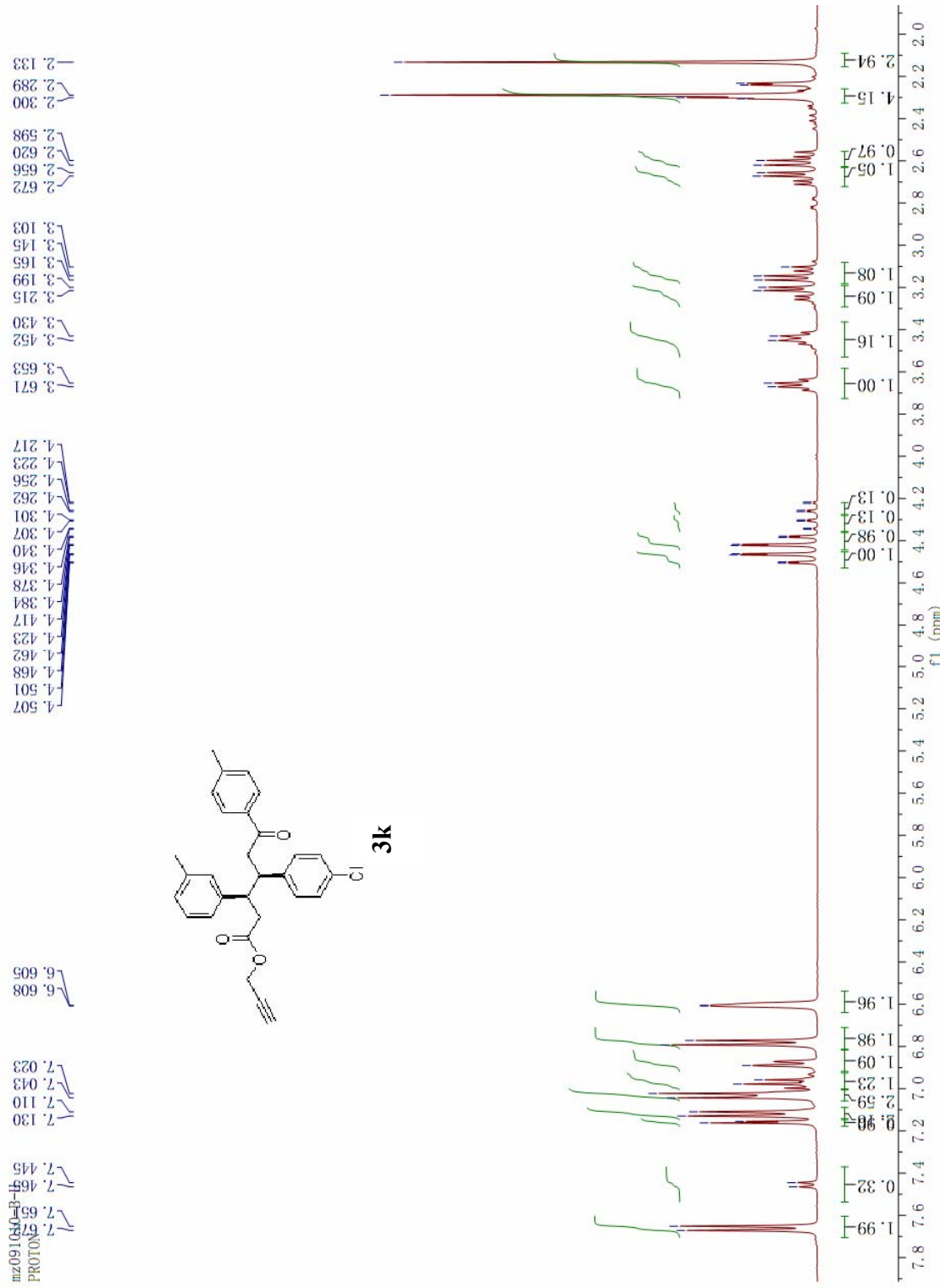

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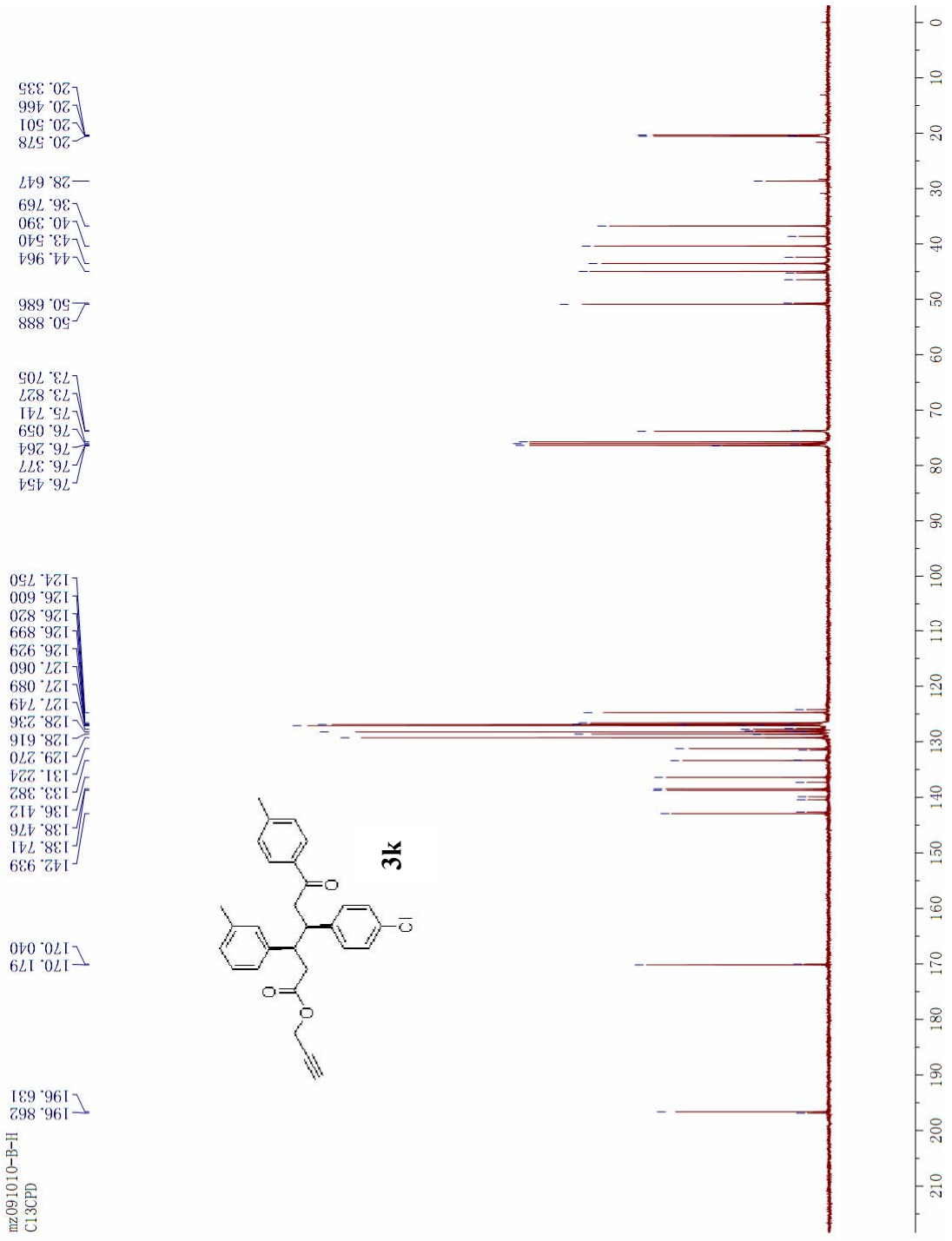

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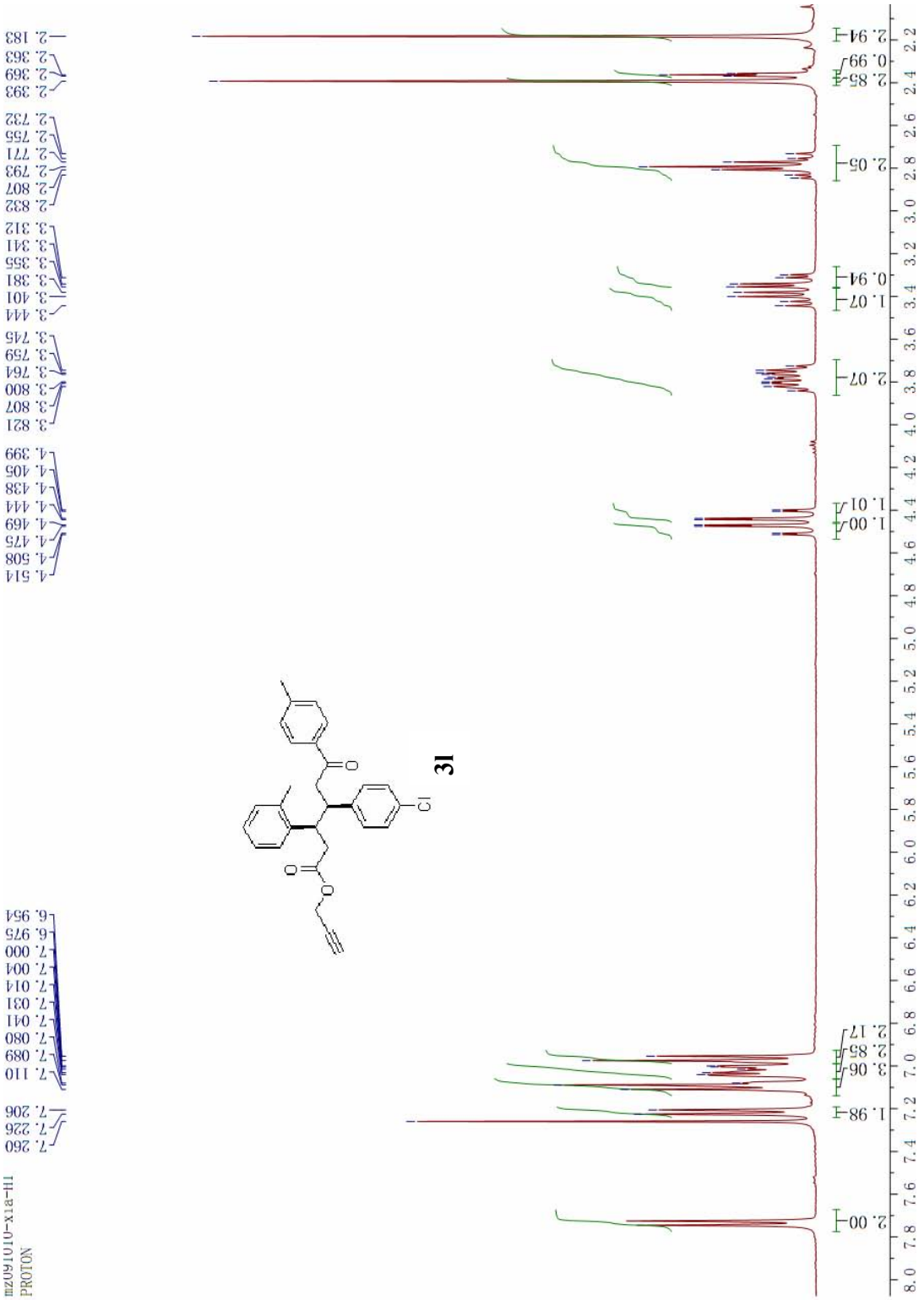
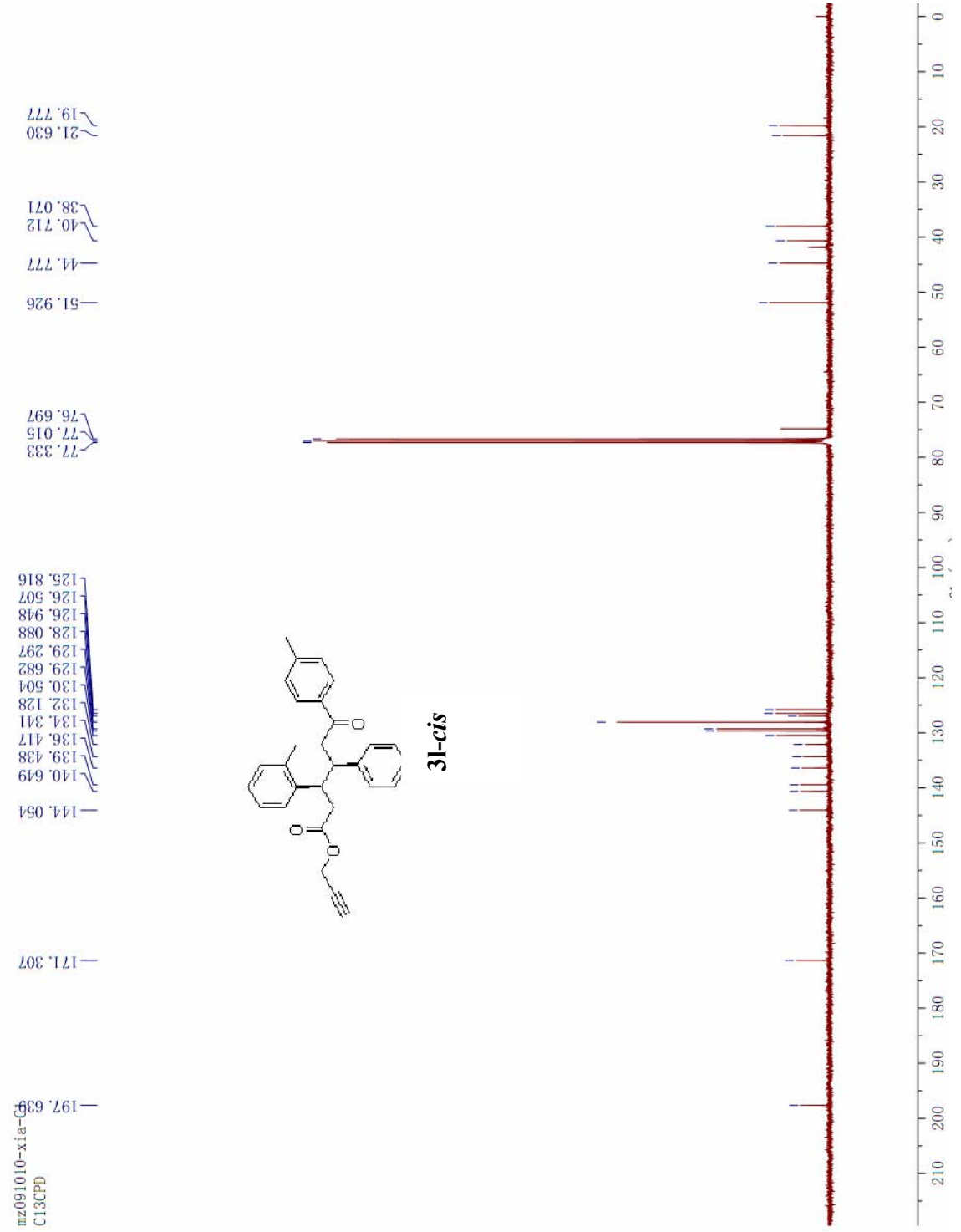


^{13}C NMR of compound 3l *cis* isomer



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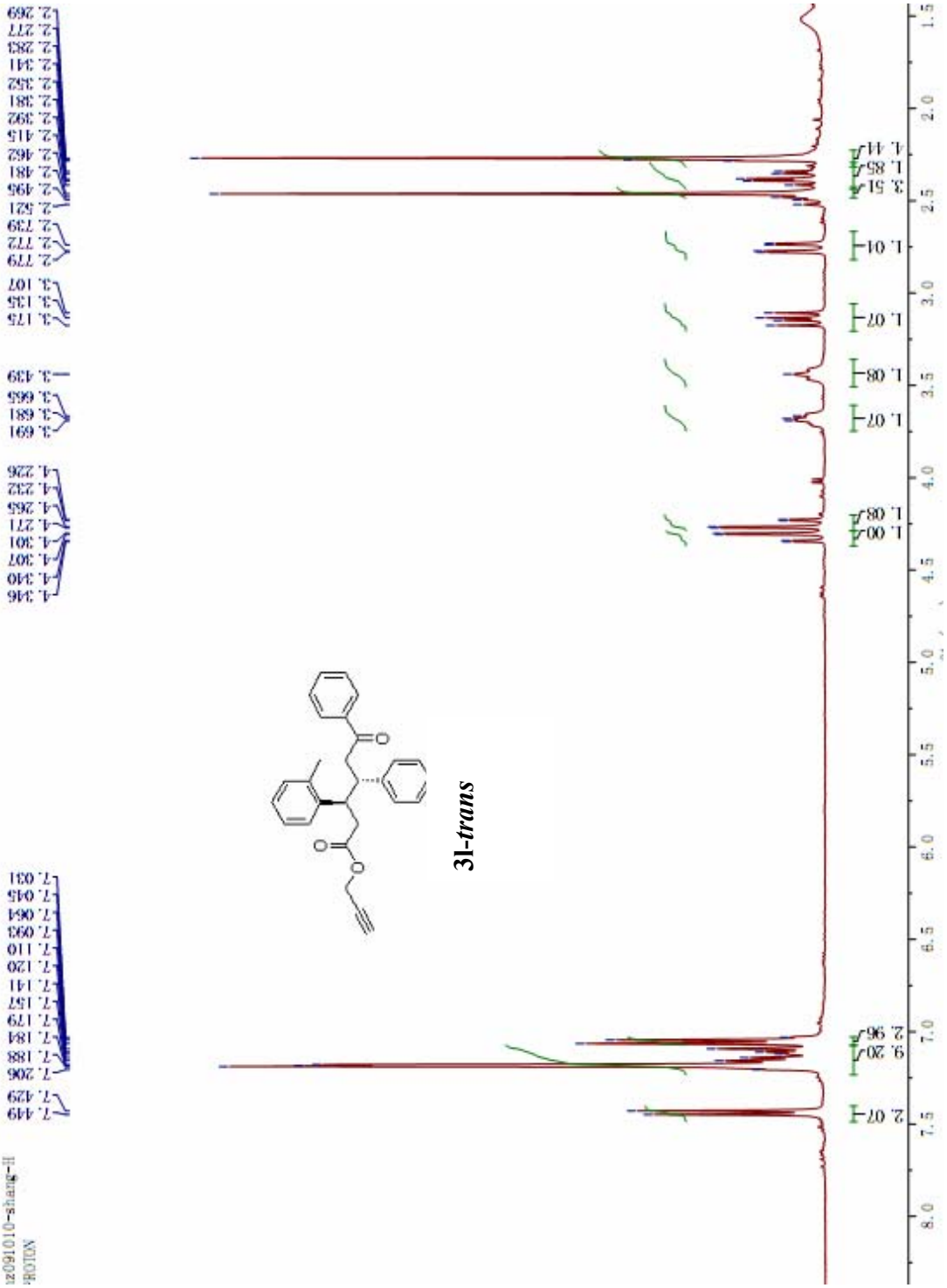

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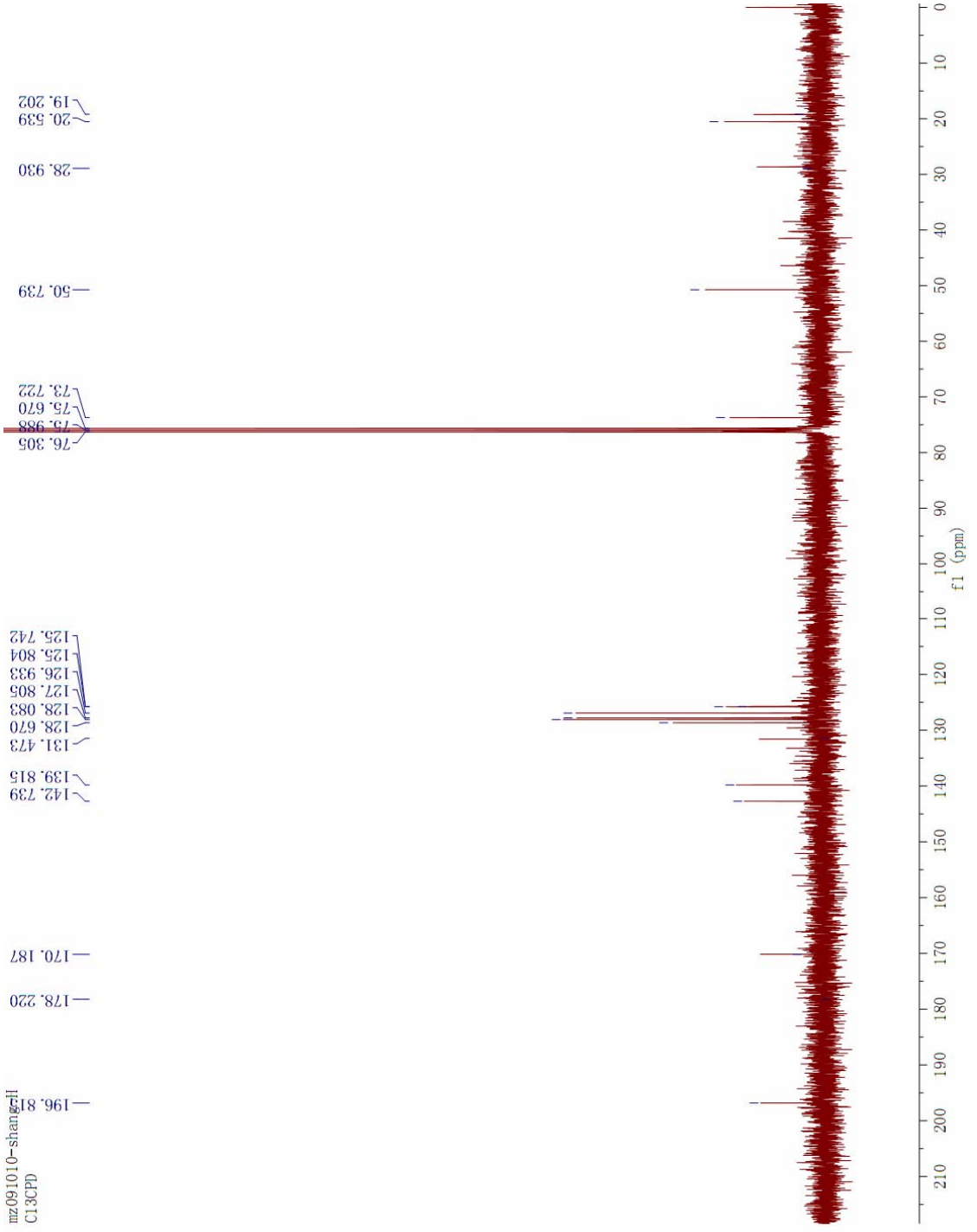

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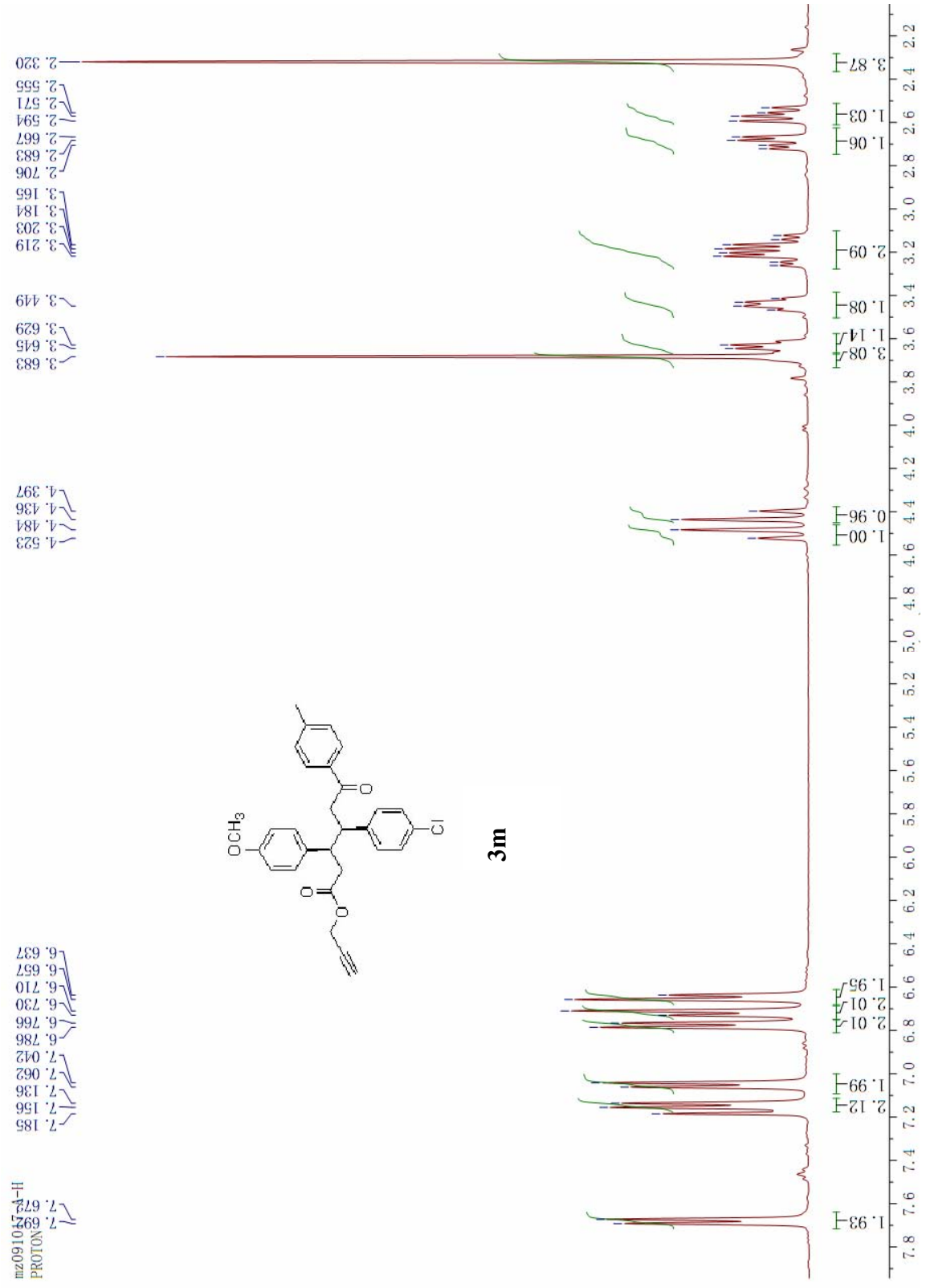

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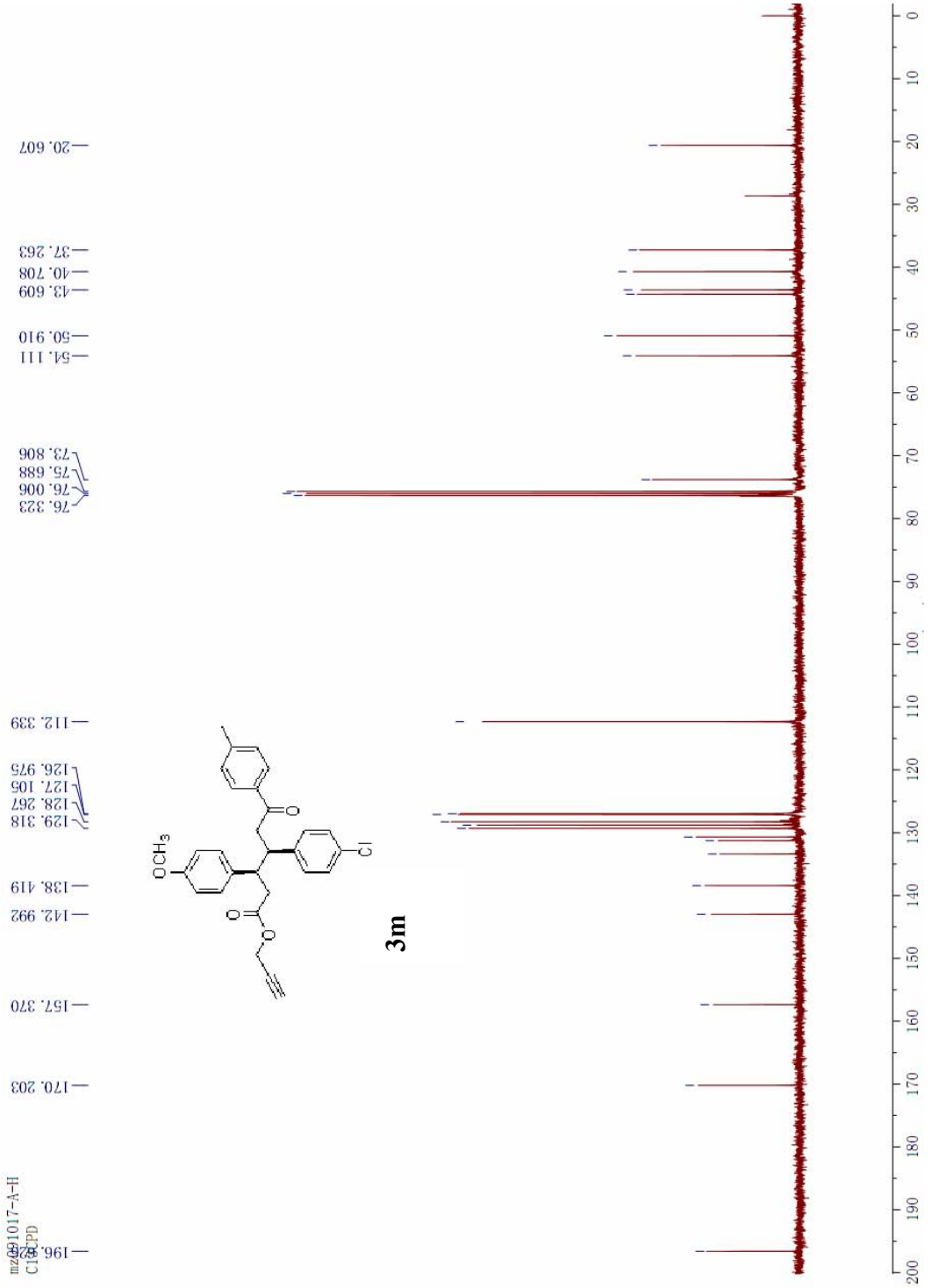

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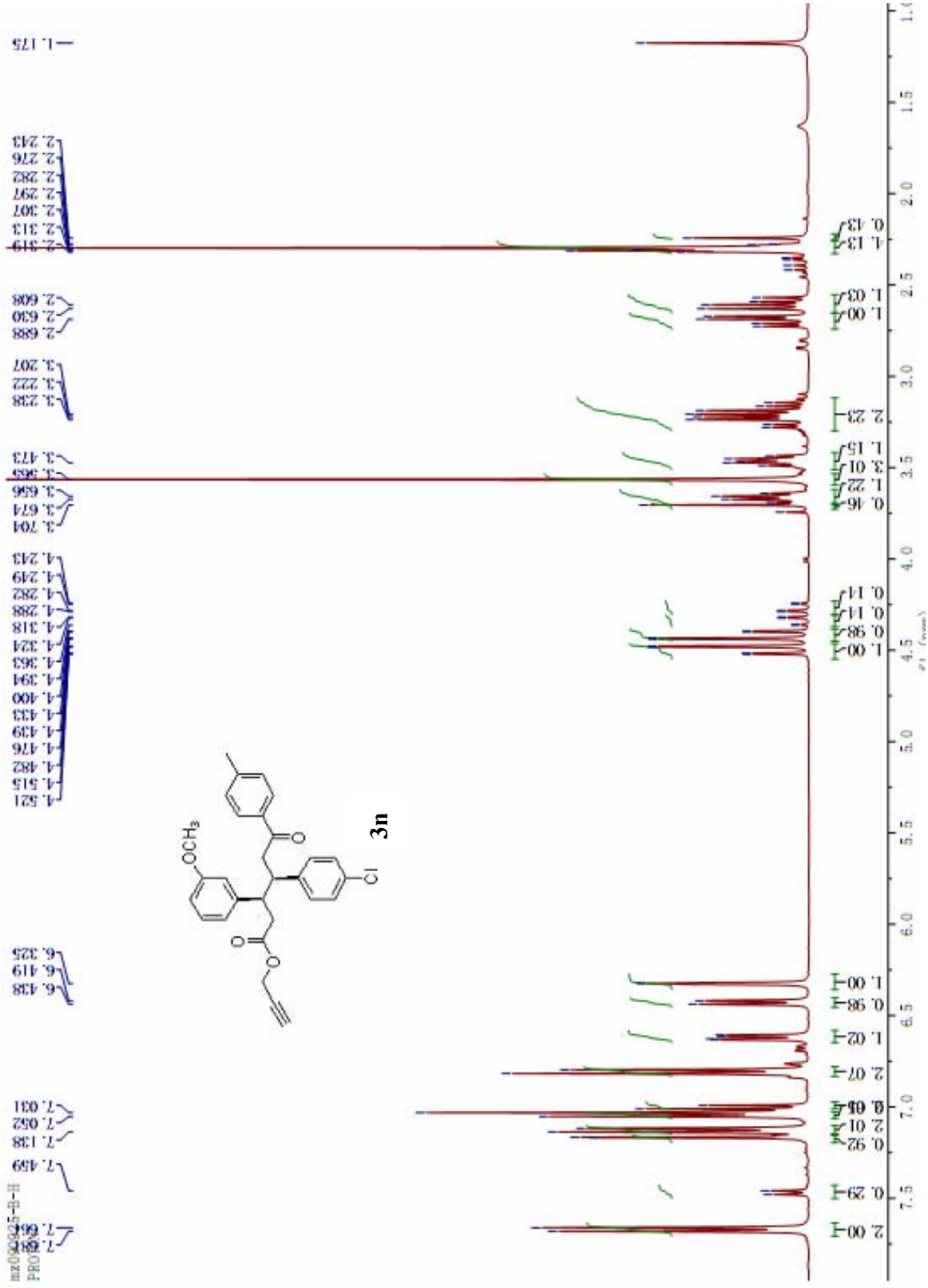

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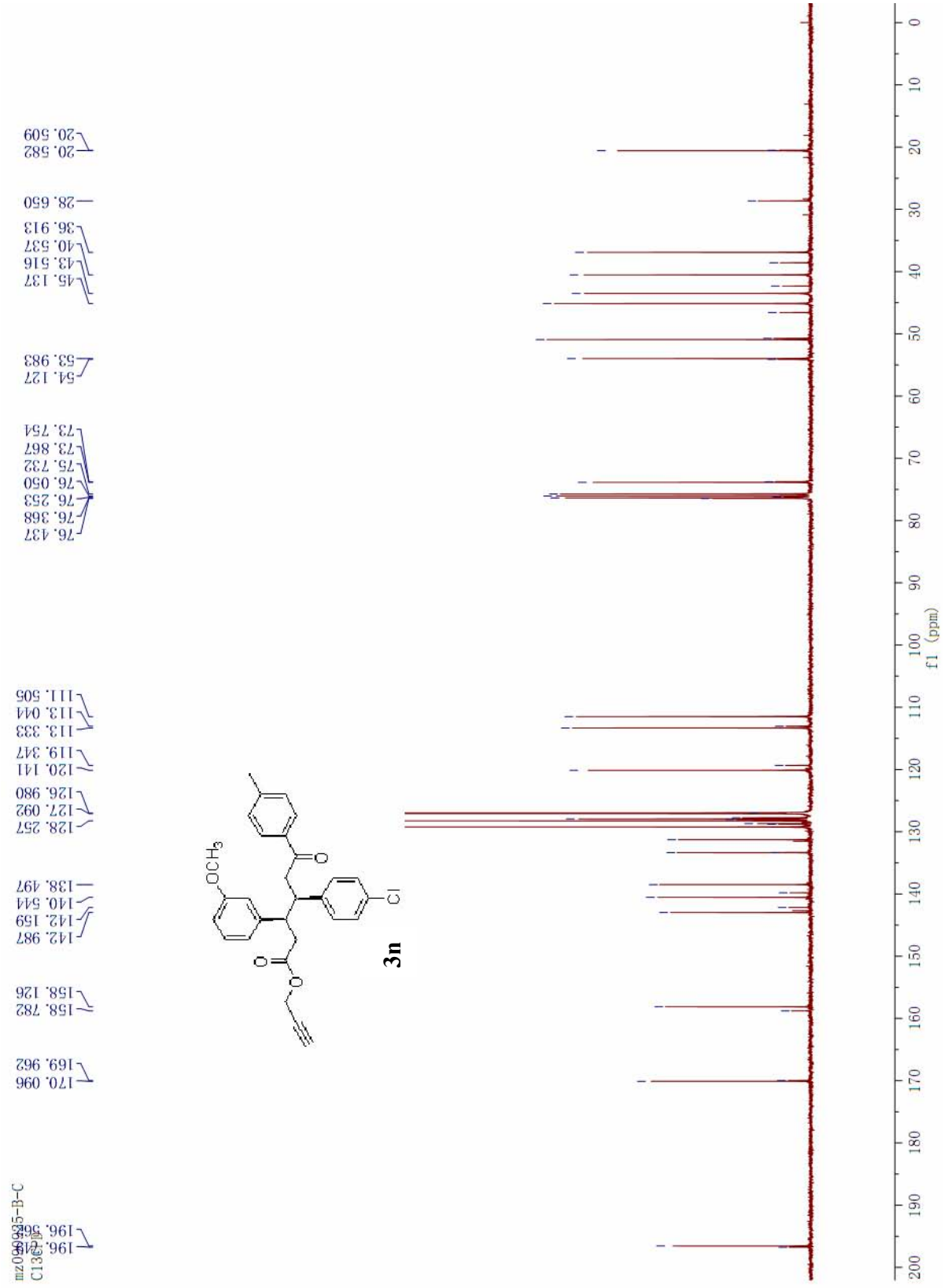

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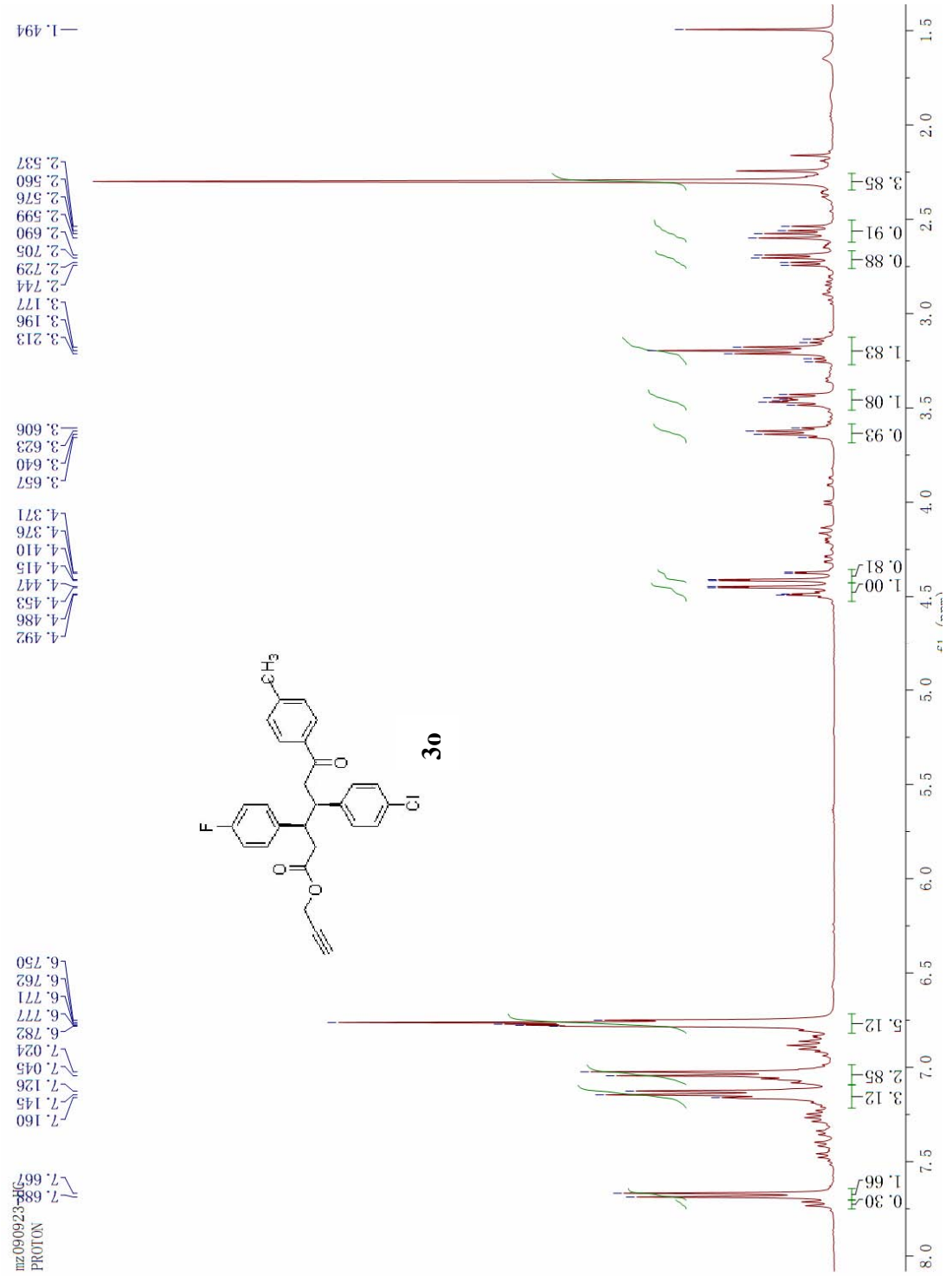

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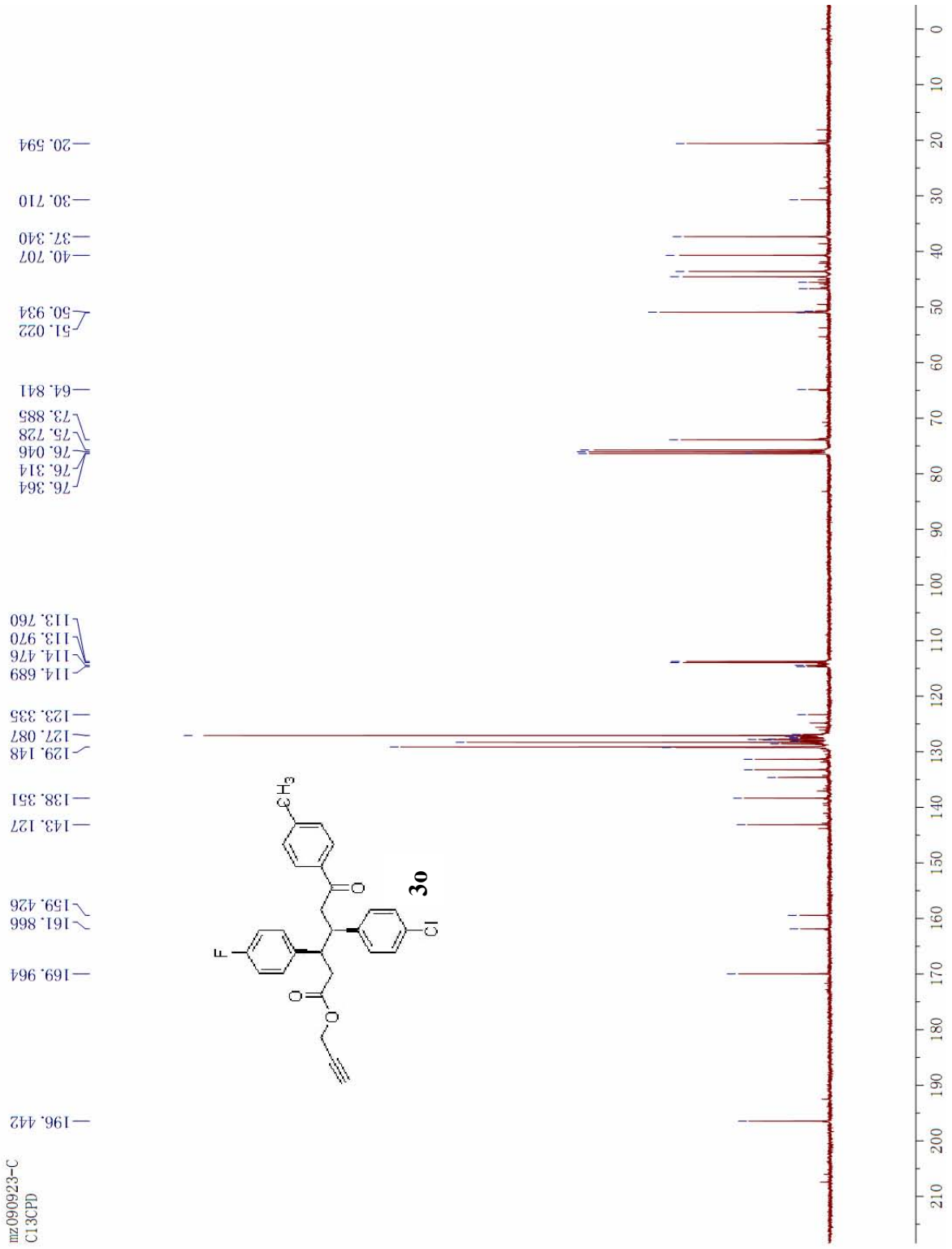

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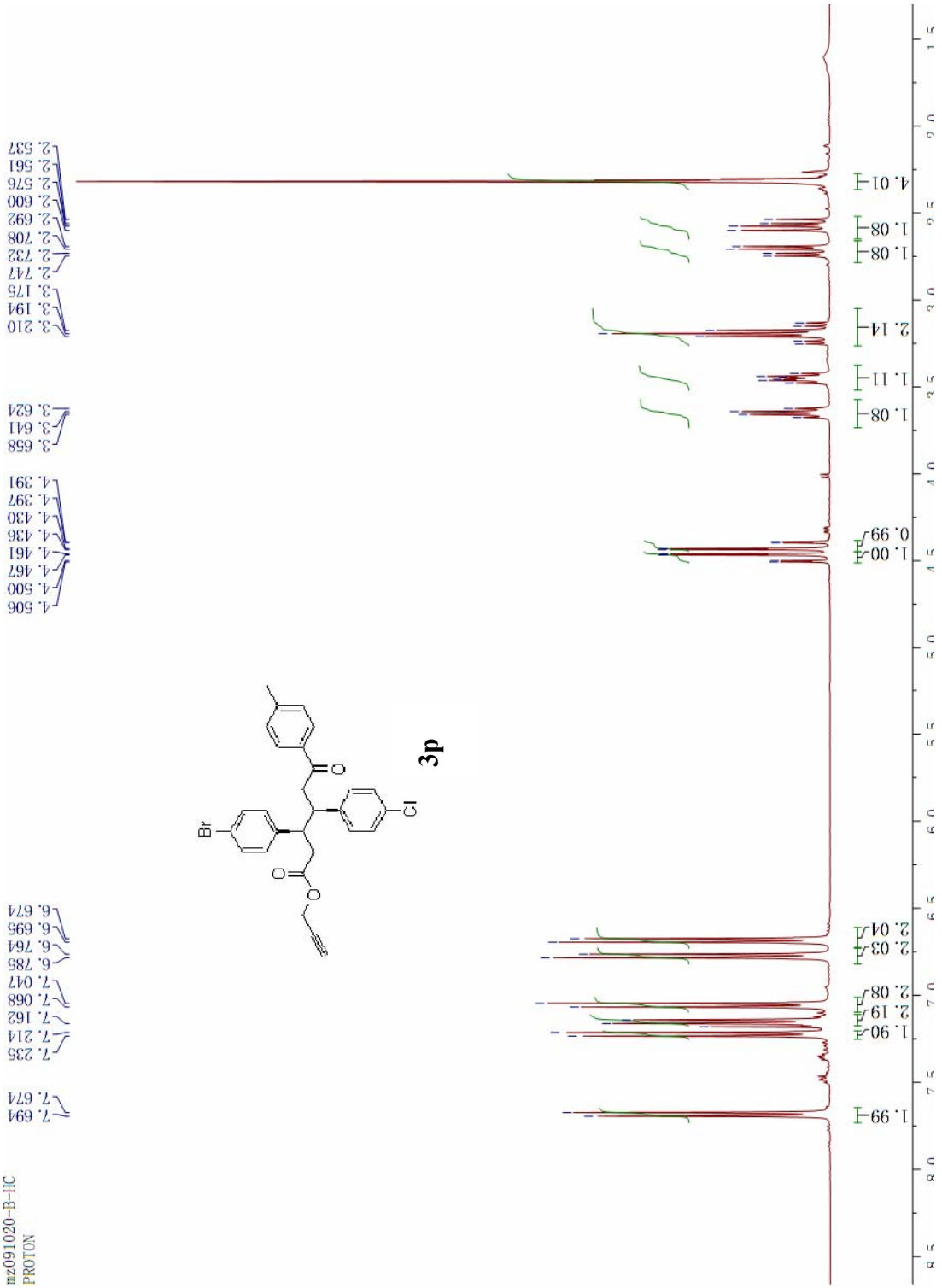

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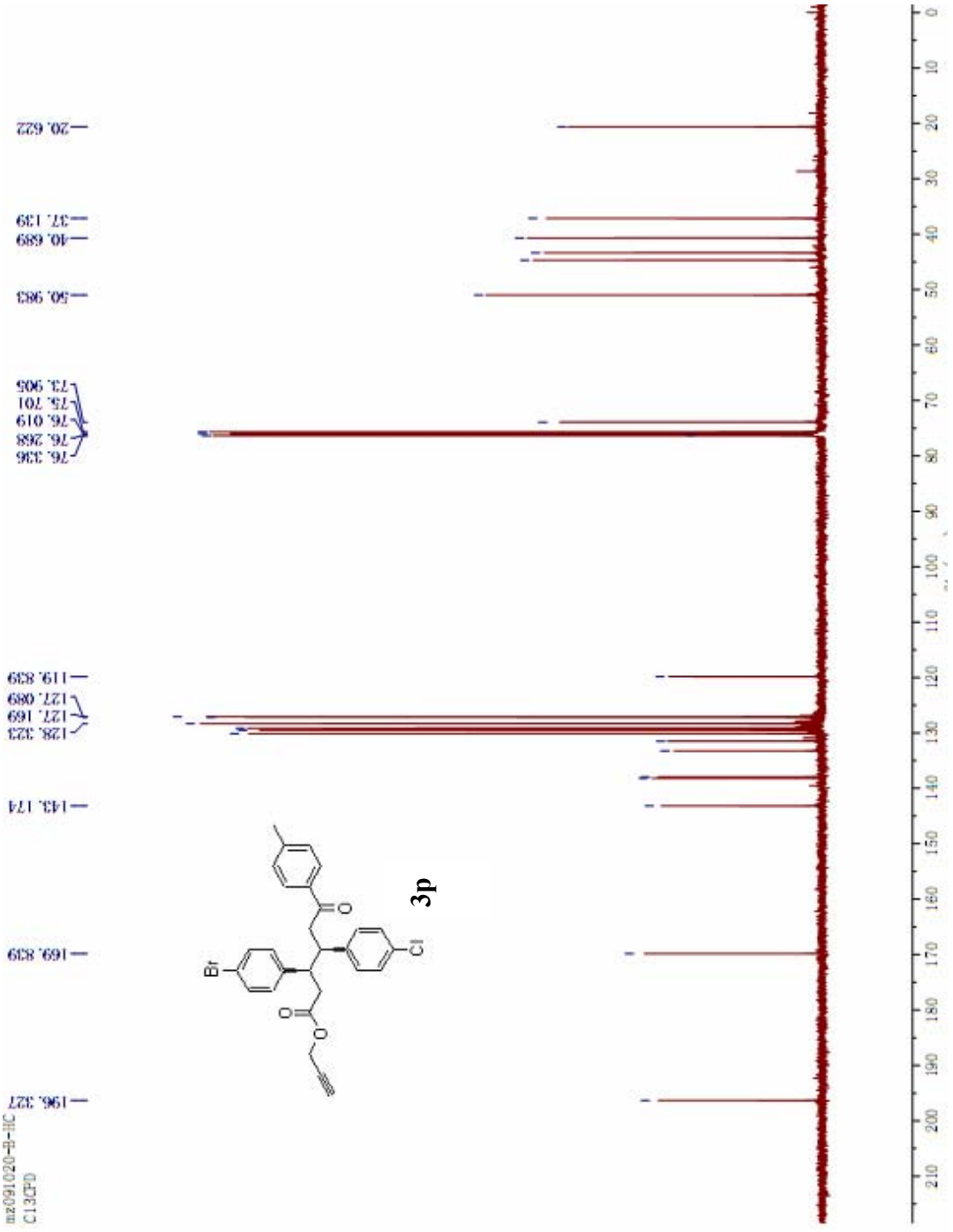

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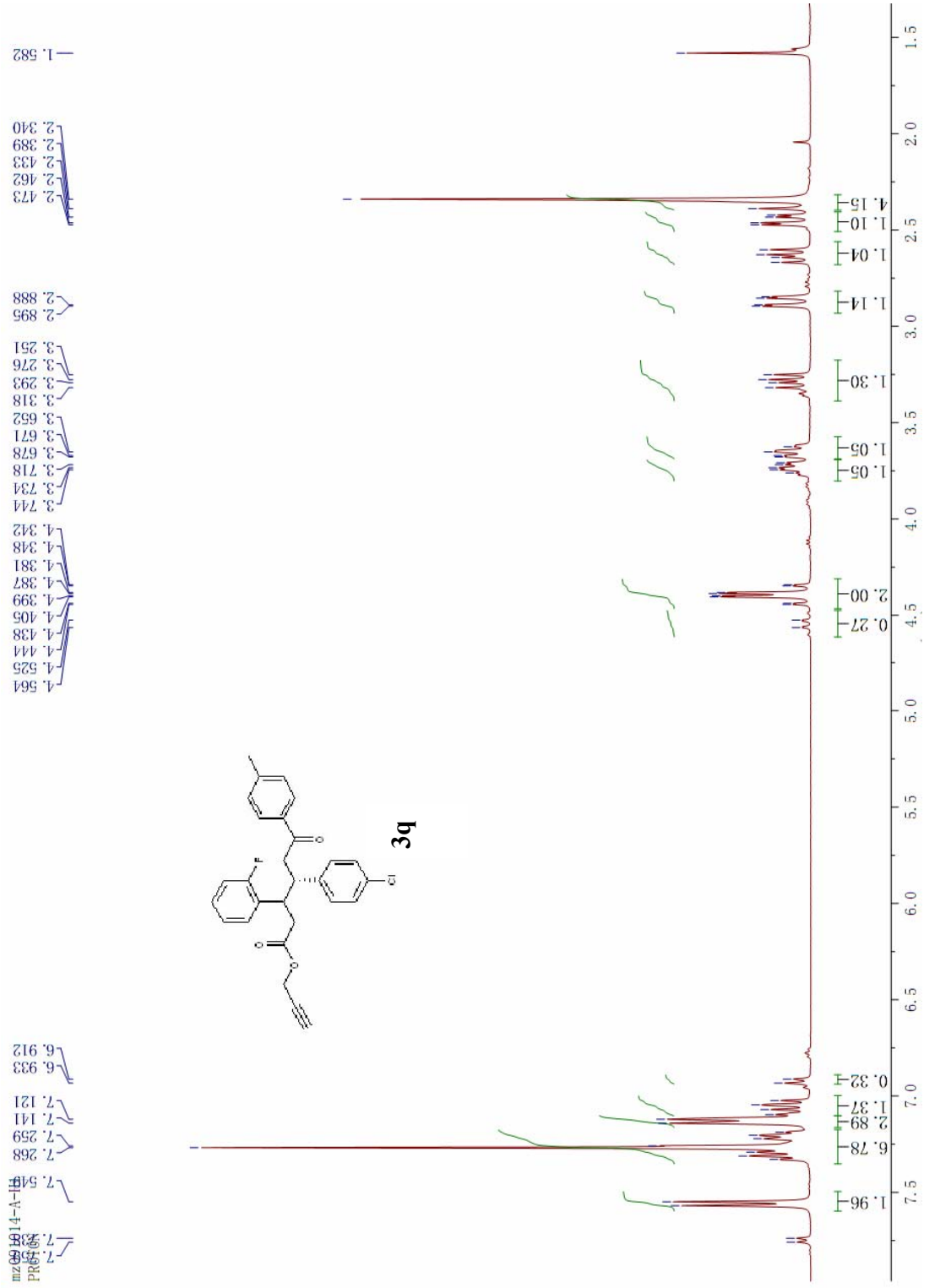

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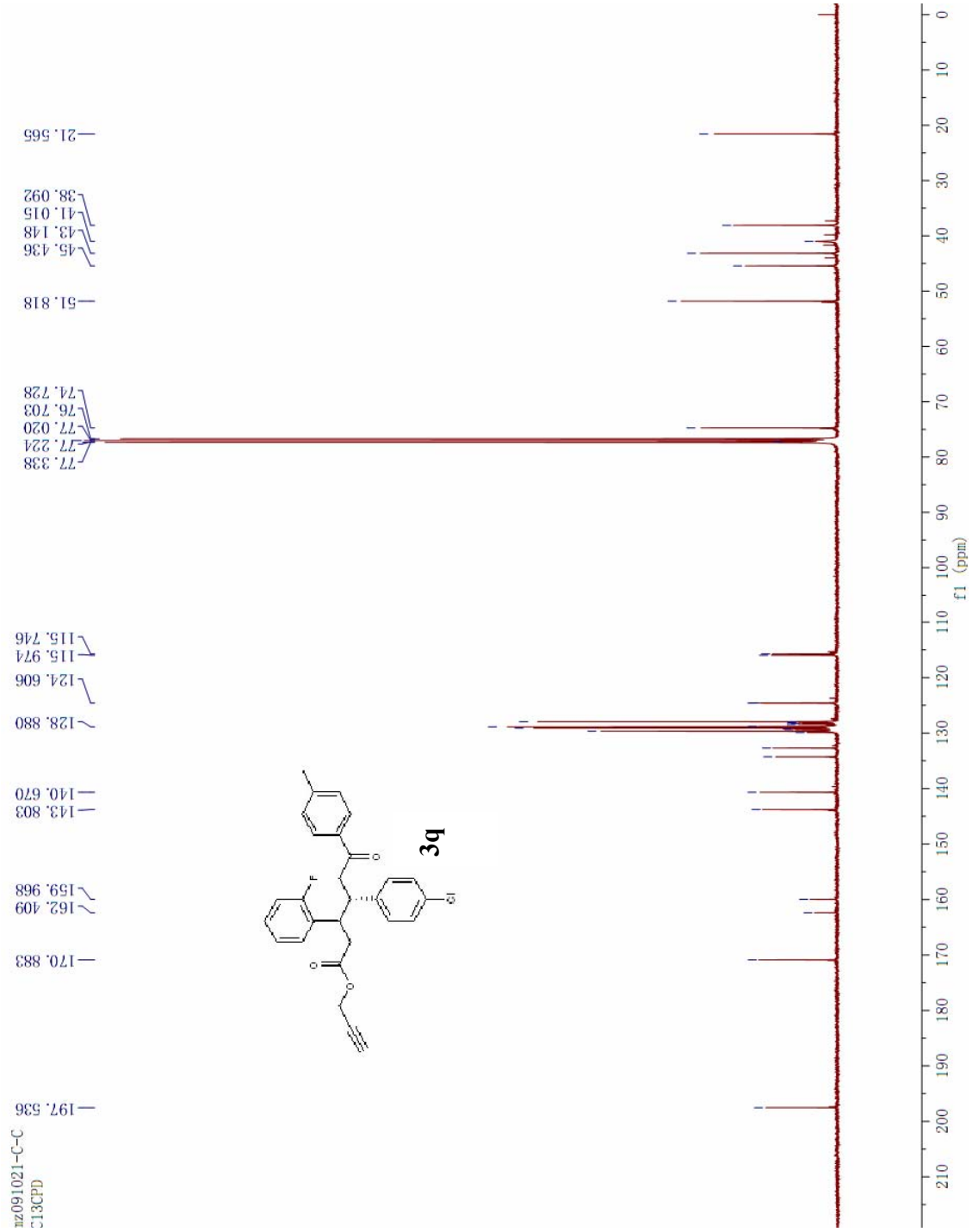

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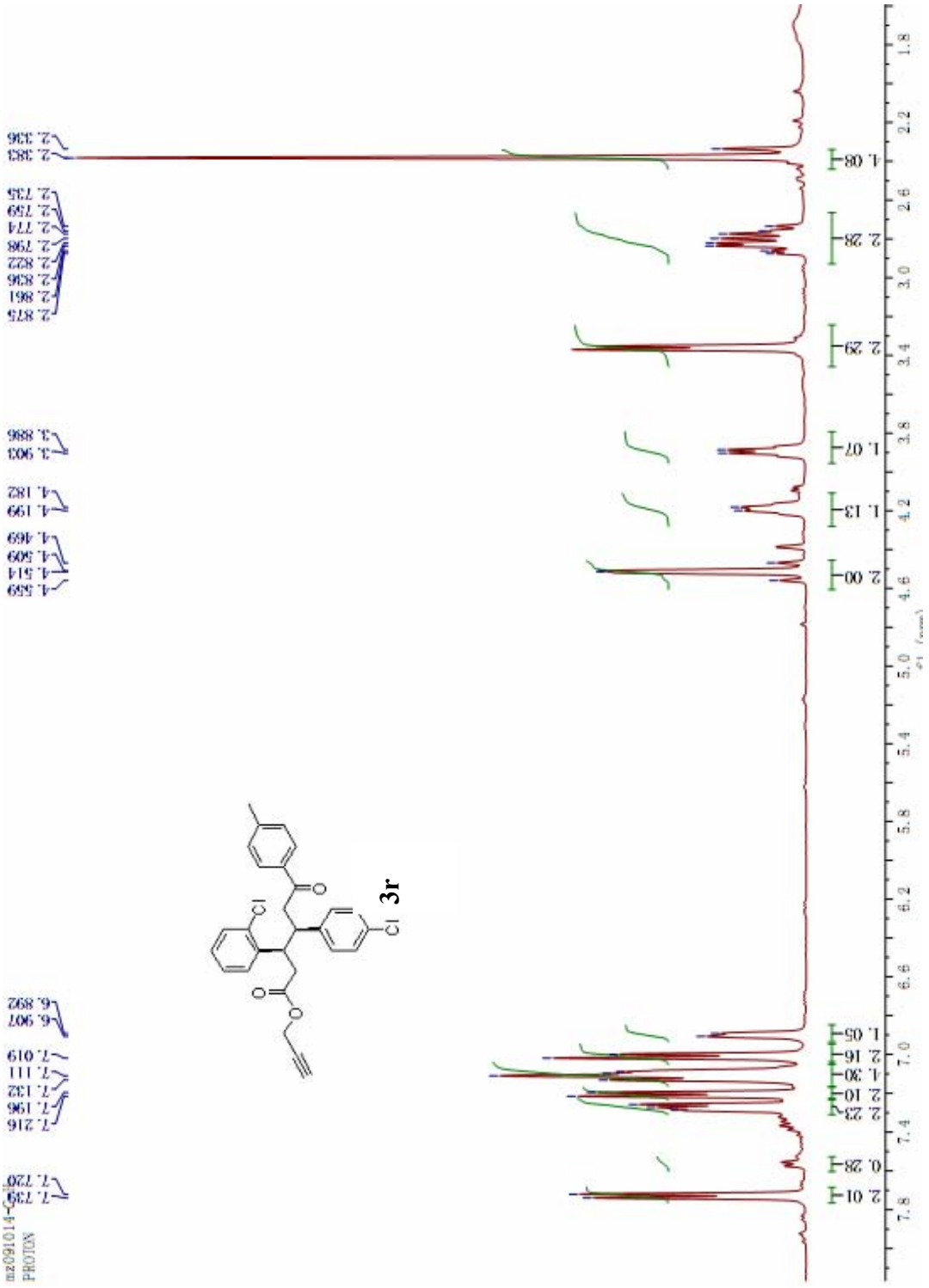

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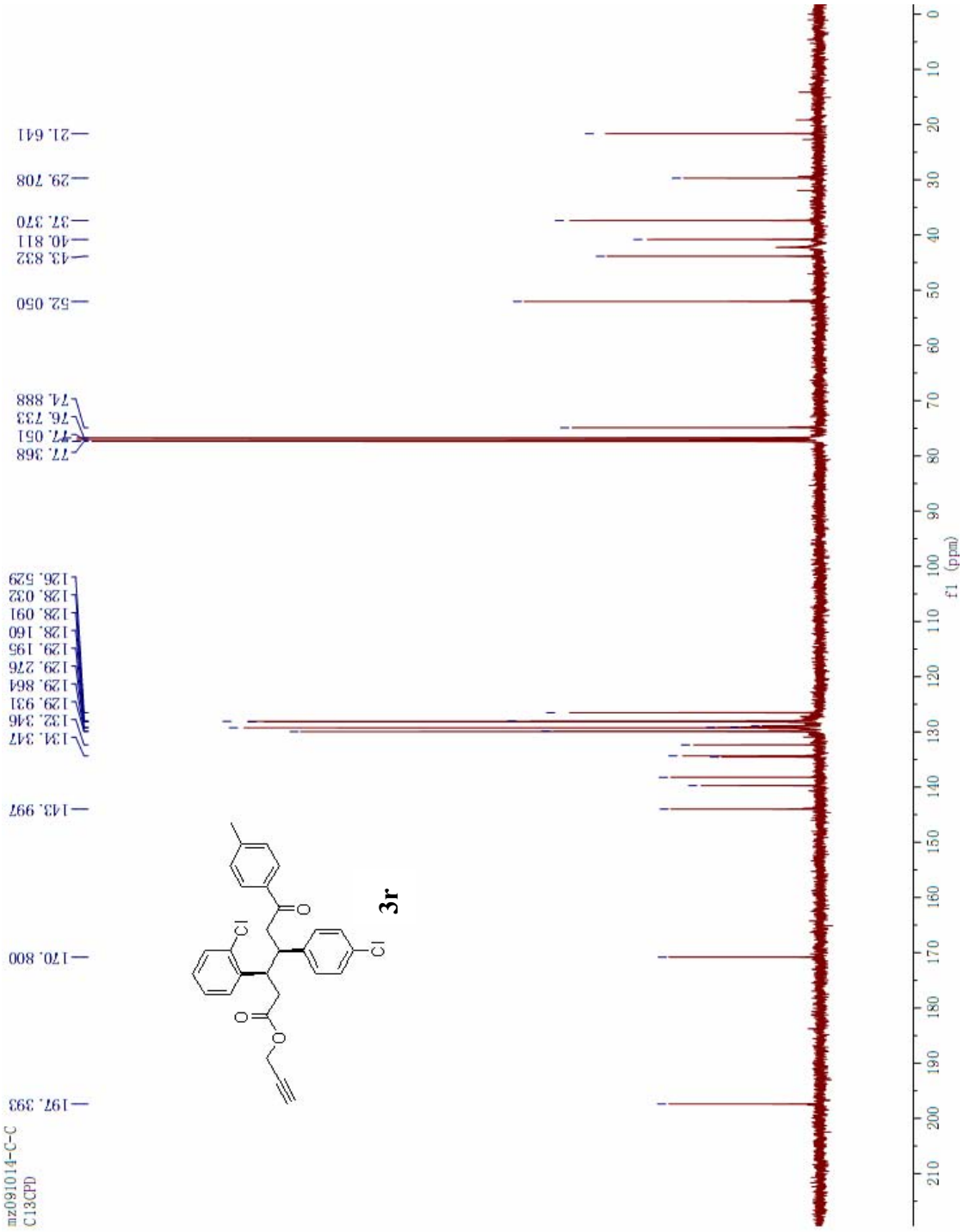

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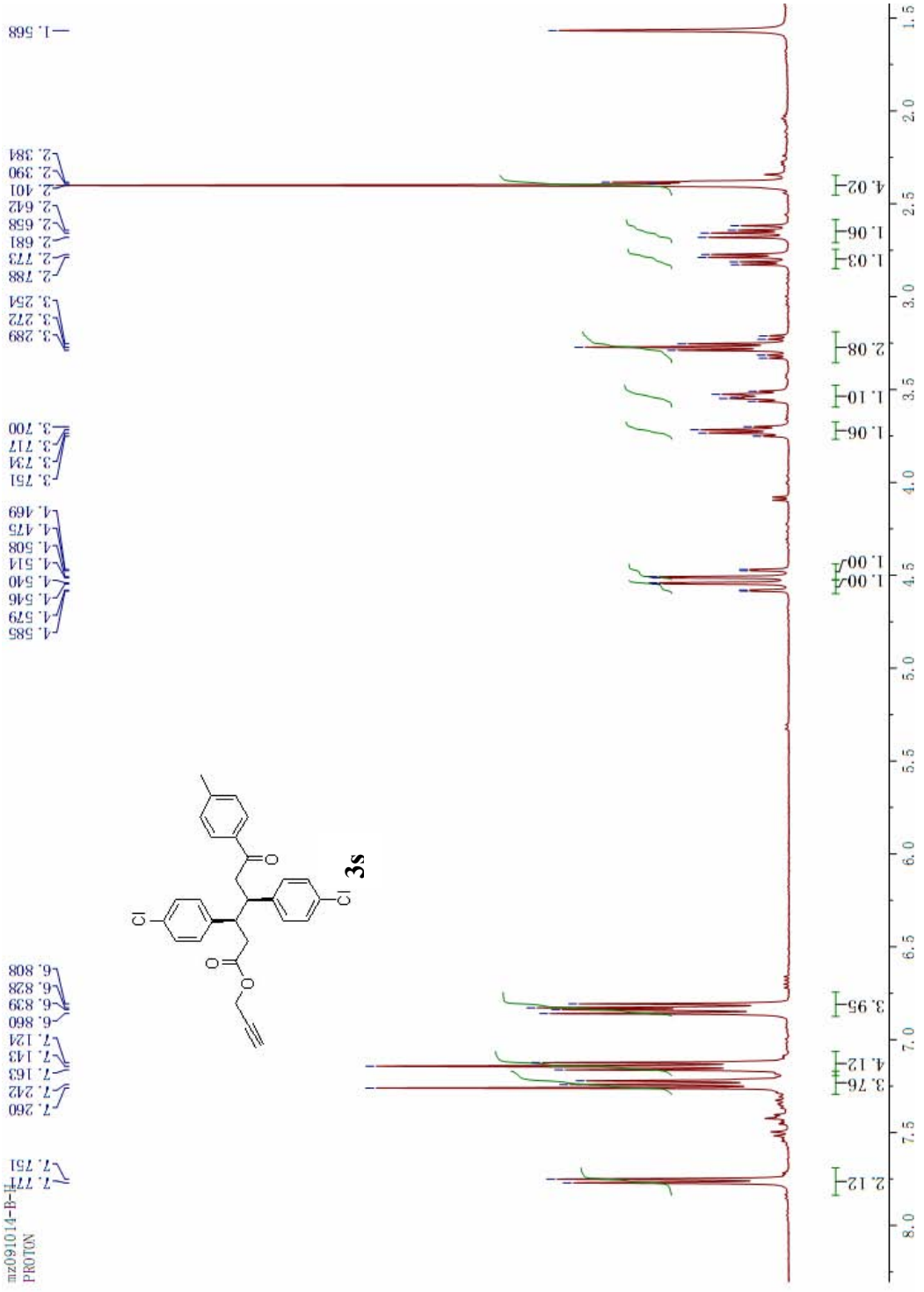

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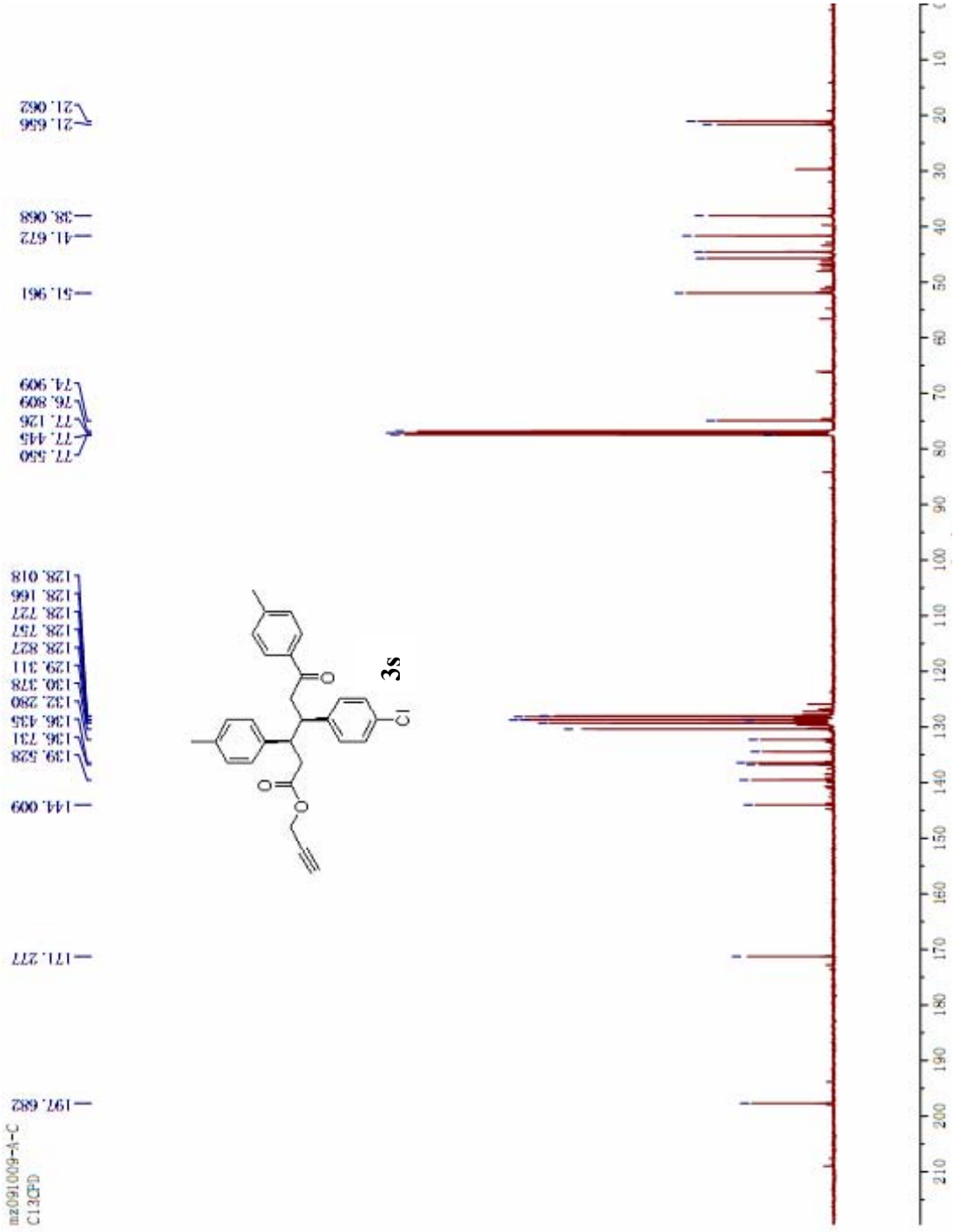

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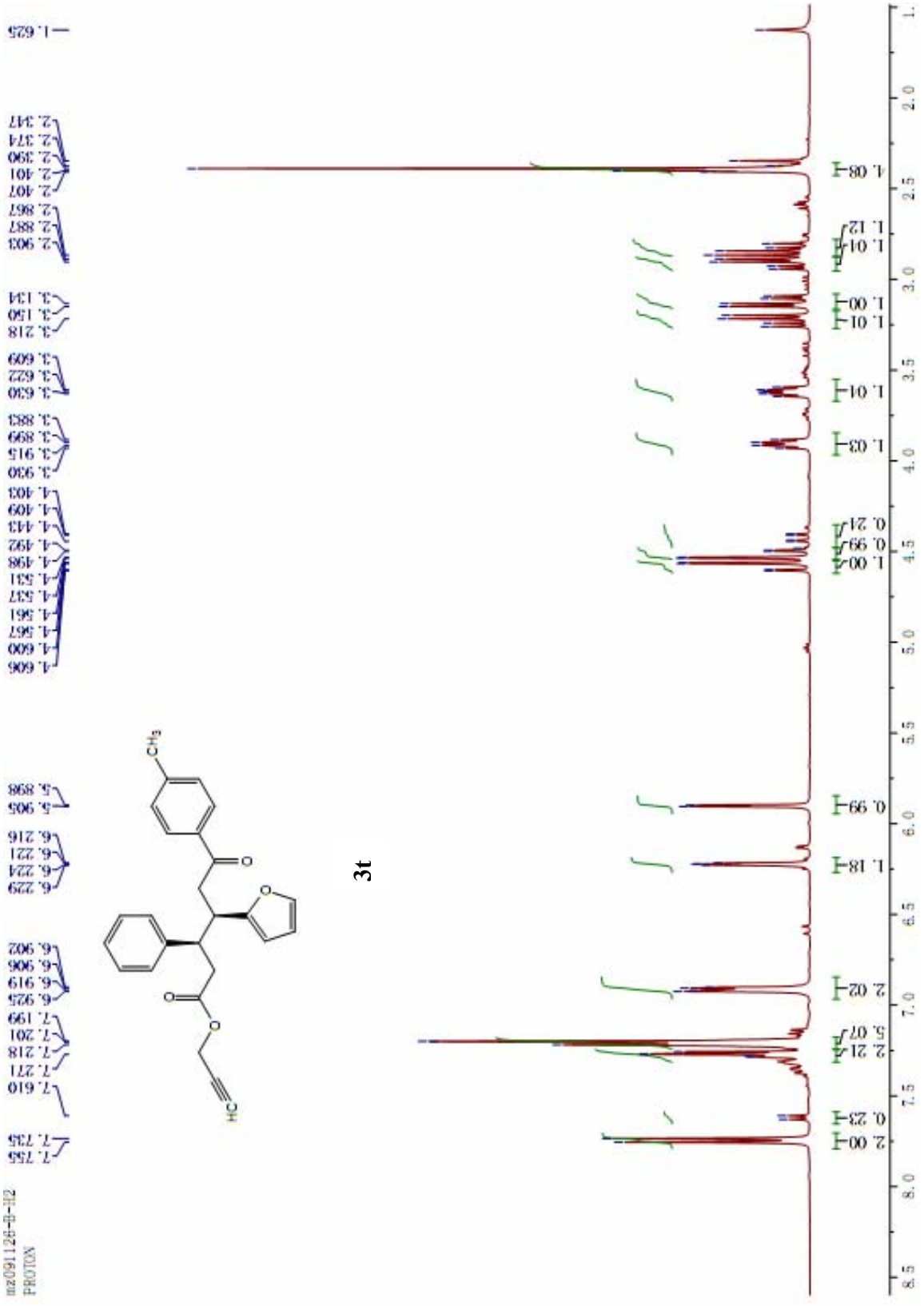

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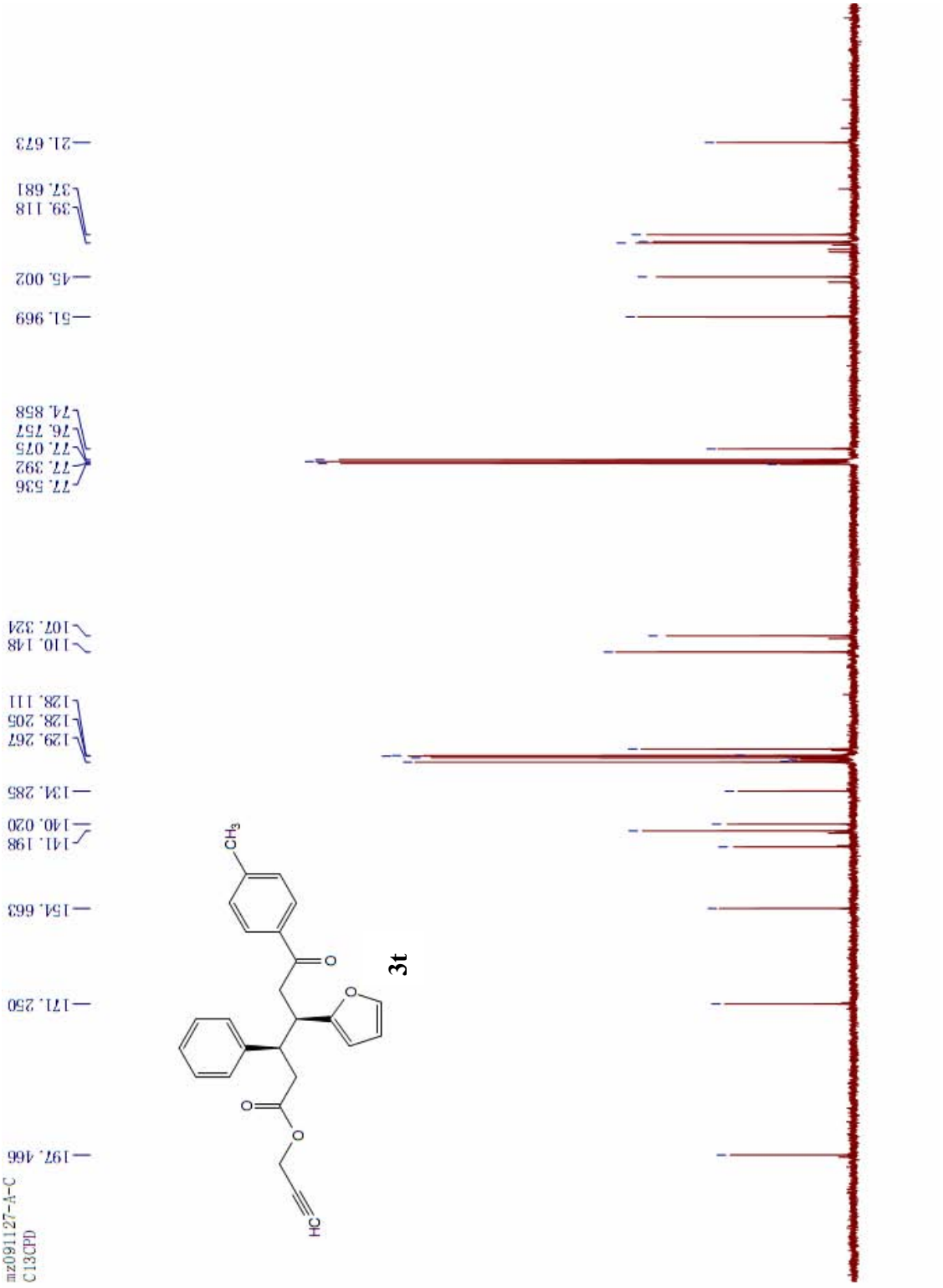

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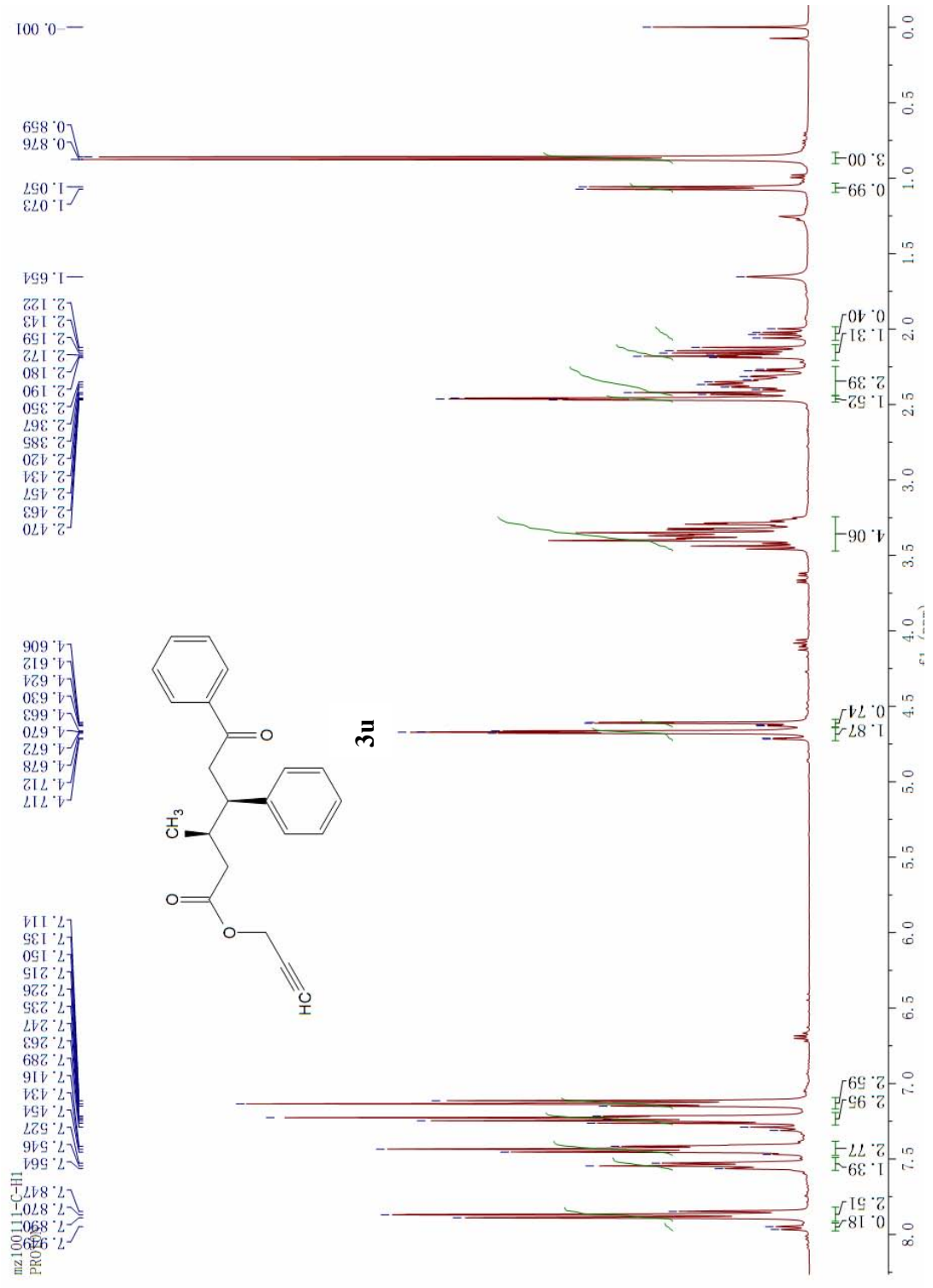

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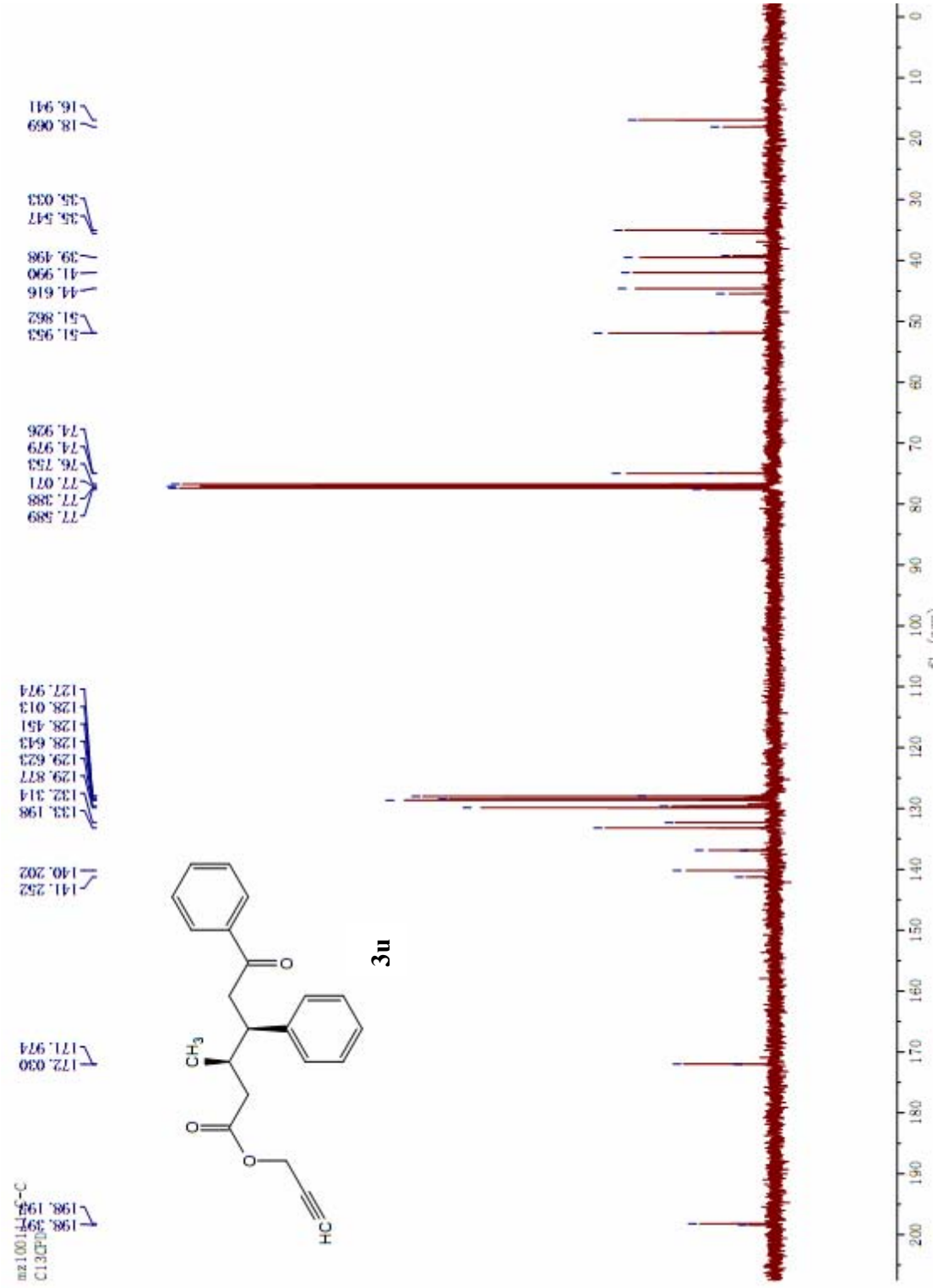

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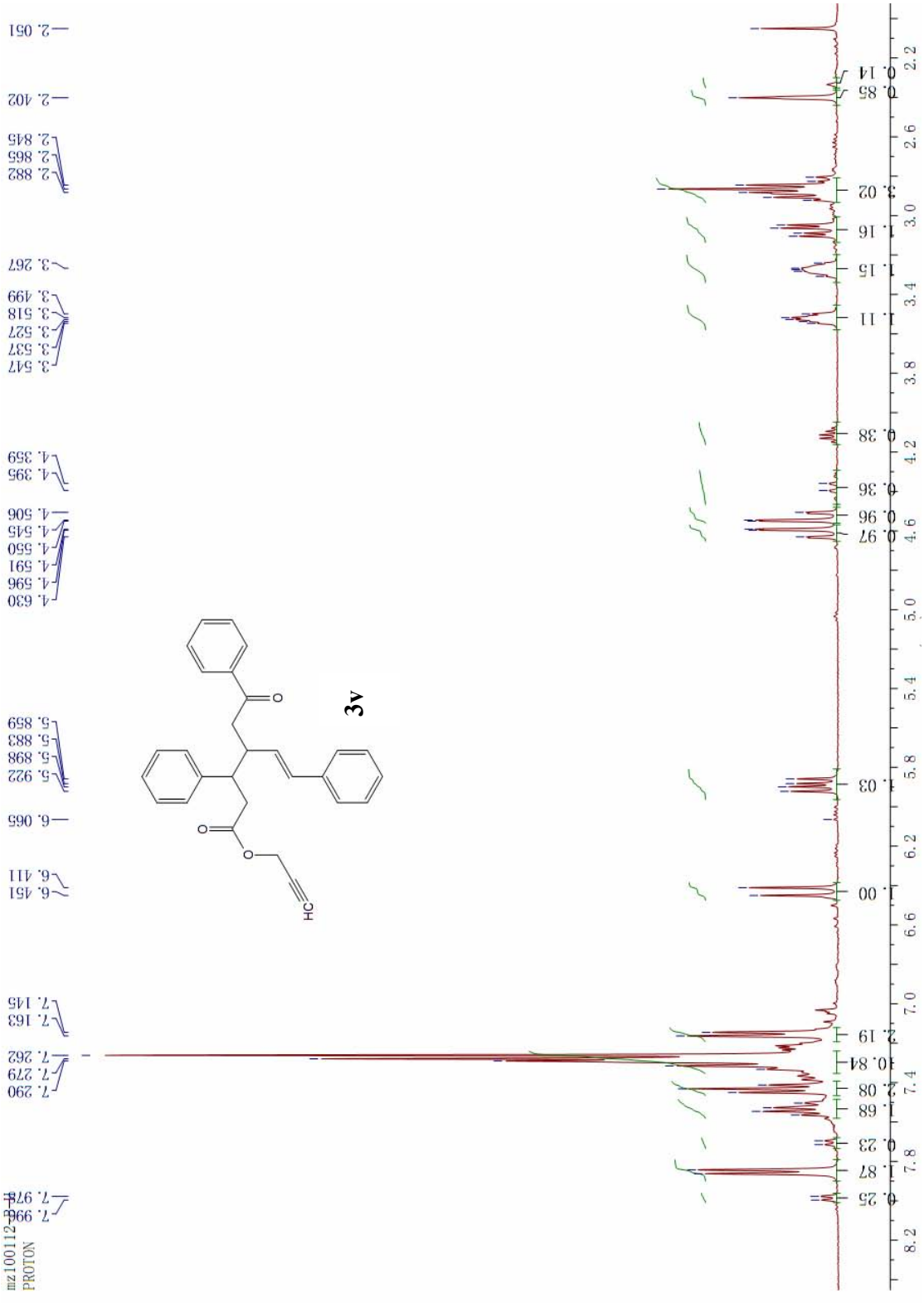

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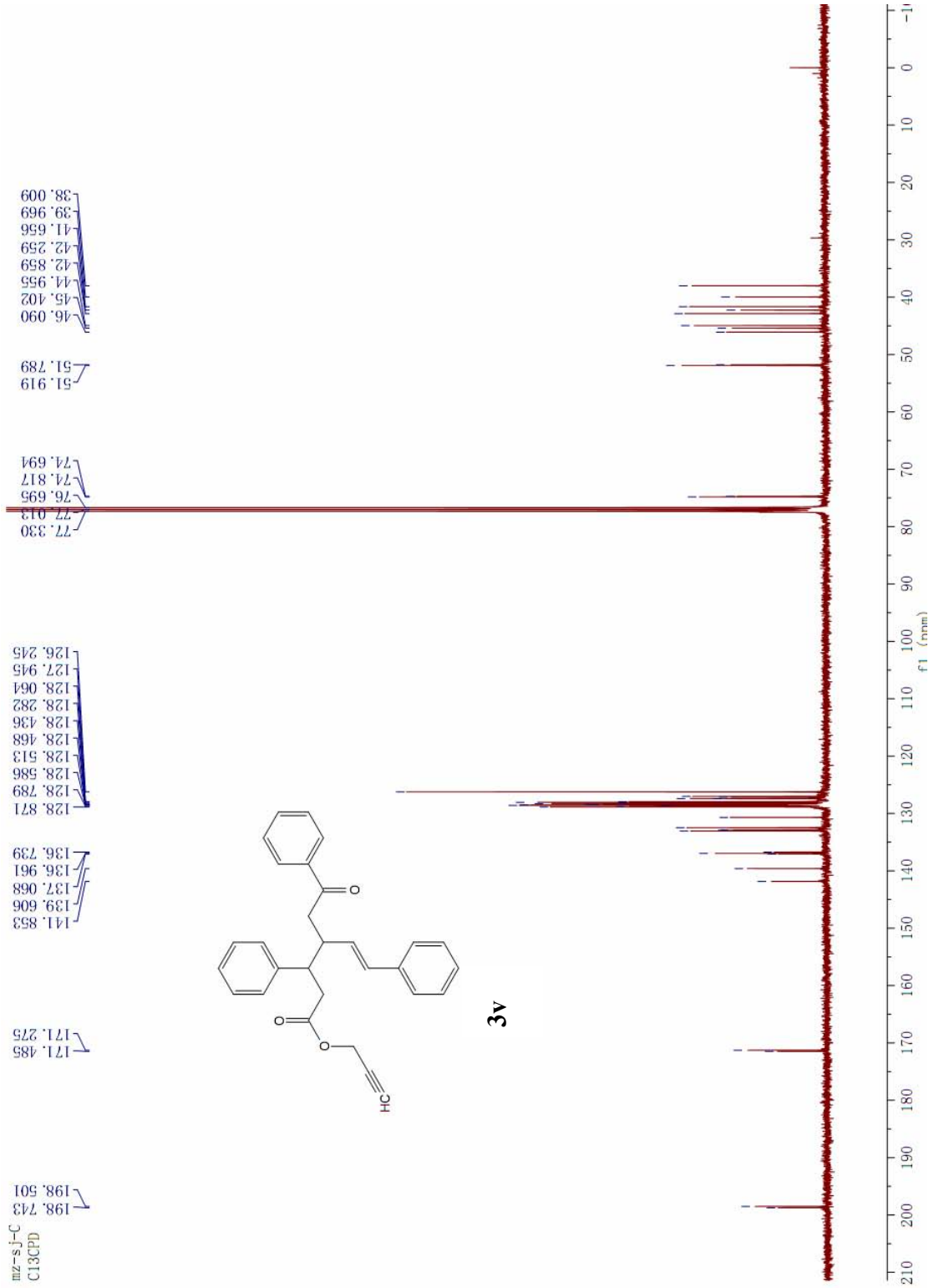

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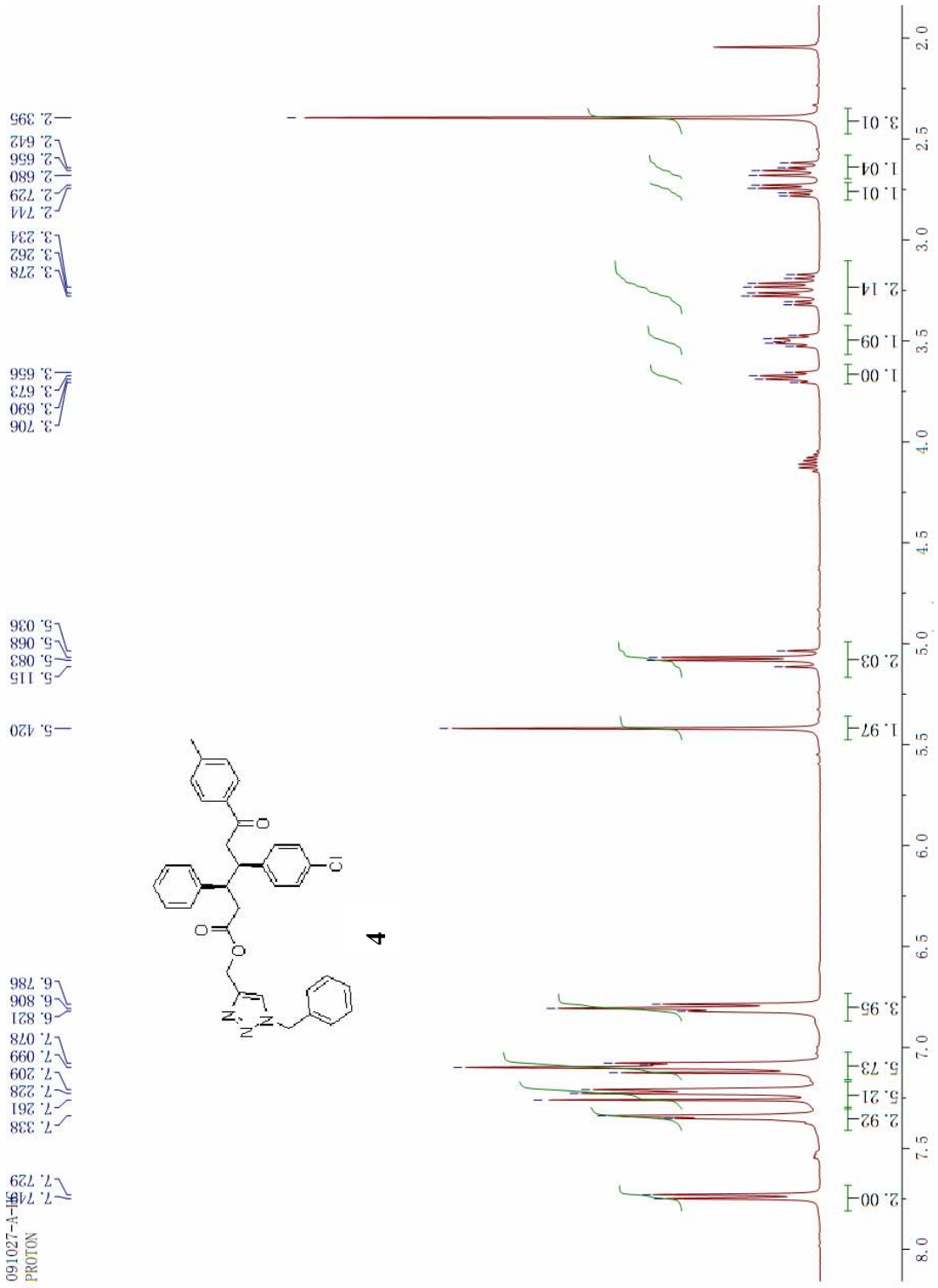

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