Synthesis, photolysis studies and *in vitro* photorelease of photolabile TRPV1 agonists and antagonists

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Electronic Supplementary Information

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General experimental methods

^{1}H NMR spectra were recorded at 300 MHz or 400 MHz, on Bruker Avance spectrometers, using deuteriochloroform (or other indicated solvent) as reference and internal deuterium lock. The chemical shift data for each signal are given as δ in units of parts per million (ppm) relative to tetramethylsilane (TMS) where δ_{TMS} = 0.00 ppm. The multiplicity of each signal is indicated by: s (singlet); br s (broad singlet); d (doublet); dd (doublet of doublets); m (multiplet) etc. *^{13}C NMR spectra* were recorded at 75.5 MHz or 100 MHz using the DEPT Q pulse sequence with broadband proton decoupling and internal deuterium lock. The chemical shift data for each signal are given as δ in units of ppm relative to TMS where δ_{TMS} = 0.00 ppm. Identical proton coupling constants (*J*) are averaged in each spectrum and reported to the nearest 0.1 Hz. *Low and high resolution mass spectra* were recorded on a Micromass LCT spectrometer using electrospray ionisation in either positive or negative polarity (ES^+ or ES^-). Certain samples were submitted to the National Mass Spectrometry Centre, Swansea. *m/z* values are reported in Daltons and followed by their percentage abundance in parentheses. *Microanalyses* were obtained on a Carlo Erber EA1110 analyser by the St Andrews University microanalysis service. *IR spectra* were recorded on a Perkin-Elmer GX FT-IR spectrometer as thin films between sodium chloride discs or as potassium bromide disks as indicated. *Absorption maxima* are reported in wavenumbers (cm^{-1}). Melting points were determined on an Electrothermal 9100 and are uncorrected. *Optical rotations* were measured on a Perkin-Elmer 341 polarimeter using cells with a path length of 1 dm. The concentration (*c*) is expressed in g/100 mL (equivalent to g/0.1 dm^3). Specific rotations are denoted $[\alpha]_D^T$ and are given in implied units of 10^{-1} deg cm^2 g^{-1} (T= ambient temperature in °C). *Analyitcal thin-layer chromatography* (TLC) was carried out on Merck silica gel 60 F_{254} pre-coated aluminium-backed plates. Visualisation of the plates was achieved using a UV lamp (λ_{max} 254 or 365 nm) or thermal development after dipping in either an ethanolic solution of phosphomolybdic acid or an ethanolic solution of 4-anisaldehyde, sulfuric acid and acetic acid. Flash column chromatography was carried out using Merck silica gel 60 (240-400 mesh), under a positive pressure of compressed air. Anhydrous CH_2Cl_2, THF, diethyl ether and hexane were obtained using a MBRAUN GmbH MB SPS-800 solvent purification system. Anhydrous DMF was purchased from Sigma Aldrich, UK and used without further purification. Where appropriate and if not stated otherwise, all non aqueous reactions were performed under an inert atmosphere of nitrogen or argon in flame-dried glassware, using a vacuum manifold with nitrogen or argon passed through 4 Å molecular sieves and self-indicating silica gel. *In vacuo* refers to the use of a rotary evaporator attached to a diaphragm pump. Hexane refers to a mixture of hexanes and brine refers to a saturated aqueous solution of sodium chloride.

3-Methoxy-4-(triisopropyloxy)benzonitrile (12) ^{1}H NMR spectrum

```
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PROCNO                   1
Date_             20061113
Time                 10.07
INSTRUM              av300
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PULPROG               zg30
TD                   32768
SOLVENT              CDCl3
NS                      16
DS                       2
SWH               4194.631 Hz
FIDRES            0.128010 Hz
AQ                3.9059956 sec
RG                    228.1
DW                  119.200 usec
DE                    6.00 usec
TE                   295.9 K
D1              1.00000000 sec
TD0                      1

======== CHANNEL f1 ========
NUC1                    1H
P1                   12.30 usec
PL1                  10.00 dB
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SI                   32768
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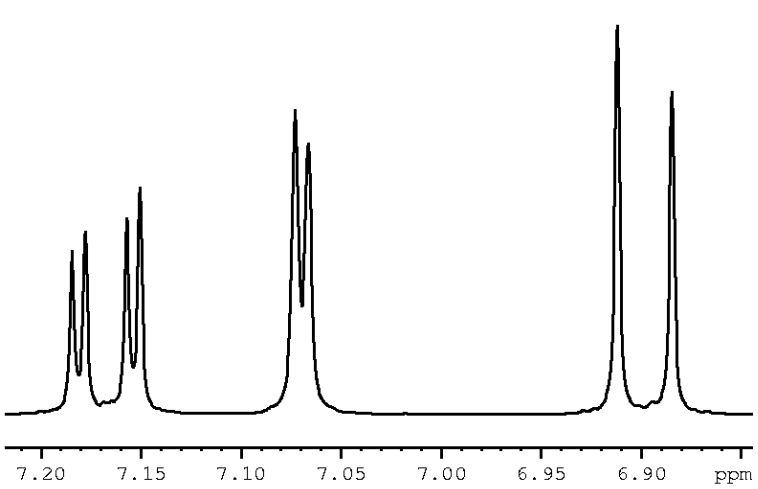

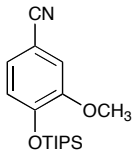

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TD                  65536
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NS                    800
DS                      8
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FIDRES            0.276427 Hz
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RG                18390.4
DW                  27.600 usec
DE                   6.00 usec
TE                  293.9 K
CNST2           145.0000000
CNST3             1.0000000
CNST4             5.0000000
D1                1.50000000 sec
d2                0.00172414 sec
d3                0.00431034 sec
D12               0.00002000 sec
D13               0.00000400 sec

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p2                   15.00 usec
PL1                   5.00 dB
SFO1            75.4587938 MHz

======== CHANNEL f2 ========
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NUC2                   1H
P3                    8.50 usec
p4                   17.00 usec
PCPD2                80.00 usec
PL2                   8.00 dB
PL12                 27.47 dB
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SF              75.4501170 MHz
WDW                     EM
SSB                      0
LB                    2.00 Hz
GB                       0
PC                    1.40
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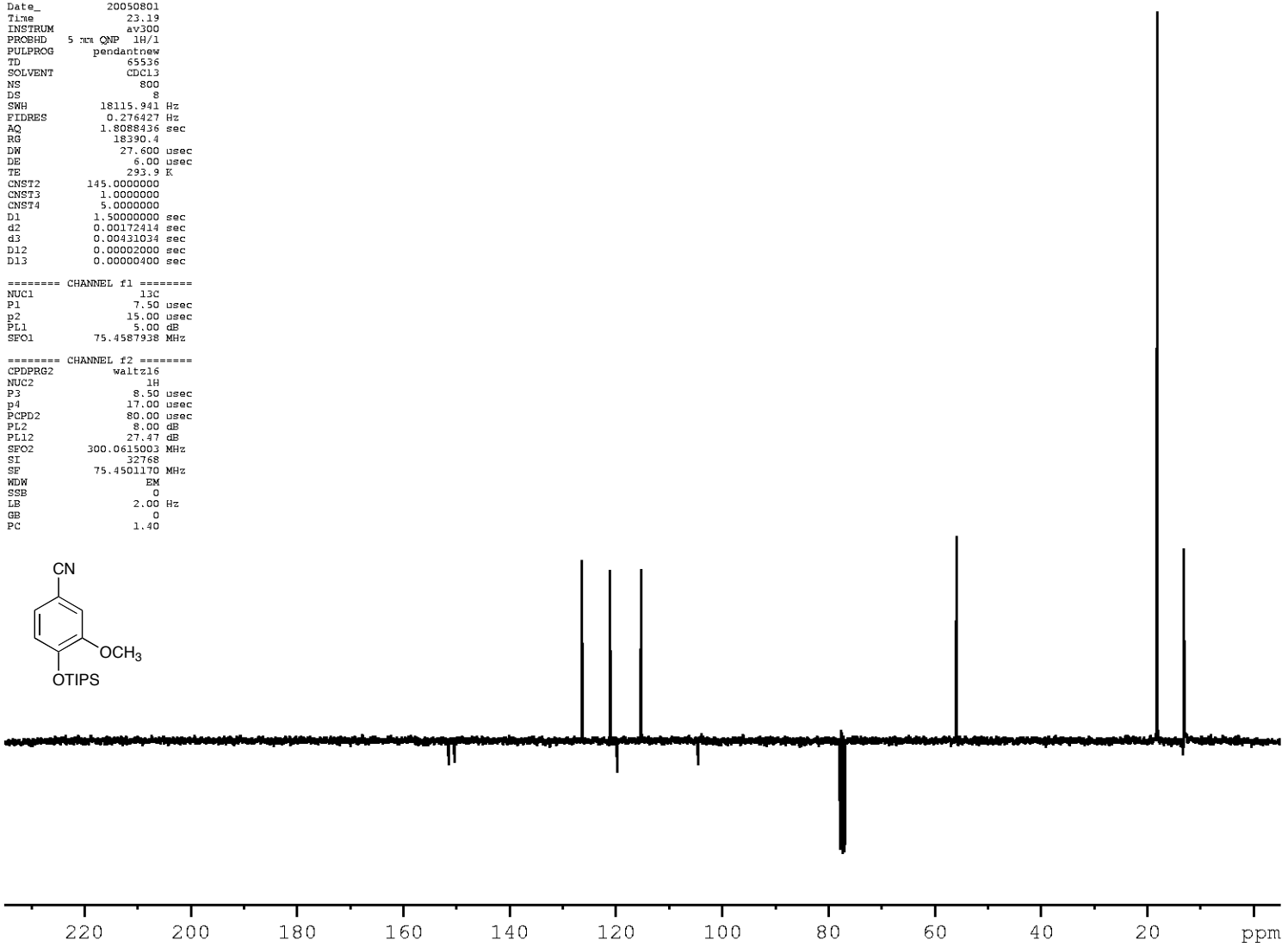

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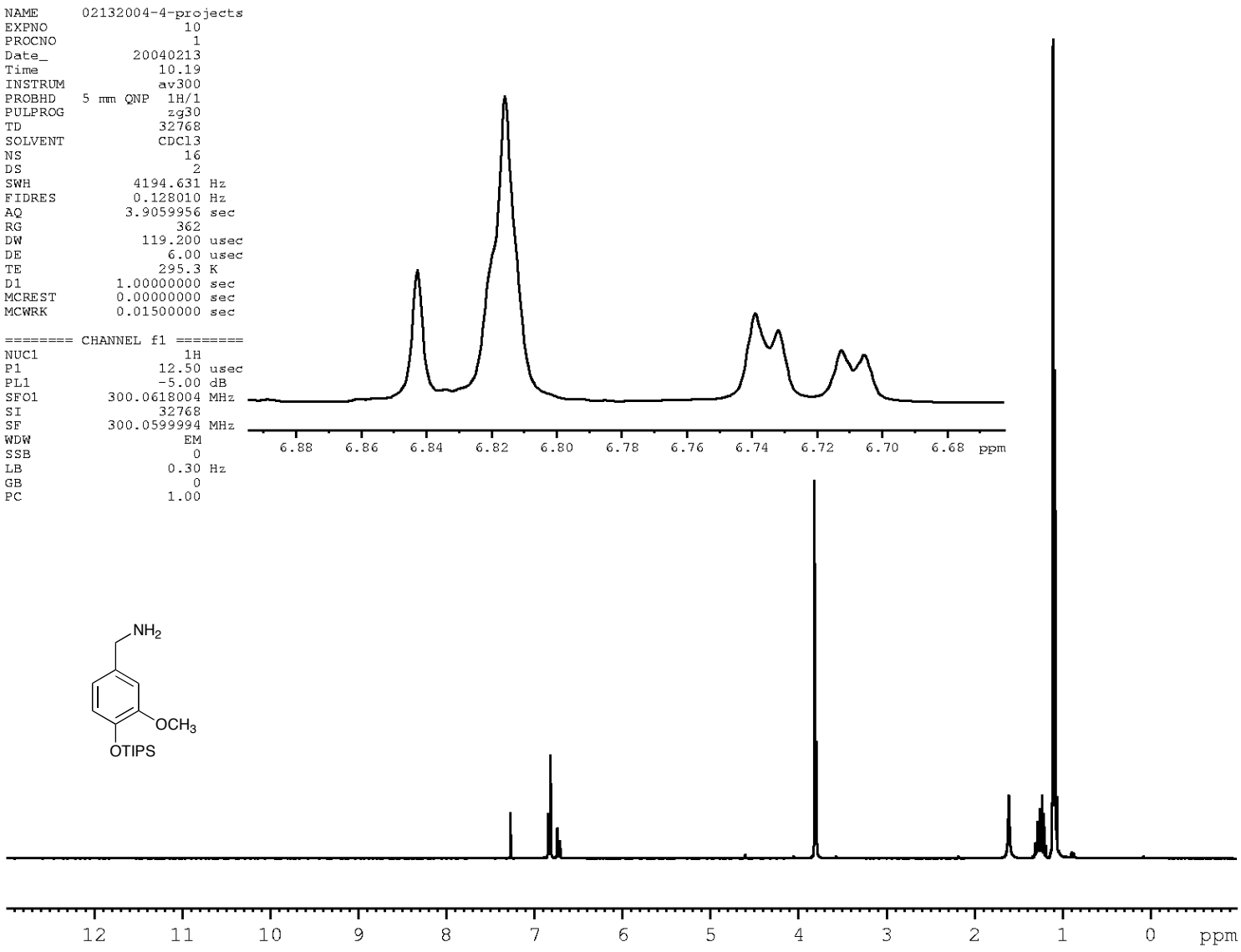

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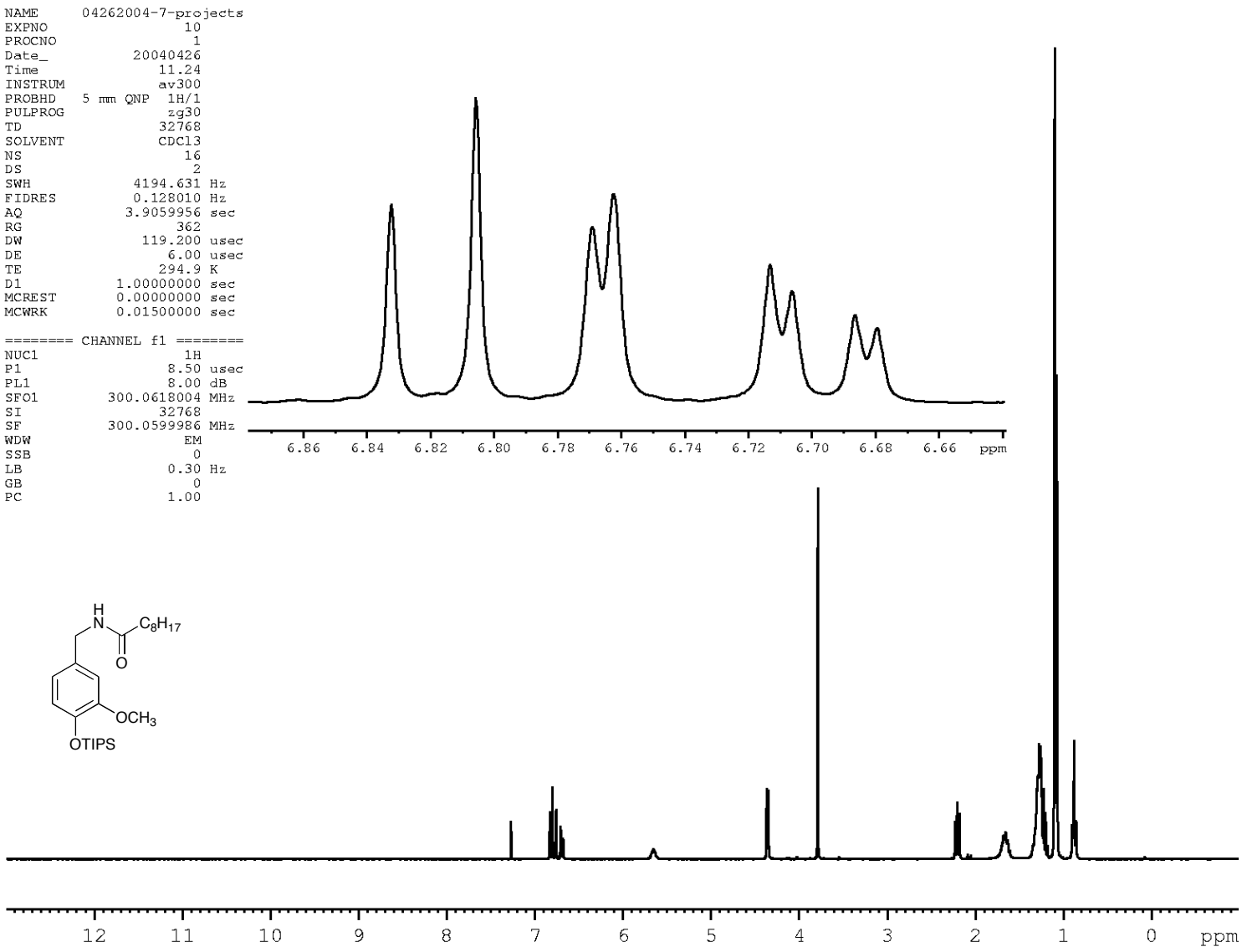

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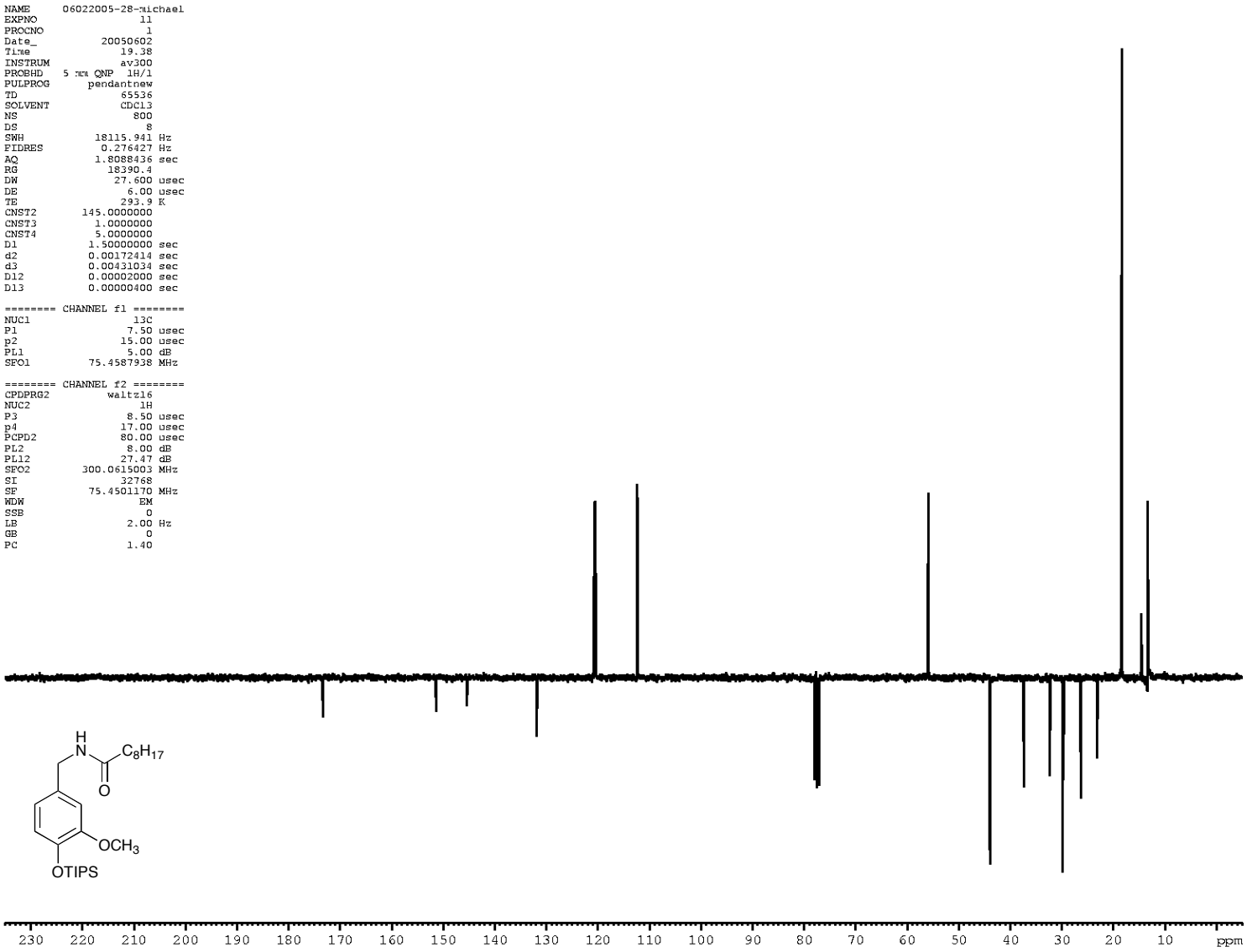

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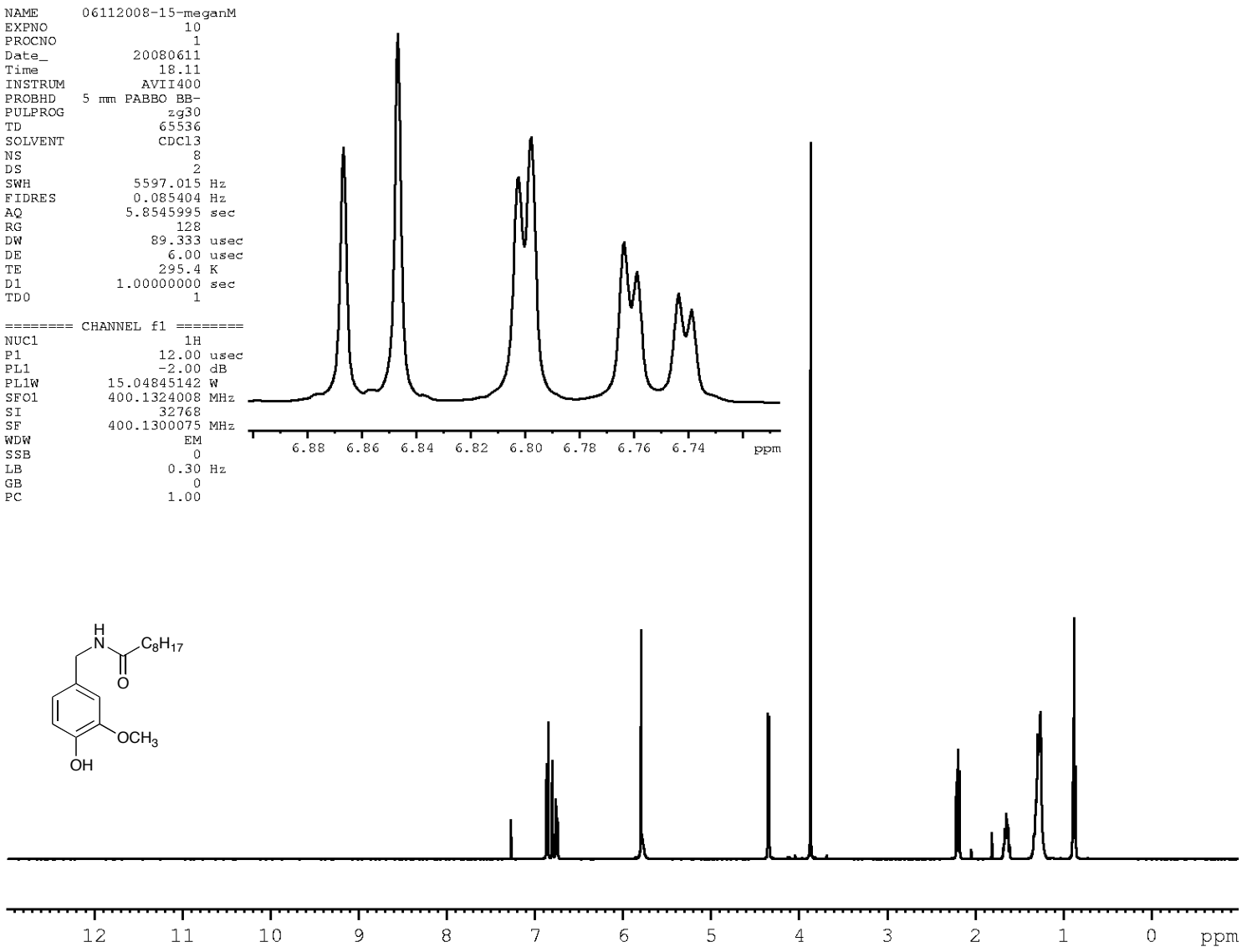

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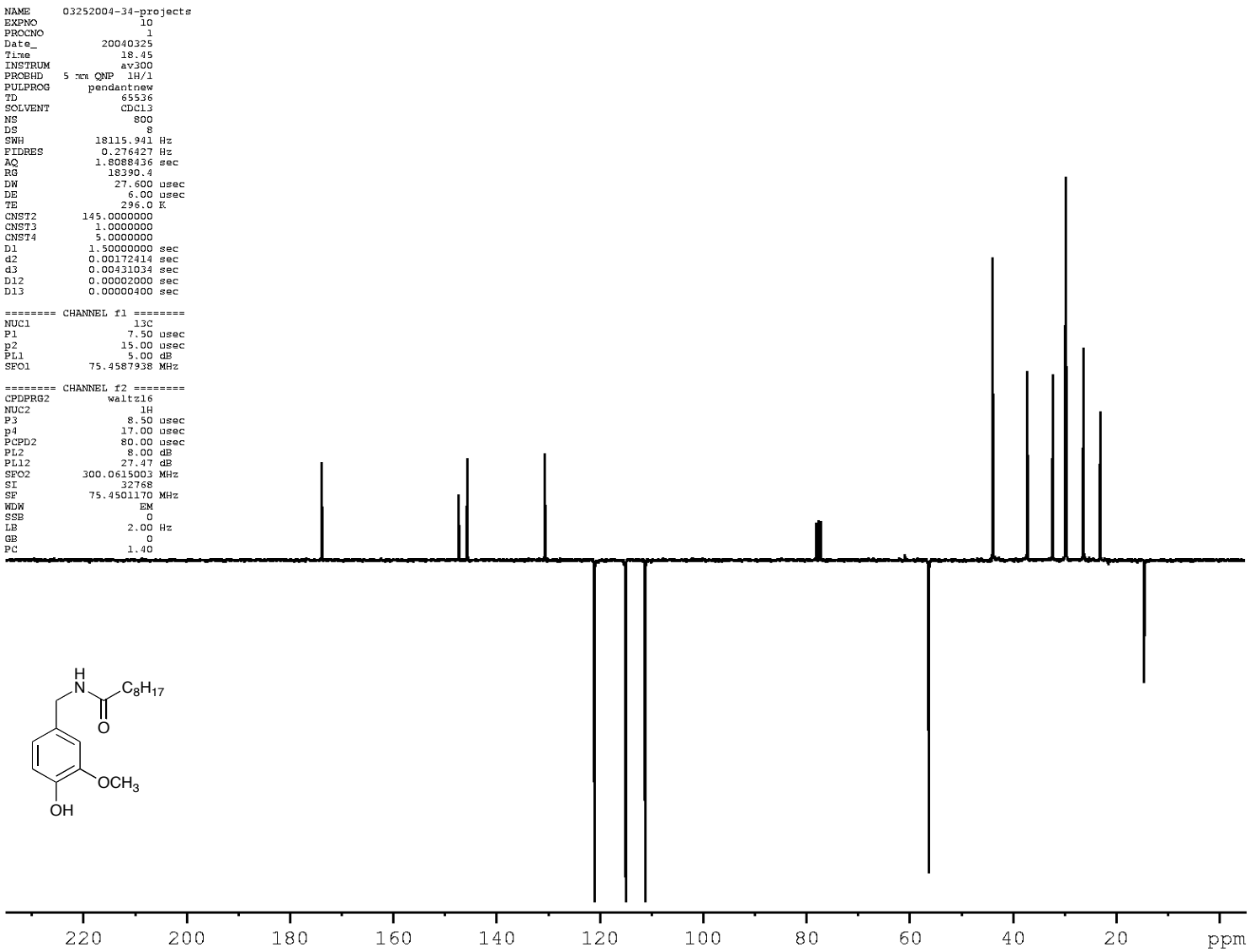

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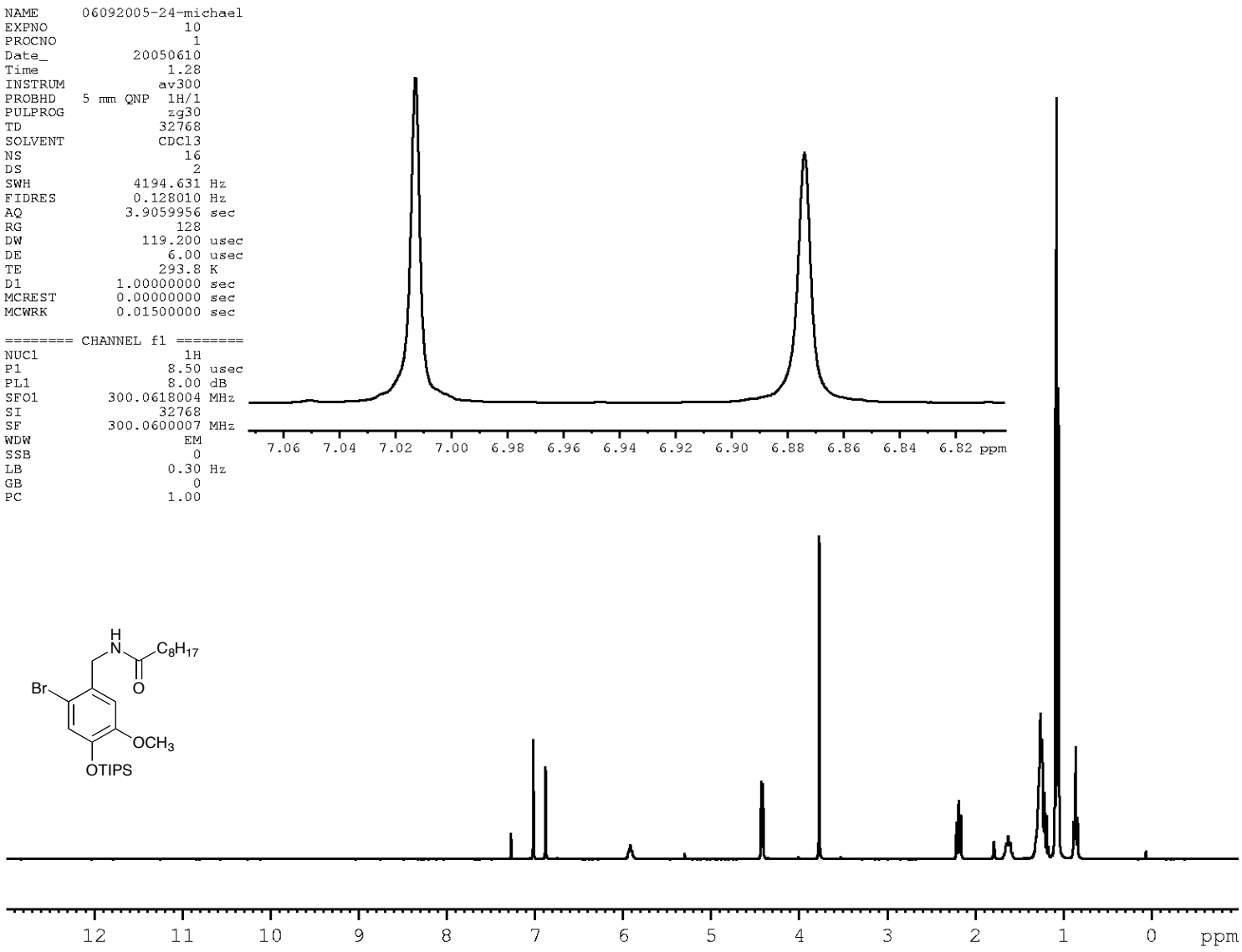

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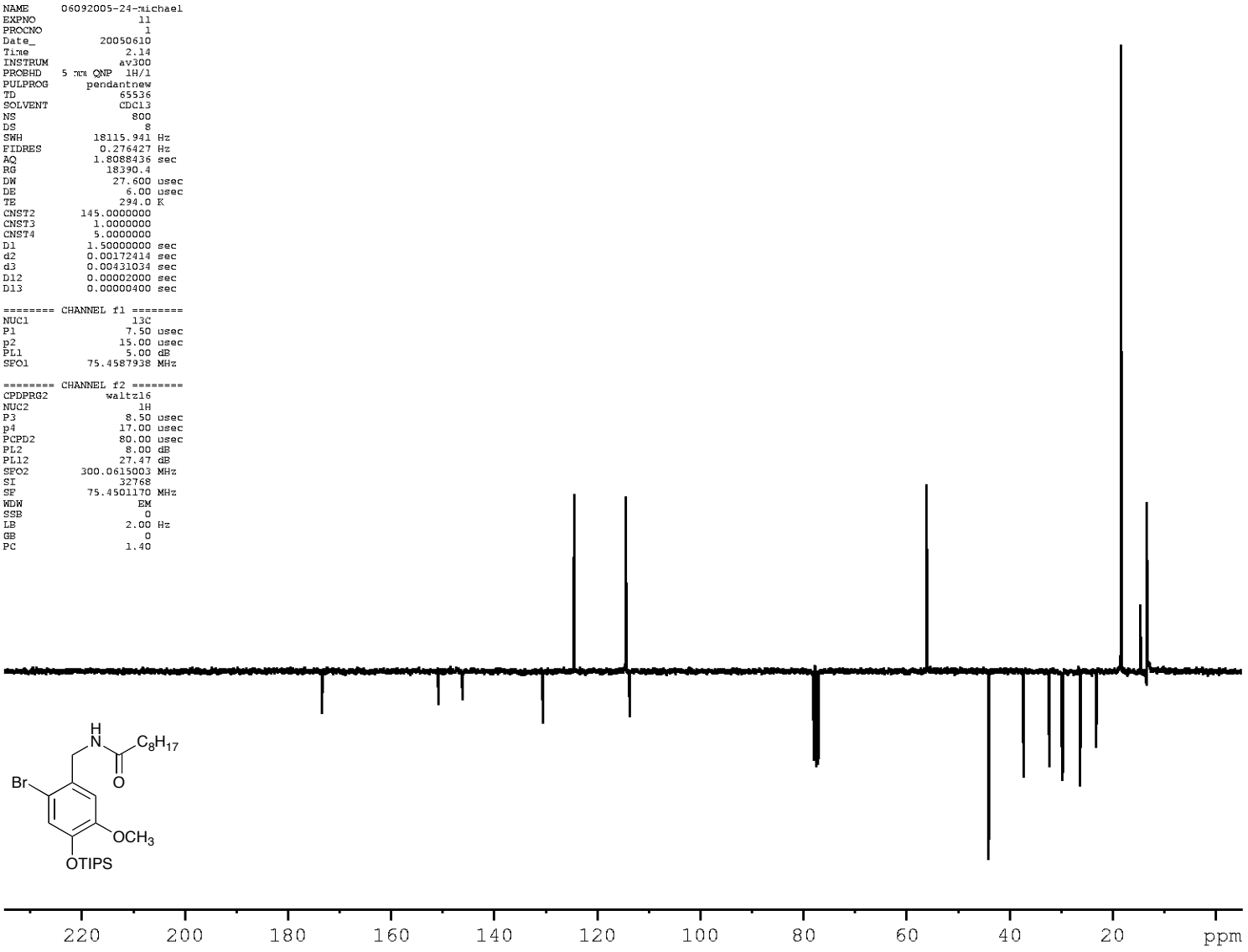

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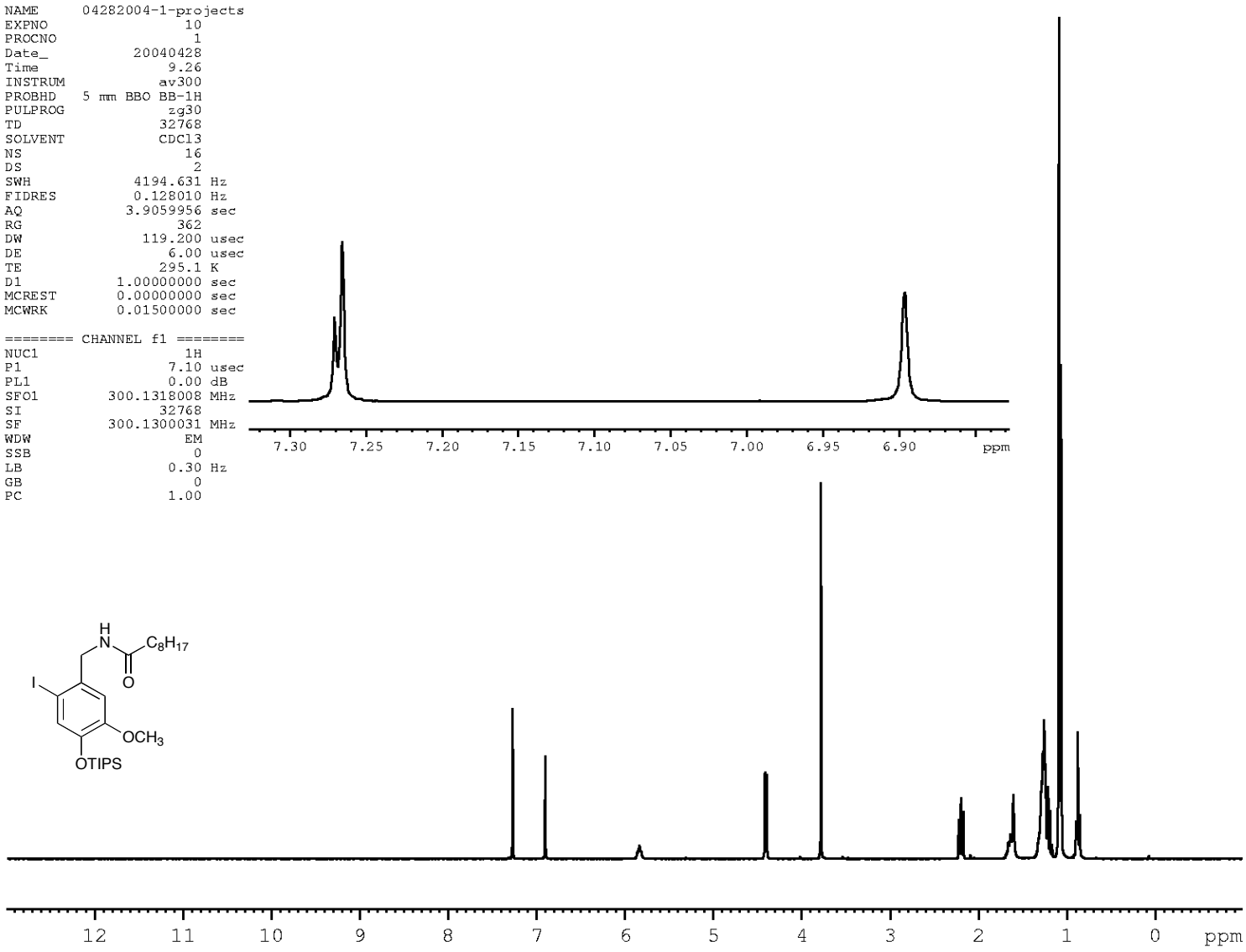

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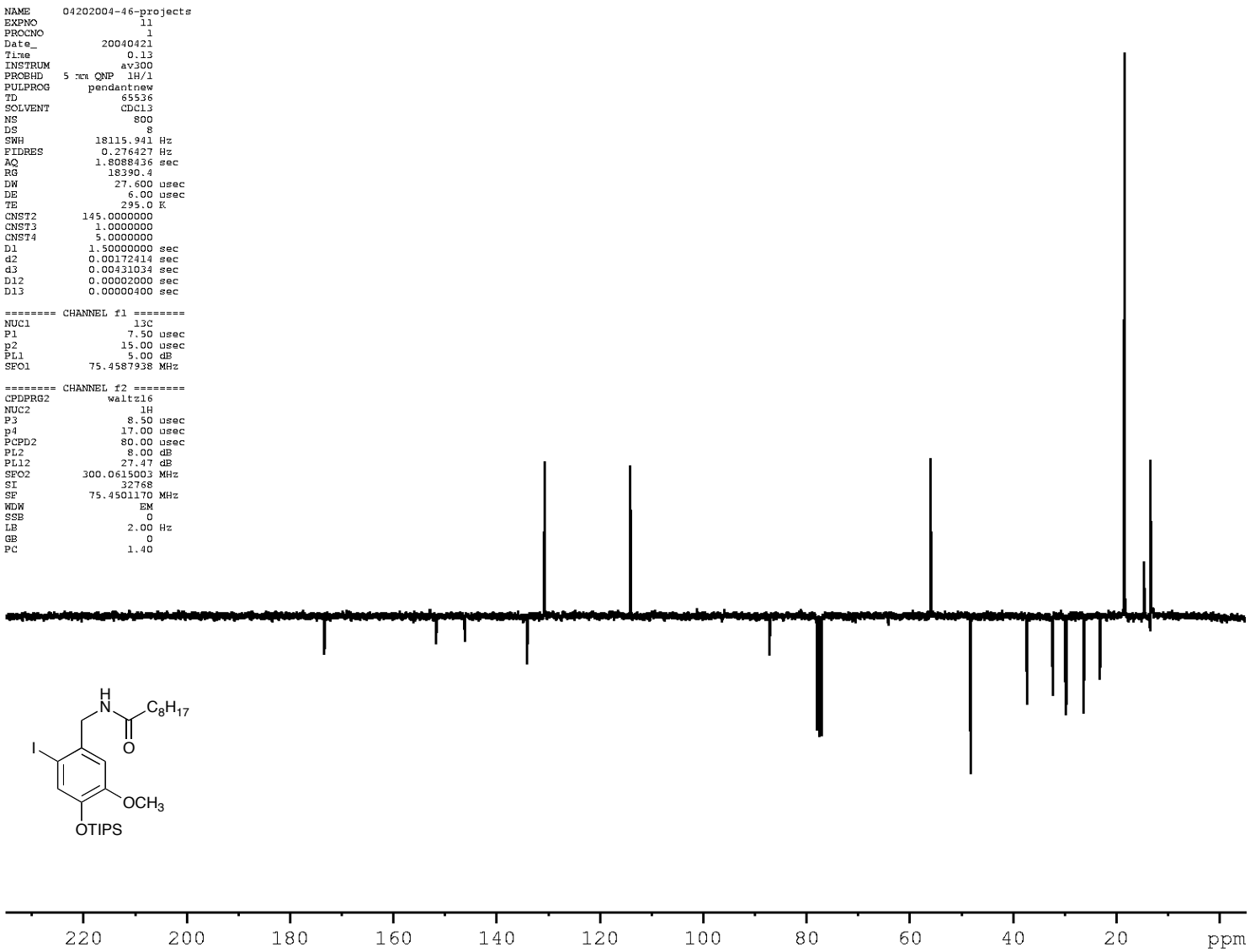

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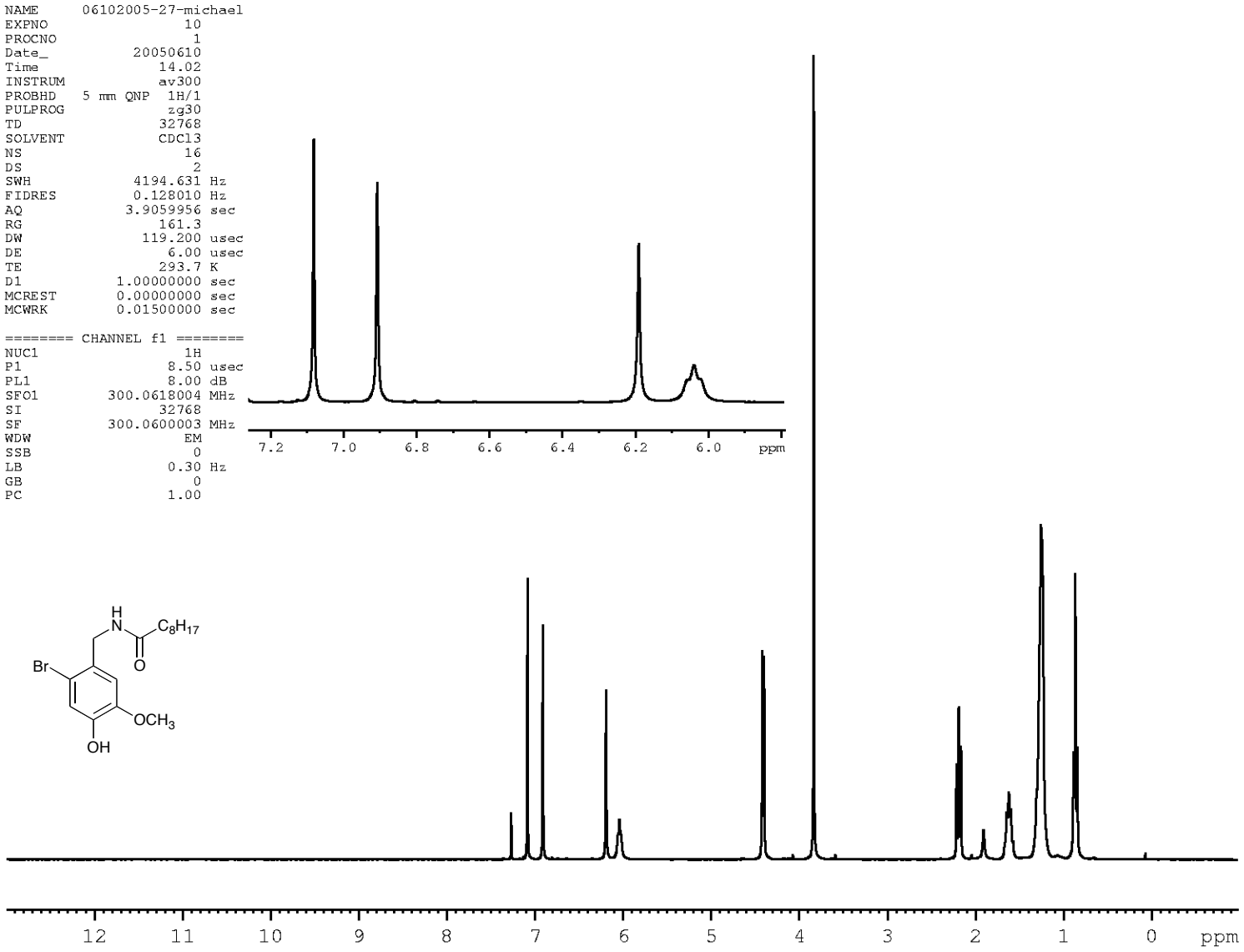

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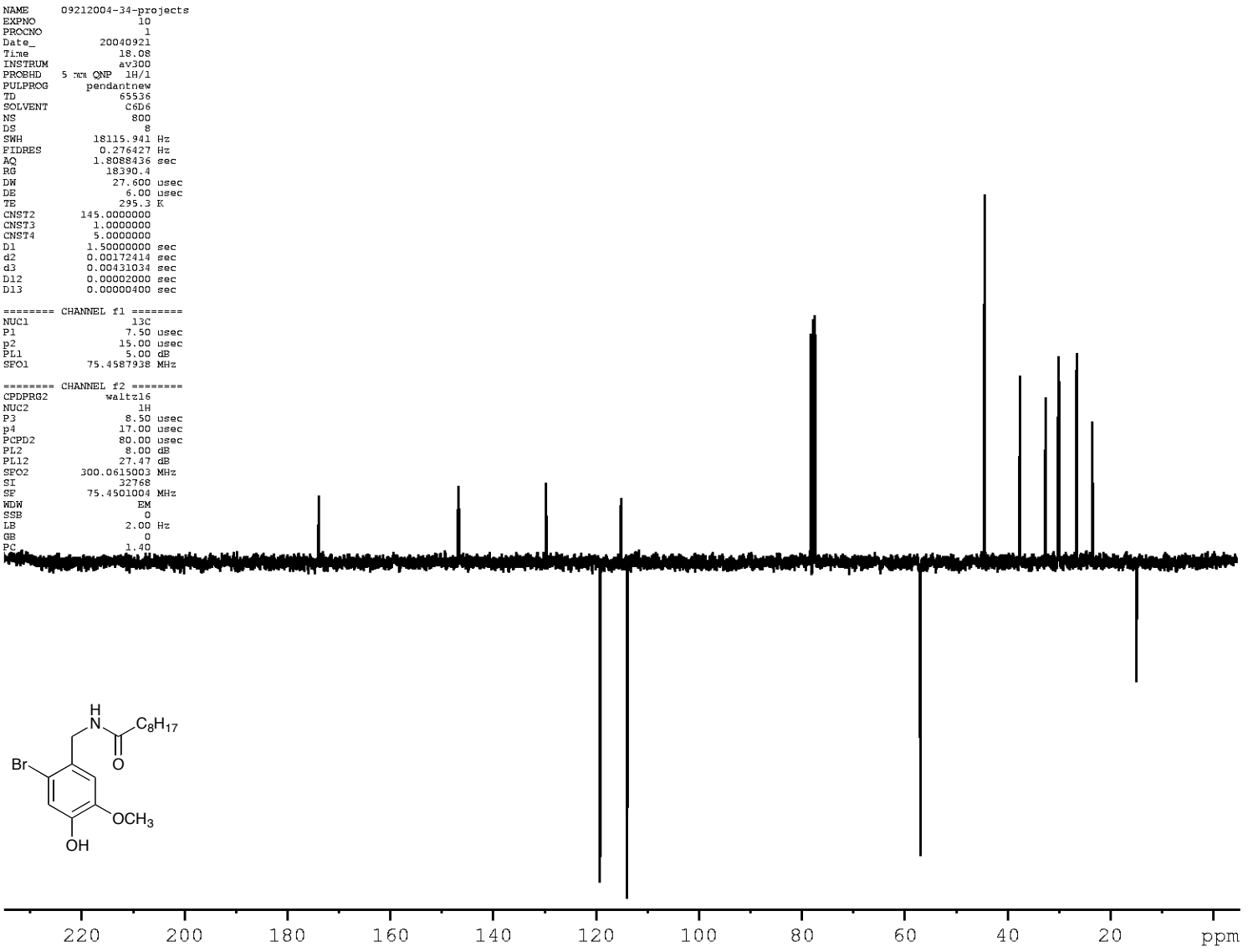

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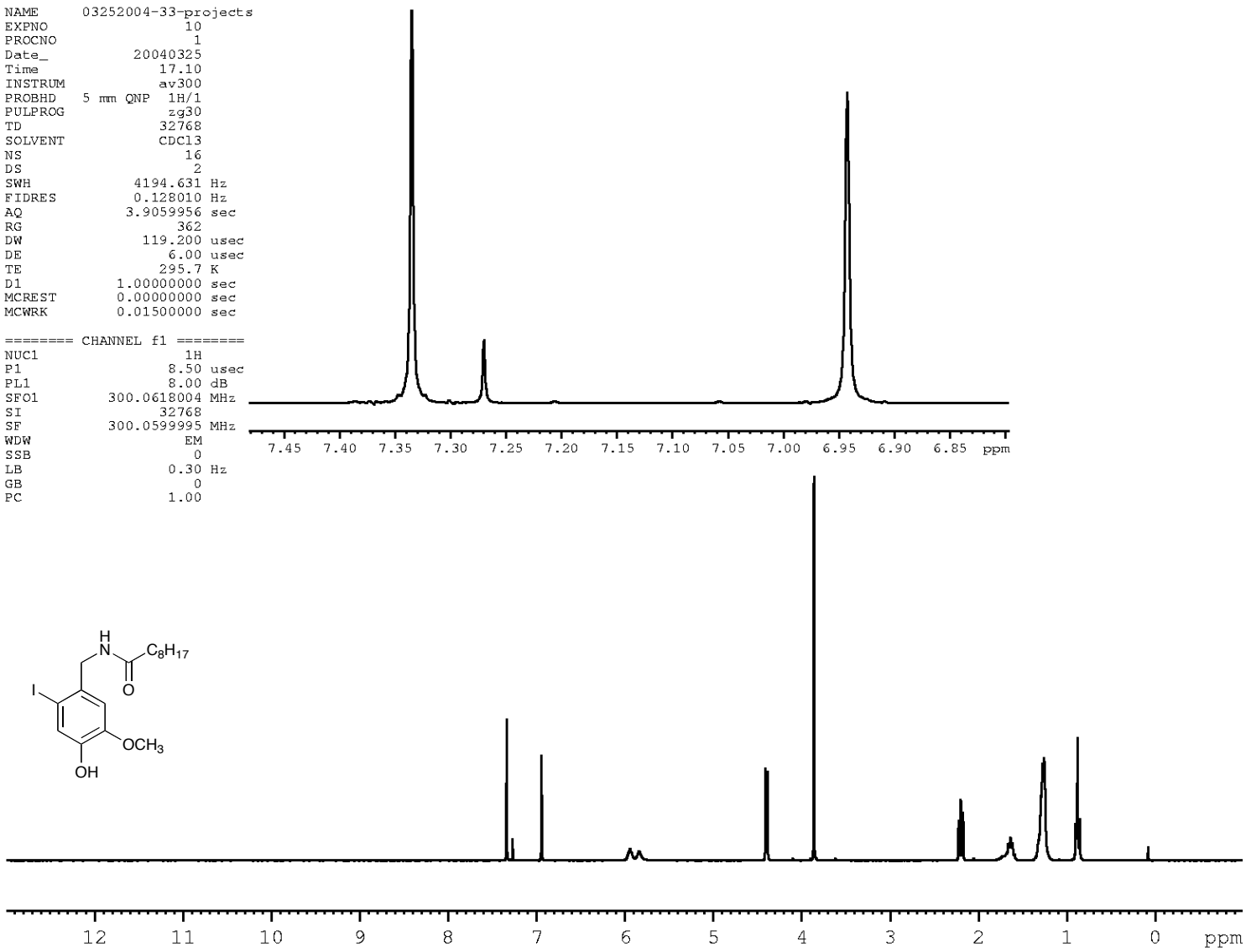

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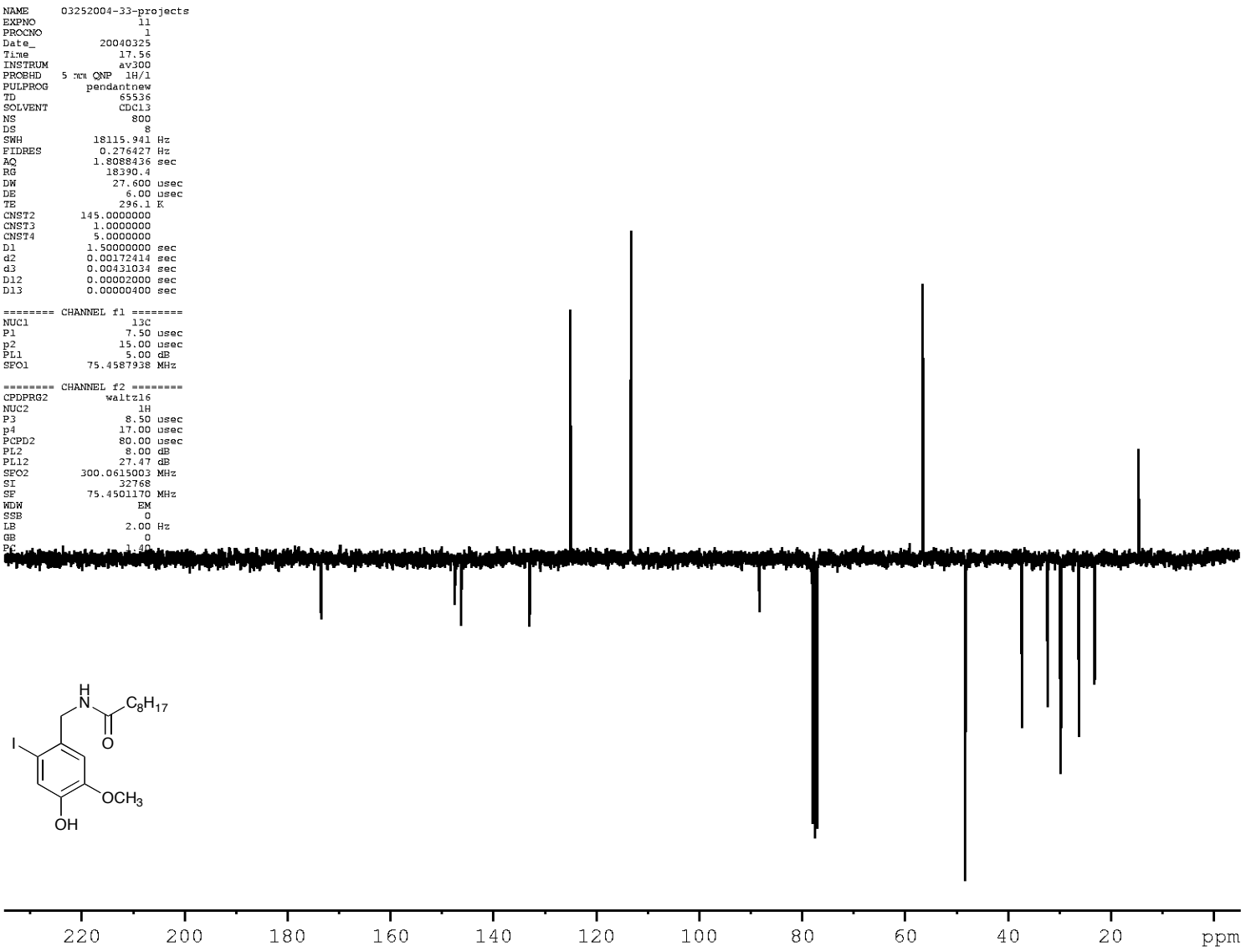

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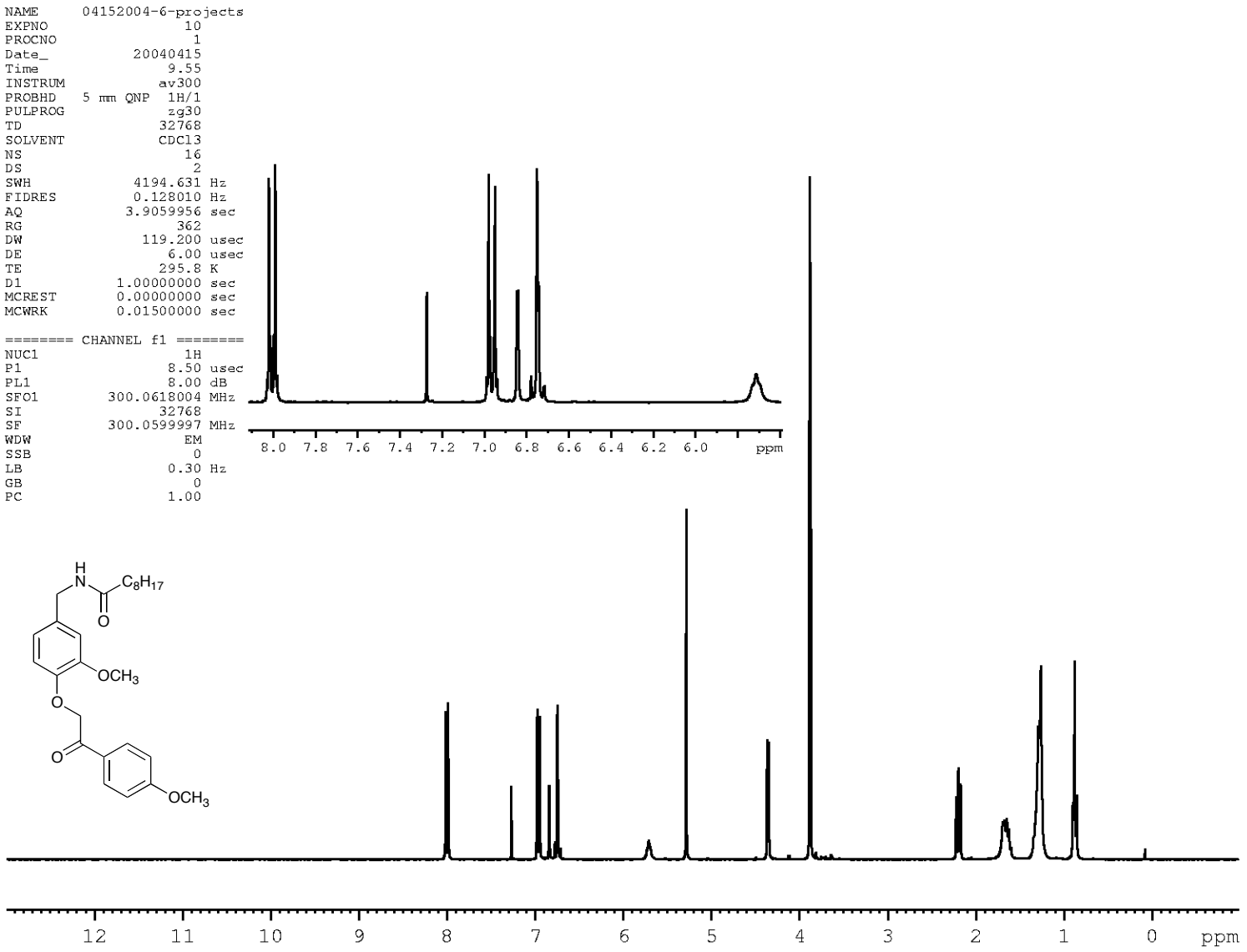

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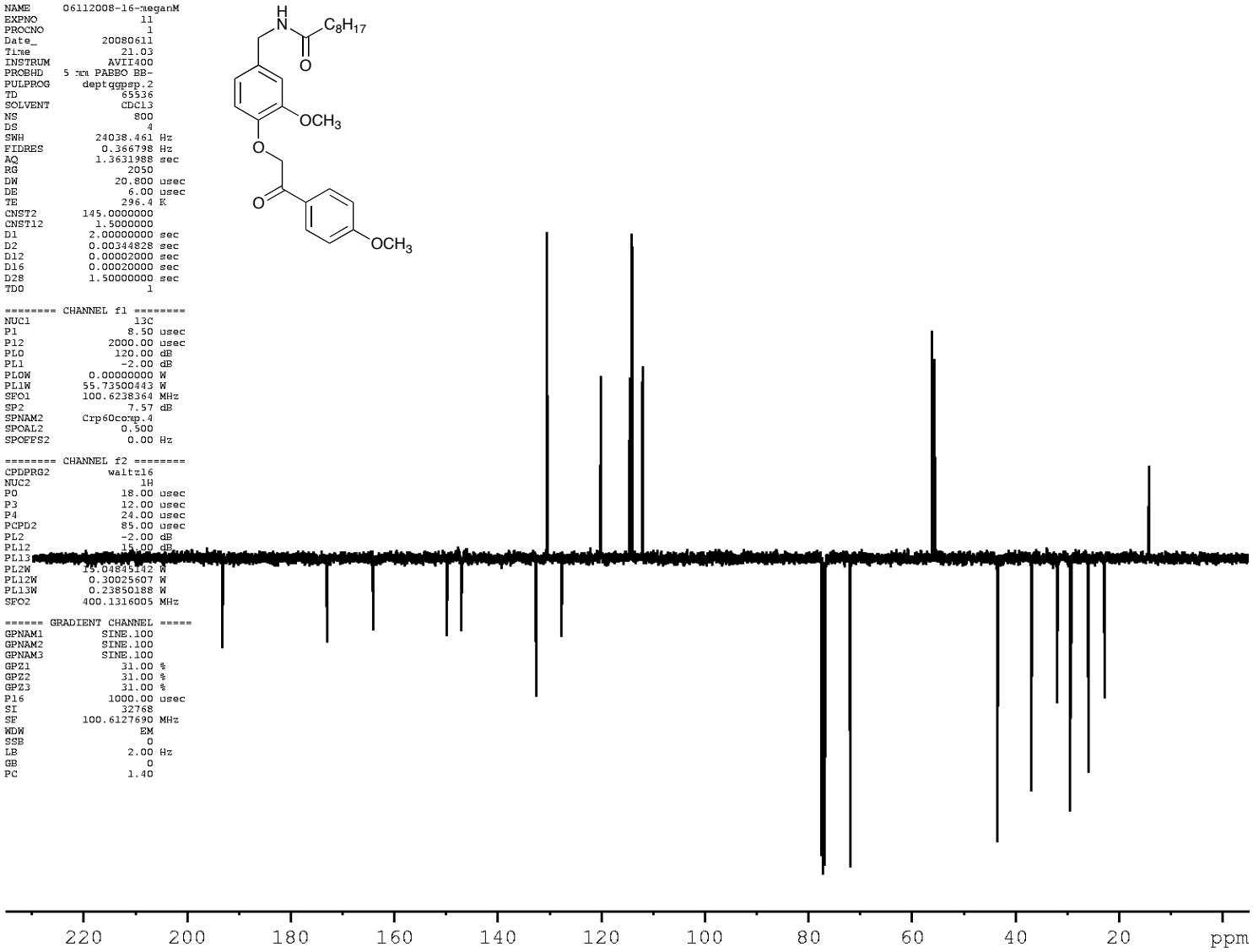

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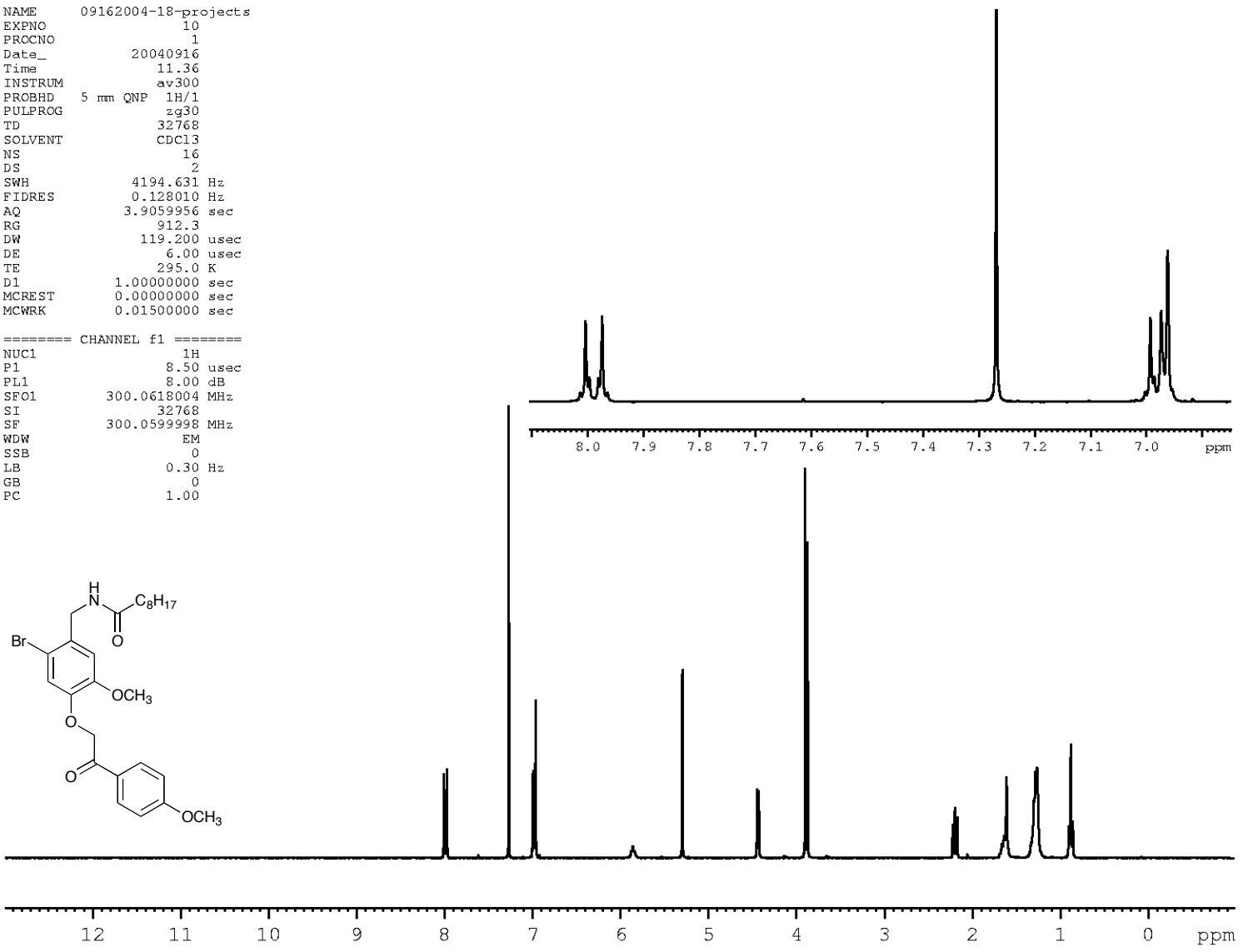

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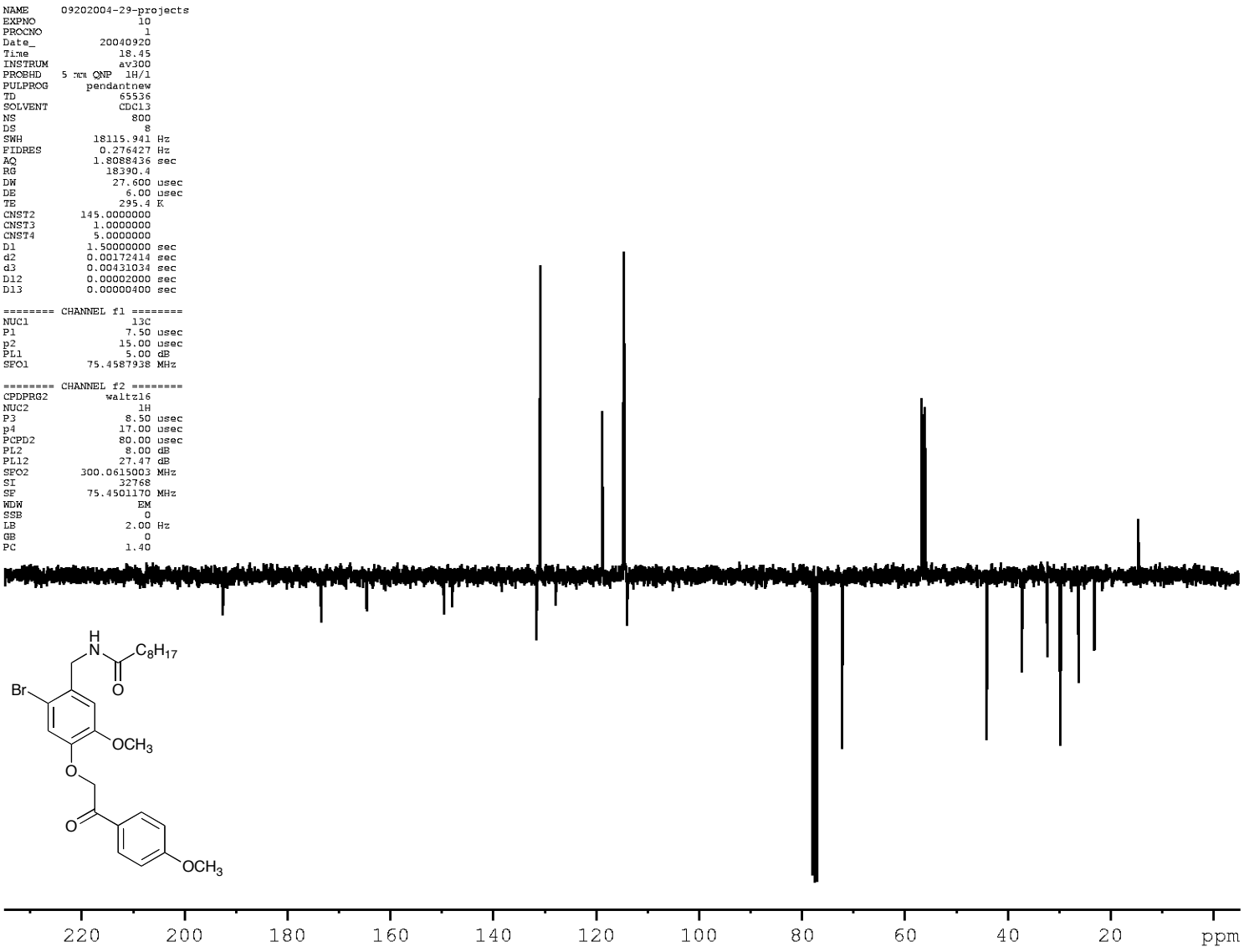

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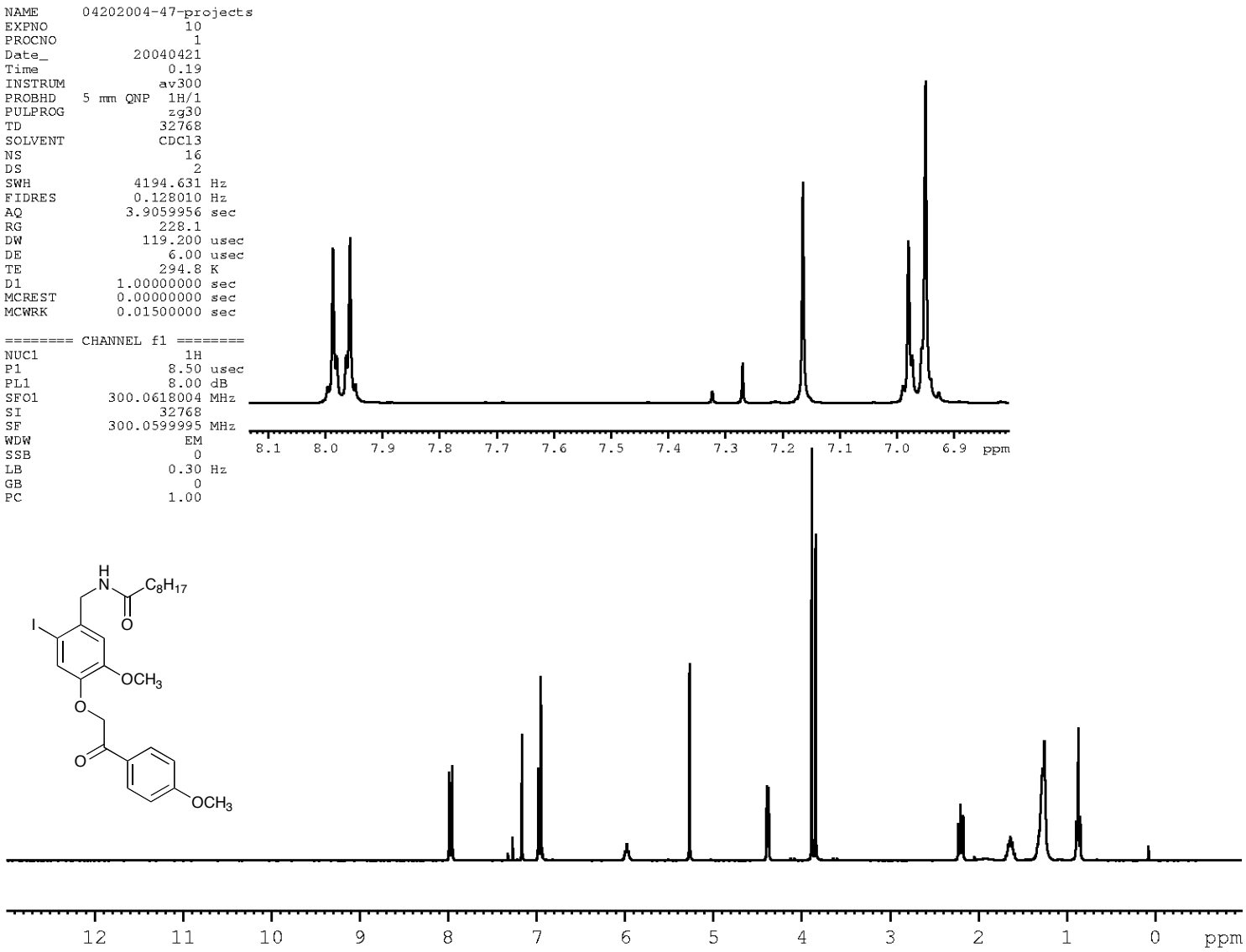

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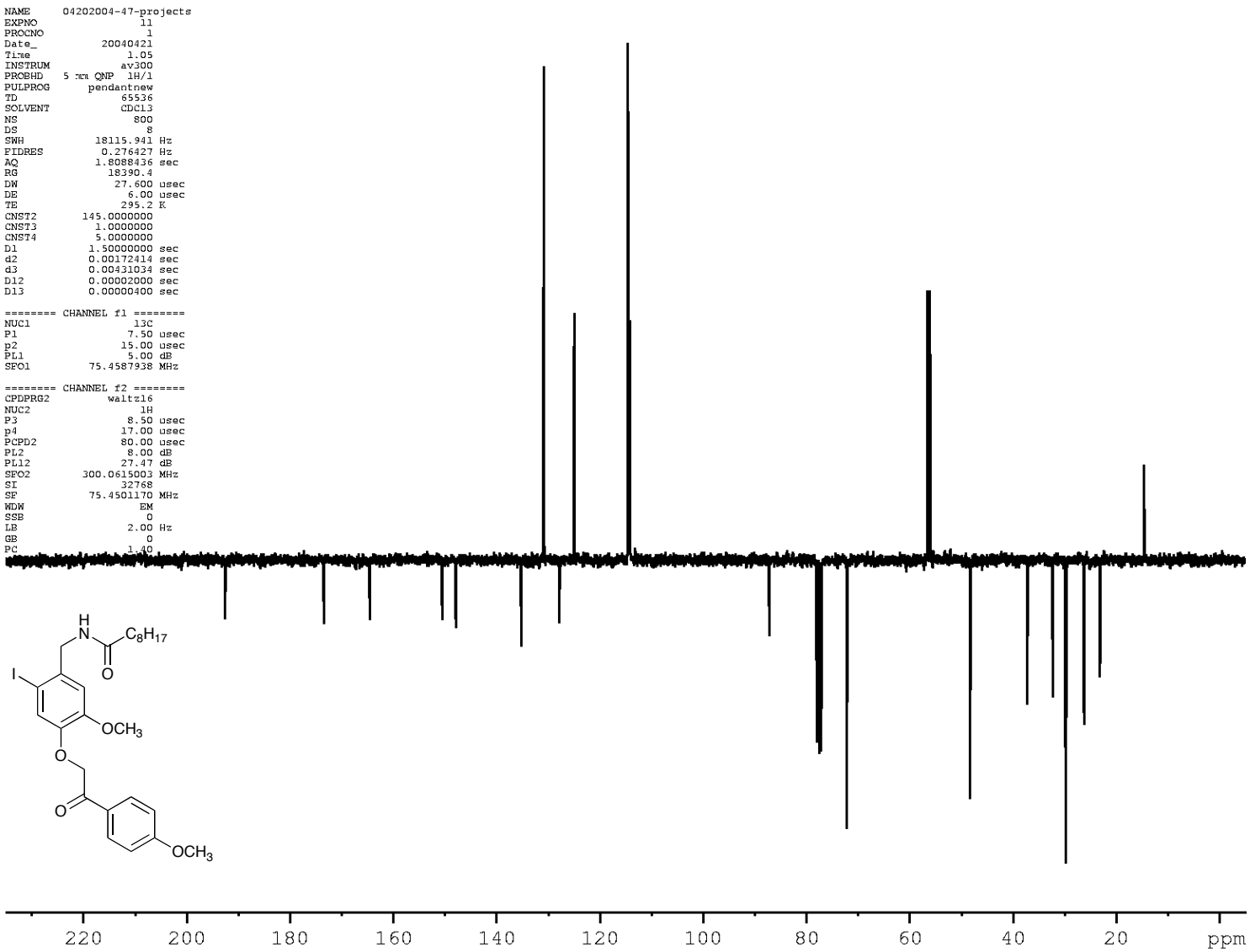

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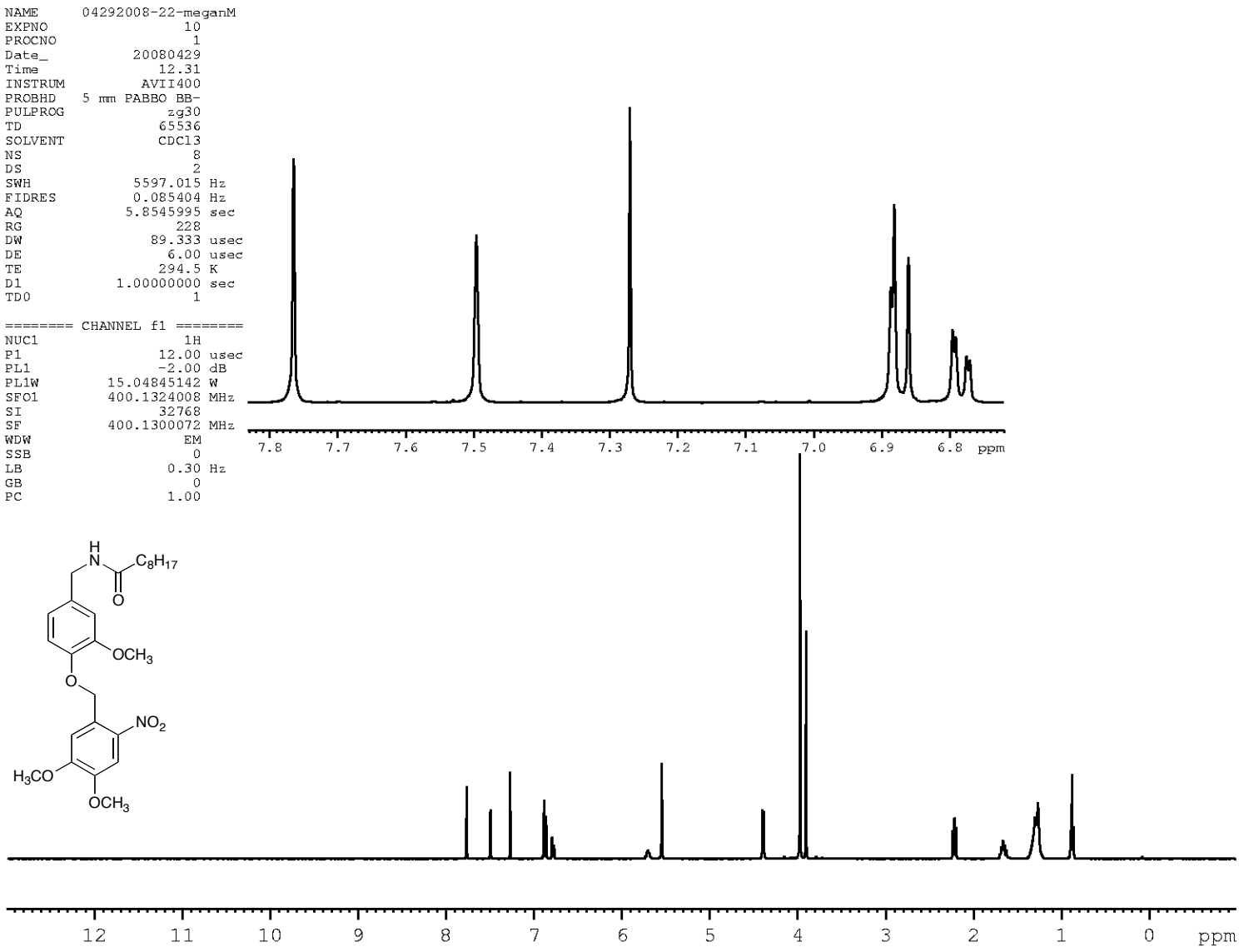

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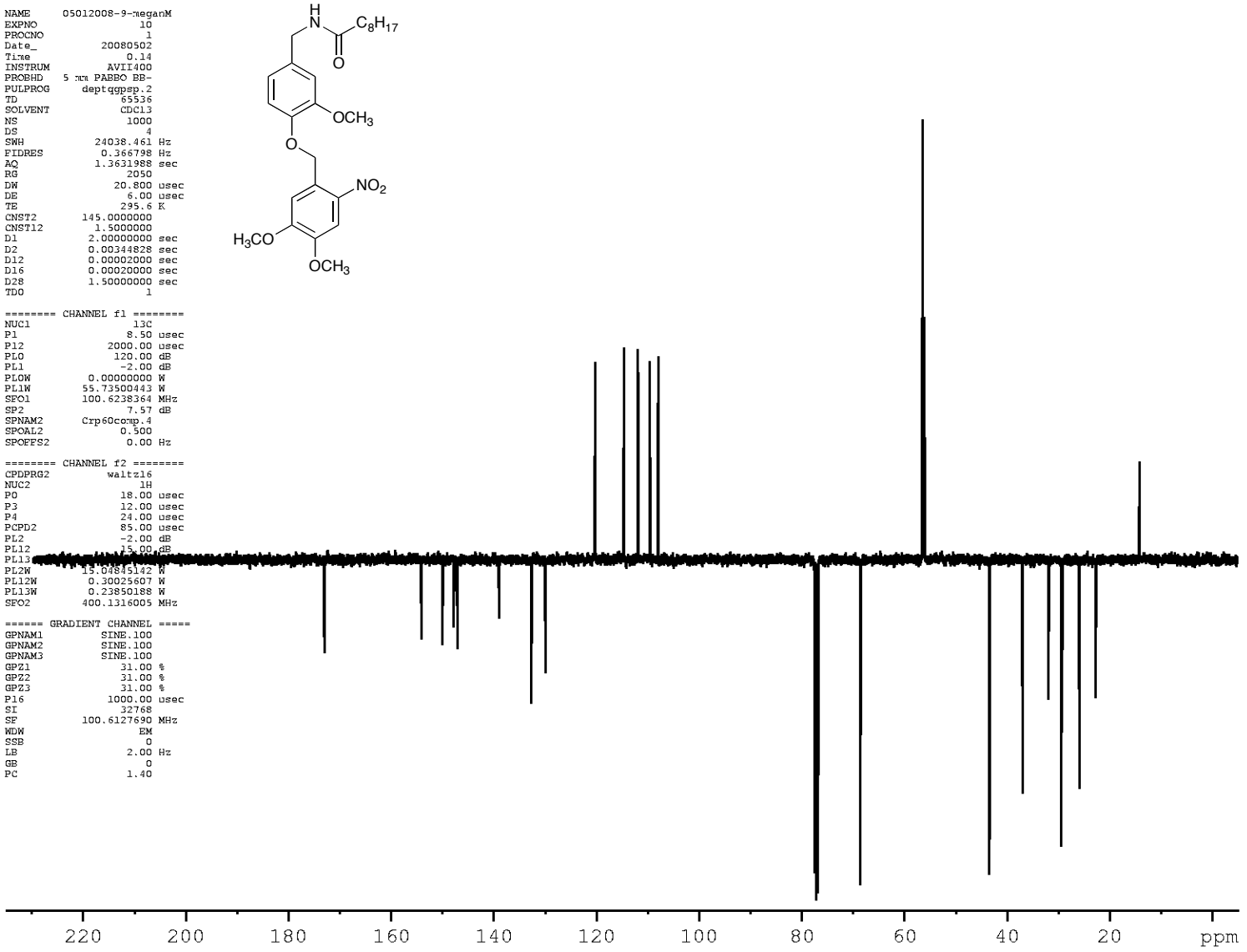

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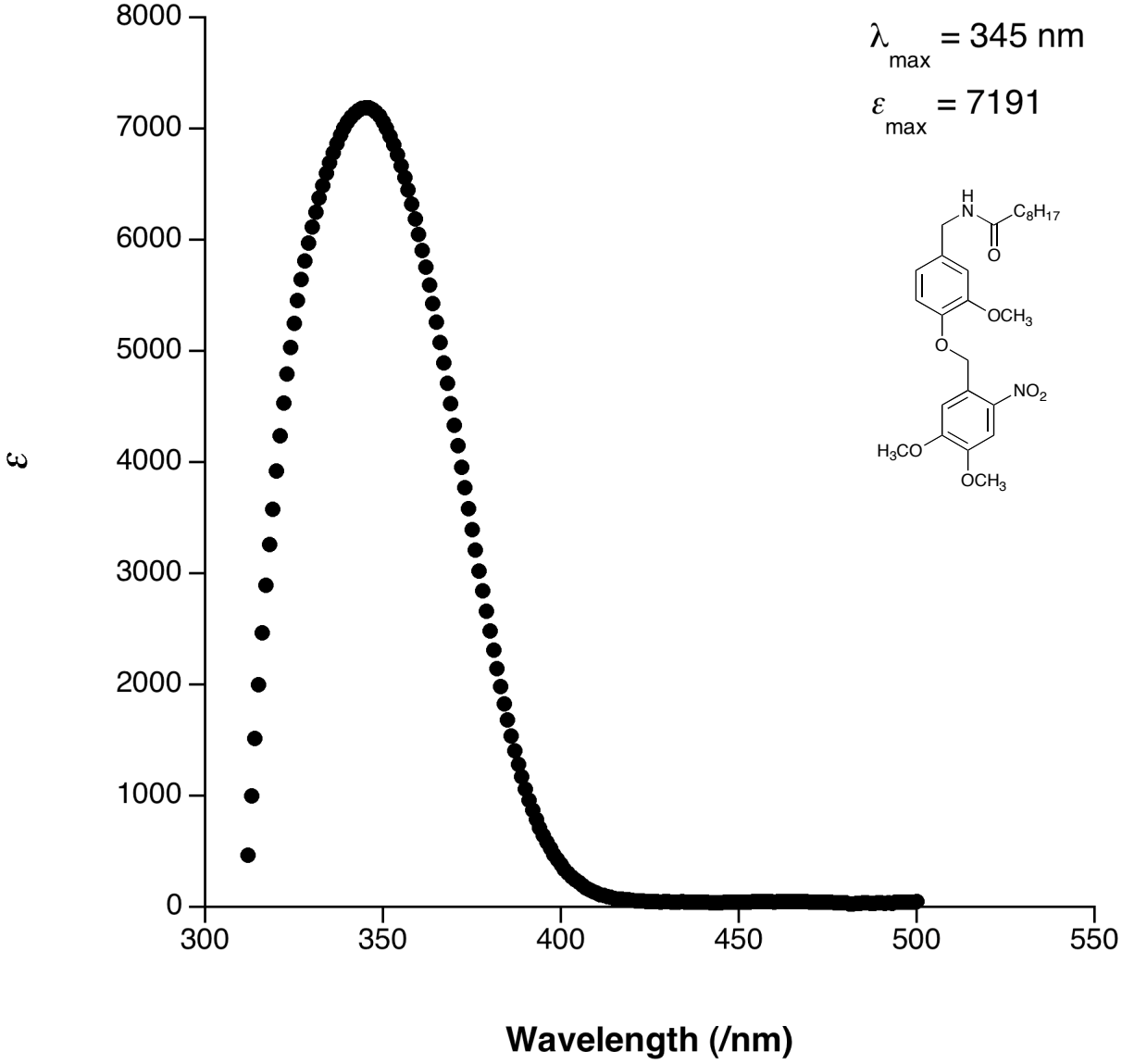

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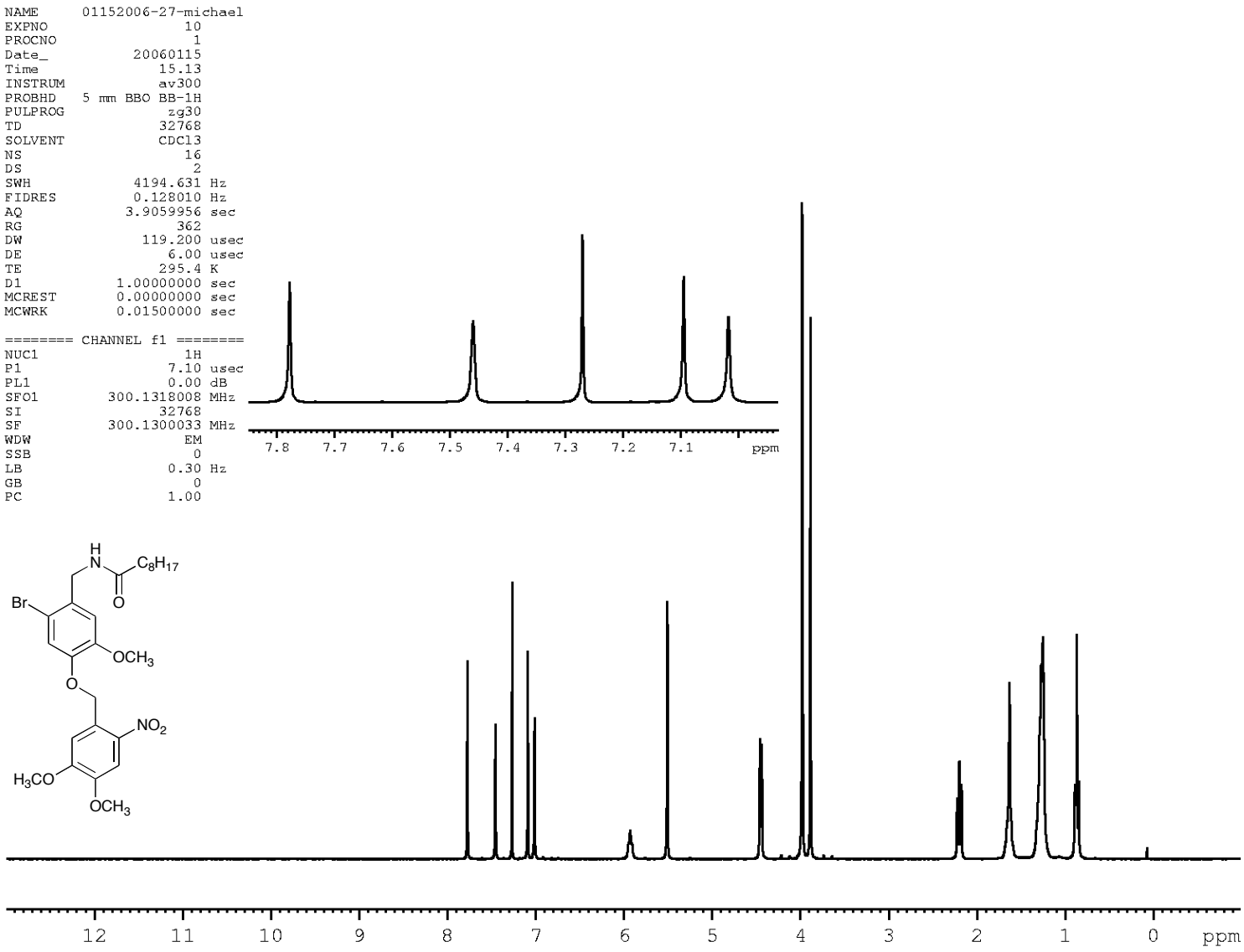

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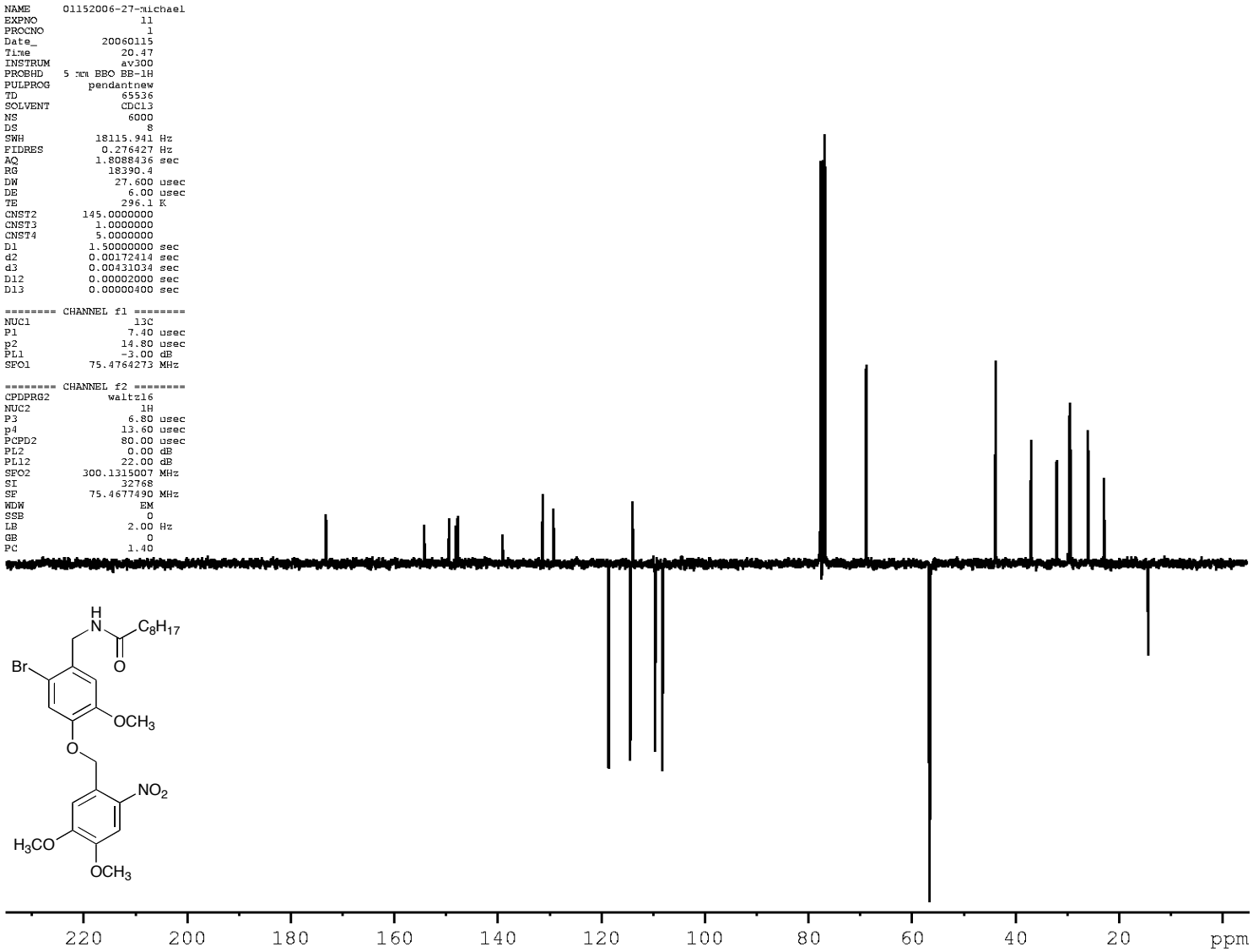

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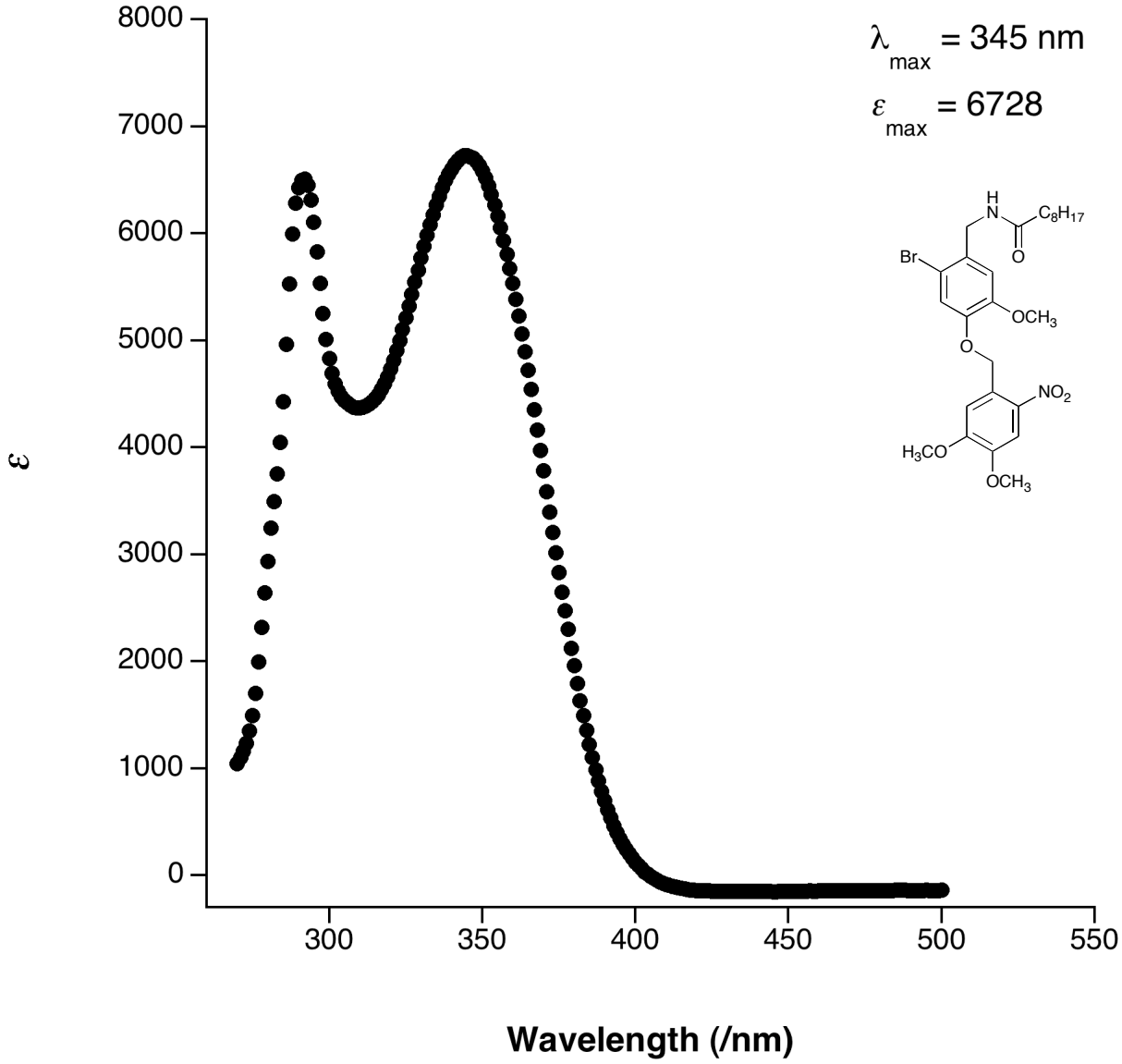

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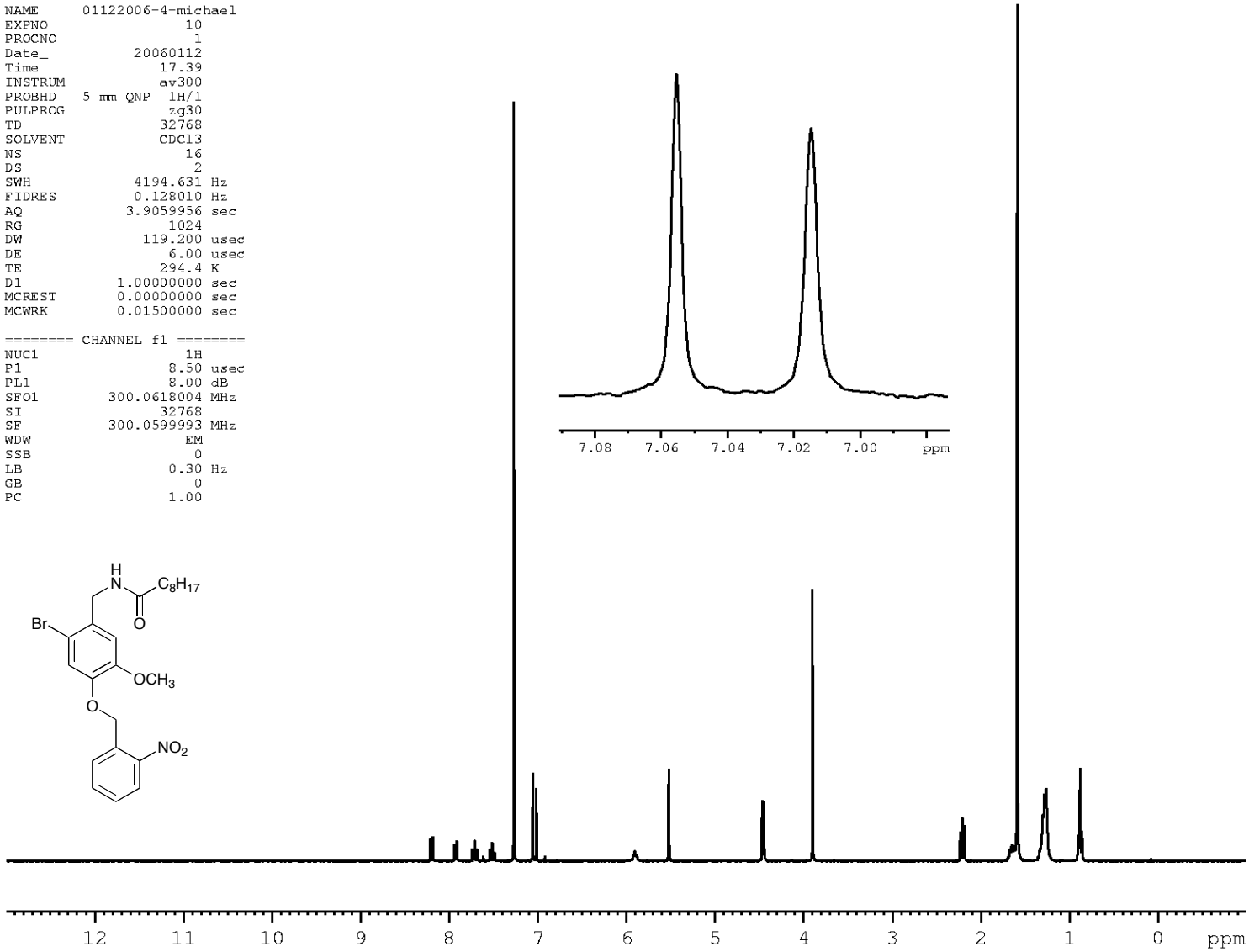

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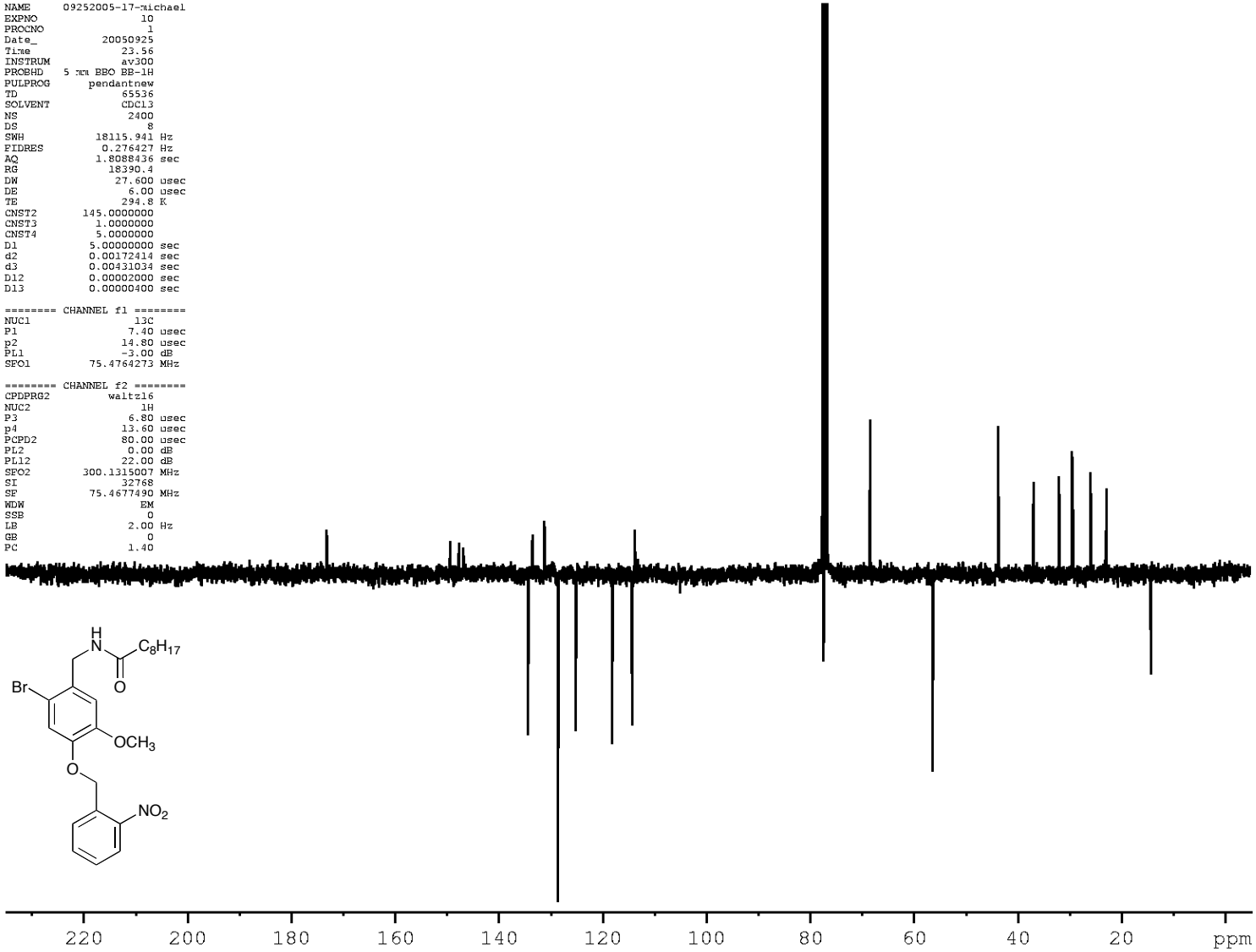

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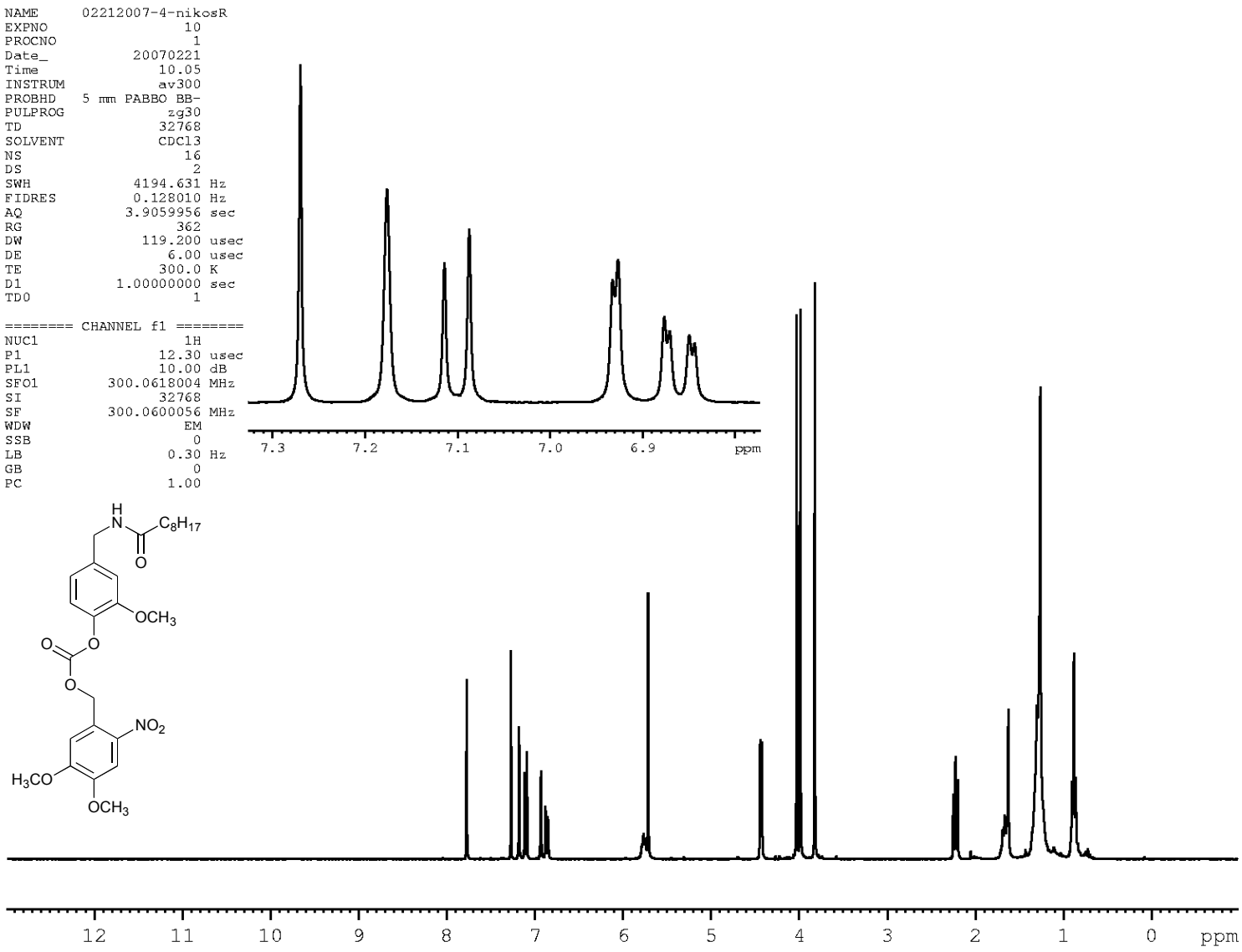

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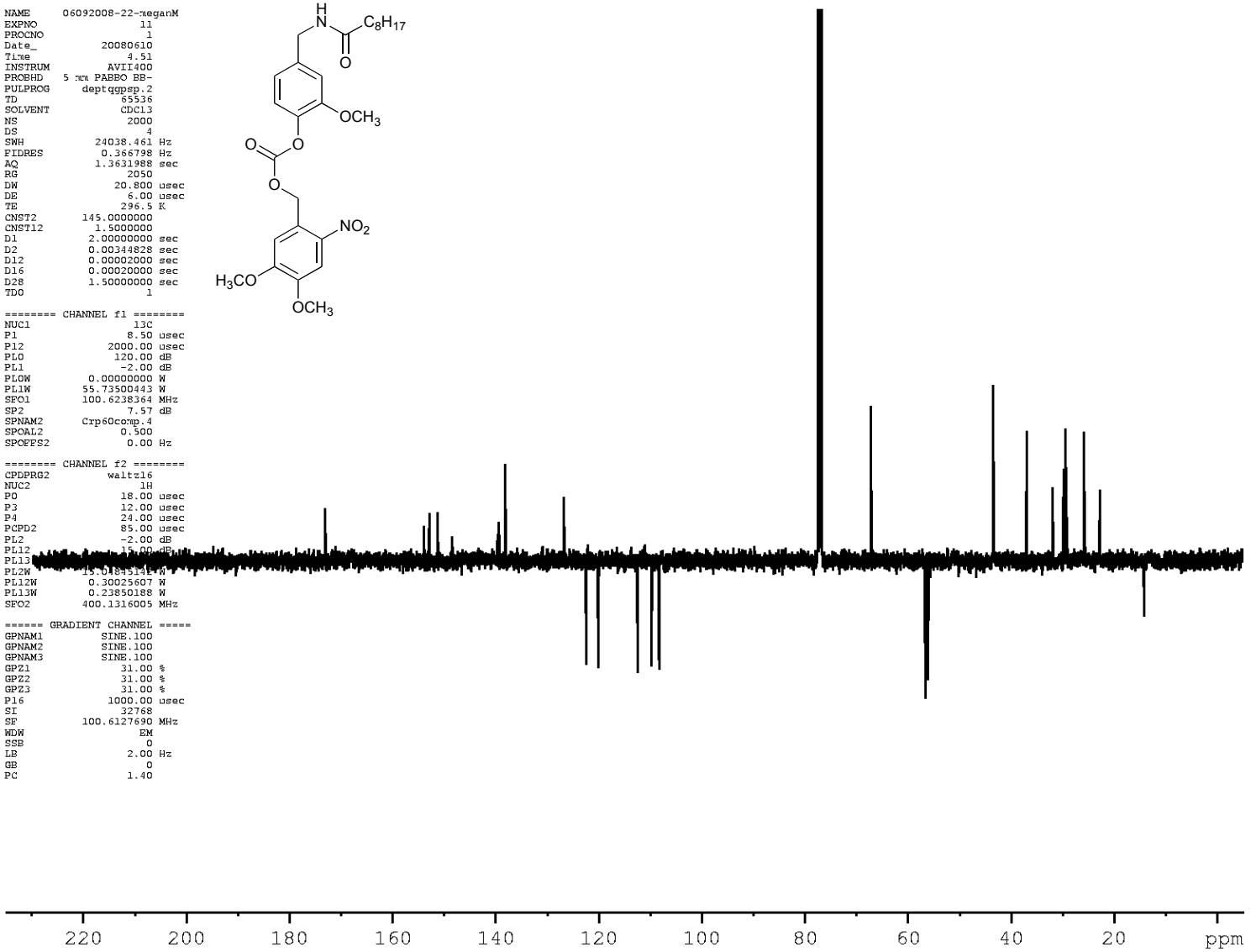

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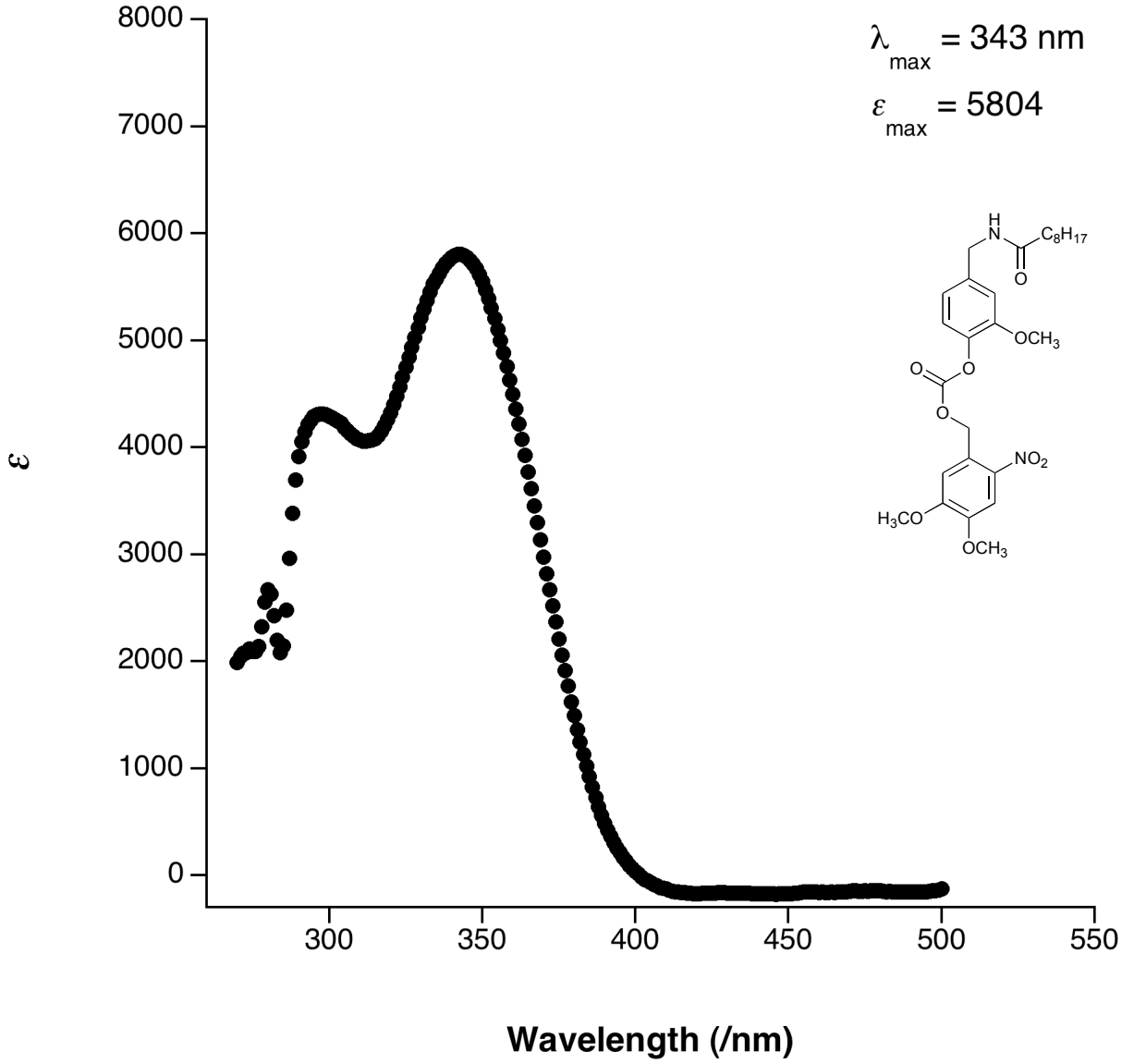

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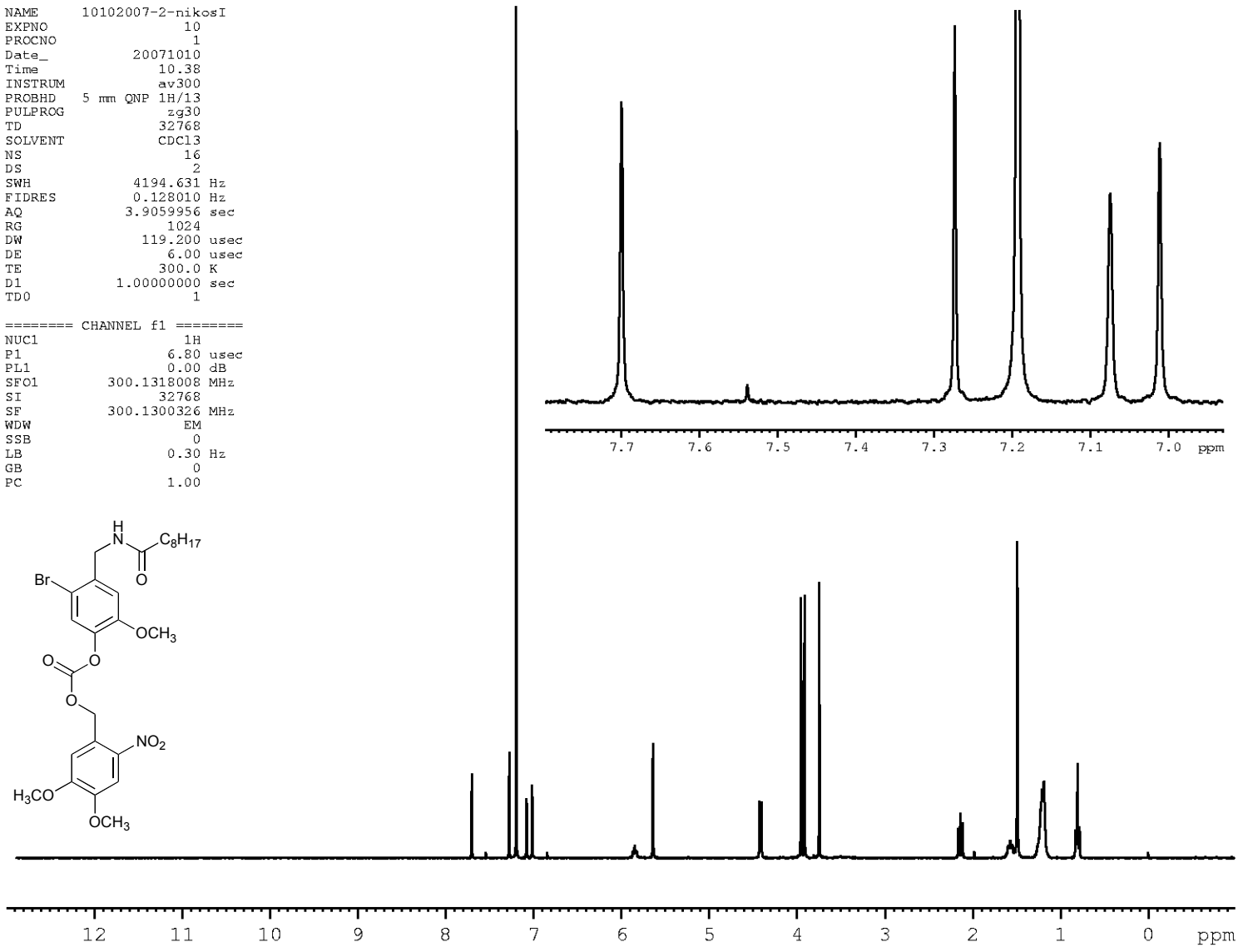

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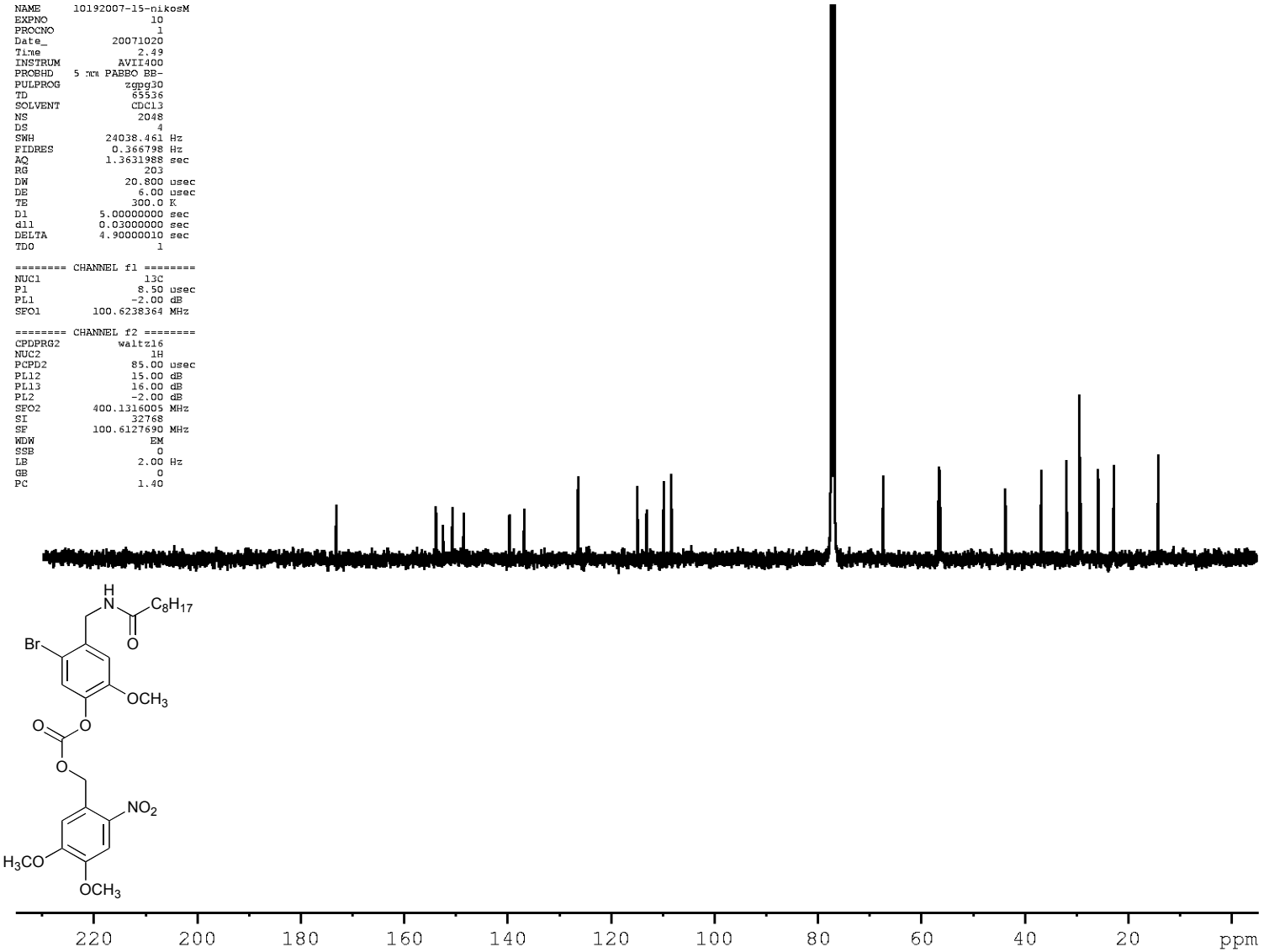

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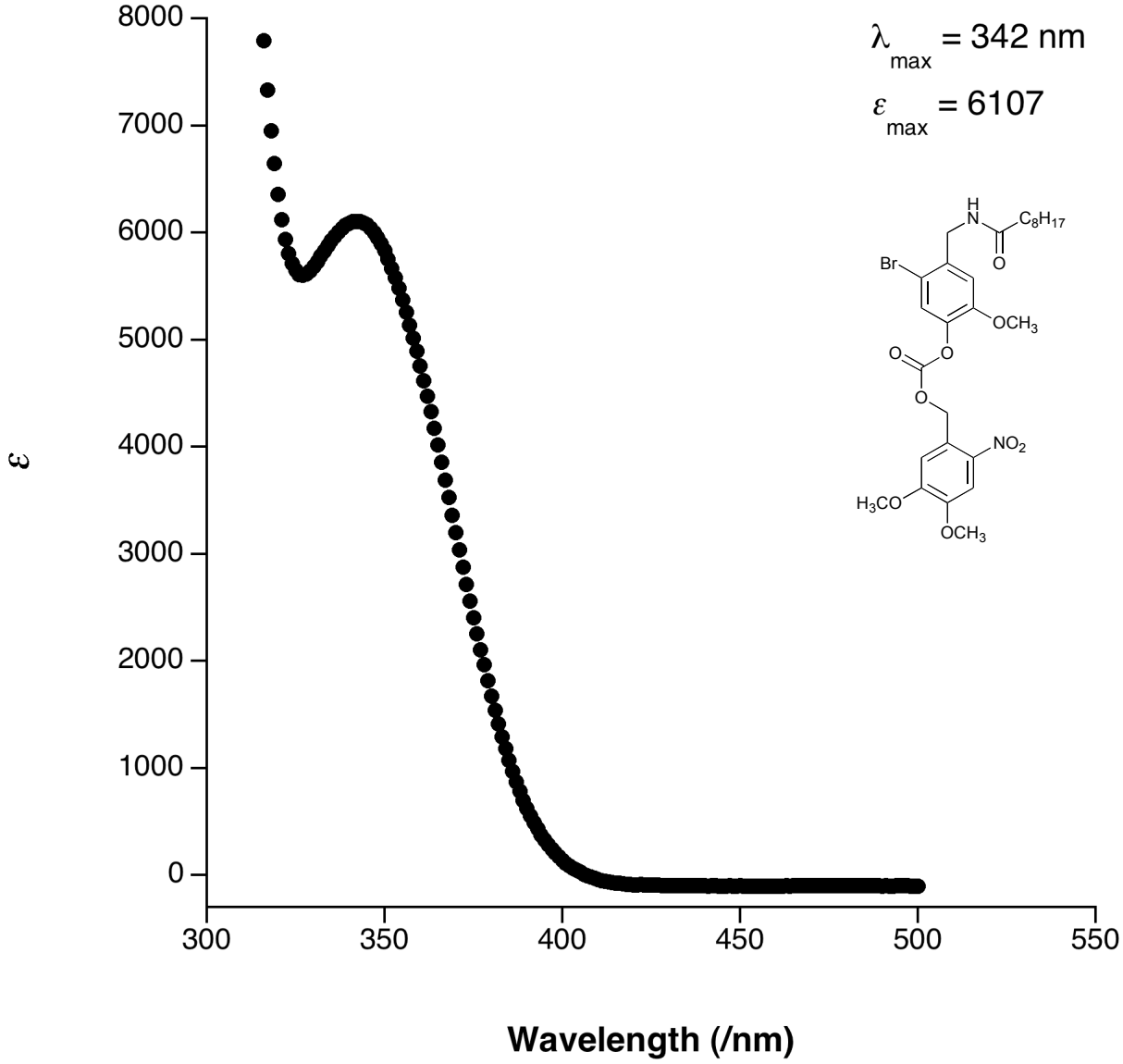

References

1. W. L. F. Armarego and C. L. L. Chai, *Purification of laboratory chemicals*, Butterworth Heinemann, 2003.