Chemistry 5361/8361 Thursday, October 3, 2002

Midterm Exam 1

Please do not open or sign this packet until you are instructed to do so.

Please write all of your answers for this exam this exam packet. Although you may use as many blue books for scratch work as you would like, the blue books will not be collected at the end of the exam or graded. Answer each question in the space provided if you can, but feel free to continue your answer on the back of the page if you need more room. (Please write a note by your answer pointing us to the continuation if you do this.) Feel free to remove the corner staple if this helps you analyze the spectra; you will have the opportunity to re-staple your exam at the end. The exam in this packet is designed to take 1 hour to complete. You will be given 2 hours total to finish the test.

This exam contains two problems, which are split into parts. Many of these parts can be answered independently. *Do not get stuck* on one part and then assume that you will be unable to answer the rest of the question—move on. In addition, partial credit will be given for incorrect but still plausible answers, so *guess* on problems you cannot answer perfectly.

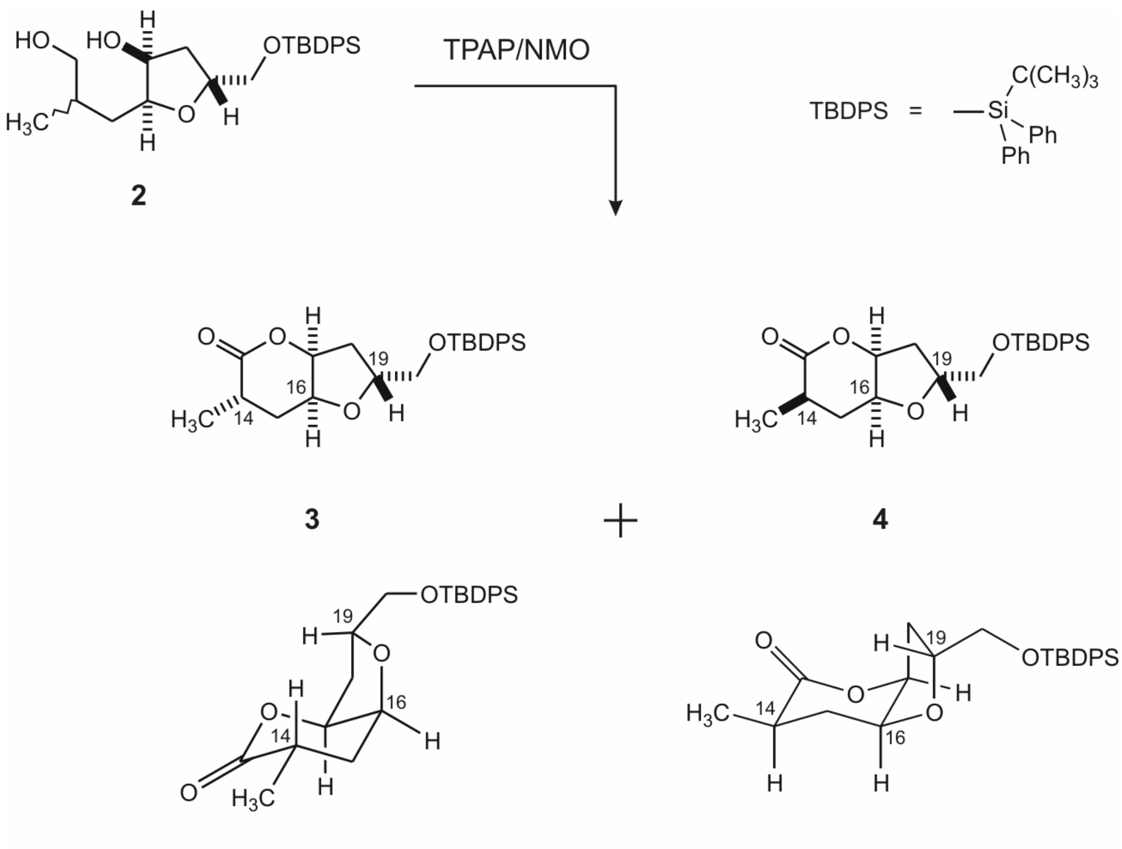
At the end of the 2 hour exam period you will be asked to return your exam to the proctor. (You may, of course, also turn the packet in earlier if you choose.) You are allowed to use any materials you brought with you before the exam. However, we ask that you not bring any materials in or out of the room while you are taking the exam. Please do not take any part of the exam packet with you when you are done; everything will be returned to you after the exams are graded.

This packet should contain 18 pages, including this one. (The last page contains a periodic table and will not be graded.) Please check to make sure that your packet contains 18 pages before beginning your exam.

Name: ____

Signature: ____

1. As part of a general strategy towards the total synthesis of azaspiracid, Amy Dounay (Forsyth Group) oxidatively converted the substituted tetrahydrofuran **2** to two diastereomeric lactones, which Amy predicted would have the structures **3** and **4**. Amy separated the two lactones and analyzed one of them extensively by NMR. This problem follows Amy's attempt to determine which structure (**3** *or* **4**) corresponded to this lactone.



(conformations drawn to maximize equatorial vs. axial groups)

Carbons in structures **3** and **4** are numbered according to their positions in the full structure of azaspiracid, and this exam will follow this same numbering scheme throughout. Amy already knew, based on previous experiments, that the ^{1}H resonance observed at δ = 4.3 ppm corresponded to H19.

Page	Description
5	^{1}H NMR, **500 MHz**, $CDCl_3$
6-7	Close-ups of page 4
8	^{1}H NMR, **500 MHz**, $CDCl_3$, decoupled at $\delta = 1.3$ ppm
9	Close-up of page 8
10	^{1}H NOE, irradiated at $\delta = 1.3$ ppm
11	^{1}H NOE, irradiated at $\delta = 2.8$ ppm

a. (10 pts) Amy began her analysis by assuming the resonance at $\delta = 1.3$ ppm belonged to the methyl group attached to C14. To what proton are the methyl group protons coupled to? What is the coupling constant observed?

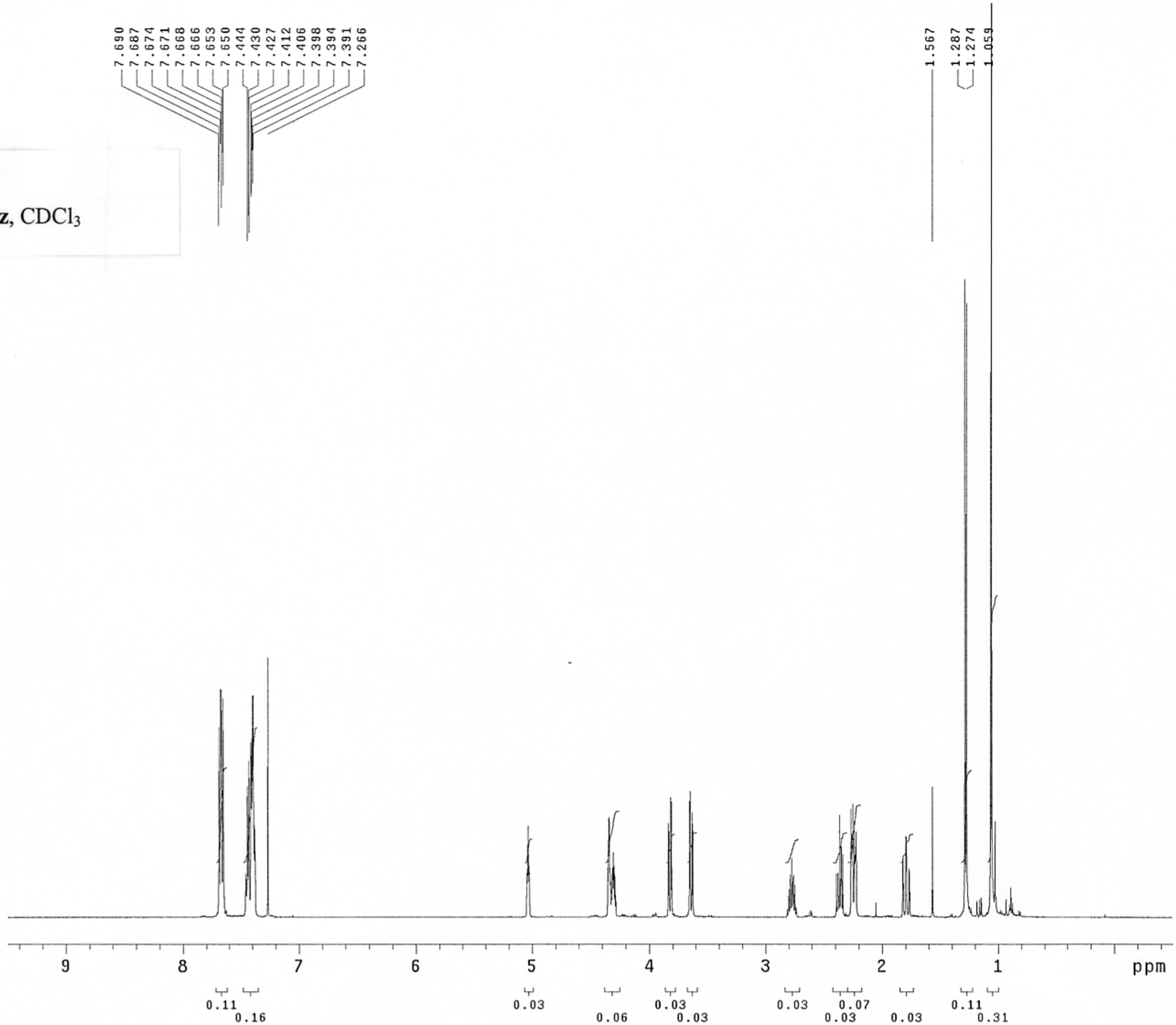
$-CH_3$ coupling partner	coupling constant (J)

b. (10 pts) To help discover the chemical shift of the methyl group's coupling partner, Amy applied a decoupling RF pulse at $\delta = 1.3$ ppm. Results of this experiment are shown on pages 8 and 9. What changes were observed in the ^{1}H NMR spectrum of the lactone as a result of decoupling?

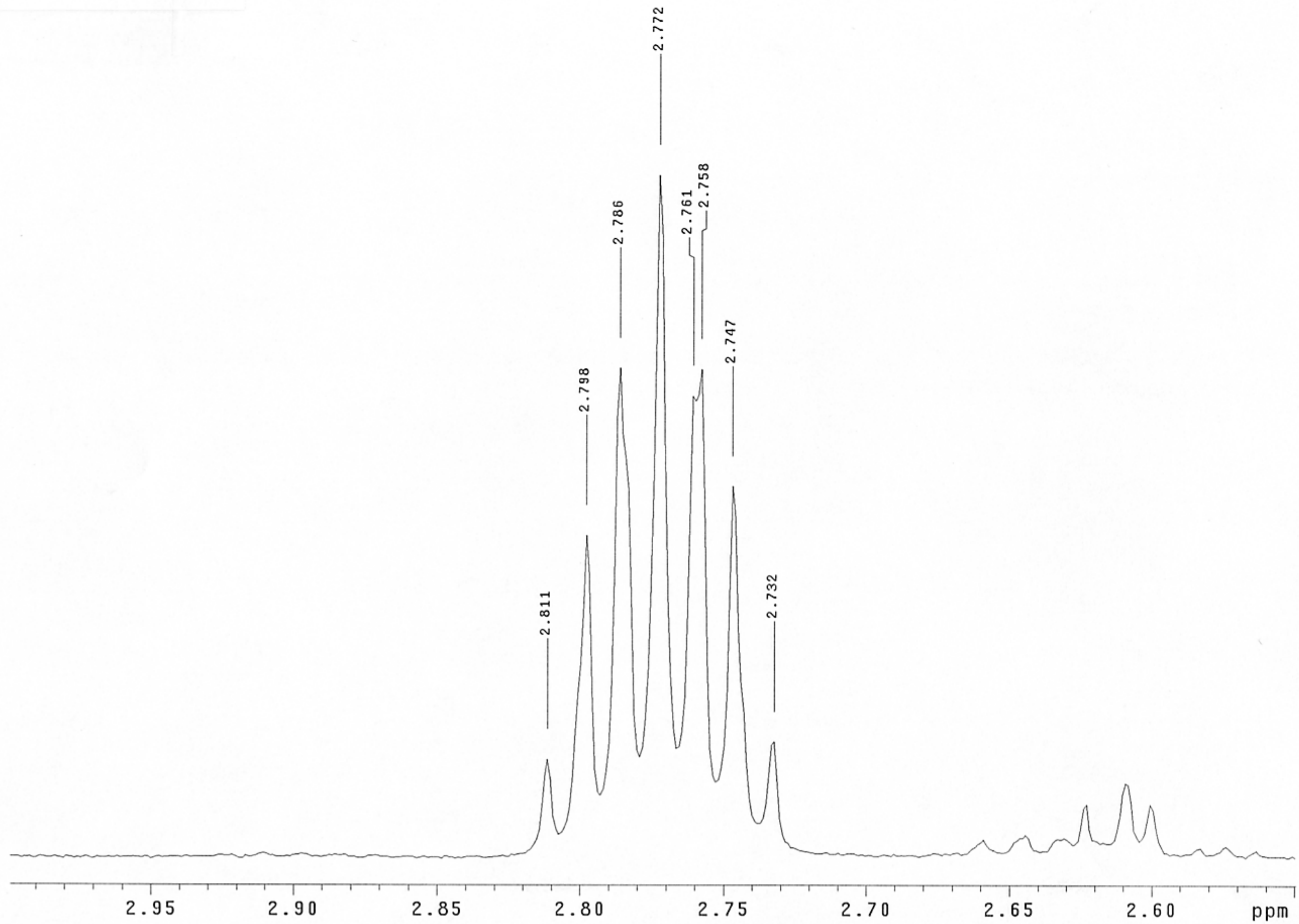
c. (10 pts) In resonances that changed, what coupling constants *J* are still observed? Do these values help you distinguish between **3** and **4** as the correct structure for the unknown?

d. (10 pts) Amy also performed nuclear Overhauser effect (NOE) experiments, pre-saturating the resonances at $\delta = 1.3$ ppm and $\delta = 2.8$ ppm (shown on pages 9 and 10, respectively). There are clearly differences in the way these experiments affected the resonance at $\delta = 4.3$ ppm, which Amy had already assigned to H19. Does this information help you distinguish between **3** and **4** as the correct structure for the unknown?

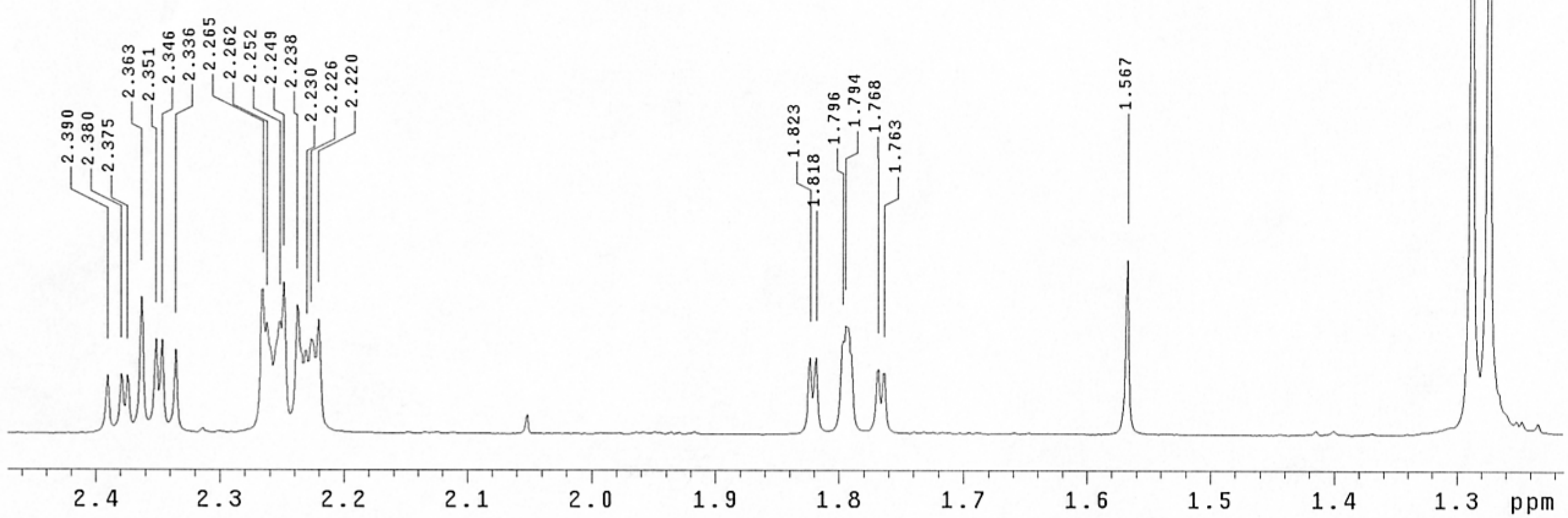
Problem 1
^{1}H NMR, **500 MHz**, $CDCl_3$



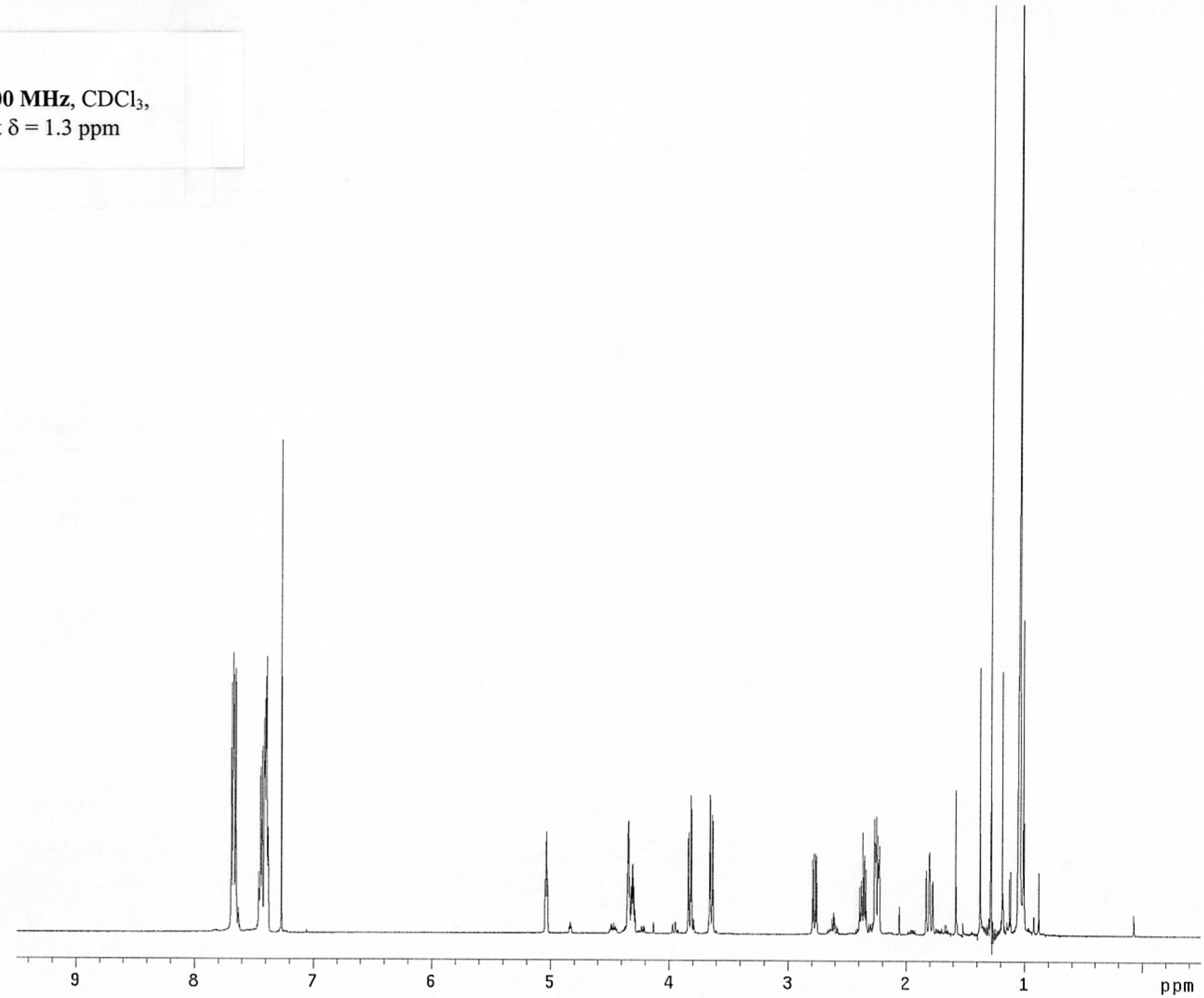
Problem 1
^{1}H NMR, **500 MHz**, $CDCl_3$
(closeup)



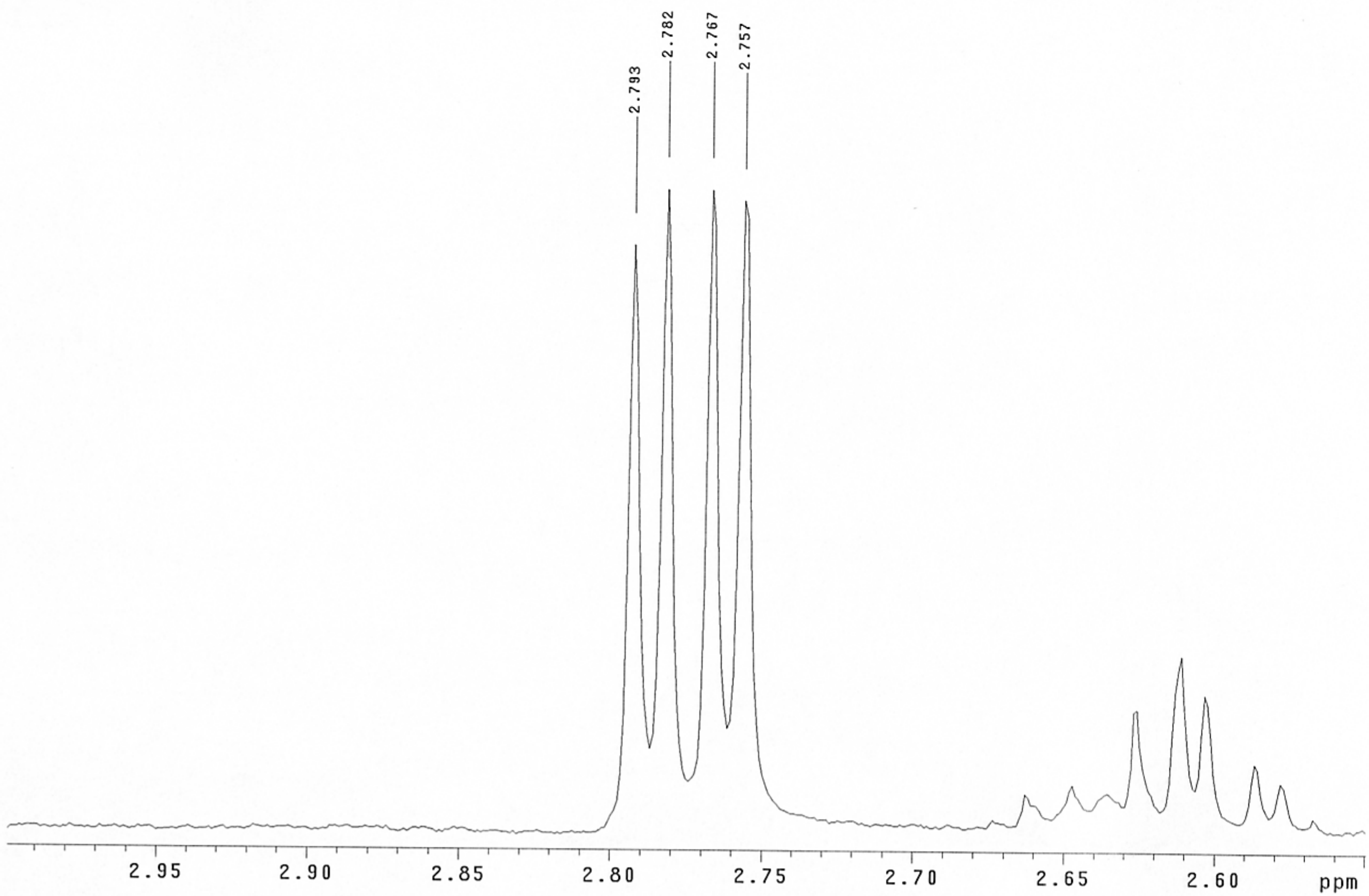
Problem 1
^1H NMR, **500 MHz**, $CDCl_3$
(closeup)



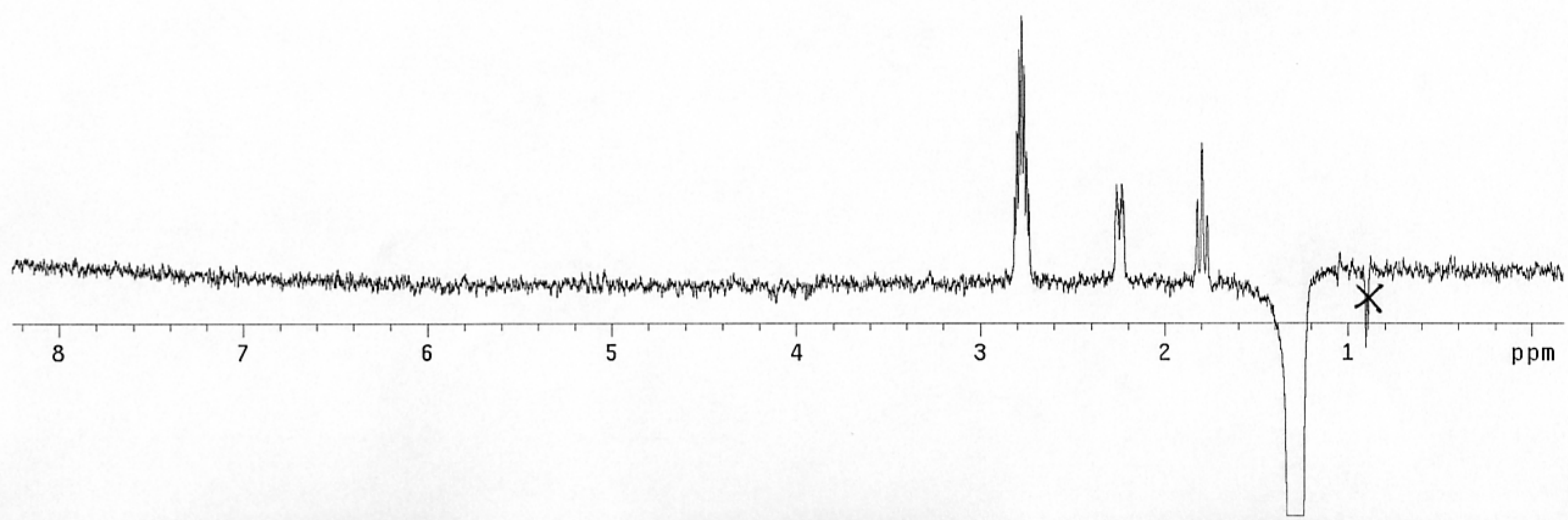
Problem 1
^{1}H NMR, **500 MHz**, $CDCl_3$,
decoupled at $\delta = 1.3$ ppm



Problem 1
^{1}H NMR, **500 MHz**, $CDCl_3$,
decoupled at $\delta = 1.3$ ppm
(closeup)

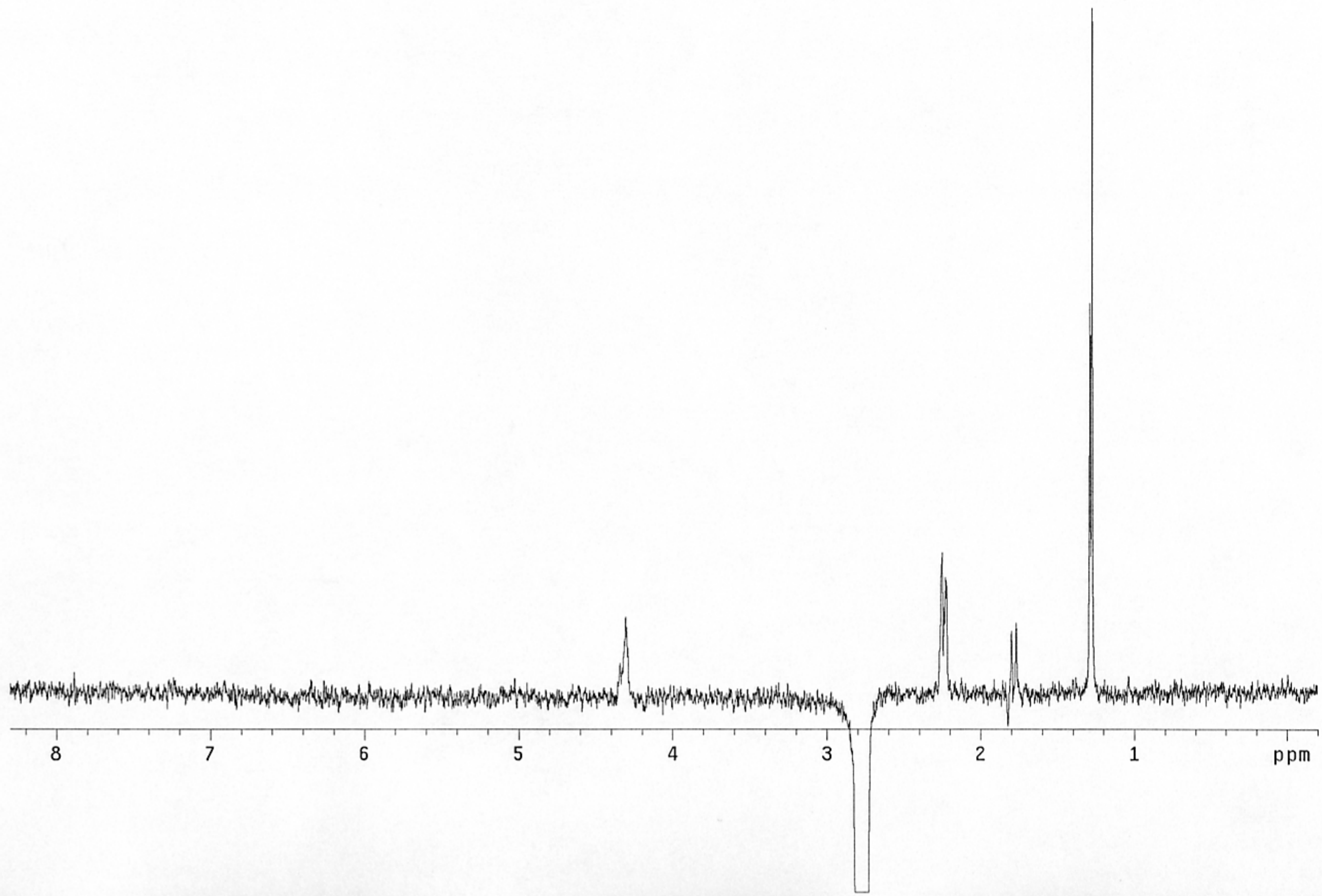


Problem 1
^{1}H NOE, irradiated at $\delta = 1.3$ ppm

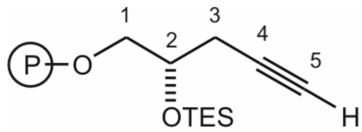


Problem 1

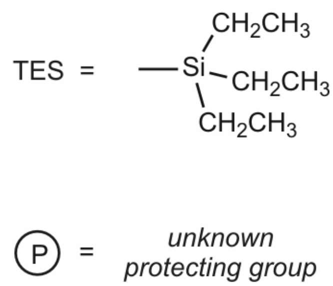
^{1}H NOE, irradiated at $\delta = 2.8$ ppm



2. The [1]H NMR spectrum and close-ups on pages 15-17 refer to the doubly protected alkynyl diol **5**. By simple mass spectrometry, **5** has a molecular mass of 334, meaning that the unknown protecting group P has a (fragment) mass of 121.



5



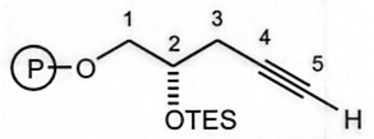
a. (30 pts) In the chart on the next page, assign chemical shifts, multiplicities, coupling partners and coupling constants to the protons in the backbone of **5**. (Ignore resonances corresponding to the protecting groups.)

b. (10 pts) What is the structure of the unknown protecting group P? *(If you do not know, guess. Partial credit will be given for correct structural elements that are part of an incorrect structure.)*

Proton	Chemical shift (δ)	Multiplicity	Coupling partners	Coupling constants (J)
1a				
1b				
2				
3a				
3b				
5				

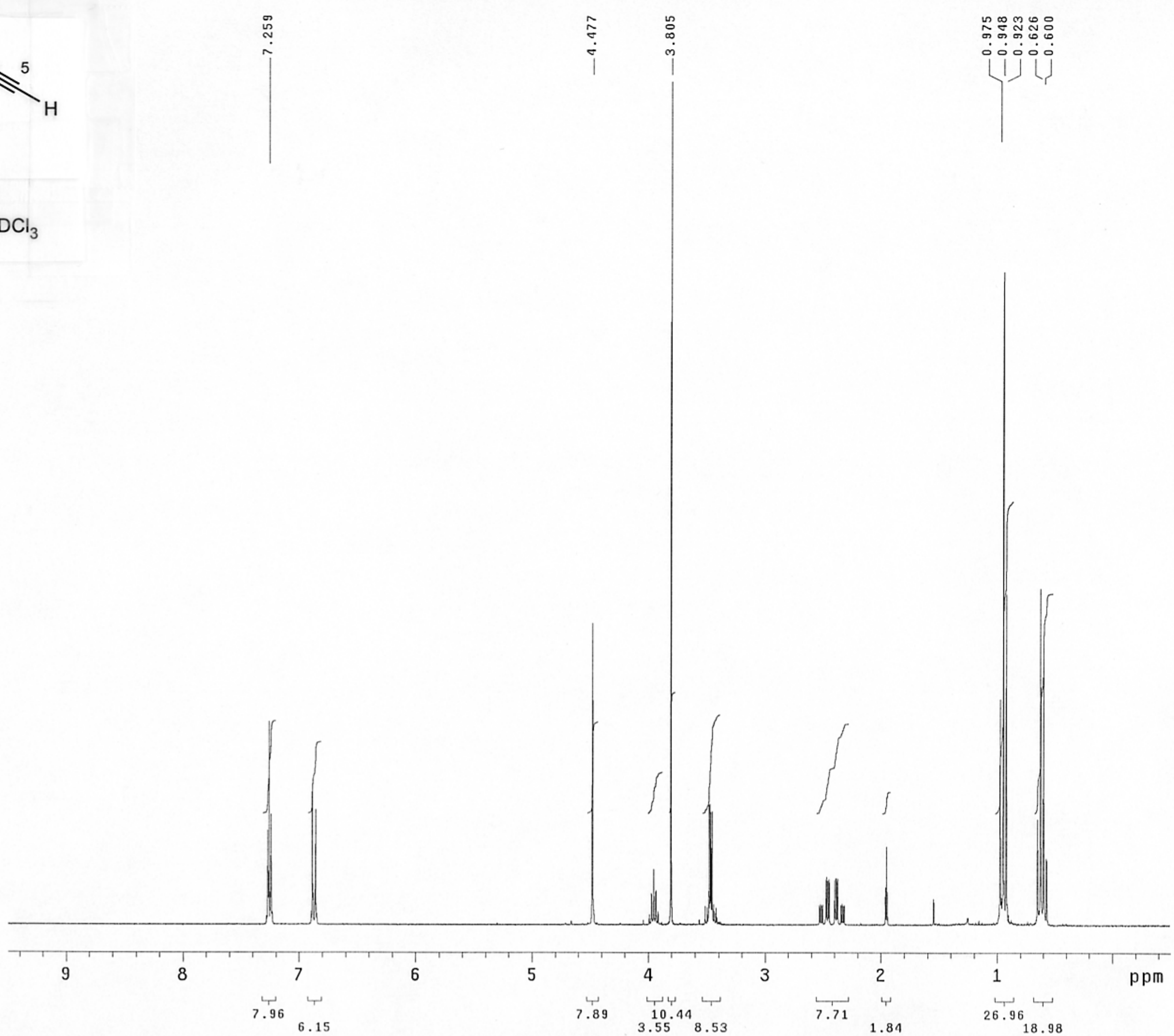
c. (10 pts) Why does the splitting pattern in the multiplet at $\delta = 3.47$ ppm look unusual? Frame your answer in terms of the chemical structure of **5**.

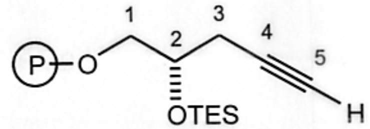
d. (10 pts) Although the resonance at $\delta = 1.95$ can be assigned to one proton, the integrated intensity of this signal is proportionally too low. Why might this be? Frame your answer in terms of the chemical structure of **5**.



5

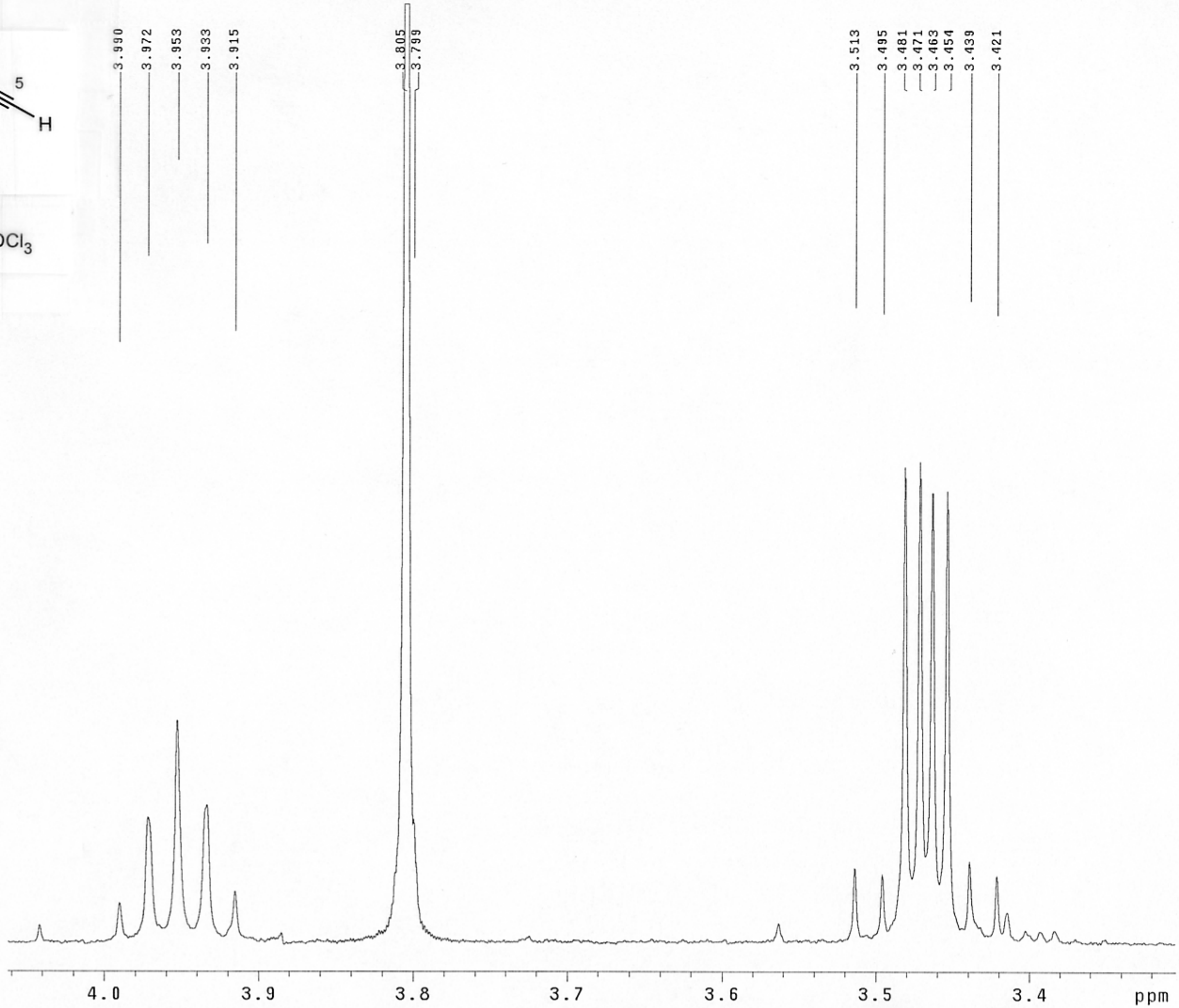
^{1}H NMR, 300 MHz, $CDCl_3$

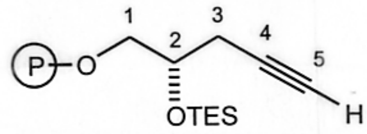




5

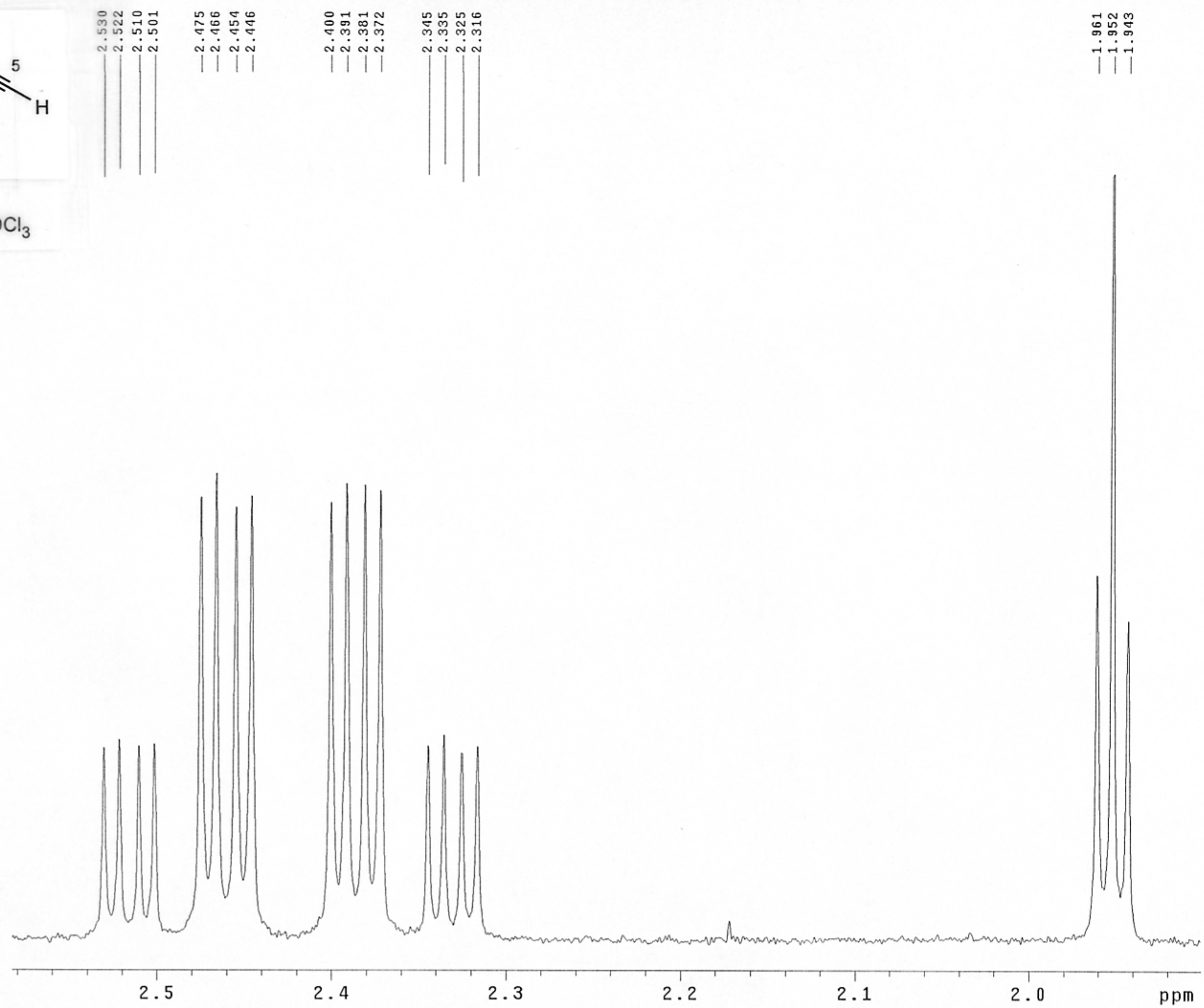
^1H NMR, 300 MHz, $CDCl_3$





5

^{1}H NMR, 300 MHz, $CDCl_3$



Periodic Table of the Elements

Key	
6	Atomic number
C	Element symbol
12.01	Atomic weight*
Carbon	Element name

PERIOD	1A	2A	3B	4B	5B	6B	7B	8B	8B	8B	1B	2B	3A	4A	5A	6A	7A	Noble gases 8A
1	1 **H** 1.008 Hydrogen																	2 **He** 4.003 Helium
2	3 **Li** 6.941 Lithium	4 **Be** 9.012 Beryllium											5 **B** 10.81 Boron	6 **C** 12.01 Carbon	7 **N** 14.01 Nitrogen	8 **O** 16 Oxygen	9 **F** 19.00 Fluorine	10 **Ne** 20.18 Neon
3	11 **Na** 22.99 Sodium	12 **Mg** 24.31 Magnesium											13 **Al** 26.98 Aluminum	14 **Si** 28.09 Silicon	15 **P** 30.97 Phosphorus	16 **S** 32.07 Sulfur	17 **Cl** 35.45 Chlorine	18 **Ar** 39.95 Argon
4	19 **K** 39.10 Potassium	20 **Ca** 40.08 Calcium	21 **Sc** 44.96 Scandium	22 **Ti** 47.867 Titanium	23 **V** 50.94 Vanadium	24 **Cr** 52.00 Chromium	25 **Mn** 54.94 Manganese	26 **Fe** 55.85 Iron	27 **Co** 58.93 Cobalt	28 **Ni** 58.70 Nickel	29 **Cu** 63.546 Copper	30 **Zn** 65.39 Zinc	31 **Ga** 69.72 Gallium	32 **Ge** 72.64 Germanium	33 **As** 74.92 Arsenic	34 **Se** 78.96 Selenium	35 **Br** 79.90 Bromine	36 **Kr** 83.80 Krypton
5	37 **Rb** 85.47 Rubidium	38 **Sr** 87.62 Strontium	39 **Y** 88.91 Yttrium	40 **Zr** 91.22 Zirconium	41 **Nb** 92.90 Niobium	42 **Mo** 95.94 Molybdenum	43 **Tc** (98) Technetium	44 **Ru** 101.07 Ruthenium	45 **Rh** 102.9 Rhodium	46 **Pd** 106.4 Palladium	47 **Ag** 107.9 Silver	48 **Cd** 112.4 Cadmium	49 **In** 114.8 Indium	50 **Sn** 118.7 Tin	51 **Sb** 121.8 Antimony	52 **Te** 127.6 Tellurium	53 **I** 126.9 Iodine	54 **Xe** 131.3 Xenon
6	55 **Cs** 132.9 Cesium	56 **Ba** 137.327 Barium	71 **Lu** 175.0 Lutetium	72 **Hf** 178.5 Hafnium	73 **Ta** 180.9479 Tantalum	74 **W** 183.84 Tungsten	75 **Re** 186.2 Rhenium	76 **Os** 190.23 Osmium	77 **Ir** 192.2 Iridium	78 **Pt** 195.1 Platinum	79 **Au** 197.0 Gold	80 **Hg** 200.6 Mercury	81 **Tl** 204.4 Thallium	82 **Pb** 207.2 Lead	83 **Bi** 209.0 Bismuth	84 **Po** (209) Polonium	85 **At** (210) Astatine	86 **Rn** (222) Radon
7	87 **Fr** (223) Francium	88 **Ra** (226) Radium	103 **Lr** (257) Lawrencium	104 **Rf** (261) Rutherfordium	105 **Db** (262) Dubnium	106 **Sg** (263) Seaborgium	107 **Bh** (262) Bohrium	108 **Hs** (265) Hassium	109 **Mt** (266) Meitnerium	110 (269)	111 (272)	112 (277)		114 (285)		116 (289)		

* Lanthanide series:	57 ***La** 138.9 Lanthanum	58 **Ce** 140.1 Cerium	59 **Pr** 140.9 Praseodymium	60 **Nd** 144.2 Neodymium	61 **Pm** (145) Promethium	62 **Sm** 150.4 Samarium	63 **Eu** 152.0 Europium	64 **Gd** 157.3 Gadolinium	65 **Tb** 158.9 Terbium	66 **Dy** 162.5 Dyprosium	67 **Ho** 164.9 Holmium	68 **Er** 167.3 Erbium	69 **Tm** 168.9 Thulium	70 **Yb** 173.0 Ytterbium
† Actinide series:	89 **†Ac** (227) Actinium	90 **Th** 232.0 Thorium	91 **Pa** (231) Protactinium	92 **U** 238.0 Uranium	93 **Np** (237) Neptunium	94 **Pu** (244) Plutonium	95 **Am** (243) Americium	96 **Cm** (247) Curium	97 **Bk** (247) Berkelium	98 **Cf** (251) Californium	99 **Es** (252) Einsteinium	100 **Fm** (257) Fermium	101 **Md** (258.10) Mendelevium	102 **No** (259) Nobelium

*Numbers in parentheses are mass numbers of the most stable or best-known isotope of radioactive elements.