CHEM 344 Final Quiz Fall 2013

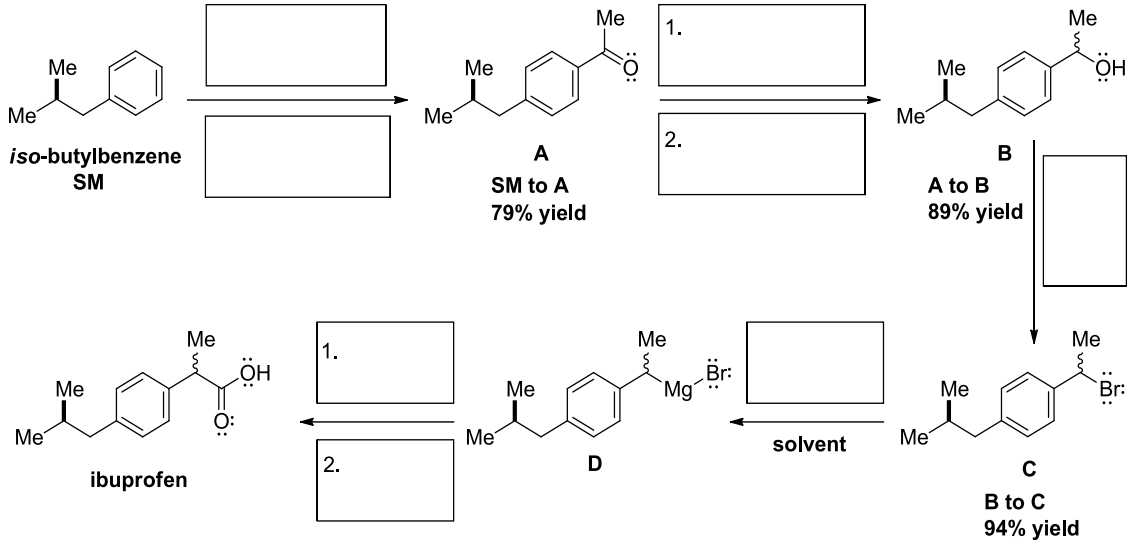
100 pts

Name:

TA Name:

CHEM 344 Final Quiz Fall 2013 **100 pts**

1) A multi-step synthesis of the NSAID ibuprofen is shown below.

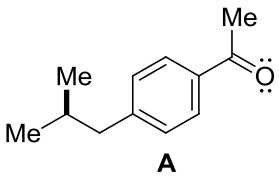


a) Fill in the boxes with the appropriate reagent(s) for each step of the synthetic route. (8 pts)

b) 2.81 g of ibuprofen was obtained from 3.78 g of compound C. Showing all work, calculate the % yield of ibuprofen. (4 pts)

c) Based upon your answer to part b) calculate the overall %yield of ibuprofen starting from *iso*-butylbenzene (SM) (2 pts).

d) The EI-MS data for compound A feature the following important peaks:

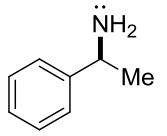


A

EI-MS: *m/z* 161 (100 %), 133 (42 %)

For each peak, draw the most likely ion in its major resonance form. Show all formal charges and lone pairs (4 pts).

e) Pure ibuprofen is isolated from the above synthetic route as a racemic mixture. The enantiomers of ibuprofen can be separated by using a chiral reagent such as (*S)*-1-phenylethylamine (shown below).

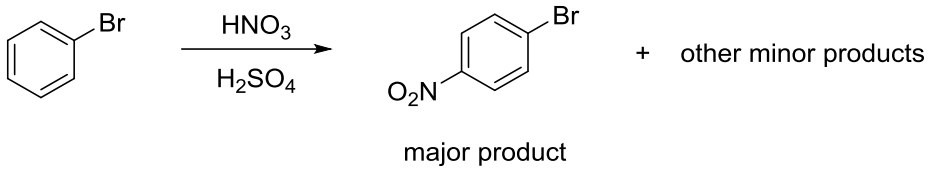


(*S*)-1-phenylethylamine

Draw the diastereomeric salts produced by reaction of (*S)*-1-phenylethylamine with racemic ibuprofen. Assign the configuration of any chiral atoms as either *R* or *S*. Show all lone pairs and formal charges. (4 pts)

f) The *R,S* salt is soluble in water but the *S,S* salt is insoluble. Suggest a procedure to separate the salts and isolate the two enantiomers of ibuprofen. (4 pts)

2) The nitration of bromobenzene with H_2SO_4/HNO_3 results in *p*-bromonitrobenzene as the major product along with (at least) two other organic products. This question will consider the formation of possible products, the ratio of products in the crude material, and the identity of each product.



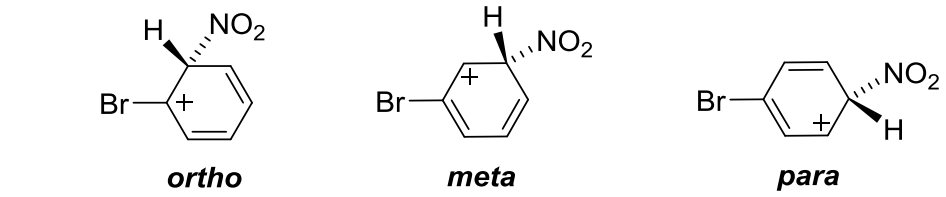
major product

a) What are the *m/z* values of the two highest abundance molecular ions of the major product? (1 pt)

b) What is the directing effect of a bromo substituent on a benzene ring? Does a bromo substituent activate or deactivate the benzene ring toward an electrophile? (Do not explain, just identify.) (1 pt)

c) What is the directing effect of a nitro (NO_2) substituent on a benzene ring? Does a nitro substituent activate or deactivate the benzene ring toward an electrophile? (Do not explain, just identify.) (1 pt)

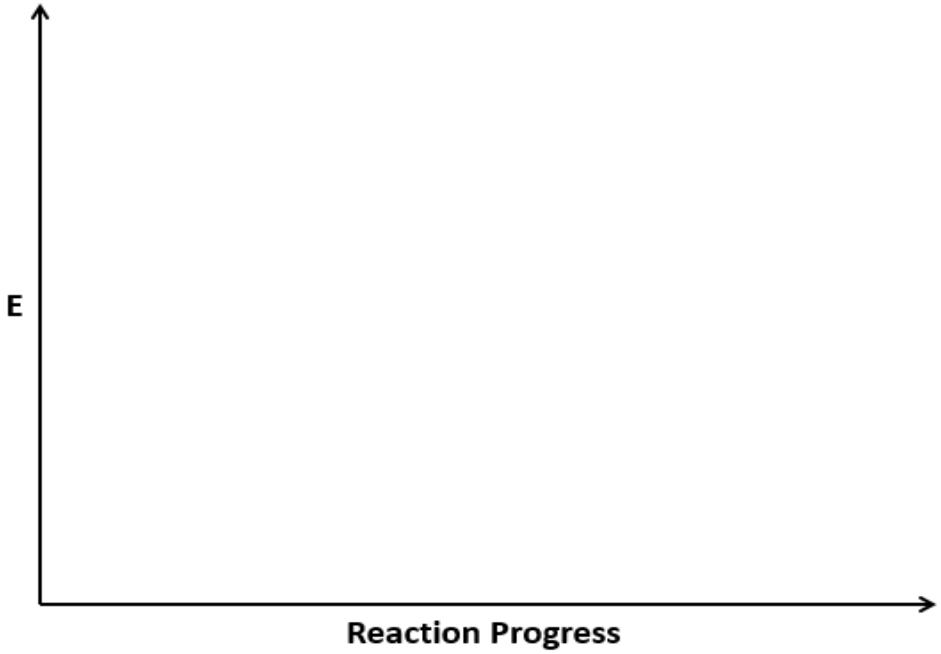
d) Use the structures of the possible arenium intermediates, the potential energy surface shown below, Hammond's postulate, and any other necessary chemical concepts to fully explain why *p*-bromonitrobenzene is the major product of the nitration of bromobenzene. (10 pts)



ortho

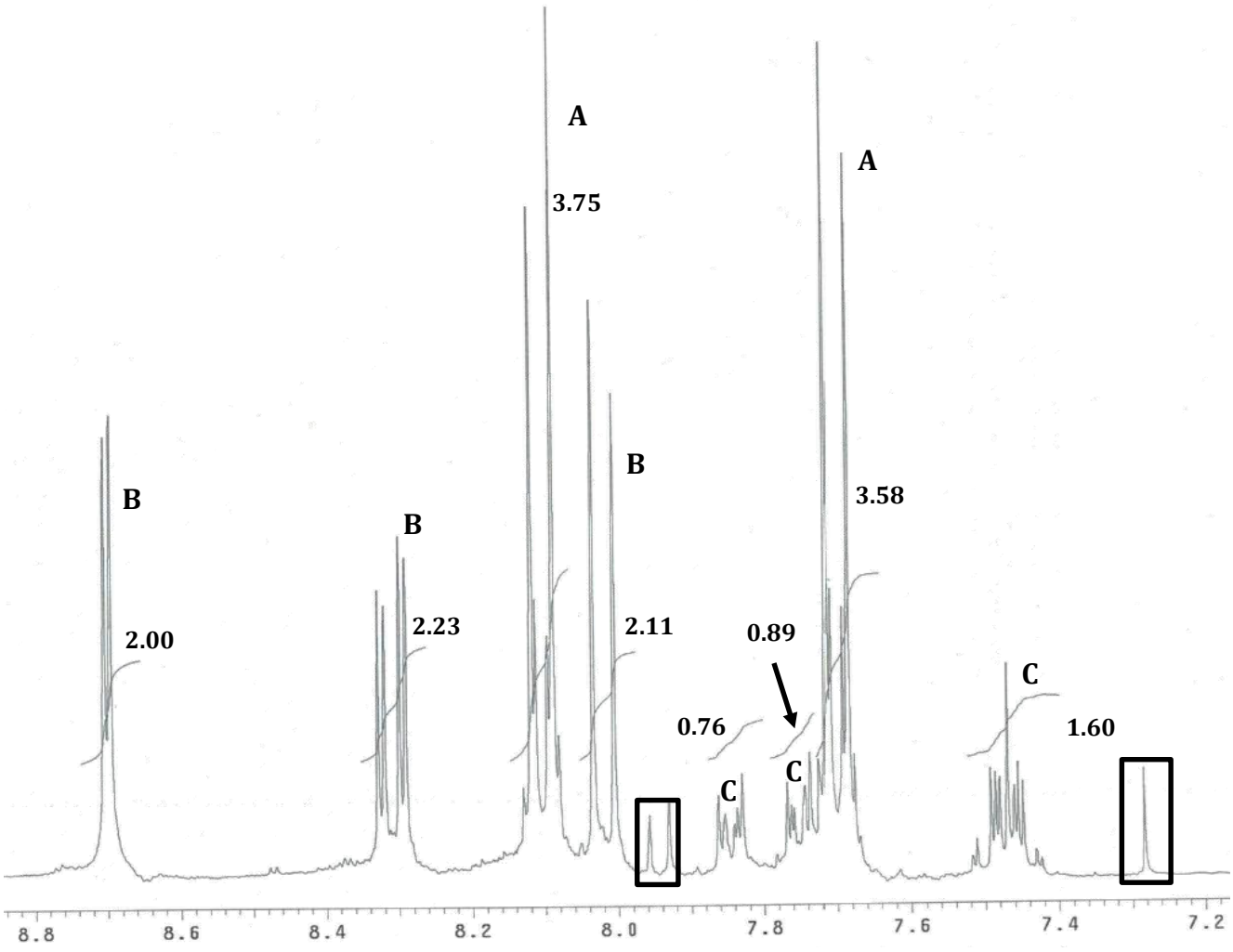
meta

para

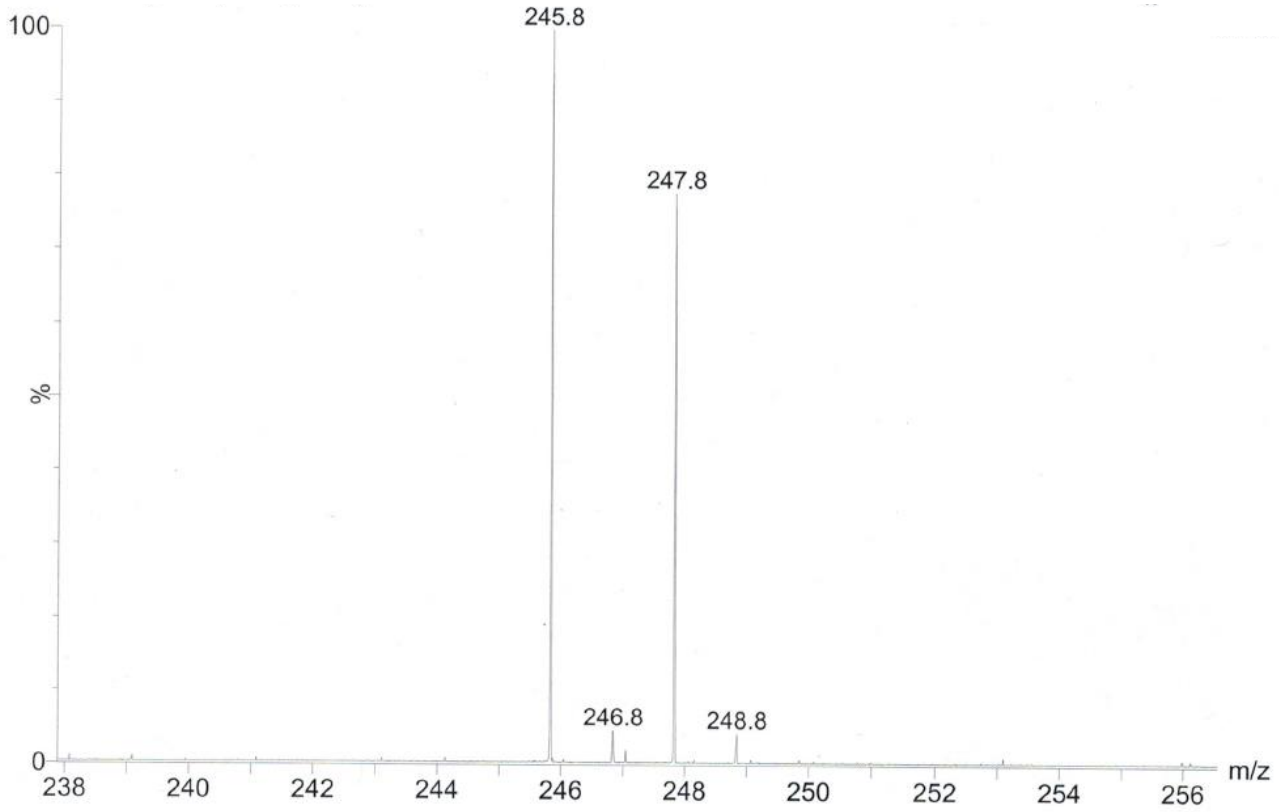


e) The ^{1}H-NMR spectrum of the crude product of the nitration of bromobenzene is shown below. The crude mixture contains 3 organic products (NMR signals labeled A, B, and C). Showing all work, calculate the relative ratios of the 3 products in terms of A:B:C (i.e. A is the most abundant and C is the least abundant of the three products, normalized to C= 1). The raw integrals are displayed next to each signal. Each product contains a single aromatic ring. Ignore the signals in the black boxes. (4 pts)

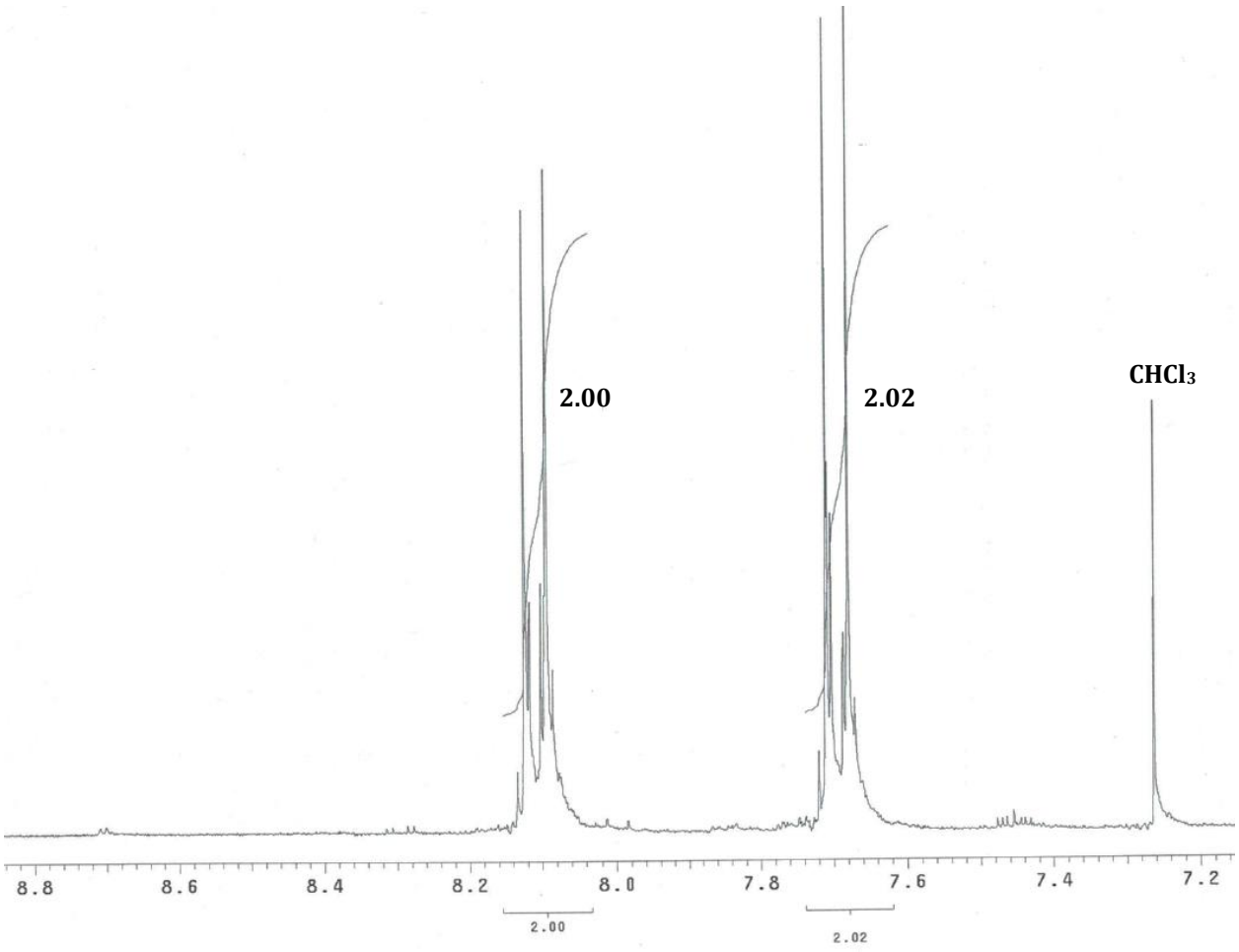
A scratch spectrum is provided at the end of the exam packet but all work for grading must be included on the spectrum on this page.



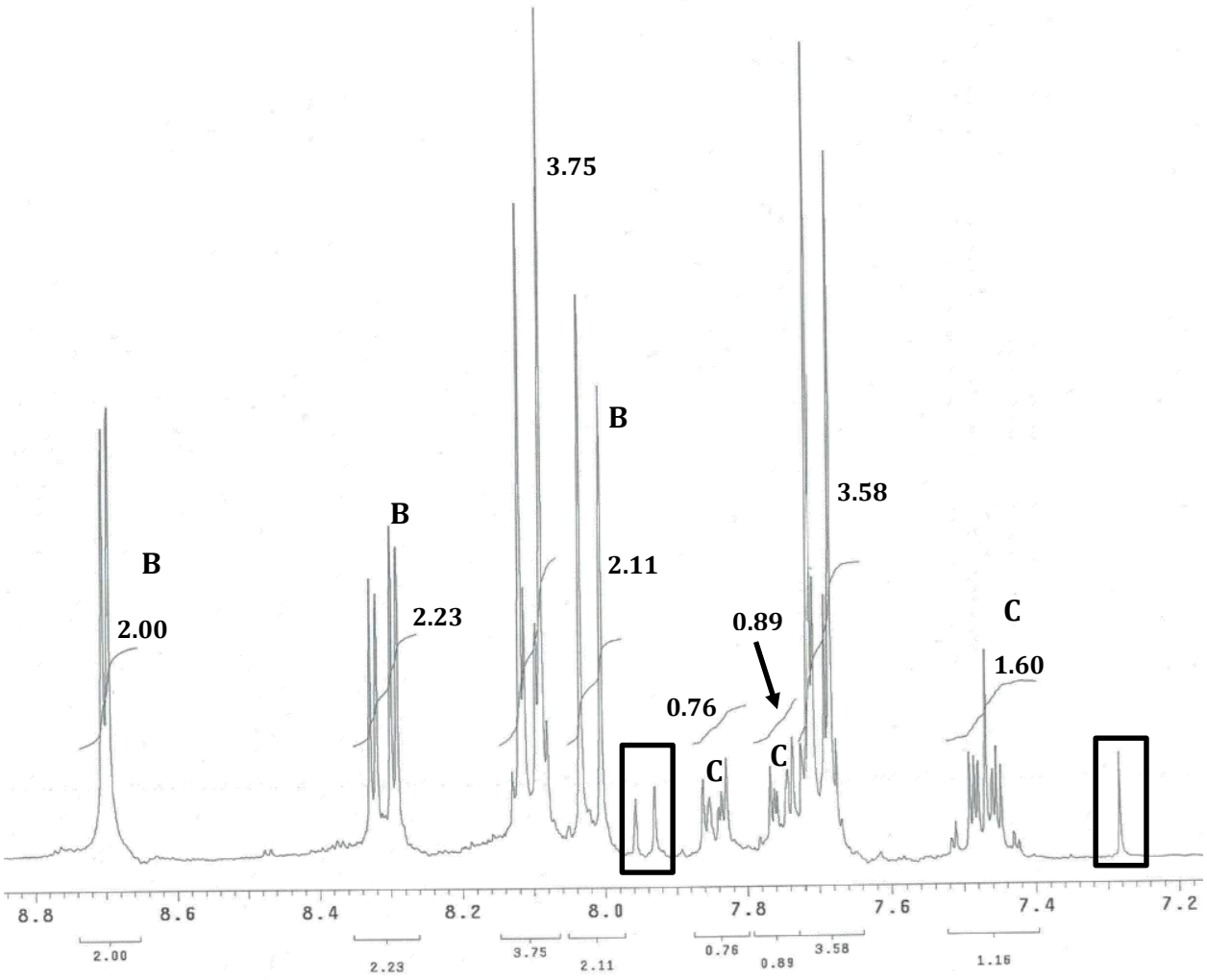
f) In addition to the ^{1}H-NMR spectrum, an EI-mass spectrum of product B was obtained. Use the EI-MS data shown below and your answer to part a) to deduce and draw the structure of product B. Show all work. (3 pts)



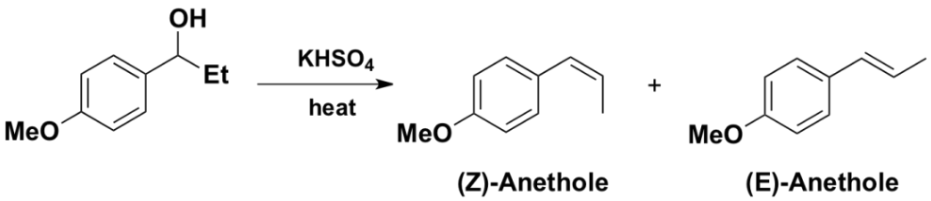
g) The crude nitration product was recrystallized from dichloromethane. The ^{1}H-NMR spectrum of the recrystallized product is shown below. Assign each of the signals in the spectrum using the H_a, H_b, etc. system. Additionally, comment upon the effectiveness of the recrystallization and explain your reasoning. (4 pts)



h) Based upon the preceding NMR and MS data draw the structures of the minor products B and C. Justify your answers based upon your chemistry knowledge and the spectra provided. Fully assign the NMR spectrum of the crude product provided below using the H_a, H_b, etc. system. (8 pts)



3) Antheole is an aromatic compound isolated from Anise, Fennel and Star Anise oils. It is commonly used in liqours such as Ouzo. A synthetic route to a mixture of (*Z*)- and (*E*)-Antheole is shown below:



a) Name the type of reaction taking place and draw a circle around the major product (2 pts).

b) Suggest another reaction that you have studied in CHEM 344 that might produce a mixture of (*Z*)- and (*E*)-Antheole. Show all necessary starting materials, reagents, and conditions. (3 pts)

c) The above reactions generate a mixture of (*Z)*- and (*E)*-Anethole. The near identical properties of the isomers makes separation difficult and so there is need for a synthetic route that is selective for each individual isomers.

The Suzuki-Miyaura coupling reaction is used to form σ–bonds between sp^2-hybridized carbon atoms. Propose a Suzuki-Miyaura synthesis of the isomer of Anethole that you circled in part a), starting from a substituted bromobenzene and any other organic compounds you require. Show all necessary reagents and conditions. (5 pts)

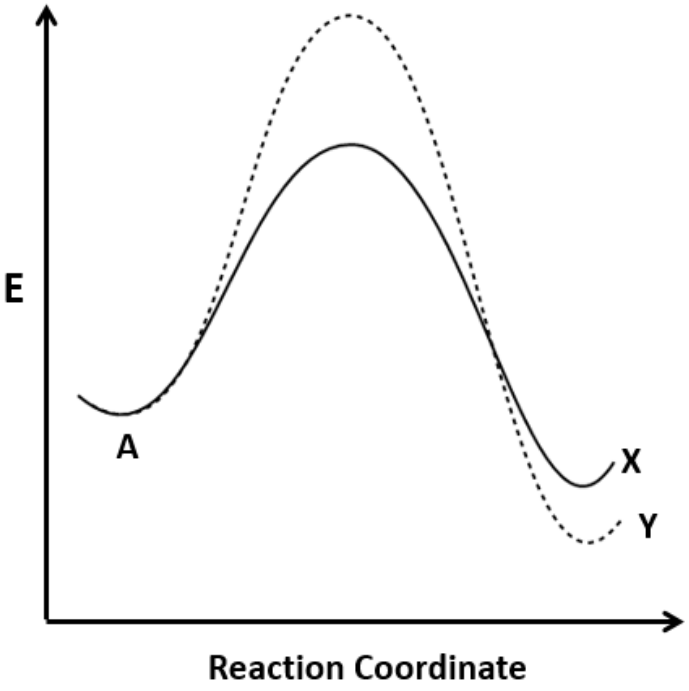
4) The potential energy surfaces a) and b) show the uncatalyzed conversions A → X+Y and B → G+H respectively.

i) On each PE surface, clearly identify the thermodynamic and kinetic product.

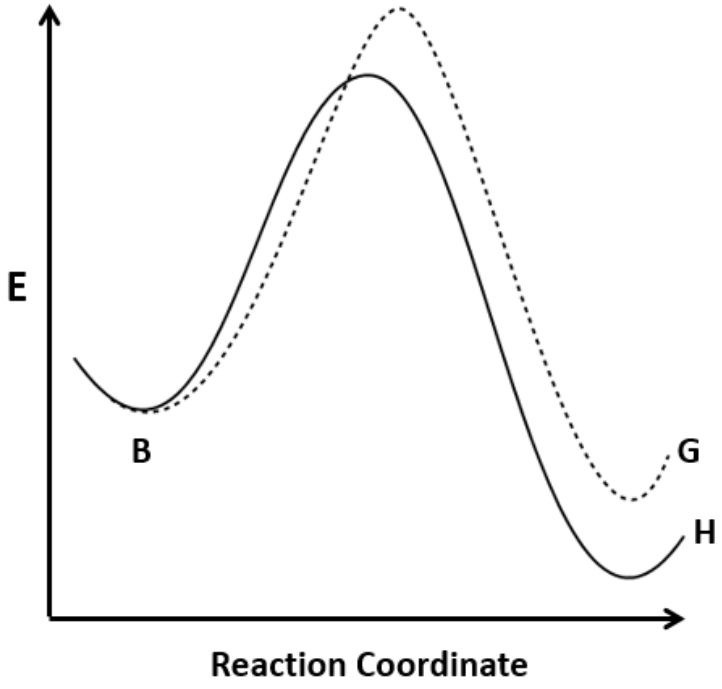
ii) on PE surface a), draw and label a possible pathway for the catalyzed process A→ X.

(6 pts total)

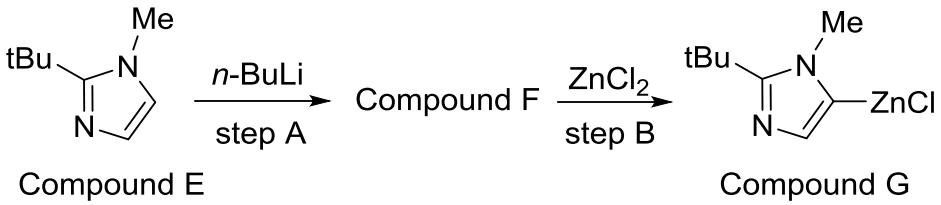
a)



b)



5) The Negishi reaction is a widely used Pd-catalyzed cross coupling that uses an organozinc reagent. The preparation of an organozinc reagent Compound G from the substituted imidazole precursor Compound E is shown below.



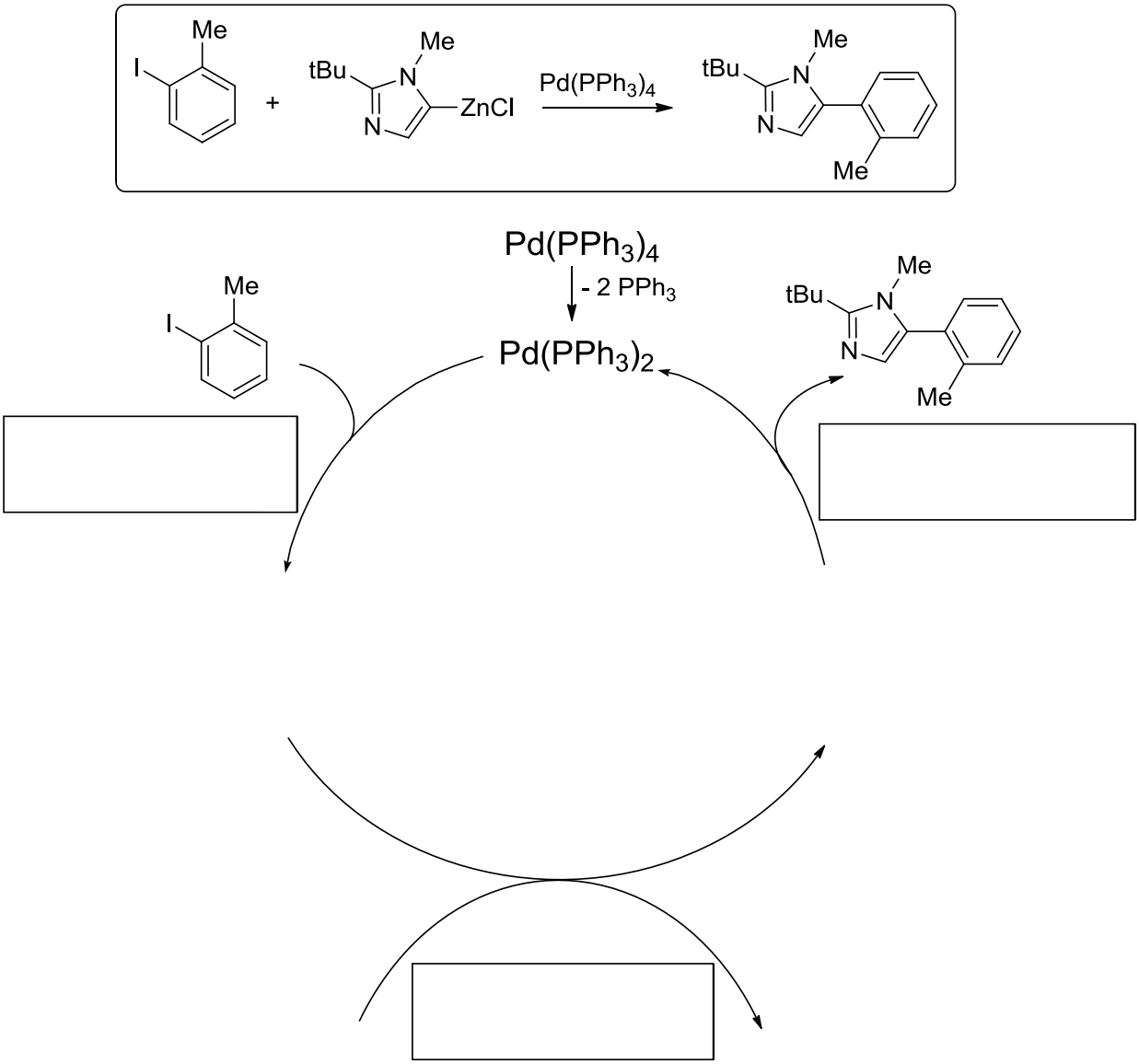
Compound E Compound G

a) Explain why *n*-BuLi is a very strong base (3 pts).

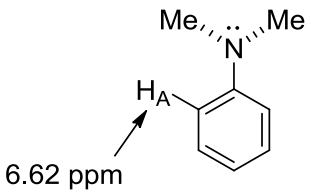
b) Draw a balanced chemical equation to show the formation of Compound F *via* the reaction of *n*-BuLi with Compound E. Show the structure of Compound F (3 pts).

c) State the name of the process occurring in step B to produce Compound G and draw the byproduct of the reaction. (2 pts)

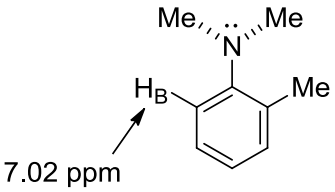
d) Complete the catalytic cycle for the Negishi coupling reaction shown below, labeling each step in the blank boxes and drawing the appropriate reagents and products of each of step. (10 pts)



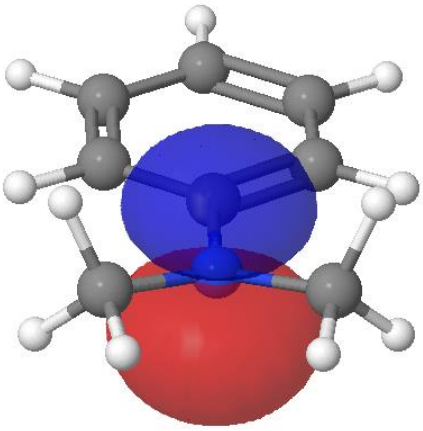
6) The aromatic amines *N,N'*-dimethylaniline (**A**) and 2-methyl-*N,N'*-dimethylaniline (**B**) are shown below. The ^{1}H-NMR chemical shift of the proton *ortho* to the NMe_2 group is given below each structure. The N-atom lone pairs are shown in the color images.

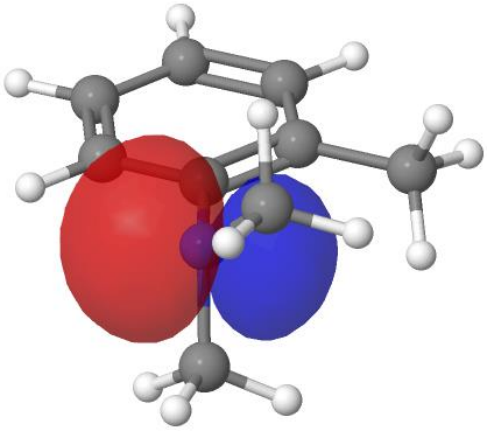


Compound A
N,N'-Dimethylaniline



Compound B
2-Methyl-N,N'-dimethylaniline





hybridization of N-lone pair in **A** $sp^{33.31}$ hybridization of N-lone pair in **B** $sp^{12.26}$

a) Draw a key resonance structure to explain the chemical shift value of H_A in compound **A** relative to the protons in benzene (δ=7.15 ppm). Clearly show all lone pairs and formal charges. (2 pts)

b) explain why the proton H_B in compound **B** is deshielded relative to the corresponding proton H_A in compound **A** (4 pts).

c) Using your answers in parts (a) & (b), explain whether **A** or **B** has the more basic nitrogen atom (2 pts).

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Name:

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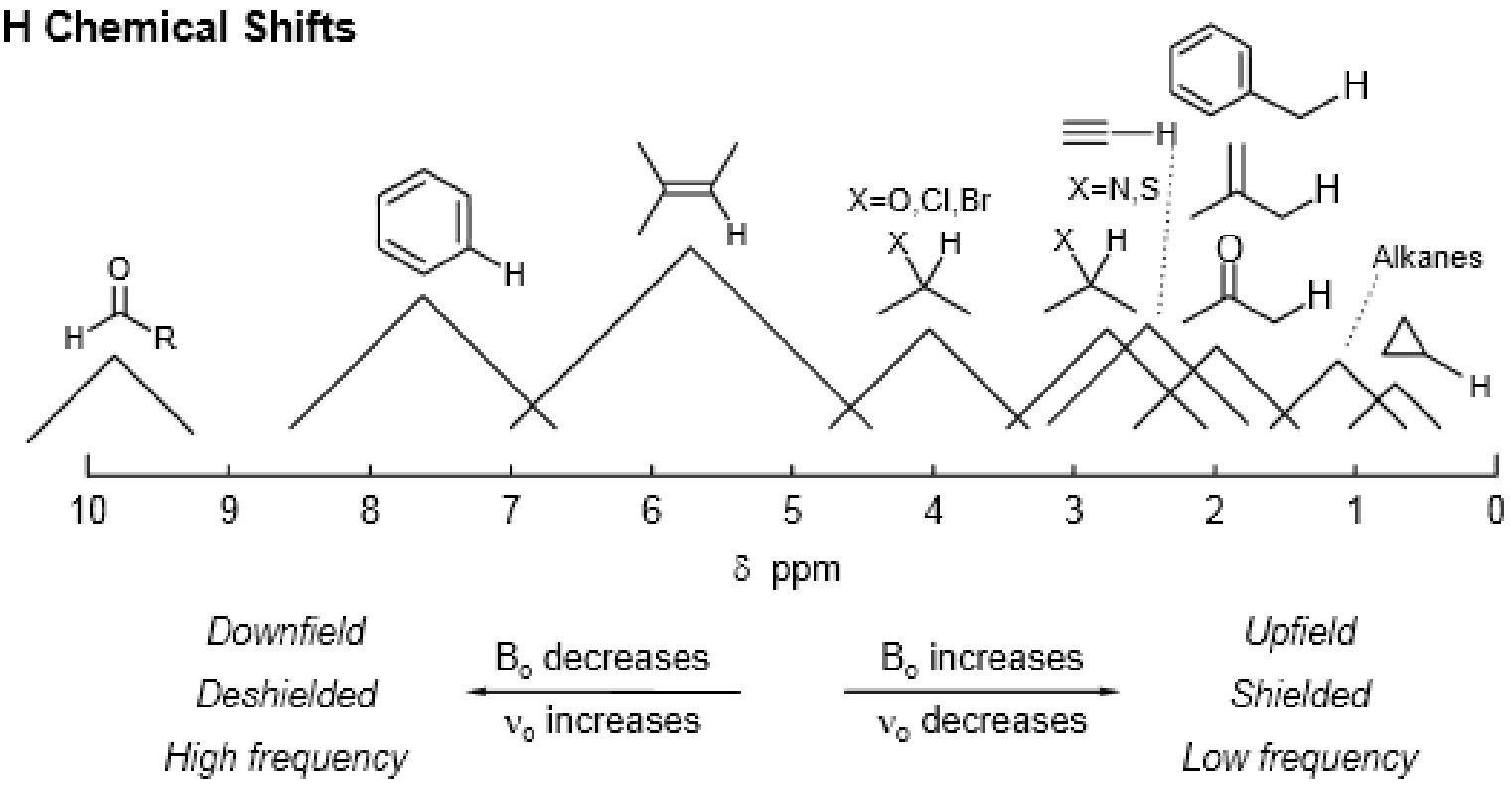
Q1	**/26**
Q2	**/32**
Q3	**/10**
Q4	**/6**
Q5	**/18**
Q6	**/8**

Total = **/100**

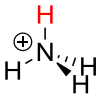
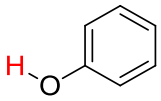
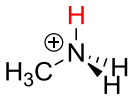
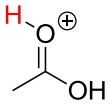
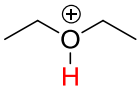
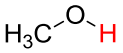
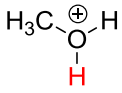
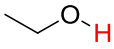
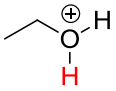
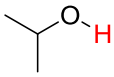
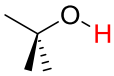
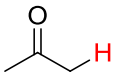
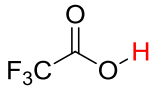
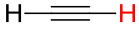
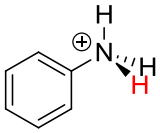
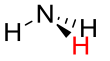
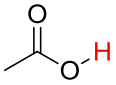
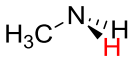
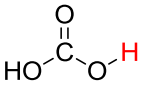
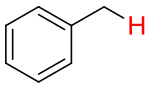
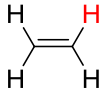
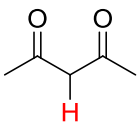
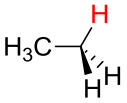
^{1}H-NMR chemical shift ranges



^{1}H-NMR coupling constants

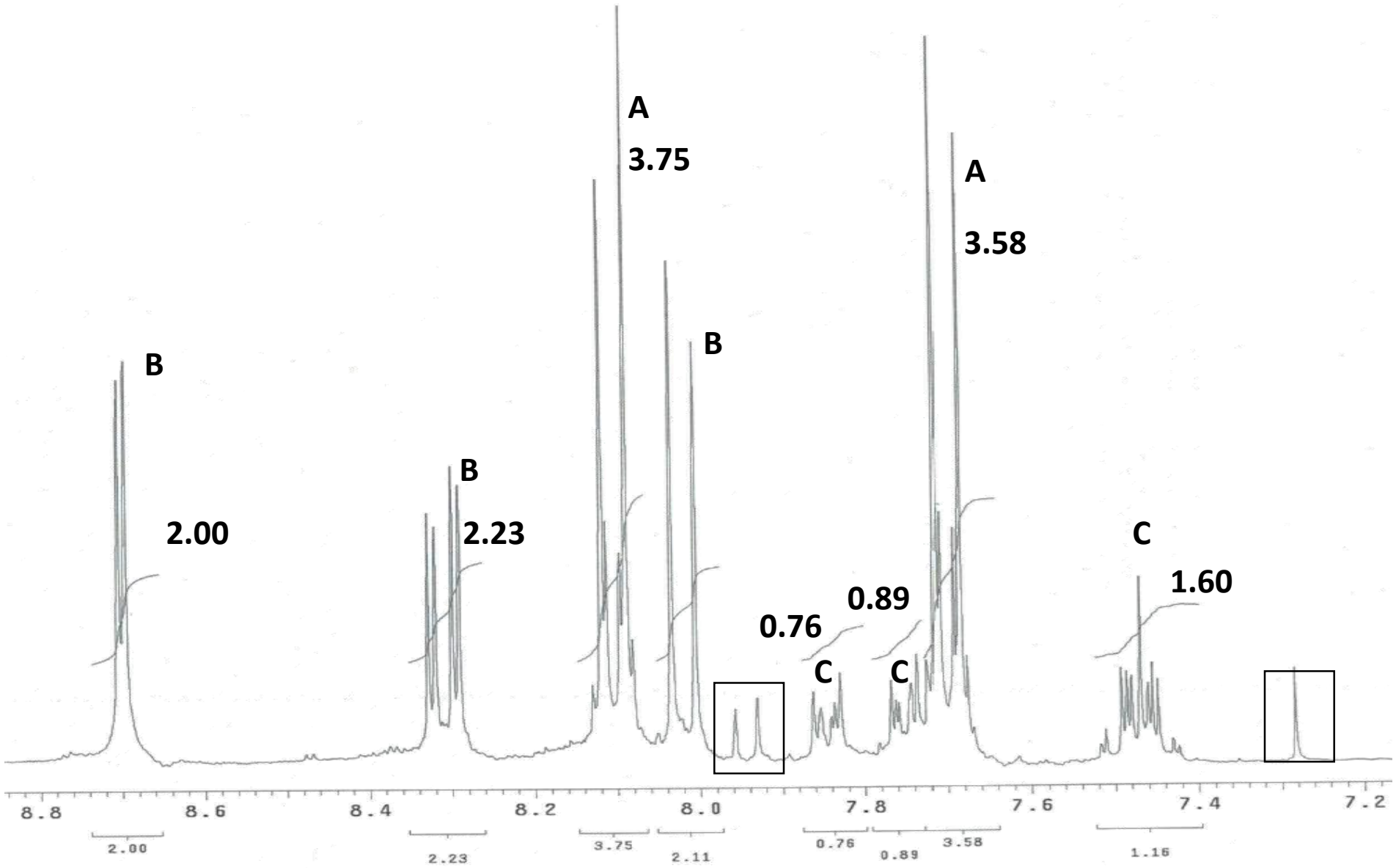
$J_{trans} > J_{cis} > J_{gem}$

$J_{ortho} > J_{meta} > J_{para}$

Acid	pK_a	Acid	pK_a
H–I	-10	H–CN	9.1
H–Br	-9		9.2
	-7.5		9.9
H–Cl	-7		10.6
	-6.2		10.7
	-3.8		15.5
H–O–SO_3H	-3*		15.7
	-2.5		16
	-2.4		16.5
	-1.74		18
H–O–NO_2	-1.4		19.2
	0.18		25
H–F	3.2	H–H	35
	4.6		38
	4.75		38
	6.35		41
	7.0		44
	9.0		50

*values differ widely depending on source from -9 to -3.

Q2 SCRATCH ^{1}H-NMR SPECTRUM – NOTHING WRITTEN ON HERE WILL BE GRADED



SCRATCH PAPER – NOTHING ON HERE WILL BE GRADED

Periodic Table of the Elements

UW-Madison

IA	IIA	IIIB	IVB	VB	VIB	VIIB	VIIIB			IB	IIB	IIIA	IVA	VA	VIA	VIIA	VIIIA
1 H 1.01																	2 He 4.00
3 Li 6.94	4 Be 9.01											5 B 10.81	6 C 12.01	7 N 14.01	8 O 16.00	9 F 19.00	10 Ne 20.18
11 Na 22.99	12 Mg 24.30											13 Al 26.98	14 Si 28.09	15 P 30.97	16 S 32.07	17 Cl 35.45	18 Ar 39.95
19 K 39.10	20 Ca 40.08	21 Sc 44.96	22 Ti 47.88	23 V 50.94	24 Cr 52.00	25 Mn 54.94	26 Fe 55.85	27 Co 58.93	28 Ni 58.69	29 Cu 63.55	30 Zn 65.39	31 Ga 69.72	32 Ge 72.61	33 As 74.92	34 Se 78.96	35 Br 79.90	36 Kr 83.80
37 Rb 85.47	38 Sr 87.62	39 Y 88.90	40 Zr 91.22	41 Nb 92.91	42 Mo 95.94	43 Tc 98	44 Ru 101.07	45 Rh 102.91	46 Pd 106.42	47 Ag 107.87	48 Cd 112.41	49 In 114.82	50 Sn 118.71	51 Sb 121.76	52 Te 127.60	53 I 126.90	54 Xe 131.29
55 Cs 132.91	56 Ba 137.33	57 La* 138.91	72 Hf 178.49	73 Ta 180.95	74 W 183.85	75 Re 186.21	76 Os 190.23	77 Ir 192.22	78 Pt 195.08	79 Au 196.97	80 Hg 200.59	81 Tl 204.38	82 Pb 207.2	83 Bi 208.98	84 Po 209	85 At 210	86 Rn 222
87 Fr 223	88 Ra 226	89 Ac* 227	104 Rf 261	105 Db 262	106 Sg 263	107 Bh 262	108 Hs 265	109 Mt 266	110 269	111 272	112						

* Lanthanides	58 Ce 140.12	59 Pr 140.91	60 Nd 144.24	61 Pm 145	62 Sm 150.36	63 Eu 151.96	64 Gd 157.25	65 Tb 158.93	66 Dy 162.50	67 Ho 164.93	68 Er 167.26	69 Tm 168.93	70 Yb 173.04	71 Lu 174.97
** Actinides	90 Th 232.04	91 Pa 231.04	92 U 238.03	93 Np 237	94 Pu 244	95 Am 243	96 Cm 247	97 Bk 247	98 Cf 251	99 Es 252	100 Fm 257	101 Md 258	102 No 259	103 Lr 262