NAME:_____ Section:__A__ Student Number:_____

Spring 2015 **Chemistry 4000 Midterm** ____/ 42 marks

INSTRUCTIONS:

1) Please read over the test carefully before beginning. You should have 8 pages of questions and a periodic table.
2) Unless otherwise stated in the question, explain all of your answers fully. Use diagrams where appropriate. When invoking any argument based on resonance, you must draw all relevant resonance structures.
3) ALL structures must be drawn showing lone pairs, non-zero formal charges and reasonable bond angles – regardless of whether they are expanded, condensed or line-bond. Marks will be deducted for poorly drawn structures.
4) Marks will be deducted for incorrect information added to an otherwise correct answer.
5) If your work is not legible, it will be given a mark of zero.
6) Calculators are not allowed. You are not permitted to have any electronic devices with you during the exam unless authorized by the instructor.
7) You may use a molecular model kit.
8) You have 2 hours to complete this test.

Confidentiality Agreement:

I agree not to discuss (or in any other way divulge) the contents of this exam until after 8:00pm Mountain Time on Wednesday, March 11th, 2015. I understand that breaking this agreement would constitute academic misconduct, a serious offense with serious consequences. The minimum punishment would be a mark of 0/42 on this exam; the maximum punishment would include expulsion from this university.

Signature: _____ Date: _____

Course: CHEM 4000A (Medicinal Chemistry)
Semester: Spring 2015
The University of Lethbridge

Question Breakdown

Q1	/ 6
Q2	/ 12
Q3	/ 11
Q4	/ 3
Q5	/ 10
BONUS	/ 1

Total	/ 42

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1. The main natural synthons are a^1, d^2 and a^3. Explain why each of these synthons has "natural" reactivity. Each explanation should include an example. **[6 marks]**

(a) a^1 synthon

(b) d^2 synthon

(c) a^3 synthon

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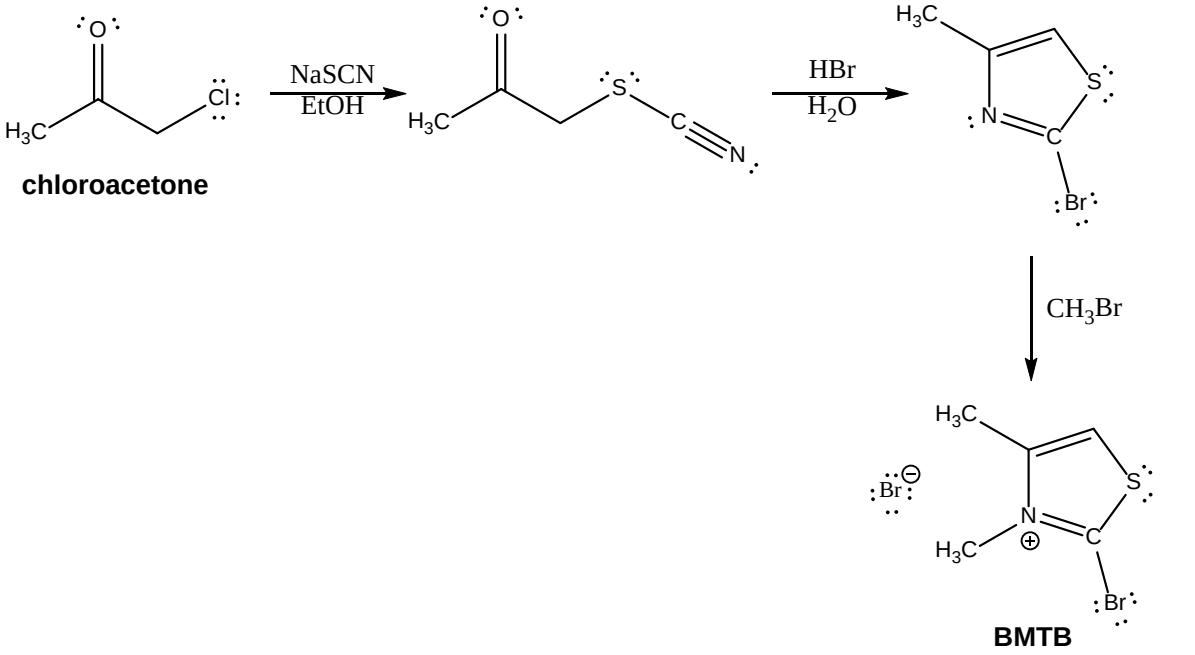
2. 2-bromo-N-methylthiazolium bromide (BMTB) was developed as a peptide coupling agent that would be better at coupling sterically hindered amino acids better than the alternatives that existed at the time. It was made in three steps from chloropropanone (aka "chloroacetone"):

[12 marks]



BMTB

(a) The thiocyanate ion (SCN^-) has two nucleophilic sites. Draw both resonance structures for SCN^- and identify the two nucleophilic sites. *[2 marks]*

(b) Draw a mechanism for the reaction of SCN^- with chloroacetone and explain the regiochemistry of this reaction. In other words, why does SCN^- react using one nucleophilic site instead of the other one and why does chloroacetone react using one electrophilic site instead of the other one? *[5 marks]*

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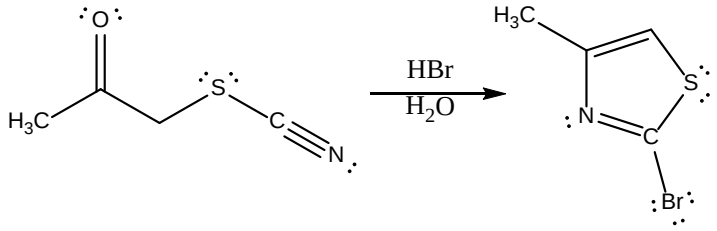
2. *continued…*

(c) Propose a reasonable mechanism for the second step in the synthesis of BMTB. *(shown below)*

[5 marks]



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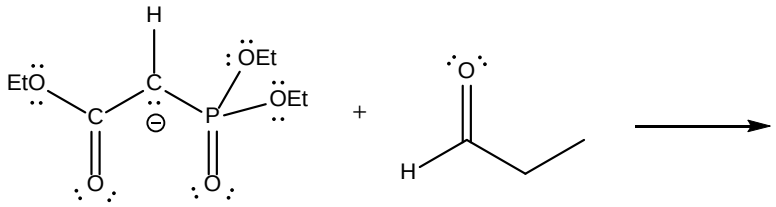
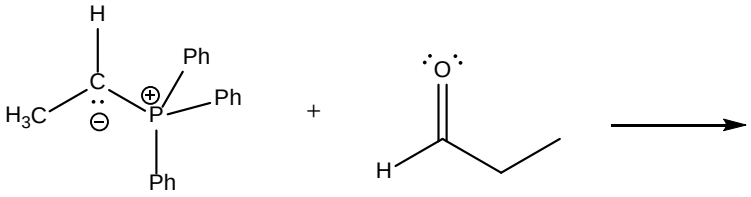
3. The Horner-Wadsworth-Emmons reaction is very similar to the Wittig reaction: **[11 marks]**

Horner-Wadsworth-Emmons Reaction



Wittig Reaction



(a) In the space provided above, draw the major organic product of each reaction. *[4 marks]*

(b) The Wittig reagent is made by reacting the $CH_3CH_2PPh_3^+$ cation with a very strong base such as BuLi; however, the Horner-Wadsworth-Emmons reagent can be made by reacting $CH_2(CO_2Et)(PO(OEt)_2)$ with a less strong base such as NaH.

i. Why does preparation of the Horner-Wadsworth-Emmons reagent not require such a strong base? *(compared to preparation of the Wittig reagent)* *[4 marks]*

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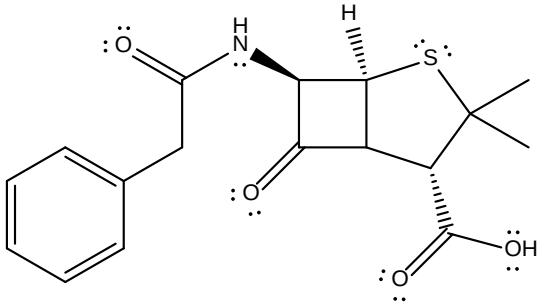
3.

(b) *continued…*

ii. Why would it be a bad idea to use BuLi as the base in preparing a Horner-Wadsworth-Emmons reagent from $CH_2(CO_2Et)(PO(OEt)_2)$? Show what would happen. *[3 marks]*

4. The structure of penicillin is shown below. Identify **one** disconnection that you would make if you were tasked with synthesizing penicillin. Explain your choice. Show the corresponding forward reaction for that step. **[3 marks]**

DO NOT TRY TO PROPOSE A WHOLE SYNTHESIS OF PENICILLIN!!!



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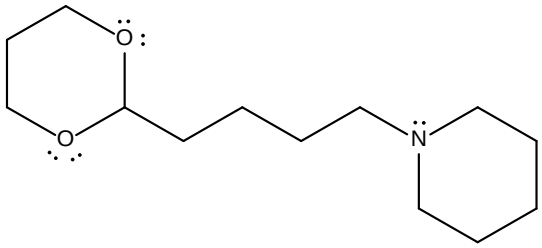
5. How would you make the molecule below? **[10 marks]**

Your answer should take the form of a retrosynthetic analysis followed by chemical equations for the reactions in the synthesis itself. Write an equation for each reaction. Show all required reagents, and number steps within a reaction if order of addition is important.

You may use any reagents that you could reasonably expect to be commercially available <u>and</u> that contain no more than 6 carbon atoms. (Exception: Reagents may contain one or more benzene rings in addition to the 6 carbon limit.)



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BONUS I recently came across a website in which a chemistry instructor told his students this following: "…begin mechanisms by drawing the most important resonance structure (lowest energy)…" Part of this statement is very VERY VERY wrong. Which part? Why? *[1 mark]*

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CHEM 1000 Standard Periodic Table

1												13	14	15	16	17	18
1.0079 **H** 1	2																4.0026 **He** 2
6.941 **Li** 3	9.0122 **Be** 4											10.811 **B** 5	12.011 **C** 6	14.0067 **N** 7	15.9994 **O** 8	18.9984 **F** 9	20.1797 **Ne** 10
22.9898 **Na** 11	24.3050 **Mg** 12	3	4	5	6	7	8	9	10	11	12	26.9815 **Al** 13	28.0855 **Si** 14	30.9738 **P** 15	32.066 **S** 16	35.4527 **Cl** 17	39.948 **Ar** 18
39.0983 **K** 19	40.078 **Ca** 20	44.9559 **Sc** 21	47.88 **Ti** 22	50.9415 **V** 23	51.9961 **Cr** 24	54.9380 **Mn** 25	55.847 **Fe** 26	58.9332 **Co** 27	58.693 **Ni** 28	63.546 **Cu** 29	65.39 **Zn** 30	69.723 **Ga** 31	72.61 **Ge** 32	74.9216 **As** 33	78.96 **Se** 34	79.904 **Br** 35	83.80 **Kr** 36
85.4678 **Rb** 37	87.62 **Sr** 38	88.9059 **Y** 39	91.224 **Zr** 40	92.9064 **Nb** 41	95.94 **Mo** 42	(98) **Tc** 43	101.07 **Ru** 44	102.906 **Rh** 45	106.42 **Pd** 46	107.868 **Ag** 47	112.411 **Cd** 48	114.82 **In** 49	118.710 **Sn** 50	121.757 **Sb** 51	127.60 **Te** 52	126.905 **I** 53	131.29 **Xe** 54
132.905 **Cs** 55	137.327 **Ba** 56	**La-Lu**	178.49 **Hf** 72	180.948 **Ta** 73	183.85 **W** 74	186.207 **Re** 75	190.2 **Os** 76	192.22 **Ir** 77	195.08 **Pt** 78	196.967 **Au** 79	200.59 **Hg** 80	204.383 **Tl** 81	207.19 **Pb** 82	208.980 **Bi** 83	(210) **Po** 84	(210) **At** 85	(222) **Rn** 86
(223) **Fr** 87	226.025 **Ra** 88	**Ac-Lr**	(261) **Rf** 104	(262) **Db** 105	(263) **Sg** 106	(262) **Bh** 107	(265) **Hs** 108	(266) **Mt** 109	(281) **Dt** 110	(283) **Rg** 111							

138.906 **La** 57	140.115 **Ce** 58	140.908 **Pr** 59	144.24 **Nd** 60	(145) **Pm** 61	150.36 **Sm** 62	151.965 **Eu** 63	157.25 **Gd** 64	158.925 **Tb** 65	162.50 **Dy** 66	164.930 **Ho** 67	167.26 **Er** 68	168.934 **Tm** 69	173.04 **Yb** 70	174.967 **Lu** 71
227.028 **Ac** 89	232.038 **Th** 90	231.036 **Pa** 91	238.029 **U** 92	237.048 **Np** 93	(240) **Pu** 94	(243) **Am** 95	(247) **Cm** 96	(247) **Bk** 97	(251) **Cf** 98	(252) **Es** 99	(257) **Fm** 100	(258) **Md** 101	(259) **No** 102	(260) **Lr** 103

Developed by Prof. R. T. Boeré