NAME:_____   Section:__A__   Student Number:_____

Fall 2012   **Chemistry 4000 Midterm**   ____/ 56 marks

INSTRUCTIONS: 1) Please read over the test carefully before beginning. You should have 7 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 Monday, October 29th, 2012. I understand that breaking this agreement would constitute academic misconduct, a serious offense with serious consequences. The minimum punishment would be a mark of 0/56 on this exam; the maximum punishment would include expulsion from this university.

Signature: _____   Date: _____
Course: CHEM 4000A (Medicinal Chemistry)
Semester: Fall 2012
The University of Lethbridge
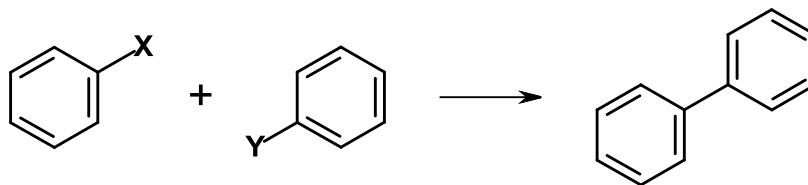
Question Breakdown

Q1	/ 7
Q2	/ 4
Q3	/ 4
Q4	/ 6
Q5	/ 6
Q6	/ 6
Q7	/ 8
Q8	/ 15

Total	/ 56

1.   You wish to perform the following reaction: **[7 marks]**

(a)   Why can you not use an S_N1 approach?   *[2 marks]*

(b)   Why can you not use an S_N2 approach?   *[2 marks]*

(c)   How would you do it?   Include specific groups to replace X and Y, and identify any other necessary reagents.   *[3 marks]*

2.   **[4 marks]**

(a)   What is meant by the term "umpolung"?   *[1 mark]*

(b)   Give an example of an umpoled synthon, and indicate what feature(s) make it umpoled.

                                                                                   [3 marks]

3.   Explain why an a^3 synthon is usually a better choice than a d^3 synthon.   **[4 marks]**
      Your answer should include an example of each.

4.   The first synthesis we worked through in problem set was that of rofecoxib (Vioxx$^®$). One of
      the key disconnections used in one of the syntheses is shown below (the thick dark line).
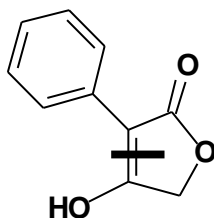
      There are two possible pairs of synthons generated by this disconnection.   **[6 marks]**

(a)   Identify each pair of synthons (clearly indicating which side of the disconnection corresponds to
      each synthon).   *[4 marks]*

(b)   Which of the pairs of synthons is preferable? Why?   *[2 marks]*

5.   Consider the following sequence of reactions.   **[6 marks]**
      There is no work-up done between reactions.
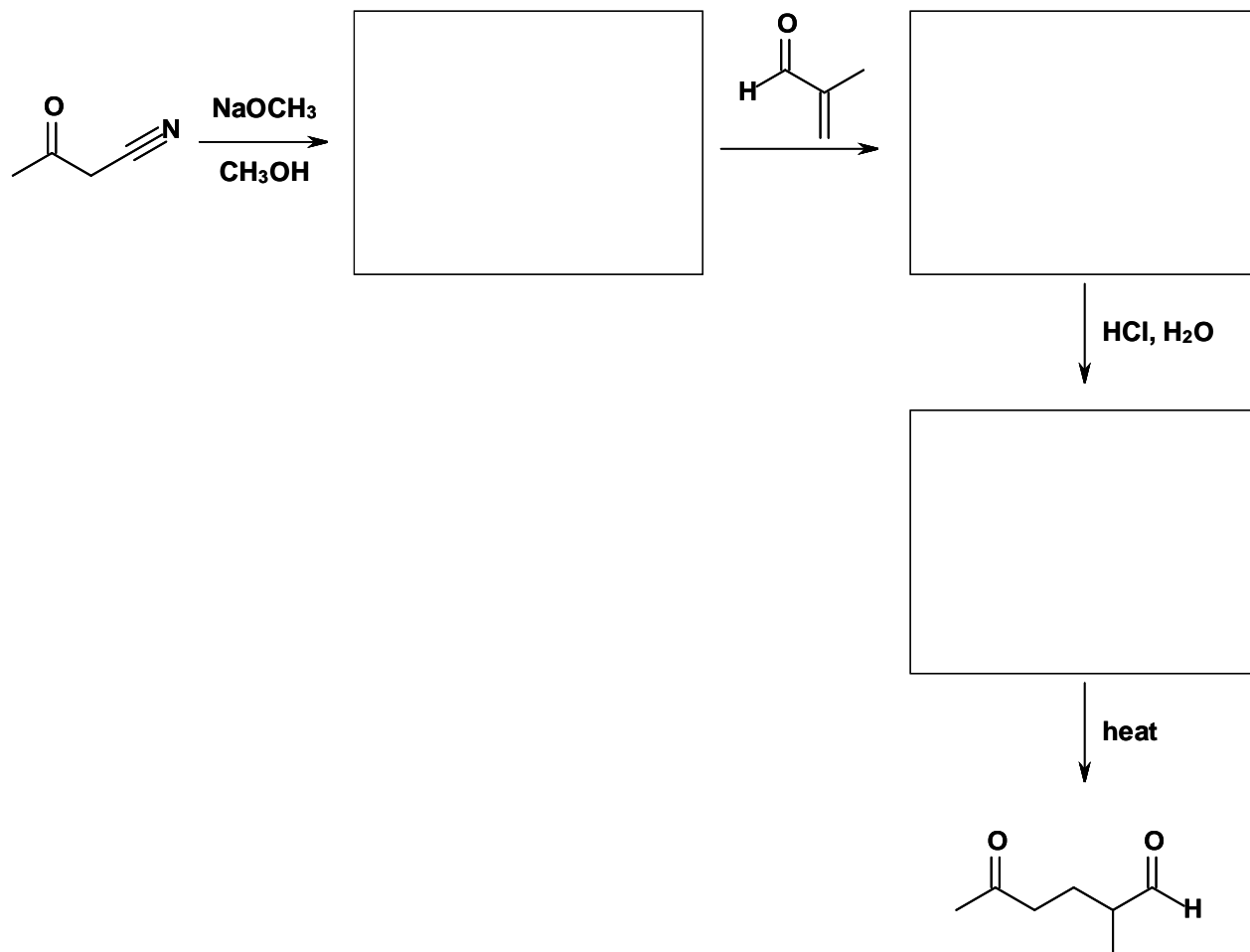
(a)   Draw the product of each step in the appropriate box.   *[3 marks]*
(b)   What was the purpose of the –CN group?   *[3 marks]*

6.   Use an argument based on hard/soft principles to explain why NaH and LiAlH$_4$ react differently
      with acetone: **[6 marks]**
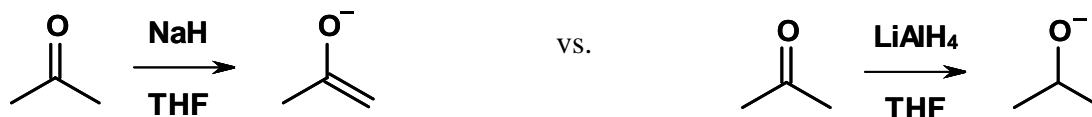
      Your answer should include a mechanism for each of the reactions shown above.

7.   One of the first steps in the synthesis of sildenafil (Viagra®) is shown below.   **[8 marks]**
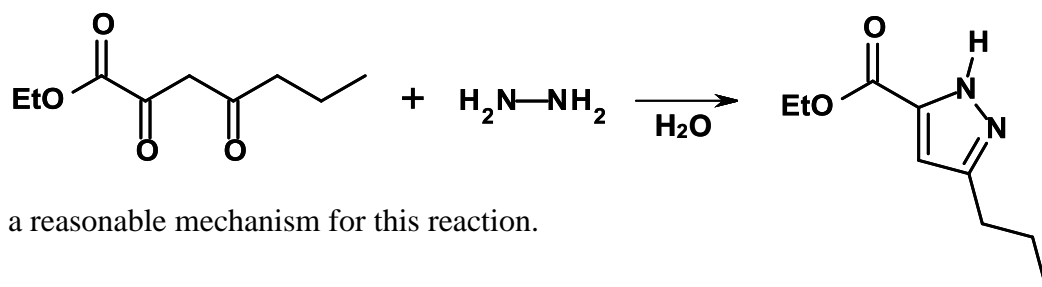
Propose a reasonable mechanism for this reaction.

8.   How would you make each of the molecules below?   **[15 marks]**

Your answers should take the form of a retrosynthetic analysis followed by chemical equations for the reactions in the synthesis itself. 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.)

If you are suggesting a multi-step synthesis, write an equation for each step.

(a)   *[5 marks]*

8.   *continued…*

(b)   *[10 marks]*

CHEM 1000 Standard Periodic Table

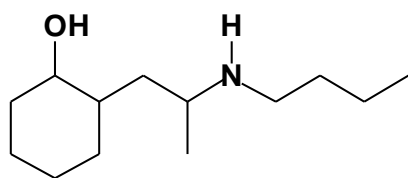| 1																	18
1.0079 **H** 1	**2**												**13**	**14**	**15**	**16**	**17**	4.0026 **He** 2
6.941 **Li** 3	9.0122 **Be** 4												10.811 **B** 5	12.011 **C** 6	14.0067 **N** 7	15.9994 **O** 8	18.9984 **F** 9	20.1797 **Ne** 10
22.9898 **Na** 11	24.3050 **Mg** 12	**3**	**4**	**5**	**6**	**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