

Heterocyclic Chemistry – Final Exam

June 12th, 2007

Professor Baran
Department of Chemistry
The Scripps Research Institute

Name: _____

Any 4-digit number you will remember: _____

This is an “open-notes” exam designed to last 2 hours that you have 4 hours to complete
Definition of "open notes": Only handwritten notes (from lectures and any other source), no copies allowed. Lecture summaries are the only handouts permitted during test.

Please present ONLY your FINAL answers on these sheets

Question 1 _____ < (15 points)

Question 2 _____ < (150 points)

Question 3 _____ < (40 points)

Question 4 _____ < (30 points)

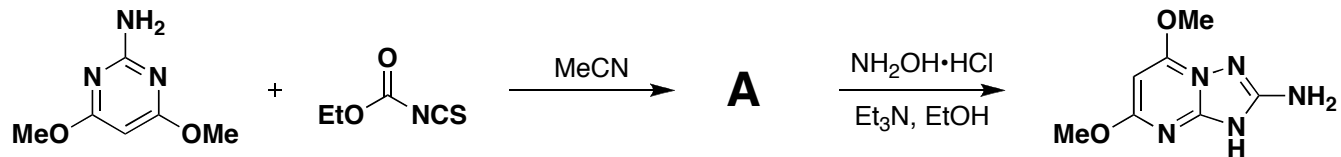
Question 5 _____ < (15 points)

Question 6 _____ < (50 points)

Bonus Question _____ < (25 points)

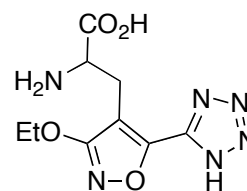
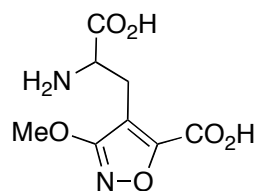
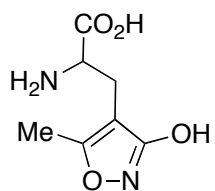
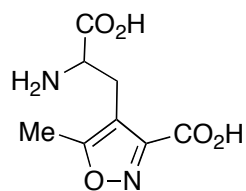
Total _____ out of 325 points

Question 1 (15 points). In Dow AgroSciences development of the herbicide pyroxsulam, they utilized the following transformation to construct the core (*Org. Proc. Res. Dev.* **2006**, *10*, 1167). Provide a plausible mechanism for this complex transformation.

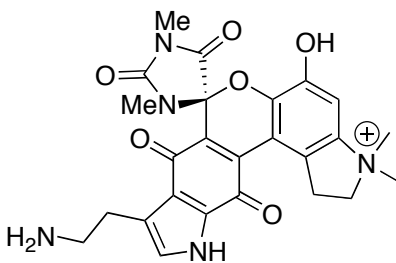


Question 2 (150 points). Choose 10 compounds from the structure sheet and propose a synthesis for each (15 points each):

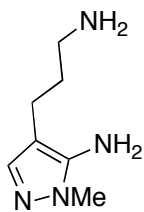
Question 3 (40 points). Provide a divergent synthetic plan for accessing the following isoxazoles
(*J. Med. Chem.* **2000**, *43*, 4910).



Question 4 (30 points). Provide a synthetic route and propose a biosynthetic pathway by which exiguamine A is likely formed.



Question 5 (15 points). Propose a synthesis for the pyrazole starting from a pyridine.



Question 6 (50 points). Deduce the structures of the following heterocycles (5 points each).

A. (C_6H_7NO) Obtained by treating 4-chloropyridine with i) NaOMe ii) MeI iii) 185 °C.

B. ($C_{15}H_{18}N_2O_2S$) Obtained by reacting 2-*N*-Boc-quinoline with 3 eq. *n*-BuLi then Me_2S_2 .

C. ($C_{16}H_{11}NO_2$) Obtained by treating isatin with NaOH followed by acetophenone in the same pot.

D. ($C_{10}H_{16}N_2$) Formed when pyrrole is treated first with $Me_2NH/CH_2O/AcOH$, then with MeI, then with piperidine.

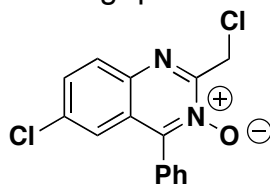
E. (C₉H₁₂OS) Obtained from treating thiophene with *N*-phenyl-*N*-methyl-formamide/POCl₃ followed by NaOH.

F. (C₇H₈O₄) Obtained from reacting methyl 3,3-dimethoxypropanoate with methyl 2-chloroethanoate in the presence of sodium methoxide and heat.

G. (C₁₄H₁₈N₂O) Formed when indole is reacted with *N*-methyl-2-pyridone/POCl₃, and then treated with aq. NaOH.

H. (C₅H₆O₂) Produced by heating 4-phenyloxazole in the presence of but-1-yn-3-one.

I. (C₁₆H₁₄ClN₃O) Product of treating the following quinazoline *N*-oxide with methylamine.



J. (C₅H₆N₂O) Treatment of 4-bromo-1-methylimidazole with *n*-BuLi at -78 °C followed by DMF quench gave a product isomeric to one in which the anion resulting from *n*-BuLi treatment was allowed to warm to 0 °C before quenching with DMF. Both were worked up under acidic conditions. What are the products for each reaction and why do they differ?

Bonus Question (25 points): In their quest for new pharmaceuticals, scientists at Pfizer have established the following route to a new medication. Provide the intermediates and final structure of this new medication.

