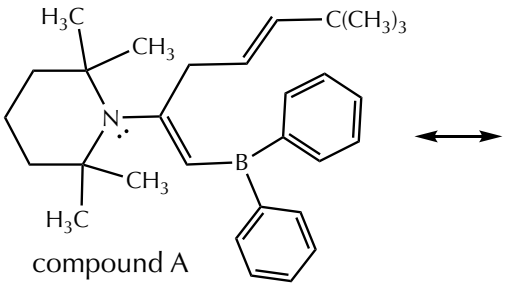
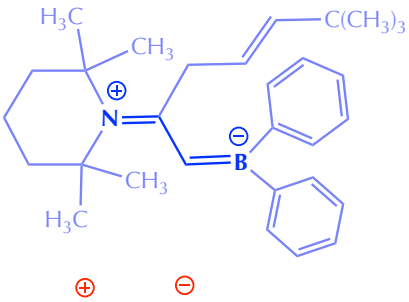
Question I (20 points) NAME _____

Compound A has many resonance contributors (*J Am Chem Soc*, **2018**, 140, 3635).

(a) Draw the single resonance contributor of compound A with all closed shell atoms. Include all necessary non-bonding electron pairs and formal charges.



compound A



core answer N=C-C=B + 2 pts
if that is OK, then +2 for redrawing the rest — 4

(b) Based on the structure drawn above, how many units of unsaturation are in compound A? — no partial — 11 — 2

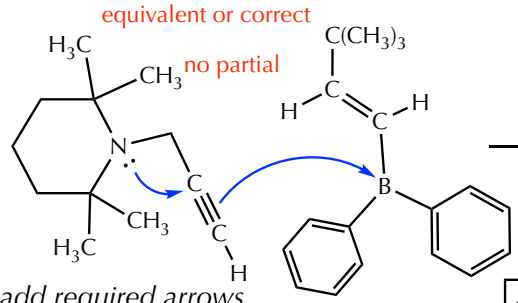
(c) What is the molecular formula of compound A? — no partial — all credit for $C_{30}H_{42}NB$ error — $C_{30}H_{42}BN$ — 2

What is the hybridization of the boron atom in compound A? — no partial — sp^2 — 2

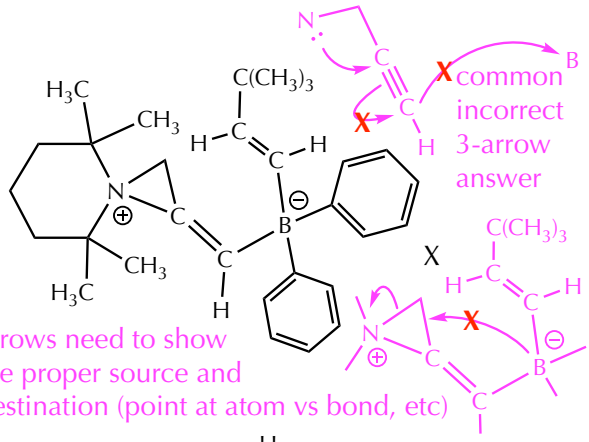
(e) What is the observable geometry of the nitrogen atom in compound A? — no partial — trigonal planar — "trigonal" alone = 0 — 2

(f) There are two steps in the reaction used to form compound A. Provide the curved arrows needed to explain the bonding changes (that is, the mechanism) for these two steps.

step 1: Note: more than 2 arrows means something different that 2 arrows does, and this is not equivalent or correct

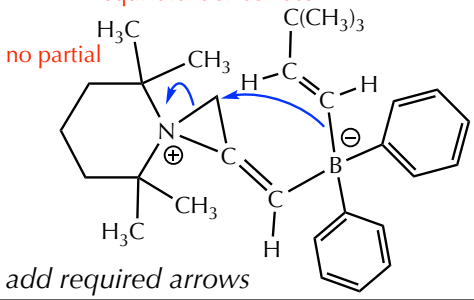


add required arrows — 4

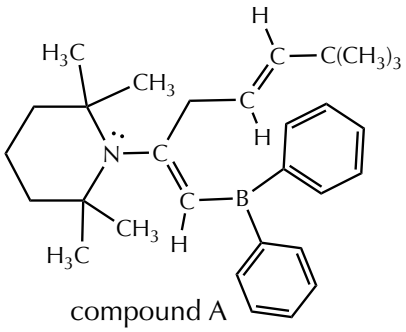


arrows need to show the proper source and destination (point at atom vs bond, etc)

step 2: Note: more than 2 arrows means something different that 2 arrows does, and this is not equivalent or correct



add required arrows — 4



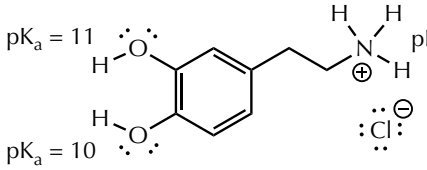
compound A

a		/04
b		/02
c		/02
d		/02
e		/02
f		/08
		/20

Question II (18 points)

NAME _____

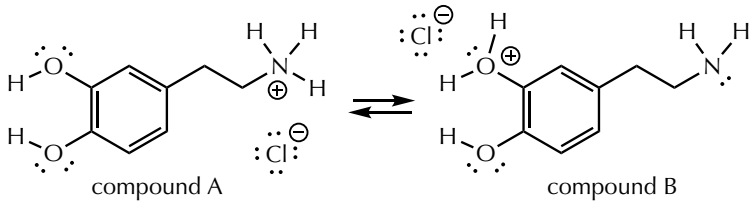
Dopamine is a hormone and neurotransmitter that plays a number of important functions in the human brain and body. Its hydrochloride salt (compound A) can be used as a drug to treat severe hypotension, bradycardia, circulatory shock, or cardiac arrest.



dopamine hydrochloride (compound A)

Compound A has three acidic protons (pK_a values of 9, 10 and 11, as shown above). Answer the following questions.

(a) One of the internal acid-base equilibria for compound A gives the isomeric compound B, whose lowest pK_a value is -4. What is the estimated equilbrium constant ([B]/[A]) for this isomerization, as drawn?

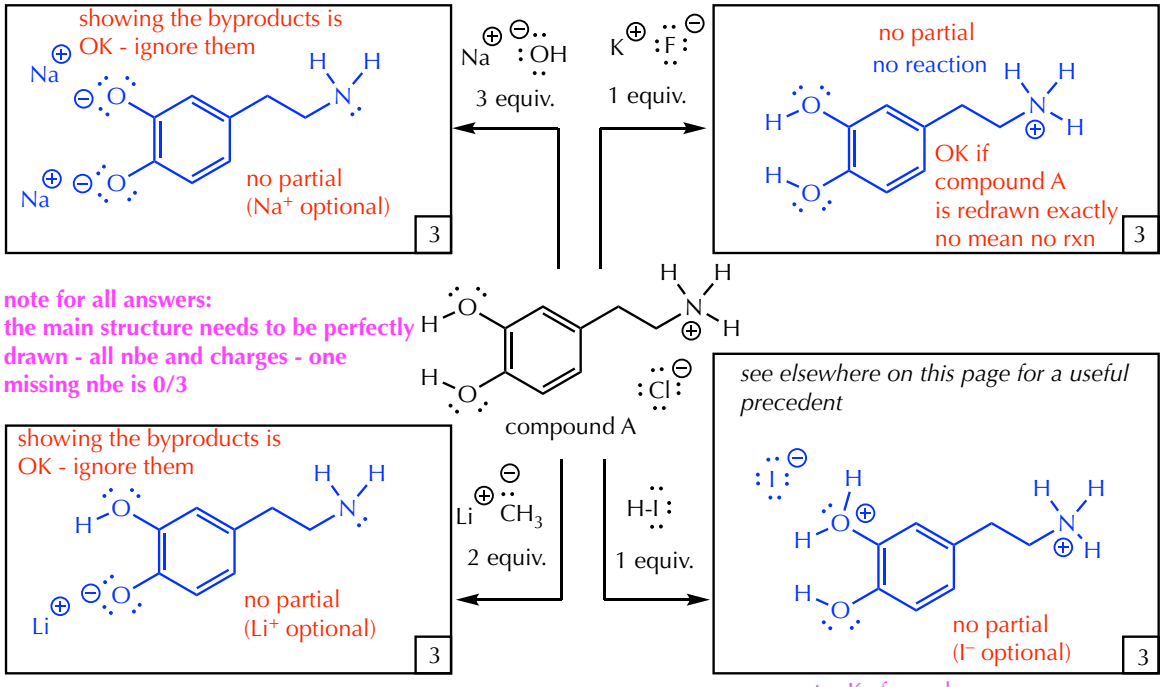


compound A compound B

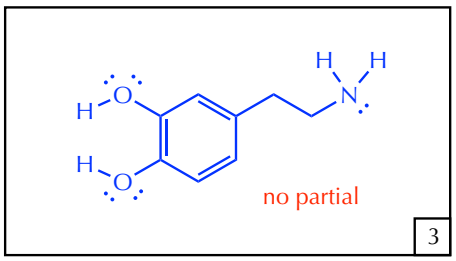
What is the estimated K_{EQ} for this isomerization? (use 10^x format)

no partial
10^{-13}
3

(b) Draw the major product for the reaction of compound A with the reagents shown below (byproducts do not need to be shown). Pay attention to the number of equivalents of added reagent, which will potentially influence the outcome. Write "no reaction" if no reaction ($K_{EQ} < 10^{-4}$) is expected.



(c) Draw the major form of compound A that would be expected to exist at pH 9.5.

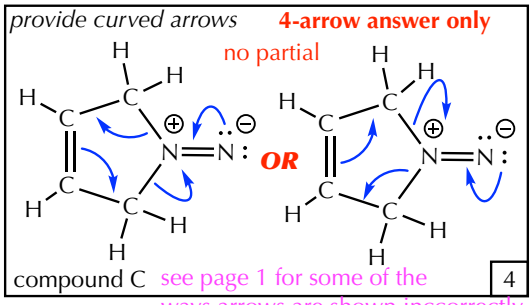


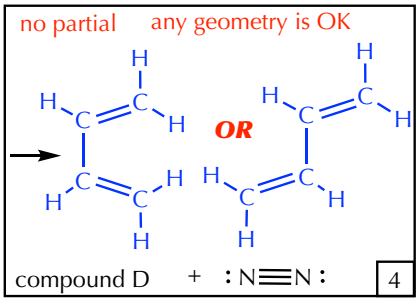
est. pKa from above is -4, so $K_{EQ} = 10^{-4-(-9)}$ is 10^5, the pKa of the product would need to be -14 for the K_{EQ} to be $< 10^{-4}$

a		/03
b		/12
c		/03
		/18

Question III (22 points) NAME _____

A. When heated, isodiazenes (such as compound C) lose molecular nitrogen and give stable organic products. In the example below, the product (compound D) accounts for all of the original atoms other than the molecule of nitrogen. Compound D is a stable, uncharged, all closed shell atom structure with the molecular formula C_4H_6. There are two different structures than compound D might be, rationally, but the fact that compound D readily adds two equivalents of molecular bromine (Br_2) to give $C_4H_6Br_4$ narrows this down to one choice. Compound D also has no sp^3 atoms. What is the structure of compound D, and what curved arrows are needed to describe its formation from compound C (*Russ Chem Rev*, **1989**, *58*, 732)?



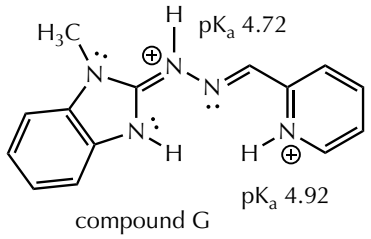


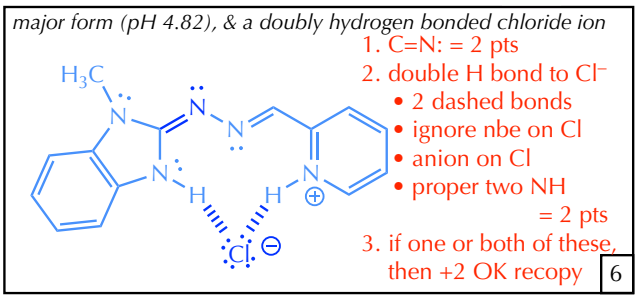
Data on compound D:
i. C_4H_6
ii. reacts with 2 Br_2 to give $C_4H_6Br_4$
iii. no sp^3 atoms
iv. remember… most reactions are not explosions and connectivity is often maintained

B. Compound G is known as a pyridyl-linked benzimidazolyl hydrazone. It has been studied for its toxicity towards human breast cancer cells and its relative nontoxic effect on other cells (*Org Lett*, **2021**, *23*, 6131). Owing to low water solubility and the experimental challenge of measuring close pK_a values, the values for its two most acidic protons were estimated by theoretical calculations. The major form of compound G in solution at pH = 4.82 is proposed to form two hydrogen bonds with a chloride anion (Cl^-) as part of its anticancer activity. Draw the structure that matches this description by following steps (a) and (b) in sequence.

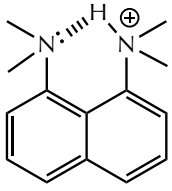
(a) Draw the structure of compound G at pH = 4.82.

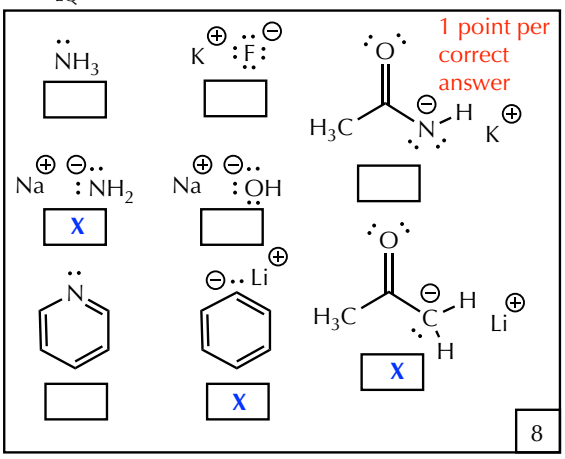
(b) Add a chloride anion to your drawing, clearly showing the anion acting to accept two H-bonds from the two most likely H-bond donors in the structure you drew for (a). Hydrogen bond notation: ııııııı





C. The experimental pK_a value of compound K is 12.1. Mark the space(s) of the reagent(s) that could be used to deprotonate compound K with a $K_{EQ} > 10^5$.



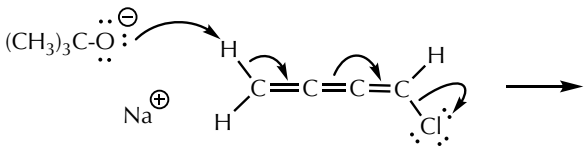


A		/08
B		/06
C		/08
		/22

Question IV (18 points) NAME _____

A. The following reaction is used to prepare a variety of naturally occurring, biologically active compounds (*J Am Chem Soc*, **2004**, *126*, 14314).

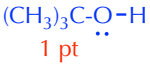
(a) Provide the structure of the product based upon the mechanism. Draw the proper geometry of the product.



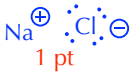
include all products

2 pts connectivity; if OK, then +2 pts for geometry

ignore nbe errors



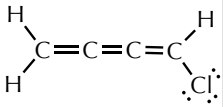
1 pt

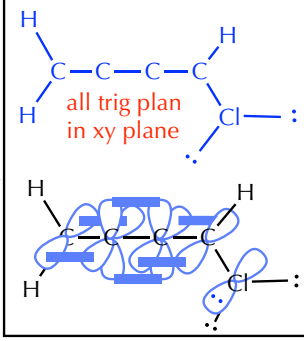


1 pt

6

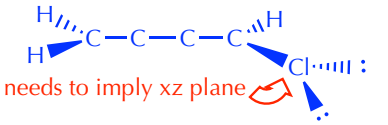
(b) Using lines, dashes, and wedges for sigma bonds and the directionality of localized nbe pairs, and p-orbitals for pi bonds and empty or filled p-orbitals, provide the 3D orbital drawing for the starting material.





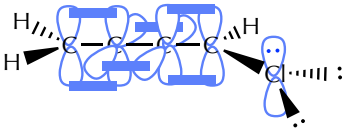
all trig plan in xy plane

localized e framework = 3; *all 5 atoms coplanar* **if not OK, then done: 0/6** b/c pi system automatically incorrect



needs to imply xz plane

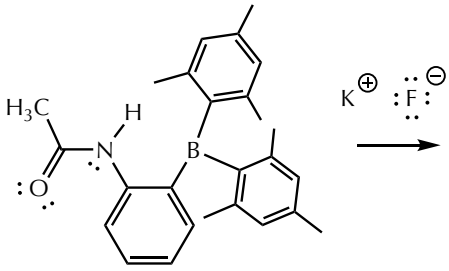
if localized OK, then for xy coplanar sp^2 there are 5 p orbitals pz and 2 py; if xz coplanar then 5 p orbitals py and 2 pz; + proper overlap and nbe = 3

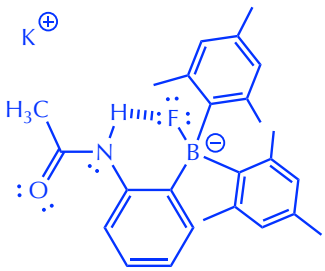


6

B. "The molecular recognition of fluoride continues to attract a great deal of attention because of the importance of this anion in dental health and in the treatment of osteoporosis…" (*Org Lett*, **2006**, *8*, 2747).

(a) The following reaction results in an ionic product in which there is an intramolecular hydrogen bond. Draw the structure of the product, including the expected hydrogen bond. Hydrogen bond notation: ııııııı





proper BF bond with (-) charge = 2 pts if not OK, 0/4

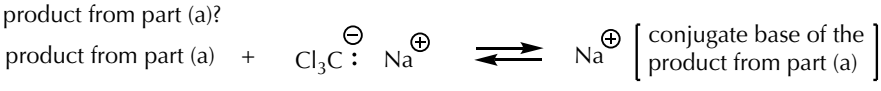
if OK, the proper hydrogen bond between F and NH = + 2 pts

ignore non-critical copy errors & K^+

4

(b) When the product from the reaction is part (a) is treated treated with one equivalent of the trichloromethyl anion (Cl_3C^-), an equilibrium is established with a K_{EQ} of $10^{3.5}$. Based on this information, what is the pK_a value of the product from part (a)?

pK_a = 25 on table



product from part (a) + Cl_3C^- Na^+ ⇌ Na^+ [conjugate base of the product from part (a)] + Cl_3CH

$K_{EQ} = 10^{3.5}$

What is the pK_a value for the product from part (a)?

no partial

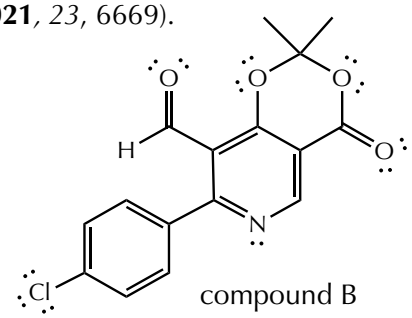
21.5

2

Aa		/06
Ab		/06
Ba		/04
Bb		/02
		/18

Question V (22 points) NAME _____

A. Pyridines are an important building block for the preparation of pharmaceuticals. Compound B was prepared using a new method to construct the ring containing the nitrogen atom (*Org Lett*, **2021**, *23*, 6669).



compound B

(a) How many delocalizable electron pairs are there in compound B?

no partial
11
2

(b) How many sp^3 hydridized atoms are there in compound B?

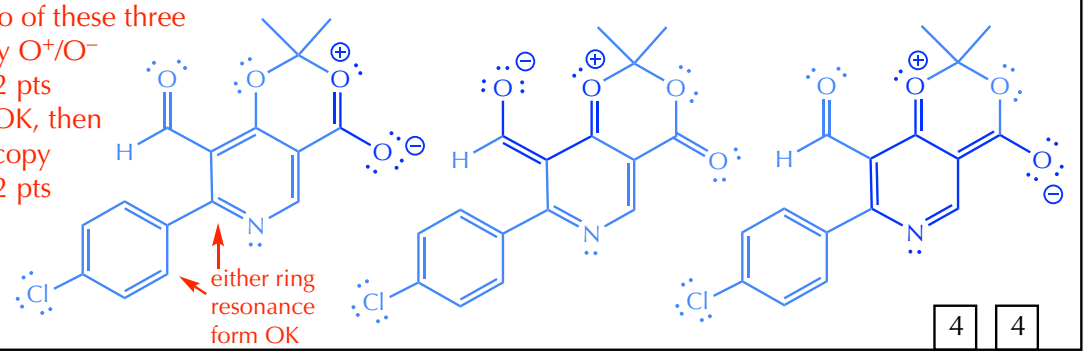
no partial
3
2

(c) How many atoms with the bent observable geometry are there in compound B?

no partial
3
2

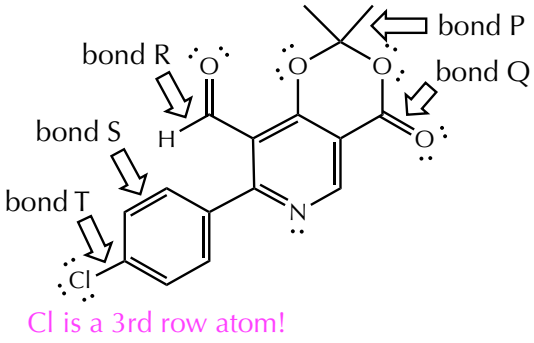
(d) There are at least three resonance contributors for compound B that contain all closed shell atoms and in which different pairs of oxygen atoms end up bearing formal charges. Draw two of these resonance contributors. Be careful to include all the necessary bonds, atoms, nbe pairs, and charges (note that non-zero formal charges are only located on two oxygen atoms in these contributors).

two of these three
key O^+/O^-
= 2 pts
If OK, then
recopy
= 2 pts



4 4

(e) Rank the indicated five bonds according to bond length.



Cl is a 3rd row atom!

longest T
P
no partial
S
Q
shortest R
4

Aa		/02
Ab		/02
Ac		/02
Ad		/08
Ae		/04
B		/04
		/22

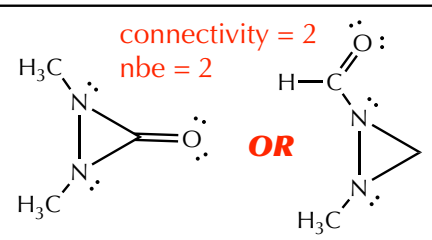
B. There are at two three compounds with the molecular formula $C_3H_6N_2O$ that satisfy all of the following criteria. Draw one of these compounds.

i. contains a three-membered ring
ii. includes a carbon-oxygen double bond
iii. does not possess a hydrogen bond donor
iv. all atoms closed shell and uncharged

(be sure to include nbe pairs in the drawing)

no NH or OH

connectivity = 2
nbe = 2



4