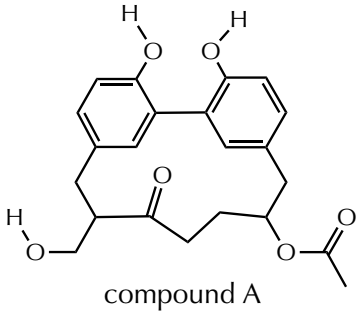
Question I (20 points) NAME _____

Compound A is one of four new cyclic diarylheptanoids isolated from bark and leaves of *Casuarina equisetifolia* L., used in traditional medicine for a variety of ailments, which are being investigated for antiviral activity (*J. Nat. Prod. 2022:* doi.org/10.1021/acs.jnatprod.2c00335).



compound A
all atoms are uncharged and closed shell

(a) Answer the following questions about compound A.

i. How many units of unsaturation does it have? [ ] 2

ii. How many nonbonding electron pairs are needed to complete the structural drawing? [ ] 2

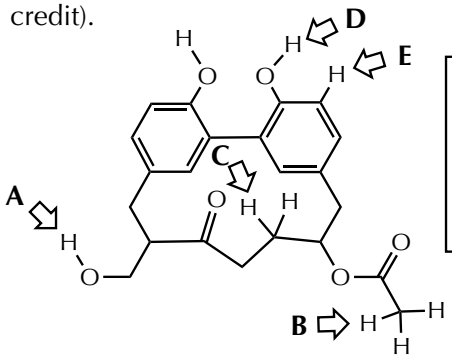
iii. How many pairs of delocalized electrons are there? [ ] 2

iv. What is the molecular formula? [ ] 2

(b) Draw another resonance contributor for compound A that is an equally significant contributor to the structure. Include all nonbonding electron pairs and formal charges.

[ ] 4

(c) Based upon the pK_a values in the table, rank the anticipated order of acidity for the five protons (**A**-**E**) in compound A that are indicated below by entering the letters A-E into the grid below (no partial credit).



most acidic				*least acidic*

4

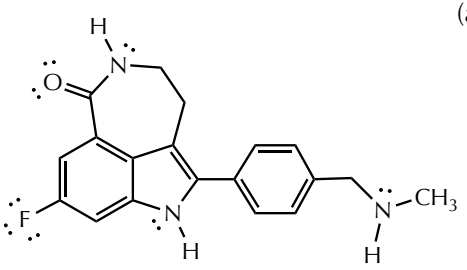
(d) Based upon the pK_a values in the table, what is the structure of the conjugate acid of compound A if it reacts with one equivalent of HCl? Provide the ionic structure for the balanced equation, including nonbonding electron pairs and any formal charges.

[ ] 4

a		/08
b		/04
c		/04
d		/04
		/20

Question II (22 points) NAME _____

Rucaparib, whose structure is shown below, is an FDA-approved drug for ovarian and prostate cancers (*J. Org. Chem.* **2022**, *87*, 4813).



rucaparib

(a) Answer the following questions about rucaparib.

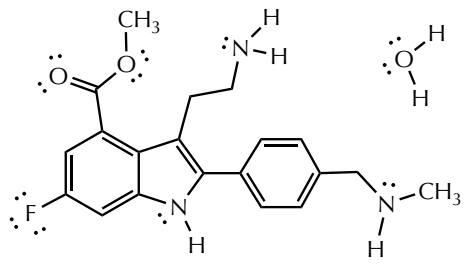
i. How many of the atoms are sp^2 hybridized? 2

ii. How many of the atoms would have an observable geometry described as "bent"? 2

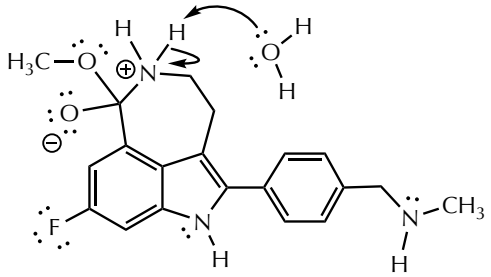
iii. How many of the atoms would have an observable geometry described as "pyramidal"? 2

(b) Provide the needed curved arrows or structures, as specified below, for some of the chemical reactions used in preparing rucaparib.

add the arrow(s) needed to describe this reaction

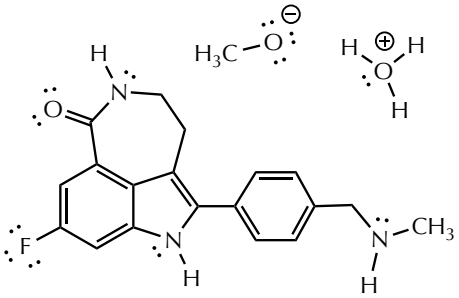


4



draw the products implied from these arrows in the space below, then provide the arrow(s) needed to give the final products

draw structure & arrow(s) 8



rucaparib

There is a single most likely Brønsted acid-base reaction that would now occur.

Draw the structures for the two products resulting from only that acid-base reaction.

4

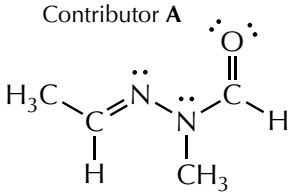
a		/06
b		/16
		/22

Question III (24 points) NAME _____

Gyromitrin is a toxin produced by some fungi known as false morels. Suspected in 1895, the structure of this active ingredient was not deduced until 1968 (*Archiv. der Pharmazie* **1968**, *301*, 294).

(a) One of the resonance contributors of gyromitrin is shown below. There are two other contributors with all closed shell atoms, a total of 0-2 non-zero formal charges, and formal charges limited to the [-1, +1] range. Draw these two resonance contributors (include nonbonding electrons and formal charges).

Contributor **A**



gyromitrin

Contributor **B** 3

Contributor **C** 3

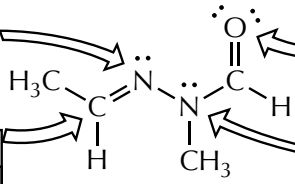
(b) Identify which contributors are the most and least signficant. Note that the three contributors need to be correct to receive credit for this part, so check your answers to part (a) carefully.

i. most significant (*circle one*): **A** **B** **C**
ii. least significant (*circle one*): **A** **B** **C** 2

(c) Identify the anticipated hybridizations, electronic geometries, or observable geometries of the indicated atoms.

i. hybridization 2

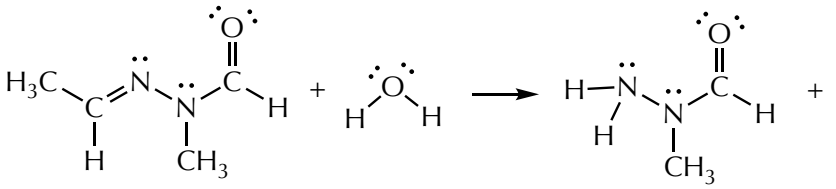
iii. electronic geometry 2



ii. observable geometry 2

iv. hybridization 2

(d) Hydrolysis of gyromitrin creates N-formyl-N-methylhydrazine, which is not only implicated in the toxicity, but it is also a cancer-causing agent (carcinogen) in even small quantities. Using the structural principles of organic reactions, what is the structure of the other product formed when gyromitrin reacts with water?



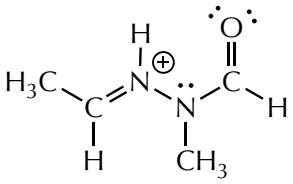
gyromitrin

N-formyl-N-methylhydrazine

4

(e) The experimental value for the pK_a of the conjugate acid of gyromitrin is 2.6. In a buffer solution whose pH equals 3.6, there is a 10:1 ratio of what two structures?

conjugate acid of gyromitrin, pK_a 2.6



At pH 3.6, there is a 10:1 ratio of what two structures?

major structure 2

minor structure 2

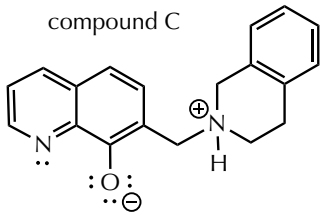
a		/06
b		/02
c		/08
d		/04
e		/04
		/24

Question IV (18 points) NAME _____

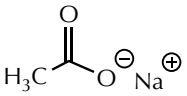
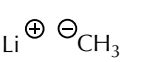
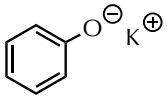
The experimental value for the pK_a of compound C is 10.68 (*J. Med. Chem.* **2022**, *65*, 7729).

(a) Which of the following compounds could prospectively deprotonate compound C with a K_{EQ} of 10^5 or greater?

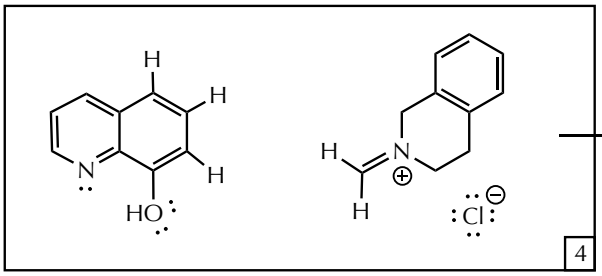
compound C



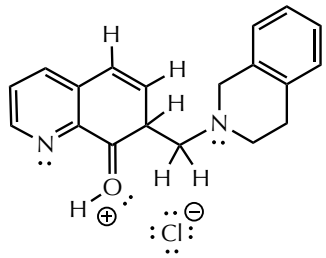
circle "yes" if the anticipated K_{EQ} for the deprotonation using that base is > 10^5 and "no" if it is not

NaH $K_{EQ} > 10^5$: yes no	 $K_{EQ} > 10^5$: yes no	 $K_{EQ} > 10^5$: yes no
NH_3 $K_{EQ} > 10^5$: yes no	 $K_{EQ} > 10^5$: yes no	$NaOCH_2CH_3$ $K_{EQ} > 10^5$: yes no
 $K_{EQ} > 10^5$: yes no	LiOH $K_{EQ} > 10^5$: yes no	8

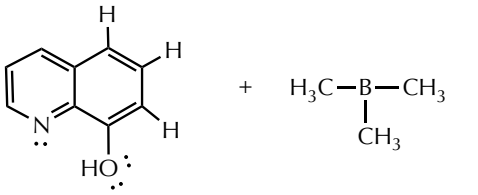
(b) Provide the curved arrows for this reaction, which was used in the preparation of compound C.



4



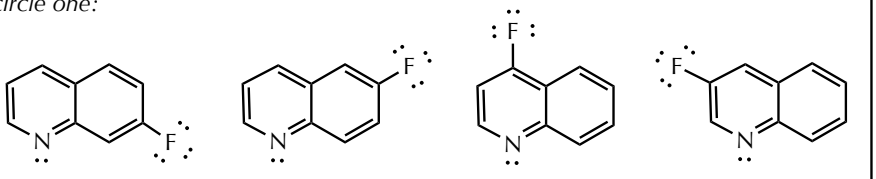
(c) When one of the two starting materials shown in part (b) reacts with one equivalent of trimethylborane, a highly selective reaction is observed. Predict the structure of the product. Do not forget to include details such as nonbonding electron pairs and formal charges, as needed.



4

(d) In the following set of closely related compounds, in which the "OH" group of the compound shown in part (c) has been replaced by a fluorine atom, one of the molecules has an observed molecular dipole moment of close to zero (0 D). Which one of these isomers is it?

circle one:

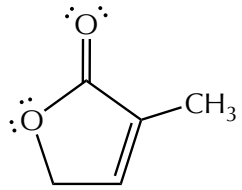


2

a		/08
b		/04
c		/04
d		/02
		/18

Question V (16 points) NAME _____

A. 3-Methyl-2(5H)-furanone is a natural product (*J. Nat. Prod.* **2022**, *85*, 1976) found in *Morithamnus crassus* (a Brazilian flowering plant) and *Achillea ageratum* (a flowering plant in the sunflower family, found throughout Europe, and used in the Middle Ages as an insect repellant).

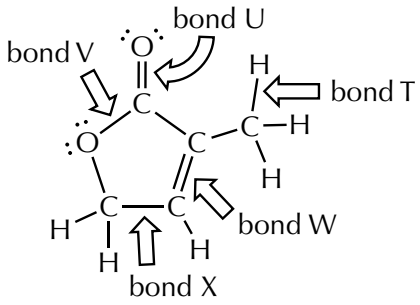


3-methyl-2(5H)-furanone

(a) Provide a 3D orbital drawing for 3-methyl-2(5H)-furanone using the standard conventions: line/dash/wedge notation for sigma bonds and the direction of localized nbe pairs, and p orbitals for pi bonds and delocalized nbe pairs. *Be sure to provide a clear and precise drawing in which all hybridized atoms are in the plane of the paper.*

8

(b) Rank the indicated five bonds according to bond length. Place the letters T-X in the grid; no partial credit.



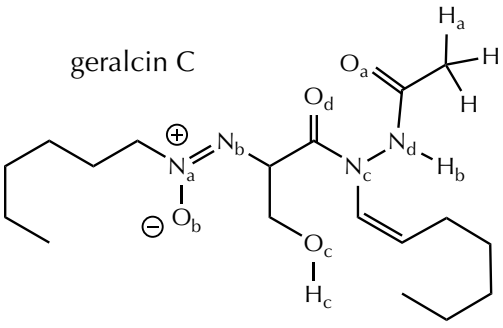
longest

shortest

4

B. The geralcins are a class of compounds isolated from *Streptomyces* sp. LMA-545. One of them, geralcin C, exhibits toxicity towards some cell lines associated with cancers. The experimental structure of geralcin C, shown below, is said to contain two distinct intramolecular hydrogen bonds between two different pairs of atoms in the structure. One of the hydrogen bonds creates a five-membered ring of atoms, while the other creates a six-membered ring. Which two combinations of atoms are the likely pairs that make up these hydrogen bonds?

geralcin C

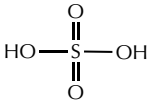
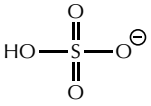
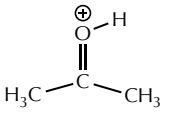
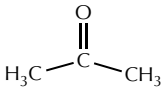


Mark (X) the two pairs that match this description. None of the atoms are participating in two hydrogen bonds.

- ☐ H_b-O_a
- ☐ H_a-N_c
- ☐ H_c-N_a
- ☐ H_b-O_d
- ☐ H_c-N_c
- ☐ H_b-O_c
- ☐ H_b-N_c
- ☐ H_c-O_d

4

Aa		/08
Ab		/04
B		/04
		/16

ACID	pK_a	CONJUGATE BASE
(strongest acid)		(weakest base)
	-12	
	-9	
	-9	
	-7.2	
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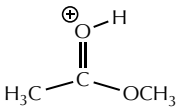
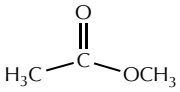
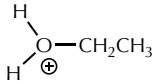
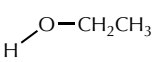
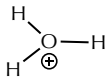
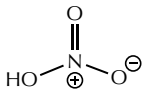
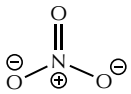
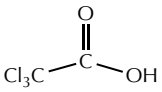
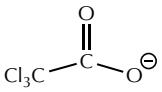
	-4.6	
	-2.4	
	-1.7	
	-1.3	
	0.64	
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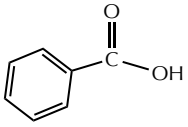
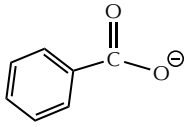
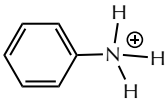
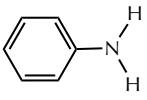
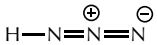
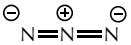
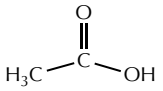
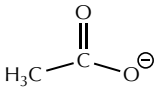
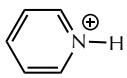
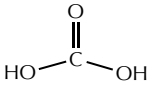
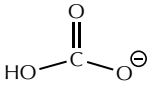
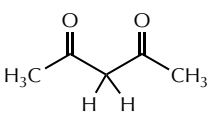
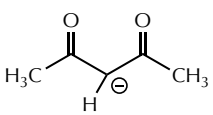
	4.2	
	4.6	
	4.7	
	4.8	
	5.2	
	6.5	
	9.1	
	9.2	

ACID	pK_a	CONJUGATE BASE
	9.4	
	10.0	
	10.2	
	10.2	
	10.5	
	10.6	
	15.0	
	15.7	
	17	
	19	
	25	
	26	
	35	
	36	
	41	
	43	
	44	
	49	
(weakest acid)		(strongest base)