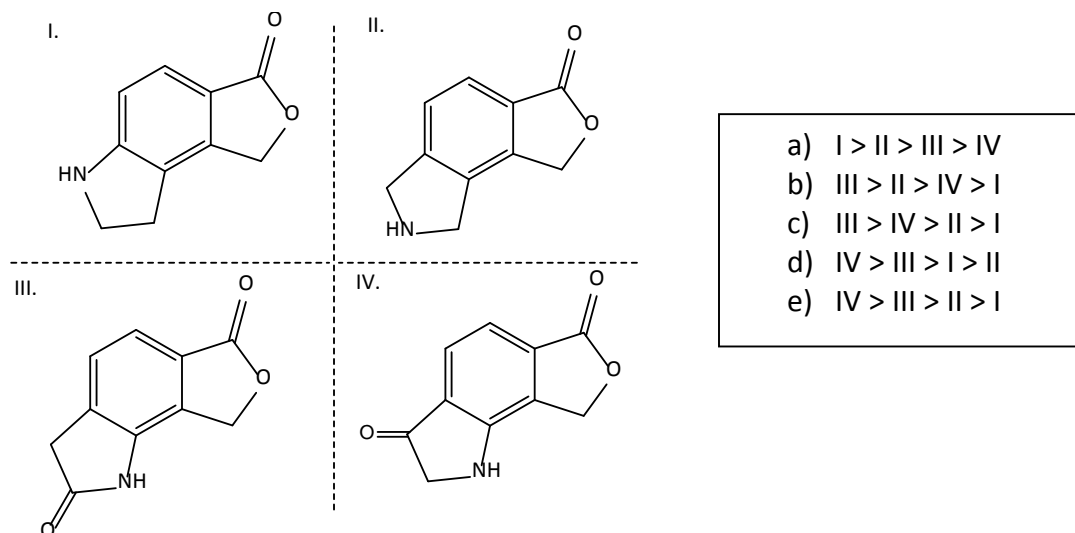
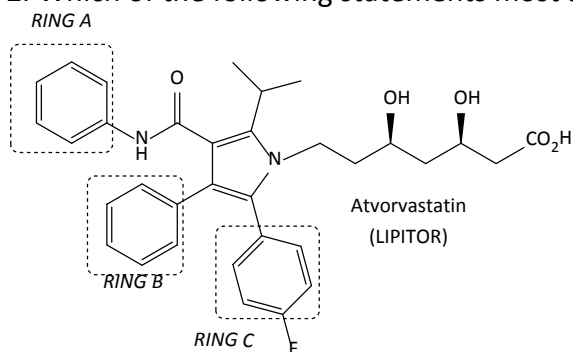


1. Rank the relative rates of reaction (fastest > slowest) of the compounds below with NaOH, H<sub>2</sub>O. **E**



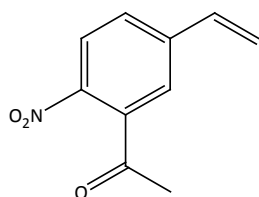
2. Which of the following statements most accurately describes the structure below? **A**



- I. The compound contains one para-substituted ring.  
 II. Ring C contains two activating groups.  
 III. Reaction with Cl<sub>2</sub>, FeCl<sub>3</sub> will occur predominantly on ring C.  
 IV. The compound contains an ionizable functional group on ring A.

- a) I  
 b) I & IV  
 c) I & III  
 d) I, II & III  
 e) II & III

3. Which reagent(s) will convert 2-nitro-5-vinylacetophenone to 2,4-diethylaniline? **C**

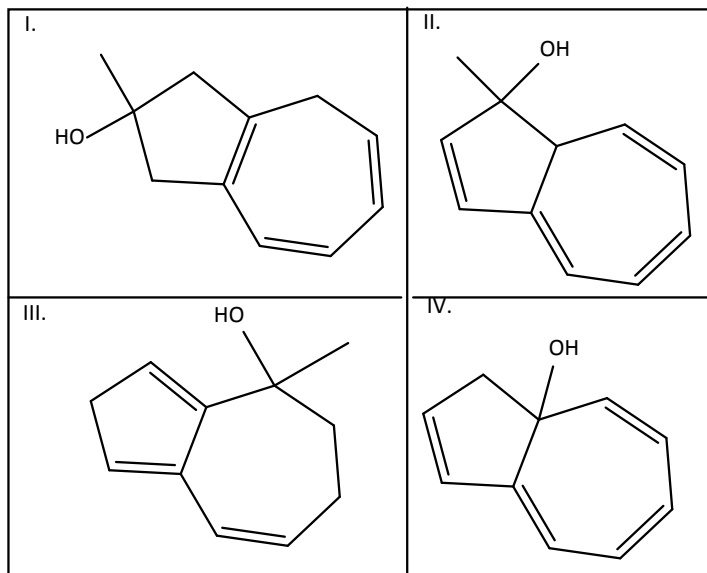


2-nitro-5-vinylacetophenone

- I. Zn(Hg), HCl  
 II. SnCl<sub>2</sub>, HCl  
 III. H<sub>2</sub>NNH<sub>2</sub>, KOH  
 IV. H<sub>2</sub>, Pt

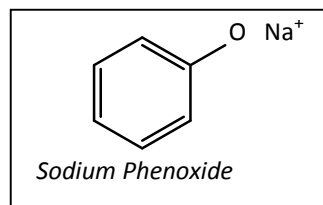
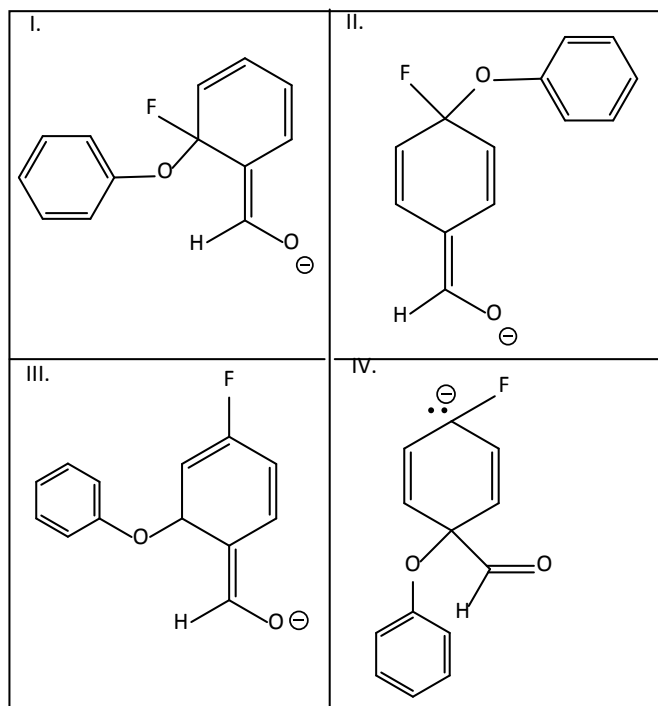
- a) I  
 b) I & II  
 c) IV  
 d) III  
 e) II

4. Rank the relative rate of the reaction of each of the compounds below with  $\text{H}_3\text{PO}_4$  from fastest to slowest (fastest>slowest). **D**



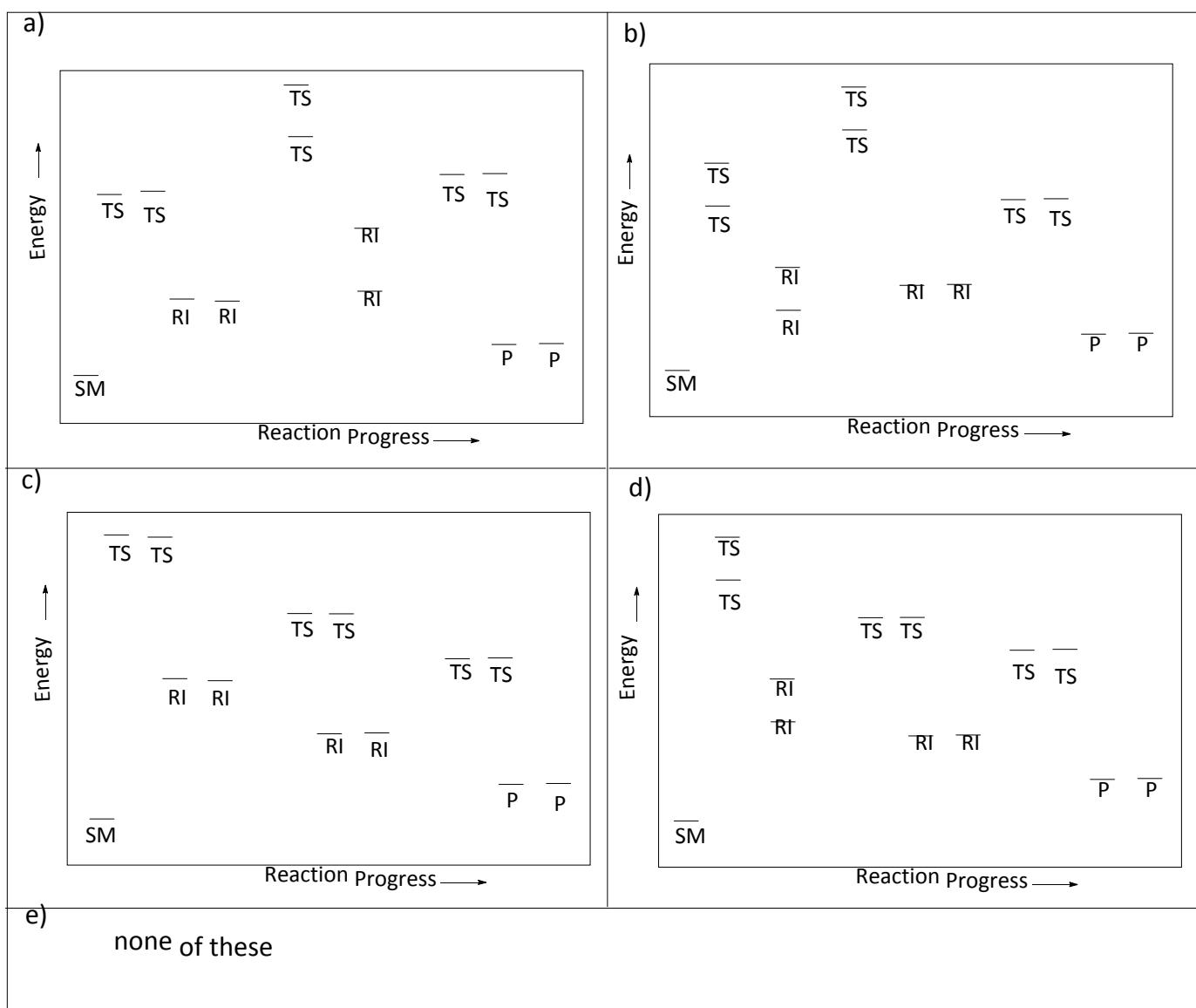
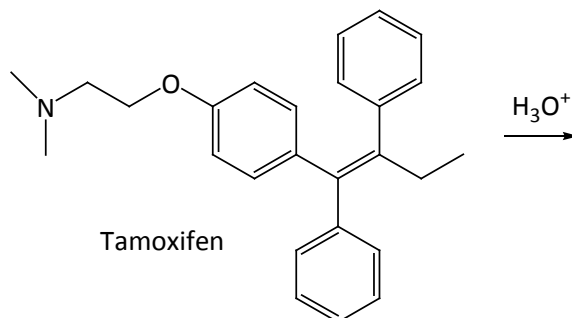
- a) I > II > III > IV  
 b) IV > III > II > I  
 c) IV = II > III > I  
 d) IV > II > III > I  
 e) II > IV > III > I

5. Which of the following structures represents a reaction intermediate that is generated upon reaction of para-fluorobenzaldehyde with sodium phenoxide? **D**

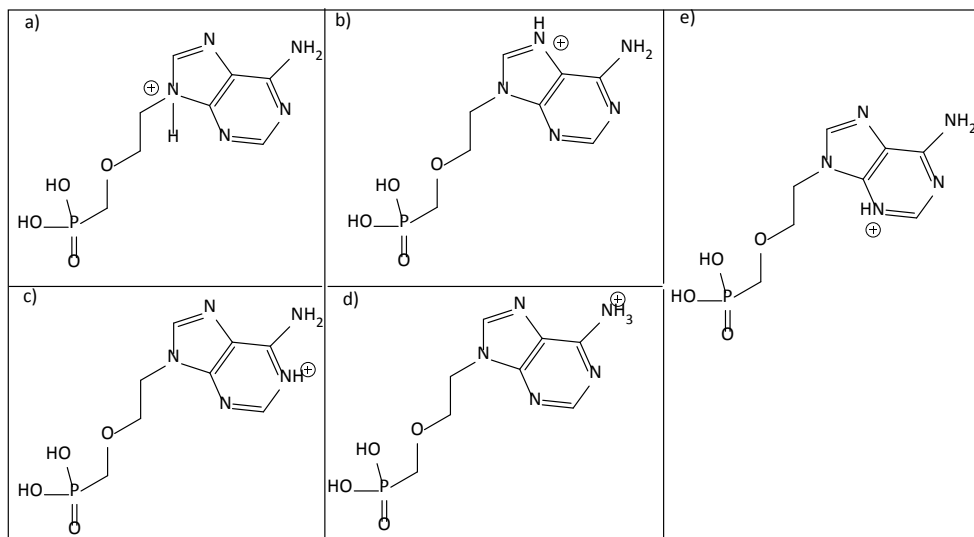
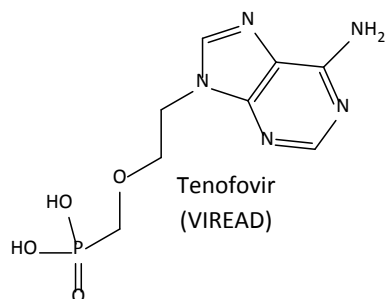


- a) I  
 b) II & IV  
 c) III  
 d) II  
 e) IV

6. Tamoxifen is a selective estrogen receptor modulator (SERM) used to treat breast cancer. Which of the following reaction energy diagrams describes the reaction of tamoxifen with  $\text{H}_3\text{O}^+$ ? (Note: Stereoisomers are not shown in the reaction energy diagram) **D**



7. Which of the following conjugate acids of tenofovir has the lowest pKa? **A**



8. Starting with benzene, which *sequence* of reagents could be used to prepare 1-bromo-3-chloro-4-isopropylbenzene? (Note: Other isomers may also form) **C**

- I. 1. isopropyl chloride, AlCl<sub>3</sub> 2. Cl<sub>2</sub>, FeCl<sub>3</sub> 3. Br<sub>2</sub>, FeBr<sub>3</sub>  
 II. 1. Cl<sub>2</sub>, FeCl<sub>3</sub> 2. Br<sub>2</sub>, FeBr<sub>3</sub> 3. isopropyl chloride, AlCl<sub>3</sub>  
 III. 1. isopropyl chloride, AlCl<sub>3</sub> 2. Br<sub>2</sub>, FeBr<sub>3</sub> 3. Cl<sub>2</sub>, FeCl<sub>3</sub>  
 IV. 1. Br<sub>2</sub>, FeBr<sub>3</sub> 2. Cl<sub>2</sub>, FeCl<sub>3</sub> 3. isopropyl chloride, AlCl<sub>3</sub>

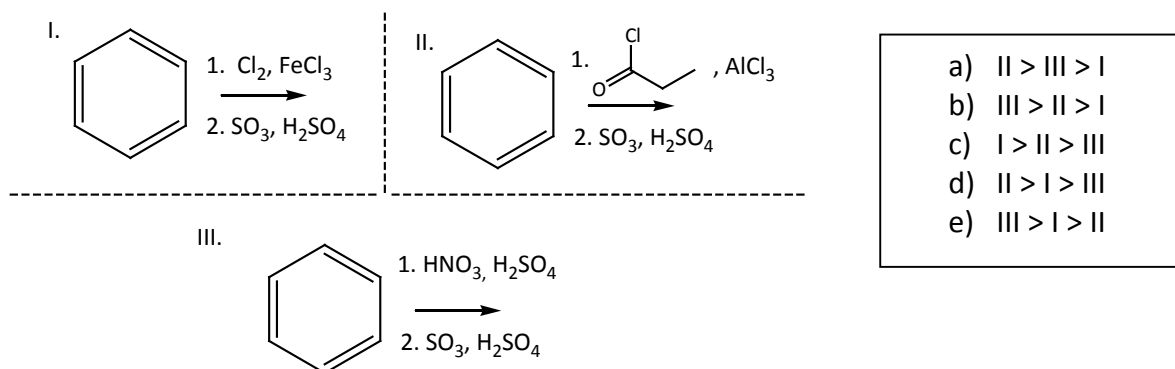
- a) II & IV  
 b) I & II  
 c) I & III  
 d) I, III & IV  
 e) I, II, III & IV

9. The pKa values of benzoic acid and phenoxy-substituted benzoic acids have been determined experimentally and are provided below. Based on these pKa values (not sigma values), which of the following statements is most consistent with this data? **D**

Acid	pKa
Benzoic acid	4.19
o-phenoxybenzoic acid	3.53
m-phenoxybenzoic acid	3.95
p-phenoxybenzoic acid	4.52

- a) Phenoxy substituents follow a resonance effect, regardless of its position on the ring.  
 b) Phenoxy substituents follow an inductive effect regardless of its position on the ring  
 c) Phenoxy substituents follow an inductive effect in the meta position and a resonance effect in the ortho and para positions.  
 d) Phenoxy substituents follow an inductive effect in the ortho and meta positions and the resonance effect in the para position  
 e) Phenoxy substituents follow an inductive effect in the ortho position and a resonance effect in the meta and para positions.

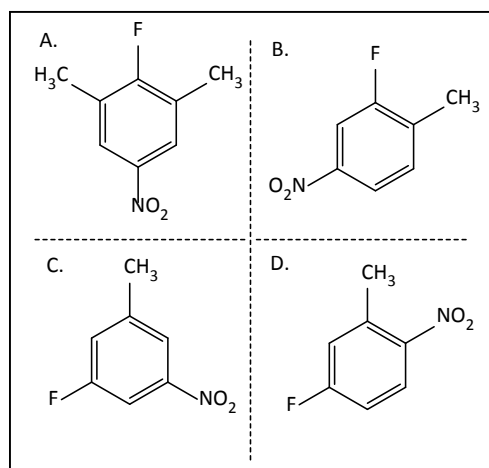
10. Rank the relative rates of formation of products from fastest to slowest (fastest>slowest) in the series of reactions below. **C**



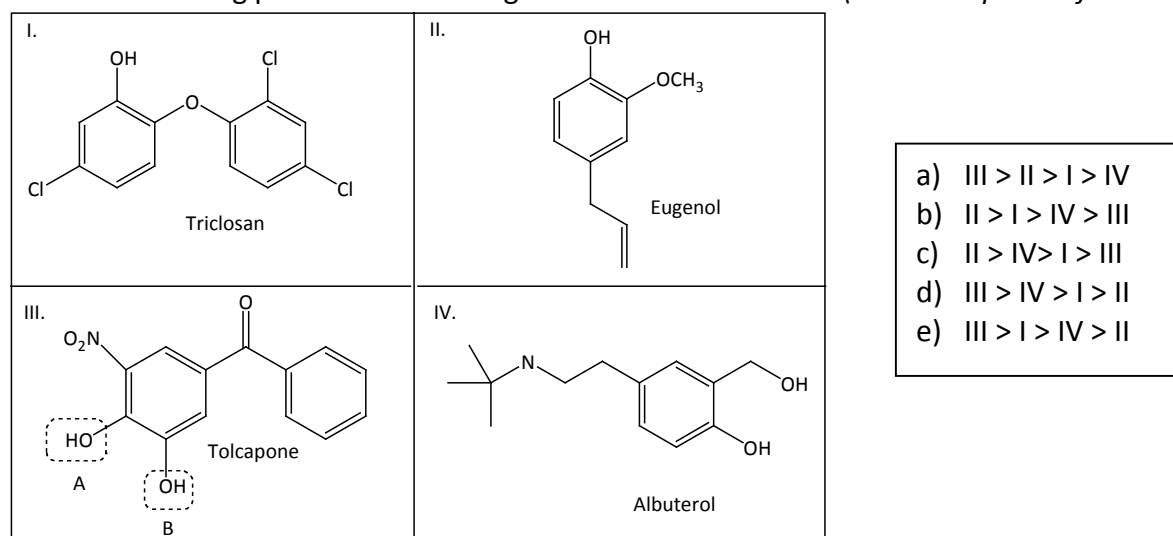
11. Match each compound (A-D) with its reaction chemistry in electrophilic aromatic substitutions (EAS) nucleophilic aromatic substitutions (NAS) and Benzyne reaction. **A**

- I. Reacts in NAS  
 II. Reacts in EAS  
 III. Reacts in Benzyne  
 IV. Does not react in EAS, NAS or Benzyne

- a) A = I    B = II, III    C = III    D = I, II, III  
 b) A = I, II    B = II, III    C = III    D = I, II, III  
 c) A = I    B = I, II, III    C = IV    D = I, II, III  
 d) A = IV    B = II, III    C = II, III    D = I, II, III  
 e) A = IV    B = II, III    C = IV    D = I, II, III



12. Rank the following phenols from strongest acid to weakest acid. (Use the B phenol for structure III) **E**

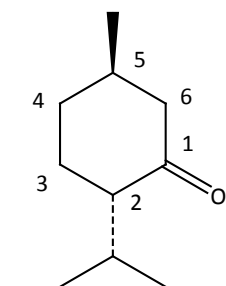


13. The *major* product(s) that would form in the monoalkylation reaction of *ortho*-dimethoxybenzene, tert-butyl alcohol and acetic acid is (are): **E**

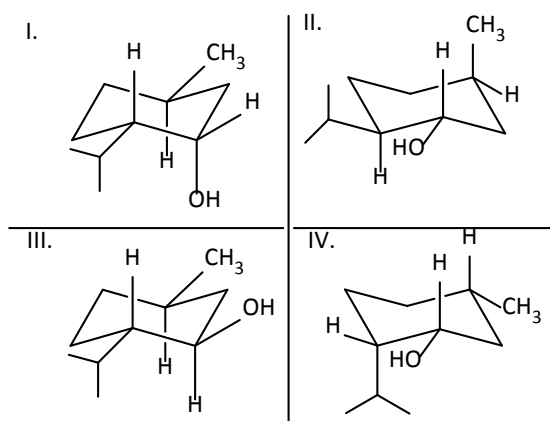
- I. 5-tert-butyl-1,3-dimethoxybenzene
- II. 1-tert-butyl-3,4-dimethoxybenzene
- III. 4-tert-butyl-1,5-dimethoxybenzene
- IV. 2-tert-butyl-1,3-dimethoxybenzene
- V. 1-tert-butyl-2,3-dimethoxybenzene

- |           |
|-----------|
| a) I & II |
| b) II     |
| c) III    |
| d) IV & V |
| e) II & V |

14. In a study by Ravichandran and Divakar (*J. Molecular Catalysis A: Chemical* 109(3) 201-208, 1996) it was demonstrated that treatment of (2*S*, 5*R*)-menthone with sodium borohydride provided (-)-menthol as the major product and (+)-neomenthol as a minor product. Which of the following compounds corresponds to (+)-neomenthol, the *minor product* of the reaction? **E**

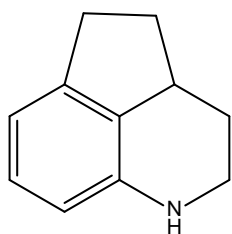


(2*S*, 5*R*)-menthone

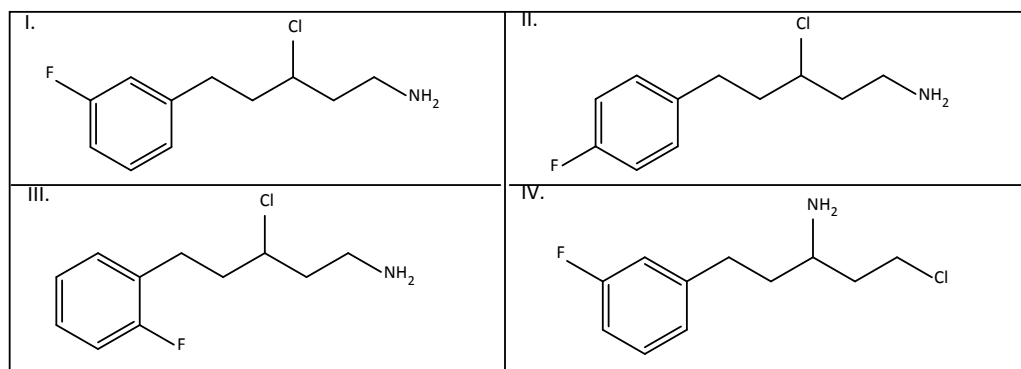


- |            |
|------------|
| a) IV      |
| b) II      |
| c) III     |
| d) II & IV |
| e) I       |

15. The compound below can be prepared through an intramolecular benzyne reaction. In this reaction, benzyne is generated with base, and the benzyne intermediate then reacts with an electrophile and nucleophile within the same molecule to give this product. Which of the following starting materials could be used to prepare the compound below through an intramolecular benzyne reaction? **B**

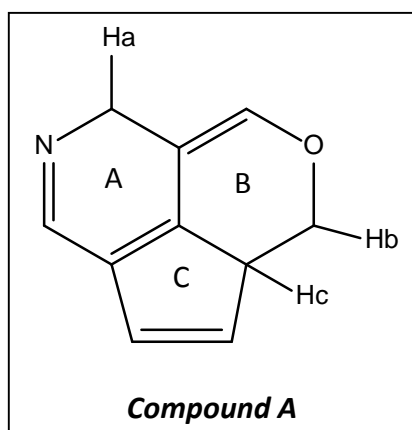


- a) I
- b) I & III
- c) II & IV
- d) III
- e) I, II, III & IV



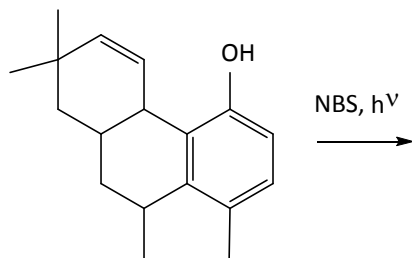
16. Which of the following statements is true as they relate to compound A below? **C**

- I. Donation of H<sub>a</sub> results in formation of a conjugate base that contains a new aromatic system that includes rings A and B.
- II. The pK<sub>a</sub> values of H<sub>a</sub>, H<sub>b</sub> and H<sub>c</sub> are approximately equal.
- III. The conjugate base that is generated by donation of H<sub>c</sub> has 6 π electrons associated with its aromatic system.
- IV. Compound A is aromatic.

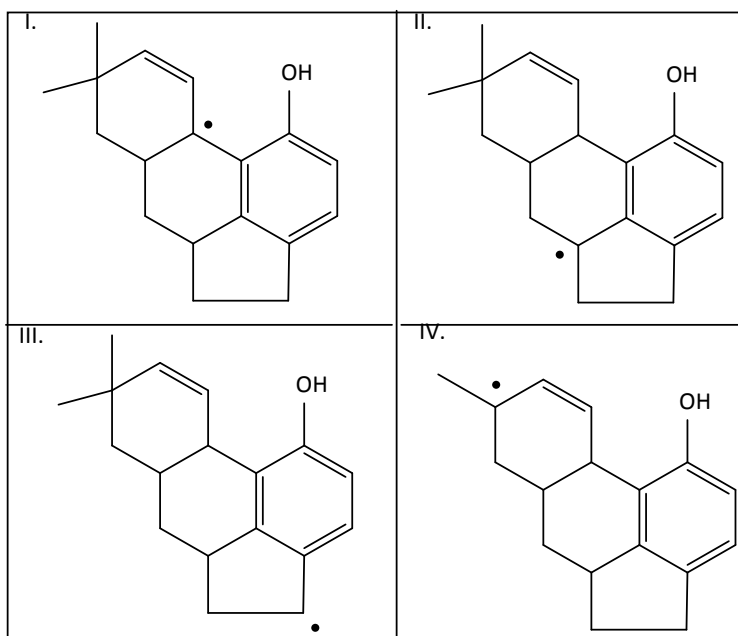


- a) I
- b) I & II
- c) III
- d) III & IV
- e) II & III

17. Which of the following reaction intermediate(s) is generated the fastest in the reaction below? **B**



- a) I & II
- b) I
- c) I, II & IV
- d) III
- e) I, II, III & IV

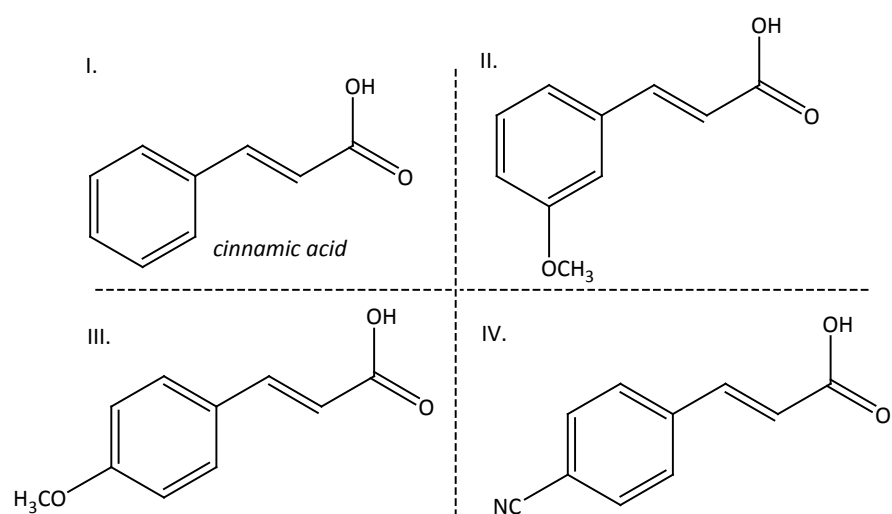


18. The major product(s) in the reaction of 4-fluoro-2-nitrotoluene with  $\text{NaNH}_2$ ,  $\text{NH}_3$  is (are): **B**

- I. 3-methyl-2-nitroaniline
- II. 4-methyl-3-nitroaniline
- III. 3-methyl-4-nitroaniline
- IV. 5-fluoro-2-methyl-3-nitroaniline

- |  |
|--|
| <ul style="list-style-type: none"> <li>a) IV</li> <li>b) II</li> <li>c) I &amp; II</li> <li>d) II &amp; III</li> <li>e) I, II &amp; III</li> </ul> |
|--|

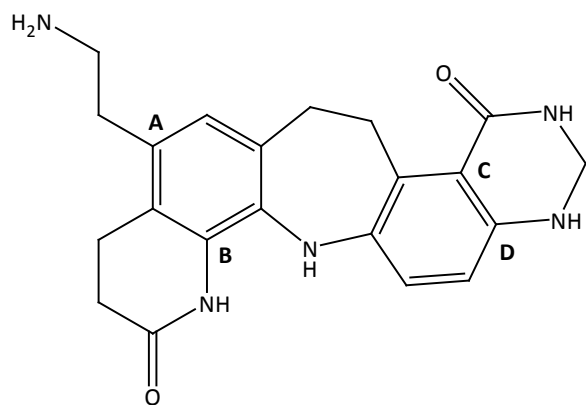
19. Cinnamic acid (I) and a series of substituted cinnamic acid compounds (II-IV) have been evaluated for activity in inhibiting the generation of glucose in the body. The relative potency of these compounds has been determined and is summarized below. Based on this data, what would be the predicted potency of m-chlorocinnamic acid (m-Cl)? **A**



<b>POTENCY</b>	
III > I > II > IV	(most potent) <span style="margin-left: 100px;">(least potent)</span>

- a) III > I > II > **m-Cl** > IV
- b) III > I > II > IV > **m-Cl**
- c) III > **m-Cl** > I > II > IV
- d) III > I > **m-Cl** > II > IV
- e) **m-Cl** > III > I > II > IV

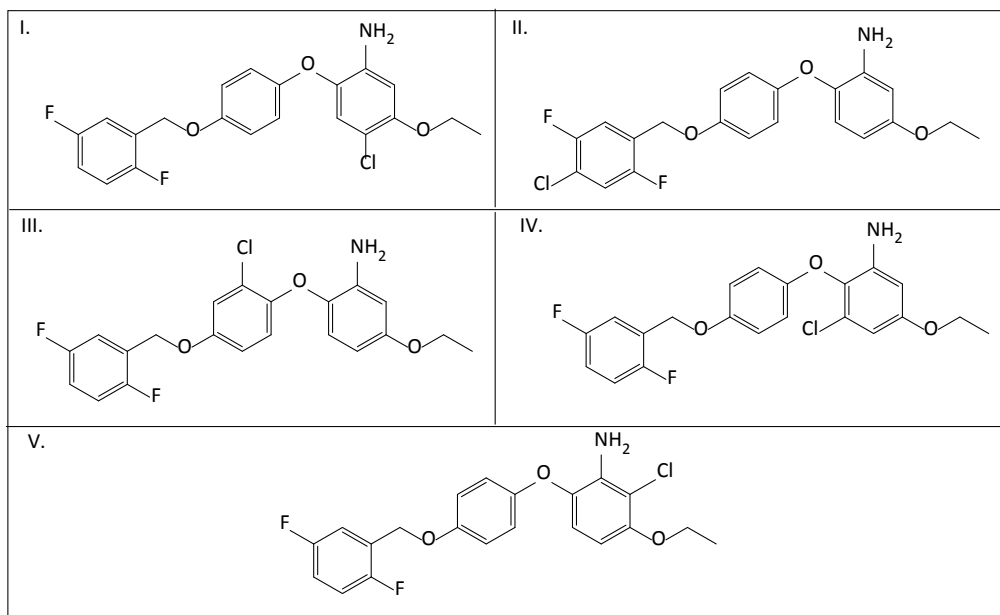
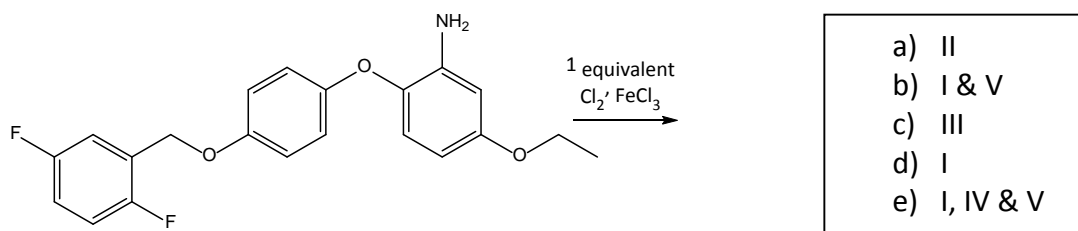
20. Sigma values may be used to predict the relative pKa values of aniline functional groups. Match the proper sigma values to the substituents labeled at carbons A, B, C and D in the compound provided below. **D**



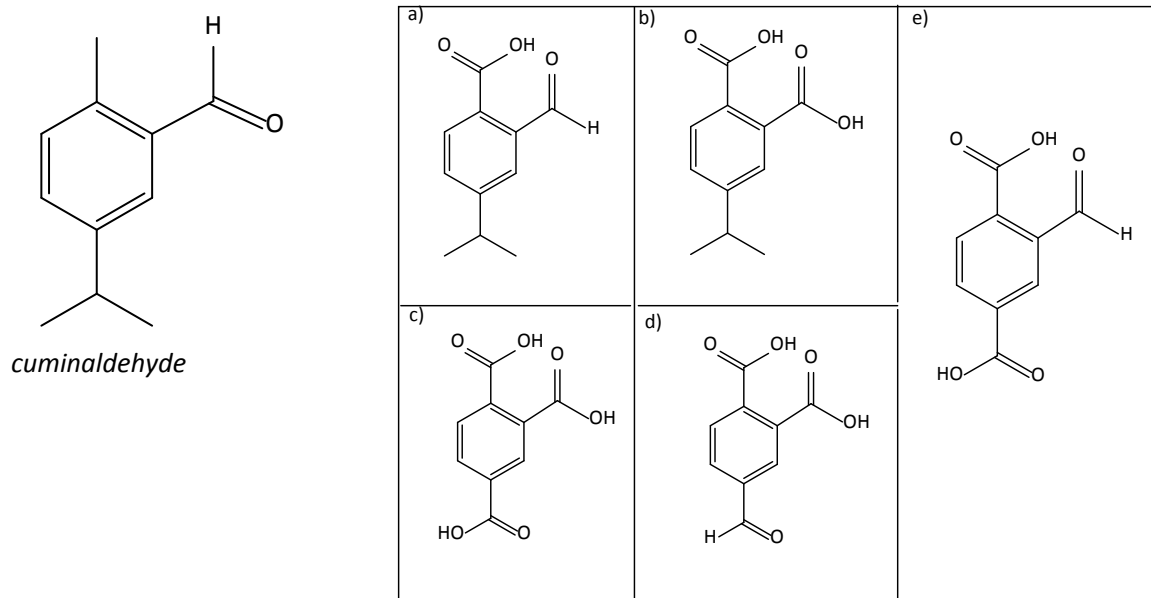
- |  |
|--|
| <ul style="list-style-type: none"> <li>a) A = ethyl B = acetamido C = acetamido D = amino</li> <li>b) A = ethyl B = amino C = acetyl D = amino</li> <li>c) A = amino B = amino C = acetyl D = amino</li> <li>d) A = ethyl B = acetamido C = acetyl D = amino</li> <li>e) A = amino B = acetamido C = acetyl D = amino</li> </ul> |
|--|



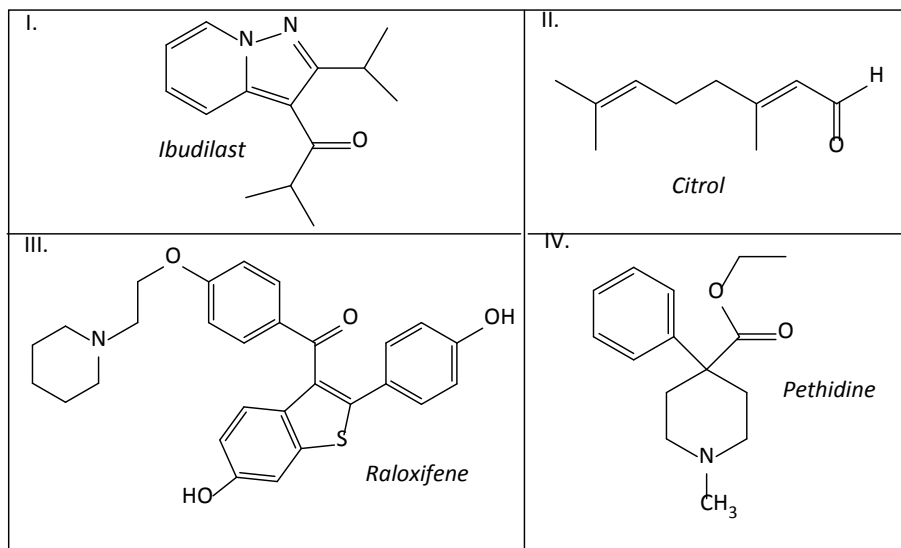
21. The major product(s) of the reaction below is (are): **D**



22. Treatment of cuminaldehyde with excess  $\text{KMnO}_4$  will provide: **C**

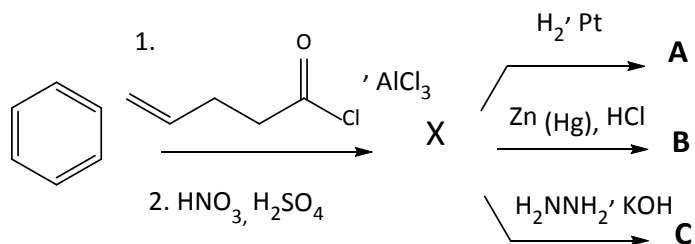


23. Which of the following compounds is prochiral in a reaction with excess  $\text{NaBH}_4$ ,  $\text{CH}_3\text{OH}$ ? **C**

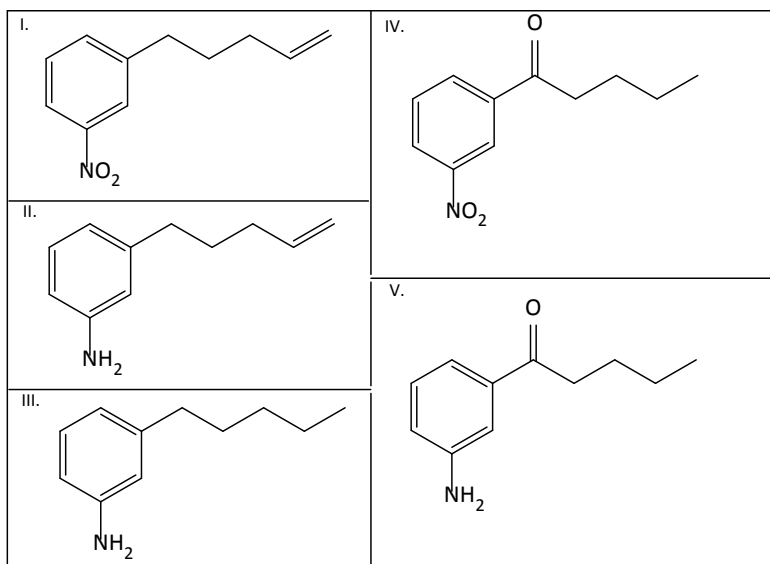


- |   |
|---|
| <p>a) I<br/>b) I, II &amp; III<br/>c) I &amp; III<br/>d) I, III &amp; IV<br/>e) I, II, III &amp; IV</p> |
|---|

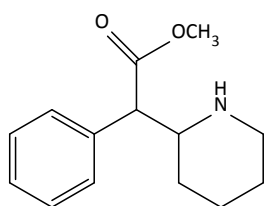
24. Identify A, B and C in the reaction scheme below. **E**



- |   |
|---|
| <p>a) A = III    B = III    C = I<br/>b) A = IV    B = II    C = I<br/>c) A = V    B = III    C = II<br/>d) A = III    B = I    C = III<br/>e) A = III    B = II    C = I</p> |
|---|

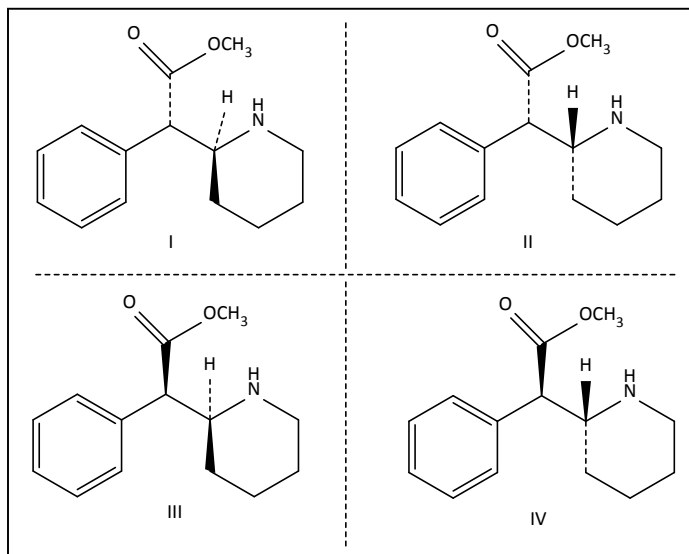


25. Methylphenidate (RITALIN) is a chiral drug sold as a racemic mixture to treat ADHD (attention deficit and hyperactivity disorder). Recently, Focalin, the *d*-isomer (R,R) of methylphenidate was approved by the FDA for treating ADHD. It has a longer duration of action and is more effective in reducing the symptoms of ADHD. Which of the following represents the racemic mixture marketed as RITALIN? **D**



Methylphenidate  
(Ritalin)

- a) I & II
- b) II & III
- c) III & IV
- d) I & IV
- e) II & IV



Substituent	Abbreviation	$\sigma$ meta	$\sigma$ para
acetamido-	AcNH-	0.21	-0.02
acetoxy-	AcO-	0.39	-0.01
acetyl-	Ac-	0.38	0.50
alkenyl-	-CH <sub>2</sub> =CH <sub>2</sub>	0.05	-0.02
amino-	NH <sub>2</sub> -	-0.16	-0.66
bromo-	Br-	0.39	0.23
tert-butyl-	(CH <sub>3</sub> ) <sub>3</sub> C-	-0.10	-0.20
chloro-	Cl-	0.37	0.23
cyano-	NC-	0.56	0.66
ethoxy-	EtO-	0.10	-0.24
ethyl-	Et-	-0.07	-0.15
fluoro-	F-	0.34	0.06
hydrogen	H-	0.00	0.00
hydroxy-	HO-	0.12	-0.37
methoxy-	MeO-	0.12	-0.27
methyl-	Me-	-0.07	-0.17
nitro-	NO <sub>2</sub> -	0.71	0.78
phenoxy-	PhO-	0.15	-0.21
phenyl-	Ph-	0.06	-0.01
trifluoromethyl	F <sub>3</sub> C-	0.43	0.54
trimethylamino-	(CH <sub>3</sub> ) <sub>3</sub> N <sup>+</sup> -	0.88	0.82

**Table 1:**  $\sigma$  values for Various Substituents

**Periodic Table of the Elements**

Representative (main group) elements		Transition metals										Representative (main group) elements							
IA												IIIA	IVA	VA	VIA	VIIA	VIIIA		
1	<b>H</b> 1.0079											5	<b>B</b> 10.811	<b>C</b> 12.011	<b>N</b> 14.007	<b>O</b> 15.999	<b>F</b> 18.998	<b>Ne</b> 20.180	
2	<b>Li</b> 6.941	<b>Be</b> 9.012											13	<b>Al</b> 26.982	<b>Si</b> 28.086	<b>P</b> 30.974	<b>S</b> 32.066	<b>Cl</b> 35.453	<b>Ar</b> 39.948
3	<b>Na</b> 22.990	<b>Mg</b> 24.305	IIIB	IVB	VB	VIB	VII B	VIII B		IB	IIB	14	<b>Ga</b> 69.723	<b>Ge</b> 72.61	<b>As</b> 74.922	<b>Se</b> 78.96	<b>Br</b> 79.904	<b>Kr</b> 83.8	
4	<b>K</b> 39.098	<b>Ca</b> 40.078	<b>Sc</b> 44.956	<b>Ti</b> 47.88	<b>V</b> 50.942	<b>Cr</b> 51.996	<b>Mn</b> 54.938	<b>Fe</b> 55.845	<b>Co</b> 58.933	<b>Ni</b> 58.69	<b>Cu</b> 63.546	<b>Zn</b> 65.39	<b>In</b> 114.82	<b>Sn</b> 118.71	<b>Sb</b> 121.76	<b>Te</b> 127.60	<b>I</b> 126.905	<b>Xe</b> 131.29	
5	<b>Rb</b> 85.468	<b>Sr</b> 87.62	<b>Y</b> 88.906	<b>Zr</b> 91.224	<b>Nb</b> 92.906	<b>Mo</b> 95.94	<b>Tc</b> 98	<b>Ru</b> 101.07	<b>Rh</b> 102.906	<b>Pd</b> 106.42	<b>Ag</b> 107.868	<b>Cd</b> 112.411	<b>Tl</b> 204.383	<b>Pb</b> 207.2	<b>Bi</b> 208.980	<b>Po</b> 209	<b>At</b> 210	<b>Rn</b> 222	
6	<b>Cs</b> 132.905	<b>Ba</b> 137.327	<b>La</b> 138.906	<b>Hf</b> 178.49	<b>Ta</b> 180.948	<b>W</b> 183.84	<b>Re</b> 186.207	<b>Os</b> 190.23	<b>Ir</b> 192.22	<b>Pt</b> 195.08	<b>Au</b> 196.967	<b>Hg</b> 200.59							
7	<b>Fr</b> 223	<b>Ra</b> 226.025	<b>Ac</b> 227.028	<b>Rf</b> 261	<b>Db</b> 262	<b>Sg</b> 263	<b>Bh</b> 262	<b>Hs</b> 265	<b>Mt</b> 266	<b>Uun</b> 269	<b>Uuu</b> 272	<b>Uub</b> 277							
			Rare earth elements																
Lanthanides			58	59	60	61	62	63	64	65	66	67	68	69	70	71			
			<b>Ce</b> 140.115	<b>Pr</b> 140.908	<b>Nd</b> 144.24	<b>Pm</b> 145	<b>Sm</b> 150.36	<b>Eu</b> 151.964	<b>Gd</b> 157.25	<b>Tb</b> 158.925	<b>Dy</b> 162.5	<b>Ho</b> 164.93	<b>Er</b> 167.26	<b>Tm</b> 168.934	<b>Yb</b> 173.04	<b>Lu</b> 174.967			
Actinides			90	91	92	93	94	95	96	97	98	99	100	101	102	103			
			<b>Th</b> 232.038	<b>Pa</b> 231.036	<b>U</b> 238.029	<b>Np</b> 237.048	<b>Pu</b> 244	<b>Am</b> 243	<b>Cm</b> 247	<b>Bk</b> 247	<b>Cf</b> 251	<b>Es</b> 252	<b>Fm</b> 257	<b>Md</b> 258	<b>No</b> 259	<b>Lr</b> 262			

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