NAME ________________________

ID # ________________________

ORGANIC CHEMISTRY II (2302)

8:00 – 8:50 am, August 4, 2015

Exam 4

If you want to pick this exam up Wednesday in class (in public), please check the box on the right: ☐

If you do not check the box, I will not bring your exam to class on Wednesday, and you will need to pick up your exam in private from Chemistry department staff in 115 Smith beginning Thursday, August 6th. Exams that are not picked up within two weeks will be disposed of.

A periodic table and a chart of amino acids and nucleic acid bases are attached to the back of this exam as an aid. Otherwise, you are not permitted to use any other materials (including notes, books, or electronic devices of any kind).

When the exam begins, please write your name at the top of the next page.

You may use pen or pencil. However, re-grades will be considered only for exams completed in pen.

Please write your answers in the boxes/spaces provided. If your answer is not in the appropriate space (say, for example, it's on the back of the page), draw us an arrow and/or note telling us where to look.

NAME ________________________

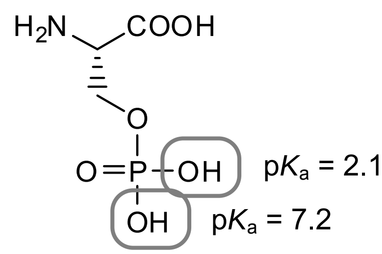
Scoring: 1. _________ / 48   4. _________ / 8

2. _________ / 9   5. _________ / 5

3. _________ / 30

Total Score: _________ / 100

1. (48 pts)
   a. L-Phosphoserine is a modified amino acid that is generated in proteins by phosphorylation of serine residues. The amino acid side chain has two acidic protons, which exhibit different pK_a values, as shown at right. What would be the structure and charge state of phosphoserine under extremely acidic conditions, at pH = 1? Then, how would the structure change with increasing pH?



L-phosphoserine

charge = +1	*charge = 0*	*charge = -1*

at pH = 1 → *with increasing pH*

   b. What would you predict for the isoelectric point (pI) of phosphoserine?

pI = [ ]

   c. If you analyzed a mixture of phosphoserine and serine by ion exchange chromatography, using a solvent gradient of increasing pH, would you expect phosphoserine to elute

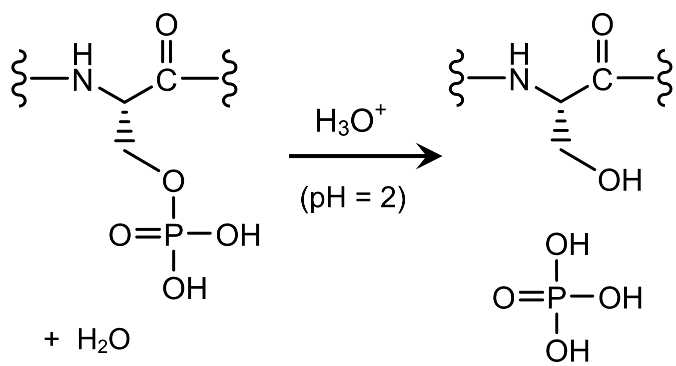
earlier   **later**   *or*   **at the same time**

relative to serine? *(Circle one answer.)*

d. At pH = 7, if a kinase enzyme were to convert serine residues on the surface of a target protein to phosphoserines, would the protein

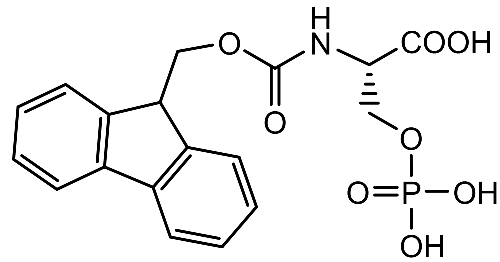
become **more positively charged?**	become **more negatively charged?**	*or*	retain **the same charge state?**	*(Circle one.)*

e. Ingested, phosphoserine-containing proteins may not survive our stomachs. Under acidic conditions, phosphoserine residues on the surfaces of proteins can undergo acid-catalyzed, nucleophilic phosphoacyl substitution, and can be hydrolyzed back to serines. Draw a mechanism (using "electron pushing") for this process. Draw each molecule and mechanistic step explicitly; don't cheat by combining multiple processes in a single step.

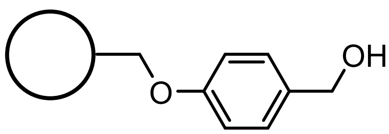


Mechanism:

f. Phosphopeptides−peptides incorporating a phosphoserine residue−can be synthesized via solid-phase peptide synthesis using the Fmoc-protected phosphoserine ("Fmoc-PS") reagent shown at right. In the box below, propose a multistep synthesis of the dipeptide phosphoserinylglycine (H_2N-PS-Gly-COOH), starting from Wang resin (drawn in the box below). You do not need to draw any chemical structures to answer this problem; you can refer to molecules by name or chemical abbreviation. In addition to the starting materials I've drawn, you can use any reagents and reactions we've learned about in class. *(Wang resin is cleaved in acid.)*

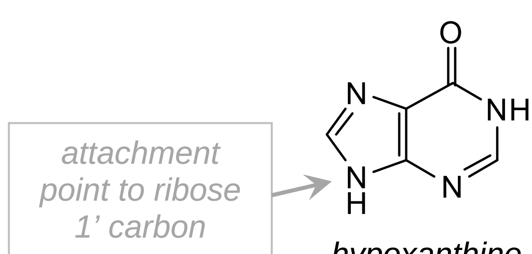


Fmoc-PS



Wang resin

2. (9 pts) Inosine is a non-natural nucleoside that is formed when a hypoxanthine base is attached at the 1' position of a ribose sugar. Inosine can be incorporated into DNA and RNA by both biological and synthetic methods.



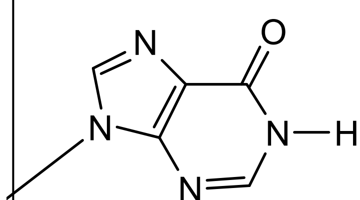
hypoxanthine

a. DNA polymerase can incorporate 2'-deoxyinosine into DNA when it accepts 2'-deoxyinosine triphosphate as a substrate. Draw the structure of 2'-deoxyinosine triphosphate.

2'-deoxyinosine triphosphate

b. Inosine can base-pair with any of the four typical DNA bases, though the DNA double helix accommodates a pyrimidine across from inosine better than a purine. Draw a base pair between the hypoxanthine base of inosine (already drawn in the box for you) and either of the two pyrimidine bases typically found in DNA. Illustrate hydrogen bonding in your drawing. You do not need to draw the sugar or phosphate parts of DNA; just draw the base.

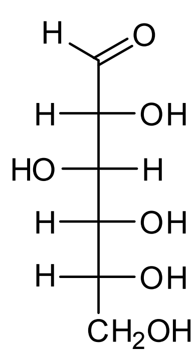
hypoxanthine-pyrimidine base pair



3. (30 pts) Lactose is a disaccharide formed from glucose and galactose; it is a glucosyl glycoside of galactose.

a. D-Galactose is the C-4 epimer of D-glucose, shown at right. Draw a Fischer projection of D-galactose in the box provided.

b. Acyclic D-galactose equilibrates with a cyclic, α-galactopyranose (6-membered ring) form. Draw both a Haworth projection and the most stable chair conformer of that cyclic form in the boxes on the next page.



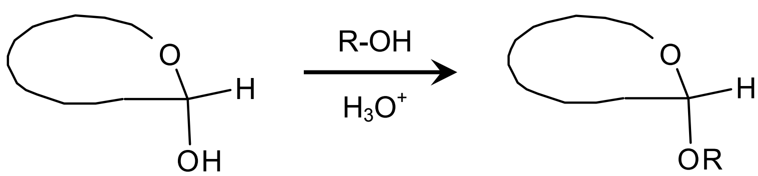
D-glucose

acyclic form of D-galactose (Fischer projection)

cyclic α-D-galactopyranose (Haworth projection)	*cyclic α-D-galactopyranose (chair conformer)*

c. Although the α-anomer of galactose that you drew is less stable than the β-anomer, the α-anomer is still stabilized by the "anomeric effect", a specific molecular orbital interaction. Illustrate that molecular orbital interaction on your chair drawing above, drawing lobes for orbitals.

d. Cyclic α-galactose (a hemiacetal) spontaneously forms glycosides (acetals) with other alcohols, like glucose, in the presence of an acid catalyst. Using my cartoon illustrations below, draw a mechanism on the next page for the formation of glycoside from galactose.

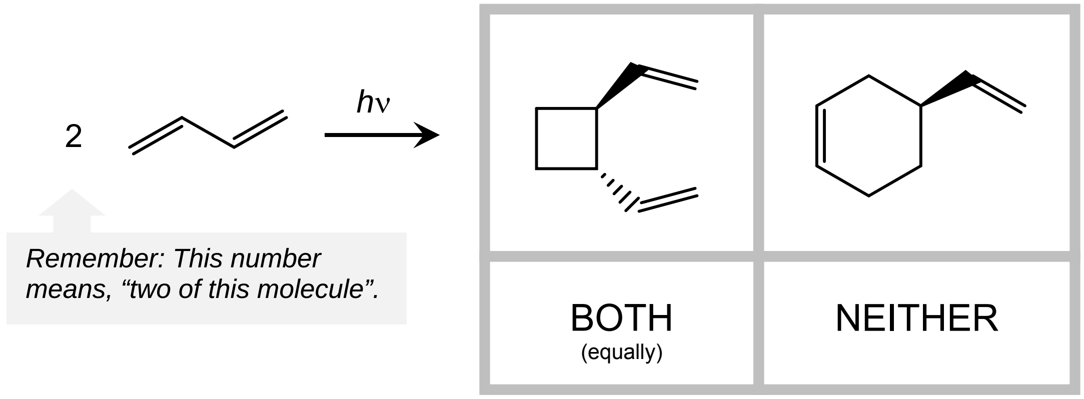


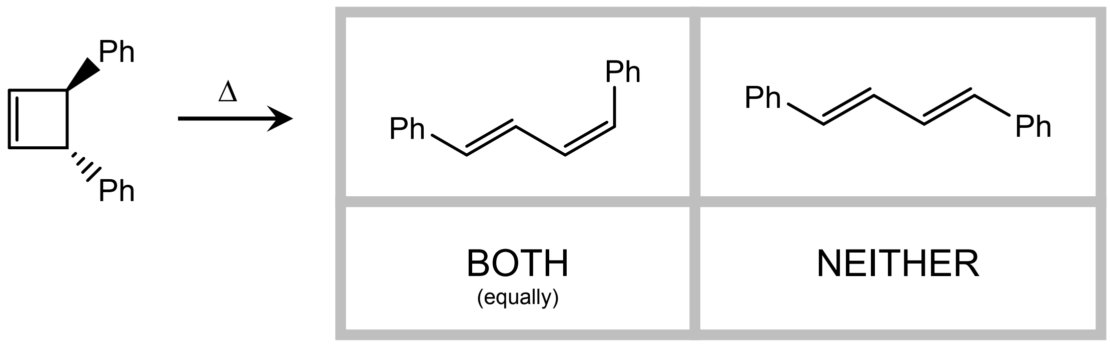
Mechanism:

e. What is the timescale of the reaction on the previous page? Does it take place spontaneously over

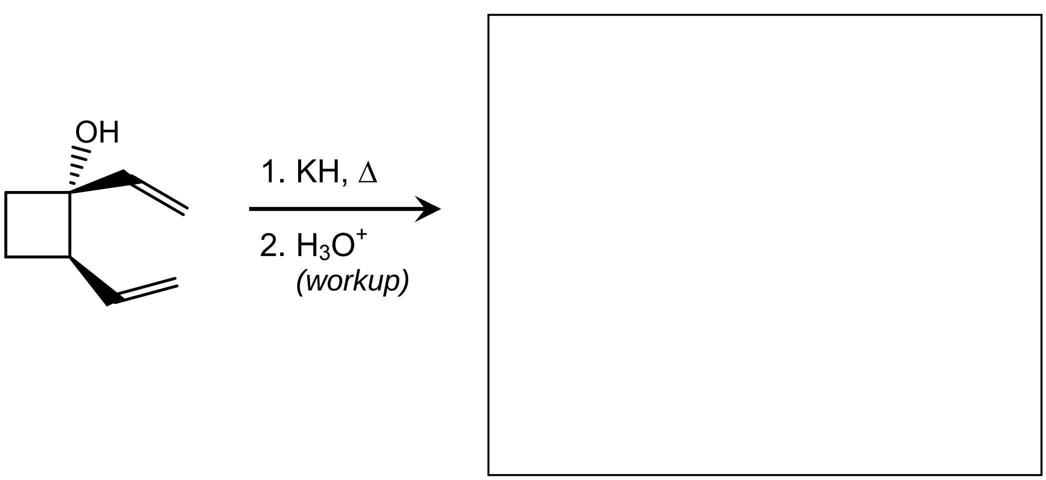
minutes? **weeks?** *or* **decades?** *(Circle one.)*

4. (8 pts) Each of the reactions below is drawn with two possible products. Circle the preferred product. If the two products are produced equally, circle "BOTH". If neither product would result from the reaction, circle "NEITHER". **Circle one answer only.**

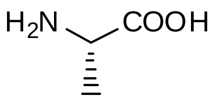




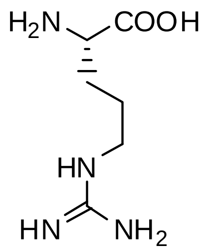
5. (5 pts) For the reaction below, fill in the empty box corresponding to product. Give only one answer. If you expect the reaction to yield multiple products, draw one major product. If the reaction yields multiple enantiomers, draw only one enantiomer in the box, and include the note "+ enantiomer".



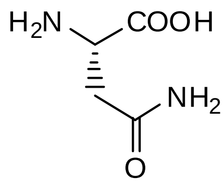
Exam 4 Chart of Amino Acids
(in Alphabetical Order)



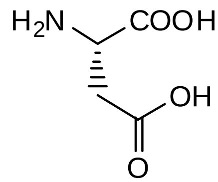
alanine
(Ala, A)



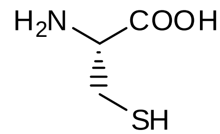
arginine
(Arg, R)



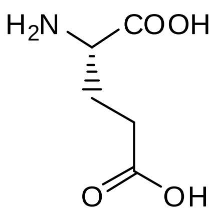
asparagine
(Asn, N)



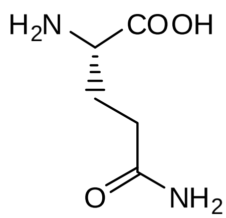
aspartic acid
(Asp, D)



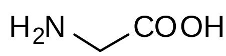
cysteine
(Cys, C)



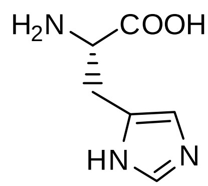
glutamic acid
(Glu, E)



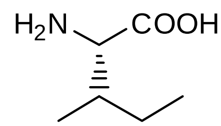
glutamine
(Gln, Q)



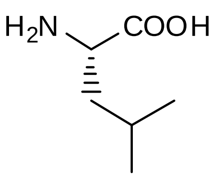
glycine
(Gly, G)



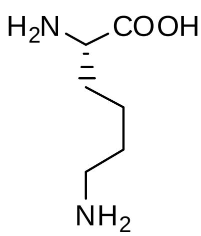
histidine
(His, H)



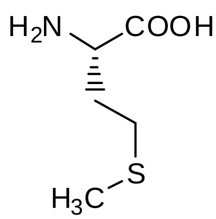
isoleucine
(Ile, I)



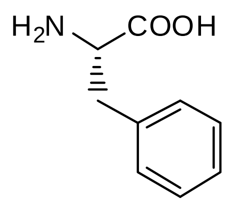
leucine
(Leu, L)



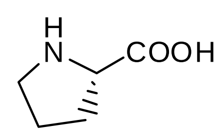
lysine
(Lys, K)



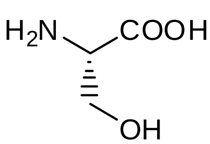
methionine
(Met, M)



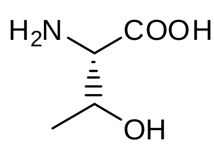
phenylalanine
(Phe, F)



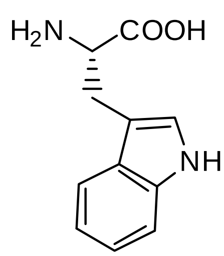
proline
(Pro, P)



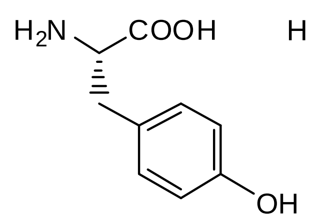
serine
(Ser, S)



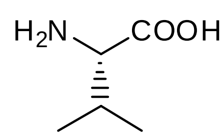
threonine
(Thr, T)



tryptophan
(Trp, W)

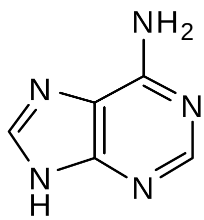


tyrosine
(Tyr, Y)

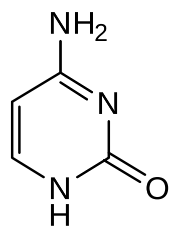


valine
(Val, V)

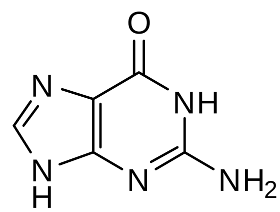
Exam 4 Chart of Nucleic Acid Bases
(in Alphabetical Order)



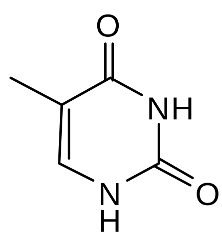
adenine
(A)



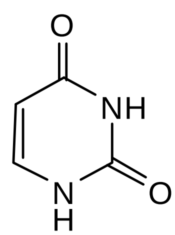
cytosine
(C)



guanine
(G)



thymine
(T)



uracil
(U)

Exam 4 Chart of Reaction Conditions

Br_2
$FeBr_3$

Cl_2
$AlCl_3$

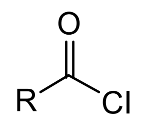
H_2SO_4
HNO_3

Sn *or* Fe
HCl/H_2O

H_2SO_4
SO_3

$KMnO_4$
^{-}OH, 100 °C

1. $NaNO_2$
   HCl
2. CuCN *or* H_3PO_2 *or* CuX *or* H_3O^+



$AlCl_3$

R-X (R = alkyl)
$AlCl_3$ *or* $FeBr_3$

Zn(Hg),
HCl/H_2O

1. N_2H_4
2. KOH, Δ

H_2
Pd-C

Li
hexane

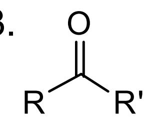
Mg
Et_2O

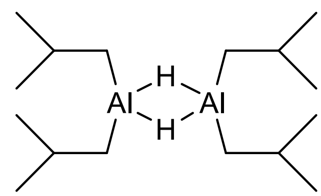
R_2CuLi

RLi

RMgX

$LiAlH(OtBu)_3$

1. PPh_3
2. *n*-BuLi
3. 



(DIBAL-H)

$Na_2Cr_2O_7$
H_2SO_4

1. $NaBH_4$
2. H_2O

1. Ag_2O
   NH_3
2. H_3O^+

1. O_3
2. H_2O

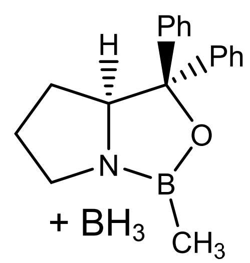
1. $LiAlH_4$
2. H_2O

$Bu_4N^+F^-$

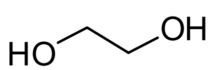
$NaNH_2$

$(COCl)_2$

$PhCH_2Br$
Ag_2O



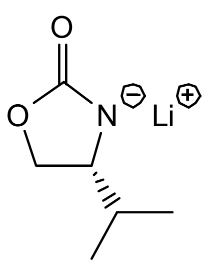
+ BH_3



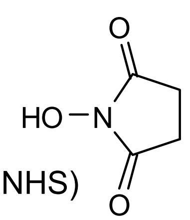
HCl

$SOCl_2$
(& pyridine, usually)

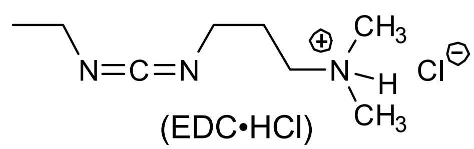
$(CH_3)_3SiCl$ {TMSCl}, *or* TBDMSCl;
Et_3N *or* imidazole

1. 

2. R-X
3. LiOH

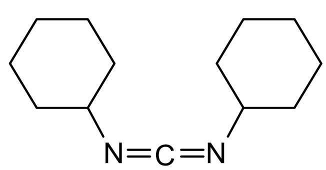


(NHS)

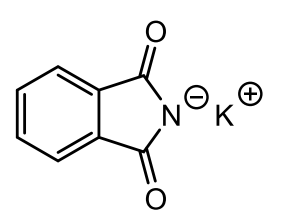


(EDC•HCl)

1. CH_3I
   (excess)
2. Ag_2O
   H_2O

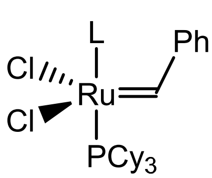


(DCC)

1. 

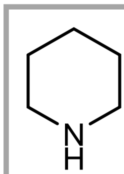
2. N_2H_4 (or ^{-}OH)

RCHO
$Na(OAc)_3BH$
or
$NaBH_3CN$



(Grubbs catalyst)

$Pd(OAc)_2$
PPh_3, NEt_3



1. NaN_3
2. PPh_3
   H_2O

HF

$CHCl_3$
KO*t*Bu

$Pd(PPh_3)_4$
NaOH

CH_2I_2
Zn(Cu)

CF_3COOH

Chemistry Reference Sheet

Key

11 — Atomic number
Na — Element symbol
Sodium — Element name
22.99 — Average atomic mass*

Period	1 1A	2 2A	3 3B	4 4B	5 5B	6 6B	7 7B	8	9 8B	10	11 1B	12 2B	13 3A	14 4A	15 5A	16 6A	17 7A	18 8A
1	1 **H** Hydrogen 1.01																	2 **He** Helium 4.00
2	3 **Li** Lithium 6.94	4 **Be** Beryllium 9.01											5 **B** Boron 10.81	6 **C** Carbon 12.01	7 **N** Nitrogen 14.01	8 **O** Oxygen 16.00	9 **F** Fluorine 19.00	10 **Ne** Neon 20.18
3	11 **Na** Sodium 22.99	12 **Mg** Magnesium 24.31											13 **Al** Aluminum 26.98	14 **Si** Silicon 28.09	15 **P** Phosphorus 30.97	16 **S** Sulfur 32.07	17 **Cl** Chlorine 35.45	18 **Ar** Argon 39.95
4	19 **K** Potassium 39.10	20 **Ca** Calcium 40.08	21 **Sc** Scandium 44.96	22 **Ti** Titanium 47.87	23 **V** Vanadium 50.94	24 **Cr** Chromium 52.00	25 **Mn** Manganese 54.94	26 **Fe** Iron 55.85	27 **Co** Cobalt 58.93	28 **Ni** Nickel 58.69	29 **Cu** Copper 63.55	30 **Zn** Zinc 65.39	31 **Ga** Gallium 69.72	32 **Ge** Germanium 72.61	33 **As** Arsenic 74.92	34 **Se** Selenium 78.96	35 **Br** Bromine 79.90	36 **Kr** Krypton 83.80
5	37 **Rb** Rubidium 85.47	38 **Sr** Strontium 87.62	39 **Y** Yttrium 88.91	40 **Zr** Zirconium 91.22	41 **Nb** Niobium 92.91	42 **Mo** Molybdenum 95.94	43 **Tc** Technetium (98)	44 **Ru** Ruthenium 101.07	45 **Rh** Rhodium 102.91	46 **Pd** Palladium 106.42	47 **Ag** Silver 107.87	48 **Cd** Cadmium 112.41	49 **In** Indium 114.82	50 **Sn** Tin 118.71	51 **Sb** Antimony 121.76	52 **Te** Tellurium 127.60	53 **I** Iodine 126.90	54 **Xe** Xenon 131.29
6	55 **Cs** Cesium 132.91	56 **Ba** Barium 137.33	57 **La** Lanthanum 138.91	72 **Hf** Hafnium 178.49	73 **Ta** Tantalum 180.95	74 **W** Tungsten 183.84	75 **Re** Rhenium 186.21	76 **Os** Osmium 190.23	77 **Ir** Iridium 192.22	78 **Pt** Platinum 195.08	79 **Au** Gold 196.97	80 **Hg** Mercury 200.59	81 **Tl** Thallium 204.38	82 **Pb** Lead 207.2	83 **Bi** Bismuth 208.98	84 **Po** Polonium (209)	85 **At** Astatine (210)	86 **Rn** Radon (222)
7	87 **Fr** Francium (223)	88 **Ra** Radium (226)	89 **Ac** Actinium (227)	104 **Rf** Rutherfordium (261)	105 **Db** Dubnium (262)	106 **Sg** Seaborgium (266)	107 **Bh** Bohrium (264)	108 **Hs** Hassium (269)	109 **Mt** Meitnerium (268)									

58 **Ce** Cerium 140.12	59 **Pr** Praseodymium 140.91	60 **Nd** Neodymium 144.24	61 **Pm** Promethium (145)	62 **Sm** Samarium 150.36	63 **Eu** Europium 151.96	64 **Gd** Gadolinium 157.25	65 **Tb** Terbium 158.93	66 **Dy** Dysprosium 162.50	67 **Ho** Holmium 164.93	68 **Er** Erbium 167.26	69 **Tm** Thulium 168.93	70 **Yb** Ytterbium 173.04	71 **Lu** Lutetium 174.97
90 **Th** Thorium 232.04	91 **Pa** Protactinium 231.04	92 **U** Uranium 238.03	93 **Np** Neptunium (237)	94 **Pu** Plutonium (244)	95 **Am** Americium (243)	96 **Cm** Curium (247)	97 **Bk** Berkelium (247)	98 **Cf** Californium (251)	99 **Es** Einsteinium (252)	100 **Fm** Fermium (257)	101 **Md** Mendelevium (258)	102 **No** Nobelium (259)	103 **Lr** Lawrencium (262)

* If this number is in parentheses, then it refers to the atomic mass of the most stable isotope.