

## Exercise 3 - CHEMICAL TOXICITY

### A. Toxicities of Chemicals

- Use one or more of the sites near the beginning of this *Exercise* to find the LD<sub>50</sub> (oral-rat) values for the compounds below. From these values, calculate the extrapolated LD<sub>50</sub> value for a 70 kg rat in units of grams. When available, also record the LD<sub>50</sub> value for humans. The site <http://chem.sis.nlm.nih.gov/chemidplus/chemidlite.jsp> is suggested for this search.

<u>Compound</u>	<u>formula</u>	<u>LD<sub>50</sub> (oral-rat)</u> <u>(mg/kg)</u>	<u>LD<sub>50</sub> for</u> <u>70 kg rat (g)</u>	<u>LD<sub>LO</sub> for</u> <u>humans (mg/kg)</u>
glucose	C <sub>6</sub> H <sub>12</sub> O <sub>6</sub>	25800	1806	na
iodine	I <sub>2</sub>	14000	980	28
ethanol	C <sub>2</sub> H <sub>6</sub> O	7060	494	1400
potassium iodide	KI	na	na	na
acetaminophen	C <sub>8</sub> H <sub>9</sub> NO <sub>2</sub>	1944	136	143-357
dichloromethane	CH <sub>2</sub> Cl <sub>2</sub>	1600	112	357
vanillin	C <sub>8</sub> H <sub>8</sub> O <sub>3</sub>	1580	111	na
caffeine	C <sub>8</sub> H <sub>10</sub> N <sub>4</sub> O <sub>2</sub>	192	13	192
nicotine	C <sub>10</sub> H <sub>14</sub> O <sub>2</sub>	50	3.5	na
arsenic(III) chloride	AsCl <sub>3</sub>	48	3.4	na
potassium cyanide	KCN	5	0.35	na
warfarin (coumadin)	C <sub>19</sub> H <sub>16</sub> O <sub>4</sub>	1.6	0.11	6.7 (man)
dioxin	C <sub>12</sub> H <sub>4</sub> Cl <sub>4</sub> O <sub>2</sub>	0.02	0.0014	na

[Note: For the following questions, assume that the LD<sub>50</sub> values for rats can be applied to humans and that an average human weighs 70 kg.]

- $(70 \text{ kg})(0.192 \text{ g/kg})(1 \text{ cup}/0.1 \text{ g}) = 1.3 \times 10^4 \text{ cups}$
  - Recognizing that the answer to #3a depends on many assumptions and has a large margin of error, is the very sad and unfortunate story reported at the site below surprising?
 

<http://the-tech.mit.edu/V118/N56/shorts.56n.html>  
[http://www.solarnavigator.net/solar\\_cola/caffeine.htm](http://www.solarnavigator.net/solar_cola/caffeine.htm)

*According to the first website, the student swallowed caffeine pills equivalent to 250 cups of coffee. This is almost double the amount that should be fatal to 50% of a 70 kg rat population and also double the amount for the low dose that can be fatal to humans (however, as noted the LD<sub>LO</sub> value because of coincidence is suspect).*
- $(70 \text{ kg})(7.06 \text{ g/kg})(1 \text{ beer}/21 \text{ g}) = 24 \text{ beers}$  (Assumes the density of beer is 1.0 g/mL, 350x0.06)
- $(70 \text{ kg})(50 \text{ mg/kg})(1 \text{ cigarette}/20 \text{ mg}) =$  consumed 180 cigarettes  
 $(70 \text{ kg})(50 \text{ mg/kg})(1 \text{ cigarette}/1 \text{ mg}) =$  smoked 3500 cigarettes
- During nuclear accidents, people exposed to radiation are sometimes advised to take potassium iodide to dilute the radioactive iodide that has been released and can be incorporated into the thyroid gland.
  - Does this sound like a wise procedure? *Unfortunately, there does not seem to be a legitimate LD<sub>50</sub> reported for KI. Some references give its value as the value for I<sub>2</sub> and others for triiodide. Probably the best estimate is the value reported for NaI of 4340 mg/kg. This value indicates a low toxicity and KI can probably be used safely if carefully administered to minimize radiation damage from radioactive iodide.*

- b. During these episodes, the media often describes the use of iodine as therapy. Explain the problem with this announcement. *Iodine and KI are two completely different chemicals. Iodine will not solve the iodide absorption problem in the thyroid and according to the human's  $LD_{LO}$  of 28mg/kg,  $I_2$  is potentially lethal if administered instead of KI.*
- c. Compare iodine's  $LD_{LO}$  value for human's with its  $LD_{50}$  value for rats and consider a comparison of the two values for other compounds in your table. Consistent with the  $LD_{LO}$  for iodine, halogens are considered to be very toxic but the  $LD_{50}$  value for rats seems to indicate a low toxicity. Critically evaluate the values. *The  $LD_{50}$  value for rats is certainly suspect although values for rabbits and mice are also surprisingly high. One possible conclusion is that iodine is much more toxic to humans than to rodents but for most compounds, the correlation is at least fair. Another conclusion is that the value of 14 g/kg is incorrect. It is not uncommon for these values to be off by a factor of 1000 as results are often reported in mg/kg and g/kg. Another possibility is that the 14 g/mg is for a solution rather than pure iodine. Once a value has been transcribed, other tabulations sometimes copy the result without checking validity.*
6. Would you consider vanillin to be a safe food additive? *111 g will kill half of the 70 kg rat population. Assuming that humans and rats have similar responses to vanillin, vanillin should be relatively safe as 111 g or about 4 oz is much more than a human would consume when vanillin is used as a flavoring.*
7. a.  $6.7 \times 10^{11}$  g or  $7.4 \times 10^5$  tons  
b.  $7.4 \times 10^5$  tons would require over 18,000 truckloads (total truck including loads are generally not allowed to exceed 40 tons) and would not go undetected.  
c.  $3.0 \times 10^3$  tons would take over 73 truckloads and would not go undetected.
8.  $1.4 \times 10^{-4}$  mL Assumes humans have same sensitivity as rats.. According to Wikipedia, a typical bite injects about  $3 \times 10^{-5}$  mL which is dangerous but not enough to kill most people.
9. Warfarin is very toxic with a rat  $LD_{50}$  of 1.6 mg/kg and therefore must be kept at a low level to prevent reaching a toxic level.
10. The  $LD_{50}$  for dioxin is much lower than for cyanide. Accidents involving dioxin have had terrible consequences.
11. It is very surprising that the evidence supporting sodium as a cause of high blood pressure is weak and there is some evidence that the culprit is actually chloride. It is very difficult to do controlled studies as sodium ion cannot be administered without the presence of a negative ion and chloride cannot be administered without the presence of a positive ion.

## Exercise 4 - Infrared Spectroscopy

$\nu = (1/2\pi c) (F/\mu)^{1/2}$  where  $\mu = \frac{M_x M_y}{M_x + M_y} =$  reduced mass with  $M_x$  and  $M_y$  representing the masses of the balls on the ends of the spring

- Using the equation above, derive the relationship between the ratio  $\nu_1/\nu_2$  of the stretching frequencies for two bonds (assuming the stretching force constant is the same for the two bonds) and the masses on the bond.

$$\nu_1/\nu_2 = (\mu_2/\mu_1)^{1/2} = (M_{2x}M_{2y}/M_{1x}M_{1y})^{1/2}[(M_{1x} + M_{1y})/(M_{2x} + M_{2y})]^{1/2}$$

- Now use the derived equation to determine the  $\nu_1/\nu_2$  ratio for a C - H bond to a C - D bond assuming the force constants are the same.

$$\nu_1/\nu_2 = (24/12)^{1/2}(13/14)^{1/2} = 1.36$$

- After you have finished the problem immediately above (#2), use the two infrared spectra below to determine the experimental value of  $\nu_1/\nu_2$  for the ratio of the stretching frequencies of C - H to C - D. Please note that the weak absorptions in the vicinity of  $2400 \text{ cm}^{-1}$  are due to an inadequate correction for the background absorption of carbon dioxide.

$$3019/2253 = 1.34$$

- Compare the result from the model to the experimental value and comment on the validity of the model.

*The difference is only 1.5%*

- Are there any other absorptions in the spectra that involve the C - D bond? Explain your answer and if so describe the type of vibration that is responsible for the absorption.

*The  $1215 \text{ cm}^{-1}$  for C-H and the  $911 \text{ cm}^{-1}$  for C-D for a ratio of 1.33 must involve the isotopes because of the sizeable shift. This is probably a bending mode and it is a little surprising the ratio is about the same as for stretching.*

- Does the hydrogen (or deuterium) have a significant effect on the stretching frequency of the C-Cl bond? Explain your answer.

*The shifts are small as expected because the isotopes are not directly involved but the shifts are measurable (e.g.,  $769 \text{ cm}^{-1}$  to  $743 \text{ cm}^{-1}$ ).*

- Is either  $\text{CHCl}_3$  or  $\text{CDCl}_3$  a good solvent for ir spectroscopy? Explain your answer. Would  $\text{CCl}_4$  have any advantages over either chloroform as an ir solvent? Explain your answer.

*$\text{CHCl}_3$  is not useful if C-H bonds are being studied and  $\text{CDCl}_3$  would have limitations if triple bonds are being studied.  $\text{CCl}_4$  would only interfere at lower and generally less important frequencies for functional group identifications but it is considerably more hazardous.*

### Group Frequencies (An Internet Exercise)

1. The odor additive in natural gas is usually a mercaptan such as methy, ethyl or *t*-butyl mercaptan.
2. What compounds are responsible for the essence of skunk?  
from: <http://chemeducator.org/sbibs/s0004002/spapers/420044ww.htm>

Table 1. Composition of the Major Volatile Components (>1%) in Anal Sac Secretion from Three Species of North American Skunks (ND = None Detected)

Compound	Striped Skunk <sup>a</sup>	Spotted Skunk <sup>b</sup>	Hog nosed Skunk <sup>c</sup>
( <i>E</i> )-2-butene-1-thiol	38–40%	30–36%	71%
3-methyl-1-butanethiol	18–26%	48–66%	ND
<i>S</i> -( <i>E</i> )-2-butenyl thioacetate	12–18%	ND	17%
<i>S</i> -3-methylbutanyl thioacetate	2–3%	ND	ND
2-phenylethanethiol	trace	2–5%	ND
2-methylquinoline	4–11%	trace	2%
2-quinolinemethanethiol	4–12%	trace	0.5%
<i>S</i> -2-quinolinemethyl thioacetate	1–4%	ND	ND

<sup>a</sup>Range of data from 4 striped skunks. <sup>b</sup>Range of data from 2 spotted skunks. <sup>c</sup>Determined from a single hog-nosed skunk.

3. Consider the names of many common explosives (TNT, nitroglycerine, ammonium nitrate). What characteristics are desirable for explosives? *The desired properties are significant amounts of nitrogen. This often leads to a highly exothermic reaction that yields many moles of gas per mole of explosive.*
4. *thiols (S-H) 2600 - 2550 cm<sup>-1</sup>  
nitro - 1550 cm<sup>-1</sup>, 1372 cm<sup>-1</sup>, conjugation lowers about 25 - 30 cm<sup>-1</sup>*

## Exercise 5 - UNKNOWNNS

- A. Searching for Unknowns. Use one or more of the sites (this part of the exercise was originally designed for use with the *Organic Chemistry Data Base*) listed under *Unknowns* on page 10 to find the best matches to the information provided in each question below. For the three cases where there are multiple possibilities, suggest a method for distinguishing among them.

#	melting pt. (°C)	boiling pt. (°C)	refractive index	infrared analysis <sup>1</sup>	possible compounds and distinguishing method
1		115	1.4100	OH CH <sub>3</sub>	<i>3-methyl-2-butanol, 3-pentanol, 2-pentanol, nmr</i>
2	122			arom., OH C=O	<i>benzoic acid</i>
3		154	1.5160	arom., CH <sub>3</sub>	<i>anisole, allylbenzene, ir or nmr</i>
4		202	1.5325	arom., C=O CH <sub>3</sub>	<i>acetophenone</i>
5	81			arom., CH <sub>3</sub>	<i>1,2,4,5-tetramethylbenzene</i>
6		78	1.3720	C=O, CH <sub>3</sub>	<i>methyl propionate, ethyl acetate, nmr</i>
7	114			arom., C=O NH, CH <sub>3</sub>	<i>acetanilide</i>
8		134	1.4585	NH, sp <sup>3</sup> C-H	<i>cyclohexylamine</i>

- B. Collections of Spectra on the Internet.

1.	Possible Compounds	Absorptions (cm <sup>-1</sup> )	Assignments	Key Compound
<u>Formula</u> C <sub>2</sub> H <sub>4</sub> O <sub>2</sub> U = 1 (= π bonds + rings)	acetic acid ethyl formate	2960 1735 1208, 1160	sp <sup>3</sup> C - H stretch C=O stretch C-O stretch	methyl formate

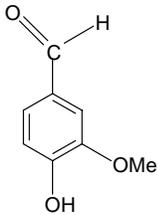
The ir spectra of acetic acid and methyl formate have at least one predictable difference. The data given do not show O - H stretch and this observation rules out acetic acid. The data are consistent with the spectrum of methyl formate given at the NIMC site.

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<sup>1</sup>The information represents the results of the interpretation of the infrared spectrum of the compound. Definitive evidence for the presence of carbon - oxygen single bonds is difficult to obtain from the ir and has not been included.

<u>Formula</u>	<u>Possible Compounds</u>	<u>Key Absorptions (cm<sup>-1</sup>)</u>	<u>Assignments</u>	<u>Compound</u>
<b>C<sub>5</sub>H<sub>8</sub></b> U = 2	<i>trans-1,3-pentadiene</i> <i>2-pentyne</i> <i>1-pentyne</i> <i>isoptene</i>	3307 2968, 2938 2120	<i>sp C-H</i> <i>sp<sup>3</sup> C-H</i> C≡C	<i>1-pentyne</i>
<b>C<sub>3</sub>H<sub>6</sub>O</b> U = 1	<i>acetone</i> <i>propanal</i> <i>2-propen-1-ol</i> <i>methyl vinyl ether</i>	no absorptions 2700 - 2900 cm <sup>-1</sup> 1715 1363	not an aldehyde C=O CH <sub>3</sub>	<i>acetone</i>
<b>C<sub>3</sub>H<sub>6</sub>O</b>	same as above	3600 - 3200 3081, 3012 2861 1645	O-H <i>sp<sup>2</sup> C-H</i> <i>sp<sup>3</sup> C-H</i> C=C	<i>2-propen-1-ol</i>
<b>C<sub>6</sub>H<sub>7</sub>N</b> U = 4	<i>aniline</i> <i>2-methylpyridine</i> <i>3-methylpyridine</i> <i>4-methylpyridine</i>	3429, 3354 3037 1929, 1839, 1706 1621, 1601	N-H <i>sp<sup>2</sup> C-H</i> <i>aromatic</i> C=C	<i>aniline</i>

2. For the compound, vanillin, perform a search for its ir spectrum. After obtaining the ir spectrum, record the energy in wave-numbers of key functional group absorptions and make assignments for the absorptions.

<u>Formula</u>	<u>Systematic Name</u>	<u>Key Absorptions (cm<sup>-1</sup>)</u>	<u>Assignments</u>	<u>Structure</u>
C <sub>8</sub> H <sub>8</sub> O <sub>3</sub>	<i>4-hydroxy-3-methoxy benzaldehyde</i>	3639 3075, 3015 2819, 2796, 2724 1698 1600, 1509 1268	O-H <i>sp<sup>2</sup> C-H</i> CO-H C=O <i>aromatic C=C</i> C-O	

- 3.

Compound	Mass	Fragment	Fragment Lost	Relative Intensity <sup>3</sup>	$\frac{P+1}{0.011P}$ <sup>(2)</sup>
propane	45	P + 1		0.88	2.9
	44	parent peak (P) or molecular ion		27.8	
	29	ethyl carbocation	methyl radical		
	15	methyl carbocation	ethyl radical		

<sup>2</sup>P+1 and P represent relative intensities of these two peaks

<sup>3</sup>Only needed for P+1 and P peaks

Compound	Mass	Fragment	Fragment Lost	Relative Intensity <sup>5</sup>	$\frac{P+1}{P}$ <sup>(4)</sup>
pentane	73	P + 1		0.69	5.0
	72	parent peak (P)		12.5	
	57	butyl	methyl		
	43	propyl	ethyl		
	29	ethyl	propyl		
acetone	59	P + 1		0.92	3.4
	58	parent peak (P)		24.8	
	43	acetyl	methyl		
	15	methyl	acetyl		

Compound	Mass	Fragment	Fragment Lost	Relative Intensity <sup>6</sup>
chloroethane	66	P + 2		32.3
	64	parent peak (P)		100
	37	<sup>37</sup> Cl <sup>+</sup>	ethyl	
	35	<sup>35</sup> Cl <sup>+</sup>	ethyl	
	29	ethyl	Cl	
	28	ethenyl	HCL	
bromobenzene	158	P + 2		64
	156	parent peak (P)		66
	81	<sup>81</sup> Br <sup>+</sup>	phenyl	
	79	<sup>79</sup> Br <sup>+</sup>	phenyl	
	77	phenyl	Br	
	51	C <sub>4</sub> H <sub>3</sub> <sup>+</sup>		

4. For pentane, the value is right on (5) but for acetone it is rather high (3.4 compared to 3.0). There are minor contributions from the oxygen and the hydrogens but they do not account for the error.
5. 75.78% chlorine-35 and 24.22% chlorine 37. Bromine 50.69% bromine-79 and 49.31% bromine-81. From the mass spectra, the results come out 75.6% and 24.4%. For bromine, 50.8%, 49.2%. These values agree better than expected for the significant figures obtainable from the NIST spectra.
6.
  - a. Is it possible to detect the presence of chlorine or bromine with confidence from either an ir or nmr spectrum? Explain your answer. *Ir group frequencies for Cl and Br are in a difficult to reach section of the ir and are not reliable. Chemical shifts caused by Br and Cl fall into the same field strength ranges as other chemical shifts. Mass spectra are much more reliable for these two elements.*
  - b. Describe how you could rather easily detect the presence of chlorine or bromine from a mass spectrum. *Inspection of the (P+2)/P ratio.*

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<sup>4</sup>P+1 and P represent relative intensities of these two peaks

<sup>5</sup>Only needed for P+1 and P peaks

<sup>6</sup>Only needed for P+2 and P peaks for this compound

7. Use the NIMC site and bring up nmr spectra of the compounds ethyl acetate, methyl acetate, methyl propionate (note that it doesn't seem to recognize methyl propanoate) and 2-butanone.
- Describe how you could distinguish among these four compounds using nmr.  
*All but methyl acetate yield a quartet, triplet and a singlet. The latter gives two singlets. The others can be distinguished on the basis of chemical shifts (ethyl acetate - low field quarted, methyl propionate - low field single, 2-butanone- no low field signals).*
  - Would it be possible to distinguish among these four compounds using ir? Explain your answer.  
*The three esters would have carbonyl frequencies at about  $1740\text{ cm}^{-1}$  and the ketone around  $1710\text{ cm}^{-1}$ . Additionally, the C-O band of the esters might be detectable. The esters could only be distinguished by comparison to actual spectra.*
8. Use the formula at the NIMC site to search for compounds with the formula  $\text{C}_9\text{H}_{12}$ .
- How many compounds come up as hits? 16
  - Of these, how many have Hnmr's in the collection? 11
  - Of the compounds with Hnmr's, how many are aromatic? 9
  - Click on cumene. Use lines to draw an Hnmr spectrum of cumene.
  - Is the Hnmr of cumene consistent with its structure? Explain your answer.  
*The septet expected for cumene should have lines with relative magnitudes 1, 6, 15, 20, 15, 6, 1. Because the first and last peaks have very low magnitudes, they will probably not be observed unless the signals are amplified.*
- C.
- 1-chloropropane, 2-chloropropane, 2-bromopropane, 2-propanol  
*2-propanol can be distinguished by ir (O-H stretch). 1-chloropropane and 2-propanol can be distinguished from each other and the other two using Hnmr. 2-chloropropane and 2-bromopropane can be distinguished using mass spectrometry.*
  - ethanol, diethyl ether, ethyl propanoate, aminoethane, acetic acid, acetamide  
*It should be possible to distinguish among all of them using functional group analysis (OH, -, high C=O, NH, N-H + C=O), in the ir or by studying chemical shifts and splitting patterns in the nmr.*
  - acetone, methyl acetate, dimethyl ether, p-xylene, cyclohexane  
*It should be possible to distinguish among all of them using functional group analysis in the ir (low C=O, high C=O, C-O + CH<sub>3</sub>, C=C + arom., -) or by studying chemical shifts and splitting patterns in the nmr.*
  - 1-pentene, 2-pentene, 3-pentene, 1-pentyne, 2-pentyne, 3-pentyne  
*The first two alkenes can be distinguished from the first two alkynes using ir (double vs triple bond). 3-pentene and 3-pentyne are problems because the multiple bonds are symmetrically substituted and these bonds will be inactive in ir although the absence of a multiple bond will indicate that the compound is one of these two. 1-pentyne and 2-pentyne can be distinguished in the ir by looking for an sp C-H stretch. Chemical shifts, splitting patterns and integration in the nmr could probably distinguish all the compounds especially if ir is first used to divide the possibilities into subgroups.*
  - pentanal, 2-pentanone, 1-pentanol, pentanoic acid  
*It should be possible to distinguish among all of them using functional group analysis in the ir (CO-H + C=O, C=O, O-H, C=O + O-H).*
  - o-xylene, m-xylene, p-xylene, ethylbenzene, cumene, ethoxybenzene  
*While it should be possible to distinguish some of these using aromatic overtones or methyl bending absorptions in the ir, none of these can be used with high confidence. Hnmr can identify the last three but will have difficulty with the distinguishing the first three. For these cases it might be necessary to compare ir on mass spectra to authentic spectra to make the id.*
  - benzyl alcohol, p-methylphenol, benzylamine, p-toluic acid  
*Ir (O-H, lower O-H, N-H, O-H + C=O) and nmr could probably distinguish among all of these.*
  - ethylbenzoate, diethylphthalate, 2-ethylnaphthoate, N,N-diethylbenzamide  
*Chemical shifts, splitting patterns and integration in the nmr could probably distinguish all the compounds although mass spectra might be needed to confidently distinguish diethylphthalate and N,N-diethylbenzamide.*