

## 8 QSAR

### Exercise 1 Predicting the Rate Constant of HFC's with Atmospheric OH•.

Open Excel. (If necessary, click Tools / Add-Ins... and choose Analysis ToolPak, ChemDraw for Excel, ChemSAR for Excel, and CombiChem for Excel and click OK.)

Click New ChemOffice Worksheet (1<sup>st</sup> icon). The title changes to ChemDraw for Excel–Book 1 and the ChemSAR tool bars are no longer grayed out.

Enter the 21 molecules listed in the table as ChemDraw .cdx files.

Click in Cell A1 and enter “Molecule”.

Click in Cell A2 and click Load Molecule (5<sup>th</sup> icon).

Locate and open the folder “HFC structures”.

Click on the cf3cf2ch2f.cdx file and click Open.

The name of the file and the structure appear in the cell.

Repeat for the remaining 20 molecules in Cells A3-A22.

Similarly, enter the structures for the two “unknown” molecules, cf3chfchfch2cf3 and ch2fchf2 in Cells A23 and A24.

Save as hfc.xls.

Enter the known experimental rate constants given in the table in Cells B2-B22. Label the column by clicking in Cell B1 and entering “rate const”.

Evaluate the log of the rate constants in Cells C2-C22 by entering “=LOG(B2)” in Cell C2, etc. Label the column by clicking in Cell C1 and entering “log k”.

Save.

Click Options... (7<sup>th</sup> icon) and click Defaults. Click OK.

Set up structural parameters to be studied in Columns D, E, and F.

Select Cells A2-A24 by clicking and dragging.

Click Select Descriptors... (1<sup>st</sup> icon) and click Defaults.

Choose Heat of Formation (HF) / Add. Click OK. A series of entries of #N/A may appear in Cells D2-D24 as calculations are carried out and it may be necessary to respond to an “error message” involving invalid text for each calculation. The values will appear in the cells. Enter “heat form” in Cell D1.

Save.

Likewise after selecting Cells A2-A24, click Select Descriptors..., Remove Heat of Formation (HF) and add HOMO Energy (Homo). Click OK. Entries of #N/A in cells E2-E24 will be replaced by numerical values. Enter “HOMO ener” in Cell E1.

Save.

Enter “H count” in cell F1 and in Cells F2-F24, enter the number of H atoms in each molecule.

Save.

(Additional structural parameters could be chosen and placed in additional

columns.)

Perform a correlation study of the log k values with the structural parameters.

Select Tools / Data Analysis... / Correlation and click OK.

Enter C2:F22 as the Input Range, B30 as the Output Range and click OK.

Which structural parameter(s) is(are) important based on the entries in the column labeled "Column 1"? \_\_\_\_\_

Save.

Evaluate the structural property equation. (We will use all three parameters, but you may choose to use only the most significant or additional parameters.)

Click in Cell A40 and enter "Analysis".

Select Tools / Data Analysis... / Regression and click OK.

Enter C2:C22 for the Input Y Range, D2:F22 for the Input X Range, and B40 for the Output Range and click OK.

Save.

Predict the logarithm of the rate constant for the "unknown" structures.

Enter "Pred cf3chfchf2cf3" in Cell A26 and

"=C56+C57\*D23+C58\*E23+C59\*F23" in Cell C 26.

List the predicted value for cf3chfchf2cf3 \_\_\_\_\_ (literature is 0.591).

Likewise enter "Pred ch2fchf2" in Cell A27 and

"=C56+C57\*D24+C58\*E24+C59\*F24" in Cell C 27.

List the predicted value for ch2fchf2 \_\_\_\_\_ (literature is 1.255).

Save.

Close and save.

Chemical Sample	Rate Constant		
		ch3cf3	1.3
cf3cf2ch2f	6.31	ch3ch2f	230
cf3ch2cf3	0.44	ch3chf2	36
cf3ch2och3	620	ch3f	17
cf3ch2ochf2	13	ch3ocf3	21
cf3chfchf3	1.6	chf2cf2cf2chcf2	4.2
cf3cho	550	chf2cf3	1.9
ch2f2	11	chf2chf2	5.7
ch2fcf3	4.9	chf2ocf3	3.4
ch2fch2f	110	chf2ochf2	25
ch2fochcf3cf3	73	chf3	0.24

**Exercise 2 Predicting  $pK_a$  for  $p$ -C<sub>2</sub>H<sub>5</sub>-benzoic Acid.**

Use the following organic acid information to determine  $pK_a$  for  $p$ -C<sub>2</sub>H<sub>5</sub>-benzoic acid. There are several structural properties that you might want to consider. List the predicted value \_\_\_\_\_ (literature value is 4.35).

Acid	$pK_a$		
benzoic	4.20	<i>p</i> -F-benzoic	4.14
<i>p</i> -Br-benzoic	3.97	<i>p</i> -NH <sub>2</sub> -benzoic	4.92
<i>p</i> -CH <sub>3</sub> O-benzoic	4.47	<i>p</i> -nitrobenzoic	3.42
<i>p</i> -Cl-benzoic	3.98	<i>p</i> -OH-benzoic	4.48