

## 8 QSAR

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

Open Project Leader.

Enter the PM3-optimized structures for the HFC molecules.

Double click in Cell A1 to open the file list to import.

Locate and open the folder "HFC structures".

Click on the cf3cf2ch2f.csf file and Shift / Click on the chf3.csf file to select all 21 HFC structures.

Click Open to insert.

Save as HFC.plp.

Enter the known experimental rate constants given in the table at the end of the exercise.

Double click the Column B header.

Choose Property of chemical sample / Next.

Scroll to experimental reaction rate / Next.

Select Manual entry / OK.

Double click Cell B1 and enter data. Be sure the respective values are used.

Move downward using the downward arrow key and repeat entering data until all values are filled in.

Save.

Evaluate the log of the rate constant.

Double click the Column C header.

Choose Analysis / Next.

Choose Algebraic Equation / Next.

Enter  $=\log_{10}(B)$  / OK.

Click the letter C above the Column C header.

Select Evaluate / Cell from the menu bar.

Save.

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

Double click the Column E header.

Choose Property of chemical sample / Next.

Scroll to heat of formation / Next.

Scroll to Hf at PM3 geometry / OK.

Double click the Column F header.

Choose Property of chemical sample / Next.

Scroll to HOMO energy / Next.

Scroll to HOMO E at PM3 geometry / OK.

Double click the Column G header.

Choose Property of chemical sample / Next.

Scroll to dipole moment / Next.

Scroll to dipole moment at PM3 geometry / OK.

Double click the Column H header.

Choose Property of chemical sample / Next.

Scroll to atom count / Next.

Scroll to hydrogen / OK.

Save.

Evaluate structural parameters in Columns E, F, G, and H.

Shift / Click letters E through H above the Column headers.

Choose Evaluate / Cell.

Save.

Set up and evaluate the correlations.

Double click the Column J header.

Choose Analysis / Next.

Choose Multiple Linear Regression / Next.

Select Predict C in left window and Using E in the right window / OK.

Click letter J above the Column header.

Select Evaluate / Cell. You may need to move the row separators to read the complete analysis of equation,  $rCV^2$ , and  $r^2$ . A small  $a$  indicator implies the prediction power is small ( $rCV^2$ ).

Repeat for Columns F, G, and H in K, L, and M, respectively.

Save.

Which structural parameter(s) is(are) important? \_\_\_\_\_

Evaluate the structural property equation.

Double click the Column O header.

Choose Analysis / Next.

Choose Multiple Linear Regression / Next.

Select Predict C in the left window and Using the appropriate letter(s) in the right window / OK.

Click letter O above the Column header.

Select Evaluate / Cell.

Save.

Is the correlation better than the separate columns? \_\_\_\_\_

Predict the rate constant for the "unknown" structures.

Enter the two "unknown" structures in Cells A23 and A24.

Highlight Cells E23 through H24 and choose Evaluate / Cells.

Highlight Cells O23 and O24 and choose Evaluate / Cells.

Save.

List the predicted values for cf3chfchf2cf3 \_\_\_\_\_ (literature is 0.591) and for ch2fchf2 \_\_\_\_\_ (literature is 1.255).

Prepare a graph of the results

Shift / click letters C and O above the Column headers.

Choose View / Scatter Plot from the menu bar.

Choose C in the left window and O in the right window / OK.

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
cf3chf3	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 optimized structures in the file “org acids” to determine  $pK_a$  for  $p$ -C<sub>2</sub>H<sub>5</sub>-benzoic acid. The values of similar organic acids are given in the table at the end of the exercise.

You might consider  $\Delta_r H$ , dipole moment, ionization potential, and partial charge on the carboxylic H. (For atomic partial charge, choose Property of Atom and two columns will appear. Use the atom ID listed in the table.)

List the predicted value \_\_\_\_\_ (literature value is 4.35).

Acid	$pK_a$	H ID			
benzoic	4.20	15	$p$ -F-benzoic	4.14	15
$p$ -Br-benzoic	3.97	15	$p$ -NH <sub>2</sub> -benzoic	4.92	15
$p$ -CH <sub>3</sub> O-benzoic	4.47	16	$p$ -nitrobenzoic	3.42	17
$p$ -Cl-benzoic	3.98	15	$p$ -OH-benzoic	4.48	15