Chemistry 4021/8021 **Computational Chemistry** 3/4 Credits

Spring Semester 2014

(Key)

1. What is your best estimate of the 298.15 K gas-phase heat of formation for *O*-methyl formaldoxime? To answer this question, do at least AM1 and PM6 calculations and some other quantum chemical model beyond semiempirical molecular orbital theory. Explain your reasoning in coming up with your best estimate. Incidentally, you may be interested to know that the equivalent heat of formation for acetaldoxime is known.

The compound *O*-methyl formaldoxime is $H_2C{=}NOCH_3$. The AM1 and PM6 levels of theory are designed to compute heats of formation directly (as the result of the SCF calculation) and the predicted heats of formation are 7.7 kcal/mol (AM1) and 4.4 kcal/mol (PM6). How accurate are these? Hard to know, although we could invoke the average error over a large number of HCNO compounds that is known for both models.

An alternative approach is to use an isodesmic reaction. Given the knowledge that the heat of formation is known for acetaldoxime (which is $CH_3CH{=}NOH$), I chose to use the reaction

$$CH_3OCH_3 + CH_3CH{=}NOH \rightarrow CH_3CH_2OH + H_2C{=}NOCH_3$$

Notice how on both sides of my equation, the total number of C–C, C–O, C=N, C–H, and O–H bonds stay the same? That should lead to cancellation in errors if I then compute the heat of formation for $H_2C{=}NOCH_3$ as the heat of *reaction* (taken from theory) minus the heat of formation of CH_3CH_2OH plus the heats of formation of CH_3OCH_3 and $CH_3CH{=}NOH$ (taken from experiment). The 298.15 K experimental heats of formation for dimethyl ether, ethanol, and acetaldoxime are –43.99, –56.0, and –5.39 kcal/mol, respectively.

I decided to do this using my AM1 and PM6 heats of formation, as well as 298.15 K enthalpies computed at the G3 and W1 levels of theory (two composite levels developed specifically for thermochemistry, the latter more accurate (and quite a bit more expensive) than the former).

Table 1. 298.15 K Enthalpies (E_h) from various levels of theory.

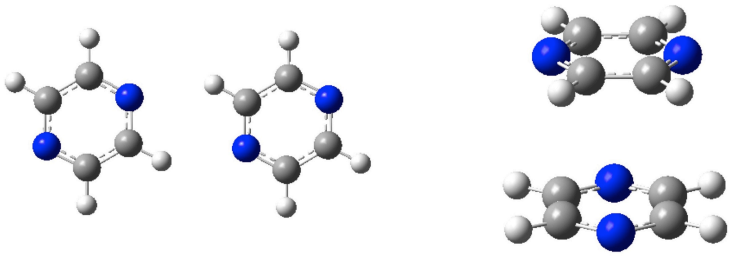
	MeOMe	EtOH	acetaldoxime	H2CNOMe
AM1	−0.084 87	−0.099 96	−0.012 76	0.012 32
PM6	−0.072 85	−0.087 33	−0.010 89	0.007 03
G3	−154.880 57	−154.899 44	−208.977 56	−208.956 80
W1U	−155.006 92	−155.026 62	−209.152 53	−209.130 37

When I use my above isodesmic protocol with the numbers in Table 1, I predict 298.15 K heats of formation for *O*-methyl formaldoxime of 12.9, 8.8, 7.8, and 8.2 kcal/mol at the AM1, PM6, G3, and W1U levels respectively.

The good agreement between G3 and W1U provides considerable confidence in these two values, the latter of which is likely to be more accurate. PM6 is remarkably good, given that it is *vastly* cheaper to compute. The AM1 isodesmic model, amusingly, is worse than the raw AM1 prediction, which is itself almost quantitatively accurate. This is a complete coincidence, of course, and if one had relied on the raw AM1 prediction one would simply have been lucky!

2. Let us revisit the pyrazine dimer from problem set 1. Using the pi-stacked geometry that was common to all 3 force fields in Problem Set 1 as a starting guess, minimize the geometry using B3LYP with the def2-svp basis set. Now, do single point energy calculations at the HF, MP2, M06-2X, and B3LYP + D3BJ (Grimme dispersion correction) levels of theory with the same basis set. How do the interaction energies from these 5 levels of theory compare for this geometry? Now, repeat the geometry optimization at the B3LYP + D3BJ/def2-svp level, and repeat the single-point calculations (substituting B3LYP without dispersion for the fifth calculation). Again, how do the interaction energies compare, and how do they vary compared to the other geometry? At the MP2 level, how does the interaction energy for the second geometry change if you switch the basis set from def2-svp to def2-tzvp? What about at the M06-2X level? How might you rationalize any trends as a function of basis set?

Using the pi-stacked geometry as an initial guess, the two optimized geometries are shown below. Without an explicit correction for dispersion, the B3LYP functional optimizes to a planar structure with two favorable C-H—N interactions. When the Grimme dispersion correction is applied, the geometry converges within 5 iterations to a similar pi-stacked geometry that was found with the force fields.



B3LYP **B3LYP + D3BJ**

The interaction energies that were calculated at both geometries with the def2-svp basis set are given below in Table 2. The interaction energy is defined as

$$E_{int} = E_{dimer} - E_{monomerA} - E_{monomerB}$$

where the energy of the dimer corresponds to the figures above, and the monomer energies are the single pyrazine molecules isolated. It can be seen in Table 2 that the results are more comparable among the 5 levels of theory for the planar geometry than for the pi-stacked geometry. For the B3LYP geometry, all levels of theory predict a favorable (negative) interaction energy, where for the B3LYP + D3BJ geometry, HF and B3LYP predict unfavorable (positive) interaction energies. This can be rationalized in that HF and B3LYP do not account for dispersion, so the favorable interactions that result from dispersion in this geometry are not accounted for.

Table. Interaction energies (in kcal/mol) computed at two geometries with 5 levels of theory using the def2-svp basis set.

	Geometry	
Level of Theory	**B3LYP**	**B3LYP + D3BJ**
HF	-3.10	+2.12
MP2	-6.33	-5.43
B3LYP	-4.50	+0.94
B3LYP + D3BJ	-6.65	-4.96
M06-2X	-5.47	-3.97

Upon increasing the basis set to def2-tzvp for the B3LYP + D3BJ geometry, the MP2 interaction energy becomes slightly more favorable, going from -5.43 kcal/mol to -5.97 kcal/mol. However, the M06-2X interaction energy becomes less favorable, going from -3.97 kcal/mol to -2.79 kcal/mol. In the case of MP2, this trend has been observed before[1] even when extrapolated to the complete basis set limit.

To rationalize why we see such changes as a function of basis set, let us first think about the variational principle. The variational principle holds for *ab initio* calculations, so the

[1] Theor Chem Acc (2012) 131:1120

process of seeking the lowest energy solutions will approach the exact energy. However, in the calculation of interaction energies, the variational principle doesn't provide us with this kind of assurance. Referring to the definition of the interaction energy above, we may do a better job in describing E_{dimer} or $E_{monomer}$ upon increasing the size of the basis set, but we have no assurance that the difference E_{int} will increase or decrease.

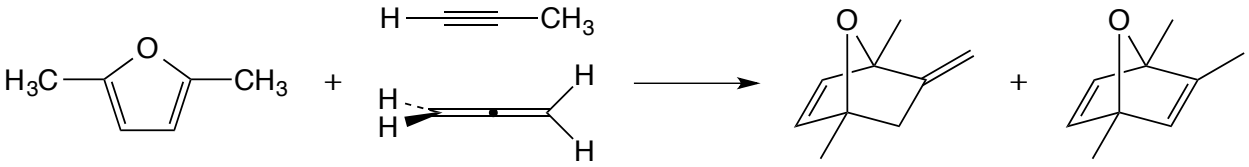
In addition to this, one may be curious to think about the description of the dimer (in the basis of the dimer) vs. the description of each monomer (in the basis of each monomer). With the def2-svp basis set, the dimer is described with 208 basis functions while each monomer is described with 104 basis functions. With the def2-tzvp basis set, the dimer is described with 420 basis functions while each monomer is described with 210 basis functions. This introduces an error known as basis set superposition error (BSSE), which has been described by some as 'the subject of more boring papers than any other topic in quantum chemistry'.[2] Since more functions are used in the calculation of the dimer, we can assume that we introduce errors since we are not using the same basis for the calculation of the monomers. A common way to correct for this error is called the counterpoise (CP) correction, where the energies of the monomers are computed in the basis of the dimer.

3. For the following problem, carry out all calculations at the M06-2X level of density functional theory (gas phase, for now). Use the 6-31G(d) basis set for all non-metal atoms; use the SDD basis set for gold.

Let's set the stage. You have an extremely unlucky synthetic organic colleague. She is cursed with glassware that seems always to have an acidic surface. Thus, whether she uses a tank of pure propyne, or a tank of pure allene, she always ends up with an equilibrated mixture of the two when she wants to use one in a reaction. At 298.15 K, what is the ratio of the two that she would find in her reaction flasks after equilibration?

The free energies predicted for propyne and allene at the M06-2X/6-31G(d) levels of theory are –116.558 41 and –116.559 95 E_h, respectively. That makes the latter more stable than the former by 0.97 kcal/mol. At 298.15 K that's a ratio of 16:84 propyne:allene.

Now, it turns out that she wants to make compound **B**, and *not* compound **A**, and they're a pain to separate if they are present as a mixture.



[2] A. J. Stone. The Theory of Intermolecular Forces. Clarendon Press: Oxford (1996).

A **B**

She's pretty certain that the free energy of activation for the acid-catalyzed process that is interconverting allene and propyne on the flask walls is about 10 kcal/mol. So, here are some questions for you to answer — do *not* include any acid catalysis in your analyses of the Diels-Alder cycloadditions:

a) Is it possible to obtain a single isomer (**A** or **B**) from the illustrated reaction of the allene/propyne mixture with 1,4-dimethylfuran? Explain your answer through invocation of the Curtin-Hammett principle.

The Curtin-Hammett principle says that the ratio of products for two competing irreversible reactions that occur in a single microscopic step from two different isomers that are in equilibrium with one another will be dictated *only* by the differential free energies of activation for the irreversible reactions *if* the free energy of activation for the interconversion of the two isomers is substantially lower than that of the irreversible reactions. So long as the Diels-Alder (DA) reactions have activation free energies well in excess of 10 kcal/mol, the Curtin-Hammett principle should hold. Computation indicates that that is the case.

b) What 298.15 K ratio of products will your colleague actually obtain? Will she be happy?

The free energies predicted for the DA transition-state (TS) structures involving propyne and allene at the M06-2X/6-31G(d) levels of theory are –424.924 28 and –424.931 10 E_h, respectively. That makes the free energy of activation for the latter (computed as the TS free energy minus the sum of the reactants' free energies, including furan at –308.429 10) more stable than the former by 3.3 kcal/mol. At 298.15 K that's a ratio of 0.4:99.6 **B**:**A**. A disaster for your colleague.

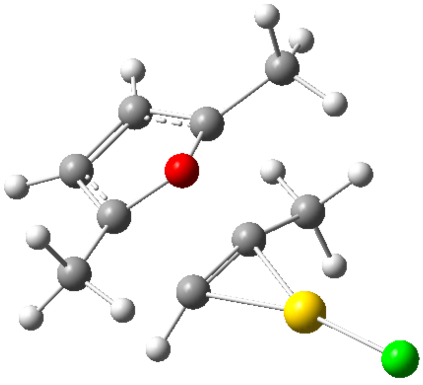
c) Your colleague asks you whether you think running the reaction in the presence of AuCl will be helpful. A great skill to a theoretician is being able to rationalize *any* result. Offer a rationale for why AuCl might lead to *more* product **B** and then another rationale for why it might lead to *less*.

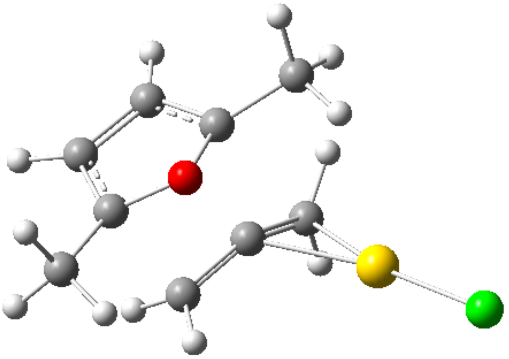
A quick survey of the literature will tell you that gold *loves* to coordinate to triple bonds, but not so much to double bonds. On the one hand, that might be bad, since it will stabilize propyne, with a full triple bond, more than the DA TS structure, which has a reduced bond order owing to new sigma bond making. On the other hand, at least there *is* some remaining pi bond order with propyne, while there will be none for coordination to allene, so perhaps AuCl will stabilize the TS structure for propyne over

allene by more than it will stabilize reactant propyne over reactant allene. Just have to do the calculation to find out.

d) Now, compute the effect of added AuCl on the reaction and the product distribution. Will your colleague's mood improve?

The free energies predicted for the DA transition-state (TS) structures involving propyne and allene at the M06-2X/6-31G(d) levels of theory, coordinating AuCl, are ever so slightly tricky. For propyne, there is no question that AuCl coordinates the triple bond. But for allene, there are two *different* TS structures, one involving AuCl coordinating the double bond that is reacting, and one involving AuCl coordinating the double bond that is *not* reacting. The latter is lower in energy than the former. Both TS structures are show below. Meanwhile, the reactant free energies must also be computed with AuCl coordination, and they are –712.413 41 and–712.412 67 E_h, respectively, for propyne and allene (so notice that AuCl does indeed coordinate more strongly to propyne, as the complex with propyne is lower in free energy than the complex with allene, even though for the bare hydrocarbons the stability was opposite). The TS free energies (for the structures shown below) are –1020.788 33 and –1020.789 25 E_h, respectively, leading to free energies of activation of 34.0 and 31.8, respectively. That makes the latter more stable than the former by 2.2 kcal/mol. At 298.15 K that's a ratio of 2.4:97.6 **B**:**A**. Not exactly a major win for gold.





e) If AuCl is not the perfect solution to the problem of making **B**, based on what you've learned thus far, what *might* you suggest as an alternative reagent to your colleague? You don't have to do calculations to bolster your suggestion (although you're welcome to), but do explain your reasoning.

Well, this is a hard one. You might imagine that, since AuCl *did* improve things, perhaps using a less coordinating counter-ion might improve things even more (e.g., gold triflate or something). You could test this by doing the calculation with Au^+, which is certainly the limit as it involves no counter-ion at all. You would find, if you did the calculation, that that would be no help at all, however. An alternative would be a gold species with a large ligand that would favor the reduced steric congestion in the propyne TS structure compared to the allene. However, AuCl only reduces the activation free energy compared to the bare hydrocarbons by about 5 kcal/mol, so if *too* much steric interaction is introduced, there will be no catalysis. Just a hard problem, darn it.

Mind you, the good organic chemists will probably notice that the adduct **B** is going to be thermodynamically preferred over adduct **A** (more substituted double bond). So, exposing the product mixture to a trace of strong acid or Br_2 is going to equilibrate the mixture to mostly **A** (I've not done the calculation to get the predicted ratio). Maybe that acidic glassware will end up being useful after all…