Analytical Cume April 2006 Crib

NMR Spectroscopy

1. (40 pts) Define the 8 of the following 10 terms. Be Brief!
Most of these terms have numbers associated with them, or a range. Put down a reasonable value or range and the unit associated with that value for full credit (some quantitative hints are given in parentheses).

A. Larmor Frequency: $\omega = \gamma B$ **the frequency of the NMR transition. Common values are 300, 400, 500, 600 800, and 900 MHz.**

B. J coupling: **Thru-bond coupling that gives rise to multiplets in the NMR spectrum. Common values are 4-10 Hz for H-H coupling.**

C. Chemical Shift Anisotropy(CSA): **Orientation-dependent frequency shift of the molecule in the solid state caused by the tensor nature of the chemical shift. Common values are 50-200 ppm for ^{13}C NMR.**

D. Magic Angle Spinning (speed): **A method to reduce CSA by averaging the CSA around an axis of 54.7 degrees w.r.t. the static magnetic field. Common values are 5kH – 35kHz.**

E. Deuterium channel (frequency): **Used to lock the frequency for ^{1}H or ^{13}C NMR using D_2O or another deuterated solvent. Common values are about 9x less that the ^{1}H Larmor frequency.**

F. Probe resonant Q factor: **Determines (in part) the S/N of the probe. Defined as the resonancefrequency over the probe resonance width. $Q = \omega_o/\Delta\omega$. Common values are 100-300.**

G. Solvent suppression (for quantitation, mention dynamic range): **Used to improve the dynamic range by reducing the enormous signal of the solvent. Reduction of the solvent can be as much as 10^5. The dynamic range of the NMR spectrometer is determined by the digitizer. Common values today are 22 bits, or 2^{22}, or about 4,000,000.**

H. Appodization: **Used to improve the S/N by multiplying the FID by a decaying function, such as an exponential function that reduces the noise at the end of the FID. It can also be used to enhance resolution at a cost of some signal distortion. Line widths of 1 Hz are typical for appodization.**

I. T_2 relaxation: **Also known as spin-spin relaxation, this term is largely responsible for the linewidth seen in the NMR spectrum. In liquids, $T_1 = T_2$, but in solids, T_2 is very short compared with T_1. Common values are around 1 s for liquid state NMR.**

K. dipolar coupling: **Thru-space coupling responsible for relaxation, this term is not observed directly in liquid state NMR, however, it is seen in solid-state NMR. Various**

methods to eliminate its broadening effect on spectrum include MAS and dipolar decoupling. Typical values for ^{1}H-^{13}C dipolar coupling are 30 kHz.

2. (10 pts) Give two reasons why larger magnetic fields are preferable. Be quantitative, as in "if the magnetic field strength is doubled the _____ changes by a factor of_____."
S/N and Resolution or chemical shift dispersion. The higher the field, the larger the S/N, which goes up roughly as the square of the field, or B^2 (actually $B^{7/4}$). The dispersion increases linearly with the field and allows one to resolve more peaks in densely crowded spectra.

3. (20 pts) Name 2 different multidimensional NMR experiments and briefly explain how they work and what they measure.

COSY – measures through bond connectivity in molecules via the ^{1}Hs. The COSY experiment consists of only 2 pulses, with an excitation and mixing pulse. The evolution time defined as the time between the two pulses is incremented during the experiment and is called the indirect (or second) dimension of the experiment. A double Fourier transform is performed to convert the time data to frequency information.

HSQC – is a more advanced experiment that measures the proton-carbon correlation for carbons that have directly bonded hydrogen atoms. This experiment incorporates two conversions of magnetization, one from protons to carbon, and the other from carbon back to protons to improve the sensitivity of the experiment. Carbon chemical shift evolution occurs during the middle of the pulse sequence.

4. (10 pts) What are the advantages and disadvantages of the ^{1}H-^{13}C heteronuclear HSQC experiment as compared to ^{1}H or ^{13}C NMR?

As described above, the HSQC has high sensitivity and also give good resolution because of the indirectly detected carbon dimension. The resolution is better than just a 1D proton or 1D carbon. However, it is not sensitive to quaternary carbons. Also, because the method uses the spins on ^{13}C during the experiment, it is less sensitive than just ^{1}H (by about 400 times) but more sensitive that just ^{13}C direct observation.

5. (10 pts) How does a cryoprobe work? (In a cryoprobe, the detection coil operates at 20K to improve the signal to noise).

In a cryoprobe, since the coil and electronics are at 20K, they have less thermal noise, thus increasing the S/N. Although the Q of the probe circuit (see above) is also increased, the probe filling factor is reduced because of the need for a dewar between the room temperature sample and the coil. The S/N gain is about 3-4, which results in a time savings of 9-16.

6. (10 pts) The combination of NMR and multivariate statistical analysis of complex samples such as urine or serum is gaining attention as a possible method for early disease detection.

What properties of the NMR experiment do you think are desirable to this end? What are some undesirable qualities of NMR and what would you do as an analytical chemist to get around these problems?

The characteristics of NMR that make it favorable for this type of analysis include NMR's high resolution and quantitation, its repeatability and limited need for sample preparation. Advanced methods can sometimes be used to improve resolution or sensitivity. NMR's lack of sensitivity can be a problem, so the use of other methods such as MS is desirable. In fact the combination of NMR and MS for the analysis of such complex samples is at the forefront of this field.

1. See page 933, in the textbook "BIOCHEMISTRY" by Voet and Voet ,second edition

2. See page 1126 (Fig. 33-5), in the textbook "BIOCHEMISTRY" by Voet and Voet, second edition

3. See page 1124-1127, in the textbook "BIOCHEMISTRY" by Voet and Voet, second edition

Also, through interactions with DNA, the histones would limit the accessibility of DNA to transcription factors and hence would act as repressors of transcription. This repression is released through chromatin remodeling, which includes acetylation of histones at specific lysine residues.

4 A. See page 1159, in the textbook "BIOCHEMISTRY" by Voet and Voet, second edition.

There are several hundred known nuclear receptors. Examples include: progesterone receptor, androgen receptor, glucocorticoid receptor, vitamin D receptor, etc

4 B. See page 1159, in the textbook "BIOCHEMISTRY" by Voet and Voet, second edition.

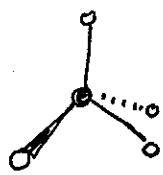
5. There are numerous examples: As an example, look up gene regulation by CREB family of transcription factors (through the cAMP/PKA pathway), and lookup the pathway regulated by cytokines through NF-κB family of transcription factors.

CRIB FOR INORG. CHEMISTRY CUME

April 1, 2006

(i) $TiBr_4$

$$Ti \xrightarrow[N_2]{liq.\ Br_2} TiBr_4 \text{ (can be distilled)}$$



Tetrahedral

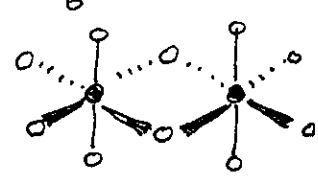
$Ti(\mathrm{IV})$ is d^0; no $d \leftrightarrow d$ transitions but $Br_\pi \rightarrow Ti_d$ electron-transfer transitions occur to give orange-yellow color.

(ii) MCl_5 M can be Nb, Ta, Mo, W or Re

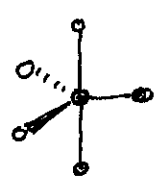
Nb, Ta, Mo & Re prep. by chlorination of the metal pwdr in a heated tube furnace *i.e.* $M + Cl_2$.

WCl_5 is formed by thermolysis of WCl_6 or reduction of this same halide.

Structures in the solid-state are



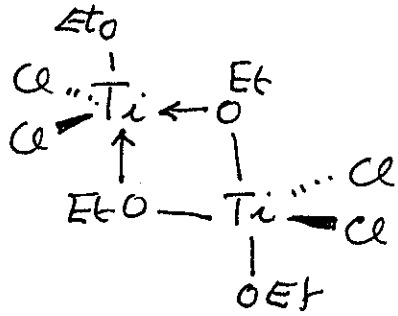
In gas phase



(trigonal bipyramidal)

Nb, Ta are d^0.
Mo, W are d^1 – pairwise interactions form M–M bond.
Re is d^2 – pairwise interactions form Re=Re bond.

(iii) e.g $TiCl_4 + 2EtOH \longrightarrow TiCl_2(OEt)_2$



Ethoxide bridged dimer Ti has approx. trigonal bipyramidal geometry.

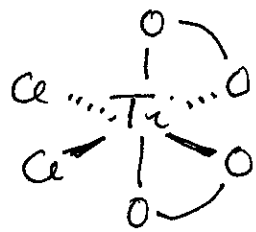
Ti(IV) is d^0; no d↔d transitions and compound is colorless.

(iv) e.g $TiCl_2(acac)_2$

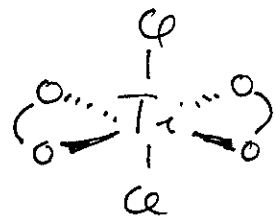
$$TiCl_4 + 2\,Hacac \xrightarrow{\text{toluene}} TiCl_2(acac)_2 + 2\,HCl$$

$TiCl_2(acac)_2$ can have a <u>cis</u> or <u>trans</u> octahedral structure.

<u>cis</u>



<u>trans</u>

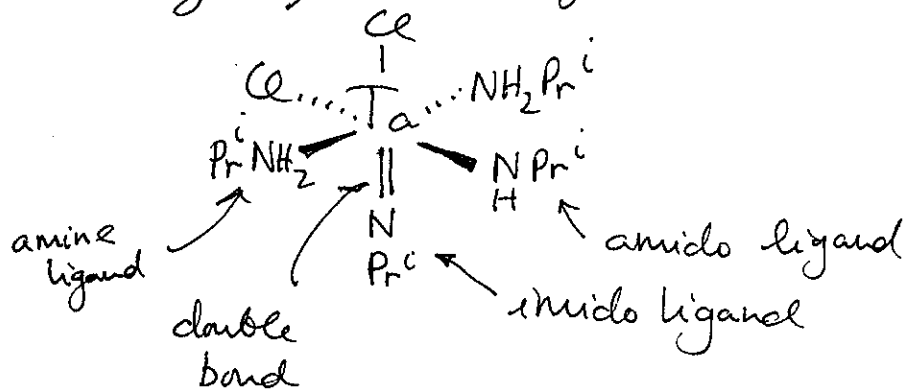


Ti(IV) is d^0; no d↔d transitions and compound is a pale yellow color.

(v) e.g $TaCl_5 + 7\,Pr^iNH_2 \longrightarrow Ta(\underline{\underline{N}}Pr^i)(NHPr^i)(NH_2Pr^i)_2Cl_2 + 3\,Pr^iNH_3^+Cl^-$

This compound can lose a NH_2Pr^i ligand to form

the dimer $[Ta(NPr^i)(NHPr^i)(NH_2Pr^i)Cl]_2$ - dimerization occurs through μ-Cl bridges.



Similar chemistry with Nb in place of Ta and Bu^tNH_2 in place of Pr^iNH_2.

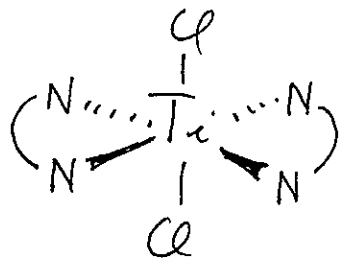
Ta(V) (and Nb(V)) is d^0; no $d \leftrightarrow d$ transitions and compound is colorless.

(vi) e.g <u>trans</u>-$TiCl_2(tmeda)_2$

$$TiCl_4 \text{ (or } TiCl_3) \xrightarrow[THF]{KC_8} TiCl_2(THF)_4$$

strong reducing agent

$$TiCl_2(tmeda)_2 \xleftarrow{tmeda}$$

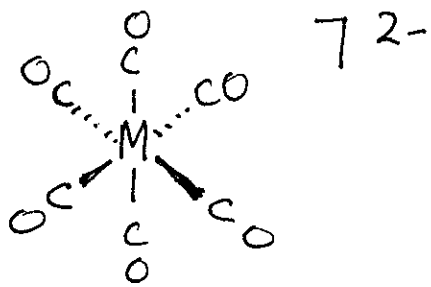


Ti(II) is d^2 so $d \leftrightarrow d$ transitions will occur; three of these are spin-allowed ($^3T_{1g} \rightarrow {}^3T_{2g}$, $^3T_{1g}(F) \rightarrow {}^3T_{1g}(P)$ and $^3T_{1g} \rightarrow {}^3A_{2g}$).

(vii) $[M(CO)_6]^{2-}$ for M = Ti, Zr or Hf

$$MCl_4 \xrightarrow[\text{or cryptand, CO, } -70^\circ C \text{ in THF}]{K^+C_{10}H_8^-\text{, crown ether}} [M(CO)_6]^{2-}$$

$K^+C_{10}H_8^-$ is a strong reducing agent; crown ether or cryptand complexes the K^+ ions.



18-e species; diamagnetic.

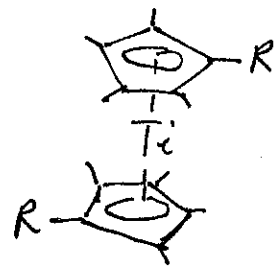
(viii) $M(\eta^5\text{-}C_5R_5)_2$ for M = V, Cr, Fe, Co, Ni.

Also possible with Ti with choice of the right R substituents —

$Ti(\eta^5\text{-}C_5Me_4R)_2$ where R = $SiMe_3$, $SiMe_2Bu^t$ etc.

$$TiCl_3 + Li^+C_5Me_4R^- \xrightarrow[\text{low T}]{THF} (\eta^5\text{-}C_5Me_4R)_2TiCl$$

$$(\eta^5\text{-}C_5Me_4R)_2Ti \xleftarrow{Na/Hg}$$



<u>Note</u>: $(\eta^5\text{-}C_5Me_5)_2Ti$ may have this structure but not yet confirmed by X-ray crystallography.

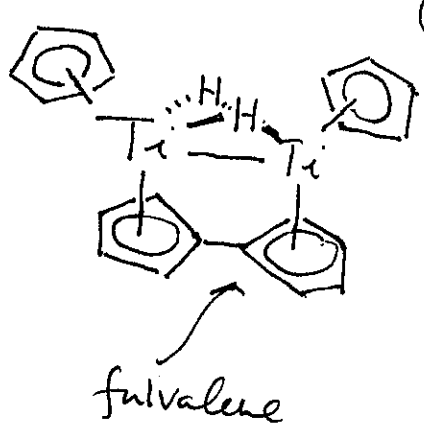
Other compounds that have the ferrocene structure are $(\eta^5\text{-}C_5Me_5)_2Re$, $\underbrace{(\eta^5\text{-}C_5Me_5)_2Ru \text{ and } (\eta^5\text{-}C_5Me_5)_2Os}_{\text{same group as Fe}}$

Ti compound has a 14-e count but still stable; Cp_2^*M triad with Fe, Ru, Os is 18-e.

(ix) Non-ferrocene structures for compounds of composition $(C_5H_5)_2M$ encountered with M = Ti, Zr, Hf, Nb, Ta and Mo:

The best known example is "titanocene".

$$TiCl_4 \xrightarrow[THF]{Na^+C_5H_5^-} (\eta^5\text{-}C_5H_5)_2TiCl_2 \xrightarrow[THF]{\text{reducing agent } Na^+C_{10}H_8^-} (C_{10}H_{10})Ti$$



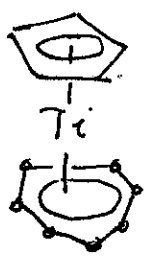
Each Ti is formally Ti(III) and therefore d^1; weak Ti–Ti bond is present.
Ti atoms have 16-e counts (15-e without Ti–Ti bond!)

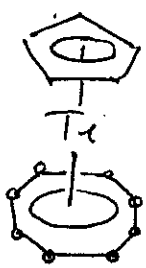
(x) $(\eta^5\text{-}C_5Me_5)Ti(\eta^7\text{-}C_7H_7)$ or $(\eta^5\text{-}C_5Me_5)Ti(\eta^8\text{-}C_8H_8)$

$$(\eta^5\text{-}C_5Me_5)TiCl_3 + C_7H_8 \xrightarrow[THF]{Mg} (\eta^5\text{-}C_5Me_5)Ti(\eta^7\text{-}C_7H_7)$$

cycloheptatriene

Replace cycloheptatriene by cyclooctatetraene to get $(\eta^5\text{-}C_5Me_5)Ti(\eta^8\text{-}C_8H_8)$.





$(\eta^5\text{-}C_5Me_5)Ti(\eta^7\text{-}C_7H_7)$ has a 16-e count (diamagnetic)

$(\eta^5\text{-}C_5Me_5)Ti(\eta^8\text{-}C_8H_8)$ has a 17-e count (paramagnetic)

If one considers formal charge assignments –

$C_5Me_5^{\ominus}$ / $C_7H_7^{\oplus}$ Ti is Ti(0)

$C_5Me_5^{\ominus}$ / $C_8H_8^{2\oplus}$ Ti is Ti(-I)

$C_5Me_5^{\ominus}$ / $C_8H_8^{2-}$ Ti is Ti(III)

} Would give same overall electron count of 17-e

10e ring

6e ring

Crib

Organic Cumulative Examination 4-1-06

(1)

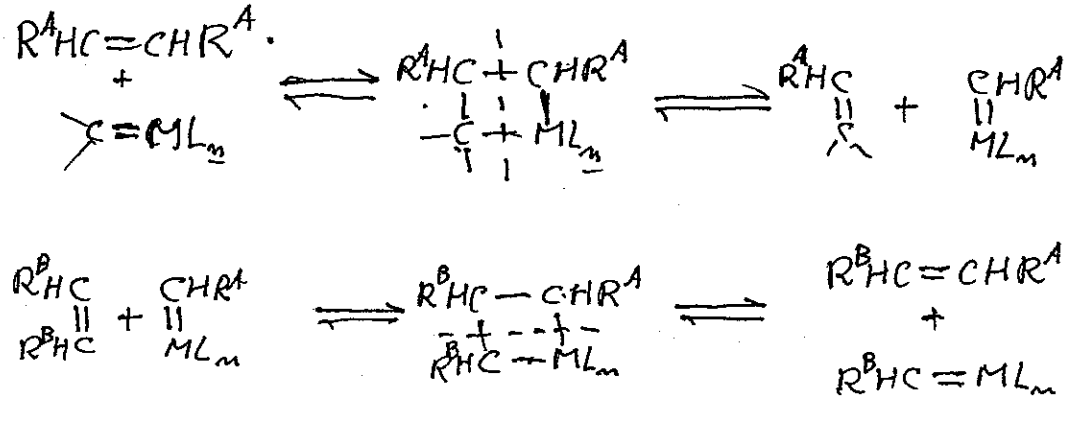
(1)(Equals) $R^AHC{=}CHR^A + R^BHC{=}CHR^B \xrightleftharpoons{\text{cat. } RuL_n} R^AHC{=}CHR^B$

- $R^AHC{=}$ and $R^BHC{=}$ may also be $R^AR^{A'}C{=}$ and $R^BR^{B'}C$
- Two alkylidene groups in one alkene may be different.

(2)(Equals) The Chauvin mechanism involves the following critical features:

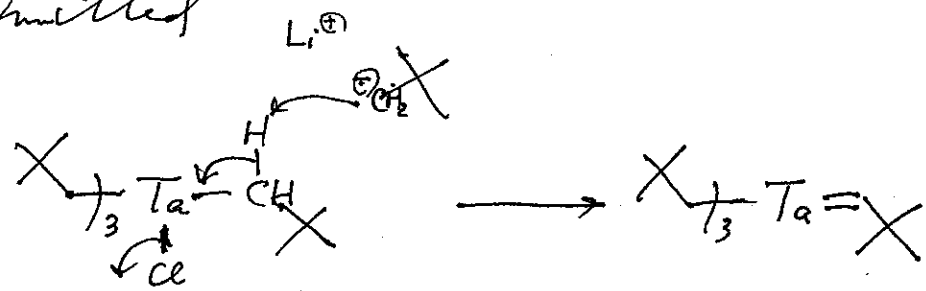
(i) formation of metal-carbene intermediate i.e., $>C{=}ML_n$

(ii) then reversible carbometalation to produce metaldacyclobutane intermediates and decarbometalation leading to olefin metathesis.

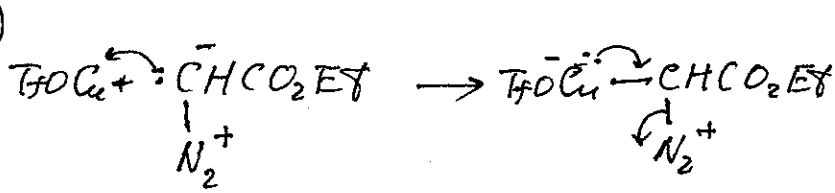


(3) Omitted

(4) (20 pts)

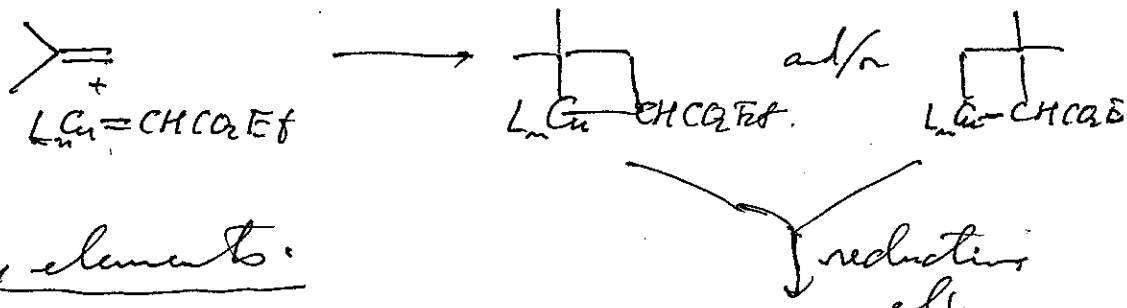


[2] (1) (20 pts)



$\longrightarrow L_nCu{=}CHCO_2Et$

L_n = TfO or something else

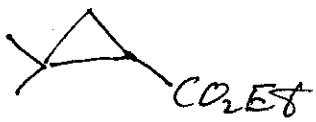


<u>Key elements:</u>

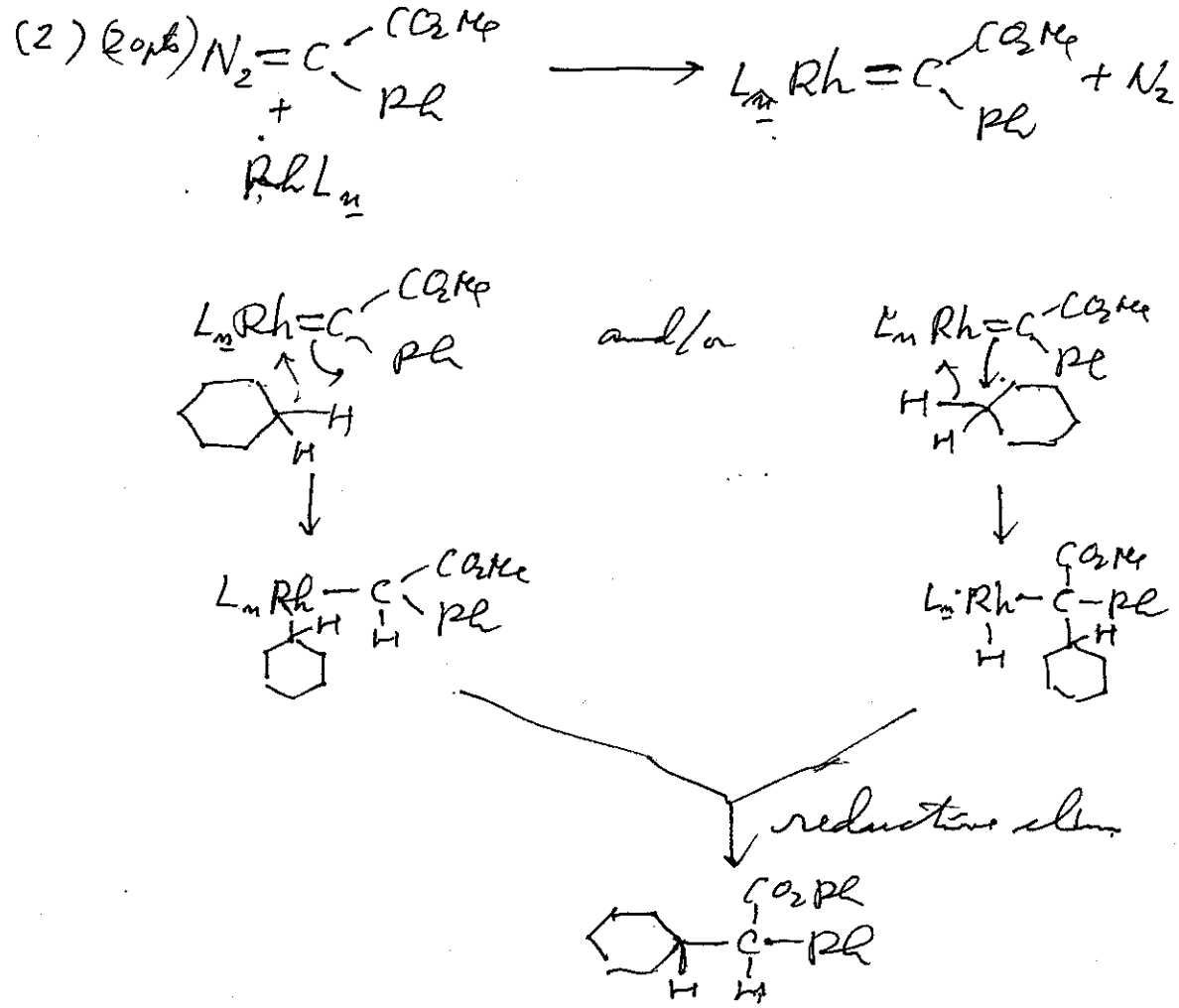
(i) Formation of $L_nCu{=}CHCO_2Et$

(ii) Its carbometalation

(iii) Reductive elimination



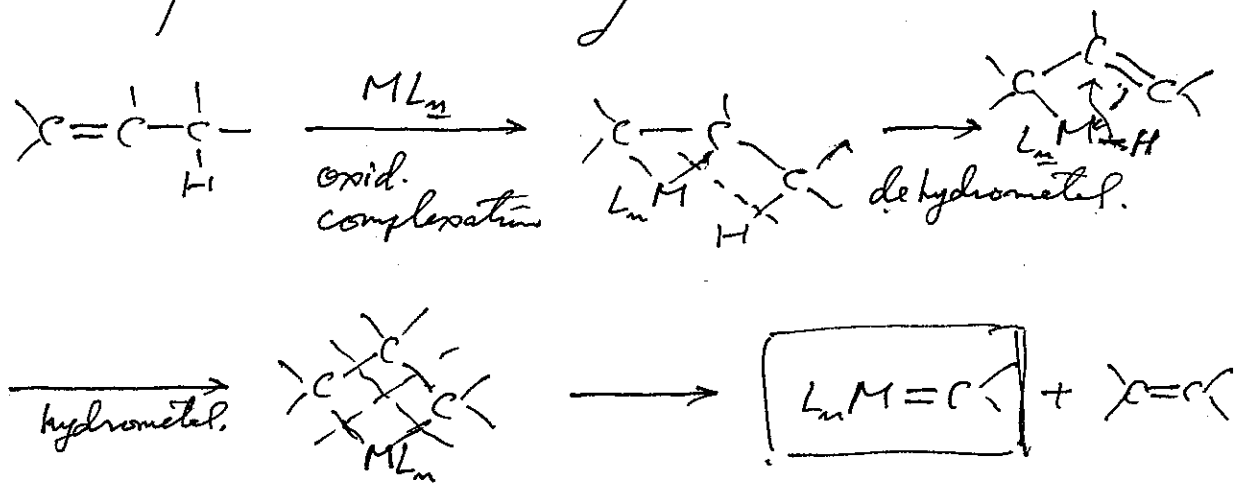
(2) (20 pts)



Bonus Question (10 pts)

One of the puzzles regarding the Chauvin mechanism was how metal-carbene species might be formed from alkenes and metal complexes that do not contain a M=C bond. With time, chemists gradually realized that there are more than one way to produce metal-carbene complexes from alkenes and metal complexes without M=C bonds. The following

is one of the most widely observable.



Physical Chemistry Cume Crib April 2006

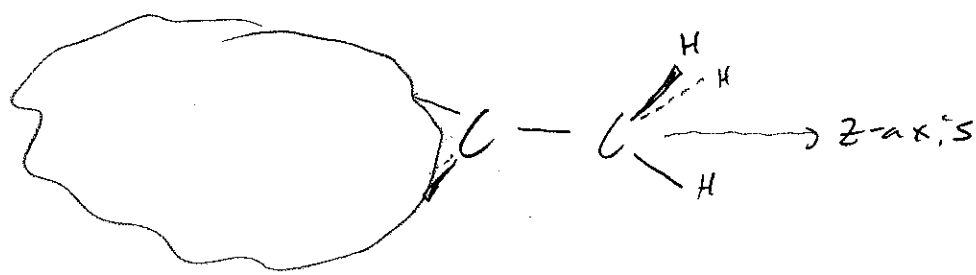
Useful Equations:

$$\int_0^\infty e^{-ax^2}dx = \sqrt{\frac{\pi}{4a}} \qquad Q = \frac{q^N}{N!} \qquad q = \sum_i g_i e^{-E_i/kT} \qquad \langle E \rangle_V = U = NkT^2 \frac{\partial \ln q}{\partial T}$$

$$\hat{H}\psi = E\psi \qquad \hbar = h/2\pi$$

$$\hat{H}_{trans}\psi_{trans} = \frac{\hat{p}^2}{2m}\psi_{trans} = E_{trans}\psi_{trans}; \quad \hat{H}_{vib}\psi_{vib} = \left(-\frac{\hbar^2}{2\mu}\frac{d^2}{dx^2} + \tfrac{1}{2}kx^2\right)\psi_{vib} = E_{vib}\psi_{vib}$$

$$\hat{H}_{rot}\psi_{rot} = \frac{\hat{L}^2}{2I}\psi_{rot} = E_{rot}\psi_{rot}; \quad \hat{L}_z = -i\hbar\frac{\partial}{\partial\phi};$$

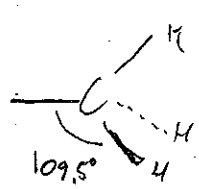


1. Consider the local torsional motion of one methyl group with respect to a larger effectively fixed molecular structure (e.g., a protein) depicted above. From your chemical intuition, do you expect the barrier for torsional inter-conversion (E_a) of a free CH_3 group to be greater than, lesser than, or comparable to kT at room temperature?

(5) probably comparable to kT @ Room temp.

2. Let's assume we are operating at a temperature high enough that $E_a \ll kT$. In this limit, the wavefunctions describing torsional motion effectively reduce down to those of a 1D rigid rotator describing the clockwise and/or counter-clockwise motions of the 3 hydrogen atoms about the C-C bond with a moment of inertia I_{CH3}. Using typical values for bond lengths and bond angles, estimate the value of I_{CH3} (in units of amu*Å^2).

(5)



- 109.5° is close enough to 90°, that will just treat it as such.

- Typical C-H bond length $\cong 1a_0 \cong 2$ Å

so $I_{CH_3} = \sum m \cdot (r - r_{com})^2 = 3 \cdot (1\,amu)(2\,Å)^2$
$\cong 12\,amu\,Å^2$

3. Derive an expression for the set of <u>normalized wavefunctions</u> describing the pseudo-rotational motion of a single CH_3 subunit using the boundary conditions $\psi_{CH3}(\phi) = \psi_{CH3}(\phi + 2\pi)$ and/or $\psi'_{CH3}(\phi) = \psi'_{CH3}(\phi + 2\pi)$ starting from a general solution of $\psi_{CH3}(\phi) = Ae^{im\phi}$, where A and m can each be any real rational number. Show that resulting the wavefunction is an eigenfunction of the angular momentum operator $\hat{L}_z$, with the z-axis defined as the C-C bond axis. What are the eigenvalues?

a) Boundary conditions:

$$\psi(\phi) = \psi(\phi + 2\pi) \quad \text{and} \quad \psi'(\phi) = \psi'(\phi + 2\pi)$$

$$Ae^{im\phi} = Ae^{im(\phi+2\pi)}$$

$$= Ae^{im\phi} \cdot e^{2im\pi} \Big\} \text{ B.C. will only be satisfied if } \left(e^{2im\pi} = 1\right)$$

$$e^{2im\pi} = \cos(2m\pi) + i\sin(2m\pi) \Big\} \text{ only } = 1 \text{ if } m \text{ is an } \underline{\text{integer}}!$$

$$\boxed{m = 0, \pm 1, \pm 2, \ldots}$$

b) Now, normalize:

$$1 = \int_{-\pi}^{\pi} \psi^* \psi \, d\phi = \int_{-\pi}^{\pi} A^2 d\phi = A^2 \cdot 2\pi \quad ; \quad A = \frac{1}{\sqrt{2\pi}}$$

$$\psi(\phi) = \frac{1}{\sqrt{2\pi}} e^{im\phi} \quad ; \quad m = 0, \pm 1, \pm 2 \ldots$$

c) Show that $\psi(\phi)$ is eF. of $\hat{L}_z$

$$\hat{L}_z = -i\hbar \frac{\partial}{\partial \phi} \quad // \quad \hat{L}_z \psi_\phi = -i\hbar \frac{\partial}{\partial \phi} Ae^{im\phi}$$

$$= -i\hbar(imAe^{im\phi}) = \underbrace{m\hbar}_{\text{eigenvalues}} \psi(\phi)$$

This is just the particle-on-a-ring result!

4. Show that the wavefunction $\psi_{CH3}(\phi)$ you derived in 3) leads to the following solution for the energy of the pseudo-rotational eigenstates. Using your calculated moment of inertial for CH_3, how does the energy of the $m = 1$ excited state compare with kT? (hint: for a 1D rigid rotator, $\hat{L}^2 = \hat{L}_z\hat{L}_z$).

$$E_m = \frac{\hbar^2 m^2}{2I_{CH3}};\ m = 0, \pm 1, \pm 2, \ldots$$

Rigid Rotator

$$\hat{H}\psi = \frac{\hat{L}^2}{2I}\psi = E\psi$$

a)

$$E\psi = \frac{1}{2I}\hat{L}_z(\hat{L}_z\psi) = \frac{-\hbar^2}{2I}\frac{\partial^2}{\partial\phi^2}\psi = \frac{-\hbar^2}{2I}\frac{\partial^2}{\partial\phi^2}Ae^{im\phi}$$

$$= \underbrace{\frac{\hbar^2 m^2}{2I}}_{E} \cdot \underbrace{Ae^{im\phi}}_{\psi} \qquad \text{Q.E.D.}$$

b) IF $I \cong 12\,\text{amu}\,\text{Å}^2$

$$E_1 = \frac{\hbar^2}{2(12\,\text{amu}\,\text{Å}^2)} = \frac{(1\times10^{-34}\,\text{Js})^2}{2(12\,\text{amu}\,\text{Å}^2)}$$

$$= \frac{1\times10^{-68}\,\text{J}^2\text{s}^2}{24\,\text{amu}\,\text{Å}^2} \times \frac{1\,\text{amu}}{2\times10^{-27}\,\text{kg}} \times \left(\frac{1\,\text{Å}}{10^{-10}\,\text{m}}\right)^2 \times \frac{1\,\text{kgm}^2/\text{s}^2}{1\,\text{J}} \cong \frac{10^{-68}\,\text{J}}{44\times10^{-47}}$$

$$\cong 2\times10^{-23}\,\text{J}$$

$$kT \cong 208\,\text{cm}^{-1} \times \frac{2\times10^{-23}\,\text{J}}{\text{cm}^{-1}} \cong 200\times \text{ greater than the}$$

energy of the pseudo-rotational transition

5. Using this expression for the energy, prove that the partition function for this torsional motion (which is formally a vibrational motion) is given by the following expression:

$$q_\phi \cong \sqrt{\frac{2\pi I_{CH3} kT}{\hbar^2}}$$

$$q_\phi = \sum_{m=-\infty}^{\infty} e^{-E_m/kT} = \sum_{m=-\infty}^{\infty} e^{-\frac{\hbar^2}{2IkT}\cdot m^2} \cong \int_{-\infty}^{\infty} e^{-\alpha m^2} dm \; ; \; \alpha = \frac{\hbar^2}{2IkT}$$

$$= 2\int_0^{\infty} e^{-\alpha m^2} dm = 2\cdot\sqrt{\frac{\pi}{4\alpha}} = \sqrt{\frac{\pi}{\alpha}}$$

$$= \sqrt{\frac{2\pi I kT}{\hbar^2}} \quad \text{Q.E.D.}$$

6. From the expression for q_ϕ, what is the contribution of this torsional motion to the molar heat capacity at constant volume C_v in terms of R (where R is the gas constant) in the limit that $E_a \ll kT$ (hint: what is the definition of heat capacity at constant volume?).

$$C_v = \left(\frac{\partial U}{\partial T}\right)_v = \frac{\partial}{\partial T}\left(NkT^2 \frac{\partial \ln q}{\partial T}\right)$$

$$= \frac{\partial}{\partial T}\left[NkT^2 \frac{\partial}{\partial T}\left(\ln\sqrt{\frac{2\pi IkT}{\hbar^2}}\right)\right] = \frac{\partial}{\partial T}\left[\frac{1}{2}NkT^2 \frac{\partial}{\partial T}\left(\underbrace{\cancel{\ln\frac{2\pi Ik}{\hbar^2}}}_{0 \text{ not a fn. of } T} + \ln T\right)\right]$$

$$= \frac{\partial}{\partial T}\left[\frac{1}{2}NkT^2 \cdot \frac{\partial}{\partial T}(\ln T)\right] = \frac{\partial}{\partial T}\left[\frac{1}{2}NkT\right] = \boxed{\frac{1}{2}Nk = \frac{1}{2}nR}$$

# of moles

7. What would you expect the contributions to the molar heat capacity to be in the other limit of $E_a \gg kT$?

IF $E_a \gg kT$, U is essentially a constant of T, and

$$C_v = \left(\frac{\partial U}{\partial T}\right)_v \cong 0$$

8. Is the $m = 0$ to $m = 1$ transition for this torsional mode infrared-active? Is it Raman active? Defend your answers.

a) Infrared: No perm. dipole + no change in dipole upon pseudo-rotation => Ir inactive.

b) Raman: No significant change in polarizability would be expected for a true pseudo rotation, so => Raman inactive.