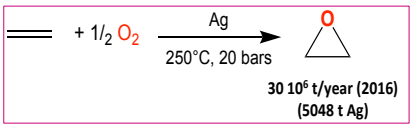
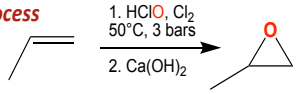
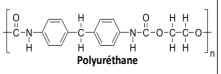
oxydations industrielles (exemples)



Chlorhydrin process

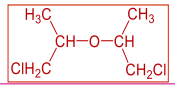


> 6 10⁶ t/year



➡ Stoechiometric and harmful conditions (HClO, HCl)

➡ Toxic and non valuable side products



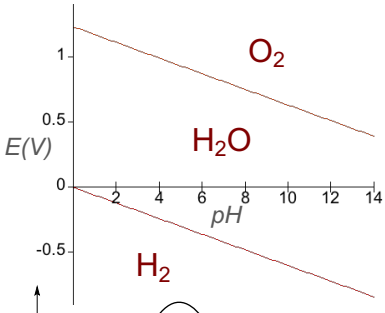
1 t propene oxide
⇒ 40 t $CaCl_2$ (6 %) aqueous solution

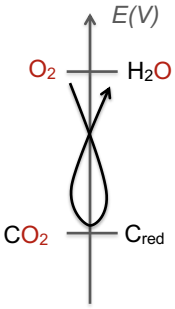
=> besoin de solutions douces, catalytiques, oxydants propres (O_2, H_2O_2)

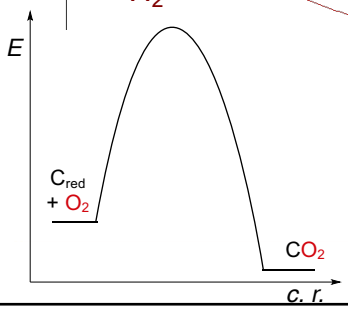
3

3

O_2 : oxydant puissant mais inerte

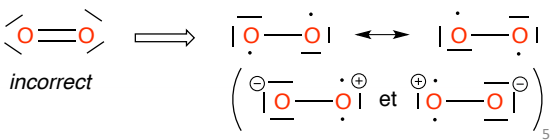






$C_{red} + O_2 \not\longrightarrow CO_2$ (+ H_2O)

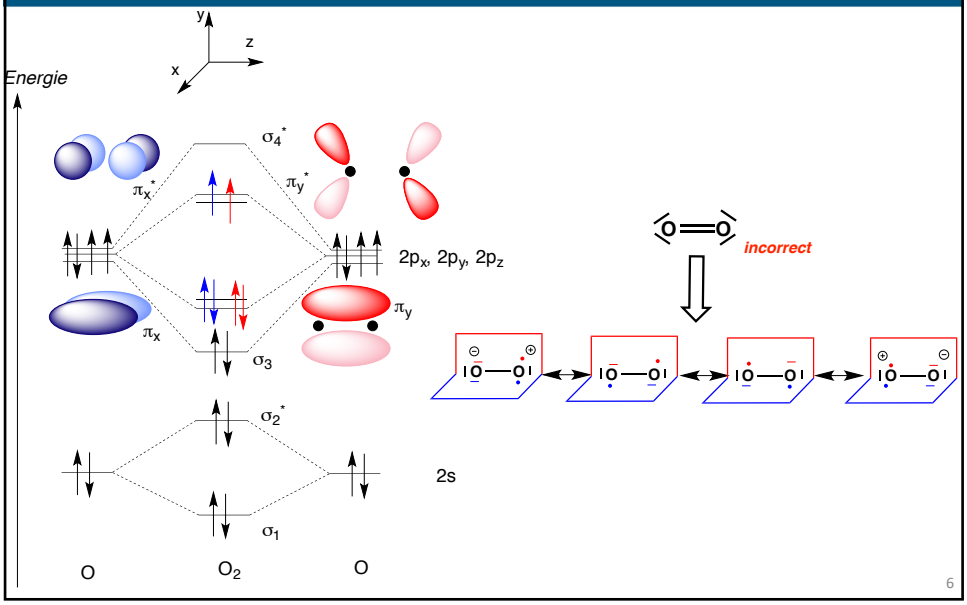
O_2 est une espèce radicalaire !!!



5

5

O_2 : structure électronique



6

O_2 : oxydant puissant mais inerte

Règles de restriction de spin de Wigner :
Le nombre d'électrons non appariés doit rester constant avant et après chaque étape d'une réaction.

1. les singulets (S=0) réagissent aisément avec les doublets (S=1/2) mais leur réaction avec les triplets (S=1) est interdite.

2. les doublets réagissent généralement plus lentement entre eux.

3. les doublets réagissent lentement avec les triplets

Barton et Sawyer (1993) :
- l'oxygène est probablement le plus important de tous les réactifs vitaux
- quel bonheur qu'il soit triplet et non singulet
- quel bonheur aussi que les complexes de cuivre et surtout de fer permettent de le domestiquer de manière à ce que nos corps soient oxydés mais seulement aux bons endroits.

7

7

propriétés de l'oxygène moléculaire.

Reaction	E° (V) vs. NHE[a]
$O_2 + e^- \rightarrow O_2^-$	-0.33^b
$O_2^- + e^- + 2\,H^+ \rightarrow H_2O_2$	$+0.89$
$H_2O_2 + e^- + H^+ \rightarrow H_2O + OH$	$+0.38$
$OH + e^- + H^+ \rightarrow H_2O$	$+2.31$
$O_2 + 2\,e^- + 2\,H^+ \rightarrow H_2O_2$	$+0.281^b$
$H_2O_2 + 2\,e^- + 2\,H^+ \rightarrow 2\,H_2O$	$+1.349$
$O_2 + 4\,H^+ + 4\,e^- \rightarrow 2\,H_2O$	$+0.815^b$

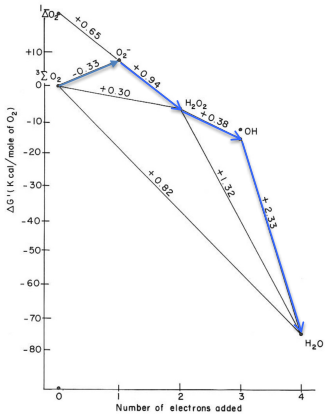
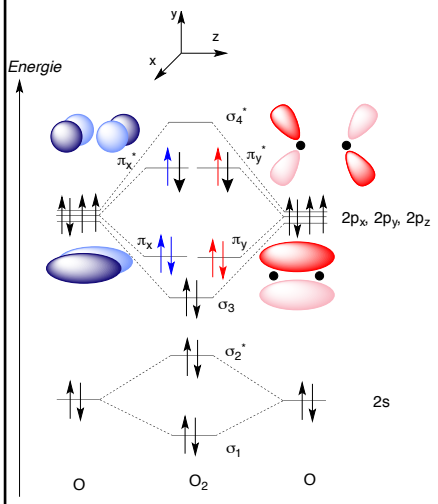


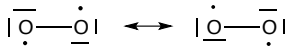
Figure 2-1. Reduction of ground-state dioxygen at pH 7 and 298°C. Note that after one uphill reduction of-ground state ($^3\Sigma_g$) dioxygen to O_2^-, all the rest are downhill. Reduction potentials are placed on the reaction lines. There is no barrier on the one-electron pathway of excited dioxygen ($^1\Delta$). Excited ($^1\Delta$) dioxygen is discussed in Chapter 2.

8

O_2 : structure électronique



O_2



indice de liaison = 2
$d_{O\text{-}O}$ = 1.21 Å
$\sigma_{O\text{-}O}$ = 1580 cm^{-1}

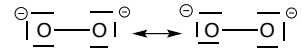
+ e$^-$

$O_2^{\bullet -}$

indice de liaison = 1.5
$d_{O\text{-}O}$ = 1.34 Å
$\sigma_{O\text{-}O}$ = 1100 cm^{-1}

+ e$^-$

O_2^{2-}



indice de liaison = 1
$d_{O\text{-}O}$ = 1.49 Å
$\sigma_{O\text{-}O}$ = 800 cm^{-1}

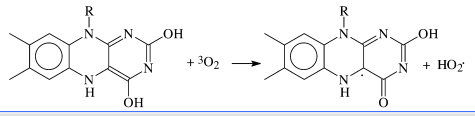
11

11

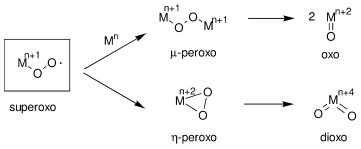
propriétés de l'oxygène moléculaire.

contournement de la barrière d'activation :

formation de radicaux libres



avec métal paramagnétique

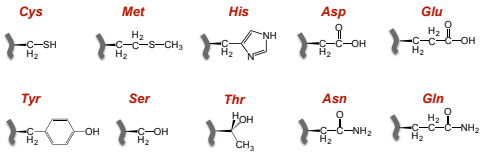


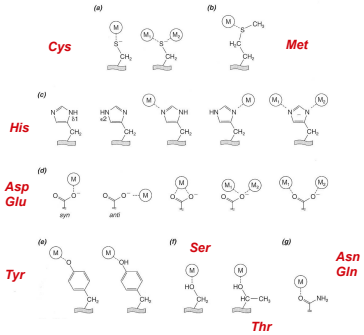
13

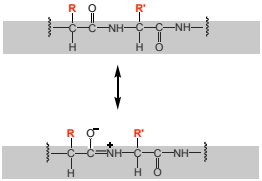
13

ligands

résidus des aminoacides







NB : barrière de rotation autour de la liaison amide de 80 kJ/mol ⇒ doublet de N délocalisé.

NB : d'autres types de ligands existent (goupes prosthétiques, cofacteurs...)

14

14

théorie HSAB – spécificité des ligands & ions métalliques.

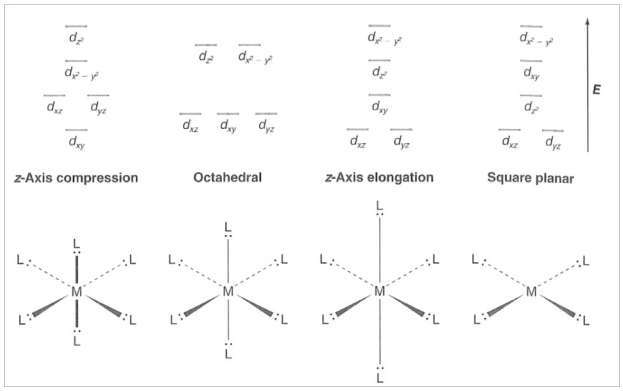
HSAB ⇒ liaisons <u>stables</u> = acide dur/base dure ou acide mou/base molle

acides durs	**intermédiaires**	**mous**
petite taille charge (DO) élevée polarisabilité faible		grande taille charge (DO) faible polarisabilité élevée
Fe^{3+}, Co^{3+}, Cr^{3+}, Mn^{2+}, Ca^{2+}, Na^{+}, Al^{3+}, Li^{+}, Mg^{2+}, H^{+}…	Fe^{2+}, Co^{2+}, Cu^{2+}, Ni^{2+}, Zn^{2+}...	Cu^{+}, Pt^{2+}, Ag^{+}...

bases dures	**intermédiaires**	**molles**
petite taille, électronégatif polarisabilité faible, difficile à oxyder		grande taille, peu électronégatif, polarisabilité grande, facile à oxyder
H_2O, OH^-, RO^-, O_2^-, F^-, Cl^-, NH_3, RNH_2, $RCOO^-$, CO_3^{2-}, PO_4^{3-},...	py, N_3^-, N_2, imidazole, $\mathbf{O_2}$, Br^-...	I^-, H_2S, RSH, RS^-, CO, CN^-, PR_3...

15

champ cristallin (champ de ligand)



série spectrochimique

$$I^- < Br^- < SCN^- < S^{2-} < Cl^- < NO_3^- < F^- < OH^- \sim RCOO^- < H_2O \sim RS^- < NH_3 \sim \text{Im (imidazole)} < \text{bpy (2,2}'\text{-bipyridine)} < CN^- < CO$$

$$Mn^{2+} < Ni^{2+} < Co^{2+} < Fe^{2+} < V^{2+} < Fe^{3+} < Co^{3+} < Mn^{3+} < Mo^{3+} < Rh^{3+} < Ru^{3+} < Pd^{4+} < Ir^{3+} < Pt^{4+}$$

18

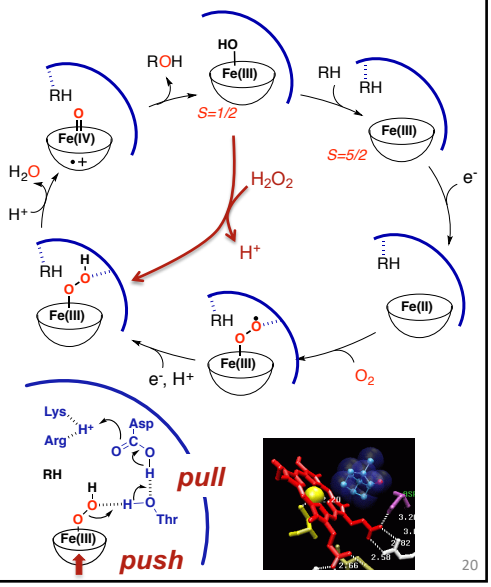
18

Reductive Activation of O_2 by cyt. P450

the paradigm

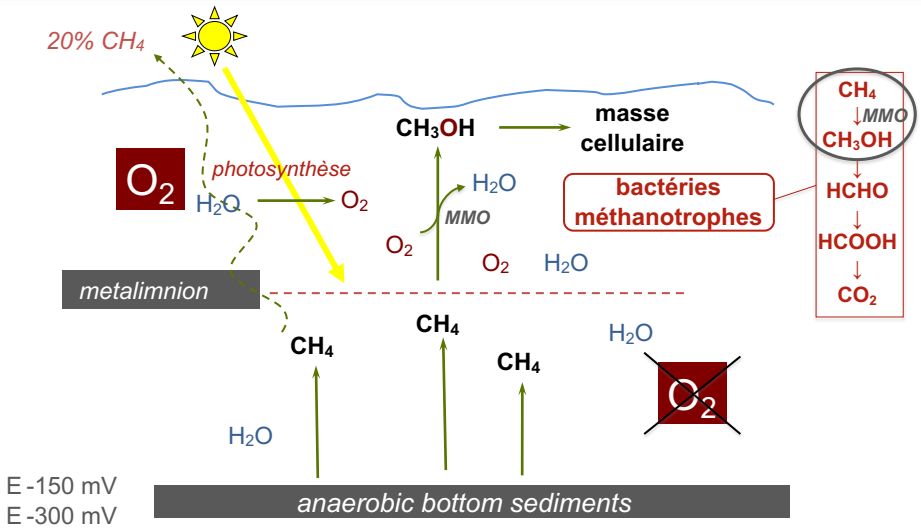
selectivity / efficiency

- 1st coordination sphere
- Substrate binding and preorganization
- Substrate triggered reactivity and 2nd sphere interactions



environnement méthanogène

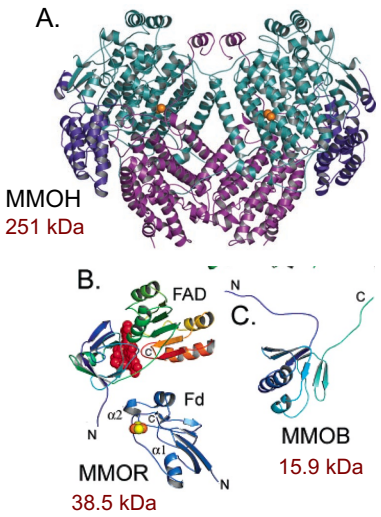
les marais



NB : consommation mondiale gaz 2012 ⇨ 3 10^9 t

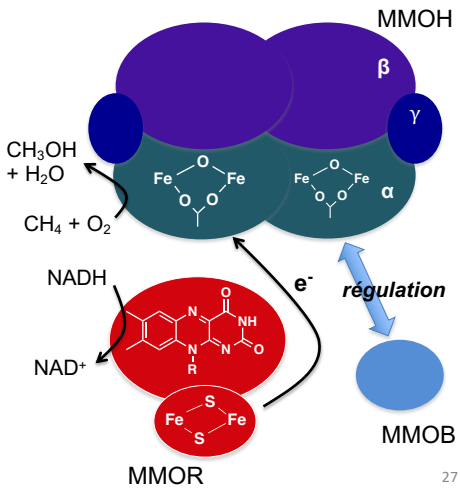
Activation réductrice de O_2 :

Méthane Monooxygénase



$CH_4 + O_2 + NADH + H^+ \rightarrow CH_3OH + H_2O + NAD^+$

($D_{C\text{-}H}$=438.4 kJ.mol^{-1}; oxydation d'alcanes ≤ C_8)



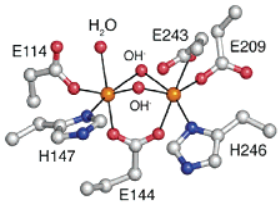
Murray, Lippard, Acc. Chem. Res., 2007, 40, 466
Sazinsky, Lippard, Acc. Chem. Res., 2006, 39, 558
Merkx et al. Angew. Chem. 2001, 40, 2782

27

27

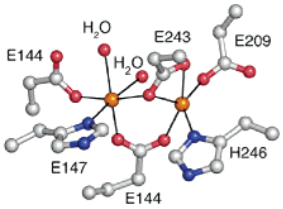
Structure du site actif

$MMOH_{ox}$



Fe^{III}-Fe^{III} 3,1 Å

$MMOH_{red}$



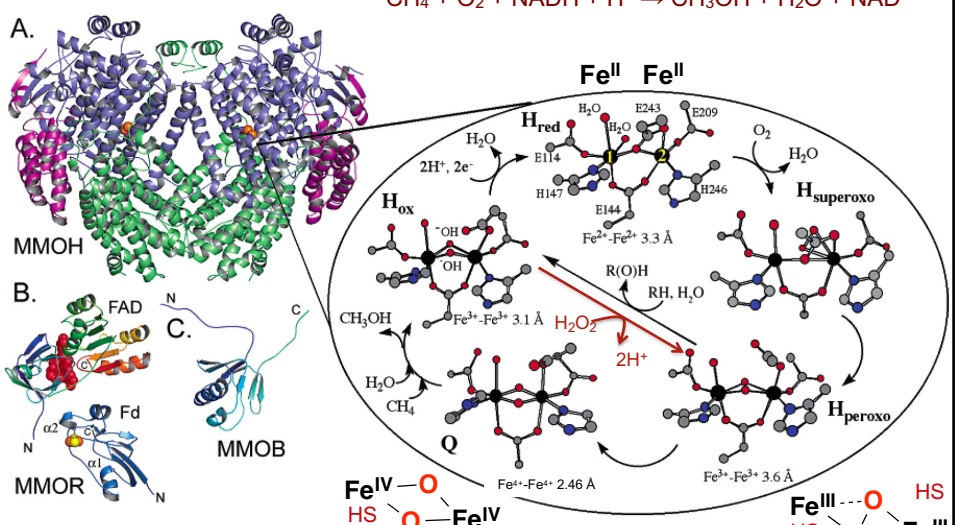
Fe^{II}-Fe^{II} 3,3 Å

Sazinsky, Lippard, Acc. Chem. Res., 2006, 39, 558
Merkx et al. Angew. Chem. 2001, 40, 2782
Murray, Lippard, Acc. Chem. Res., 2007, 40, 466

28

proposition de cycle catalytique

$CH_4 + O_2 + NADH + H^+ \rightarrow CH_3OH + H_2O + NAD^+$



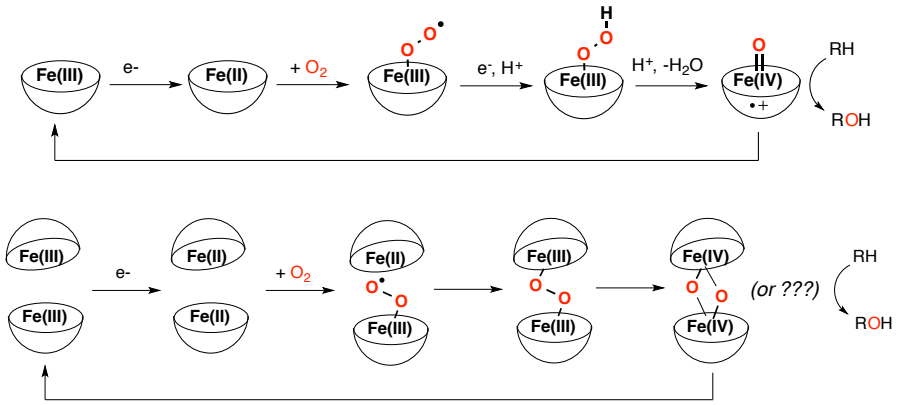
350 (3600); 420 (7200)
δ_1 = 0,21 mm.s^{-1}, ΔE_{Q1} = 0,68 mm.s^{-1}
δ_2 = 0,14 mm.s^{-1}, ΔE_{Q2} = 0,55 mm.s^{-1}
d(Fe-Fe) = 2.46 Å (EXAFS) ?

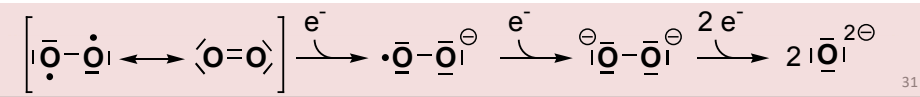
420 nm (4000 L.mol^{-1}.cm^{-1}); 725 nm (1800 L.mol^{-1}.cm^{-1})

30

Activation réductrice de O_2 :

MMO vs. P450





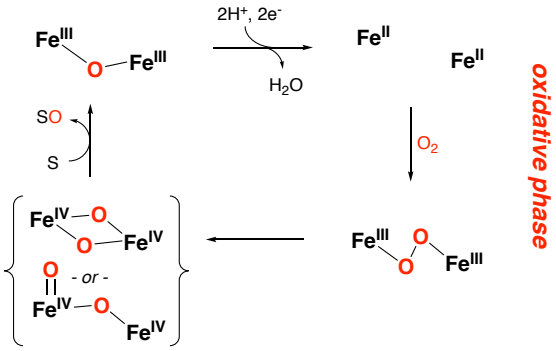
31

31

Interaction entre composants

le dilemme des oxygénases

reductive phase



Convenient assembly of protein complexes (MMOH, MMOB, MMOR) :

- electron consumption ⟷ substrate hydroxylation;

- protection of reactive oxygenated diiron intermediates (→reduction by reductase);

⇨ *Possible competition between MMOB and MMOR for a shared binding site on MMOH.*

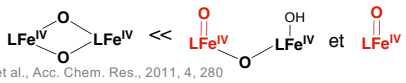
Murray, Lippard, Acc. Chem. Res., 2007, 40, 466

32

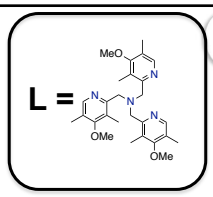
32

structure de l'intermédiaire Q

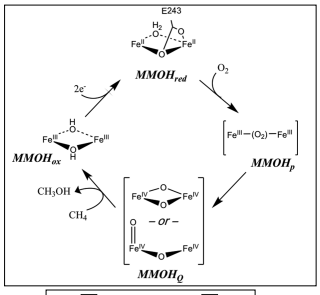
compared reactivity of $Fe^{IV}O$ model complexes
(O-atom transfer and C-H bond cleavage):

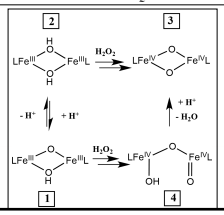


Tienberg et al., Acc. Chem. Res., 2011, 4, 280
Xue et al. Nat. Chem 2010, 2, 400

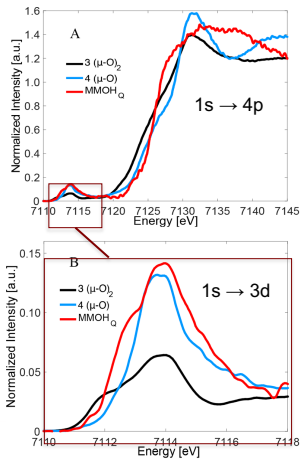


compared spectroscopic properties of Q and model complexes





HERFD XAS



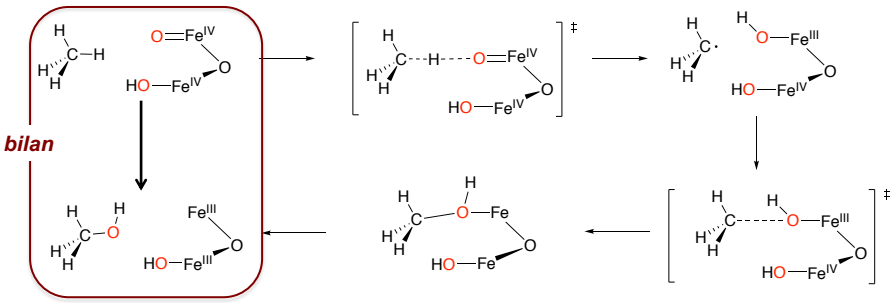
J. Am. Chem. Soc. 2017, 139, 18024

33

33

hydroxylation du méthane par $MMOH_Q$

a possible mechanism



KIE observed for $MMOH_Q$ decay : 50-100 for CH_4 vs CD_4.
KIE observed for product formation : 19.3 for CH_4 vs CD_4; 3.9 for the intramolecular effect in CD_3H.

The reaction of CD_4 with $^{18}O_2$ results in 100 % $CD_3{}^{18}OH$.
⇒ no exchange of oxygen or methyl hydrogen atoms with the solvent.

34

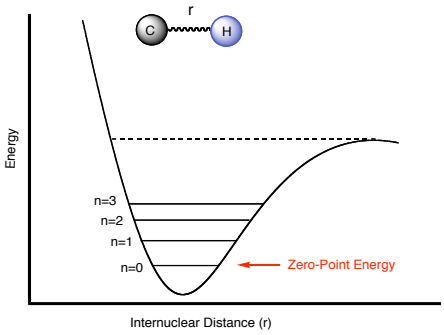
34

Kinetic Isotope Effect

KIE : *mechanistic phenomenon where isotopically substituted molecules react at different rates*
⇨ Interpretation of the rate differences provides information on the rate determining step (rds)

Primary isotope effect : labelled bond is made or broken in the rds
Secondary isotope effect : labelled bond is not made or broken in the rds
Normal isotope effect : $k_H/k_D > 1$
Inverse isotope effect : $k_H/k_D < 1$

vibrational energy levels of chemical bonds (harmonic oscillator) :
depends on the bond stretch frequency, thus on the reduced mass of the two connected atoms



$$\nu_{C-H} = \frac{1}{2\pi}\sqrt{\frac{k}{\mu_{C-H}}}$$

reduced mass :

$$\mu_{C-H} = \frac{m_c \times m_H}{m_c + m_H} = \frac{12}{13}$$

$$E_n = h\nu(n + \frac{1}{2})$$

NB : 99.9 % of C-H bonds are in the ground vibrational state (n=0) at RT.
⇨ the ZPE forms the basis for the reactivity differences between isotopomers

35

Kinetic Isotope Effect

Primary isotope effect : C-H vs C-D homolytic cleavage

$$R\text{-}(H/D) \xrightarrow{k} \text{Product} \qquad k_{C\text{-}H} \neq k_{C\text{-}D}$$

μ_{C-H}=0.92	ν_{C-H} = 2900cm^{-1}	ZPE=4.15 kcal.mol^{-1}	rel. rate=6.9 (300K)
μ_{C-D}=1.71	ν_{C-D} = 2100cm^{-1}	ZPE=3.0 kcal.mol^{-1}	rel. rate=1 (300K)

$$\frac{k_{C-H}}{k_{C-D}} = e^{\frac{-\Delta ZPE}{RT}} = e^{\frac{1.15\times10^3\times4.18}{8.32\times300}} = 6.86$$

classical limit