***Supplement 16: Brown’s Markovnikoff & Anti-Markovnikoff Routes to Alcohols***

***from Alkenes***

 ***ORGANIC CHEMISTRY I***

H.C. Brown, 1979 Nobel Laureate in Chemistry from Purdue University, was instrumental in devising rapid, high yield and specific reaction pathways that have helped a generation of synthetic chemists build and tailor everything from anti-cancer drugs to agricultural pesticides. Two of his most famous reactions are the oxymercuration/demercuration reaction of alkene to an markovnikoff addition alcohol , and the hydroboration/oxidation reaction of alkene to an anti-Markovnikoff addition alcohol. Both syntheses are entirely specific in their addition sites, take literally only a minute or so at room temperature, and regularly provide 90+ percent yields. Both take advantage of a carbocation-like `bridgehead’ intermediate. Because they take two steps, I refer to the reactions as the `Brown’ two

step.

**Oxymercuration/demercuration route to Markovnikoff alcohols**

The overall reaction here, illustrated in the case of isobutylene is:

 Hg(OAc)2 NaBH4/OH-

 (CH3)2 C=CH2 -----------> (CH3 )­2 C-CH2 ----------> (CH3 )2 C-CH2 + Hg

 | | | |

 OH HgOAc OH H

The suggested mechanism to the critical mercurial intermediate follows a bridgehead

pattern where the mercury (II) acetate =Hg(OAc)2 adds across the top of the alkene πbond

**1) bridgehead formation (note: OAc- = acetate anion= CH3COO-)**





after the bridgehead is formed, the mercury leans a bit to the right (as in the halonium mechanism with Br) to place the + charge on the more substituted side. Water’s OH then acts as an nucleophile and attacks the `leaning’ bridgehead at the (+) end, simultaneously forming a C-OH bond and transferring an H from water to the OAc-.

**2) aqueous hydroxyl insertion**



**NaBH4/OH-**

The remaining reduction (demercuration) step is not mechanistically important, and amounts to having BH4- reduce the Hg2+ to Hgo and transfer an H



from BH4- to the new alcohol as shown tothe left.

**+ NaOAc + Hgo** + **borates**

 oxymercuration-demercuration is now considered too dangerous to carry out.

**Hydroboration-oxidation route to Anti-Markovnikoff Alcohols**

The hydroboration-oxidation pathway features a Brown hallmark, boron chemistry. It is well-described in your text. The overall reaction in the case of isobutylene is:

 **BH3**H2O2/OH-

 (CH3)2 C=CH2 -----------> (CH3 )­2 C-CH2 ----------> (CH3)2C-CH2

 | | | |

 **H****BH2** **H**  OH

The initial step of the reaction to the borohydride intermediate is the now familiar

bridgehead form, created by borane (BH3), which is supposedly generated from scission of

B2H6 (diborane=BH3-BH3)

**1)** **bridgehead formation**



A second, somewhat controversial step is suggested by Brown. The initial bridgehead supposedly gives way to 4 center-4-electron bond created by a hydritic (-)H in BH3, `bonding’ to the positive side of the bridgehead (which is again, the more substituted side)

**2) 4-center, 4-electron bond formation**



The 4-center, 4-electron system then reverts to its final form, where the hydride

says goodbye to the borane and bonds to the more substituted carbon.

**3) formation of borohydride intermediate from 4-center, 4-electron structure**





Subsequent oxidation to the final, anti-Markovnikoff alcohol is clearly described in your text, wherein the HOOH

 creates another `bridgehead’ between itself **H2O2/OH-** and BH2 then displaces it with OH to form the final, anti-Markovnikoff alcohol

 + B**H2**OH