Quadrant II – Transcript and Related Materials

Programme: Bachelor of Science (Second Year)

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Unit: Unit II – Amines and Diazonium salts

Module Name: Hofmann versus Saytzeff Elimination

Module No: 15

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Notes

NOTES: Hofmann Elimination versus Saytzeff or Zaitsev Elimination in Amines

Amines, on conversion to their quaternary ammonium salts, *undergo* elimination reactions to give the corresponding alkenes. This occurs in the presence of base. {This entire process is known as Hofmann Exhaustive Methylation or Hofmann Degradation or Hofmann Elimination}. JM1290(Michael B. Smith, 2013). The alkyl halides undergo elimination of HX by loss of halide ion and proton from the adjacent C.

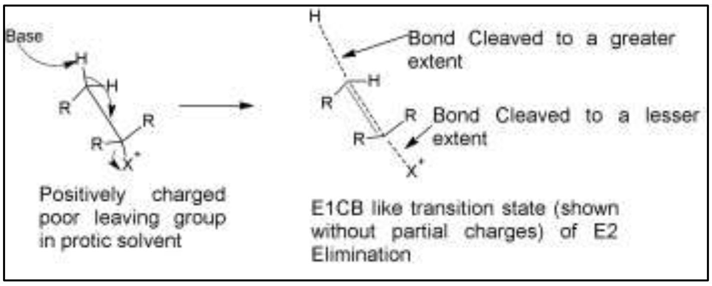
As proposed by Ingold et al in 1927, the mechanism of elimination is usually bimolecular E2 in protic solvents (Finar, 319)(I L Finar, 1963) for positively charged poor leaving groups ie ammonium ions. The mechanism followed for neutral leaving groups like halogen is usually either E2 or E1.

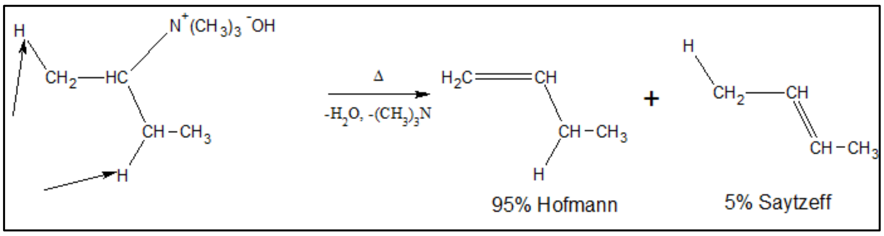
E1 eliminations involve loss of a good leaving group thereby resulting in the formation of carbocation which then loses the proton from adjacent carbon so as to give the most stable alkene as the major product i.e. by following saytzeff rule.

E2 elimination is a one step process which involves loss of HX under the influence of base.

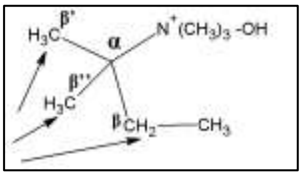
E1CB mechanism involves the formation of carbanion by loss of acidic hydrogen under the influence of base. This carbanion then losses the leaving group thereby resulting in the formation of alkene.

For acyclic ammonium hydroxides the mechanism that dominates in this elimination is E_2-Elimination with E_1CB like transition state. Here the C-H bond is cleaved to a greater extent than that of C-X bond. Thus, more carbanion like character of transition state is obtained.





This then leads to the loss of more acidic H, which will ultimately lead to the formation of Hofmann product as the major product. .i.e the less substituted C-C double bond. But, in general terms a more substituted C_C double bond is more stable than the less substituted one due to hyperconjugation.



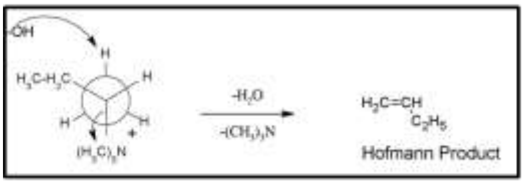
There are two reasons for Hofmann product being the major product i.e.

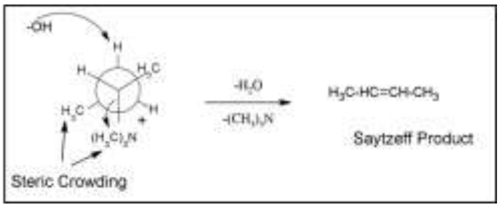
- Acidity of β-H and Negative Inductive Effect of the positively charged poor leaving groups i.e. the ammonium ion.
- Steric Effects: not much considered

Acidity of β-H and Negative Inductive Effect of the positively charged poor leaving groups i.e. the ammonium ion: acidity of the β hydrogen is decreased by the presence of the electron-donating alkyl groups. Thus the C-H acidity decreases in the series C*prim*-H, C*sec*-H , C*tert*-H. It is the more acidic hydrogen that is removed by the base. Of course, the CH3 hydrogen atoms would still be more acidic than the Me2CH hydrogen even if a neutral leaving group were present, but the explanation presented was that acidity matters with charged and not with neutral leaving groups, because the charged groups exert a strong electron-withdrawing effect, making differences in acidity greater than they are with the less electron-withdrawing neutral groups.

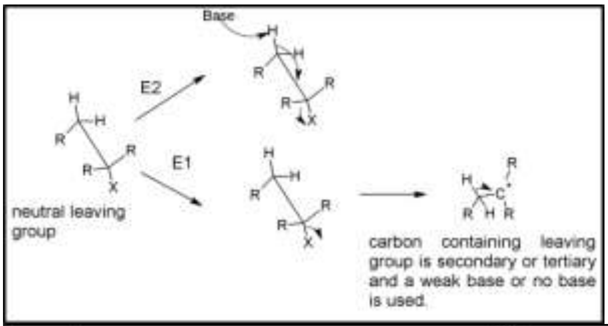
The mechanism of elimination is usually E2 in protic solvents. But, it will have E_1CB like transition state due to the positively charged poor leaving groups which has EW character.

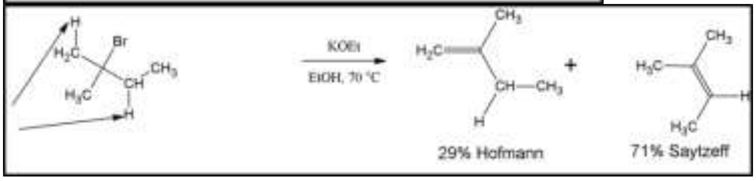
- E2 eliminations are actually one-step eliminations. Still, in an E2 transition state the C¬H bond can be broken to a different extent than the C¬N bond. If the C¬H bond is broken to a greater extent than the C¬N bond, we have an E2 elimination with an E1cb-like distortion of the transition state geometry. Thus, acidity of C-H bond will determine the rate of the reaction.
- 2. Steric Effects due to the bulky tetra substituted ammonium species-this explanation is proposed by Brown et al in 1957 (Finar, pg 319): the NR3 groups in the substrate are relatively large because they are branched. Therefore, they allow an attacking base more readily access to the structural element C^{β}_*prim*¬H relative to C^{β} *sec*—H and to the structural element
- C^{β} *sec*—H relative to C^{β}*tert*—H. (ref Bruckner)This effect may not be related to E1CB mechanism





Alkyl haildes undergo elimination via either E1 or E2 mechanism. If the alkyl halide is secondary or tertiary then there is more probability of the substrate undergoing E1 due to the stable carbocation formed. E1 mechanism is still more favourable in presence of weak base or no base. In both the mechanisms Saytzeff product is the major product being the most stable one. At even modest concentration of base E2 mechanism is much faster than E1.





The reasons for Saytzeff product being the major product are

- No impact of acidity of β-H, being a neutral leaving group unlike ammonium ion. This is based on what is discussed earlier for quaternary ammonium ion.
- Energy of E2 transition state reduces as partial C=C stability increases.

  Here, there will be partial double bond character in E2 transition state and more stable C-C partial double bond will stabilise the TS. Thus, more stable Saytzeff product will be favoured.
- In the E1 mechanism, R.D.S. is the formation of carbocation.

Here the first step is R.D.S thus, the second step proceeds to give the most stable product i.e. the Saytzeff product.

So to summarise, we can conclude that acyclic quaternary ammonium ions give Hoffmann as the major product and alkyl halides give Saytzeff as the major product.

References

1.Francis Carey, 2000. Organic Chemistry. McGraw-Hill.

2. I L Finar, 1963. Organic Chemistry the Fundamental Principles, 4th ed. Longman.

3. Michael B. Smith, 2013. March’s Advanced Organic Chemistry Reactions, Mechanisms, and Structure. JohnWiley & Sons.

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