6 NUCLEOPHILIC REACTIONS: PROPERTIES AND SUBSTITUTION REACTIONS OF ALKYL HALIDES

SOLUTIONS TO PROBLEMS

6.1 (a) *cis*-1-Bromo-2-methylcyclohexane

(b) *cis*-1-Bromo-3-methylcyclohexane

(c) 2,3,4-Trimethylheptane

6.2 (a) 3° (b) alkenyl (vinylic) (c) 2° (d) aryl (e) 1°

6.3 (a) $CH_3-\ddot{I}: + CH_3CH_2-\ddot{O}:^- \longrightarrow CH_3-\ddot{O}-CH_2CH_3 + :\ddot{I}:^-$

Substrate; Nucleophile; Leaving group

(b) $:\ddot{I}:^- + CH_3CH_2-\ddot{B}r: \longrightarrow CH_3CH_2-\ddot{I}: + :\ddot{B}r:^-$

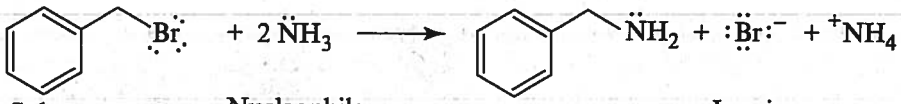
Nucleophile; Substrate; Leaving group

(c) $2\,CH_3\ddot{O}H + (CH_3)_3C-\ddot{C}l: \longrightarrow (CH_3)_3C-\ddot{O}-CH_3 + :\ddot{C}l:^- + CH_3\overset{+}{O}H_2$

Nucleophile; Substrate; Leaving group

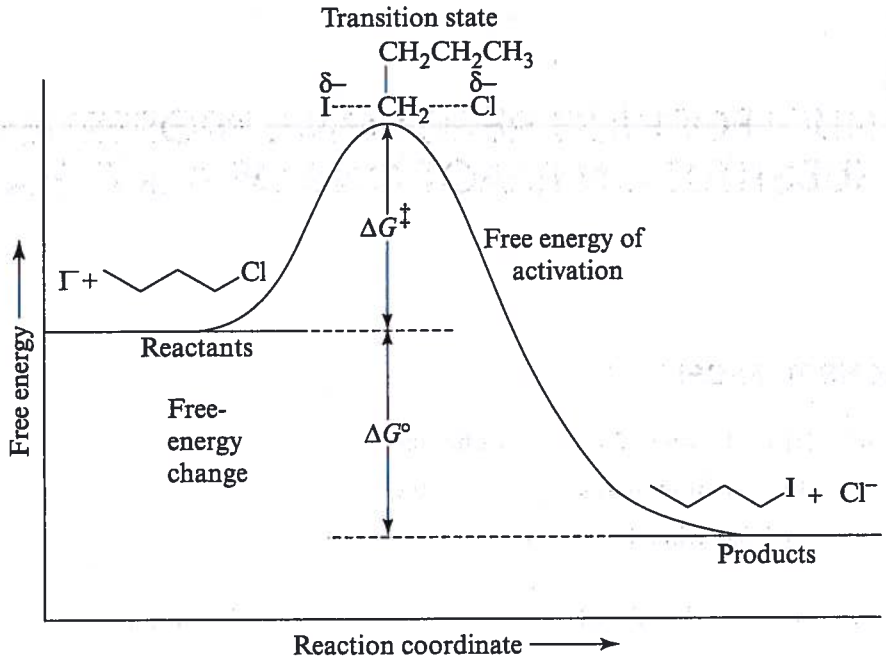
(d) 

Substrate; Nucleophile; Leaving group

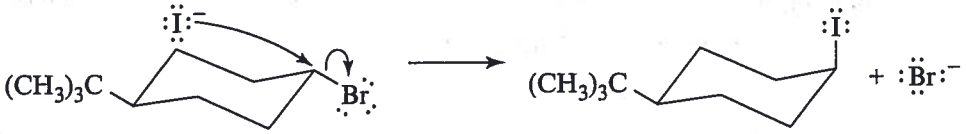
(e) 

Substrate; Nucleophile; Leaving group

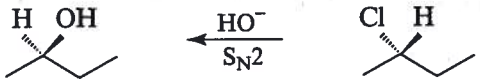
6.4



6.5



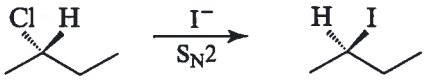
6.6 (a) We know that when a secondary alkyl halide reacts with hydroxide ion by substitution, the reaction occurs with *inversion of configuration* because the reaction is S_N2. If we know that the configuration of (–)-2-butanol (from Section 5.8C) is that shown here, then we can conclude that (+)-2-chlorobutane has the opposite configuration.



(*R*)-(–)-2-Butanol
$[\alpha]_D^{25°} = -13.52$

(*S*)-(+)-2-Chlorobutane
$[\alpha]_D^{25°} = +36.00$

(b) Again the reaction is S_N2. Because we now know the configuration of (+)-2-chlorobutane to be (*S*) [cf., part (a)], we can conclude that the configuration of (–)-2-iodobutane is (*R*).

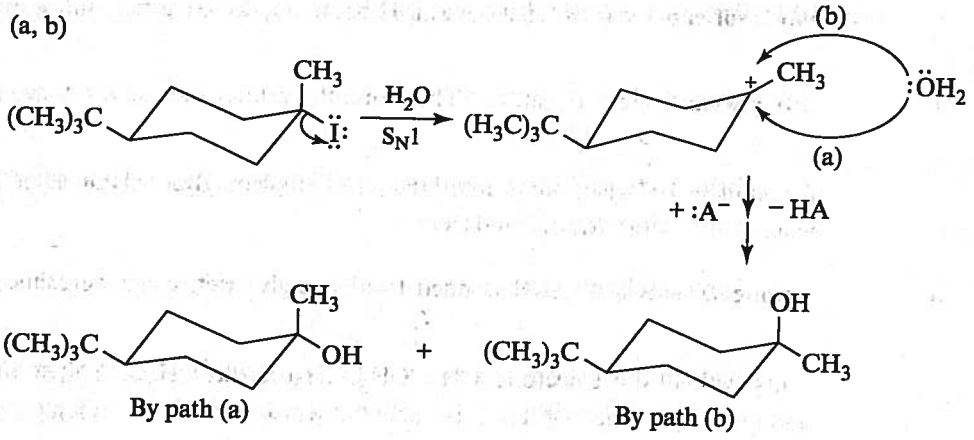


(*S*)-(+)-2-Chlorobutane (*R*)-(–)-2-Iodobutane

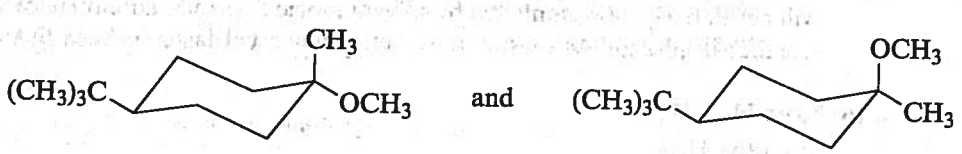
(+)-2-Iodobutane has the (*S*) configuration.

6.7 (b) < (c) < (a) in order of increasing stability

6.8 (a, b)



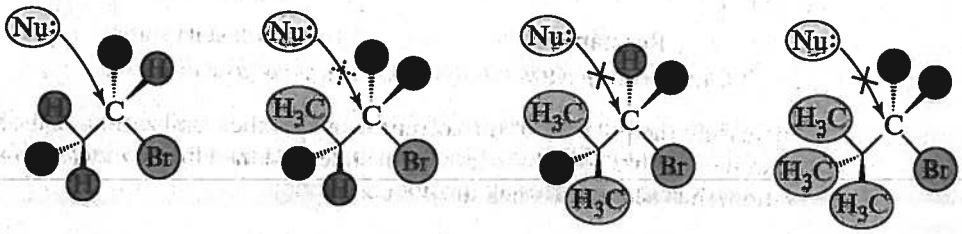
6.9



6.10 (c) is most likely to react by an S_N1 mechanism because it is a tertiary alkyl halide, whereas (a) is primary and (b) is secondary.

6.11 (a) Being primary halides, the reactions are most likely to be S_N2, with the nucleophile in each instance being a molecule of the solvent (i.e., a molecule of ethanol).

(b) Steric hindrance is provided by the substituent or substituents on the carbon β to the carbon bearing the leaving group. With each addition of a methyl group at the β carbon (below), the number of pathways open to the attacking nucleophile becomes fewer.



6.12 $NC^- > CH_3O^- > CH_3CO_2^- > CH_3CO_2H > CH_3OH$
Order of decreasing nucleophilicity in methanol

6.13 $CH_3S^- > CH_3O^- > CH_3CO_2^- > CH_3SH > CH_3OH$
Order of decreasing nucleophilicity in methanol

6.14 **Protic solvents** are those that have an H bonded to an oxygen or nitrogen (or to another strongly electronegative atom). Therefore, the protic solvents are formic acid, $HCOH$; formamide, $HCNH_2$; ammonia, NH_3; and ethylene glycol, $HOCH_2CH_2OH$. In other words, choices (a), (d), (f), and (h).

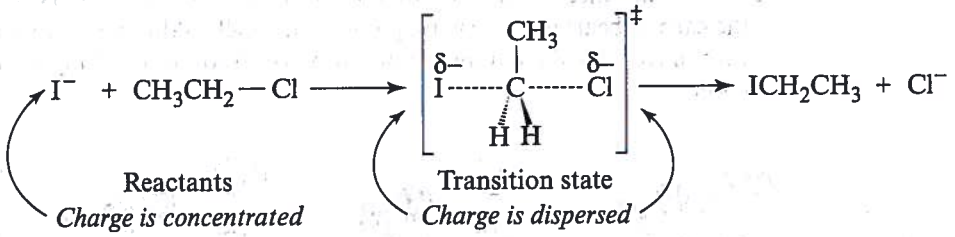
Aprotic solvents lack an H bonded to a strongly electronegative element. Aprotic solvents in this list are acetone, CH_3CCH_3; acetonitrile, $CH_3C{\equiv}N$; sulfur dioxide, SO_2; and trimethylamine, $N(CH_3)_3$. In other words, choices (b), (c), (e), and (g).

6.15 The reaction is an S_N2 reaction. In the polar aprotic solvent (DMF), the nucleophile (CN^-) will be relatively unencumbered by solvent molecules, and, therefore, it will be more reactive than in ethanol. As a result, the reaction will occur faster in *N*,*N*-dimethylformamide.

6.16 (a) CH_3O^-
(b) H_2S
(c) $(CH_3)_3P$

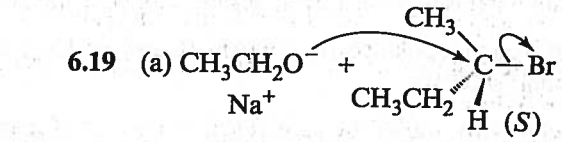
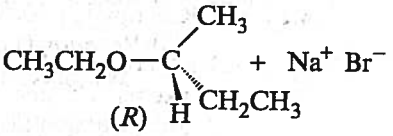
6.17 (a) Increasing the percentage of water in the mixture increases the polarity of the solvent. (Water is more polar than methanol.) Increasing the polarity of the solvent increases the rate of the solvolysis because separated charges develop in the transition state. The more polar the solvent, the more the transition state is stabilized (Section 6.13D).

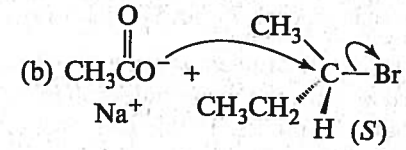
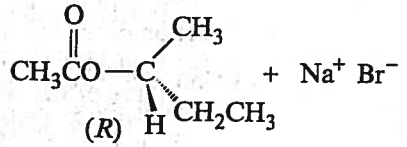
(b) In an S_N2 reaction of this type, the charge becomes dispersed in the transition state:

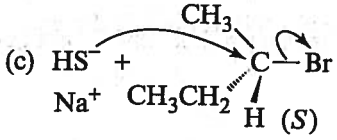
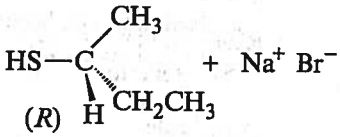


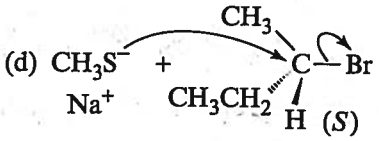
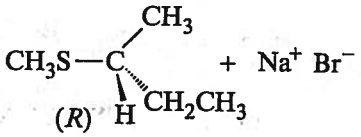
Increasing the polarity of the solvent increases the stabilization of the reactant I^- more than the stabilization of the transition state, and thereby increases the free energy of activation, thus decreasing the rate of reaction.

6.18 $CH_3OSO_2CF_3 > CH_3I > CH_3Br > CH_3Cl > CH_3F > {}^{14}CH_3OH$
(Most reactive) (Least reactive)

6.19 (a) $CH_3CH_2O^-\ Na^+$ +  inversion, S_N2 →  + $Na^+\ Br^-$

(b) $CH_3CO^-\ Na^+$ +  inversion, S_N2 →  + $Na^+\ Br^-$

(c) $HS^-\ Na^+$ +  inversion, S_N2 →  + $Na^+\ Br^-$

(d) $CH_3S^-\ Na^+$ +  inversion, S_N2 →  + $Na^+\ Br^-$

Relative Rates of Nucleophilic Substitution

6.20 (a) 1-Bromopropane would react more rapidly because, being a primary halide, it is less hindered.

(b) 1-Iodobutane, because iodide ion is a better leaving group than chloride ion.

(c) 1-Chlorobutane, because the carbon bearing the leaving group is less hindered than in 1-chloro-2-methylpropane.

(d) 1-Chloro-3-methylbutane, because the carbon bearing the leaving group is less hindered than in 1-chloro-2-methylbutane.

(e) 1-Chlorohexane, because it is a primary halide. Phenyl halides are unreactive in S_N2 reactions.

6.21 (a) Reaction (1), because ethoxide ion is a stronger nucleophile than ethanol.

(b) Reaction (2), because the ethyl sulfide ion is a stronger nucleophile than the ethoxide ion in a protic solvent. (Because sulfur is larger than oxygen, the ethyl sulfide ion is less solvated and it is more polarizable.)

(c) Reaction (2), because triphenylphosphine [$(C_6H_5)_3P$] is a stronger nucleophile than triphenylamine. (Phosphorus atoms are larger than nitrogen atoms.)

(d) Reaction (2), because in an S_N2 reaction the rate depends on the concentration of the substrate and the nucleophile. In reaction (2) the concentration of the nucleophile is twice that of the reaction (1).

6.22 (a) Reaction (2), because bromide ion is a better leaving group than chloride ion.

(b) Reaction (1), because water is a more polar solvent than methanol, and S_N1 reactions take place faster in more polar solvents.

(c) Reaction (2), because the concentration of the substrate is twice that of reaction (1). The major reaction would be E2. (However, the problem asks us to consider that small portion of the overall reaction that proceeds by an S_N1 pathway.)

(d) Considering only S_N1 reactions, as the problem specifies, both reactions would take place at the same rate because S_N1 reactions are independent of the concentration of the nucleophile. The predominant process in this pair of reactions would be E2, however.

(e) Reaction (1), because the substrate is a tertiary halide. Phenyl halides are unreactive in S_N1 reactions.

Synthesis

6.23 (a) 

(b) 

(c) 

(d) 

(e) 

(f) 

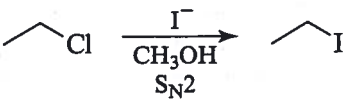
(g) 

(h) 

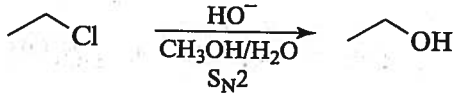
(i) 

6.24 Possible methods are given here.

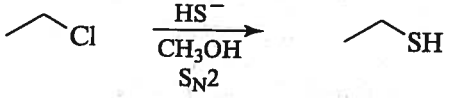
(a) $CH_3Cl \xrightarrow[S_N2]{I^- \; CH_3OH} CH_3I$

(b) 

(c) $CH_3Cl \xrightarrow[CH_3OH/H_2O]{HO^-} CH_3OH$ (S_N2)

(d)  (S_N2)

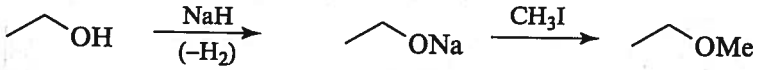
(e) $CH_3Cl \xrightarrow[CH_3OH]{HS^-} CH_3SH$ (S_N2)

(f)  (S_N2)

(g) $CH_3I \xrightarrow[DMF]{^-CN} CH_3CN$

(h) 

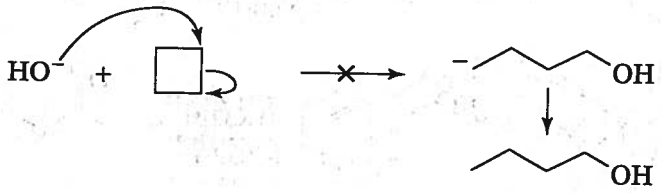
(i) $CH_3OH \xrightarrow[(-H_2)]{NaH} CH_3ONa \xrightarrow[CH_3OH]{CH_3I} CH_3OCH_3$

(j) 

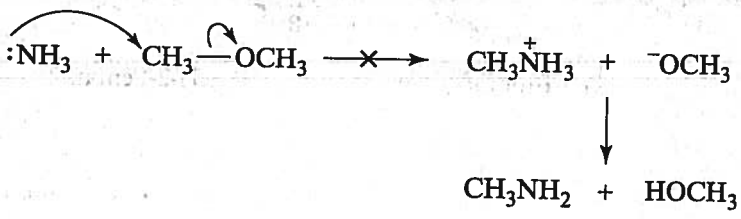
6.25 (a) The reaction will not take place because the leaving group would have to be a methyl anion, a very powerful base, and a very poor leaving group.

(b) The reaction will not take place because the leaving group would have to be a hydride ion, a very powerful base, and a very poor leaving group.

(c) The reaction will not take place because the leaving group would have to be a carbanion, a very powerful base, and a very poor leaving group.



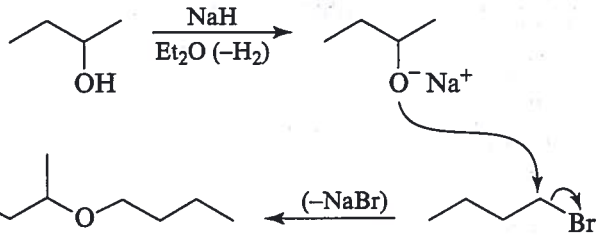
(d) The reaction will not take place because the leaving group would have to be a CH_3O^- ion, a strong base, and a very poor leaving group.



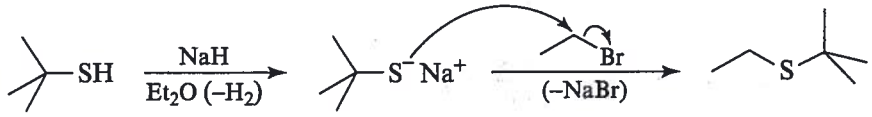
(e) The reaction will not take place because the first reaction that would take place would be an acid-base reaction that would convert the ammonia to an ammonium ion. An ammonium ion, because it lacks an electron pair, is not nucleophilic.



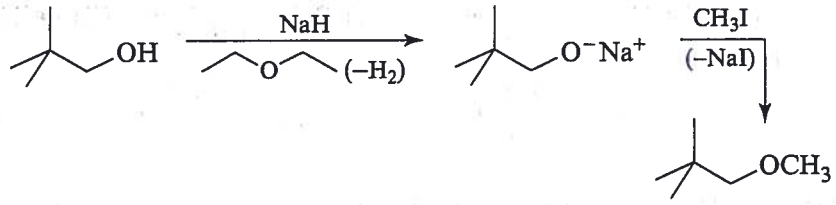
6.26 (a)



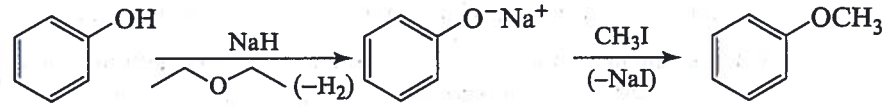
(b)



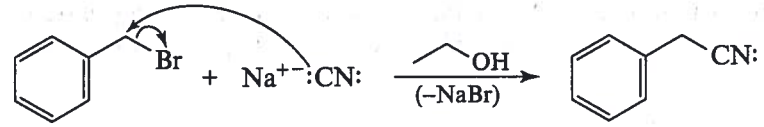
(c)



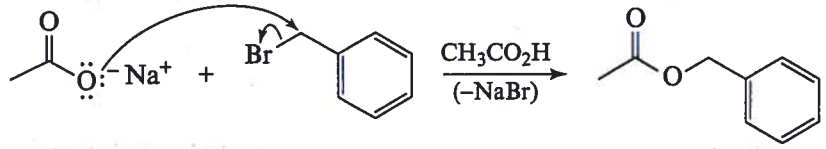
(d)



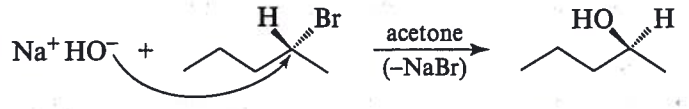
(e)



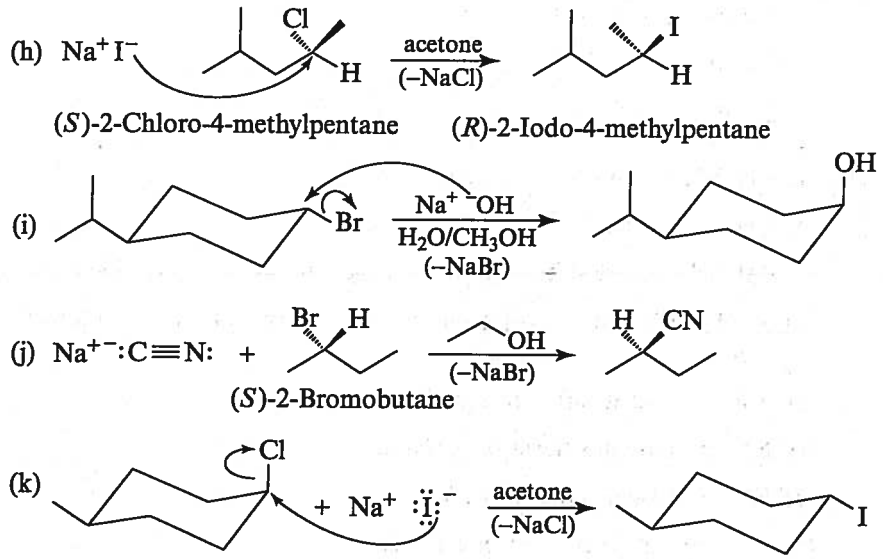
(f)



(g)

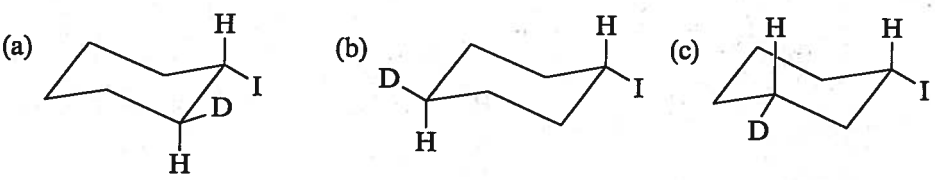


(*R*)-2-Bromopentane (*S*)-2-Pentanol

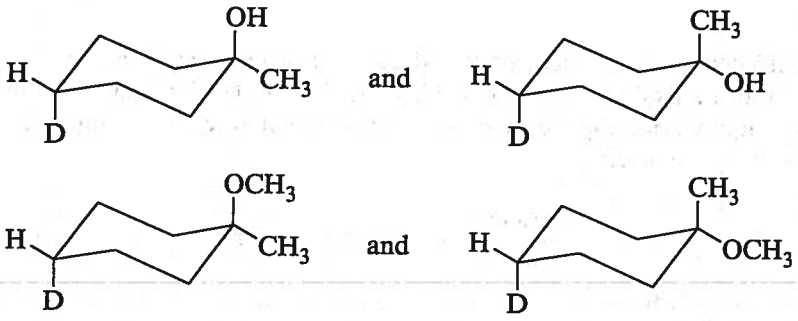


General S_N1 and S_N2

6.27 (a), (b), and (c) are all S_N2 reactions and, therefore, proceed with inversion of configuration. The products are



(d) is an S_N1 reaction. The carbocation that forms can react with either nucleophile (H_2O or CH_3OH) from either the top or bottom side of the molecule. Four substitution products (below) would be obtained. (Considerable elimination by an E1 path would also occur.)



6.28 (a) S_N2 because the substrate is a 1° halide.

(b) Rate = $k\,[CH_3CH_2Cl][I^-]$

$= 5 \times 10^{-5}\ L\ mol^{-1}s^{-1} \times 0.1\ mol\ L^{-1} \times 0.1\ mol\ L^{-1}$

Rate = $5 \times 10^{-7}\ mol\ L^{-1}s^{-1}$