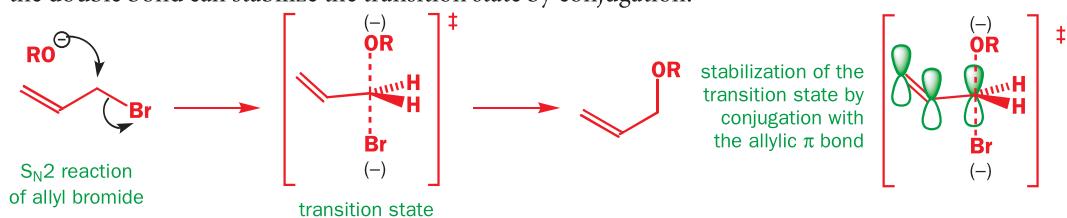


### Structural variation and the S<sub>N</sub>2 mechanism

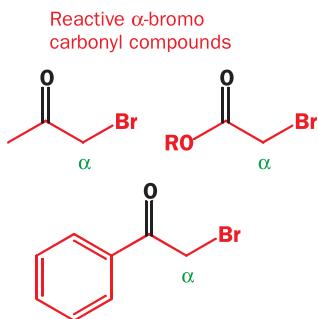
We have already established that methyl and primary alkyl compounds react well by the S<sub>N</sub>2 mechanism, while secondary alkyl compounds *can* do so. There are other important structural features that also encourage the S<sub>N</sub>2 mechanism. Two, allyl and benzyl compounds, also encourage the S<sub>N</sub>1 mechanism.

Here you see a typical S<sub>N</sub>2 reaction of allyl bromide. We have drawn the transition state for this reaction. This is not because we want to encourage you to do this for all S<sub>N</sub>2 reactions but so that we can explain the role of the allyl system. Allyl compounds react rapidly by the S<sub>N</sub>2 mechanism because the double bond can stabilize the transition state by conjugation.



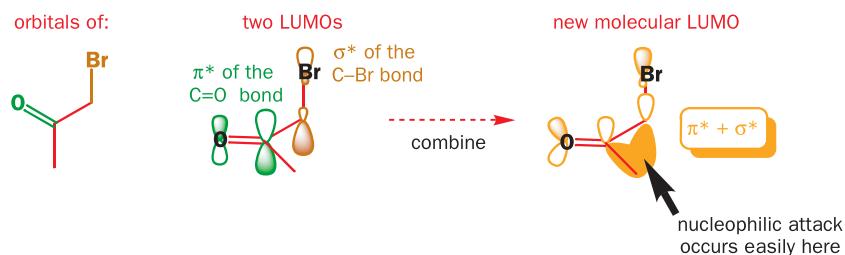
The benzyl group acts in much the same way using the  $\pi$  system of the benzene ring for conjugation with the p orbital in the transition state.

S<sub>N</sub>2 reaction of benzyl bromide



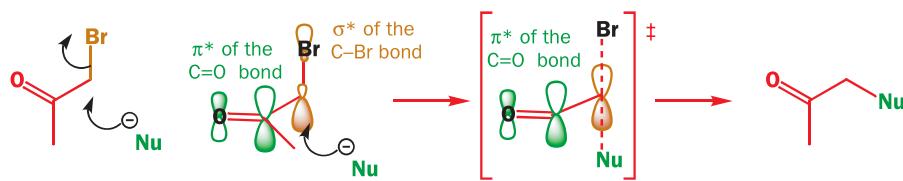
Since the p orbital in question has electrons in it—it shares a pair of electrons with the nucleophile and the leaving group—more effective conjugation is possible with an electron-deficient  $\pi$  bond. The most important example is the carbonyl group: carbon electrophiles like those in the margin give the fastest S<sub>N</sub>2 reactions.

With  $\alpha$ -bromo carbonyl compounds, substitution leads to two electrophilic groups on neighbouring carbon atoms. Each has a low-energy empty orbital,  $\pi^*$  from C=O and  $\sigma^*$  from C-Br (this is what makes them electrophilic), and these can combine to form a molecular LUMO ( $\pi^* + \sigma^*$ ) lower in energy than either. Nucleophilic attack will occur easily where this new orbital has its largest coefficients, shown in orange on the diagram.

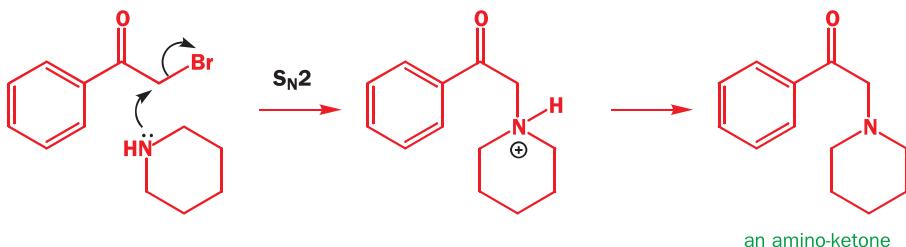


This orange area is on one side of the carbonyl group and in the usual place at the back of the C-Br bond. Each group has become more electrophilic because of the presence of the other—the C=O group makes the C-Br bond more reactive and the Br makes the C=O group more reactive. Another way to put this is that the carbonyl group stabilizes the transition state by overlap of its  $\pi^*$  orbital with the full p orbital of the carbon atom under attack. The nucleophile may well attack the carbonyl group but this will be reversible whereas displacement of bromide is irreversible.

transition state for nucleophilic attack on an  $\alpha$ -bromo-ketone



There are many examples of this type of reaction. Reactions with amines go well and the amino-ketone products are widely used in the synthesis of drugs.



### Variation of rate with structure

Some actual data may help at this point. The rates of reaction of the following alkyl chlorides with KI in acetone at 50 °C broadly confirm the patterns we have just analysed. These are relative rates with respect to *n*-BuCl

as a 'typical primary halide'. You should not take too much notice of precise figures but rather observe the trends and notice that the variations are quite large—the full range from 0.02 to 100 000 is eight powers of ten.



**Table 17.10 Relative rates of S<sub>N</sub>2 reactions of alkyl chlorides with the iodide ion**

| Alkyl chloride | Relative rate | Comments   |
|----------------|---------------|--|
| Me—Cl          | 200           | least hindered alkyl chloride  |
|                | 0.02          | secondary alkyl chloride; slow because of steric hindrance   |
|                | 79            | allyl chloride accelerated by $\pi$ conjugation in transition state  |
|                | 200           | benzyl chloride slightly more reactive than allyl: benzene ring better at $\pi$ conjugation than isolated double bond                                      |
|                | 920           | conjugation with oxygen lone pair accelerates reaction   |
|                | 100 000       | conjugation with carbonyl group much more effective than with simple alkene or benzene ring. These $\alpha$ -carbonyl halides are the most reactive of all |