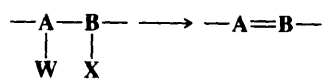
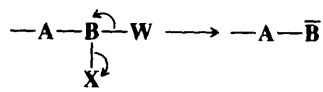
17
ELIMINATIONS

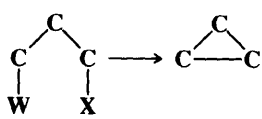
When two groups are lost from adjacent atoms so that a new double (or triple) bond is



formed the reaction is called β *elimination*; one atom is the α, the other the β atom. In an α elimination both groups are lost from the same atom to give a carbene (or a nitrene):



In a γ elimination, a three-membered ring is formed:



Some of these processes were discussed in Chapter 10. Another type of elimination involves the expulsion of a fragment from within a chain or ring (X—Y—Z → X—Z + Y). Such reactions are called *extrusion reactions*. This chapter discusses β elimination and (beginning on p. 1045) extrusion reactions; however, β elimination in which both X and W are hydrogens are oxidation reactions and are treated in Chapter 19.

MECHANISMS AND ORIENTATION

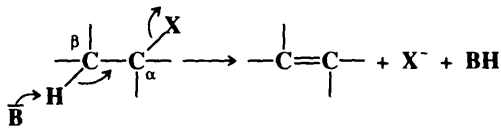
β elimination reactions may be divided into two types; one type taking place largely in solution, the other (pyrolytic eliminations) mostly in the gas phase. In the reactions in solution one group leaves with its electrons and the other without, the latter most often being hydrogen. In these cases we refer to the former as the leaving group or nucleofuge. For pyrolytic eliminations there are two principal mechanisms, one pericyclic and the other a free-radical pathway. A few photochemical eliminations are also known (the most important is Norrish type II cleavage of ketones, p. 243), but these are not generally of synthetic importance[1] and will not be discussed further. In most β eliminations the new bonds are

[1]For synthetically useful examples of Norrish type II cleavage, see Neckers; Kellogg; Prins; Schoustra *J. Org. Chem.* **1971**, *36*, 1838.

C=C or C≡C; our discussion of mechanisms is largely confined to these cases.[2] Mechanisms in solution (E2, E1, E1cB) are discussed first.

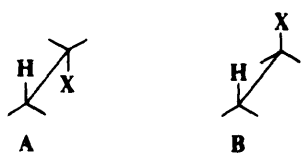
The E2 Mechanism

In the E2 mechanism (elimination, bimolecular), the two groups depart simultaneously, with the proton being pulled off by a base:



The mechanism thus takes place in one step and kinetically is second order: first order in substrate and first order in base. The IUPAC designation is $A_xH D_H D_N$, or more generally (to include cases where the electrofuge is not hydrogen), $A_n D_E D_N$. It is analogous to the SN2 mechanism (p. 294) and often competes with it. With respect to the substrate, the difference between the two pathways is whether the species with the unshared pair attacks the carbon (and thus acts as a nucleophile) or the hydrogen (and thus acts as a base). As in the case of the SN2 mechanism, the leaving group may be positive or neutral and the base may be negatively charged or neutral.

Among the evidence for the existence of the E2 mechanism are: (1) the reaction displays the proper second-order kinetics; (2) when the hydrogen is replaced by deuterium in second-order eliminations, there is an isotope effect of from 3 to 8, consistent with breaking of this bond in the rate-determining step.[3] However, neither of these results alone could prove an E2 mechanism, since both are compatible with other mechanisms also (e.g., see E1cB p. 991). The most compelling evidence for the E2 mechanism is found in stereochemical studies.[4] As will be illustrated in the examples below, the E2 mechanism is stereospecific: the five atoms involved (including the base) in the transition state must be in one plane. There are two ways for this to happen. The H and X may be trans to one another (**A**) with a dihedral angle of 180°, or they may be cis (**B**) with a dihedral angle of 0°.[5] Conformation



[2]For a monograph on elimination mechanisms, see Saunders; Cockerill *Mechanisms of Elimination Reactions*; Wiley: New York, 1973. For reviews, see Gandler, in Patai *Supplement A: The Chemistry of Double-bonded Functional Groups*, vol. 2, pt. 1; Wiley: New York, 1989, pp. 733-797; Aleskerov; Yufit; Kucherov *Russ. Chem. Rev.* **1978,** *47*, 134-147; Cockerill; Harrison, in Patai *The Chemistry of Functional Groups, Supplement A*, pt. 1; Wiley: New York, 1977, pp. 153-221; Willi *Chimia* **1977,** *31*, 93-101; More O'Ferrall, in Patai *The Chemistry of the Carbon-Halogen Bond*, pt. 2; Wiley: New York, 1973, pp. 609-675; Cockerill, in Bamford; Tipper *Comprehensive Chemical Kinetics*, vol. 9; Elsevier: New York, 1973, pp. 163-372; Saunders *Acc. Chem. Res.* **1976,** *9*, 19-25; Stirling *Essays Chem.* **1973,** *5*, 123-149; Bordwell *Acc. Chem. Res.* **1972,** *5*, 374-381; Fry *Chem. Soc. Rev.* **1972,** *1*, 163-210; LeBel *Adv. Alicyclic Chem.* **1971,** *3*, 195-290; Bunnett *Surv. Prog. Chem.* **1969,** *5*, 53-93; in Patai *The Chemistry of Alkenes*, vol. 1; Wiley: New York, 1964, the articles by Saunders, pp. 149-201 (eliminations in solution); and by Maccoll, pp. 203-240 (pyrolytic eliminations); Köbrich *Angew. Chem. Int. Ed. Engl.* **1965,** *4*, 49-68, pp. 59-63 [*Angew. Chem.* 77, 75-94] (for the formation of triple bonds).

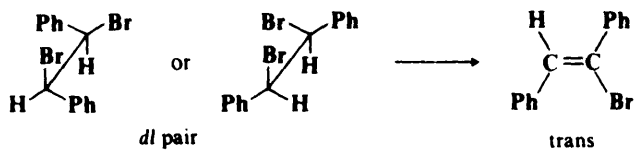
[3]See, for example, Saunders; Edison *J. Am. Chem. Soc.* **1960,** *82*, 138; Shiner; Smith *J. Am. Chem. Soc.* **1958,** *80*, 4095, **1961,** *83*, 593. For a review of isotope effects in elimination reactions, see Fry, Ref. 2.

[4]For reviews, see Bartsch; Závada *Chem. Rev.* **1980,** *80*, 453-494; Coke *Sel. Org. Transform.* **1972,** *2*, 269-307; Sicher *Angew. Chem. Int. Ed. Engl.* **1972,** *11*, 200-214 [*Angew. Chem. 84*, 177-191], *Pure Appl. Chem.* **1971,** *25*, 655-666; Saunders; Cockerill, Ref. 2, pp. 105-163; Cockerill, Ref. 2, pp. 217-235; More O'Ferrall, Ref. 2, pp. 630-640.

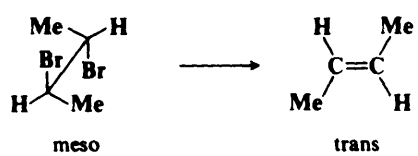
[5]DePuy; Morris; Smith; Smat *J. Am. Chem. Soc.* **1965,** *87*, 2421.

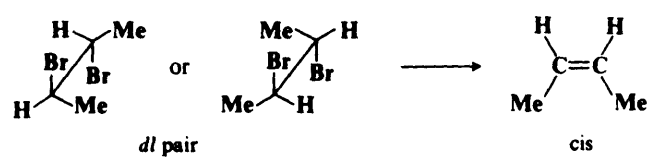
A is called *anti-periplanar*, and this type of elimination, in which H and X depart in opposite directions, is called *anti elimination*. Conformation **B** is *syn-periplanar*, and this type of elimination, with H and X leaving in the same direction, is called *syn elimination*. Many examples of both kinds have been discovered. In the absence of special effects (discussed below) anti elimination is usually greatly favored over syn elimination, probably because **A** is a staggered conformation (p. 139) and the molecule requires less energy to reach this transition state than it does to reach the eclipsed transition state **B**. A few of the many known examples of predominant or exclusive anti elimination follow.

1. Elimination of HBr from *meso*-1,2-dibromo-1,2-diphenylethane gave *cis*-2-bromostilbene, while the (+) or (−) isomer gave the trans olefin. This stereospecific result, which



was obtained in 1904,[6] demonstrates that in this case elimination is anti. Many similar examples have been discovered since. Obviously, this type of experiment need not be restricted to compounds that have a meso form. Anti elimination requires that an erythro *dl* pair (or either isomer) give the cis olefin, and the threo *dl* pair (or either isomer) give the trans isomer, and this has been found many times. Anti elimination has also been demonstrated in cases where the electrofuge is not hydrogen. In the reaction of 2,3-dibromobutane with iodide ion, the two bromines are removed (**7-29**). In this case the meso compound gave the trans olefin and the *dl* pair the cis:[7]

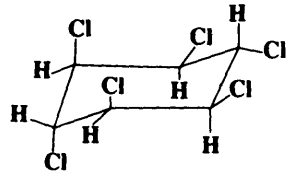




2. In open-chain compounds the molecule can usually adopt that conformation in which H and X are anti-periplanar. However, in cyclic systems this is not always the case. There

[6]Pfeiffer *Z. Phys. Chem.* **1904,** *48*, 40.
[7]Winstein; Pressman; Young *J. Am. Chem. Soc.* **1939,** *61*, 1645.

are nine stereoisomers of 1,2,3,4,5,6-hexachlorocyclohexane: seven meso forms and a *dl* pair (see p. 131). Four of the meso compounds and the *dl* pair (all that were then known) were subjected to elimination of HCl. Only one of these (**1**) has no Cl trans to an H. Of



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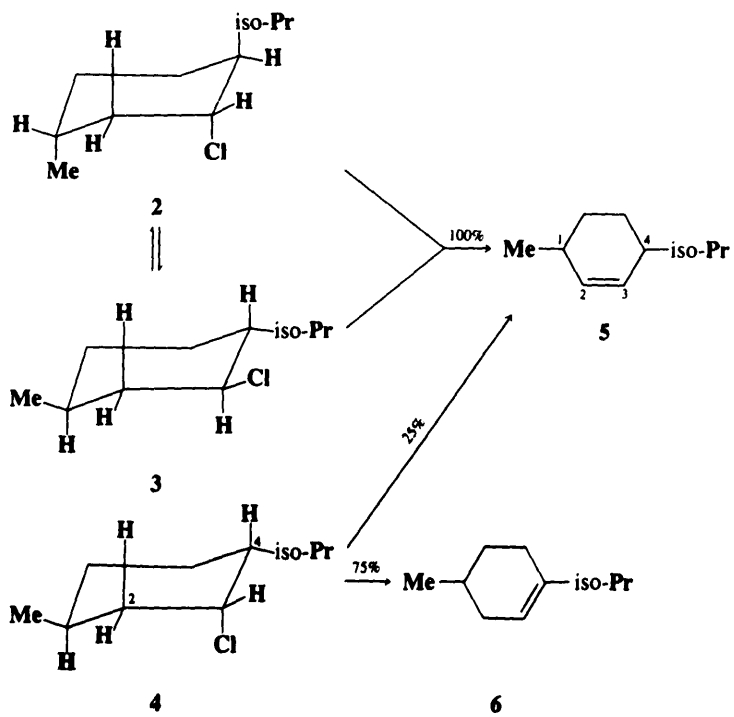
the other isomers, the fastest elimination rate was about three times as fast as the slowest, but the rate for **1** was 7000 times slower than that of the slowest of the other isomers.[8] This result demonstrates that with these compounds anti elimination is greatly favored over syn elimination, though the latter must be taking place on **1**, very slowly, to be sure.

3. The preceding result shows that elimination of HCl in a six-membered ring proceeds best when the H and X are trans to each other. However, there is an additional restriction. Adjacent trans groups on a six-membered ring can be diaxial or diequatorial (p. 144) and the molecule is generally free to adopt either conformation, though one may have a higher energy than the other. Anti-periplanarity of the leaving groups requires that they be diaxial, even if this is the conformation of higher energy. The results with menthyl and neomenthyl chlorides are easily interpretable on this basis. Menthyl chloride has two chair conformations,



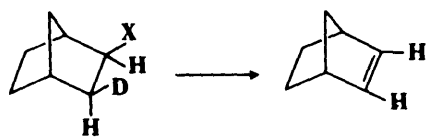
[8]Cristol *J. Am. Chem. Soc.* **1947**, *69*, 338; Cristol; Hause; Meek *J. Am. Chem. Soc.* **1951**, *73*, 674.

2 and **3**. **3**, in which the three substituents are all equatorial, is the more stable. The more stable chair conformation of neomenthyl chloride is **4**, in which the chlorine is axial; there are axial hydrogens on both C-2 and C-4. The results are: neomenthyl chloride gives rapid E2 elimination and the olefin produced is predominantly **6** (**6**/**5** ratio is about 3:1) in accord with Zaitsev's rule (p. 998). Since an axial hydrogen is available on both sides, this factor does not control the direction of elimination and Zaitsev's rule is free to operate. However, for menthyl chloride, elimination is much slower and the product is entirely the anti-Zaitsev **5**. It is slow because the unfavorable conformation **2** has to be achieved before elimination can take place, and the product is **5** because only on this side is there an axial hydrogen.[9]

4. That anti elimination also occurs in the formation of triple bonds is shown by elimination from *cis*- and *trans*-HOOC—CH=CCl—COOH. In this case the product in both cases is HOOCC≡CCOOH, but the trans isomer reacts about 50 times faster than the cis compound.[10]

Some examples of syn elimination have been found in molecules where H and X could not achieve an anti-periplanar conformation.

1. The deuterated norbornyl bromide (**7**, X = Br) gave 94% of the product containing no deuterium.[11] Similar results were obtained with other leaving groups and with bicy-



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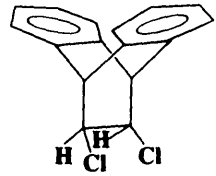
clo[2.2.2] compounds.[12] In these cases the exo X group cannot achieve a dihedral angle of 180° with the endo β hydrogen because of the rigid structure of the molecule. The dihedral angle here is about 120°. These leaving groups prefer syn elimination with a dihedral angle of about 0° to anti elimination with an angle of about 120°.

2. The molecule **8** is a particularly graphic example of the need for a planar transition state. In **8** each Cl has an adjacent hydrogen trans to it, and if planarity of leaving groups



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were not required, anti elimination could easily take place. However, the crowding of the rest of the molecule forces the dihedral angle to be about 120°, and elimination of HCl from

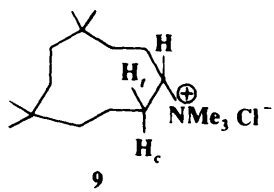
[9]Hughes; Ingold; Rose *J. Chem. Soc.* **1953**, 3839.
[10]Michael *J. Prakt. Chem.* **1895**, *52*, 308. See also Marchese; Naso; Modena *J. Chem. Soc. B* **1968**, 958.
[11]Kwart; Takeshita; Nyce *J. Am. Chem. Soc.* **1964**, *86*, 2606.
[12]For example, see Bird; Cookson; Hudec; Williams *J. Chem. Soc.* **1963**, 410; Stille; Sonnenberg; Kinstle *J. Am. Chem. Soc.* **1966**, *88*, 4922; Coke; Cooke *J. Am. Chem. Soc.* **1967**, *89*, 6701; DePuy; Naylor; Beckman *J. Org. Chem.* **1970**, *35*, 2750; Brown; Liu *J. Am. Chem. Soc.* **1970**, *92*, 200; Sicher; Pánkova, Závada; Kniežo; Orahovats *Collect. Czech. Chem. Commun.* **1971**, *36*, 3128; Bartsch; Lee *J. Org. Chem.* **1991**, *56*, 212, 2579.

8 is much slower than from corresponding nonbridged compounds.[13] (Note that syn elimination from **8** is even less likely than anti elimination.) Syn elimination can take place from the trans isomer of **8** (dihedral angle about 0°); this isomer reacted about eight times faster than **8**.[13]

The examples so far given illustrate two points. (1) Anti elimination *requires* a dihedral angle of 180°. When this angle cannot be achieved, anti elimination is greatly slowed or prevented entirely. (2) For the simple systems so far discussed syn elimination is not found to any significant extent unless anti elimination is greatly diminished by failure to achieve the 180° angle.

As noted in Chapter 4 (p. 156), six-membered rings are the only ones among rings of four to thirteen members in which strain-free anti-periplanar conformations can be achieved. It is not surprising, therefore, that syn elimination is least common in six-membered rings. Cooke and Coke subjected cycloalkyltrimethylammonium hydroxides to elimination (**7-6**) and found the following percentages of syn elimination with ring size: four-membered, 90%; five-membered, 46%; six-membered, 4% seven-membered, 31 to 37%.[14] It should be noted that the NMe_3^+ group has a greater tendency to syn elimination than do other common leaving groups such as OTs, Cl, and Br.

Other examples of syn elimination have been found in medium-ring compounds, where both cis and trans olefins are possible (p. 128). As an illustration, we can look at experiments performed by Závada, Svoboda, and Sicher.[15] These workers subjected 1,1,4,4-tetramethyl-7-cyclodecyltrimethylammonium chloride (**9**) to elimination and obtained mostly *trans*- but



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trans and cis olefins

also some *cis*-tetramethylcyclodecenes as products. (Note that *trans*-cyclodecenes, though stable, are less stable than the cis isomers). In order to determine the stereochemistry of the reaction, they repeated the elimination, this time using deuterated substrates. They found that when **9** was deuterated in the trans position (H_t = D), there was a substantial isotope effect in the formation of *both* cis and trans olefins, but when **9** was deuterated in the cis position (H_c = D), there was *no* isotope effect in the formation of either olefin. Since an isotope effect is expected for an E2 mechanism,[16] these results indicated that *only* the trans hydrogen (H_t) was lost, whether the product was the cis or the trans isomer.[17] This in turn means that the cis isomer must have been formed by anti elimination and the trans isomer by syn elimination. (Anti elimination could take place from approximately the conformation shown, but for syn elimination the molecule must twist into a conformation in which the C—H_t and C—NMe_3^+ bonds are syn-periplanar.) This remarkable result, called the *syn-anti dichotomy*, has also been demonstrated by other types of evidence.[18] The fact

[13]Cristol; Hause *J. Am. Chem. Soc.* **1952,** *74*, 2193.

[14]Cooke; Coke *J. Am. Chem. Soc.* **1968,** *90*, 5556. See also Coke; Smith; Britton *J. Am. Chem. Soc.* **1975,** *97*, 4323.

[15]Závada; Svoboda; Sicher *Tetrahedron Lett.* **1966,** 1627, *Collect. Czech. Chem. Commun.* **1968,** *33*, 4027.

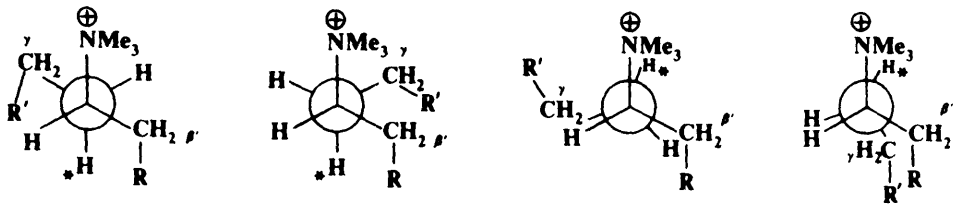
[16]Other possible mechanisms, such as E1cB (p. 991) or α',β elimination (p. 1018), were ruled out in all these cases by other evidence.

[17]This conclusion has been challenged by Coke, Ref. 4.

[18]Sicher; Závada; Krupička *Tetrahedron Lett.* **1966,** 1619; Sicher; Závada *Collect. Czech. Chem. Commun.* **1967,** *32*, 2122; Závada; Sicher *Collect. Czech. Chem. Commun.* **1967,** *32*, 3701. For a review, see Bartsch; Závada, Ref. 4.

that syn elimination in this case predominates over anti (as indicated by the formation of trans isomer in greater amounts than cis) has been explained by conformational factors.[19] The syn-anti dichotomy has also been found in other medium-ring systems (8- to 12-membered),[20] though the effect is greatest for 10-membered rings. With leaving groups,[21] the extent of this behavior decreases in the order $NMe_3^+ > OTs > Br > Cl$, which parallels steric requirements. When the leaving group is uncharged, syn elimination is favored by strong bases and by weakly ionizing solvents.[22]

Syn elimination and the syn-anti dichotomy have also been found in open-chain systems, though to a lesser extent than in medium-ring compounds. For example, in the conversion of 3-hexyl-4-*d*-trimethylammonium ion to 3-hexene with potassium *sec*-butoxide, about 67% of the reaction followed the syn-anti dichotomy.[23] In general syn elimination in open-chain systems is only important in cases where certain types of steric effect are present. One such type is compounds in which substituents are found on both the β′ and the γ carbons (the unprimed letter refers to the branch in which the elimination takes place). The factors that cause these results are not completely understood, but the following conformational effects have been proposed as a partial explanation.[24] The two anti- and two syn-periplanar conformations are, for a quaternary ammonium salt:



In order for an E2 mechanism to take place a base must approach the proton marked *. In **C** this proton is shielded on both sides by R and R′. In **D** the shielding is on only one side. Therefore, when anti elimination does take place in such systems, it should give more cis product than trans. Also, when the normal anti elimination pathway is hindered sufficiently to allow the syn pathway to compete, the anti → trans route should be diminished more than the anti → cis route. When syn elimination begins to appear, it seems clear that **E**, which is less eclipsed than **F**, should be the favored pathway and syn elimination should generally give the trans isomer. In general, deviations from the syn-anti dichotomy are greater on the trans side than on the cis. Thus, trans olefins are formed partly or mainly by syn elimination, but cis olefins are formed entirely by anti elimination. Predominant syn

[19]For discussions, see Ref. 4.

[20]For example, see Coke; Mourning *J. Am. Chem. Soc.* **1968,** *90*, 5561, where the experiment was performed on cyclooctyltrimethylammonium hydroxide, and *trans*-cyclooctene was formed by a 100% syn mechanism, and *cis*-cyclooctene by a 51% syn and 49% anti mechanism.

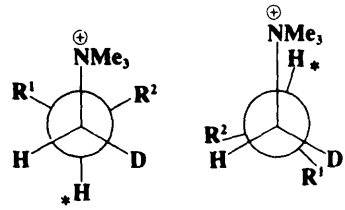
[21]For examples with other leaving groups, see Závada; Krupička; Sicher *Chem. Commun.* **1967,** 66, *Collect. Czech. Chem. Commun.* **1968,** *33*, 1393; Sicher; Jan; Schlosser *Angew. Chem. Int. Ed. Engl.* **1971,** *10*, 926 [*Angew. Chem. 83*, 1012]; Závada; Pánková *Collect. Czech. Chem. Commun.* **1980,** *45*, 2171.

[22]See, for example, Sicher; Závada *Collect. Czech. Chem. Commun.* **1968,** *33*, 1278.

[23]Bailey; Saunders *Chem. Commun.* **1968,** 1598, *J. Am. Chem. Soc.* **1970,** *92*, 6904. For other examples of syn elimination and the syn-anti dichotomy in open-chain systems, see Pánková; Sicher; Závada *Chem. Commun.* **1967,** 394; Pánková; Vítek; Vašíčková; Řeřicha; Závada *Collect. Czech. Chem. Commun.* **1972,** *37*, 3456; Schlosser; An *Helv. Chim. Acta* **1979,** *62*, 1194; Sugita; Nakagawa; Nishimoto; Kasai; Ichikawa *Bull. Chem. Soc. Jpn.* **1979,** *52*, 871; Pánková; Kocián; Krupička; Závada *Collect. Czech. Chem. Commun.* **1983,** *48*, 2944.

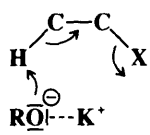
[24]Bailey; Saunders, Ref. 23; Chiao; Saunders *J. Am. Chem. Soc.* **1977,** *99*, 6699.

elimination has also been found in compounds of the form $R^1R^2CHCHDNMe_3^+$, where R^1 and R^2 are both bulky.[25] In this case also the conformation leading to syn elimination (**H**) is less strained than **G**, which gives anti elimination. **G** has three bulky groups (including NMe_3^+) in the gauche position to each other.



G **H**

It was mentioned above that weakly ionizing solvents promote syn elimination when the leaving group is uncharged. This is probably caused by ion pairing, which is greatest in nonpolar solvents.[26] Ion pairing can cause syn elimination with an uncharged leaving group by means of the transition state shown in **10.** This effect was graphically illustrated by



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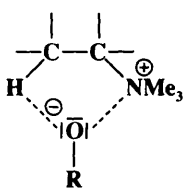
elimination from 1,1,4,4-tetramethyl-7-cyclodecyl bromide.[27] The ratio of syn to anti elimination when this compound was treated with *t*-BuOK in the nonpolar benzene was 55.0. But when the crown ether dicyclohexano-18-crown-6 was added (this compound selectively removes K^+ from the *t*-BuO^- K^+ ion pair and thus leaves *t*-BuO^- as a free ion), the syn/anti ratio decreased to 0.12. Large decreases in the syn/anti ratio on addition of the crown ether were also found with the corresponding tosylate and with other nonpolar solvents.[28] However, with positively charged leaving groups the effect is reversed. Here, ion pairing *increases* the amount of anti elimination.[29] In this case a relatively free base (e.g., PhO^-) can be attracted to the leaving group, putting it in a favorable position for attack on the syn β hydrogen, while ion pairing would reduce this attraction.



[25]Tao; Saunders *J. Am. Chem. Soc.* **1983,** *105*, 3183; Dohner; Saunders *J. Am. Chem. Soc.* **1986,** *108*, 245.

[26]For reviews of ion pairing in this reaction, see Bartsch; Závada, Ref. 4; Bartsch *Acc. Chem. Res.* **1975,** *8*, 239-245.

[27]Svoboda; Hapala; Závada *Tetrahedron Lett.* **1972,** 265.

[28]For other examples of the effect of ion pairing, see Bayne; Snyder *Tetrahedron Lett.* **1971,** 571; Bartsch; Wiegers *Tetrahedron Lett.* **1972,** 3819; Fiandanese; Marchese; Naso; Sciacovelli *J. Chem. Soc., Perkin Trans. 2* **1973,** 1336; Borchardt; Swanson; Saunders *J. Am. Chem. Soc.* **1974,** *96*, 3918; Mano; Sera; Maruyama *Bull. Chem. Soc. Jpn.* **1974,** *47*, 1758; Závada; Pánková; Svoboda *Collect. Czech. Chem. Commun.* **1976,** *41*, 3778; Baciocchi; Ruzziconi; Sebastiani *J. Org. Chem.* **1979,** *44*, 3718; Croft; Bartsch *Tetrahedron Lett.* **1983,** *24*, 2737; Kwart; Gaffney; Wilk *J. Chem. Soc., Perkin Trans. 2* **1984,** 565.

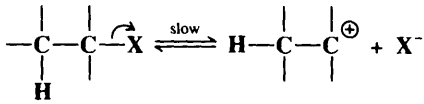
[29]Borchardt; Saunders *J. Am. Chem. Soc.* **1974,** *96*, 3912.

We can conclude that anti elimination is generally favored in the E2 mechanism, but that steric (inability to form the anti-periplanar transition state), conformational, ion-pairing, and other factors cause syn elimination to intervene (and even predominate) in some cases.

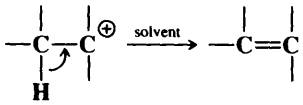
The E1 Mechanism

The E1 mechanism is a two-step process in which the rate-determining step is ionization of the substrate to give a carbocation that rapidly loses a β proton to a base, usually the solvent:

Step 1



Step 2

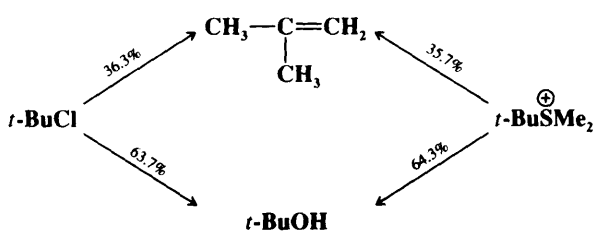


The IUPAC designation is $D_N + D_E$ (or $D_N + D_H$). This mechanism normally operates without an *added* base. Just as the E2 mechanism is analogous to and competes with the SN2, so is the E1 mechanism related to the SN1. In fact, the first step of the E1 is exactly the same as that of the SN1 mechanism. The second step differs in that the solvent pulls a proton from the β carbon of the carbocation rather than attacking it at the positively charged carbon, as in the SN1 process. In a pure E1 reaction (i.e., without ion pairs, etc.) the product should be completely nonstereospecific, since the carbocation is free to adopt its most stable conformation before giving up the proton.

Some of the evidence for the E1 mechanism is as follows:

1. The reaction exhibits first-order kinetics (in substrate) as expected. Of course the solvent is not expected to appear in the rate equation, even if it were involved in the rate-determining step (p. 222), but this point can be easily checked by adding a small amount of the conjugate base of the solvent. It is generally found that such an addition does not increase the rate of the reaction. If this more powerful base does not enter into the rate-determining step, it is unlikely that the solvent does. An example of an E1 mechanism with a rate-determining second step (proton transfer) has been reported.[30]

2. If the reaction is performed on two molecules that differ only in the leaving group (for example, *t*-BuCl and *t*-$BuSMe_2^+$), the rates should obviously be different, since they depend on the ionizing ability of the molecule. However, once the carbocation is formed, if the solvent and the temperature are the same, it should suffer the same fate in both cases, since the nature of the leaving group does not affect the second step. This means that *the ratio of elimination to substitution should be the same*. The compounds mentioned in the example were solvolyzed at 65.3°C in 80% aqueous ethanol with the following results:[31]



[30]Baciocchi; Clementi; Sebastiani; Ruzziconi *J. Org. Chem.* **1979**, *44*, 32.
[31]Cooper; Hughes; Ingold; MacNulty *J. Chem. Soc.* **1948**, 2038.

Although the rates were greatly different (as expected with such different leaving groups), the product ratios were the same, within 1%. If this had taken place by a second-order mechanism, the nucleophile would not be expected to have the same ratio of preference for attack at the β hydrogen compared to attack at a *neutral* chloride as for attack at the β hydrogen compared to attack at a *positive* SMe_2 group.

3. Many reactions carried out under first-order conditions on systems where E2 elimination is anti proceed quite readily to give olefins where a cis hydrogen must be removed, often in preference to the removal of a trans hydrogen. For example, menthyl chloride (**2,** p. 985), which by the E2 mechanism gave only **5,** under E1 conditions gave 68% **6** and 32% **5,** since the steric nature of the hydrogen is no longer a factor here, and the more stable olefin (Zaitsev's rule, p. 998) is predominantly formed.

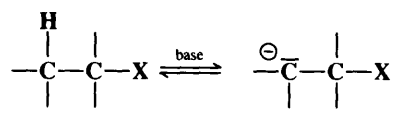
4. If carbocations are intermediates, we should expect rearrangements with suitable substrates. These have often been found in elimination reactions performed under E1 conditions.

E1 reactions can involve ion pairs, just as is true for SN1 reactions (p. 302).[32] This effect is naturally greatest for nondissociating solvents: it is least in water, greater in ethanol, and greater still in acetic acid. It has been proposed that the ion-pair mechanism (p. 305) extends to elimination reactions too, and that the SN1, SN2, E1, and E2 mechanisms possess in common an ion-pair intermediate, at least occasionally.[33]

The E1cB Mechanism[34]

In the E1 mechanism, X leaves first and then H. In the E2 mechanism the two groups leave at the same time. There is a third possibility: the H leaves first and then the X. This is a two-step process, called the *E1cB mechanism*, or the *carbanion mechanism*, since the intermediate is a carbanion:

Step 1



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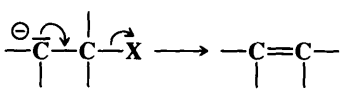
Step 2



The name E1cB comes from the fact that it is the conjugate base of the substrate that is giving up the leaving group (see the SN1cB mechanism, p. 356). The IUPAC designation is $A_nD_E + D_N$ or $A_{xh}D_H + D_N$ (see p. 290). We can distinguish three limiting cases: (1) The carbanion returns to starting material faster than it forms product: step 1 is reversible;

[32]Cocivera; Winstein *J. Am. Chem. Soc.* **1963,** *85,* 1702; Smith; Goon *J. Org. Chem.* **1969,** *34,* 3127; Bunnett; Eck *J. Org. Chem.* **1971,** *36,* 897; Sridharan; Vitullo *J. Am. Chem. Soc.* **1977,** *99,* 8093; Seib; Shiner; Sendijarević; Humski *J. Am. Chem. Soc.* **1978,** *100,* 8133; Jansen; Koshy; Mangru; Tidwell *J. Am. Chem. Soc.* **1981,** *103,* 3863; Coxon; Simpson; Steel; Whiteling *Tetrahedron* **1984,** *40,* 3503; Thibblin *J. Am. Chem. Soc.* **1987,** *109,* 2071, *J. Phys. Org. Chem.* **1989,** *2,* 15.

[33]Sneen; Robbins *J. Am. Chem. Soc.* **1969,** *91,* 3100, Sneen *Acc. Chem. Res.* **1973,** 6, 46-53. See, however, McLennan *J. Chem. Soc., Perkin Trans. 2* **1972,** 1577.

[34]For reviews, see Cockerill; Harrison, Ref. 2, pp. 158-178; Hunter *Intra-Sci. Chem. Rep.* **1973,** 7(3), 19-26; McLennan *Q. Rev., Chem. Soc.* **1967,** *21,* 490-506. For a general discussion, see Koch *Acc. Chem. Res.* **1984,** *17,* 137-144.

step 2 is slow. (2) Step 1 is the slow step, and formation of product is faster than return of the carbanion to starting material. In this case step 1 is essentially irreversible. (3) Step 1 is rapid, and the carbanion goes slowly to product. This case occurs only with the most stable carbanions. Here, too, step 1 is essentially irreversible. These cases have been given the designations: (1) $(E1cB)_R$, (2) $(E1cB)_I$ (or $E1cB_{irr}$), and (3) $(E1)_{anion}$. Their characteristics are listed in Table 17.1.[35] Investigations of the reaction order are generally not very useful (except for case 3 which is first order), because cases 1 and 2 are second order and thus difficult or impossible to distinguish from the E2 mechanism by this procedure.[36] We would expect the greatest likelihood of finding the E1cB mechanism in substrates that have (a) a poor nucleofuge and (b) an acidic hydrogen, and most investigations have concerned such substrates. The following is some of the evidence in support of the E1cB mechanism.

1. The first step of the $(E1cB)_R$ mechanism involves a reversible exchange of protons between the substrate and the base. In that case, if deuterium is present in the base, recovered starting material should contain deuterium. This was found to be the case in the treatment of $Cl_2C{=}CHCl$ with NaOD to give $ClC{\equiv}CCl$. When the reaction was stopped before completion, there *was* deuterium in the recovered olefin.[37] A similar result was found for pentahaloethanes.[38] These substrates are relatively acidic. In both cases the electron-withdrawing halogens increase the acidity of the hydrogen, and in the case of trichloroethylene there is the additional factor that a hydrogen on an sp^2 carbon is more acidic than one on an sp^3 carbon (p. 269). Thus, the E1cB mechanism is more likely to be found in eliminations yielding triple bonds than in those giving double bonds. Another likely place for the E1cB mechanism should be in reaction of a substrate like $PhCH_2CH_2Br$, since the carbanion is stabilized by resonance with the phenyl group. Nevertheless, no deuterium exchange was found here.[39] If this type of evidence is a guide, then it may be inferred that the $(E1cB)_R$ mechanism is quite rare, at least for eliminations with common leaving groups such as Br, Cl, or OTs, which yield C=C double bonds.

2. When the reaction

$$p\text{-}NO_2C_6H_4{-}CH_2{-}CH_2{-}NR_3^+ + B^- \longrightarrow p\text{-}NO_2C_6H_4{-}CH{=}CH_2 + BH + NR_3$$

was carried out in water containing acetohydroxamate buffers, a plot of the rate against the buffer concentration was curved and the rate leveled off at high buffer concentrations, indicating a change in rate-determining step.[40] This rules out an E2 mechanism, which has only one step. When D_2O was used instead of H_2O as solvent, there was an initial inverse solvent isotope effect of 7.7 (the highest inverse solvent isotope effect yet reported). That is, the reaction took place faster in D_2O than in H_2O. This is compatible only with an E1cB mechanism in which the proton-transfer step is not entirely rate-determining. The isotope effect arises from a partitioning of the carbanion intermediate **11.** This intermediate either can go to product or it can revert to starting compound, which requires taking a proton from the solvent. In D_2O the latter process is slower (because the O—D bond of D_2O cleaves less easily than the O—H bond of H_2O), reducing the rate at which **11** returns to

[35]This table, which appears in Cockerill; Harrison, Ref. 2, p. 161, was adapted from a longer one in Bordwell, Ref. 2, p. 375.

[36]$(E1cB)_I$ cannot be distinguished from E2 by this means, because it has the identical rate law: Rate = k[substrate][B^-]. The rate law for $(E1cB)_R$ is different: Rate = k[substrate][B^-]/[BH], but this is often not useful because the only difference is that the rate is also dependent (inversely) on the concentration of the conjugate acid of the base, and this is usually the solvent, so that changes in its concentration cannot be measured.

[37]Houser; Bernstein; Miekka; Angus *J. Am. Chem. Soc.* **1955,** *77*, 6201.

[38]Hine; Wiesboeck; Ghirardelli *J. Am. Chem. Soc.* **1961,** *83*, 1219; Hine; Wiesboeck; Ramsay *J. Am. Chem. Soc.* **1961,** *83*, 1222.

[39]Skell; Hauser *J. Am. Chem. Soc.* **1945,** *67*, 1661.

[40]Keeffe; Jencks *J. Am. Chem. Soc.* **1983,** *105*, 265.

TABLE 17.1 Kinetic predictions for base-induced β-eliminations[35]

$$\overline{B} + (D)H-C_\beta-C_\alpha-X \longrightarrow BH + C=C + \overline{X}$$

Mechanism	Kinetic[a] order	β-hydrogen exchange faster than elimination	General or specific base catalysis	k_H/k_D	Electron withdrawal at C_β[d]	Electron release at C_α[d]	Leaving-group isotope effect or element effect
$(E1)_{anion}$	1	Yes	General[c]	1.0	Rate decrease	Rate increase	Substantial
$(E1cB)_R$	2	Yes	Specific	1.0	Small rate increase	Small rate increase	Substantial
$(E1cB)_{ip}$	2	No	General[e]	1.0 → 1.2	Small rate increase	Small rate increase	Substantial
$(E1cB)_I$	2	No	General	2 → 8	Rate increase	Little effect	Small to negligible
E2[b]	2	No	General	2 → 8	Rate increase	Small rate increase	Small

[a]All mechanisms exhibit first-order kinetics in substrate.
[b]Only transition states with considerable carbanion character considered in this table.
[c]Specific base catalysis predicted if extent of substrate ionization reduced from almost complete.
[d]Effect on rate assuming no change in mechanism is caused; steric factors upon substitution at C_α and C_β have not been considered. The rate predictions are geared to substituent effects such as those giving rise to Hammett reaction constants on β- and α-aryl substitution.
[e]Depends on whether ion pair assists in removal of leaving group.

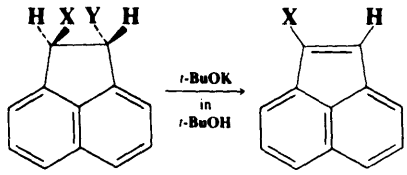
starting compound. With the return reaction competing less effectively, the rate of conversion of **11** to product is increased.

3. We have predicted that the E1cB mechanism would be most likely to be found with substrates containing acidic hydrogens and poor leaving groups. Compounds of the type ZCH_2CH_2OPh, where Z is an electron-withdrawing group (e.g., NO_2, SMe_2^+, $ArSO_2$, CN, COOR, etc.), belong to this category, because OPh is a very poor leaving group (p. 352). There is much evidence to show that the mechanism here is indeed E1cB.[41] Isotope effects, measured for $MeSOCD_2CH_2OPh$ and $Me_2\overset{\oplus}{S}CD_2CH_2OPh$ with NaOD in D_2O, are about 0.7. This is compatible with an $(E1cB)_R$ mechanism, but not with an E2 mechanism for which an isotope effect of perhaps 5 might be expected (of course, an E1 mechanism is precluded by the extremely poor nucleofugal ability of OPh). The fact that k_H/k_D is less than the expected value of 1 is attributable to solvent and secondary isotope effects. Among other evidence for an E1cB mechanism in these systems is that changes in the identity of Z had a dramatic effect on the relative rates: a span of 10^{11} between NO_2 and COO^-. Note that elimination from substrates of the type $RCOCH_2CH_2Y$ is the reverse of Michael-type addition to C=C bonds. We have seen (p. 741) that such addition involves initial attack by a nucleophile Y and subsequent attack by a proton. Thus the initial loss of a proton from substrates of this type (i.e., an E1cB mechanism) is in accord with the principle of microscopic reversibility.[42] It may also be recalled that benzyne formation (p. 647) can occur by such a

[41]Crosby; Stirling *J. Chem. Soc. B* **1970,** 671, 679; Redman; Stirling *Chem. Commun.* **1970,** 633; Cann; Stirling *J. Chem. Soc., Perkin Trans. 2* **1974,** 820. For other examples; see Fedor *J. Am. Chem. Soc.* **1969,** *91*, 908; More O'Ferrall; Slae *J. Chem. Soc. B* **1970,** 260; Kurzawa; Leffek *Can. J. Chem.* **1977,** *55*, 1696.
[42]Patai; Weinstein; Rappoport *J. Chem. Soc.* **1962,** 1741. See also Hilbert; Fedor *J. Org. Chem.* **1978,** *43*, 452.

process. It has been suggested that all base-initiated eliminations wherein the proton is activated by a strong electron-withdrawing group are E1cB reactions,[43] but there is evidence that this is not the case—that when there is a good nucleofuge, the mechanism is E2 even when strong electron-withdrawing groups are present.[44] On the other hand, Cl^- has been found to be a leaving group in an E1cB reaction.[45]

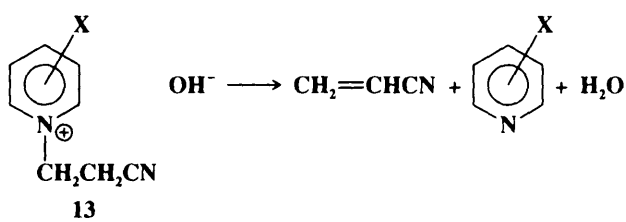
Of the three cases of the E1cB mechanism, the one most difficult to distinguish from E2 is $(E1cB)_I$. One way to make this distinction is to study the effect of a change in leaving group. This was done in the case of the three acenaphthylenes **12,** where it was found that (1) the three rates were fairly similar, the largest being only about four times that of the



	X	Y
a	Br	Cl
b	Cl	Cl
c	Cl	F

12

smallest, and (2) in compound c (X = Cl, Y = F), the only product contained Cl and no F, i.e., only the poorer nucleofuge F departed while Cl remained.[46] Result (1) rules out all the E1cB mechanisms except $(E1cB)_I$, because the others should all have considerable leaving group effects (Table 17.1). An ordinary E2 mechanism should also have a large leaving group effect, but an E2 mechanism with substantial carbanionic character (see the next section) might not. However, no E2 mechanism can explain result (2), which can be explained by the fact that an α Cl is more effective than an α F in stabilizing the planar carbanion that remains when the proton is lost. Thus (as in the somewhat similar case of aromatic nucleophilic substitution, see p. 653), when X^- leaves in the second step, the one that leaves is not determined by which is the better nucleofuge, but by which has had its β hydrogen removed.[47] Additional evidence for the existence of the $(E1cB)_I$ mechanism was the observation of a change in the rate-determining step in the elimination reaction of N-(2-cyanoethyl)pyridinium ions **13,** treated with base, when X was changed.[48] Once again,



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the demonstration that two steps are involved precludes the one-step E2 mechanism.

[43]Bordwell; Vestling; Yee *J. Am. Chem. Soc.* **1970,** *92,* 5950; Bordwell, Ref. 2.

[44]Marshall; Thomas; Stirling *J. Chem. Soc., Perkin Trans. 2,* **1977,** 1898, 1914; Fishbein; Jencks *J. Am. Chem. Soc.* **1988,** *110,* 5075, 5087; Banait; Jencks *J. Am. Chem. Soc.* **1990,** *112,* 6950.

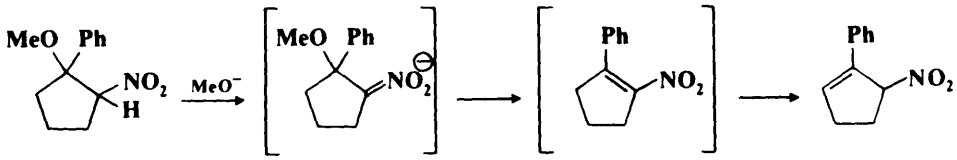
[45]Ölwegård; McEwen; Thibblin; Ahlberg *J. Am. Chem. Soc.* **1985,** *107,* 7494.

[46]Baciocchi; Ruzziconi; Sebastiani *J. Org. Chem.* **1982,** *47,* 3237.

[47]For other evidence for the existence of the $(E1cB)_I$ mechanism, see Bordwell; Vestling; Yee, Ref. 43; Fedor; Glave *J. Am. Chem. Soc.* **1971,** *93,* 985; Redman; Thomas; Stirling *J. Chem. Soc., Perkin Trans. 2* **1978,** 1135; Thibblin *Chem. Scr.* **1980,** *15,* 121; Carey; More O'Ferrall; Vernon *J. Chem. Soc., Perkin Trans. 2* **1982,** 1581; Baciocchi; Ruzziconi *J. Org. Chem.* **1984,** *49,* 3395; Jarczewski; Waligorska; Leffek *Can. J. Chem.* **1985,** *63,* 1194; Gula; Vitale; Dostal; Trometer; Spencer *J. Am. Chem. Soc.* **1988,** *110,* 4400; Garay; Cabaleiro *J. Chem. Res. (S)* **1988,** 388; Gandler; Storer; Ohlberg *J. Am. Chem. Soc.* **1990,** *112,* 7756.

[48]Bunting; Toth; Heo; Moors *J. Am. Chem. Soc.* **1990,** *112,* 8878. See also Bunting; Kanter *J. Am. Chem. Soc.* **1991,** *113,* 6950.

4. An example of an $(E1)_{anion}$ mechanism has been found with the substrate **14,** which when treated with methoxide ion undergoes elimination to **16,** which is unstable under the

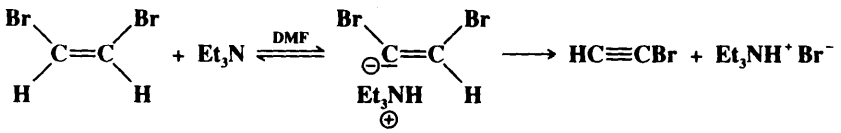


14 **15** **16**

reaction conditions and rearranges as shown.[49] Among the evidence for the proposed mechanism in this case were kinetic and isotope-effect results, as well as the spectral detection of **15.**[50]

5. In many eliminations to form C=O and C≡N bonds the initial step is loss of a positive group (normally a proton) from the oxygen or nitrogen. These may also be regarded as E1cB processes.

There is evidence that some E1cB mechanisms can involve carbanion ion pairs, e.g.,[51]



This case is designated $(E1cB)_{ip}$; its characteristics are shown in Table 17.1.

The E1–E2–E1cB Spectrum

In the three mechanisms so far considered the similarities are greater than the differences. In each case there is a leaving group that comes off with its pair of electrons and another group (usually hydrogen) that comes off without them. The only difference is in the order of the steps. It is now generally accepted that there is a spectrum of mechanisms ranging from one extreme, in which the leaving group departs well before the proton (pure E1), to the other extreme, in which the proton comes off first and then, after some time, the leaving group follows (pure E1cB). The *pure* E2 case would be somewhere in the middle, with both groups leaving simultaneously. However, most E2 reactions are not exactly in the middle, but somewhere to one side or the other. For example, the nucleofuge might depart just before the proton. This case may be described as an E2 reaction with a small amount of E1 character. The concept can be expressed by the question: In the transition state, which bond (C—H or C—X) has undergone more cleavage?[52]

[49]Bordwell; Yee; Knipe *J. Am. Chem. Soc.* **1970,** *92,* 5945.

[50]For other examples of this mechanism, see Rappoport *Tetrahedron Lett.* **1968,** 3601; Berndt *Angew. Chem. Int. Ed. Engl.* **1969,** *8,* 613 [*Angew. Chem. 81,* 567]; Albeck; Hoz; Rappoport *J. Chem. Soc., Perkin Trans. 2* **1972,** 1248, **1975,** 628.

[51]Kwok; Lee; Miller *J. Am. Chem. Soc.* **1969,** *91,* 468. See also Lord; Naan; Hall *J. Chem. Soc. B* **1971,** 220; Rappoport; Shohamy *J. Chem. Soc. B* **1971,** 2060; Fiandanese; Marchese; Naso *J. Chem. Soc., Chem. Commun.* **1972,** 250; Koch; Dahlberg; Toczko; Solsky *J. Am. Chem. Soc.* **1973,** *95,* 2029; Hunter; Shearing *J. Am. Chem. Soc.* **1973,** *95,* 8333; Thibblin; Ahlberg *J. Am. Chem. Soc.* **1977,** *99,* 7926, **1979,** *101,* 7311; Thibblin; Bengtsson; Ahlberg *J. Chem. Soc., Perkin Trans. 2* **1977,** 1569; Petrillo; Novi; Garbarino; Dell'Erba; Mugnoli *J. Chem. Soc., Perkin Trans. 2* **1985,** 1291.

[52]For discussions, see Cockerill; Harrison, Ref. 2, pp. 178-189; Saunders *Acc. Chem. Res.*, Ref. 2; Bunnett, Ref. 2; Saunders; Cockerill, Ref. 2, pp. 47-104; Bordwell, Ref. 2.

One way to determine just where a given reaction stands on the E1–E2–E1cB spectrum is to study isotope effects, which ought to tell something about the behavior of bonds in the transition state.[53] For example, $CH_3CH_2NMe_3^+$ showed a nitrogen isotope effect (k^{14}/k^{15}) of 1.017, while $PhCH_2CH_2NMe_3^+$ gave a corresponding value of 1.009.[54] It would be expected that the phenyl group would move the reaction toward the E1cB side of the line, which means that for this compound the C—N bond is not as greatly broken in the transition state as it is for the unsubstituted one. The isotope effect bears this out, for it shows that in the phenyl compound, the mass of the nitrogen has less effect on the reaction rate than it does in the unsubstituted compound. Similar results have been obtained with SR_2^+ leaving groups by the use of $^{32}S/^{34}S$ isotope effects[55] and with Cl ($^{35}Cl/^{37}Cl$).[56] The position of reactions along the spectrum has also been studied from the other side of the newly forming double bond by the use of H/D and H/T isotope effects,[57] though interpretation of these results is clouded by the fact that β hydrogen isotope effects are expected to change smoothly from small to large to small again as the degree of transfer of the β hydrogen from the β carbon to the base increases[58] (recall—p. 227—that isotope effects are greatest when the proton is half-transferred in the transition state), by the possibility of secondary isotope effects (e.g., the presence of a β deuterium or tritium may cause the leaving group to depart more slowly), and by the possibility of tunneling[59] (see footnote 55 in Chapter 6). Other isotope-effect studies have involved labeled α or β carbon, labeled α hydrogen, or labeled base.[53]

Another way to study the position of a given reaction on the spectrum involves the use of β aryl substitution. Since a positive Hammet ρ value is an indication of a negatively charged transition state, the ρ value for substituted β aryl groups should increase as a reaction moves from E1-like to E1cB-like along the spectrum. This has been shown to be the case in a number of studies;[60] e.g., ρ values of $ArCH_2CH_2X$ increase as the leaving-group ability of X decreases. A typical set of ρ values was: X = I, 2.07; Br, 2.14; Cl, 2.61; SMe_2^+, 2.75; F, 3.12.[61] As we have seen, decreasing leaving-group ability correlates with increasing E1cB character.

Still another method measures volumes of activation.[62] These are negative for E2 and positive for E1cB mechanisms. Measurement of the activation volume therefore provides a continuous scale for deciding just where a reaction lies on the spectrum.

[53]For a review, see Fry, Ref. 2. See also Hasan; Sims; Fry. *J. Am. Chem. Soc.* **1983,** *105*, 3967; Pulay; Fry *Tetrahedron Lett.* **1986,** *27*, 5055.

[54]Ayrey; Bourns; Vyas *Can. J. Chem.* **1963,** *41*, 1759. Also see Simon; Müllhofer *Chem. Ber.* **1963,** 96, 3167, **1964,** *97*, 2202, *Pure Appl. Chem.* **1964,** *8*, 379, 536; Smith; Bourns *Can. J. Chem.* **1970,** *48*, 125.

[55]Saunders; Zimmerman *J. Am. Chem. Soc.* **1964,** *86*, 3789; Wu; Hargreaves; Saunders *J. Org. Chem.* **1985,** *50*, 2392.

[56]Grout; McLennan; Spackman *J. Chem. Soc., Perkin Trans. 2* **1977,** 1758.

[57]For example, see Saunders; Edison *J. Am. Chem. Soc.* **1960,** *82*, 138; Hodnett; Sparapany *Pure Appl. Chem.* **1964,** *8*, 385, 537; Finley; Saunders *J. Am. Chem. Soc.* **1967,** *89*, 898; Ghanbarpour; Willi *Liebigs Ann. Chem.* **1975,** 1295; Simon; Müllhofer, Ref. 54; Thibblin *J. Am. Chem. Soc.* **1988,** *110*, 4582; Smith; Amin *Can. J. Chem.* **1989,** *67*, 1457.

[58]There is controversy as to whether such an effect has been established in this reaction: See Cockerill *J. Chem. Soc. B* **1967,** 964; Blackwell *J. Chem. Soc., Perkin Trans. 2* **1976,** 488.

[59]For examples of tunneling in elimination reactions, see Miller; Saunders *J. Org. Chem.* **1981,** *46*, 4247 and previous papers in this series. See also Shiner; Smith, Ref. 3; McLennan *J. Chem. Soc., Perkin Trans. 2* **1977,** 1753; Fouad; Farrell *Tetrahedron Lett.* **1978,** 4735; Koth; McLennan; Koch; Tumas; Dobson; Koch *J. Am. Chem. Soc.* **1983,** *105*, 1930; Kwart; Wilk *J. Org. Chem.* **1985,** *50*, 817; Amin; Price; Saunders *J. Am. Chem. Soc.* **1990,** *112*, 4467.

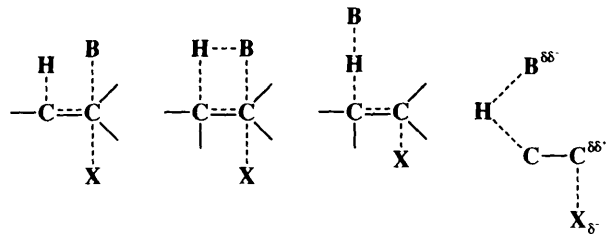
[60]Saunders; Bushman; Cockerill *J. Am. Chem. Soc.* **1968,** *90*, 1775; Oae; Yano *Tetrahedron* **1968,** *24*, 5721; Yano; Oae *Tetrahedron* **1970,** *26*, 27, 67; Blackwell; Buckley; Jolley; MacGibbon *J. Chem. Soc., Perkin Trans. 2* **1973,** 169; Smith; Tsui *J. Am. Chem. Soc.* **1973,** *95*, 4760, *Can. J. Chem.* **1974,** *52*, 749.

[61]DePuy; Froemsdorf *J. Am. Chem. Soc.* **1957,** *79*, 3710; DePuy; Bishop *J. Am. Chem. Soc.* **1960,** *82*, 2532, 2535.

[62]Brower; Muhsin; Brower *J. Am. Chem. Soc.* **1976,** *98*, 779. For a review, see van Eldik; Asano; le Noble *Chem. Rev.* **1989,** *89*, 549-688.

The E2C Mechanism[63]

Certain alkyl halides and tosylates undergo E2 eliminations faster when treated with such weak bases as Cl^- in polar aprotic solvents or PhS^- than with the usual E2 strong bases such as RO^- in ROH.[64] In order to explain these results Parker and co-workers proposed[65] that there is a spectrum[66] of E2 transition states in which the base can interact in the transition state with the α carbon as well as with the β hydrogen. At one end of this spectrum is a mechanism (called E2C) in which, in the transition state, the base interacts mainly with the



E2C **17** E2H **18**

carbon. The E2C mechanism is characterized by strong nucleophiles that are weak bases. At the other extreme is the normal E2 mechanism, here called E2H to distinguish it from E2C, characterized by strong bases. **17** represents a transition state between these extremes. Additional evidence[67] for the E2C mechanism is derived from Brønsted equation considerations (p. 258), from substrate effects, from isotope effects, and from the effects of solvents on rates.

However, the E2C mechanism has been criticized, and it has been contended that all the experimental results can be explained by the normal E2 mechanism.[68] McLennan has suggested that the transition state is that shown as **18.**[69] An ion-pair mechanism has also been proposed.[70] Although the actual mechanisms involved may be a matter of controversy, there is no doubt that a class of elimination reactions exists that is characterized by second-order attack by weak bases.[71] These reactions also have the following general characteris-

[63]For reviews, see McLennan *Tetrahedron* **1975,** *31*, 2999-3010; Ford *Acc. Chem. Res.* **1973,** 6, 410-415; Parker *CHEMTECH* **1971,** 297-303.

[64]For example; see Winstein; Darwish; Holness *J. Am. Chem. Soc.* **1956,** *78*, 2915; de la Mare; Vernon *J. Chem. Soc.* **1956,** 41; Eliel; Ro *Tetrahedron* **1958,** *2*, 353; Bunnett; Davis; Tanida *J. Am. Chem. Soc.* **1962,** *84*, 1606; McLennan *J. Chem. Soc. B* **1966,** 705, 709; Hayami; Ono; Kaji *Bull. Chem. Soc. Jpn.* **1971,** *44*, 1628.

[65]Parker; Ruane; Biale; Winstein *Tetrahedron Lett.* **1968,** 2113.

[66]This is apart from the E1–E2–E1cB spectrum.

[67]Lloyd; Parker *Tetrahedron Lett.* **1968,** 5183, **1970,** 5029; Cook; Parker; Ruane *Tetrahedron Lett.* **1968,** 5715; Alexander; Ko; Parker; Broxton *J. Am. Chem. Soc.* **1968,** *90*, 5049; Ko; Parker *J. Am. Chem. Soc.* **1968,** *90*, 6447; Parker; Ruane; Palmer; Winstein *J. Am. Chem. Soc.* **1972,** *94*, 2228; Biale; Parker; Stevens; Takahashi; Winstein *J. Am. Chem. Soc.* **1972,** *94*, 2235; Cook; Hutchinson; Parker *J. Org. Chem.* **1974,** *39*, 3029; Cook; Hutchinson; MacLeod; Parker *J. Org. Chem.* **1974,** *39*, 534; Cook *J. Org. Chem.* **1976,** *41*, 2173; Muir; Parker *Aust. J. Chem.* **1983,** *36*, 1667; Kwart; Wilk *J. Org. Chem.* **1985,** *50*, 3038.

[68]Anderson; Ang; England; McCann; McLennan *Aust. J. Chem.* **1969,** *22*, 1427; Bunnett; Baciocchi *J. Org. Chem.* **1967,** *32*, 11, **1970,** *35*, 76; Jackson; McLennan; Short; Wong *J. Chem. Soc., Perkin Trans. 2* **1972,** 2308; McLennan; Wong *Tetrahedron Lett.* **1970,** 881, *J. Chem. Soc., Perkin Trans. 2* **1972,** 279, **1974,** 1818; Bunnett; Eck *J. Am. Chem. Soc.* **1973,** *95*, 1897, 1900; Ford; Pietsek *J. Am. Chem. Soc.* **1975,** *97*, 2194; Loupy *Bull. Soc. Chim. Fr.* **1975,** 2662; Miller; Saunders *J. Am. Chem. Soc.* **1979,** *101*, 6749; Bunnett; Sridharan; Cavin *J. Org. Chem.* **1979,** *44*, 1463; Bordwell; Mrozack *J. Org. Chem.* **1982,** *47*, 4813; Bunnett; Migdal *J. Org. Chem.* **1989,** *54*, 3037, 3041.

[69]McLennan, Ref. 63, *J. Chem. Soc., Perkin Trans. 2* **1977,** 293, 298; McLennan; Lim *Aust. J. Chem.* **1983,** *36*, 1821. For an opposing view, see Kwart; Gaffney *J. Org. Chem.* **1983,** *48*, 4502.

[70]Ford, Ref. 63.

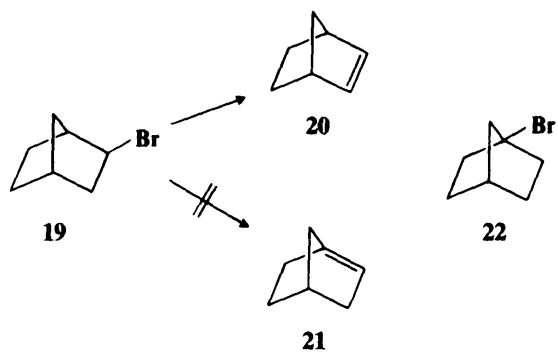
[71]For convenience, we will refer to this class of reactions as E2C reactions, though the actual mechanism is in dispute.

tics:[72] (1) they are favored by good leaving groups; (2) they are favored by polar aprotic solvents; (3) the reactivity order is tertiary > secondary > primary, the opposite of the normal E2 order (p. 1003); (4) the elimination is always anti (syn elimination is not found), but in cyclohexyl systems, a diequatorial anti elimination is about as favorable as a diaxial anti elimination (unlike the normal E2 reaction, p. 985); (5) they follow Zaitsev's rule (see below), where this does not conflict with the requirement for anti elimination.

Orientation of the Double Bond

With some substrates, a β hydrogen is present on only one carbon and (barring rearrangements) there is no doubt as to the identity of the product. For example, $PhCH_2CH_2Br$ can give only $PhCH{=}CH_2$. However, in many other cases two or three olefinic products are possible. In the simplest such case, a *sec*-butyl compound can give either 1-butene or 2-butene. There are a number of rules that enable us to predict, in many instances, which product will predominantly form.[73]

1. No matter what the mechanism, a double bond does not go to a bridgehead carbon unless the ring sizes are large enough (Bredt's rule, see p. 160). This means, for example, not only that **19** gives only **20** and not **21** (indeed **21** is not a known compound), but also that **22** does not undergo elimination.



2. No matter what the mechanism, if there is a double bond (C=C or C=O) or an aromatic ring already in the molecule that can be in conjugation with the new double bond, the conjugated product usually predominates, sometimes even when the stereochemistry is unfavorable (for an exception, see p. 1001).

3. In the E1 mechanism the leaving group is gone before the choice is made as to which direction the new double bond takes. Therefore the direction is determined almost entirely by the relative stabilities of the two (or three) possible olefins. In such cases *Zaitsev's rule*[74] *operates*. This rule states that *the double bond goes mainly toward the most highly substituted carbon*. That is, a *sec*-butyl compound gives more 2-butene than 1-butene, and 3-bromo-

[72]Biale; Parker; Smith; Stevens; Winstein *J. Am. Chem. Soc.* **1970,** *92*, 115; Lloyd; Muir; Parker *Tetrahedron Lett.* **1971,** 3015; Beltrame; Biale; Lloyd; Parker; Ruane; Winstein *J. Am. Chem. Soc.* **1972,** *94*, 2240; Beltrame; Ceccon; Winstein *J. Am. Chem. Soc.* **1972,** *94*, 2315.

[73]For a review of orientation in cycloalkyl systems, see Hückel; Hanack *Angew. Chem. Int. Ed. Engl.* **1967,** 6, 534-544 [*Angew. Chem.* 79, 555-565].

[74]Often given the German spelling: Saytzeff.

2,3-dimethylpentane gives more 2,3-dimethyl-2-pentene than either 3,4-dimethyl-2-pentene or 2-ethyl-3-methyl-1-butene. Thus Zaitsev's rule predicts that the olefin predominantly formed will be the one with the largest possible number of alkyl groups on the C=C carbons, and in most cases this is what is found. From heat of combustion data (see p. 23) it is known that olefin stability increases with alkyl substitution, though just why this should be is a matter of conjecture. The most common explanation is hyperconjugation. For E1 eliminations Zaitsev's rule governs the orientation whether the leaving group is neutral or positive, since, as already mentioned, the leaving group is not present when the choice of direction is made. This statement does not hold for E2 eliminations, and it may be mentioned here, for contrast with later results, that E1 elimination of $Me_2CHCHMeSMe_2^+$ gave 91% of the Zaitsev product and 9% of the other.[75] However, there *are* cases in which the leaving group affects the direction of the double bond in E1 eliminations.[76] This may be attributed to ion pairs; that is, the leaving group is not completely gone when the hydrogen departs. Zaitsev's rule breaks down in cases where the non-Zaitsev product is more stable for steric reasons. For example, E1 or E1-like eliminations of 1,2-diphenyl-2-X-propanes $PhMeCXCH_2Ph$ were reported to give about 50% $CH_2{=}CPhCH_2Ph$, despite the fact that the double bond of the Zaitsev product ($PhMeC{=}CHPh$) is conjugated with two benzene rings.[77]

4. For the anti E2 mechanism a trans β proton is necessary; if this is available in only one direction, that is the way the double bond will form. Because of the free rotation in acyclic systems (except where steric hindrance is great), this is a factor only in cyclic systems. Where trans β hydrogens are available on two or three carbons, two types of behavior are found, depending on substrate structure and the nature of the leaving group. Some compounds follow Zaitsev's rule and give predominant formation of the most highly substituted olefin, but others follow *Hofmann's rule: the double bond goes mainly toward the least highly substituted carbon*. Though many exceptions are known, the following general statements can be made: In most cases, compounds containing uncharged nucleofuges (those that come off as negative ions) follow Zaitsev's rule, just as they do in E1 elimination, no matter what the structure of the substrate. However, elimination from compounds with charged nucleofuges, e.g., NR_3^+, SR_2^+ (those that come off as neutral molecules), follow Hofmann's rule if the substrate is acyclic,[78] but Zaitsev's rule if the leaving group is attached to a six-membered ring.[79]

Much work has been devoted to searching for the reasons for the differences in orientation. Since Zaitsev orientation almost always gives the thermodynamically more stable isomer, what needs to be explained is why in some cases the less stable Hofmann product predominates. Three explanations have been offered for the change in orientation in acyclic systems with a change from uncharged to charged nucleofuges. The first of these, by Hughes and Ingold,[80] is that Hofmann orientation is caused by the fact that the acidity of the β hydrogen is decreased by the presence of the electron-donating alkyl groups. For example, under E2 conditions $Me_2CHCHMeSMe_2^+$ gives more of the Hofmann product; it is the more acidic hydrogen that is removed by the base.

[75]de la Mare *Prog. Stereochem.* **1954,** *1*, 112.

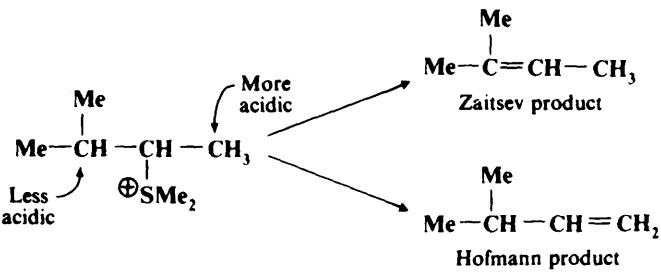
[76]Cram; Sahyun *J. Am. Chem. Soc.* **1963,** *85*, 1257; Silver *J. Am. Chem. Soc.* **1961,** *83*, 3482.

[77]Ho; Smith *Tetrahedron* **1970,** *26*, 4277.

[78]An example of an acyclic quaternary ammonium salt that follows Zaitsev's rule is found in Feit; Saunders *J. Am. Chem. Soc.* **1970,** *92*, 5615.

[79]For examples where Zaitsev's rule is followed with charged leaving groups in cyclohexyl systems, see Gent; McKenna *J. Chem. Soc* **1959,** 137; Hughes; Wilby *J. Chem. Soc.* **1960,** 4094; Brownlee; Saunders *Proc. Chem. Soc.* **1961,** *314*; Booth; Franklin; Gidley *J. Chem. Soc. C* **1968,** 1891. For a discussion of the possible reasons for this, see Saunders; Cockerill, Ref. 2, pp. 192-193.

[80]For summaries of this position, see Ingold *Proc. Chem. Soc.* **1962,** 265-274; Banthorpe; Hughes; Ingold *J. Chem. Soc.* **1960,** 4054.



Of course, the CH_3 hydrogens would still be more acidic than the Me_2CH hydrogen even if a neutral leaving group were present, but the explanation of Hughes and Ingold is 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.[80] The explanation of Bunnett[81] is similar. According to this, the change to a positive leaving group causes the mechanism to shift toward the E1cB end of the spectrum, where there is more C—H bond breaking in the rate-determining step and where, consequently, acidity is more important. In this view, when there is a neutral leaving group, the mechanism is more E1-like, C—X bond breaking is more important, and olefin stability determines the direction of the new double bond. The third explanation, by H. C. Brown, is completely different. In this picture, field effects are unimportant, and the difference in orientation is largely a steric effect caused by the fact that charged groups are usually larger than neutral ones. A CH_3 group is more open to attack than a CH_2R group and a CHR_2 group is still less easily attacked. Of course, these considerations also apply when the leaving group is neutral, but, according to Brown, they are much less important here because the neutral groups are smaller and do not block access to the hydrogens as much. Brown showed that Hofmann elimination increases with the size of the leaving group. Thus the percentage of 1-ene obtained from $CH_3CH_2CH_2CHXCH_3$ was as follows (X listed in order of increasing size): Br, 31%; I, 30%; OTs, 48%; SMe_2^+, 87%; SO_2Me, 89%; NMe_3^+, 98%.[82] Hofmann elimination was also shown to increase with increase in bulk of the substrate.[83] With large enough compounds, Hofmann orientation can be obtained even with halides, e.g., *t*-amyl bromide gave 89% of the Hofmann product. Even those who believe in the acidity explanations concede that these steric factors operate in extreme cases.[84]

There is one series of results incompatible with the steric explanation—E2 elimination from the four 2-halopentanes gave the following percentages of 1-pentene: F, 83%; Cl, 37%; Br, 25%; I, 20%.[85] The same order was found for the four-2-halohexanes.[86] Although there is some doubt about the relative steric requirements of Br, Cl, and I, there is no doubt that F is the smallest of the halogens, and if the steric explanation were the only valid one, the fluoroalkanes could not give predominant Hofmann orientation. Another result that argues against the steric explanation is the effect of changing the nature of the base. An experiment in which the effective size of the base was kept constant while its basicity was increased (by

[81]Bunnett, Ref. 2.
[82]Brown; Wheeler *J. Am. Chem. Soc.* **1956,** *78*, 2199.
[83]Brown; Moritani; Nakagawa *J. Am. Chem. Soc.* **1956,** *78*, 2190; Brown; Moritani *J. Am. Chem. Soc.* **1956,** *78*, 2203; Bartsch *J. Org. Chem.* **1970,** *35*, 1334. See also Charton *J. Am. Chem. Soc.* **1975,** *97*, 6159.
[84]For example, see Banthorpe; Hughes; Ingold *J. Chem. Soc.* **1960,** 4054.
[85]Saunders; Fahrenholtz; Caress; Lowe; Schreiber *J. Am. Chem. Soc.* **1965,** *87*, 3401. Similar results were obtained by Brown; Klimisch *J. Am. Chem. Soc.* **1966,** *88*, 1425.
[86]Bartsch; Bunnett *J. Am. Chem. Soc.* **1968,** *90*, 408.

using as bases a series of $XC_6H_4O^-$ ions) showed that the percentage of Hofmann elimination increased with increasing base strength, though the size of the base did not change.[87] These results are in accord with the explanation of Bunnett, since an increase in base strength moves an E2 reaction closer to the E1cB end of the spectrum. In further experiments, a large series of bases of different kinds was shown to obey linear free-energy relationships between basicity and percentage of Hofmann elimination,[88] though certain very large bases (e.g., 2,6-di-*t*-butyl-phenoxide) did not obey the relationships, steric effects becoming important in these cases. How large the base must be before steric effects are observed depends on the pattern of alkyl substitution in the substrate, but not on the nucleofuge.[89] One further result may be noted. In the gas phase, elimination of H and BrH^+ or H and ClH^+ using Me_3N as the base predominantly followed Hofmann's rule,[90] although BrH^+ and ClH^+ are not very large.

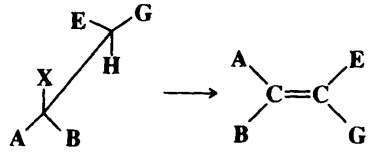
5. Only a few investigations on the orientation of syn E2 eliminations have been carried out, but these show that Hofmann orientation is greatly favored over Zaitsev.[91]

6. In the E1cB mechanism the question of orientation seldom arises because the mechanism is generally found only where there is an electron-withdrawing group in the β position, and that is where the double bond goes.

7. As already mentioned, E2C reactions show a strong preference for Zaitsev orientation.[92] In some cases this can be put to preparative use. For example, the compound $PhCH_2CHOTsCHMe_2$ gave about 98% $PhCH{=}CHCHMe_2$ under the usual E2 reaction conditions (*t*-BuOK in *t*-BuOH). In this case the double bond goes to the side with more hydrogens because on that side it will be able to conjugate with the benzene ring. However, with the weak base $Bu_4N^+ Br^-$ in acetone the Zaitsev product $PhCH_2CH{=}CMe_2$ was formed in 90% yield.[93]

Steric Orientation of the Double Bond

When elimination takes place on a compound of the form CH_3—CABX or CHAB—CGGX, the new olefin does not have cis–trans isomerism, but for compounds of the form CHEG—CABX (E and G *not* H) (**23**) and CH_2E—CABX (**24**), cis and trans isomers are possible. When the anti E2 mechanism is in operation, **23** gives the isomer arising from



23

[87]Froemsdorf; Robbins *J. Am. Chem. Soc.* **1967,** *89*, 1737. See also Froemsdorf; Dowd; Leimer *J. Am. Chem. Soc.* **1966,** *88*, 2345; Bartsch; Kelly; Pruss *Tetrahedron Lett.* **1970,** 3795; Feit; Breger; Capobianco; Cooke; Gitlin *J. Am. Chem. Soc.* **1975,** *97*, 2477; Ref. 78.

[88]Bartsch; Pruss; Bushaw; Wiegers *J. Am. Chem. Soc.* **1973,** *95*, 3405; Bartsch; Roberts; Cho *J. Org. Chem.* **1979,** *44*, 4105.

[89]Bartsch; Read; Larsen; Roberts; Scott; Cho *J.Am. Chem. Soc.* **1979,** *101*, 1176.

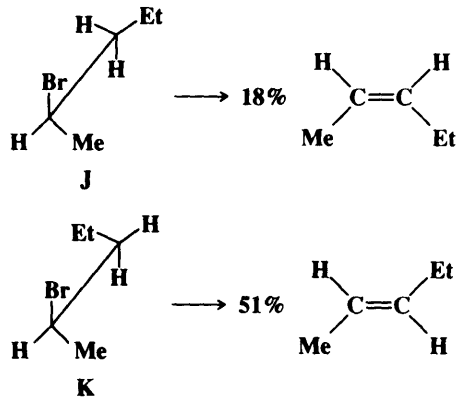
[90]Angelini; Lilla; Speranza *J. Am. Chem. Soc.* **1989,** *111*, 7393.

[91]Sicher; Svoboda; Pánková; Závada *Collect. Czech. Chem. Commun.* **1971,** *36*, 3633; Bailey; Saunders *J. Am. Chem. Soc.* **1970,** *92* 6904.

[92]For example; see Ono *Bull. Chem. Soc. Jpn.* **1971,** *44*, 1369; Bailey; Saunders *J. Org. Chem.* **1973,** *38*, 3363; Muir; Parker *J. Org. Chem.* **1976,** *41*, 3201.

[93]Lloyd; Muir; Parker, Ref. 72.

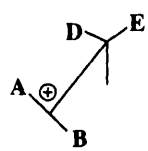
trans orientation of X and H and, as we have seen before (p. 984), an erythro compound gives the cis olefin and a threo compound the trans. For **24** two conformations are possible for the transition state; these lead to different isomers and often both are obtained. However, the one that predominates is often determined by an eclipsing effect.[94] For example, Zaitsev elimination from 2-bromopentane can occur as follows:



In conformation **J** the ethyl group is between Br and Me, while in **K** it is between Br and H. This means that **K** is more stable, and most of the elimination should occur from this conformation. This is indeed what happens, and 51% of the trans isomer is formed (with KOEt) compared to 18% of the cis (the rest is the Hofmann product).[95] These effects become larger with increasing size of A, B, and E.

However, eclipsing effects are not the only factors that affect the cis/trans ratio in anti E2 eliminations. Other factors are the nature of the leaving group, the base, the solvent, and the substrate. Not all these effects are completely understood.[96]

For E1 eliminations, if there is a free carbocation (**25**), it is free to rotate, and no matter



(D may be H)

25

what the geometry of the original compound, the more stable situation is the one where the larger of the D–E pair is opposite the smaller of the A–B pair and the corresponding olefin should form. If the carbocation is not completely free, then to that extent, E2-type products are formed. Similar considerations apply in E1cB eliminations.[97]

[94]See Cram; Greene; DePuy *J. Am. Chem. Soc.* **1956,** *78,* 790; Cram, in Newman *Steric Effects in Organic Chemistry*; Wiley: New York, 1956, pp. 338-345.

[95]Brown; Wheeler *J. Am. Chem. Soc.* **1956,** *78* 2199.

[96]For discussions, see Bartsch; Bunnett *J. Am. Chem. Soc.* **1969,** *91,* 1376, 1382; Feit; Saunders *J. Am. Chem. Soc.* **1970,** 92, 1630, 5615; Alunni; Baciocchi *J. Chem. Soc., Perkin Trans. 2* **1976,** 877; Saunders; Cockerill, Ref. 2, pp. 165-193.

[97]See, for example, Redman; Thomas; Stirling *J. Chem. Soc., Chem. Commun.* **1978,** 43.

REACTIVITY

In this section we examine the effects of changes in the substrate, base, leaving group, and medium on (1) overall reactivity, (2) E1 vs. E2 vs. E1cB,[98] and (3) elimination vs. substitution.

Effect of Substrate Structure

1. *Effect on reactivity.* We refer to the carbon containing the nucleofuge (X) as the α carbon and to the carbon that loses the positive species as the β carbon. Groups attached to the α or β carbons can exert at least four kinds of influence:

a. They can stabilize or destabilize the incipent double bond (both α and β groups).

b. They can stabilize or destabilize an incipient negative charge, affecting the acidity of the proton (β groups only).

c. They can stabilize or destabilize an incipient positive charge (α groups only).

d. They can exert steric effects (e.g., eclipsing effects) (both α and β groups).

Effects a and d can apply in all three mechanisms, though steric effects are greatest for the E2 mechanism. Effect b does not apply in the E1 mechanism, and effect c does not apply in the E1cB mechanism. Groups such as Ar and C=C increase the rate by any mechanism, whether they are α or β (effect a). Electron-withdrawing groups increase the acidity when in the β position, but have little effect in the α position unless they also conjugate with the double bond. Thus Br, Cl, CN, Ts, NO_2, CN, and SR in the β position all increase the rate of E2 eliminations.

2. *Effect on E1 vs. E2 vs. E1cB.* α alkyl and α aryl groups stabilize the carbocation character of the transition state, shifting the spectrum toward the E1 end. β alkyl groups also shift the mechanism toward E1, since they *decrease* the acidity of the hydrogen. However, β aryl groups shift the mechanism the other way (toward E1cB) by stabilizing the carbanion. Indeed, as we have seen (p. 993), all electron-withdrawing groups in the β position shift the mechanism toward E1cB.[99] α alkyl groups also increase the extent of elimination with weak bases (E2C reactions).

3. *Effect on elimination vs. substitution.* Under second-order conditions α branching increases elimination, to the point where tertiary substrates undergo few SN2 reactions, as we saw in Chapter 10. For example, Table 17.2 shows results on some simple alkyl bromides. Similar results were obtained with SMe_2^+ as the leaving group.[100] Two reasons can be presented for this trend. One is statistical: as α branching increases, there are usually more hydrogens for the base to attack. The other is that α branching presents steric hindrance to attack of the base at the carbon. Under first-order conditions, increased α branching also increases the amount of elimination (E1 vs. SN1), though not so much, and usually the substitution product predominates. For example, solvolysis of *t*-butyl bromide gave only 19% elimination[101] (compare with Table 17.2). β branching also increases the amount of E2 elimination with respect to SN2 substitution (Table 17.2), not because elimination is faster but because the SN2 mechanism is so greatly slowed (p. 339). Under first-order conditions too, β branching favors elimination over substitution, probably for steric reasons.[102]However, E2 eliminations from compounds with charged leaving groups are slowed

[98]For discussions, see Cockerill; Harrison, Ref. 2, pp. 178-189.

[99]For a review of eliminations with COOH, COOR, $CONH_2$, and CN groups in the β position, see Butskus; Denis *Russ. Chem. Rev.* **1966,** *35*, 839-850.

[100]Hughes; Ingold; Maw *J. Chem. Soc.* **1948,** 2072; Hughes; Ingold; Woolf *J. Chem. Soc.* **1948,** 2084.

[101]Hughes; Ingold; Maw *J. Chem. Soc.* **1948,** 2065.

[102]Brown; Berneis *J. Am. Chem. Soc.* **1953,** *75*, 10.

TABLE 17.2 The effect of α and β branching on the rate of E2 elimination and the amount of olefin formed

The reactions were between the alkyl bromide and OEt^-. The rate for isopropyl bromide was actually greater than that for ethyl bromide, if the temperature difference is considered. Neopentyl bromide, the next compound in the β-branching series, cannot be compared because it has no β-hydrogen and cannot give an elimination product without rearrangement.

Substrate	Temperature, °C	Olefin, %	Rate × 10^5 of E2 reaction	Reference
CH_3CH_2Br	55	0.9	1.6	103
$(CH_3)_2CHBr$	25	80.3	0.237	104
$(CH_3)_3CBr$	25	97	4.17	101
$CH_3CH_2CH_2Br$	55	8.9	5.3	103
CH_3CHCH_2Br (CH$_3$ branch)	55	59.5	8.5	103

by β branching. This is related to Hofmann's rule (p. 999). Electron-withdrawing groups in the β position not only increase the rate of E2 eliminations and shift the mechanisms toward the E1cB end of the spectrum but also increase the extent of elimination as opposed to substitution.

Effect of the Attacking Base

1. *Effect on E1 vs. E2 vs. E1cB.* In the E1 mechanism, an external base is generally not required: The solvent acts as the base. Hence, when external bases are added, the mechanism is shifted toward E2. Stronger bases and higher base concentrations cause the mechanism to move toward the E1cB end of the E1–E2–E1cB spectrum.[105] However, weak bases in polar aprotic solvents can also be effective in elimination reactions with certain substrates (the E2C reaction). Normal E2 elimination has been accomplished with the following bases:[106] H_2O, NR_3, OH^-, OAc^-, OR^-, OAr^-, NH_2^-, CO_3^{2-}, $LiAlH_4$, I^-, CN^-, and organic bases. However, the only bases of preparative importance in the normal E2 reaction are OH^-, OR^-, and NH_2^-, usually in the conjugate acid as solvent, and certain amines. Weak bases effective in the E2C reaction are Cl^-, Br^-, F^-, OAc^-, and RS^-. These bases are often used in the form of their R_4N^+ salts.

2. *Effect on elimination vs. substitution.* Strong bases not only benefit E2 as against E1, but also benefit elimination as against substitution. With a high concentration of strong base in a nonionizing solvent, bimolecular mechanisms are favored and E2 predominates over SN2. At low base concentrations, or in the absence of base altogether, in ionizing solvents, unimolecular mechanisms are favored, and the SN1 mechanism predominates over the E1. In Chapter 10, it was pointed out that some species are strong nucleophiles though weak bases (p. 349). The use of these obviously favors substitution, except that, as we have seen, elimination can predominate if polar aprotic solvents are used. It has been shown for the

[103]Dhar; Hughes; Ingold; Masterman *J. Chem. Soc.* **1948,** 2055.
[104]Dhar; Hughes; Ingold *J. Chem. Soc.* **1948,** 2058.
[105]For a review, see Baciocchi *Acc. Chem. Res.* **1979,** *12,* 430-436. See also Baciocchi; Ruzziconi; Sebastiani *J. Org. Chem.* **1980,** *45,* 827.
[106]This list is from Banthorpe *Elimination Reactions*; Elsevier: New York, 1963, p. 4.

base CN^- that in polar aprotic solvents, the less the base is encumbered by its counterion in an ion pair (i.e., the freer the base), the more substitution is favored at the expense of elimination.[107]

Effect of the Leaving Group

1. *Effect on reactivity.* The leaving groups in elimination reactions are similar to those in nucleophilic substitution. E2 eliminations have been performed with the following groups: NR_3^+, PR_3^+, SR_2^+, OHR^+, SO_2R, OSO_2R, OCOR, OOH OOR, NO_2,[108] F, Cl, Br, I, and CN (*not* OH_2^+). E1 eliminations have been carried out with: NR_3^+, SR_2^+, OH_2^+, OHR^+, OSO_2R, OCOR, Cl, Br, I, and N_2^+.[109] However, the major leaving groups for preparative purposes are OH_2^+ (always by E1) and Cl, Br, I, and NR_3^+ (usually by E2).

2. *Effect on E1 vs. E2 vs. E1cB.* Better leaving groups shift the mechanism toward the E1 end of the spectrum, since they make ionization easier. This effect has been studied in various ways. One way already mentioned was a study of ρ values (p. 996). Poor leaving groups and positively charged leaving groups shift the mechanism toward the E1cB end of the spectrum because the strong electron-withdrawing field effects increase the acidity of the β hydrogen.[110] The E2C reaction is favored by good leaving groups.

3. *Effect on elimination vs. substitution.* As we have already seen (p. 990), for first-order reactions the leaving group has nothing to do with the competition between elimination and substitution, since it is gone before the decision is made as to which path to take. However, where ion pairs are involved, this is not true, and results have been found where the nature of the leaving group does affect the product.[111] In second-order reactions, the elimination/substitution ratio is not greatly dependent on a halide leaving group, though there is a slight increase in elimination in the order I > Br > Cl. When OTs is the leaving group, there is usually much more substitution. For example, n-$C_{18}H_{37}Br$ treated with *t*-BuOK gave 85% elimination, while n-$C_{18}H_{37}OTs$ gave, under the same conditions, 99% substitution.[112] On the other hand, positively charged leaving groups increase the amount of elimination.

Effect of the Medium

1. *Effect of solvent on E1 vs. E2 vs. E1cB.* With any reaction a more polar environment enhances the rate of mechanisms that involve ionic intermediates. For neutral leaving groups, it is expected that E1 and E1cB mechanisms will be aided by increasing polarity of solvent and by increasing ionic strength. With certain substrates, polar aprotic solvents promote elimination with weak bases (the E2C reaction).

2. *Effect of solvent on elimination vs. substitution.* Increasing polarity of solvent favors SN2 reactions at the expense of E2. In the classical example, alcoholic KOH is used to effect elimination, while the more polar aqueous KOH is used for substitution. Charge-dispersal discussions, similar to those on p. 358,[113] only partially explain this. In most solvents SN1

[107]Loupy; Seyden-Penne *Bull. Soc. Chim. Fr.* **1971,** 2306.

[108]For a review of eliminations in which NO_2 is a leaving group, see Ono, in Feuer; Nielsen *Nitro Compounds; Recent Advances in Synthesis and Chemistry*; VCH: New York, 1990,pp. 1-135, pp. 86-126.

[109]These lists are from Banthorpe, Ref. 106, pp. 4, 7.

[110]For a discussion of leaving-group ability, see Stirling *Acc. Chem. Res.* **1979,** *12*, 198-203. See also Varma; Stirling *J. Chem. Soc., Chem. Commun.* **1981,** 553.

[111]For example, see Skell; Hall *J. Am. Chem. Soc.* **1963,** *85* 2851; Cocivera; Winstein, Ref. 32; Feit; Wright *J. Chem. Soc., Chem. Commun.* **1975,** 776. See, however, Cavazza *Tetrahedron Lett.* **1975,** 1031.

[112]Veeravagu; Arnold; Eigenmann *J. Am. Chem. Soc.* **1964,** *86*, 3072.

[113]Cooper; Dhar; Hughes; Ingold; MacNulty; Woolf *J. Chem. Soc.* **1948,** 2043.

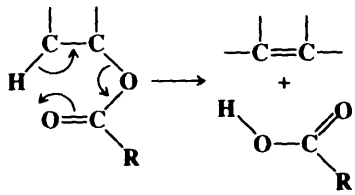
reactions are favored over E1. E1 reactions compete best in polar solvents that are poor nucleophiles, especially dipolar aprotic solvents.[114] A study made in the gas phase, where there is no solvent, has shown that when 1-bromopropane reacts with MeO^- only elimination takes place—no substitution—even with this primary substrate.[115]

3. *Effect of temperature.* Elimination is favored over substitution by increasing temperature, whether the mechanism is first or second order.[116] The reason is that the activation energies of eliminations are higher than those of substitutions (because eliminations have greater changes in bonding).

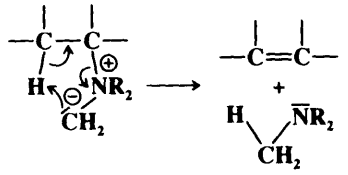
MECHANISMS AND ORIENTATION IN PYROLYTIC ELIMINATIONS

Mechanisms[117]

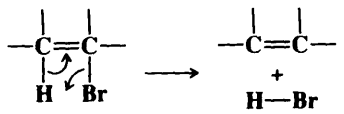
Several types of compound undergo elimination on heating, with no other reagent present. Reactions of this type are often run in the gas phase. The mechanisms are obviously different from those already discussed, since all those require a base (which may be the solvent) in one of the steps, and there is no base or solvent present in pyrolytic elimination. Two mechanisms have been found to operate. One involves a cyclic transition state, which may be four-, five-, or six-membered. Examples of each size are:



(7-3)



(7-7)



(7-13)

In this mechanism the two groups leave at about the same time and bond to each other as they are doing so. The designation is Ei in the Ingold terminology and cyclo-$D_E D_N A_n$ in the IUPAC system. The elimination must be syn and, for the four- and five-membered transition states, the four or five atoms making up the ring must be coplanar. Coplanarity

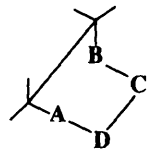
[114]Aksnes; Stensland *Acta Chem. Scand.* **1989,** *43*, 893, and references cited therein.

[115]Jones; Ellison *J. Am. Chem. Soc.* **1989,** *111*, 1645. For a different result with other reactants, see Lum; Grabowski *J. Am. Chem. Soc.* **1988,** *110*, 8568.

[116]Cooper; Hughes; Ingold; Maw; MacNulty *J. Chem. Soc.* **1948,** 2049.

[117]For reviews, see Taylor, in Patai *The Chemistry of Functional Groups, Supplement B*, pt. 2; Wiley: New York, 1979, pp. 860-914; Smith; Kelly *Prog. Phys. Org. Chem.* **1971,** *8*, 75-234, pp. 76-143, 207-234; in Bamford; Tipper, Ref. 2, vol. 5, 1972, the articles by Swinbourne, pp. 149-233 (pp. 158-188), and by Richardson; O'Neal, pp. 381-565 (pp. 381-446); Maccoll, Ref. 2, *Adv. Phys. Org. Chem.* **1965,** *3*, 91-122. For reviews of mechanisms in pyrolytic eliminations of halides, see Egger; Cocks; in Patai *The Chemistry of the Carbon–Halogen Bond*, pt. 2; Wiley: New York, 1973, pp. 677-745; Maccoll *Chem. Rev.* **1969,** *69*, 33-60.

is not required for the six-membered transition state, since there is room for the outside atoms when the leaving atoms are staggered.

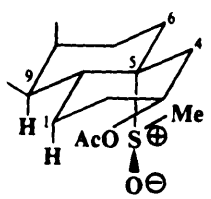


As in the E2 mechanism, it is not necessary that the C—H and C—X bond be equally broken in the transition state. In fact, there is also a spectrum of mechanisms here, ranging from a mechanism in which C—X bond breaking is a good deal more advanced than C—H bond breaking to one in which the extent of bond breaking is virtually identical for the two bonds. Evidence for the existence of the Ei mechanism is:

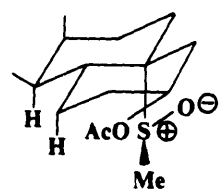
1. The kinetics are first order, so only one molecule of the substrate is involved in the reaction (that is, if one molecule attacked another, the kinetics would be second order in substrate).[118]

2. Free-radical inhibitors do not slow the reactions, so no free-radical mechanism is involved.[119]

3. The mechanism predicts exclusive syn elimination, and this behavior has been found in many cases.[120] The evidence is inverse to that for the anti E2 mechanism and generally involves the following facts: (1) an erythro isomer gives a trans olefin and a threo isomer gives a cis olefin; (2) the reaction takes place only when a cis β hydrogen is available; (3) if, in a cyclic compound, a cis hydrogen is available on only one side, the elimination goes in that direction. Another piece of evidence involves a pair of steroid molecules. In 3β-acetoxy-(*R*)-5α-methylsulfinylcholestane (**26** shows rings A and B of this compound) and in 3β-acetoxy-(*S*)-5α-methylsulfinylcholestane (**27:** rings A and B), the *only* difference is the



26



27

(7-12)

configuration of oxygen and methyl about the sulfur. Yet pyrolysis of **26** gave only elimination to the 4-side (86% 4-ene), while **27** gave predominant elimination to the 6-side (65% 5-ene and 20% 4-ene).[121] Models show that interference from the 1- and 9-hydrogens causes the two groups on the sulfur to lie *in front of it* with respect to the rings, rather than behind it. Since the sulfur is chiral, this means that in **26** the oxygen is near the 4-hydrogen, while in **27** it is near the 6 hydrogen. This experiment is compatible only with syn elimination.[122]

4. ^{14}C isotope effects for the Cope elimination (**7-8**) show that both the C—H and C—N bonds have been extensively broken in the transition state.[123]

[118]O'Connor; Nace *J. Am. Chem. Soc.* **1953,** *75*, 2118.

[119]Barton; Head; Williams *J. Chem. Soc.* **1953,** 1715.

[120]In a few instances anti or nonstereoselective elimination has been found; this behavior is generally ascribed to the intervention of other mechanisms. For example, see Bordwell; Landis *J. Am. Chem. Soc.* **1958,** *80*, 2450, 6383; Briggs; Djerassi *J. Org. Chem.* **1968,** *33*, 1625; Smissman; Li; Creese *J. Org. Chem.* **1970,** *35*, 1352.

[121]Jones; Saeed *Proc. Chem. Soc.* **1964,** 81. See also Goldberg; Sahli *J. Org. Chem.* **1967,** *32*, 2059.

[122]For other evidence for syn elimination, see Curtin; Kellom *J. Am. Chem. Soc.* **1953,** *75*, 6011; Skell; Hall *J. Am. Chem. Soc.* **1964,** *86*, 1557; Bailey; Bird *J. Org. Chem.* **1977,** *42*, 3895.

[123]Wright; Sims; Fry *J. Am. Chem. Soc.* **1983,** *105*, 3714.

5. Some of these reactions have been shown to exhibit negative entropies of activation, indicating that the molecules are more restricted in geometry in the transition state than they are in the starting compound.

Where a pyrolytic elimination lies on the mechanistic spectrum seems to depend mostly on the leaving group. When this is halogen, all available evidence suggests that in the transition state the C—X bond is cleaved to a much greater extent than the C—H bond, i.e., there is a considerable amount of carbocation character in the transition state. This is in accord with the fact that a completely nonpolar four-membered cyclic transition state violates the Woodward–Hoffmann rules (see the similar case of **5-49**). Evidence for the carbocation-like character of the transition state when halide is the leaving group is that relative rates are in the order I > Br > Cl[124] (see p. 352), and that the effects of substituents on reaction rates are in accord with such a transition state.[125] Rate ratios for pyrolysis of some alkyl bromides at 320°C were: ethyl bromide, 1; isopropyl bromide, 280; *t*-butyl bromide, 78,000. Also, α-phenylethyl bromide had about the same rate as *t*-butyl bromide. On the other hand, β-phenylethyl bromide was only slightly faster than ethyl bromide.[126] This indicates that C—Br cleavage was much more important in the transition state than C—H cleavage, since the incipient carbocation was stabilized by α alkyl and α aryl substitution, while there was no incipient carbanion to be stabilized by β aryl substitution. These substituent effects, as well as those for other groups, are very similar to the effects found for the SN1 mechanism and thus in very good accord with a carbocation-like transition state.

For carboxylic esters, the rate ratios were much smaller,[127] though still in the same order, so that this reaction is closer to a pure Ei mechanism, though the transition state still has some carbocationic character. Other evidence for a greater initial C—O cleavage with carboxylic esters is that a series of 1-arylethyl acetates followed σ^+ rather than σ, showing carbocationic character at the 1 position.[128] The extent of E1 character in the transition state increases in the following order of ester types: acetate < phenylacetate < benzoate < carbamate < carbonate.[129] Cleavage of xanthates (**7-4**), cleavage of sulfoxides (**7-12**), the Cope reaction (**7-8**), and reaction **7-7** are probably very close to straight Ei mechanisms.[130]

The second type of pyrolysis mechanism is completely different and involves free radicals. Initiation occurs by pyrolytic homolytic cleavage. The remaining steps may vary, and a few are shown:

Initiation $\quad R_2CHCH_2X \longrightarrow R_2CHCH_2\cdot + X\cdot$

Propagation $\quad R_2CHCH_2X + X\cdot \longrightarrow R_2\dot{C}CH_2X + HX$

$\quad R_2\dot{C}CH_2X \longrightarrow R_2C{=}CH_2 + X\cdot$

Termination (disproportionation)

$$2R_2\dot{C}CH_2X \longrightarrow R_2C{=}CH_2 + R_2CXCH_2X$$

[124]Maccoll, Ref. 2, pp. 215-216.

[125]For reviews of such studies, see Maccoll, Ref. 117.

[126]For rate studies of pyrolysis of some β-alkyl substituted ethyl bromides, see Chuchani; Rotinov; Dominguez; Martin *Int. J. Chem. Kinet.* **1987,** *19*, 781.

[127]For example, see Scheer; Kooyman; Sixma *Recl. Trav. Chim. Pays-Bas* **1963,** *82*, 1123. See also Louw; Vermeeren; Vogelzang *J. Chem. Soc., Perkin Trans. 2* **1983,** 1875.

[128]Taylor; Smith; Wetzel *J. Am. Chem. Soc.* **1962,** *84*, 4817; Smith; Jones; Brown *J. Org. Chem.* **1963,** *28*, 403; Taylor *J. Chem. Soc., Perkin Trans. 2* **1978,** 1255. See also Ottenbrite; Brockington *J. Org. Chem.* **1974,** *39*, 2463; Jordan; Thorne *J. Chem. Soc., Perkin Trans. 2* **1984,** 647; August; McEwen; Taylor *J. Chem. Soc., Perkin Trans. 2* **1987,** 1683, and other papers in this series; Al-Awadi *J. Chem. Soc., Perkin Trans. 2* **1990,** 2187.

[129]Taylor *J. Chem. Soc., Perkin Trans. 2* **1975,** 1025.

[130]For a review of the mechanisms of **7-12**, **7-8**, and the pyrolysis of sulfilimines, see Oae; Furukawa *Tetrahedron* **1977,** *33*, 2359-2367.

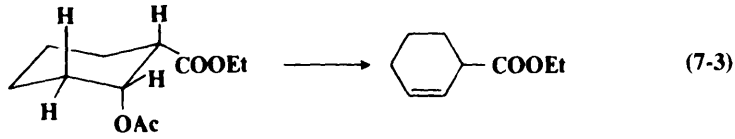
Free-radical mechanisms are mostly found in pyrolyses of polyhalides and of primary monohalides,[131] though they also have been postulated in pyrolysis of certain carboxylic esters.[132] Much less is known about these mechanisms and we shall not consider them further. Free-radical eliminations in solution are also known but are rare.[133]

Orientation in Pyrolytic Eliminations

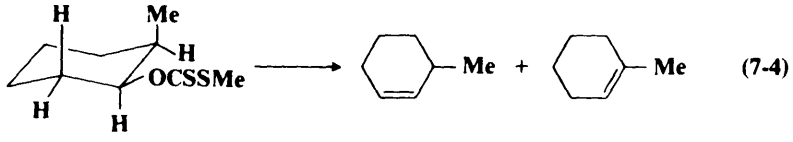
As in the E1–E2–E1cB mechanistic spectrum, Bredt's rule applies; and if a double bond is present, a conjugated system will be preferred, if sterically possible. Apart from these considerations, the following statements can be made for Ei eliminations:

1. In the absence of considerations mentioned below, orientation is statistical and is determined by the number of β hydrogens available (therefore *Hofmann's rule* is followed). For example, *sec*-butyl acetate gives 55 to 62% 1-butene and 38 to 45% 2-butene,[134] which is close to the 3:2 distribution predicted by the number of hydrogens available.[135]

2. A cis β hydrogen is required. Therefore in cyclic systems, if there is a cis hydrogen on only one side, the double bond will go that way. However, when there is a six-membered transition state, this does not necessarily mean that the leaving groups must be cis to each other, since such transition states need not be completely coplanar. If the leaving group is axial, then the hydrogen obviously must be equatorial (and consequently cis to the leaving group), since the transition state cannot be realized when the groups are both axial. But if the leaving group is equatorial, it can form a transition state with a β hydrogen that is either axial (hence, cis) or equatorial (hence, trans). Thus **28,** in which the leaving group is most likely axial, does not form a double bond in the direction of the carbethoxyl group, even though that would be conjugated, because there is no equatorial hydrogen on that side. Instead it gives 100% **29.**[136] On the other hand, **30,** with an equatorial leaving group, gives



28 **29** (7-3)



30 (7-4)

[131]For example, see Barton; Howlett *J. Chem. Soc.* **1949,** 155, 165.

[132]For example, see Rummens *Recl. Trav. Chim. Pays-Bas* **1964,** *83*, 901; Louw; Kooyman *Recl. Trav. Chim. Pays-Bas* **1965,** *84*, 1511.

[133]For examples; see Kampmeier; Geer; Meskin; D'Silva *J. Am. Chem. Soc.* **1966,** *88*, 1257; Kochi; Singleton; Andrews *Tetrahedron* **1968,** *24*, 3503; Boothe; Greene; Shevlin *J. Org. Chem.* **1980,** *45*, 794; Stark; Nelson; Jensen *J. Org. Chem.* **1980,** *45*, 420; Kochi *Organic Mechanisms and Catalysis*; Academic Press: New York, 1978, pp. 346-349; Kamimura; Ono *J. Chem. Soc., Chem. Commun.* **1988,** 1278.

[134]Froemsdorf; Collins; Hammond; DePuy *J. Am. Chem. Soc.* **1959,** *81*, 643; Haag; Pines *J. Org. Chem.* **1959,** *24*, 877.

[135]DePuy; King *Chem. Rev.* **1960,** *60*, 431-445, have tables showing the product distribution for many cases.

[136]Bailey; Baylouny *J. Am. Chem. Soc.* **1959,** *81*, 2126.

about 50% of each olefin, even though, for elimination to the 1-ene, the leaving group must go off with a trans hydrogen.[137]

3. In some cases, especially with cyclic compounds, the more stable olefin forms and Zaitsev's rule applies. For example, menthyl acetate gives 35% of the Hofmann product and 65% of the Zaitsev, even though a cis β hydrogen is present on both sides and the statistical distribution is the other way. A similar result was found for the pyrolysis of menthyl chloride.[138]

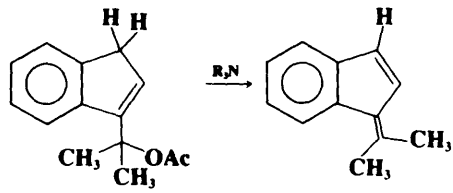
4. There are also steric effects. In some cases the direction of elimination is determined by the need to minimize steric interactions in the transition state or to relieve steric interactions in the ground state.

1,4 Conjugate Eliminations

1,4 eliminations of the type

$$\text{H—C—C=C—C—X} \longrightarrow \text{C=C—C=C}$$

are much rarer than conjugate additions (Chapter 15), but some examples are known.[140] One such is[141]



REACTIONS

First we consider reactions in which a C=C or a C≡C bond is formed. From a synthetic point of view, the most important reactions for the formation of double bonds are **7-1** (usually by an E1 mechanism), **7-6, 7-13,** and **7-29** (usually by an E2 mechanism), and **7-3, 7-4,** and **7-8** (usually by an Ei mechanism). The only synthetically important method for the formation of triple bonds is **7-13.**[142] In the second section we treat reactions in which C≡N bonds and C=N bonds are formed, and then eliminations that give C=O bonds and diazoalkanes. Finally, we discuss extrusion reactions.

Reactions in Which C=C and C≡C Bonds are Formed

A. Reactions in Which Hydrogen is Removed from One Side. In **7-1** to **7-5** the other leaving atom is oxygen. In **7-6** to **7-10** it is nitrogen. For reactions in which hydrogen is removed from both sides, see **9-1** to **9-6.**

[137]Botteron; Shulman *J. Org. Chem.* **1962,** *27,* 2007.

[138]Barton; Head; Williams *J. Chem. Soc.* **1952,** 453; Bamkole; Maccoll *J. Chem. Soc. B* **1970,** 1159.

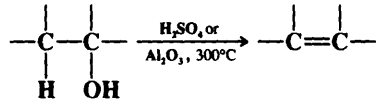
[139]Taylor, Ref. 117, pp. 885-890; Smith; Mutter; Todd *J. Org. Chem.* **1977,** *42,* 44; Chuchani; Dominguez *Int. J. Chem. Kinet.* **1981,** *13,* 577; Hernández A.; Chuchani *Int. J. Chem. Kinet* **1983,** *15,* 205.

[140]For a review of certain types of 1,4 and 1,6 eliminations, see Wakselman *Nouv. J. Chem.* **1983,** *7,* 439-447.

[141]Thibblin; Onyido; Ahlberg *Chem. Scr.* **1982,** *19,* 145; Thibblin *J. Chem. Soc., Perkin Trans. 2* **1986,** 321; Ölwegård; Ahlberg *Acta Chem. Scand.* **1990,** *44,* 642. For studies of the stereochemistry of 1,4 eliminations, see Hill; Bock *J. Am. Chem. Soc.* **1978,** *100,* 637; Moss; Rickborn *J. Org. Chem.* **1986,** *51,* 1992; Ölwegård; Ahlberg *J. Chem. Soc., Chem. Commun.* **1989,** 1279.

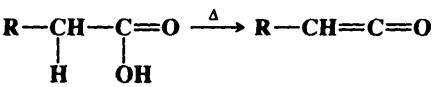
[142]For reviews of methods for preparing alkynes, see Friedrich, in Patai; Rappoport *The Chemistry of Functional Groups, Supplement C,* pt. 2; Wiley: New York, 1983; pp. 1376-1384; Ben-Efraim, in Patai *The Chemistry of the Carbon-Carbon Triple Bond,* pt. 2; Wiley: New York, 1978, pp. 755-790. For a comparative study of various methods, see Mesnard; Bernadou; Miginiac *J. Chem. Res. (S)* **1981,** 270, and other papers in this series.

7-1 Dehydration of Alcohols
Hydro-hydroxy-elimination

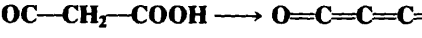


Dehydration of alcohols can be accomplished in several ways. H_2SO_4 and H_3PO_4 are common reagents, but in many cases these lead to rearrangement products and to ether formation (**0-16**). If the alcohol can be evaporated, vapor-phase elimination over Al_2O_3 is an excellent method since side reactions are greatly reduced. This method has even been applied to such high-molecular-weight alcohols as 1-dodecanol.[143] Other metallic oxides (e.g., Cr_2O_3, TiO_2, WO_3) have also been used, as have been sulfides, other metallic salts, and zeolites. Another method of avoiding side reactions is the conversion of alcohols to esters, and the pyrolysis of these (**7-3** to **7-5**). The ease of dehydration increases with α branching, and tertiary alcohols are dehydrated so easily with only a trace of acid that it sometimes happens even when the investigator desires otherwise. It may also be recalled that the initial alcohol products of many base-catalyzed condensations dehydrate spontaneously (Chapter 16) because the new double bond can be in conjugation with one already there. Many other dehydrating agents[144] have been used on occasion: P_2O_5, I_2, $ZnCl_2$, BF_3–etherate, dimethyl sulfoxide, $KHSO_4$, anhydrous $CuSO_4$, and phthalic anhydride, among others. Secondary and tertiary alcohols can also be dehydrated, without rearrangements, simply on refluxing in HMPA.[145] With nearly all reagents, dehydration follows Zaitsev's rule. An exception involves the passage of hot alcohol vapors over thorium oxide at 350 to 450°C, under which conditions Hofmann's rule is followed,[146] and the mechanism is probably different.

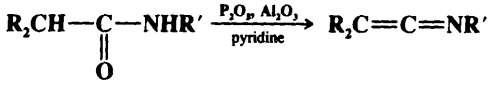
Carboxylic acids can be dehydrated by pyrolysis, the product being a ketene:



Ketene itself is commercially prepared in this manner. In a similar reaction, carbon suboxide is produced by heating malonic acid with P_2O_5:



Carboxylic acids have also been converted to ketenes by treatment with certain reagents, among them TsCl,[147] dicyclohexylcarbodiimide,[148] and 1-methyl-2-chloropyridinium iodide (*Mukaiyama's reagent*).[149] Analogously, amides can be dehydrated with P_2O_5, pyridine, and Al_2O_3 to give ketenimines:[150]



[143]For example, see Spitzin; Michailenko; Pirogowa *J. Prakt. Chem.* **1964,** [4] *25*, 160; Bertsch; Greiner; Kretzschmar; Falk *J. Prakt. Chem.* **1964,** [4] *25*, 184.

[144]For a list of reagents, with references, see Larock *Comprehensive Organic Transformations*; VCH: New York, 1989, pp. 151-152.

[145]Monson *Tetrahedron Lett.* **1971,** 567; Monson; Priest *J. Org. Chem.* **1971,** *36*, 3826; Lomas; Sagatys; Dubois *Tetrahedron Lett.* **1972,** 165.

[146]Lundeen; Van Hoozer *J. Am. Chem. Soc.* **1963,** *85*, 2180, *J. Org. Chem.* **1967,** *32*, 3386. See also Davis *J. Org. Chem.* **1982,** *47*, 900; Iimori; Ohtsuka; Oishi *Tetrahedron Lett.* **1991,** *32*, 1209.

[147]Brady; Marchand; Giang; Wu *Synthesis* **1987,** 395, *J. Org. Chem.* **1987,** *52*, 3457.

[148]Olah; Wu; Farooq *Synthesis* **1989,** 568.

[149]Ref. 147; Funk; Abelman; Jellison *Synlett* **1989,** 36.

[150]Stevens; Singhal *J. Org. Chem.* **1964,** *29*, 34.

There is no way in which dehydration of alcohols can be used to prepare triple bonds: *gem*-diols and vinylic alcohols are not normally stable compounds and *vic*-diols[151] give either conjugated dienes or lose only 1 mole of water to give an aldehyde or ketone.

When proton acids catalyze alcohol dehydration, the mechanism is E1.[152] The principal process involves conversion of ROH to ROH_2^+ and cleavage of the latter to R^+ and H_2O, though with some acids a secondary process probably involves conversion of the alcohol to an inorganic ester and ionization of *this* (illustrated for H_2SO_4):

$$\mathbf{ROH \xrightarrow{H_2SO_4} ROSO_2OH \longrightarrow R^+ + HSO_4^-}$$

Note that these mechanisms are the reverse of those involved in the acid-catalyzed hydration of double bonds (**5-2**), in accord with the principle of microscopic reversibility. With anhydrides (e.g., P_2O_5, phthalic anhydride) as well as with some other reagents such as HMPA,[153] it is likely that an ester is formed, and the leaving group is the conjugate base of the corresponding acid. In these cases the mechanism can be E1 or E2. The mechanism with Al_2O_3 and other solid catalysts has been studied extensively but is poorly understood.[154]

Dehydration of alcohols has also been accomplished by treating the *alkoxide* form of the alcohol with bromoform.[155] This reaction is called *deoxidation*. It is known that bromoform in basic solution gives rise to dibromocarbene, and the following mechanism is likely:

$$\mathbf{RO^- + \overline{C}Br_2 \xrightarrow{-Br^-} R{-}O{-}\overline{C}{-}Br \xrightarrow[-CO]{-Br^-} R^{\oplus}} \longrightarrow \text{alkenes}$$

Note that the cleavage of the intermediate ROCBr is analogous to cleavage of RN_2^+ (p. 355) and the product distribution is similar.[156] Magnesium alkoxides (formed by ROH + $Me_2Mg \rightarrow$ ROMgMe) have been decomposed thermally, by heating at 195-340°C to give the alkene, CH_4, and MgO.[157] Syn elimination is found and an Ei mechanism is likely. Similar decomposition of aluminum and zinc alkoxides has also been accomplished.[158]

OS **I,** 15, 183, 226, 280, 345, 430, 473, 475; **II,** 12, 368, 408, 606; **III,** 22, 204, 237, 312, 313, 353, 560, 729, 786; **IV,** 130, 444, 771; **V,** 294; **VI,** 307, 901; **VII,** 210, 241, 363, 368, 396; **65,** 12, 98. See also OS **VII,** 63; **67,** 125; **69,** 199. No attempt has been made to list olefin-forming dehydrations accompanying condensations or rearrangements.

7-2 Cleavage of Ethers to Olefins
Hydro-alkoxy-elimination

$$\mathbf{-\overset{|}{\underset{|}{C}}-\overset{|}{\underset{OR}{\underset{|}{C}}}- \xrightarrow{R'Na} -\overset{|}{C}=\overset{|}{C}- + RONa + R'H}$$

[151]For a review on the dehydration of 1,2 and 1,3 diols, see Bartók; Molnár, in Patai *The Chemistry of Functional Groups, Supplement E*, pt. 2; Wiley: New York, 1980, pp. 721-760.

[152]For reviews of dehydration mechanisms, see Vinnik; Obraztsov *Russ. Chem. Rev.* **1990,** *59*, 63-77; Saunders; Cockerill, Ref. 2, pp. 221-274, 317-331; Knözinger, in Patai *The Chemistry of the Hydroxyl Group*, pt. 2; Wiley: New York, 1971, pp. 641-718.

[153]See, for example, Kawanisi; Arimatsu; Yamaguchi; Kimoto *Chem. Lett.* **1972,** 881.

[154]For reviews, see Beránek; Kraus; in Bamford; Tipper, Ref. 2, vol. 20, 1978, pp. 274-295; Pines *Intra-Sci. Chem. Rep.* **1972,** *6*(2), 1-42, pp. 17-21; Noller; Andréu; Hunger *Angew. Chem. Int. Ed. Engl.* **1971,** *10*, 172-181 [*Angew. Chem. 83*, 185-194]; Knözinger *Angew. Chem. Int. Ed. Engl.* **1968,** *7*, 791-805 [*Angew. Chem. 80*, 778-792]; Pines; Manassen *Adv. Catal.* **1966,** *16*, 49-93; Ref. 152. See also Berteau; Ruwet; Delmon *Bull. Soc. Chim. Belg.* **1985,** *94*, 859.

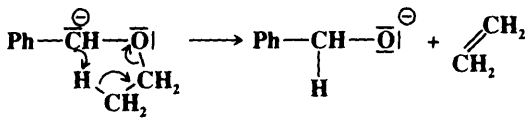
[155]Skell; Starer *J. Am. Chem. Soc.* **1959,** *81*, 4117.

[156]See, for example, Lee; Hahn *Can J. Chem.* **1967,** *45*, 2129.

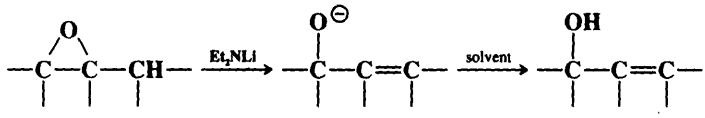
[157]Ashby; Willard; Goel *J. Org. Chem.* **1979,** *44*, 1221.

[158]Ref. 157; Brieger; Watson; Barar; Shene *J. Org. Chem.* **1979,** *44*, 1340.

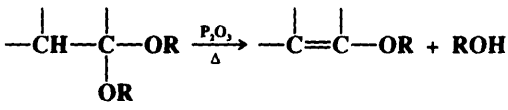
Olefins can be formed by the treatment of ethers with very strong bases, such as alkylsodium or alkyllithium compounds or sodium amide,[159] though there are usually side reactions too. The reaction is aided by electron-withdrawing groups in the β position, and, for example, $EtOCH_2CH(COOEt)_2$ can be converted to $CH_2{=}C(COOEt)_2$ without any base at all, but simply on heating.[160] *t*-Butyl ethers are cleaved more easily than others. Several mechanisms are possible. In many cases the mechanism is probably E1cB or on the E1cB side of the mechanistic spectrum,[161] since the base required is so strong, but it has been shown (by the use of $PhCD_2OEt$) that $PhCH_2OEt$ reacts by the five-membered Ei mechanism:[162]



Epoxides can be converted to allylic alcohols[163] by treatment with several reagents, including lithium diethylamide,[164] *t*-butyldimethylsilyl iodide,[165] methylmagnesium N-cyclohexylisopropylamide,[166] i-Pr_2NLi–*t*-BuOK (the *LIDAKOR reagent*),[167] and a diethylaluminum dialkylamide R_2NAlEt[168] (an alternative procedure is given in **7-12**). When an optically active reagent is used, optically active allylic alcohols can be produced from achiral epoxides.[169]



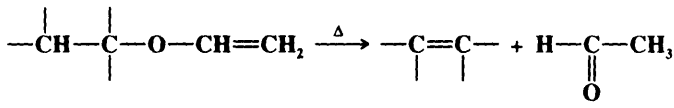
Ethers have also been converted to olefins and alcohols by passing vapors over hot P_2O_5 or Al_2O_3 (this method is similar to **7-1**), but this is not a general reaction. However, acetals can be converted to enol ethers in this manner:



This can also be done at room temperature by treatment with trimethylsilyl triflate and a tertiary amine[170] or with Me_3SiI in the presence of hexamethyldisilazane.[171]

[159]For a review, see Maercker *Angew. Chem. Int. Ed. Engl.* **1987,** *26*, 972-989 [*Angew. Chem. 99*, 1002-1019].
[160]Feely; Boekelheide *Org. Synth. IV*, 298.
[161]For an investigation in the gas phase, see DePuy; Bierbaum *J. Am. Chem. Soc.* **1981,** *103*, 5034.
[162]Letsinger; Pollart *J. Am. Chem. Soc.* **1956,** *78*, 6079.
[163]For reviews, see Smith *Synthesis* **1984,** 629-656, pp. 637-642; Crandall; Apparu *Org. React.* **1983,** *29*, 345-443. For a list of reagents, with references, see Ref. 144, pp. 117-118.
[164]See, for example, Cope; Brown; Lee *J. Am. Chem. Soc.* **1958,** *80*, 2855; Kissel; Rickborn *J. Org. Chem.* **1972,** *37*, 2060; Crandall; Crawley *Org. Synth. VI*, 948.
[165]Detty *J. Org. Chem.* **1980,** *45*, 924. For another silyl reagent, see Murata; Suzuki; Noyori *J. Am. Chem. Soc.* **1979,** *101*, 2738.
[166]Mosset; Manna; Viala; Falck *Tetrahedron Lett.* **1986,** *27*, 299.
[167]Mordini; Ben Rayana; Margot; Schlosser *Tetrahedron* **1990,** *46*, 2401.
[168]For a review, see Yamamoto; Nozaki *Angew. Chem. Int. Ed. Engl.* **1978,** *17*, 169-175 [*Angew. Chem. 90*, 180-186]. See also Yasuda; Tanaka; Yamamoto; Nozaki *Bull. Chem. Soc. Jpn.* **1979,** *52*, 1752.
[169]Su; Walder; Zhang; Scheffold *Helv. Chim. Acta* **1988,** *71*, 1073, and references cited therein.
[170]Gassman; Burns *J. Org. Chem.* **1988,** *53*, 5574.
[171]Miller; McKean *Tetrahedron Lett.* **1982,** *23*, 323. For another method, see Marsi; Gladysz *Organometallics* **1982,** *1*, 1467.

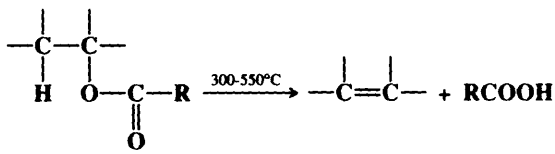
Enol ethers can be pyrolyzed to olefins and aldehydes in a manner similar to that of **7-3:**



The rate of this reaction for R—O—CH=CH_2 increased in the order Et < i-Pr < *t*-Bu.[172] The mechanism is similar to that of **7-3.**

OS **IV,** 298, 404; **V,** 25, 642, 859, 1145; **VI,** 491, 564, 584, 606, 683, 948; **65,** 98.

7-3 Pyrolysis of Esters of Carboxylic Acids
Hydro-acyloxy-elimination



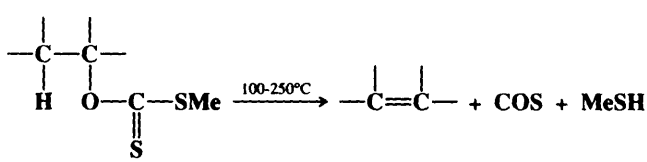
Carboxylic esters in which the alkyl group has a β hydrogen can be pyrolyzed, most often in the gas phase, to give the corresponding acid and an olefin.[173] No solvent is required. Since rearrangement and other side reactions are few, the reaction is synthetically very useful and is often carried out as an indirect method of accomplishing **7-1.** The yields are excellent and the workup is easy. Many olefins have been prepared in this manner. For higher olefins (above about C_{10}) a better method is to pyrolyze the alcohol in the presence of acetic anhydride.[174]

The mechanism is Ei (see p. 1006). Lactones can be pyrolyzed to give unsaturated acids, provided that the six-membered transition state required for Ei reactions is available (it is not available for five- and six-membered lactones, but it is for larger rings[175]). Amides give a similar reaction but require higher temperatures.

Allylic acetates give dienes when heated with certain palladium[176] or molybdenum[177] compounds.

OS **III,** 30; **IV,** 746; **V,** 235.

7-4 The Chugaev Reaction



[172]McEwen; Taylor *J. Chem. Soc., Perkin Trans. 2* **1982,** 1179. See also Taylor *J. Chem. Soc., Perkin Trans. 2* **1988,** 737.

[173]For a review, see DePuy; King, Ref. 135, pp. 432-444. For some procedures, see Jenneskens; Hoefs; Wiersum *J. Org. Chem.* **1989,** *54,* 5811, and references cited therein.

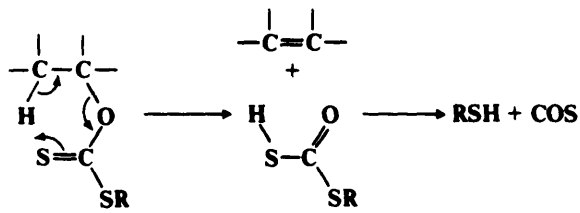
[174]Aubrey; Barnatt; Gerrard *Chem. Ind. (London)* **1965,** 681.

[175]See, for example, Bailey; Bird, Ref. 122.

[176]For a review, see Heck *Palladium Reagents in Organic Synthesis*; Academic Press: New York, 1985, pp. 172-178.

[177]Trost; Lautens; Peterson *Tetrahedron Lett.* **1983,** *24,* 4525.

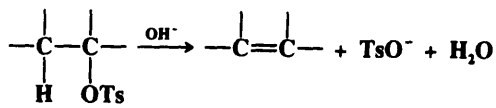
Methyl xanthates are prepared by treatment of alcohols with NaOH and CS_2 to give RO—CS—SNa, followed by treatment of this with methyl iodide.[178] Pyrolysis of the xanthate to give the olefin, COS, and the thiol is called the *Chugaev reaction*.[179] The reaction is thus, like **7-3**, an indirect method of accomplishing **7-1**. The temperatures required with xanthates are lower than with ordinary esters, which is advantageous because possible isomerization of the resulting olefin is minimized. The mechanism is Ei, similar to that of **7-3**. For a time there was doubt as to which sulfur atom closed the ring, but now there is much evidence, including the study of ^{34}S and ^{13}C isotope effects, to show that it is the C=S sulfur:[180]



The mechanism is thus exactly analogous to that of **7-3**.

OS **VII**, 139.

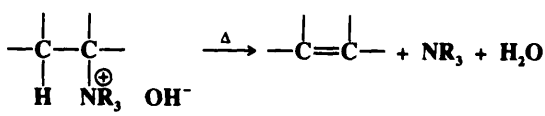
7-5 Decomposition of Other Esters
Hydro-tosyloxy-elimination



Several types of inorganic ester can be cleaved to olefins by treatment with bases. Esters of sulfuric, sulfurous, and other acids undergo elimination in solution by E1 or E2 mechanisms, as do tosylates and other esters of sulfonic acids.[181] It has been shown that bis(tetra-*n*-butylammonium) oxalate $(Bu_4N^+)_2(COO^-)_2$ is an excellent reagent for inducing tosylates to undergo elimination rather than substitution.[182] Aryl sulfonates have also been cleaved without a base. Esters of 2-pyridinesulfonic acid and 8-quinolinesulfonic acid gave olefins in high yields simply on heating, without a solvent.[183] Esters of $PhSO_2OH$ and TsOH behaved similarly when heated in a dipolar aprotic solvent such as Me_2SO or HMPA.[184]

OS, **VI**, 837; **VII**, 117.

7-6 Cleavage of Quaternary Ammonium Hydroxides
Hydro-trialkylammonio-elimination



[178]For a method of preparing xanthates from alcohols in one laboratory step, see Lee; Chan; Wong; Wong *Synth. Commun.* **1989**, *19*, 547.

[179]For reviews, see DePuy; King, Ref. 135, pp. 444-448; Nace *Org. React.* **1962**, *12*, 57-100.

[180]Bader; Bourns *Can. J. Chem.* **1961**, *39*, 348.

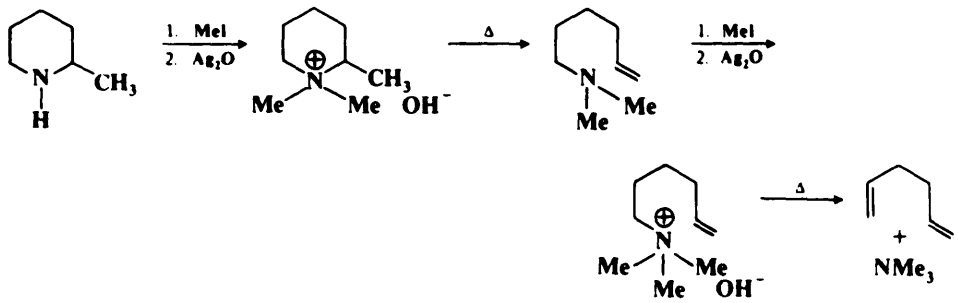
[181]For a list of reagents used for sulfonate cleavages, with references, see Ref. 144, pp. 153-154.

[182]Corey; Terashima *Tetrahedron Lett.* **1972**, 111.

[183]Corey; Posner; Atkinson; Wingard; Halloran; Radzik; Nash *J. Org. Chem.* **1989**, *54*, 389.

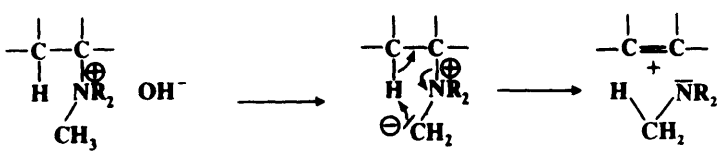
[184]Nace *J. Am. Chem. Soc.* **1959**, *81*, 5428.

Cleavage of quaternary ammonium hydroxides is the final step of the process known as *Hofmann exhaustive methylation* or *Hofmann degradation*.[185] In the first step, a primary, secondary, or tertiary amine is treated with enough methyl iodide to convert it to the quaternary ammonium iodide (**0-43**). In the second step, the iodide is converted to the hydroxide by treatment with silver oxide. In the cleavage step an aqueous or alcoholic solution of the hydroxide is distilled, often under reduced pressure. The decomposition generally takes place at a temperature between 100 and 200°C. Alternatively, the solution can be concentrated to a syrup by distillation or freeze-drying.[186] When the syrup is heated at low pressures, the cleavage reaction takes place at lower temperatures than are required for the reaction in the ordinary solution, probably because the base (OH^- or RO^-) is less solvated.[187] The reaction has never been an important synthetic tool, but in the 19th century and the first part of the 20th century it saw much use in the determination of the structure of unknown amines, especially alkaloids. In many of these compounds the nitrogen is in a ring, or even at a ring junction, and in such cases the olefin still contains nitrogen. Repetitions of the process are required to remove the nitrogen completely, e.g.,



A side reaction involving nucleophilic substitution to give an alcohol ($R_4N^+ OH^- \rightarrow ROH + R_3N$) generally accompanies the normal elimination reaction[188] but seldom causes trouble. However, when none of the four groups on the nitrogen has a β hydrogen, substitution is the only reaction possible. On heating $Me_4N^+ OH^-$ in water, methanol is obtained, though without a solvent the product is not methanol but dimethyl ether.[189]

The mechanism is usually E2. Hofmann's rule is generally obeyed by acyclic and Zaitsev's rule by cyclohexyl substrates (p. 999). In certain cases, where the molecule is highly hindered, a five-membered Ei mechanism, similar to that in **7-7**, has been shown to operate. That is, the OH^- in these cases does not attract the β hydrogen, but instead removes one of the methyl hydrogens:



[185]For reviews, see Bentley, in Bentley; Kirby *Elucidation of Organic Structures by Physical and Chemical Methods*, 2nd ed. (vol. 4 of Weissberger *Techniques of Chemistry*), pt. 2; Wiley: New York, 1973, pp. 255-289; White; Woodcock, in Patai *The Chemistry of the Amino Group*; Wiley: New York, 1968, pp. 409-416; Cope; Trumbull *Org. React.* **1960**, *11*, 317-493.

[186]Archer *J. Chem. Soc. C* **1971**, 1327.

[187]Saunders; Cockerill, Ref. 2, pp. 4-5.

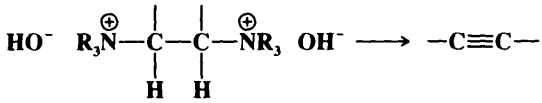
[188]Baumgarten *J. Chem. Educ.* **1968**, *45*, 122.

[189]Musker *J. Am. Chem. Soc.* **1964**, *86*, 960. *J. Chem. Educ.* **1968**, *45*, 200; Musker; Stevens *J. Am. Chem. Soc.* **1968**, *90*, 3515; Tanaka; Dunning; Carter *J. Org. Chem.* **1966**, *31*, 3431.

The obvious way to distinguish between this mechanism and the ordinary E2 mechanism is by the use of deuterium labeling. For example, if the reaction is carried out on a quaternary hydroxide deuterated on the β carbon ($R_2CDCH_2NMe_3^+$ OH^-), the fate of the deuterium indicates the mechanism. If the E2 mechanism is in operation, the trimethylamine produced would contain no deuterium (which would be found only in the water). But if the mechanism is Ei, the amine would contain deuterium. In the case of the highly hindered compound $(Me_3C)_2CDCH_2NMe_3^+$ OH^-, the deuterium did appear in the amine, demonstrating an Ei mechanism for this case.[190] With simpler compounds, the mechanism is E2, since here the amine was deuterium-free.[191]

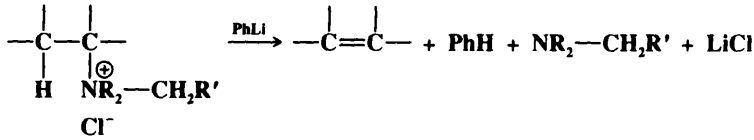
When the nitrogen bears more than one group possessing a β hydrogen, which group cleaves? The Hofmann rule says that *within* a group the hydrogen on the least alkylated carbon cleaves. This tendency is also carried over to the choice of which group cleaves: thus ethyl with three β hydrogens cleaves more readily than any longer *n*-alkyl group, all of which have two β hydrogens. "The β hydrogen is removed most readily if it is located on a methyl group, next from RCH_2, and least readily from R_2CH."[192] In fact, the Hofmann rule as first stated[193] in 1851 applied only to which group cleaved, not to the orientation within a group; the latter could not have been specified in 1851, since the structural theory of organic compounds was not formulated until 1857-1860. Of course, the Hofmann rule (applied to which group cleaves *or* to orientation within a group) is superseded by conjugation possibilities. Thus $PhCH_2CH_2NMe_2Et^+$ OH^- gives mostly styrene instead of ethylene.

Triple bonds have been prepared by pyrolysis of 1,2-bis salts.[194]



OS **IV,** 980; **V,** 315, 608; **VI,** 552. Also see OS **V,** 621, 883; **VI,** 75.

7-7 Cleavage of Quaternary Ammonium Salts with Strong Bases
Hydro-trialkylammonio-elimination



When quaternary ammonium halides are treated with strong bases (e.g., PhLi, KNH_2 in liquid NH_3[195]), an elimination can occur that is similar in products, though not in mechanism,

[190]Cope; Mehta *J. Am. Chem Soc.* **1963,** *85*, 1949. See also Baldwin; Banthorpe; Loudon; Waller *J. Chem. Soc. B* **1967,** 509.

[191]Cope; LeBel; Moore; Moore *J. Am. Chem. Soc.* **1961,** *83*, 3861.

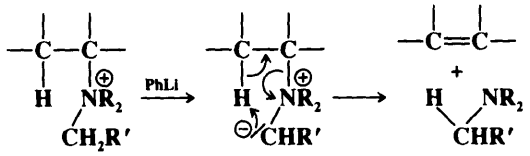
[192]Cope; Trumbull, Ref. 185, p. 348.

[193]Hofmann *Liebigs Ann. Chem.* **1851,** *78*, 253.

[194]For a review, see Franke; Ziegenbein; Meister *Angew. Chem.* **1960,** *72*, 391-400, pp. 397-398.

[195]Bach; Andrzejewski *J. Am. Chem. Soc.* **1971,** *93*, 7118; Bach; Bair; Andrzejewski *J. Am. Chem. Soc.* **1972,** *94*, 8608. *J. Chem. Soc., Chem. Commun.* **1974,** 819.

to **7-6.** This is an alternative to **7-6** and is done on the quaternary ammonium halide, so that it is not necessary to convert this to the hydroxide. The mechanism is Ei:

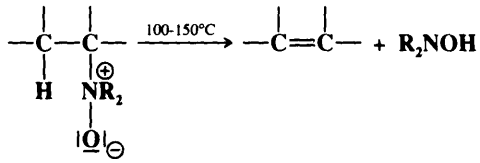


Ylide

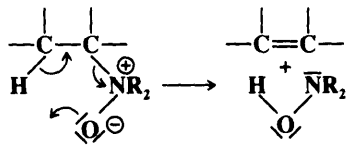
An α′ hydrogen is obviously necessary in order for the ylide to be formed. This type of mechanism is called α′,β elimination, since a β hydrogen is removed by the α′ carbon. The mechanism has been confirmed by labeling experiments similar to those described at **7-6,**[196] and by isolation of the intermediate ylides.[197] An important synthetic difference between this and most instances of **7-6** is that syn elimination is observed here and anti elimination in **7-6,** so products of opposite configuration are formed when the olefin exhibits cis–trans isomerism.

An alternative procedure that avoids the use of a very strong base is heating the salt with KOH in polyethylene glycol monomethyl ether.[198]

7-8 Cleavage of Amine Oxides
Hydro-(Dialkyloxidoammonio)-elimination



Cleavage of amine oxides to produce an alkene and a hydroxylamine is called the *Cope reaction* (not to be confused with the Cope *rearrangement*, **8-34**). It is an alternative to **7-6** and **7-7.**[199] The reaction is usually performed with a mixture of amine and oxidizing agent (see **9-28**) without isolation of the amine oxide. Because of the mild conditions side reactions are few, and the olefins do not usually rearrange. The reaction is thus very useful for the preparation of many olefins. A limitation is that it does not open 6-membered rings containing hetero nitrogen, though it does open rings of 5 and 7 to 10 members.[200] Rates of the reaction increase with increasing size of α and β substituents.[201] The reaction can be carried out at room temperature in dry Me_2SO or THF.[202] The elimination is a stereoselective syn process,[203] and the five-membered Ei mechanism operates:



[196]Weygand; Daniel; Simon *Chem. Ber.* **1958,** *91*, 1691; Bach; Andrzejewski; Bair *J. Chem. Soc., Chem. Commun.* **1974,** 820; Bach; Knight *Tetrahedron Lett.* **1979,** 3815.

[197]Wittig; Polster *Liebigs Ann. Chem.* **1958,** *612*, 102; Wittig; Burger *Liebigs Ann. Chem.* **1960,** *632*, 85.

[198]Hünig; Öller; Wehner *Liebigs Ann. Chem.* **1979,** 1925.

[199]For reviews, see Cope; Trumbull, Ref. 185, pp. 361-370; DePuy; King, Ref. 135, pp. 448-451.

[200]Cope; LeBel *J. Am. Chem. Soc.* **1960,** *82*, 4656; Cope; Ciganek; Howell; Schweizer *J. Am. Chem. Soc.* **1960,** *82*, 4663.

[201]Závada; Pánková; Svoboda *Collect. Czech. Chem. Commun.* **1973,** *38*, 2102.

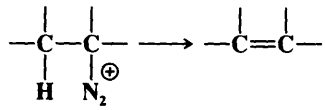
[202]Cram; Sahyun; Knox *J. Am. Chem. Soc.* **1962,** *84*, 1734.

[203]See, for example, Bach; Andrzejewski; Dusold *J. Org. Chem.* **1973,** *38*, 1742.

Almost all evidence indicates that the transition state must be planar. Deviations from planarity as in **7-3** (see p. 1006) are not found here, and indeed this is why six-membered heterocyclic nitrogen compounds do not react. Because of the stereoselectivity of this reaction and the lack of rearrangement of the products, it is useful for the formation of trans cycloolefins (eight-membered and higher).

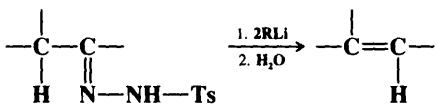
OS **IV,** 612.

7-9 Olefins from Aliphatic Diazonium Salts
Hydro-diazonio-elimination

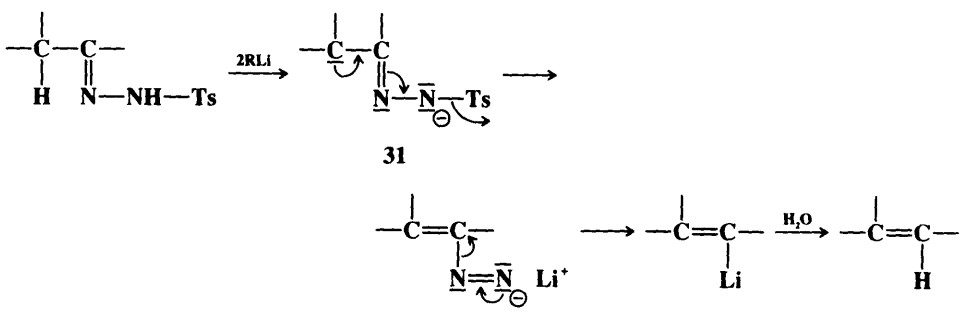


The treatment of aliphatic amines with nitrous acid is not a useful method for the preparation of olefins any more than it is for the preparation of alcohols (p. 355), though some olefin is usually formed in such reactions.

7-10 Decomposition of Toluene-*p*-sulfonylhydrazones



Treatment of the tosylhydrazone of an aldehyde or a ketone with a strong base leads to the formation of an olefin, the reaction being formally an elimination accompanied by a hydrogen shift.[204] The reaction (called the *Shapiro reaction*) has been applied to tosylhydrazones of many aldehydes and ketones. The most useful method synthetically involves treatment of the substrate with at least two equivalents of an organolithium compound[205] (usually MeLi) in ether, hexane, or tetramethylenediamine.[206] This procedure gives good yields of alkenes without side reactions and, where a choice is possible, predominantly gives the less highly substituted olefin. Tosylhydrazones of α,β-unsaturated ketones give conjugated dienes.[207] The mechanism[208] has been formulated as:



31

32 **33**

[204]For reviews, see Adlington; Barrett *Acc. Chem. Res.* **1983,** *16*, 55-59; Shapiro *Org. React.* **1976,** *23*, 405-507.

[205]Shapiro; Heath *J. Am. Chem. Soc.* **1967,** *89*, 5734; Kaufman; Cook; Shechter; Bayless; Friedman *J. Am. Chem. Soc.* **1967,** *89*, 5736; Shapiro *Tetrahedron Lett.* **1968,** 345; Meinwald; Uno *J. Am. Chem. Soc.* **1968,** *90*, 800.

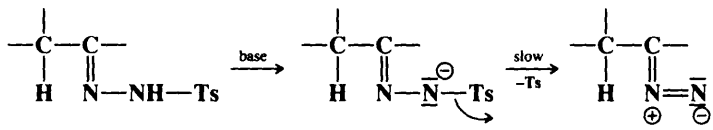
[206]Stemke; Bond *Tetrahedron Lett.* **1975,** 1815.

[207]See Dauben; Rivers; Zimmerman *J. Am. Chem. Soc.* **1977,** *99*, 3414.

[208]For a review of the mechanism, see Casanova; Waegell *Bull. Soc. Chim. Fr.* **1975,** 922-932.

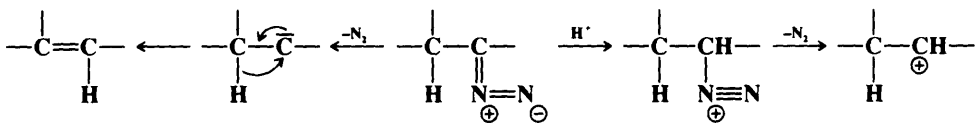
Evidence for this mechanism is: (1) two equivalents of RLi are required; (2) the hydrogen in the product comes from the water and not from the adjacent carbon, as shown by deuterium labeling;[209] and (3) the intermediates **31-33** have been trapped.[210] This reaction, when performed in tetramethylenediamine, can be a synthetically useful method[211] of generating vinylic lithium compounds (**33**), which can be trapped by various electrophiles such as D_2O (to give deuterated alkenes), CO_2 (to give α,β-unsaturated carboxylic acids—**6-34**), or DMF (to give α,β-unsaturated aldehydes—**0-105**).

The reaction also takes place with other bases (e.g., LiH,[213] Na in ethylene glycol, NaH, $NaNH_2$) or with smaller amounts of RLi, but in these cases side reactions are common and the orientation of the double bond is in the other direction (to give the more highly substituted olefin). The reaction with Na in ethylene glycol is called the *Bamford–Stevens reaction*.[214] For these reactions two mechanisms are possible—a carbenoid and a carbocation mechanism.[215] The side reactions found are those expected of carbenes and carbocations. In general, the carbocation mechanism is chiefly found in protic solvents and the carbenoid mechanism in aprotic solvents. Both routes involve formation of a diazo compound (**34**) which in some cases can be isolated.



34

In fact, this reaction has been used as a synthetic method for the preparation of diazo compounds.[216] In the absence of protic solvents **34** loses N_2, and hydrogen migrates, to give the olefin product. The migration of hydrogen may immediately follow, or be simultaneous with, the loss of N_2. In a protic solvent, **34** becomes protonated to give the diazonium ion **35** which loses N_2 to give the corresponding carbocation which may then undergo elimination



34 **35**

(**7-9**) or give other reactions characteristic of carbocations. A diazo compound is an intermediate in the formation of olefins by treatment of N-nitrosoamides with a rhodium(II) catalyst.[217]

[209]Ref. 205; Shapiro; Hornaman *J. Org. Chem.* **1974,** *39*, 2302.

[210]Shapiro; Lipton; Kolonko; Buswell; Capuano *Tetrahedron Lett.* **1975,** 1811, Ref. 206; Lipton; Shapiro *J. Org. Chem.* **1978,** *43*, 1409.

[211]See Traas; Boelens; Takken *Tetrahedron Lett.* **1976,** 2287; Stemke; Chamberlin; Bond *Tetrahedron Lett.* **1976,** 2947.

[212]For a review, see Chamberlin; Bloom *Org. React.* **1990,** *39*, 1-83.

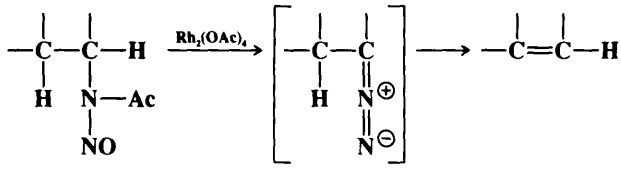
[213]Biellmann; Pète *Bull. Soc. Chim. Fr.* **1967,** 675.

[214]Bamford; Stevens *J. Chem. Soc.* **1952,** 4735.

[215]Powell; Whiting *Tetrahedron* **1959,** *7*, 305, **1961,** *12* 168; DePuy; Froemsdorf *J. Am. Chem. Soc.* **1960,** *82*, 634; Bayless; Friedman; Cook; Shechter *J. Am. Chem. Soc.* **1968,** *90*, 531; Nickon; Werstiuk *J. Am. Chem. Soc.* **1972,** *94*, 7081.

[216]For a review, see Regitz; Maas *Diazo Compounds*; Academic Press: New York, 1986, pp. 257-295. For an improved procedure, see Wulfman; Yousefian; White *Synth. Commun.* **1988,** *18*, 2349.

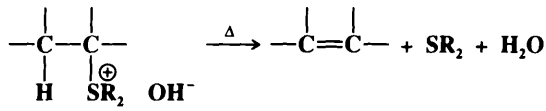
[217]Godfrey; Ganem *J. Am. Chem. Soc.* **1990,** *112*, 3717.

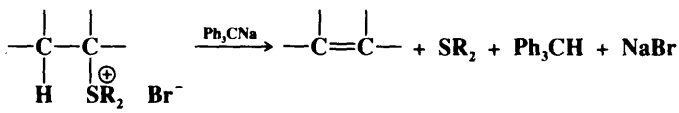


See also **7-28.**

OS **VI,** 172; **VII,** 77. For the preparation of a diazo compound, see OS **VII,** 438.

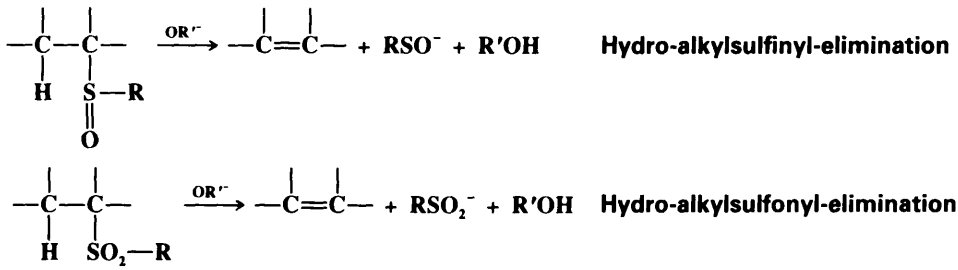
7-11 Cleavage of Sulfonium Compounds
Hydro-dialkylsulfonio-elimination





Sulfonium compounds undergo elimination similar to that of their ammonium counterparts (**7-6** and **7-7**) in scope and mechanism. The decomposition by heat of sulfonium hydroxides has been known for many years.[218] The ylide reaction was discovered more recently.[219] Neither is important synthetically.

7-12 Cleavage of Sulfoxides, Selenoxides, and Sulfones



Sulfones and sulfoxides with a β hydrogen undergo elimination on treatment with an alkoxide or, for sulfones,[220] even with OH^-.[221] In mechanism, these reactions belong on the E1–E2–E1cB spectrum.[222] Although the leaving groups are uncharged, the orientation follows Hofmann's rule, not Zaitsev's. Sulfoxides (but not sulfones) also undergo elimination on pyrolysis

[218]For a discussion, see Knipe, in Stirling *The Chemistry of the Sulphonium Group*, pt. 1; Wiley: New York, 1981, pp. 334-347.

[219]Franzen; Mertz *Chem. Ber.* **1960,** *93,* 2819. For a review, see Block *Reactions of Organosulfur Compounds*; Academic Press: New York, 1978, pp. 112-117.

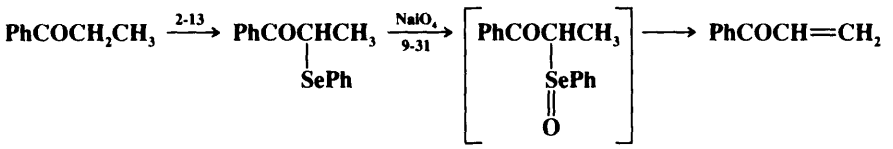
[220]Certain sulfones undergo elimination with 5% HCl in THF: Yoshida; Saito *Chem. Lett.* **1982,** 165.

[221]Hofmann; Wallace; Argabright; Schriesheim *Chem. Ind. (London)* **1963,** 1234.

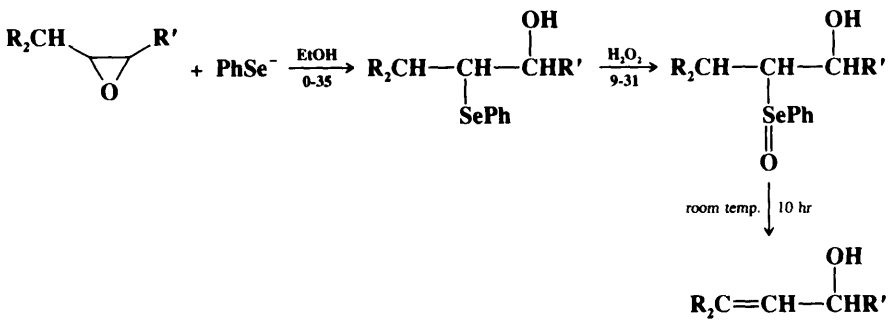
[222]Hofmann; Wallace; Schriesheim *J. Am. Chem. Soc.* **1964,** *86,* 1561.

at about 80°C in a manner analogous to **7-8.** The mechanism is also analogous, being the five-membered Ei mechanism with syn elimination.[223] Selenoxides[224] and sulfinate esters $R_2CH—CHR—SO—OMe$[225] also undergo elimination by the Ei mechanism, the selenoxide reaction taking place at room temperature. The reaction with selenoxides has been extended to the formation of triple bonds.[226]

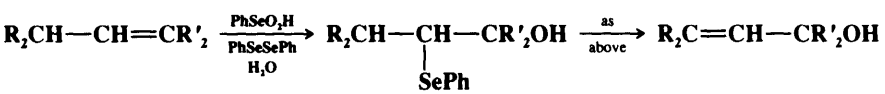
Both the selenoxide[227] and sulfoxide[228] reactions have been used in a method for the conversion of ketones, aldehydes, and carboxylic esters to their α,β-unsaturated derivatives (illustrated for the selenoxide).



Because of the mildness of the procedure, this is probably the best means of accomplishing this conversion. The selenoxide reaction has been used in a procedure for the conversion of epoxides to allylic alcohols.[229]



In another process, an olefin is converted to a rearranged allylic alcohol.[230]



[223]Kingsbury; Cram *J. Am. Chem. Soc.* **1960,** *82*, 1810; Walling; Bollyky *J. Org. Chem.* **1964,** *29*, 2699; Entwistle; Johnstone *Chem. Commun.* **1965,** 29; Yoshimura; Tsukurimichi; Iizuka; Mizuno; Isaji; Shimasaki *Bull. Chem. Soc. Jpn.* **1989,** *62*, 1891.

[224]For reviews, see Back, in Patai *The Chemistry of Organic Selenium and Telurium Compounds*, vol. 2; Wiley: New York, 1987, pp. 91-213, pp. 95-109; Paulmier *Selenium Reagents and Intermediates in Organic Synthesis*; Pergamon: Elmsford, NY, 1986, pp. 132-143; Reich *Acc. Chem. Res.* **1979,** *12*, 22-30, in Trahanovsky *Oxidation in Organic Chemistry*, pt. C; Academic Press: New York, 1978, pp. 15-101; Sharpless; Gordon; Lauer; Patrick; Singer; Young *Chem. Scr.* **1975,** *8A*; 9-13. See also Liotta *Organoselenium Chemistry*; Wiley: New York, 1987.

[225]Jones; Higgins *J. Chem. Soc. C* **1970,** 81.

[226]Reich; Willis *J. Am. Chem. Soc.* **1980,** *102*, 5967.

[227]Clive *J. Chem. Soc., Chem. Commun.* **1973,** 695; Reich; Reich; Renga *J. Am. Chem. Soc.* **1973,** *95*, 5813; Reich; Renga; Reich *J. Org. Chem.* **1974,** *39*, 2133, *J. Am. Chem. Soc.* **1975,** *97*, 5434; Sharpless; Lauer; Teranishi *J. Am. Chem. Soc.* **1973,** *95*, 6137; Grieco; Miyashita *J. Org. Chem.* **1974,** *39*, 120. For lists of reagents, with references, see Ref. 144, pp. 149-150.

[228]Trost; Salzmann; Hiroi *J. Am. Chem. Soc.* **1976,** *98*, 4887. For a review of this and related methods, see Trost *Acc. Chem. Res.* **1978,** *11*, 453-461.

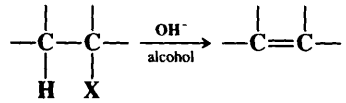
[229]Sharpless; Lauer *J. Am. Chem. Soc.* **1973,** *95*, 2697.

[230]Hori; Sharpless *J. Org. Chem.* **1978,** *43*, 1689; Reich; Wollowitz; Trend; Chow; Wendelborn *J. Org. Chem.* **1978,** *43*, 1697. See also Reich *J. Org. Chem.* **1974,** *39*, 428; Clive *J. Chem. Soc., Chem. Commun.* **1974,** 100; Sharpless; Lauer *J. Org. Chem.* **1974,** *39*, 429.

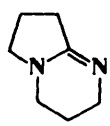
See p. 473 for another application of the selenoxide reaction. Allylic sulfoxides undergo 1,4 elimination to give dienes.[231]

OS **VI,** 23, 737; **67,** 157.

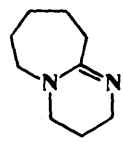
7-13 Dehydrohalogenation of Alkyl Halides
Hydro-halo-elimination



The elimination of HX from an alkyl halide is a very general reaction and can be accomplished with chlorides, fluorides, bromides, and iodides.[232] Hot alcoholic KOH is the most frequently used base, though stronger bases[233] (OR^-, NH_2^-, etc.) or weaker ones (e.g., amines) are used where warranted.[234] The bicyclic amidines 1,5-diazabicyclo[3.4.0]nonene-5 (DBN)[235] and 1,8-diazabicyclo[5.4.0]undecene-7 (DBU)[236] are good reagents for difficult cases.[237]



DBN



DBU

Dehydrohalogenation with the non-ionic base $(Me_2N)_3P{=}N{-}P(NMe_2)_2{=}NMe$ is even faster.[238] Phase transfer catalysis has been used with OH^- as base.[239] As previously mentioned (p. 997), certain weak bases in dipolar aprotic solvents are effective reagents for dehydrohalogenation. Among those most often used for synthetic purposes are LiCl or LiBr–$LiCO_3$ in DMF.[240] Dehydrohalogenation has also been effected by heating of the alkyl halide in HMPA with no other reagent present.[241] As in nucleophilic substitution (p. 352), the order of leaving group reactivity is I > Br > Cl > F.[242]

[231]de Groot; Jansen; Reuvers; Tedjo *Tetrahedron Lett.* **1981,** *22,* 4137.

[232]For a review of eliminations involving the carbon–halogen bond, see Baciocchi, in Patai; Rappoport *The Chemistry of Functional Groups, Supplement D,* pt. 2; Wiley: New York, 1983, pp. 1173-1227.

[233]Triphenylmethylpotassium rapidly dehydrohalogenates secondary alkyl bromides and iodides, in over 90% yields, at 0°C: Anton; Crabtree *Tetrahedron Lett.* **1983,** *24,* 2449.

[234]For a list of reagents, with references, see Ref. 144, pp. 131-133.

[235]Truscheit; Eiter *Liebigs Ann. Chem.* **1962,** *658,* 65; Oediger; Kabbe; Möller; Eiter *Chem. Ber.* **1966,** *99,* 2012; Vogel; Klärner *Angew. Chem. Int. Ed. Engl.* **1968,** *7,* 374 [*Angew. Chem. 80,* 402].

[236]Oediger; Möller *Angew. Chem. Int. Ed. Engl.* **1967,** *6,* 76 [*Angew. Chem. 79,* 53]; Wolkoff *J. Org. Chem.* **1982,** *47,* 1944.

[237]For a review of these reagents, see Oediger; Möller; Eiter *Synthesis* **1972,** 591.

[238]Schwesinger; Schlemper *Angew. Chem. Int. Ed. Engl.* **1987,** *26,* 1167 [*Angew. Chem. 99,* 1212].

[239]Kimura; Regen *J. Org. Chem.* **1983,** *48,* 195; Halpern; Zahalka; Sasson; Rabinovitz *J. Org. Chem.* **1985,** *50,* 5088. See also Barry; Bram; Decodts; Loupy; Pigeon; Sansoulet *J. Org. Chem.* **1984,** *49,* 1138.

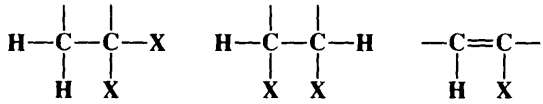
[240]For a discussion, see Fieser; Fieser *Reagents for Organic Syntheses,* vol. 1; Wiley: New York, 1967, pp. 606-609. For a review of alkali-metal fluorides in this reaction, see Yakobson; Akhmetova *Synthesis* **1983,** 169-184, pp. 170-173.

[241]Hanna *Tetrahedron Lett.* **1968,** 2105; Monson *Chem. Commun.* **1971,** 113; Hutchins; Hutchins; Milewski *J. Org. Chem.* **1972,** *37,* 4190.

[242]Matsubara; Matsuda; Hamatani; Schlosser *Tetrahedron* **1988,** *44,* 2855.

Tertiary halides undergo elimination most easily. Eliminations of chlorides, bromides, and iodides follow Zaitsev's rule, except for a few cases where steric effects are important (for an example, see p. 1000). Eliminations of fluorides follow Hofmann's rule (p. 1000).

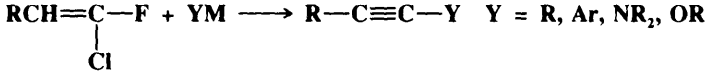
This reaction is by far the most important way of introducing a triple bond into a molecule.[243] This can be accomplished with substrates of the types:[244]



When the base is $NaNH_2$ 1-alkynes predominate (where possible), because this base is strong enough to form the salt of the alkyne, shifting any equilibrium between 1- and 2-alkynes. When the base is OH^- or OR^-, the equilibrium tends to be shifted to the internal alkyne, which is thermodynamically more stable. If another hydrogen is suitably located (e.g., —CRH—CX_2—CH_2—), allene formation can compete, though alkynes are usually more stable.

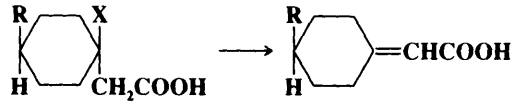
Dehydrohalogenation is generally carried out in solution, with a base, and the mechanism is usually E2, though the E1 mechanism has been demonstrated in some cases. However, elimination of HX can be accomplished by pyrolysis of the halide, in which case the mechanism is Ei (p. 1006) or, in some instances, the free-radical mechanism (p. 1008). Pyrolysis is normally performed without a catalyst at about 400°C. The pyrolysis reaction is not generally useful synthetically, because of its reversibility. Less work has been done on pyrolysis with a catalyst[245] (usually a metallic oxide or salt), but the mechanisms here are probably E1 or E2.

A combination elimination and substitution reaction has been used to synthesize alkynes. In this reaction a compound RCH=CFCl is treated with YM, where M is a metal and Y may be alkyl, aryl, NR_2, or OR:



Alkynes, ynamines,[246] and acetylenic ethers[247] can be prepared in this manner.[248]

In the special case of the prochiral carboxylic acids **36**, dehydrohalogenation with an



36

optically active lithium amide gave an optically active product with enantiomeric excesses as high as 82%.[249]

[243]For reviews, see Ben-Efraim, Ref. 142; Köbrich; Buck, in Viehe *Acetylenes*; Marcel Dekker: New York, 1969, pp. 100-134; Ref. 194, pp. 391-397; Köbrich, Ref. 2, pp. 50-53.

[244]For a list of reagents, with references, see Ref. 144, pp. 289-291.

[245]For a review, see Noller; Andréu; Hunger, Ref. 154.

[246]For a review of methods for the synthesis of ynamines, see Collard-Motte; Janousek *Top. Curr. Chem.* **1986,** *130*, 89-131.

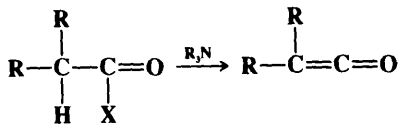
[247]For a review of acetylenic ethers, see Radchenko; Petrov *Russ. Chem. Rev.* **1989,** *58*, 948-966.

[248]Viehe *Angew. Chem. Int. Ed. Engl.* **1963,** *2*, 477 [*Angew. Chem. 75*, 638]. For reviews of ynamines, see Ficini *Tetrahedron* **1976,** *32*, 1448-1486; Viehe, in Viehe, Ref. 243, pp. 861-912.

[249]Duhamel; Ravard; Plaquevent; Plé; Davoust *Bull. Soc. Chim. Fr.* **1990,** 787.

OS **I,** 191, 205, 209, 438; **II,** 10, 17, 515; **III,** 125, 209, 270, 350, 506, 623, 731, 785; **IV,** 128, 162, 398, 404, 555, 608, 616, 683, 711, 727, 748, 755, 763, 851, 969; **V,** 285, 467, 514; **VI,** 87, 210, 327, 361, 368, 427, 462, 505, 564, 862, 883, 893, 954, 991, 1037; **VII,** 126, 319, 453, 491; **65,** 32, 68, 90; **69,** 238. Also see OS **VI,** 968.

7-14 Dehydrohalogenation of Acyl Halides and Sulfonyl Halides
Hydro-halo-elimination



Ketenes can be prepared by treatment of acyl halides with tertiary amines. The scope is broad, and most acyl halides possessing an α hydrogen give the reaction, but if at least one R is hydrogen, only the ketene dimer, not the ketene, is isolated. However, if it is desired to use a reactive ketene in a reaction with a given compound, the ketene can be generated in situ in the presence of the given compound.[250]

Closely related is the reaction of tertiary amines with sulfonyl halides that contain an α hydrogen. In this case the initial product is the highly reactive sulfene, which cannot be

$$\mathbf{RCH_2SO_2Cl} \xrightarrow{R_3N} \underset{\text{Sulfene}}{\mathbf{[RCH{=}SO_2]}} \longrightarrow \mathbf{RCH{=}CHR} + \text{other products}$$

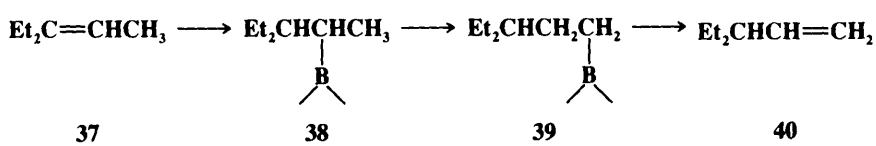
isolated but reacts further to give products, one of which may be the alkene that is the dimer of RCH.[251] Reactions of sulfenes in situ are also common (for example, see **6-62**).

OS **IV,** 560; **V,** 294, 877; **VI,** 549, 1037; **VII,** 232; **68,** 32.

7-15 Elimination of Boranes
Hydro-boranetriyl-elimination

$$\mathbf{(R_2CH{-}CH_2)_3B} + \mathbf{3}\ \text{1-decene} \rightleftharpoons \mathbf{3R_2C{=}CH_2} + \mathbf{[CH_3(CH_2)_8CH_2]_3B}$$

Trialkylboranes are formed from an olefin and BH_3 (**5-12**). When the resulting borane is treated with another olefin, an exchange reaction occurs.[252] This is an equilibrium process that can be shifted by using a large excess of olefin, by using an unusually reactive olefin, or by using an olefin with a higher boiling point than the displaced olefin and removing the latter by distillation. The reaction is useful for shifting a double bond in the direction opposite to that resulting from normal isomerization methods (**2-2**). This cannot be accomplished simply by treatment of a borane such as **38** with an olefin, because elimination in this reaction follows Zaitsev's rule: It is in the direction of the most stable olefin, and the product would be **37,** not **40.** However, if it is desired to convert **37** to **40,** this can be accomplished by converting **37** to **38,** isomerizing **38** to **39** (**8-11**) and then subjecting **39** to the exchange



37 **38** **39** **40**

[250]For a review of this procedure, see Luknitskii; Vovsi *Russ. Chem. Rev.* **1969,** *38,* 487-494.

[251]For reviews of sulfenes, see Ref. 1729 in Chapter 10.

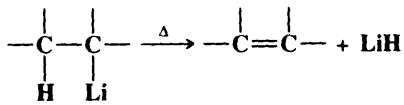
[252]Brown; Bhatt; Munekata; Zweifel *J. Am. Chem. Soc.* **1967,** *89,* 567; Taniguchi *Bull. Chem. Soc. Jpn.* **1979,** *52,* 2942.

reaction with a higher-boiling olefin, e.g., 1-decene,whereupon **40** is produced. In the usual isomerizations (**2-2**), **40** could be isomerized to **37**, but not the other way around. The reactions **38** → **39** and **39** → **40** proceed essentially without rearrangement. The mechanism is probably the reverse of borane addition (**5-12**).

A similar reaction, but irreversible, has been demonstrated for alkynes.[253]

$$(R_2CH{-}CH_2)_3B + R'C{\equiv}CR' \longrightarrow 3R_2C{=}CH_2 + (R'CH{=}CR')_3B$$

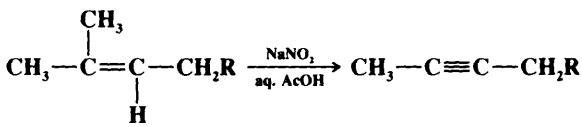
7-16 Pyrolysis of Alkali-Metal Organometallic Compounds
Hydro-metallo-elimination



Solid lithium hydride and an olefin can be obtained by heating alkyllithium compounds containing a β hydrogen.[254] The reaction has also been applied to alkylsodium and alkylpotassium compounds.[255] Grignard reagents gave olefins when thermally decomposed in nonsolvating solvents, e.g., cumene.[256] Alkenes have also been obtained from RLi and RMgX in solution, by treatment with ethylene and $NiCl_2$ or with certain other reagents.[257] Nitroalkenes have been obtained by cleavage of H and HgCl from β-nitro mercuric halides[258] (prepared by nitromercuration—see **5-7**). The mechanism is generally believed to be a four-centered pericyclic one (Ei).[259]

OS **68**, 148.

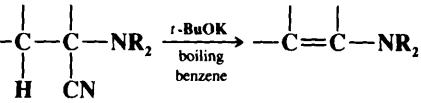
7-17 Conversion of Alkenes to Alkynes
Hydro-methyl-elimination



Alkenes of the form shown lose the elements of methane when treated with sodium nitrite in acetic acid and water, to form alkynes in moderate-to-high yields.[260] The R may contain additional unsaturation as well as OH, OR, OAc, C=O, and other groups, but the $Me_2C{=}CHCH_2{-}$ portion of the substrate is necessary for the reaction to take place. The mechanism is complex, beginning with a nitration that takes place with allylic rearrangement [$Me_2C{=}CHCH_2R \rightarrow H_2C{=}CMeCH(NO_2)CH_2R$], and involving several additional intermediates.[261] The CH_3 lost from the substrate appears as CO_2, as demonstrated by the trapping of this gas.[261]

[253]Hubert *J. Chem. Soc.* **1965**, 6669.
[254]Ziegler; Gellert *Liebigs Ann. Chem.* **1950**, *567*, 179.
[255]For example, see Finnegan *Chem. Ind. (London)* **1962**, 895, *Tetrahedron Lett.* **1963**, 851.
[256]Zakharkin; Okhlobystin; Strunin *J. Organomet. Chem.* **1965**, *4*, 349; Lefrançois; Gault *J. Organomet. Chem.* **1969**, *16*, 7; Dymova; Grazhulene; Kuchinskii; Kuznetsov *Bull. Acad. Sci. USSR; Div. Chem. Sci.* **1971**, *20*, 1532.
[257]Reetz; Stephan *Liebigs Ann. Chem.* **1980**, 171, and previous papers in this series. See also Laycock; Baird *Tetrahedron Lett.* **1978**, 3307; Baudin; Julia; Rolando; Verpeaux *Tetrahedron Lett.* **1984**, *25*, 3203.
[258]Corey; Estreicher *J. Am. Chem. Soc.* **1978**, *100*, 6294.
[259]See, for example, Li; San Filippo *Organometallics* **1983**, *2*, 554.
[260]Abidi *Tetrahedron Lett.* **1986**, *27*, 267, *J. Org. Chem.* **1986**, *51*, 2687.
[261]Corey; Seibel; Kappos *Tetrahedron Lett.* **1987**, *28*, 4921.

7-18 Dehydrocyanation
Hydro-cyano-elimination

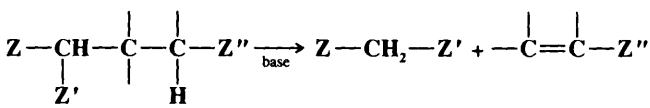


Enamines can be prepared from α-cyano tertiary amines by treatment with KOH or *t*-BuOK in boiling benzene or toluene, or in *t*-butyl methyl ether at room temperature.[262]

7-19 Decarbonylation of Acyl Halides
Hydro-chloroformyl-elimination

Acyl chlorides containing an α hydrogen are smoothly converted to olefins, with loss of HCl and CO, on heating with chlorotris(triphenylphosphine)rhodium, with metallic platinum, or with certain other catalysts.[263] The mechanism probably involves conversion of RCH_2CH_2COCl to RCH_2CH_2—$RhCO(Ph_3P)_2Cl_2$ followed by a concerted syn elimination of Rh and H.[264] See also **4-41** and **9-13.**

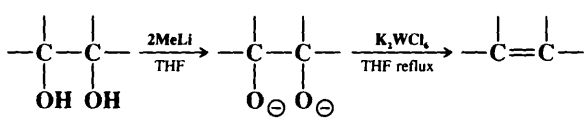
7-20 Reversal of the Michael Reaction
Hydro-bis(ethoxycarbonyl)methyl-elimination, etc.



Olefins can be formed on base cleavage of Michael adducts. (See **5-17.** Z is defined on p. 741) In some cases cleavage occurs simply on heating, without basic catalysis.

B. Reactions in Which Neither Leaving Atom is Hydrogen

7-21 Deoxygenation of Vicinal Diols
Dihydroxy-elimination



vic-Diols can be deoxygenated by treatment of the dilithium dialkoxide with the tungsten halide K_2WCl_6, or with certain other tungsten reagents, in refluxing THF.[265] Tetrasubstituted diols react most rapidly. The elimination is largely, but not entirely, syn. Several other

[262]Ahlbrecht; Raab; Vonderheid *Synthesis* **1979,** 127; Ahlbrecht; Raab *Synthesis* **1980,** 320.

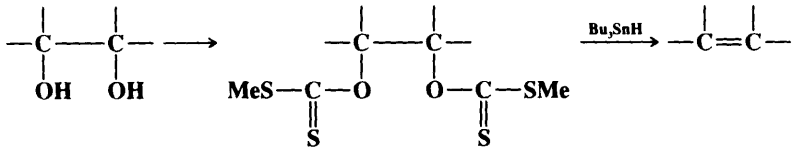
[263]Tsuji; Ohno *J. Am. Chem. Soc.* **1966,** *88,* 3452, **1968,** *90,* 94; Ohno; Tsuji *J. Am. Chem. Soc.* **1968,** *90,* 99. For a review, see Tsuji; Ohno *Synthesis* **1969,** 157-169. For extensions to certain other acid derivatives, see Minami; Nisar; Yuhara; Shimizu; Tsuji *Synthesis* **1987,** 992.

[264]Lau; Becker; Huang; Baenziger; Stille *J. Am. Chem. Soc.* **1977,** *99,* 5664.

[265]Sharpless; Flood *J. Chem. Soc., Chem. Commun.* **1972,** 370; Sharpless; Umbreit; Nieh; Flood *J. Am. Chem. Soc.* **1972,** *94,* 6538.

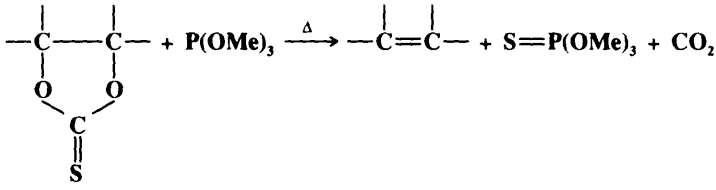
methods have been reported,[266] in which the diol is deoxygenated directly, without conversion to the dialkoxide. These include treatment with titanium metal,[267] with TsOH–NaI,[268] with Ph_2PCl–imidazole–I_2 in toluene,[269] and with PBr_3–CuBr–ether at low temperatures, followed by zinc powder.[270]

vic-Diols can also be deoxygenated indirectly, through sulfonate ester derivatives. For example, *vic*-dimesylates and *vic*-ditosylates have been converted to alkenes by treatment, respectively, with naphthalene–sodium[271] and with NaI in dimethylformamide.[272] In another procedure, the diols are converted to bisdithiocarbonates (bis xanthates), which undergo



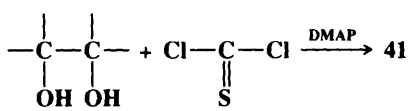
elimination (probably by a free-radical mechanism) when treated with tri-*n*-butylstannane in toluene or benzene.[273] *vic*-Diols can also be deoxygenated through cyclic derivatives (**7-22**).

7-22 Cleavage of Cyclic Thionocarbonates



41

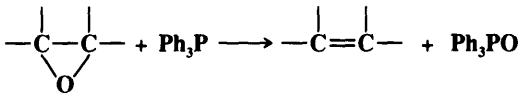
Cyclic thionocarbonates (**41**) can be cleaved to olefins (the *Corey–Winter reaction*)[274] by heating with trimethyl phosphite[275] or other trivalent phosphorus compounds[276] or by treatment with bis(1,5-cyclooctadiene)nickel.[277] The thionocarbonates can be prepared by treatment of 1,2-diols with thiophosgene and 4-dimethylaminopyridine (DMAP):[278]



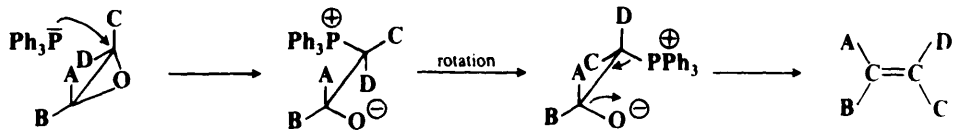
[266]For a list of reagents, with references, see Ref. 144, pp. 155-156.
[267]McMurry; Fleming *J. Org. Chem.* **1976,** *41*, 896; McMurry *Acc. Chem. Res.* **1983,** *16*, 405-411.
[268]Sarma; Sharma *Chem. Ind. (London)* **1987,** 96.
[269]Liu; Classon; Samuelsson *J. Org. Chem.* **1990,** *55*, 4273.
[270]Tanaka; Yasuda; Yamamoto; Nozaki *J. Am. Chem. Soc.* **1975,** *97*, 3252.
[271]Carnahan; Closson *Tetrahedron Lett.* **1972,** 3447.
[272]Dafaye *Bull Soc. Chim. Fr.* **1968,** 2099.
[273]Barrett; Barton; Bielski *J. Chem. Soc., Perkin Trans. 1* **1979,** 2378.
[274]For reviews, see Block *Org. React.* **1984,** *30*, 457-566; Sonnet *Tetrahedron* **1980,** *36*, 557-604, pp. 593-598; Mackie, in Cadogan *Organophosphorus Reagents in Organic Synthesis*; Academic Press: New York, 1979, pp. 354-359; Block, Ref. 219, pp. 229-235.
[275]Corey; Winter *J. Am. Chem. Soc.* **1963,** *85*, 2677.
[276]Corey *Pure Appl. Chem.* **1967,** *14*, 19-37, pp. 32-33.
[277]Semmelhack; Stauffer *Tetrahedron Lett.* **1973,** 2667. For another method, see Vedejs; Wu *J. Org. Chem.* **1974,** *39*, 3641.
[278]Corey; Hopkins *Tetrahedron Lett.* **1982,** *23*, 1979.

The elimination is of course syn, so the product is sterically controlled. Olefins that are not sterically favored can be made this way in high yield, e.g., *cis*-$PhCH_2CH{=}CHCH_2Ph$.[279] Certain other 5-membered cyclic derivatives of 1,2-diols can also be converted to alkenes.[280]

7-23 The Conversion of Epoxides to Olefins
epi-Oxy-elimination



Epoxides can be converted to olefins[281] by treatment with triphenylphosphine[282] or triethyl phosphite $P(OEt)_3$.[283] The first step of the mechanism is nucleophilic substitution (**0-49**), followed by a four-center elimination. Since inversion accompanies the substitution, the overall elimination is anti, i.e., if two groups A and C are cis in the epoxide, they will be trans in the olefin:



betaine

Alternatively, the epoxide can be treated with lithium diphenylphosphide Ph_2PLi, and the product quaternized with methyl iodide.[284] Olefins have also been obtained from epoxides by reaction with a large number of reagents,[285] among them Li in THF,[286] TsOH and NaI,[287] trimethylsilyl iodide,[288] dimethyl diazomalonate,[289] PI_3,[290] P_2I_4,[291] AlI_3,[292] $Mg–I_2–Et_2O$,[293] F_3COOH–NaI,[294] 9-diazofluorene and uv light,[295] SmI_2,[296] titanocene dichloride–Mg,[297]

[279]Corey; Carey; Winter *J. Am. Chem. Soc.* **1965,** *87*, 934.

[280]See Hines; Peagram; Whitham; Wright *Chem. Commun.* **1968,** 1593; Josan; Eastwood *Aust. J. Chem.* **1968,** *21*, 2013; Hiyama; Nozaki *Bull. Chem. Soc. Jpn.* **1973,** *46*, 2248; Marshall; Lewellyn *J. Org. Chem.* **1977,** *42*, 1311; Breuer; Bannet *Tetrahedron* **1978,** *34*, 997; Hanessian; Bargiotti; LaRue *Tetrahedron Lett.* **1978,** 737; Hatanaka; Tanimoto; Oida; Okano *Tetrahedron Lett.* **1981,** *22*, 5195; Ando; Ohhara; Takase *Chem. Lett.* **1986,** 879; King; Posner; Mak; Yang *Tetrahedron Lett.* **1987,** *28*, 3919; Beels; Coleman; Taylor *Synlett* **1990,** 479.

[281]For reviews, see Wong; Fok; Wong *Heterocycles* **1987,** *26*, 1345-1382; Sonnet, Ref. 274, pp. 576-586.

[282]Wittig; Haag *Chem. Ber.* **1955,** *88*, 1654.

[283]Scott *J. Org. Chem.* **1957,** *22*, 1118.

[284]Vedejs; Fuchs *J. Am. Chem. Soc.* **1971,** *93*, 4070, **1973,** *95*, 822.

[285]For a list of reagents, with references, see Ref. 144, pp. 140-142.

[286]Gurudutt; Ravindranath *Tetrahedron Lett.* **1980,** *21*, 1173.

[287]Baruah; Sharma; Baruah *Chem. Ind. (London)* **1983,** 524.

[288]Denis; Magnane; Van Eenoo; Krief *Nouv. J. Chim.* **1979,** *3*, 705. For other silyl reagents, see Reetz; Plachky *Synthesis* **1976,** 199; Dervan; Shippey *J. Am. Chem. Soc.* **1976,** *98*, 1265; Caputo; Mangoni; Neri; Palumbo *Tetrahedron Lett.* **1981,** *22*, 3551.

[289]Martin; Ganem *Tetrahedron Lett.* **1984,** *25*, 251.

[290]Denis, et al., Ref. 288.

[291]Suzuki; Fuchita; Iwasa; Mishina *Synthesis* **1978,** 905; Ref. 290.

[292]Sarmah; Barua *Tetrahedron Lett.* **1988,** *29*, 5815.

[293]Chowdhury *J. Chem. Res. (S)* **1990,** 192.

[294]Sarma; Sharma *Chem. Ind. (London)* **1984,** 712.

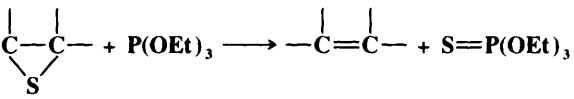
[295]Shields; Schuster *Tetrahedron Lett.* **1987,** *28*, 853.

[296]Girard; Namy; Kagan *J. Am. Chem. Soc.* **1980,** *102*, 2693; Matsukawa; Tabuchi; Inanaga; Yamaguchi *Chem. Lett.* **1987,** 2101.

[297]Schobert *Angew. Chem. Int. Ed. Engl.* **1988,** *27*, 855 [*Angew. Chem. 100*, 869]. See also Yadav; Shekharam; Gadgil *J. Chem. Soc., Chem. Commun.* **1990,** 843.

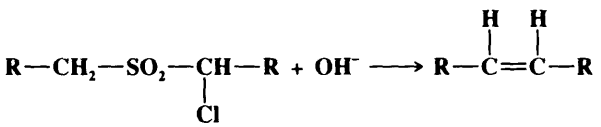
$Fe(CO)_5$,[298] $TiCl_3$–$LiAlH_4$,[299] $FeCl_3$–BuLi,[300] the tungsten reagents mentioned in **7-21**,[265] and NaI–NaOAc–Zn–AcOH.[301] The last-mentioned method is actually a variation of **7-31**, since iodohydrins are intermediates. Some of these methods give syn elimination.

7-24 The Conversion of Episulfides to Olefins
epi-Thio-elimination

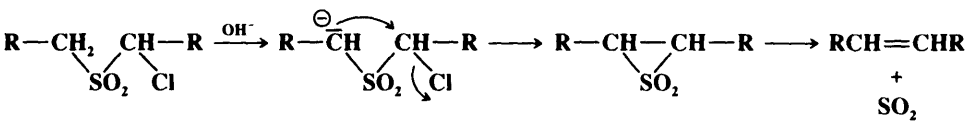


Episulfides[302] can be converted to olefins in a reaction similar in appearance to **7-23**.[303] However, in this case the elimination is syn, so the mechanism cannot be the same as that of **7-23**. The phosphite attacks not the carbon, but the sulfur. Among other reagents that convert episulfides to olefins are Bu_3SnH,[304] P_2I_4,[304] certain rhodium complexes,[305] $LiAlH_4$[306] (this compound behaves quite differently with epoxides, see **0-80**), and methyl iodide.[307] Episulfoxides can be converted to olefins and sulfur monoxide simply by heating.[308]

7-25 The Ramberg-Bäcklund Reaction
Ramberg-Bäcklund halosulfone transformation



The reaction of an α-halo sulfone with a base to give an olefin is called the *Ramberg–Bäcklund reaction*.[309] The reaction is quite general for α-halo sulfones with an α′ hydrogen, despite the unreactivity of α-halo sulfones in normal SN2 reactions (p. 344). Halogen reactivity is in the order I > Br ⩾ Cl. Phase transfer catalysis has been used.[310] In general, mixtures of cis and trans isomers are obtained, but usually the less stable cis isomer predominates. The mechanism involves formation of an episulfone and then elimination of



[298]Alper; Des Roches *Tetrahedron Lett.* **1977**, 4155.

[299]McMurry; Silvestri; Fleming; Hoz; Grayston *J. Org. Chem.* **1978**, *43*, 3249.

[300]Fujisawa; Sugimoto; Ohta *Chem. Lett.* **1975**, 883.

[301]Cornforth; Cornforth; Mathew *J. Chem. Soc.* **1959**, 112. See also Yamada; Goto; Nagase; Kyotani; Hirata *J. Org. Chem.* **1978**, *43*, 2076; Sonnet *Synthesis* **1980**, 828.

[302]For a review of this reaction, see Sonnet, Ref. 274, pp. 587-590. For a review of episulfides, see Goodman; Reist, in Kharasch; Meyers *The Chemistry of Organic Sulfur Compounds*, vol. 2; Pergamon: Elmsford, NY, 1966, pp. 93-113.

[303]Neureiter; Bordwell *J. Am. Chem. Soc.* **1959**, *81*, 578; Davis *J. Org. Chem.* **1957**, *23*, 1767.

[304]Schauder; Denis; Krief *Tetrahedron Lett.* **1983**, *24*, 1657.

[305]Calet; Alper *Tetrahedron Lett.* **1986**, *27*, 3573.

[306]Lightner; Djerassi *Chem. Ind. (London)* **1962**, 1236; Latif; Mishriky; Zeid *J. Prakt. Chem.* **1970**, *312*, 421.

[307]Culvenor; Davies; Heath *J. Chem. Soc.* **1949**, 282; Helmkamp; Pettitt *J. Org. Chem.* **1964**, *29*, 3258.

[308]Hartzell; Paige *J. Am. Chem. Soc.* **1966**, *88*, 2616, *J. Org. Chem.* **1967**, *32*, 459; Aalbersberg; Vollhardt *J. Am. Chem. Soc.* **1977**, *99*, 2792.

[309]For reviews, see Paquette *Org. React.* **1977**, *25*, 1-71, *Mech. Mol. Migr.* **1968**, *1*, 121-156, *Acc. Chem. Res.* **1968**, *1*, 209-216; Meyers; Matthews; Ho; Kolb; Parady, in Smith *Catalysis in Organic Synthesis*; Academic Press: New York, 1977, pp. 197-278; Rappe, in Patai *The Chemistry of the Carbon–Halogen Bond*, Ref. 2, pt. 2, pp. 1105-1110; Bordwell *Acc. Chem. Res.* **1970**, *3*, 281-290, pp. 285-286; in Janssen *Organosulfur Chemistry*; Wiley: New York, 1967, pp. 271-284.

[310]Hartman; Hartman *Synthesis* **1982**, 504.

SO_2. There is much evidence for this mechanism,[311] including the isolation of the episulfone intermediate,[312] and the preparation of episulfones in other ways and the demonstration that they give olefins under the reaction conditions faster than the corresponding α-halo sulfones.[313] Episulfones synthesized in other ways (e.g., **6-62**) are reasonably stable compounds but eliminate SO_2 to give olefins when heated or treated with base.

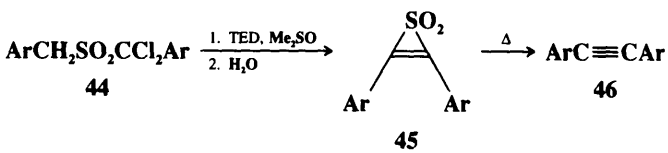
If the reaction is run on the unsaturated bromo sulfones $RCH_2CH{=}CHSO_2CH_2Br$ (prepared by reaction of $BrCH_2SO_2Br$ with $RCH_2CH{=}CH_2$ followed by treatment with Et_3N), the dienes $RCH{=}CHCH{=}CH_2$ are produced in moderate-to-good yields.[314] The compound mesyltriflone $CF_3SO_2CH_2SO_2CH_3$ can be used as a synthon for the tetraion $^{2-}C{=}C^{2-}$. Successive alkylation (**0-94**) converts it to $CF_3SO_2CR^1R^2SO_2CHR^3R^4$ (anywhere from one to four alkyl groups can be put in), which, when treated with base, gives $R^1R^2C{=}CR^3R^4$.[315] The nucleofuge here is the $CF_3SO_2^-$ ion.

2,5-Dihydrothiophene-1,1-dioxides (**42**) and 2,7-dihydrothiepin-1,1-dioxides (**43**)

42 **43**

undergo analogous 1,4 and 1,6 eliminations, respectively (see also **7-48**). These are concerted reactions and, as predicted by the orbital-symmetry rules (p. 846), the former[316] is a suprafacial process and the latter[317] an antarafacial process. The rules also predict that elimination of SO_2 from episulfones cannot take place by a concerted mechanism (except antarafacially, which is unlikely for such a small ring), and the evidence shows that this reaction occurs by a nonconcerted pathway.[318] The eliminations of SO_2 from **42** and **43** are examples of *cheletropic reactions*,[319] which are defined as reactions in which two σ bonds that terminate at a single atom (in this case the sulfur atom) are made or broken in concert.[320]

α,α-Dichlorobenzyl sulfones (**44**) react with an excess of the base triethylenediamine in



44 **45** **46**

dimethyl sulfoxide at room temperature to give 2,3-diarylthiiren-1,1-dioxides (**45**), which can be isolated.[321] Thermal decomposition of **45** gives the alkynes **46**.[322]

[311]See, for example, Bordwell; Cooper *J. Am. Chem. Soc.* **1951,** *73*, 5187; Paquette *J. Am. Chem. Soc.* **1964,** *86*, 4089; Neureiter *J. Am. Chem. Soc.* **1966,** *88*, 558; Bordwell; Wolfinger *J. Org. Chem.* **1974,** *39*, 2521; Bordwell; Doomes *J. Org. Chem.* **1974,** *39*, 2526, 2531.

[312]Sutherland; Taylor *Tetrahedron Lett.* **1989,** *30*, 3267.

[313]Bordwell; Williams; Hoyt; Jarvis *J. Am. Chem. Soc.* **1968,** *90*, 429; Bordwell; Williams *J. Am. Chem. Soc.* **1968,** *90*, 435.

[314]Block; Aslam; Eswarakrishnan; Gebreyes; Hutchinson; Iyer; Laffitte; Wall *J. Am. Chem. Soc.* **1986,** *108*, 4568.

[315]Hendrickson; Boudreaux; Palumbo *J. Am. Chem. Soc.* **1986,** *108*, 2358.

[316]Mock *J. Am. Chem. Soc.* **1966,** *88*, 2857; McGregor; Lemal *J. Am. Chem. Soc.* **1966,** *88*, 2858.

[317]Mock *J. Am. Chem. Soc.* **1969,** *91*, 5682.

[318]Ref. 313. See also Vilsmaier; Tropitzsch; Vostrowsky *Tetrahedron Lett.* **1974,** 3987.

[319]For a review, see Mock, in Marchand; Lehr *Pericyclic Reactions*, vol. 2; Academic Press: New York, 1977, pp. 141-179.

[320]Woodward; Hoffmann *The Conservation of Orbital Symmetry*; Academic Press: New York, 1970, pp. 152-163.

[321]Philips; Swisher; Haidukewych; Morales *Chem. Commun.* **1971,** 22.

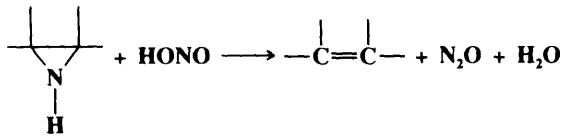
[322]Carpino; McAdams; Rynbrandt; Spiewak *J. Am. Chem. Soc.* **1971,** *93*, 476; Philips; Morales *J. Chem. Soc., Chem. Commun.* **1977,** 713.

A Ramberg–Bäcklund-type reaction has been carried out on the α-halo *sulfides* $ArCHClSCH_2Ar$, which react with *t*-BuOK and PPh_3 in refluxing THF to give the alkenes $ArCH{=}CHAr$.[323]

The Ramberg–Bäcklund reaction can be regarded as a type of extrusion reaction (see p. 1045).

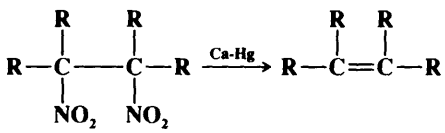
OS **V,** 877; **VI,** 454, 555; **65,** 90.

7-26 The Conversion of Aziridines to Olefins
epi-Imino-elimination



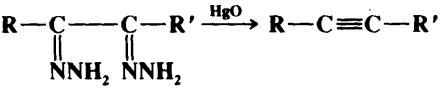
Aziridines not substituted on the nitrogen atom react with nitrous acid to produce olefins.[324] An N-nitroso compound is an intermediate (**2-51**); other reagents that produce such intermediates also give olefins. The reaction is stereospecific: cis aziridines give cis olefins and trans aziridines give trans olefins.[325] Aziridines carrying N-alkyl substituents can be converted to olefins by treatment with ferrous iodide[326] or with *m*-chloroperbenzoic acid.[327] An N-oxide intermediate (**9-28**) is presumably involved in the latter case.

7-27 Conversion of Vicinal Dinitro Compounds to Olefins
Dinitro-elimination



Tetrasubstituted *vic*-dinitro compounds have been converted to olefins by treatment with amalgamated calcium.[328] Various functional groups, such as CN and COOR, did not affect the reaction. Other reagents that have been used include sodium sulfide in DMF,[329] nickel boride and ultrasound,[330] Bu_3SnH,[331] and $SnCl_2$.[332] Radical-ion mechanisms are likely in all these cases.

7-28 The Conversion of Dihydrazones to Alkynes
Dihydrazono-bielimination



[323]Mitchell *Tetrahedron Lett.* **1973,** 4395. For a similar reaction without base treatment, see Pommelet; Nyns; Lahousse; Merényi; Viehe *Angew. Chem. Int. Ed. Engl.* **1981,** *20,* 585 [*Angew. Chem. 93,* 594].

[324]For reviews, see Sonnet, Ref. 274, pp. 591-592; Dermer; Ham *Ethylenimine and other Aziridines*; Academic Press: New York, 1969, pp. 293-295.

[325]Clark; Helmkamp *J. Org. Chem.* **1964,** *29,* 1316; Carlson; Lee *Tetrahedron Lett.* **1969,** 4001.

[326]Imamoto; Yukawa *Chem. Lett.* **1974,** 165.

[327]Heine; Myers; Peltzer *Angew. Chem. Int. Ed. Engl.* **1970,** *9,* 374 [*Angew. Chem. 82,* 395].

[328]Kornblum; Cheng *J. Org. Chem.* **1977,** *42,* 2944.

[329]Kornblum; Boyd; Pinnick; Smith *J. Am. Chem. Soc.* **1971,** *93,* 4316.

[330]Madjdabadi; Beugelmans; Lechavallier *Synth. Commun.* **1989,** *19,* 1631.

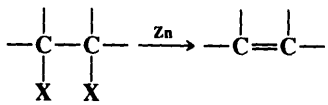
[331]Ono; Miyake; Tamura; Hamamoto; Kaji *Chem. Lett.* **1981,** 1139.

[332]Fukunaga; Kimura *Bull. Chem. Soc. Jpn.* **1979,** *52,* 1107.

1,2-Dihydrazones can be made to lose two moles of nitrogen to give alkynes by treatment with HgO, Ag_2O, $CuCl_2$–O_2–pyridine, or certain other reagents.[333] R and R′ may be alkyl or aryl. Highly strained seven- and eight-membered cycloalkynes (see p. 159), as well as large cycloalkynes, have been obtained by this reaction.[334]

OS **IV,** 377. See also OS **VI,** 791.

7-29 Dehalogenation of Vicinal Dihalides
Dihalo-elimination



Dehalogenation has been accomplished with many reagents, the most common being zinc, magnesium, and iodide ion.[335] Among reagents used less frequently have been phenyllithium, phenylhydrazine, $CrCl_2$, naphthalene–sodium,[336] Na–NH_3,[337] Na_2S in DMF,[338] Na_2Te,[339] and $LiAlH_4$.[340] Electrochemical reduction has also been used.[341] Though the reaction usually gives good yields, it is not very useful because the best way to prepare *vic*-dihalides is by the addition of halogen to a double bond (**5-26**). One useful feature of this reaction is that there is no doubt about the *position* of the new double bond, so that it can be used to give double bonds exactly where they are wanted. For example, allenes, which are not easily prepared by other methods, can be prepared from X—C—CX_2—C—X or X—C—CX=C— systems.[342] Cumulenes have been obtained from 1,4 elimination:

$$\mathbf{BrCH_2{-}C{\equiv}C{-}CH_2Br + Zn \longrightarrow CH_2{=}C{=}C{=}CH_2}$$

Triple bonds can be prepared from X—C=C—X or X_2C—CX_2 systems,[343] but availability considerations are even more extreme here. 1,4 Elimination of BrC—C=C—CBr has been used to prepare conjugated dienes C=C—C=C.[344]

The reaction can be carried out for any combination of halogens, except where one is fluorine. Mechanisms are often complex and depend on the reagent and reaction conditions.[345] For different reagents, mechanisms involving carbocations, carbanions, and free-radical intermediates, as well as concerted mechanisms, have been proposed. When the reagent is zinc, anti stereospecificity has been observed in some cases,[346] but not in others.[347]

[333]For a list of reagents, with references, see Ref. 144, p. 293.

[334]For example, see Blomquist; Liu *J. Am. Chem. Soc.* **1953,** *75,* 2153; Krebs; Kimling *Tetrahedron Lett.* **1970,** 761; Tsuji; Kezuka; Toshida; Takayanagi; Yamamoto *Tetrahedron* **1983,** *39,* 3279.

[335]For a review of this reaction, see Baciocchi, in Patai; Rappoport, Ref. 232; pt. 1, pp. 161-201.

[336]Scouten; Barton; Burgess; Story; Garst *Chem. Commun.* **1969,** 78; Garst; Pacifici; Singleton; Ezzel; Morris *J. Am. Chem. Soc.* **1975,** *97,* 5242.

[337]Allred; Beck; Voorhees *J. Org. Chem.* **1974,** *39,* 1426.

[338]Fukunaga; Yamaguchi *Synthesis* **1981,** 879. See also Nakayama; Machida; Hoshino *Tetrahedron Lett.* **1983,** *24* 3001; Landini; Milesi; Quadri; Rolla *J. Org. Chem.* **1984,** *49,* 152.

[339]Suzuki; Inouye *Chem. Lett.* **1985,** 225. See also Huang; Hou *Synth. Commun.* **1988,** *18,* 2201.

[340]For a lists of reagents, with references, see Ref. 144, pp. 133-135.

[341]See Shono *Electroorganic Chemistry as a New Tool in Organic Synthesis*; Springer: New York, 1984, pp. 145-147; Fry *Synthetic Organic Electrochemistry*, 2nd ed.; Wiley: New York, 1989, pp. 151-154.

[342]For reviews of allene formation, see Schuster; Coppola *Allenes in Organic Synthesis*; Wiley: New York, 1984, pp. 9-56; Landor, in Landor *The Chemistry of the Allenes*, vol. 1; Academic Press: New York, 1982; pp. 19-233; Taylor *Chem. Rev.* **1967,** *67,* 317-359.

[343]For a review, see Köbrich; Buck; in Viehe, Ref. 243, pp. 134-138.

[344]Engman; Byström *J. Org. Chem.* **1985,** *50,* 3170.

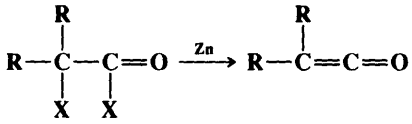
[345]For discussion, see Saunders; Cockerill, Ref. 2, pp. 332-368; Ref. 335.

[346]For example, see House; Ro *J. Am. Chem. Soc.* **1958,** *80,* 182; Gordon; Hay *J. Org. Chem.* **1968,** *33,* 427.

[347]For example, see Stevens; Valicenti *J. Am. Chem. Soc.* **1965,** *87,* 838; Sicher; Havel; Svoboda *Tetrahedron Lett.* **1968,** 4269.

OS **III,** 526, 531; **IV,** 195, 268; **V,** 22, 255, 393, 901; **VI,** 310, **VII,** 241. Also see OS **IV,** 877, 914, 964.

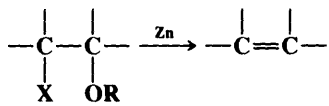
7-30 Dehalogenation of α-Halo Acyl Halides
Dihalo-elimination



Ketenes can be prepared by dehalogenation of α-halo acyl halides with zinc or with triphenylphosphine.[348] The reaction generally gives good results when the two R groups are aryl or alkyl, but not when either one is hydrogen.[349]

OS **IV,** 348; **68,** 41.

7-31 Elimination of a Halogen and a Hetero Group
Alkoxy-halo-elimination



The elimination of OR and halogen from β-halo ethers is called the *Boord reaction*. It can be carried out with zinc, magnesium, sodium, or certain other reagents.[350] The yields are high and the reaction is of broad scope. β-Halo acetals readily yield vinylic ethers X—C—C(OR)$_2$ → —C=C—OR. Besides β-halo ethers, the reaction can also be carried out on compounds of the formula X—C—C—Z, where X is halogen and Z is OCOR, OTs,[351] NR_2,[352] or SR.[353] Z may also be OH, but then X is limited Br and I. Like **7-29,** this method ensures that the new double bond will be in a specific position. The fact that magnesium causes elimination in these cases limits the preparation of Grignard reagents from these compounds. It has been shown that treatment of β-halo ethers and esters with zinc gives nonstereospecific elimination,[354] so the mechanism was not E2. An E1cB mechanism was postulated because of the poor leaving-group ability of OR and OCOR. Bromohydrins can be converted to olefins (elimination of Br, OH) in high yields by treatment with $LiAlH_4$–$TiCl_3$.[355]

OS **III,** 698, **IV,** 748; **VI,** 675.

[348]Darling; Kidwell *J. Org. Chem.* **1968,** *33,* 3974.

[349]For a procedure that gives 60 to 65% yields when one R = H, see McCarney; Ward *J. Chem. Soc., Perkin Trans. 1* **1975,** 1600. See also Masters; Sorensen; Ziegler *J. Org. Chem.* **1986,** *51,* 3558.

[350]See Ref. 144, pp. 136-139, for reagents that produce olefins from β-halo ethers and esters, and from halohydrins.

[351]Cristol; Rademacher *J. Am. Chem. Soc.* **1959,** *81,* 1600; Reeve; Brown; Steckel *J. Am. Chem. Soc.* **1971,** *93,* 4607.

[352]Gurien *J. Org. Chem.* **1963,** *28,* 878.

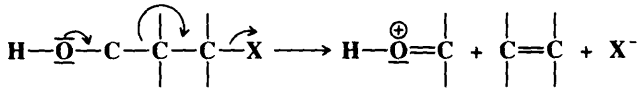
[353]Amstutz *J. Org. Chem.* **1944,** *9,* 310.

[354]House; Ro, Ref. 346.

[355]McMurry; Hoz *J. Org. Chem.* **1975,** *40,* 3797.

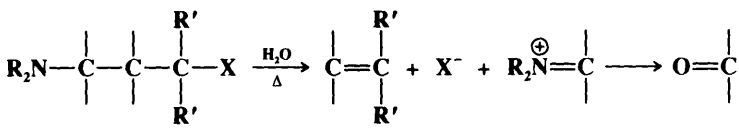
Fragmentations

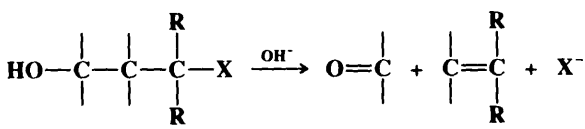
When carbon is the positive leaving group (the electrofuge) in an elimination, the reaction is called *fragmentation*.[356] These processes occur on substrates of the form W—C—C—X, where X is a normal nucleofuge (e.g., halogen, OH_2^+, OTs, NR_3^+, etc.) and W is a positive-carbon electrofuge. In most of the cases W is HO—C— or R_2N—C—, so that the positive charge on the carbon atom is stabilized by the unshared pair of the oxygen or nitrogen, e.g.,



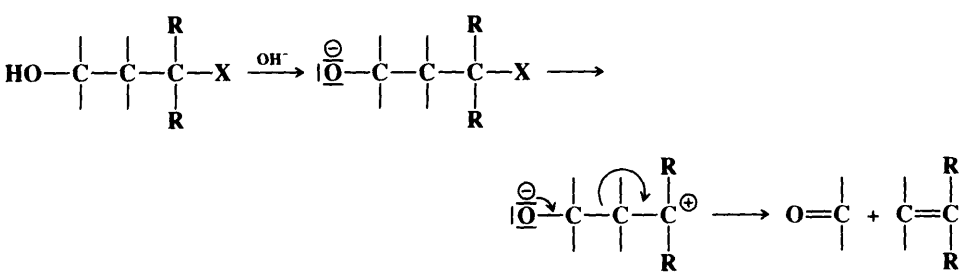
The mechanisms are mostly E1 or E2. We shall discuss only a few fragmentations, since many are possible and not much work has been done on most of them. Reactions **7-32** to **7-36** and **7-38** may be considered fragmentations. See also **9-13** and **9-14.**

7-32 Fragmentation of γ-Amino and γ-Hydroxy Halides
Dialkylaminoalkyl-halo-elimination, etc.





γ-Dialkylamino halides undergo fragmentation when heated with water to give an olefin and an iminium salt, which under the reaction conditions is hydrolyzed to an aldehyde or ketone (**6-2**).[357] γ-Hydroxy halides and tosylates are fragmented with base. In this instance the base does not play its usual role in elimination reactions but instead serves to remove a proton from the OH group, which enables the carbon leaving group to come off more easily:



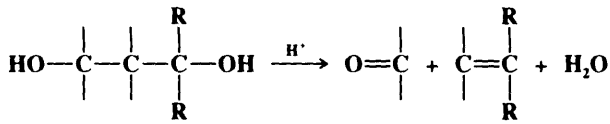
[356]For reviews, see Becker; Grob, in Patai, *The Chemistry of Functional Groups, Supplement A*, Ref. 2, pt. 2, pp. 653-723; Grob *Angew. Chem. Int. Ed. Engl.* **1969,** *8*, 535-546 [*Angew. Chem. 81*, 543-554]; Grob; Schiess *Angew. Chem. Int. Ed. Engl.* **1967,** *6*, 1-15 [*Angew. Chem. 79*, 1-14].

[357]Grob; Ostermayer; Raudenbusch *Helv. Chim. Acta* **1962,** *45*, 1672.

The mechanism of these reactions is often E1. However, in at least some cases, an E2 mechanism operates.[358] It has been shown that stereoisomers of cyclic γ-amino halides and tosylates in which the two leaving groups can assume an anti-periplanar conformation react by the E2 mechanism, while those isomers in which the groups cannot assume such a conformation either fragment by the E1 mechanism or do not undergo fragmentation at all, but in either case give rise to side products characteristic of carbocations.[359]

γ-Dialkylamino alcohols do not give fragmentation, since for ionization the OH group must be converted to OH_2^+ and this would convert NR_2 to NR_2H^+, which does not have the unshared pair necessary to form the double bond with the carbon.[360]

7-33 Fragmentation of 1,3-Diols
Hydroxyalkyl-hydroxy-elimination



1,3-Diols in which at least one OH group is tertiary or is located on a carbon with aryl substituents can be cleaved by acid treatment.[361] The reaction is most useful synthetically when at least one of the OH groups is on a ring.[362]

7-34 Decarboxylation of β-Hydroxy Carboxylic Acids and of β-Lactones
Carboxy-hydroxy-elimination

An OH and a COOH group can be eliminated from β-hydroxy carboxylic acids by refluxing with excess dimethylformamide dimethyl acetal.[363] Mono-, di-, tri-, and tetrasubstituted olefins have been prepared by this method in good yields.[364] There is evidence that the mechanism involves E1 or E2 elimination from the zwitterionic intermediate $^-O_2C-\overset{|}{\underset{|}{C}}-\overset{|}{\underset{|}{C}}-OCH{=}NMe_2^+$.[365] The reaction has also been accomplished[366] under extremely mild conditions (a few seconds at 0°C) with PPh_3 and diethyl azodicarboxylate EtOOC—N=N—COOEt.[367] In a related procedure, β-lactones undergo thermal decar-

[358]Grob; Schwarz *Helv. Chim. Acta* **1964,** *47*, 1870; Fischer; Grob *Helv. Chim. Acta* **1978,** *61*, 2336.

[359]Bottini; Grob; Schumacher; Zergenyi *Helv. Chim. Acta* **1966,** *49*, 2516; Burckhardt; Grob; Kiefer *Helv. Chim. Acta* **1967,** *50*, 231; Grob; Kiefer; Lutz; Wilkens *Helv. Chim. Acta* **1967,** *50*, 416; Geisel; Grob; Wohl *Helv. Chim. Acta* **1969,** *52*, 2206.

[360]Grob; Hoegerle; Ohta *Helv. Chim. Acta* **1962,** *45*, 1823.

[361]Zimmerman; English *J. Am. Chem. Soc.* **1954,** *76*, 2285, 2291, 2294.

[362]For a review of such cases, see Caine *Org. Prep. Proced. Int.* **1988,** *20*, 1-51.

[363]Hara; Taguchi; Yamamoto; Nozaki *Tetrahedron Lett.* **1975,** 1545.

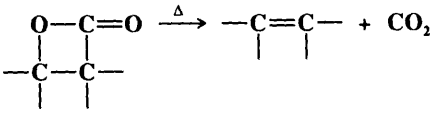
[364]For a 1,4 example of this reaction, see Rüttimann; Wick; Eschenmoser *Helv. Chim. Acta* **1975,** *58*, 1450.

[365]Mulzer; Brüntrup *Tetrahedron Lett.* **1979,** 1909.

[366]For another method, see Tanzawa; Schwartz *Organometallics* **1990,** *9*, 3026.

[367]Mulzer; Brüntrup *Angew. Chem. Int. Ed. Engl.* **1977,** *16*, 255 [*Angew. Chem. 89*, 265]; Mulzer; Lammer *Angew. Chem. Int. Ed. Engl.* **1983,** *22*, 628 [*Angew. Chem. 95*, 629].

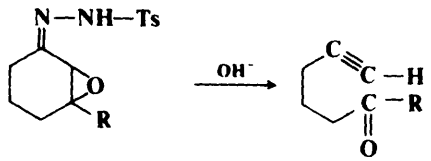
boxylation to give olefins in high yields. The reaction has been shown to be a stereospecific



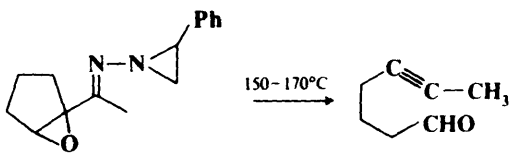
syn elimination.[368] There is evidence that this reaction also involves a zwitterionic intermediate.[369]

There are no OS references, but see OS **VII,** 172, for a related reaction.

7-35 Fragmentation of α,β-Epoxy Hydrazones
Eschenmoser–Tanabe ring cleavage



Cyclic α,β-unsaturated ketones[370] can be cleaved by treatment with base of their epoxy tosylhydrazone derivatives to give acetylenic ketones.[371] The reaction can be applied to the formation of acetylenic aldehydes (R = H) by using the corresponding, 2,4-dinitrotosylhydrazone derivatives.[372] Hydrazones (e.g., **47**) prepared from epoxy ketones and ring-sub-

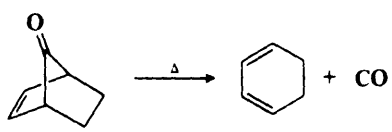


47

stituted N-aminoaziridines undergo similar fragmentation when heated.[373]

OS **VI,** 679.

7-36 Elimination of CO and CO_2 from Bridged Bicyclic Compounds
seco-Carbonyl-1/4/elimination



48

[368]Noyce; Banitt *J. Org. Chem.* **1966,** *31,* 4043; Adam; Baeza; Liu *J. Am. Chem. Soc.* **1972,** *94,* 2000; Krapcho; Jahngen *J. Org. Chem.* **1974,** *39,* 1322, 1650; Mageswaran; Sultanbawa *J. Chem. Soc., Perkin Trans. 1* **1976,** 884; Adam; Martinez; Thompson; Yany *J. Org. Chem.* **1981,** *46,* 3359.

[369]Mulzer; Zippel; Brüntrup *Angew. Chem. Int. Ed. Engl.* **1980,** *19,* 465 [*Angew. Chem. 92,* 469]; Mulzer; Zippel *Tetrahedron Lett.* **1980,** *21,* 751. See also Moyano; Pericaas; Valentí *J. Org. Chem.* **1989,** 573.

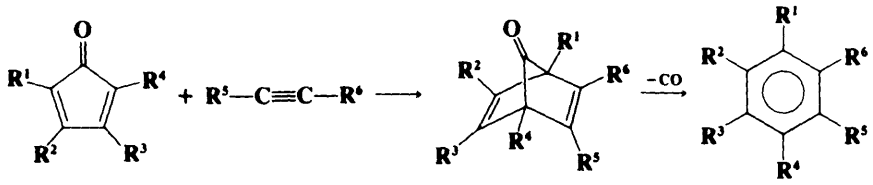
[370]For other methods of fragmentation of α,β-epoxy ketone derivatives, see MacAlpine; Warkentin *Can. J. Chem.* **1978,** *56,* 308, and references cited therein.

[371]Eschenmoser; Felix; Ohloff *Helv. Chim. Acta* **1967,** *50,* 708; Tanabe; Crowe; Dehn; Detre *Tetrahedron Lett.* **1967,** 3739; Tanabe; Crowe; Dehn *Tetrahedron Lett.* **1967,** 3943.

[372]Corey; Sachdev *J. Org. Chem.* **1975,** *40,* 579.

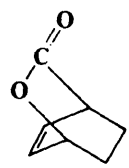
[373]Felix, Müller; Horn; Joos; Schreiber; Eschenmoser *Helv. Chim. Acta* **1972,** *55,* 1276.

On heating, bicyclo[2.2.1]hept-2,3-en-7-ones (**48**) usually lose CO to give cyclohexadienes,[374] in a type of reverse Diels–Alder reaction. Bicyclo[2.2.1]heptadienones (**49**) undergo the



49

reaction so readily (because of the stability of the benzene ring produced) that they cannot generally be isolated. The parent **49** has been obtained at 10-15 K in an Ar matrix, where its spectrum could be studied.[375] **48** and **49** can be prepared by Diels–Alder reactions between a cyclopentadienone and an alkyne or olefin, so that this reaction is a useful method for the preparation of specifically substituted benzene rings and cyclohexadienes.[376] Unsaturated bicyclic lactones of the type **50** can also undergo the reaction, losing CO_2. See also **7-47.**



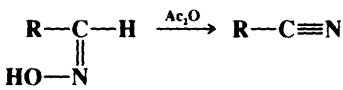
50

OS **III,** 807; **V,** 604, 1037.

Reversal of the Diels–Alder reaction may be considered a fragmentation. See **5-47.**

Reactions in Which C≡N or C=N Bonds Are Formed

7-37 Dehydration of Aldoximes and Similar Compounds *C*-Hydro-*N*-hydroxy-elimination



Aldoximes can be dehydrated to nitriles[377] by many dehydrating agents, of which acetic anhydride is the most common. Among reagents that are effective under mild conditions[378]

[374]For a review, see Stark; Duke, Ref. 444, pp. 16-46.

[375]Birney; Berson *J. Am. Chem. Soc.* **1985,** *107,* 4553; *Tetrahedron* **1986,** *42,* 1561; LeBlanc; Sheridan *J. Am. Chem. Soc.* **1985,** *107,* 4554; Birney; Wiberg; Berson *J. Am. Chem. Soc.* **1988,** *110,* 6631.

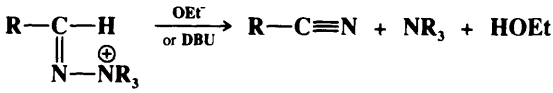
[376]For a review with many examples; see Ogliaruso; Romanelli; Becker *Chem. Rev.* **1965,** *65,* 261-367, pp. 300-348. For references to this and related reactions, see Ref. 144, pp. 101-103.

[377]For reviews, see Friedrich, in Patai; Rappoport, Ref. 142, pt. 2, pp. 1345-1390; Friedrich; Wallenfels in Rappoport *The Chemistry of the Cyano Group*; Wiley: New York, 1970, pp. 92-96. For a review of methods of synthesizing nitriles, see Fatiadi, in Patai; Rappoport, Ref. 142, pt. 2, pp. 1057-1303.

[378]For lists of some other reagents, with references, see Molina; Alajarin; Vilaplana *Synthesis* **1982,** 1016; Aizpurua; Palomo *Nouv. J. Chim.* **1983,** *7,* 465; Attanasi; Palma; Serra-Zanetti *Synthesis* **1983,** 741; Juršić *Synth. Commun.* **1989,** *19,* 689.

(room temperature) are ethyl orthoformate and H^+,[379] Ph_3P–CCl_4,[380] trichloromethyl chloroformate $ClCOOCCl_3$,[381] methyl (or ethyl) cyanoformate ROCOCN,[382] trifluoromethane sulfonic anhydride,[383] P_2I_4,[291] SeO_2,[384] CS_2 under phase transfer conditions,[385] Cl_3COCl–Et_3N,[386] and chloromethylene dimethylammonium chloride $Me_2N{=}CHCl^+\ Cl^-$.[387] Electrochemical synthesis has also been used.[388] The reaction is most successful when the H and OH are anti. Various alkyl and acyl derivatives of aldoximes, for example, RCH=NOR, RCH=NOCOR, $RCH{=}NOSO_2Ar$, etc., also give nitriles, as do chlorimines RCH=NCl (the latter with base treatment).[389] N,N-dichloro derivatives of primary amines give nitriles on pyrolysis: $RCH_2NCl_2 \rightarrow RCN$.[390]

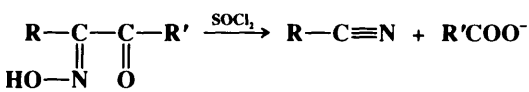
Quaternary hydrazonium salts (derived from aldehydes) give nitriles when treated with OEt^-[391] or DBU (p. 1023):[392]



as do dimethylhydrazones $RCH{=}NNMe_2$ when treated with Et_2NLi and HMPA.[393] All these are methods of converting aldehyde derivatives to nitriles. For the conversion of aldehydes directly to nitriles, without isolation of intermediates, see **6-22.**

OS **II,** 622; **III,** 690.

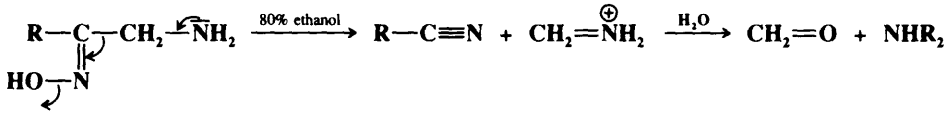
7-38 The Conversion of Ketoximes to Nitriles
C-Acyl-*N*-hydroxy-elimination



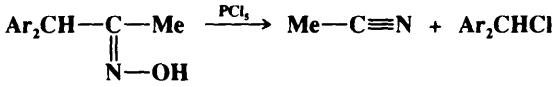
Certain ketoximes can be converted to nitriles by the action of proton or Lewis acids.[394] Among these are oximes of α-diketones (illustrated above), α-keto acids, α-dialkylamino ketones, α-hydroxy ketones, β-keto ethers, and similar compounds.[395] These are fragmen-

[379]Rogić; Van Peppen; Klein; Demmin *J. Org. Chem.* **1974,** *39*, 3424.
[380]Kim; Chung; Ryu *Synth. Commun.* **1990,** *20*, 2785.
[381]Mai; Patil *Synthesis* **1986,** 1037.
[382]Thomas; Greyn *Synthesis* **1990,** 129.
[383]Hendrickson; Blair; Keehn; *Tetrahedron Lett.* **1976,** 603.
[384]Sosnovsky; Krogh *Synthesis* **1978,** 703.
[385]Shinozaki; Imaizumi; Tajima *Chem. Lett.* **1983,** 929.
[386]Saednya *Synthesis* **1983,** 748.
[387]Dulcere *Tetrahedron Lett.* **1981,** *22*, 1599.
[388]See Shono; Matsumura; Tsubata; Kamada; Kishi *J. Org. Chem.* **1989,** *54*, 2249.
[389]Hauser; Le Maistre; Rainsford *J. Am. Chem. Soc.* **1935,** *57*, 1056.
[390]Roberts; Rittberg; Kovacic *J. Org. Chem.* **1981,** *46*, 4111.
[391]Smith; Walker *J. Org. Chem.* **1962,** *27*, 4372; Grandberg *J. Gen. Chem. USSR* **1964,** *34*, 570; Grundon; Scott *J. Chem. Soc.* **1964,** 5674; Ioffe; Zelenina *J. Org. Chem. USSR* **1968,** *4*, 1496.
[392]Moore; Stupp *J. Org. Chem.* **1990,** *55*, 3374.
[393]Cuvigny; Le Borgne; Larchevêque; Normant *Synthesis* **1976,** 237.
[394]For reviews, see Gawley *Org. React.* **1988,** *35*, 1-420; Conley; Ghosh *Mech. Mol. Migr.* **1971,** *4*, 197-308, pp. 197-251; McCarty; in Patai *The Chemistry of the Carbon–Nitrogen Double Bond*; Wiley: New York, 1970, pp. 416-439; Casanova; in Rappoport, Ref. 377, pp. 915-932.
[395]For more complete lists with references, see Olah; Vankar; Berrier *Synthesis* **1980,** 45; Conley; Ghosh, Ref. 394.

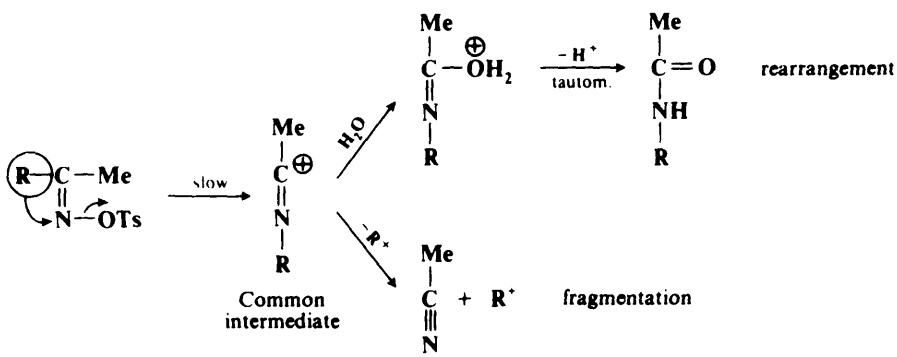
tation reactions, analogous to **7-32** and **7-33.** For example, α-dialkylamino ketoximes also give amines and aldehydes or ketones besides nitriles:[396]



The reaction that normally occurs on treatment of a ketoxime with a Lewis or proton acid is the Beckmann rearrangement (**8-18**); fragmentations are considered side reactions, often called "abnormal" or "second-order" Beckmann rearrangements.[397] Obviously, the substrates mentioned are much more susceptible to fragmentation than are ordinary ketoximes, since in each case an unshared pair is available to assist in removal of the group cleaving from the carbon. However, fragmentation is a side reaction even with ordinary ketoximes[398] and, in cases where a particularly stable carbocation can be cleaved, may be the main reaction:[399]



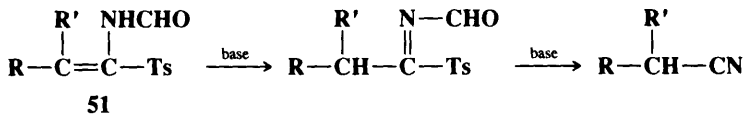
There are indications that the mechanism at least in some cases first involves a rearrangement and then cleavage. The ratio of fragmentation to Beckmann rearrangement of a series of oxime tosylates RC(=NOTs)Me was not related to the solvolysis rate but *was* related to the stability of R^+ (as determined by the solvolysis rate of the corresponding RCl), which showed that fragmentation did not take place in the rate-determining step.[400] It may be postulated then that the first step in the fragmentation and in the rearrangement is the same and that this is the rate-determining step. The product is determined in the second step:



However, in other cases the simple E1 or E2 mechanisms operate.[401]

[396]Fischer; Grob; Renk *Helv. Chim. Acta* **1962,** *45*, 2539; Fischer; Grob *Helv. Chim. Acta* **1963,** *46*, 936.
[397]See the discussion in Ferris *J. Org. Chem.* **1960,** *25*, 12.
[398]See, for example, Hill; Conley *J. Am. Chem. Soc.* **1960,** *82*, 645.
[399]Hassner; Nash *Tetrahedron Lett.* **1965,** 525.
[400]Grob; Fischer; Raudenbusch; Zergenyi *Helv. Chim.Acta* **1964,** *47*, 1003.
[401]Ahmad; Spenser *Can. J. Chem.* **1961,** *39*, 1340; Ferris; Johnson; Gould *J. Org. Chem.* **1960,** *25*, 1813; Grob; Sieber *Helv. Chim. Acta* **1967,** *50*, 2520; Green; Pearson *J. Chem. Soc. B* **1969,** 593.

The fragmentation of N-(1-tosyl-1-alkenyl)formamides (**51**) by refluxing with NaOMe in MeOH is a step in the conversion of a ketone to a nitrile,[402] since **51** can be prepared by

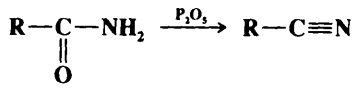


51

treatment of ketones with $TsCH_2NC$ (p. 949). The overall conversion is RR'C=O to RR'CHCN.

OS **V**, 266.

7-39 Dehydration of Unsubstituted Amides
NN-Dihydro-*C*-oxo-bielimination



Unsubstituted amides can be dehydrated to nitriles.[403] Phosphorous pentoxide is the most common dehydrating agent for this reaction, but many others, including $POCl_3$, PCl_5, CCl_4–Ph_3P,[404] $TiCl_4$–base,[405] HMPA,[406] Cl_3COCl–Et_3N,[407] $MeOOCN^{\ominus}SO_2\overset{\oplus}{N}Et_3$ (the Burgess reagent),[408] nitrilium salts,[409] cyanuric chloride,[410] $Me_2N{=}CHCl^+\ Cl^-$,[411] trimethylsilyl polyphosphate,[412] and $SOCl_2$ have also been used.[413] It is possible to convert an acid to the nitrile, without isolation of the amide, by heating its ammonium salt with the dehydrating agent,[414] or by other methods.[415] Acyl halides can also be directly converted to nitriles by heating with sulfamide $(NH_2)_2SO_2$.[416] The reaction may be formally looked on as a β elimination from the enol form of the amide RC(OH)=NH, in which case it is like **7-37**, except that H and OH have changed places. In some cases, for example, with $SOCl_2$, the mechanism probably *is* through the enol form, with the dehydrating agent forming an ester with the OH group, for example, RC(OSOCl)=NH, which undergoes elimination by the E1 or E2 mechanism.[417] N,N-Disubstituted ureas give cyanamides ($R_2N{-}CO{-}NH_2 \rightarrow R_2N{-}CN$) when dehydrated with $CHCl_3$–NaOH under phase transfer conditions.[418]

[402]Schöllkopf; Schröder *Angew. Chem. Int. Ed. Engl.* **1973,** *12*, 407 [*Angew. Chem. 85*, 402].

[403]For reviews, see Bieron; Dinan; in Zabicky *The Chemistry of Amides*; Wiley: New York, 1970, pp. 274-283; Friedrich; Wallenfels, Ref. 377, pp. 96-103; Friedrich, Ref. 377.

[404]Yamato; Sugasawa *Tetrahedron Lett.* **1970,** 4383; Appel; Kleinstück; Ziehn *Chem. Ber.* **1971,** *104*, 1030; Harrison; Hodge; Rogers *Synthesis* **1977,** 41.

[405]Lehnert *Tetrahedron Lett.* **1971,** 1501.

[406]Monson; Priest *Can. J. Chem.* **1971,** *49*, 2897.

[407]Saednya *Synthesis* **1985,** 184.

[408]Claremon; Phillips *Tetrahedron Lett.* **1988,** *29*, 2155.

[409]Jochims; Glocker *Chem. Ber.* **1990,** *123*, 1537.

[410]Olah; Narang; Fung; Gupta *Synthesis* **1980,** 657.

[411]Barger; Riley *Synth. Commun.* **1980,** *10*, 479.

[412]Yokoyama; Yoshida; Imamoto *Synthesis* **1982,** 591. See also Rao; Rambabu; Srinivasan *Synth. Commun.* **1989,** *19*, 1431.

[413]For a list of reagents, with references, see Ref. 144, pp. 991-992.

[414]See, for example, Imamoto; Takaoka; Yokoyama *Synthesis* **1983,** 142.

[415]For a list of methods, with references, see Ref. 144, pp. 976-977.

[416]Hulkenberg; Troost *Tetrahedron Lett.* **1982,** *23*, 1505.

[417]Rickborn; Jensen *J. Org. Chem.* **1962,** *27*, 4608.

[418]Schroth; Kluge; Frach; Hodek; Schädler *J. Prakt. Chem.* **1983,** *325*, 787.

N-Alkyl-substituted amides can be converted to nitriles and alkyl chlorides by treatment with PCl_5. This is called the *von Braun reaction* (not to be confused with the other von

$$\mathbf{R'CONHR + PCl_5 \longrightarrow R'CN + RCl}$$

Braun reaction, **0-73**). In a similar reaction, treatment of N-alkyl-substituted amides with chlorotris(triphenylphosphine)rhodium $RhCl(PPh_3)_3$ or certain other catalysts give nitriles and the corresponding alcohols.[419]

OS **I,** 428; **II,** 379; **III,** 493, 535, 584, 646, 768; **IV,** 62, 144, 166, 172, 436, 486, 706; **VI,** 304, 465.

7-40 Conversion of Primary Nitro Compounds to Nitriles

$$\mathbf{RCH_2{-}NO_2 \xrightarrow[\text{pyridine}]{PCl_3} RC{\equiv}N}$$

Nitriles can be obtained in one step by treatment of primary nitro compounds with PCl_3 and pyridine.[420] R may be alkyl or aryl and may contain C=C double bonds or various functional groups. Yields are moderate to good. The reaction has also been carried out with $Me_3N{-}SO_2$ and with HMPA.[421] Primary azides RCH_2N_3 have been converted to nitriles RCN with Pd metal.[422] Primary nitro compounds RCH_2NO_2 were converted to nitrile oxides $RC\overset{\oplus}{N}{-}\overset{\ominus}{O}$ by treatment with ClCOOEt or $PhSO_2Cl$ in the presence of Et_3N.[423]

7-41 Conversion of N-Alkylformamides to Isocyanides
CN-Dihydro-*C*-oxo-bielimination

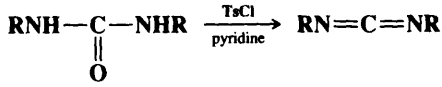
$$\mathbf{H{-}\underset{\underset{\displaystyle O}{\|}}{C}{-}NH{-}R \xrightarrow[R_3N]{COCl_2} \overset{\ominus}{C}{\equiv}\overset{\oplus}{N}{-}R}$$

Isocyanides can be prepared by elimination of water from N-alkylformamides with phosgene and a tertiary amine.[424] Other reagents, among them TsCl in quinoline, $POCl_3$ and a tertiary amine,[425] $Me_2N{=}CHCl^+\ Cl^-$,[426] di-2-pyridyl sulfite,[427] triflic anhydride–$(i\text{-}Pr)_2NEt$,[428] $Ph_3P{-}CCl_4{-}Et_3N$,[429] and $Ph_3PBr_2{-}Et_3N$[430] have also been employed.

OS **V,** 300, 772; **VI,** 620, 751, 987. See also OS **VII,** 27.

[419]Blum; Fisher; Greener *Tetrahedron* **1973,** *29*, 1073.
[420]Wehrli; Schaer *J. Org. Chem.* **1977,** *42*, 3956.
[421]Olah; Vankar; Gupta *Synthesis*; **1979,** 36. For another method, see Urpí; Vilarrasa *Tetrahedron Lett.* **1990,** *31*, 7497.
[422]Hayashi; Ohno; Oka *Bull. Chem. Soc. Jpn.* **1976,** *49*, 506. See also Jarvis; Nicholas *J. Org. Chem.* **1979,** *44*, 2951.
[423]Shimizu; Hayashi; Shibafuchi; Teramura *Bull. Chem. Soc. Jpn.* **1986,** *59*, 2827.
[424]For reviews, see Hoffmann; Gokel; Marquarding; Ugi, in Ugi *Isonitrile Chemistry*; Academic Press: New York, 1971, pp. 10-17; Ugi; Fetzer; Eholzer; Knupfer; Offermann *Angew. Chem. Int. Ed. Engl.* **1965,** *4*, 472-484 [*Angew. Chem. 77*, 492-504], *Newer Methods Prep. Org. Chem.* **1968,** *4*, 37-66.
[425]See Obrecht; Herrmann; Ugi *Synthesis* **1985,** 400.
[426]Walborsky; Niznik *J. Org. Chem.* **1972,** *37*, 187.
[427]Kim; Yi *Tetrahedron Lett.* **1986,** *27*, 1925.
[428]Baldwin; O'Neil *Synlett* **1991,** 603.
[429]Appel; Kleinstück; Ziehn *Angew. Chem. Int. Ed. Engl.* **1971,** *10*, 132 [*Angew. Chem. 83*, 143].
[430]Bestmann; Lienert; Mott *Liebigs Ann. Chem.* **1968,** *718*, 24.

7-42 Dehydration of N,N'-Disubstituted Ureas and Thioureas
1/*N*,3/*N*-Dihydro-2/*C*-oxo-bielimination



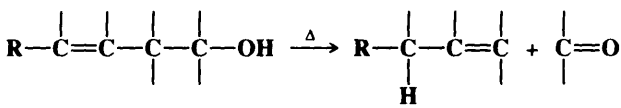
Carbodiimides[431] can be prepared by the dehydration of N,N'-disubstituted ureas with various dehydrating agents,[432] among which are TsCl in pyridine, $POCl_3$, PCl_5, P_2O_5–pyridine, TsCl (with phase-transfer catalysis),[433] and Ph_3PBr_2–Et_3N.[430] H_2S can be removed from the corresponding thioureas by treatment with HgO, NaOCl, phosgene,[434] or diethyl azodicarboxylate–triphenylphospine.[435]

OS **V,** 555; **VI,** 951.

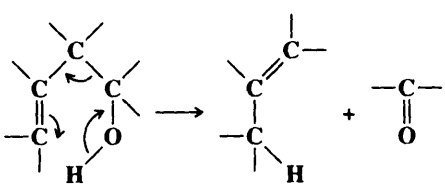
Reactions in Which C=O Bonds Are Formed

Many elimination reactions in which C=O bonds are formed were considered in Chapter 16, along with their more important reverse reactions. Also see **2-40** and **2-41.**

7-43 Pyrolysis of β-Hydroxy Olefins
O-Hydro-*C*-allyl-elimination



When pyrolyzed, β-hydroxy olefins cleave to give olefins and aldehydes or ketones.[436] Olefins produced this way are quite pure, since there are no side reactions. The mechanism has



been shown to be pericylic, primarily by observations that the kinetics are first order[437] and that, for ROD, the deuterium appeared in the allylic position of the new olefin.[438] This

[431]For a review of the reactions in this section, see Bocharov *Russ. Chem. Rev.* **1965,** *34*, 212-219. For a review of carbodiimide chemistry; see Williams; Ibrahim *Chem. Rev.* **1981,** *81*, 589-636.

[432]For some others not mentioned here, see Sakai; Fujinami; Otani; Aizawa *Chem. Lett.* **1976,** 811; Shibanuma; Shiono; Mukaiyama *Chem. Lett.* **1977,** 575; Kim; Yi *J. Org. Chem.* **1986,** *51*, 2613, Ref. 427.

[433]Jászay; Petneházy; Tóke; Szajáni *Synthesis* **1987,** 520.

[434]Ulrich; Sayigh *Angew. Chem. Int. Ed. Engl.* **1966,** *5*, 704-712 [*Angew. Chem. 78*, 761-769], *Newer Methods Prep. Org. Chem.* **1971,** *6*, 223-242.

[435]Mitsunobu; Kato; Tomari *Tetrahedron* **1970,** *26*, 5731.

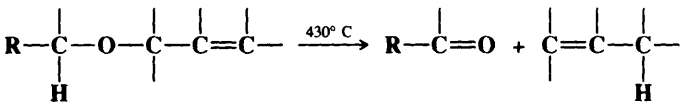
[436]Arnold; Smolinsky *J. Am. Chem. Soc.* **1959,** *81*, 6643. For a review, see Marvell; Whalley, in Patai, Ref. 152, pt. 2, pp. 729-734.

[437]Smith; Yates *J. Chem. Soc.* **1965,** 7242; Voorhees; Smith *J. Org. Chem.* **1971,** *36*, 1755.

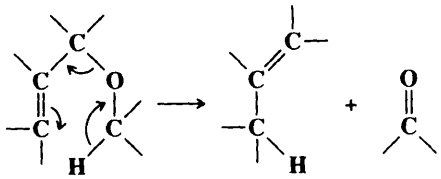
[438]Arnold; Smolinsky *J. Org. Chem.* **1960,** *25*, 128; Smith; Taylor *Chem. Ind. (London)* **1961,** 949.

mechanism is the reverse of that for the oxygen analog of the ene synthesis (**6-53**). β-Hydroxyacetylenes react similarly to give the corresponding allenes and carbonyl compounds.[439] The mechanism is the same despite the linear geometry of the triple bonds.

7-44 Pyrolysis of Allylic Ethers
***C*-Hydro-*O*-allyl-elimination**

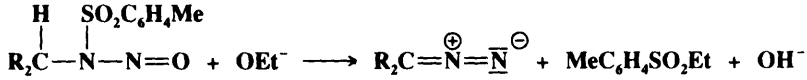


Pyrolysis of allylic ethers that contain at least one α hydrogen gives olefins and aldehydes or ketones. The reaction is closely related to **7-43**, and the mechanism is also pericyclic[440]

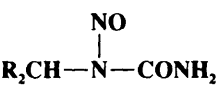


Reactions in Which N=N Bonds Are Formed

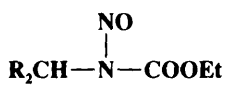
7-45 Eliminations to Give Diazoalkanes
***N*-Nitrosoamine-diazoalkane transformation**



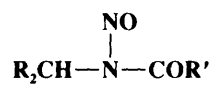
Various N-nitroso-N-alkyl compounds undergo elimination to give diazoalkanes.[441] One of the most convenient methods for the preparation of diazomethane involves base treatment of N-nitroso-N-methyl-*p*-toluenesulfonamide (illustrated above, with R = H).[442] However, other compounds commonly used are (base treatment is required in all cases):



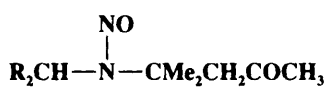
N-nitroso-N-alkylureas



N-nitroso-N-alkylcarbamates



N-nitroso-N-alkyl amides



N-nitroso-N-alkyl-4-amino-4-methyl-2-pentanones

[439]Viola; MacMillan; Proverb; Yates *J. Am. Chem. Soc.* **1971**, *93*, 6967; Viola; Proverb; Yates; Larrahondo *J. Am. Chem. Soc.* **1973**, *95*, 3609.

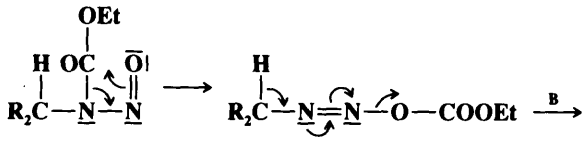
[440]Cookson; Wallis *J. Chem. Soc. B.* **1966**, 1245; Kwart; Slutsky; Sarner *J. Am. Chem. Soc.* **1973**, *95*, 5242; Egger; Vitins *Int. J. Chem. Kinet.* **1974**, *6*, 429.

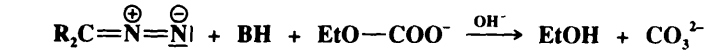
[441]For a review, see Regitz; Maas *Diazo Compounds*; Academic Press: New York, 1986, pp. 296-325. For a review of the preparation and reactions of diazomethane, see Black *Aldrichimica Acta* **1983**, *16*, 3-10. For discussions, see Cowell; Ledwith *Q. Rev., Chem. Soc.* **1970**, *24*, 119-167, pp. 126-131; Smith *Open-chain Nitrogen Compounds*; W. A. Benjamin: New York, 1966, especially pp. 257-258, 474-475, in vol. 2.

[442]de Boer; Backer *Org. Synth. IV* 225, 250; Hudlicky *J. Org. Chem.* **1980**, *45*, 5377.

All these compounds can be used to prepare diazomethane, though the sulfonamide, which is commercially available, is most satisfactory. (N-Nitroso-N-methylcarbamate and N-nitroso-N-methylurea give good yields, but are highly irritating and carcinogenic.[443]) For higher diazoalkanes the preferred substrates are nitrosoalkylcarbamates.

Most of these reactions probably begin with a 1,3 nitrogen-to-oxygen rearrangement, followed by the actual elimination (illustrated for the carbamate):

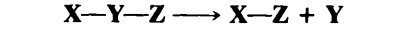




OS **II,** 165; **III,** 119, 244; **IV,** 225, 250; **V,** 351; **VI,** 981.

Extrusion Reactions

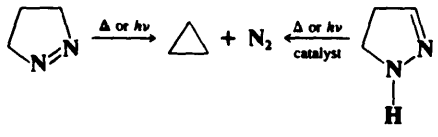
We consider an *extrusion reaction*[444] to be one in which an atom or group Y connected to two other atoms X and Z is lost from a molecule, leading to a product in which X is bonded directly to Z.



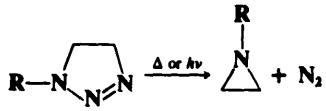
Reactions **4-41** and **7-25** also fit this definition. Reaction **7-36** does not fit the definition, but is often also classified as an extrusion reaction. An extrusibility scale has been developed, showing that the ease of extrusion of the common Y groups is in the order: —N=N— > —COO— > —SO_2— > —CO—.[445]

7-46 Extrusion of N_2 from Pyrazolines, Pyrazoles, and Triazolines

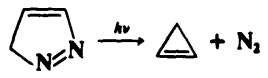
Azo-extrusion



52 53



54



55

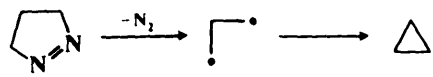
[443]Searle *Chem. Br.* **1970,** *6,* 5-10.

[444]For a monograph, see Stark; Duke *Extrusion Reactions*; Pergamon: Elmsford, NY, 1967. For a review of extrusions that are photochemically induced, see Givens *Org. Photochem.* **1981,** *5,* 227-346.

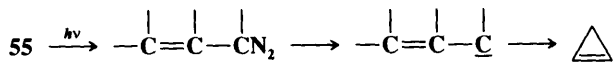
[445]Paine; Warkentin *Can. J. Chem.* **1981,** *59,* 491.

1-Pyrazolines (**52**) can be converted to cyclopropane and N_2 on photolysis[446] or pyrolysis.[447] The tautomeric 2-pyrazolines (**53**), which are more stable than **52**, also give the reaction, but in this case an acidic or basic catalyst is required, the function of which is to convert **53** to **52**.[448] In the absence of such catalysts, **53** do not react.[449] In a similar manner, triazolines (**54**) are converted to aziridines.[450] Side reactions are frequent with both **52** and **54**, and some substrates do not give the reaction at all. However, the reaction has proved synthetically useful in many cases. In general, photolysis gives better yields and fewer side reactions than pyrolysis with both **52** and **54**. 3*H*-Pyrazoles[451] (**55**) are stable to heat, but in some cases can be converted to cyclopropenes on photolysis,[452] though in other cases other types of products are obtained.

There is much evidence that the mechanism[453] of the 1-pyrazoline reactions generally involves diradicals, though the mode of formation and detailed structure (e.g., singlet vs.

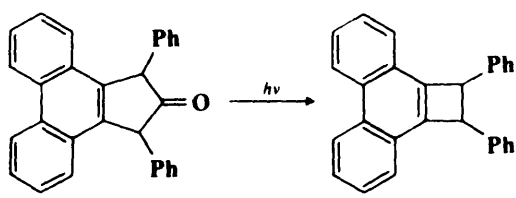


triplet) of these radicals may vary with the substrate and reaction conditions. The reactions of the 3*H*-pyrazoles have been postulated to proceed through a diazo compound that loses N_2 to give a vinylic carbene.[454]



OS **V**, 96, 929. See also OS **66**, 142.

7-47 Extrusion of CO or CO_2
Carbonyl-extrusion



56 **57**

[446]Van Auken; Rinehart *J. Am. Chem. Soc.* **1962**, *84*, 3736.

[447]For reviews of the reactions in this section, see Adam; De Lucchi *Angew. Chem. Int. Ed. Engl.* **1980**, *19*, 762-779 [*Angew. Chem. 92*, 815-832]; Meier; Zeller *Angew. Chem. Int. Ed. Engl.* **1977**, *16*, 835-851 [*Angew. Chem. 89*, 876-890]; Stark; Duke, Ref. 444, pp. 116-151. For a review of the formation and fragmentation of cyclic azo compounds, see Mackenzie; in Patai *The Chemistry of the Hydrazo, Azo, and Azoxy Groups*, pt. 1; Wiley: New York, 1975, pp. 329-442.

[448]For example, see Jones; Sanderfer; Baarda *J. Org. Chem.* **1967**, *32*, 1367.

[449]McGreer; Wai; Carmichael *Can. J. Chem.* **1960**, *38*, 2410; Kocsis; Ferrini; Arigoni; Jeger *Helv. Chim. Acta* **1960**, *43*, 2178.

[450]For a review, see Scheiner *Sel. Org. Transform.* **1970**, *1*, 327-362.

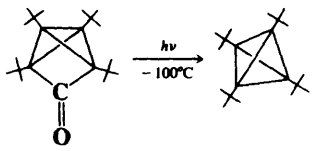
[451]For a review of 3*H*-pyrazoles, see Sammes; Katritsky *Adv. Heterocycl. Chem.* **1983**, *34*, 2-52.

[452]Closs; Böll *J. Am. Chem. Soc.* **1963**, *85*, 3904, *Angew. Chem. Int. Ed. Engl.* **1963**, *2*, 399 [*Angew. Chem. 75*, 640]; Ege *Tetrahedron Lett.* **1963**, 1667; Closs; Böll; Heyn; Dev *J. Am. Chem. Soc.* **1968**, *90*, 173; Franck-Neumann; Buchecker *Tetrahedron Lett.* **1969**, 15; Pincock; Morchat; Arnold *J. Am. Chem. Soc.* **1973**, *95*, 7536.

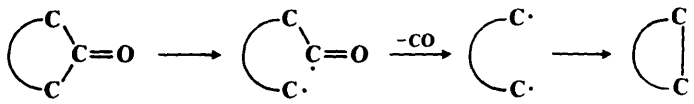
[453]For a review of the mechanism; see Engel *Chem. Rev.* **1980**, *80*, 99-150. See also Engel; Nalepa *Pure Appl. Chem.* **1980**, *52*, 2621; Engel; Gerth *J. Am. Chem. Soc.* **1983**, *105*, 6849; Reedich; Sheridan *J. Am. Chem. Soc.* **1988**, *110*, 3697.

[454]Closs; Böll; Heyn; Dev, Ref. 452; Pincock; Morchat; Arnold, Ref. 452.

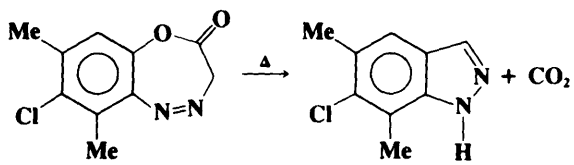
Though the reaction is not general, certain cyclic ketones can be photolyzed to give ring-contracted products.[455] In the example above, the tetracyclic ketone **56** was photolyzed to give **57**.[456] This reaction was used to synthesize tetra-*t*-butyltetrahedrane:[457]



The mechanism probably involves a Norrish type I cleavage (p. 243), loss of CO from the resulting radical, and recombination of the radical fragments.

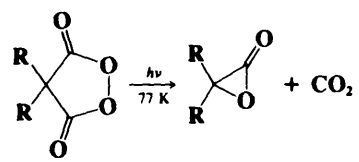


Certain lactones extrude CO_2 on heating or on irradiation, examples being pyrolysis of **58**,[458]



58

and the formation of α-lactones by photolysis of 1,2-dioxolane-3,5-diones.[459]



Decarboxylation of β-lactones (see **7-34**) may be regarded as a degenerate example of this reaction. Unsymmetrical diacyl peroxides RCO—OO—COR′ lose two molecules of CO_2 when photolyzed in the solid state to give the product RR′.[460] Electrolysis was also used, but yields were lower. This is an alternative to the Kolbe reaction (**4-38**). See also **7-36** and **7-51.**

There are no OS references, but see OS **VI,** 418, for a related reaction.

[455]For reviews of the reactions in this section, see Redmore; Gutsche *Adv. Alicyclic Chem.* **1971,** *3*, 1-138, pp. 91-107; Stark; Duke, Ref. 444, pp. 47-71.

[456]Cava; Mangold *Tetrahedron Lett.* **1964,** 1751.

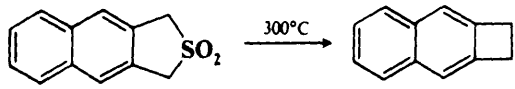
[457]Maier; Pfriem; Schäfer; Matusch *Angew. Chem. Int. Ed. Engl.* **1978,** *17*, 520 [*Angew. Chem. 90*, 552].

[458]Ried; Dietrich *Angew. Chem. Int. Ed. Engl.* **1963,** *2*, 323 [*Angew. Chem. 75*, 476]; Ried; Wagner *Liebigs Ann. Chem.* **1965,** *681*, 45.

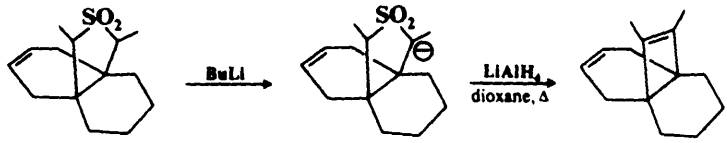
[459]Chapman; Wojtkowski; Adam; Rodriquez; Rucktäschel *J. Am. Chem. Soc.* **1972,** *94*, 1365.

[460]Feldhues; Schäfer *Tetrahedron* **1985,** *41*, 4195, 4213, **1986,** *42*, 1285; Lomölder; Schäfer *Angew. Chem. Int. Ed. Engl.* **1987,** *26*, 1253 [*Angew. Chem. 99*, 1282].

7-48 Extrusion of SO_2
Sulfonyl-extrusion



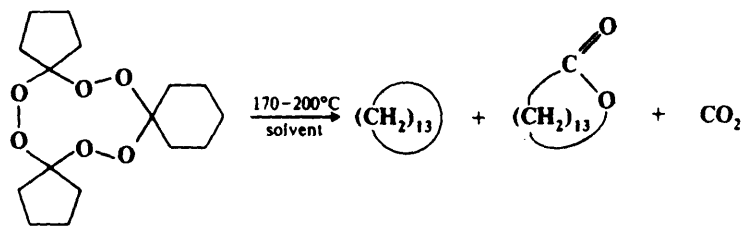
In a reaction similar to **7-47,** certain sulfones, both cyclic and acylic,[461] extrude SO_2 on heating or photolysis to give ring-contracted products.[462] An example is the preparation of naphtho(*b*)cyclobutene shown above.[463] In a different kind of reaction, five-membered cyclic sulfones can be converted to cyclobutenes by treatment with butyllithium followed by $LiAlH_4$,[464] e.g.,



This method is most successful when both the α and α′ position of the sulfone bear alkyl substituents. See also **7-25.**

OS **VI,** 482.

7-49 The Story Synthesis



59

When cycloalkylidene peroxides (e.g., **59**) are heated in an inert solvent (e.g., decane), extrusion of CO_2 takes place; the products are the cycloalkane containing three carbon atoms less than the starting peroxide and the lactone containing two carbon atoms less[465] (the *Story synthesis*).[466] The two products are formed in comparable yields, usually about 15 to 25% each. Although the yields are low, the reaction is useful because there are not many other ways to prepare large rings. The reaction is versatile, having been used to prepare rings of every size from 8 to 33 members. The method is also applicable to dimeric

[461]See, for example, Gould; Tung; Turro; Givens; Matuszewski *J. Am. Chem. Soc.* **1984,** *106,* 1789.

[462]For reviews of extrusions of SO_2, see Vögtle; Rossa *Angew. Chem. Int. Ed. Engl.* **1979,** *18,* 515-529 [*Angew. Chem. 91,* 534-549]; Stark; Duke, Ref. 444, pp. 72-90; Kice, in Kharasch; Meyers, Ref. 302, pp. 115-136. For a review of extrusion reactions of S, Se, and Te compounds, see Guziec; SanFilippo *Tetrahedron* **1988,** *44,* 6241-6285.

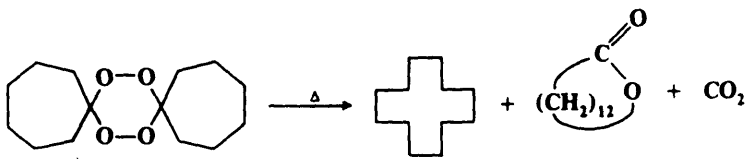
[463]Cava; Shirley *J. Am. Chem. Soc.* **1960,** *82,* 654.

[464]Photis; Paquette *J. Am. Chem. Soc.* **1974,** *96,* 4715.

[465]Story; Denson; Bishop; Clark; Farine *J. Am. Chem. Soc.* **1968,** *90,* 817; Sanderson; Story; Paul *J. Org. Chem.* **1975,** *40,* 691; Sanderson; Paul; Story *Synthesis* **1975,** 275.

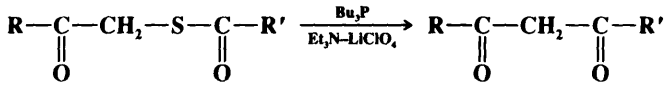
[466]For a review, see Story; Busch *Adv. Org. Chem.* **1972,** *8,* 67-95, pp. 79-94.

cycloalkylidene peroxides, in which case the cycloalkane and lactone products result from loss of two molecules and one molecule of CO_2, respectively, e.g.,



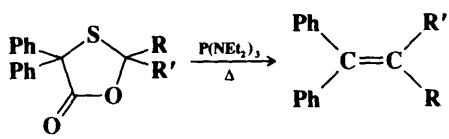
Both dimeric and trimeric cycloalkylidene peroxides can be synthesized[467] by treatment of the corresponding cyclic ketones with H_2O_2 in acid solution.[468] The trimeric peroxide is formed first and is subsequently converted to the dimeric compound.[469]

7-50 Formation of β-Dicarbonyl Compounds by Extrusion of Sulfur
Thio-extrusion



Thioesters containing a β keto group in the alkyl portion can be converted to β-diketones by treatment with a tertiary phosphine under basic conditions.[470] The starting thioesters can be prepared by the reaction between a thiol acid and an α-halo ketone (similar to **0-24**).
OS **VI**, 776.

7-51 Olefin Synthesis by Twofold Extrusion
Carbon dioxide,thio-extrusion



60

4,4-Diphenyloxathiolan-5-ones (**60**) give good yields of the corresponding olefins when heated with tris(diethylamino)phosphine.[471] This reaction is an example of a general type:

[467]For synthesis of mixed trimeric peroxides (e.g., **59**), see Sanderson; Zeiler *Synthesis* **1975**, 388; Paul; Story; Busch; Sanderson *J. Org. Chem.* **1976**, *41*, 1283.

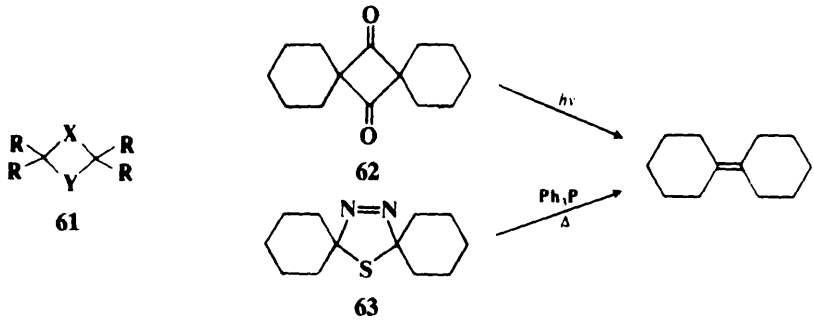
[468]Kharasch; Sosnovsky *J. Org. Chem.* **1958**, *23*, 1322; Ledaal *Acta Chem. Scand.* **1967**, *21*, 1656. For another method, see Sanderson; Zeiler *Synthesis* **1975**, 125.

[469]Story; Lee; Bishop; Denson; Busch *J. Org. Chem.* **1970**, *35*, 3059. See also Sanderson; Wilterdink; Zeiler *Synthesis* **1976**, 479.

[470]Roth; Dubs; Götschi; Eschenmoser *Helv. Chim. Acta* **1971**, *54*, 710. For a review of thio-extrusion, see Williams; Harpp *Sulfur Rep.* **1990**, *10*, 103-191.

[471]Barton; Willis *J. Chem. Soc., Perkin Trans. 1* **1972**, 305.

olefin synthesis by twofold extrusion of X and Y from a molecule of the type **61**.[472] Other examples are photolysis of 1,4-diones[473] (e.g., **62**) and treatment with Ph_3P of the azo sulfide



63.[474] **60** can be prepared by the condensation of thiobenzilic acid $Ph_2C(SH)COOH$ with aldehydes or ketones.

OS **V**, 297.

[472]For a review of those in which X or Y contains S, Se, or Te, see Guziec; SanFilippo, Ref. 462.

[473]Turro; Leermakers; Wilson; Neckers; Byers; Vesley *J. Am. Chem. Soc.* **1965**, *87*, 2613.

[474]Barton; Smith; Willis *Chem. Commun.* **1970**, 1226; Barton; Guziec; Shahak *J. Chem. Soc., Perkin Trans. 1* **1974**, 1794. See also Bee; Beeby; Everett; Garratt *J. Org. Chem.* **1975**, *40*, 2212; Back; Barton; Britten-Kelly; Guziec *J. Chem. Soc., Perkin Trans. 1* **1976**, 2079; Guziec; Moustakis *J. Chem. Soc., Chem. Commun.* **1984**, 63.