Fragmentation reaction

Fragmentation reactions, which are similar to β-elimination reactions, can be useful for the formation of alkenes, particularly from carbocyclic compounds. Fragmentation reactions occur most easily from conformationally locked 1,3-difunctionalized compounds, in which the breaking C-X and C-C bonds (highlighted) are aligned antiperiplanar.

The reaction is referred to as the Grob fragmentation and proceeds by a concerted mechanism, to give an alkene in which the stereochemistry is governed by the relative orientation of the groups in the cyclic precursor. For example, the decalin derivative 1, in which the tosyloxy group and the adjacent ring junction hydrogen atom are cis, gave E-5-cyclodecenone in high yield, whereas the isomer 2, in which the tosyloxy group and the hydrogen atom are trans, gave the Z-isomer (i.e. in each case the relative orientation of the hydrogen atoms in the precursor is retained in the alkene). In these derivatives, there is an antiperiplanar arrangement of the breaking bonds. Fragmentation reactions may be used to prepare cyclic or acyclic alkenes from cyclic precursors. The stereochemistry of the alkene can be set up by controlling the relative stereochemistry of the cyclic substrate, a process that is normally relatively easy. The ketone 5, for example, an intermediate in a synthesis of juvenile hormone, was obtained stereospecifically from the bicyclic compound 3 using two successive fragmentation steps. The geometry of the intermediates 2 and 3 allows easy fragmentation at each stage.
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The fragmentation reaction is not restricted to monosulfonates of 1,3-diols, and various leaving groups together with various electron-releasing groups can be used. The borate species formed by hydroboration (on the less-hindered face) of the alkene 6, followed by nucleophilic addition of hydroxide, fragments to the diene 7.

Fragmentation of the hydrazones of \( \text{\textsuperscript{\textdegree}} \)-epoxy ketones is known as the Eschenmoser fragmentation. Deprotonation of the hydrazone promotes ring-opening of the epoxide to give an alkoxy species. This alkoxy species then fragments, displacing nitrogen gas and the sulfinate, to give an alkynone. For example, this reaction was made use of in a synthesis of exo-brevicomin, starting with the epoxy ketone 8.
ALKENES FROM ALKYNES

The most obvious method for the formation of alkenes from alkynes is by partial reduction. This reaction can be effected in high yield with a palladium–calcium carbonate catalyst that has been partially deactivated by addition of lead(II) acetate or quinoline (Lindlar’s catalyst). It is aided by the fact that the more electrophilic alkynes are adsorbed on the electron-rich catalyst surface more strongly than the corresponding alkenes. An important feature of these reductions is their high stereoselectivity. In most cases the product consists very largely of the thermodynamically less stable Z-alkene and partial catalytic hydrogenation of alkynes provides one of the most convenient routes to Z-1,2-disubstituted alkenes. For example, reduction of stearolic acid over Lindlar’s catalyst gave 95% of the alkene oleic acid (2.48). Partial reduction of alkynes with Lindlar’s catalyst has been invaluable in the synthesis of carotenoids and many other natural products with Z-1,2-disubstituted alkenes.

In contrast, reduction of alkynes to E-1,2-disubstituted alkenes is possible using sodium metal in liquid ammonia. This method therefore complements the formation of Z-alkenes by catalytic hydrogenation.
Carbon–carbon double bonds are not normally reduced by metal–ammonia reducing agents and the reduction of the triple bond is therefore selective, such that none of the saturated product is formed. It is thought that the reaction takes place by stepwise addition of two electrons, the first electron adding to the triple bond to give an intermediate radical anion which is protonated by the ammonia to give a vinyl radical. The second electron adds to give a vinyl anion which adopts the more-stable $E$-configuration and is protonated to give the $E$-alkene.

$\text{C}_3\text{H}_7\text{C}=\text{C}-(\text{CH}_2)_7\text{OH} \xrightarrow{i, \text{Na, NH}_3} \xrightarrow{\text{ii, NH}_4\text{Cl}} \text{C}_3\text{H}_7\text{C}=\text{C}(\text{CH}_2)_7\text{OH}$

Attempts to partially reduce terminal alkynes by this method normally fail as the alkyne reacts to give the alkylnyl sodium species (sodium acetylide), which resists reduction because of the negative charge on the alkylnyl carbon atom. In the presence of ammonium sulfate, however, the terminal alkyne is preserved and reduction gives the terminal alkene. This method can be preferable to catalytic hydrogenation, which sometimes gives small amounts of the saturated hydrocarbons that may be difficult to separate from the alkene. Reduction of a terminal alkyne can be suppressed by converting it to its sodium salt by reaction with sodium amide, thereby allowing the selective reduction of an internal triple bond in the same molecule. 1,7-Undecadiyne, for example, was converted to $E$-7-undecen-1-yne in high yield.

$\text{C}_3\text{H}_7\text{C}=\text{C}-(\text{CH}_2)_4\text{C}=\text{CH} \xrightarrow{\text{NaNH}_2, \text{NH}_3} \xrightarrow{\text{ii, NH}_4\text{Cl}} \text{C}_3\text{H}_7\text{C}=\text{C}(\text{CH}_2)_4\text{C}=\text{C}^- \xrightarrow{i, \text{Na, NH}_3} \text{C}_3\text{H}_7\text{C}=\text{C}(\text{CH}_2)_4\text{C}=\text{Cl}$

Partial reduction of alkynes by using hydrogenation with Lindlar’s catalyst or by using sodium in liquid ammonia provides $Z$- or $E$-alkenes respectively, although these conditions are not always ideal and other methods have been developed. Reduction of alkynes to $Z$-alkenes is possible by hydroboration and protonolysis. Monohydroboration of alkynes is possible using dialkylboranes, catecholborane 51, or other substituted boranes. The product alkenylborane is reactive and is not normally isolated. Protonolysis occurs readily with carboxylic acids and takes place with retention of alkene configuration. Therefore, since hydroboration occurs by syn
addition of the hydrogen and boron atom, 1,2-disubstituted alkynes can be converted to Z-alkenes with high stereoselectivity.

Treatment of the intermediate alkenylborane, such as 2 or 3, with iodine in the presence of a base (such as sodium hydroxide or methoxide) forms, stereoselectively, a Z-1,2-disubstituted or trisubstituted alkene. Transfer of one alkyl group from boron to the adjacent carbon atom occurs stereospecifically, resulting, after anti elimination of boron and iodine, in a new alkene in which the two substituents of the original alkyne become trans to each other (2.53, 2.54).
In comparison, no rearrangement can occur using alkenylboronic acids, derived from hydroboration of alkynes with catecholborane 51, followed by hydrolysis. Treatment of the alkenylboronic acid with sodium hydroxide and iodine results in the replacement of the boronic acid group by iodine with retention of configuration (2.55). However, treatment with bromine, followed by base, results in substitution with inversion of configuration (2.56). In each case the reaction is highly stereoselective. The inversion of configuration in the bromination can be accounted for by invoking the usual anti addition of bromine across the double bond, followed by base-induced anti elimination of boron and bromine.

Hydroalumination of disubstituted alkynes with lithium hydridodiisobutylmethylaluminate, obtained from diisobutylaluminium hydride and methylithium, results in anti addition across the triple bond. Subsequent reaction with aldehydes gives allylic alcohols, with CO2 gives -unsaturated acids and with iodine gives alkenyl iodides, isomeric with the products obtained in the reaction sequences using diisobutylaluminium hydride. Thus the isomeric -methylcrotonic acids are obtained from 2-butyne.
Anti addition across an alkyne can be accomplished with lithium aluminium hydride. This is particularly popular using propargylic alcohols and occurs with very high stereoselectivity. If the reduction is effected in the presence of sodium methoxide and the crude reduction product is treated with iodine, then the final product is exclusively the 3-iodoallylic alcohol. In contrast, reduction with lithium aluminium hydride and aluminium chloride, followed by iodination, gives the 2-iodoallylic alcohol.

This reaction works only if there is a hydroxy or an ether functional group near to the alkyne, because it relies on delivery of the reducing agent to the triple bond through complexation to this oxygen atom.
Making alkenes by addition to alkynes offers two distinct advantages. Firstly, although the reaction is not connective in the sense that the Wittig and Julia reactions are, the starting materials can often be made straightforwardly by alkylation of alkynyl anions. Secondly, the same alkyne can be used to make either $E$- or $Z$-alkene—an advantage shared with the Peterson reaction but here the starting material is much easier to make. In some early work on sphingosine (a constituent of cell membranes), some Swiss chemists needed to make both $E$- and $Z$-isomers of the naturally occurring compound. This was an easy task once they had made the alkyne.