

SYNTHESIS OF ALKENES BY FRAGMENTATION REACTIONS; MECHANISTIC VIEWS; THE ORGANIC CHEMISTRY NOTEBOOK SERIES, A DIDACTICAL APPROACH, Nº 5

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ABSTRACT

This is the fifth chapter in the series published by the same authors: “The Organic Chemistry Notebook Series, a Didactical Approach”.

Here we offer the mechanistic views of the synthesis of alkenes by fragmentation reactions. The aim of this series of studies is to help students to have a graphical view of organic synthesis reactions of diverse nature. Fragmentation reactions can conduct to the synthesis of alkenes. This is not a common method, but useful under determined conditions. For example, the fragmentation of monotonuene-*p*-sulphonates or methanesulphonates of suitable cyclic 1,3-diols is reviewed and the corresponding mechanism proposed. The preparation of *E*-cyclodecenone and cyclodecadienes by fragmentation of substituted decalylboranes is also described mechanistically. The description of the fragmentation of bicyclic compounds to afford alkenes like macrolides from acetaltosylate is also included here. The preparation of acyclic alkenes from cyclic precursors is also mechanistically described here. We have used a series of reactions reviewed by W. Carruthers, and we have proposed didactical and mechanistic views for them. This latest approach is included in the synthetic methods reviewed by W. Carruthers with respect to the “Formation of carbon-carbon double bonds”. *Spanish title:* Síntesis de alquenos por reacciones de fragmentación; vistas mecanísticas; De la serie: El cuaderno de notas de química orgánica, un enfoque didáctico, Nº5.

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ANALYSIS AND MECHANISTIC PROPOSALS

*Fragmentation of monotonuene-*p*-sulphonates or methanesulphonates*

As academics we are concerned with the didactical importance of covering the needs of debutant students in organic synthesis. This is the fifth study in: “The Organic Chemistry Notebook Series, a Didactical Approach” [1-4]. Fragmentation reactions can conduct to the synthesis of alkenes. This is not a common method, but useful under determined circumstances. For example, the fragmentation of monotonuene-*p*-sulphonates or methanesulphonates of suitable cyclic 1,3-diols on treatment with base is reviewed and the corresponding mechanism proposed [5,6]. Characteristically, when the bonds C-X and C_(a)-C_(b) are arranged in a *trans* anti-parallel manner, the reaction happens very rapidly in a concerted way to provide an alkene whose stereochemistry exclusively depends on the relative orientation of groups in the cyclic compound of start. See Figure 1.

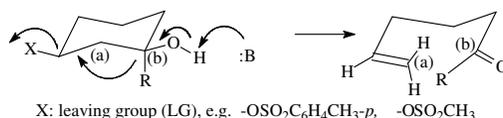


Figure 1. Fragmentation of cycle to give an alkene activated by base; reviewed by W. Carruthers [5]

An example of this reaction is the decalin structure **1** where the tosyloxy LG and its adjacent angular H are *cis* whose fragmentation gives rise to (*E*)-cyclodecenone (Figure 2). In the other hand, in the isomer **2**, where the tosyloxy LG and the vicinal angular H are *trans*, the fragmentation conducts to the isomer (*Z*)-cyclodecenone (Figure

3). In both cases (**1** and **2**, Figure 2 and 3, respectively) the relative orientation of the hydrogen atoms (H-9 and H-10, and H-9 and H-8) in the decalin structure is retained in the alkene [5]. Compounds **1** and **2** under treatment with base experiment an easy breaking of the *trans* antiparallel bonds [5] in contrast with the less immediate and less selective breaking of the anti parallel arrangement of bonds as in compound **3**. The treatment of **3** with base gives a mixture of products containing only a very small amount of (*E*)-cyclodecenone. “This reaction has been used to prepare a variety of *Z*- and *E*-cyclodecenone and cyclononenone derivatives, notably in the course of the synthesis of caryophyllene” [5,6].

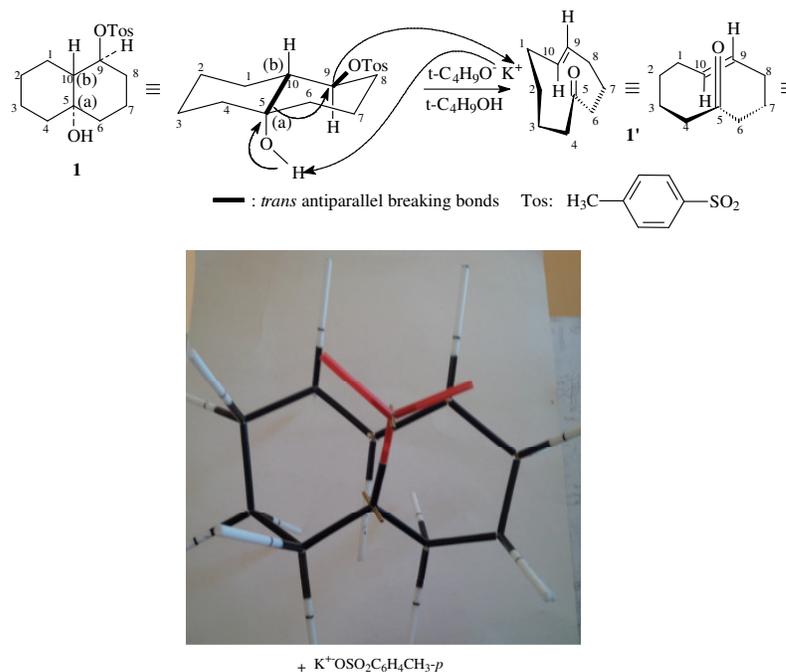


Figure 2. Synthesis of (*E*)-cyclodecenone by fragmentation of decalin structure, reviewed by W. Carruthers [5]; mechanistic views proposals

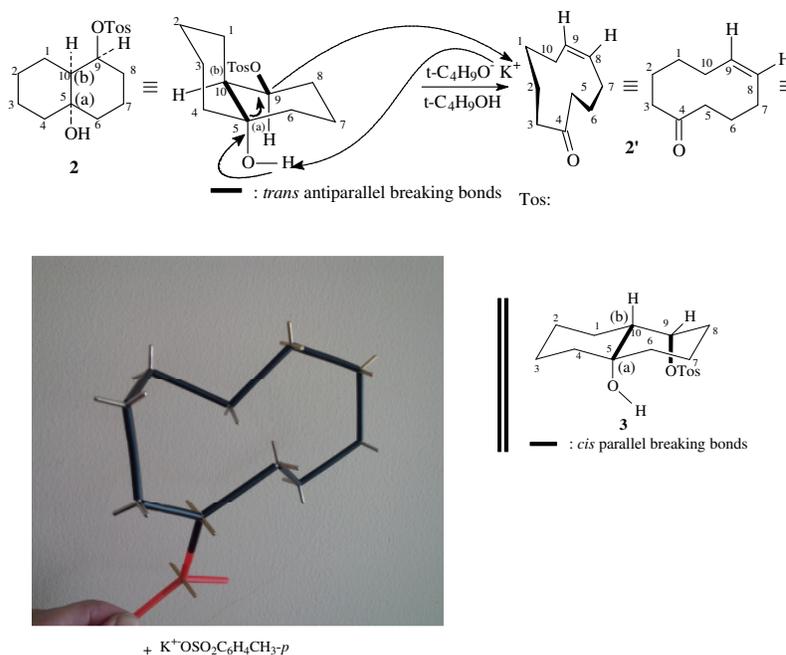


Figure 3. Synthesis of (*z*)-cyclodecenone by fragmentation of decalin structure, reviewed by W. Carruthers [5]; mechanistic views proposals

This reaction was used in an extended way to produce cyclodecadienes [5,7,8]. The appropriately substituted decalylboranes (readily available from the appropriate alkenes obtained by hydroboration) served to this purpose [5,7,8]. See Figure 4.

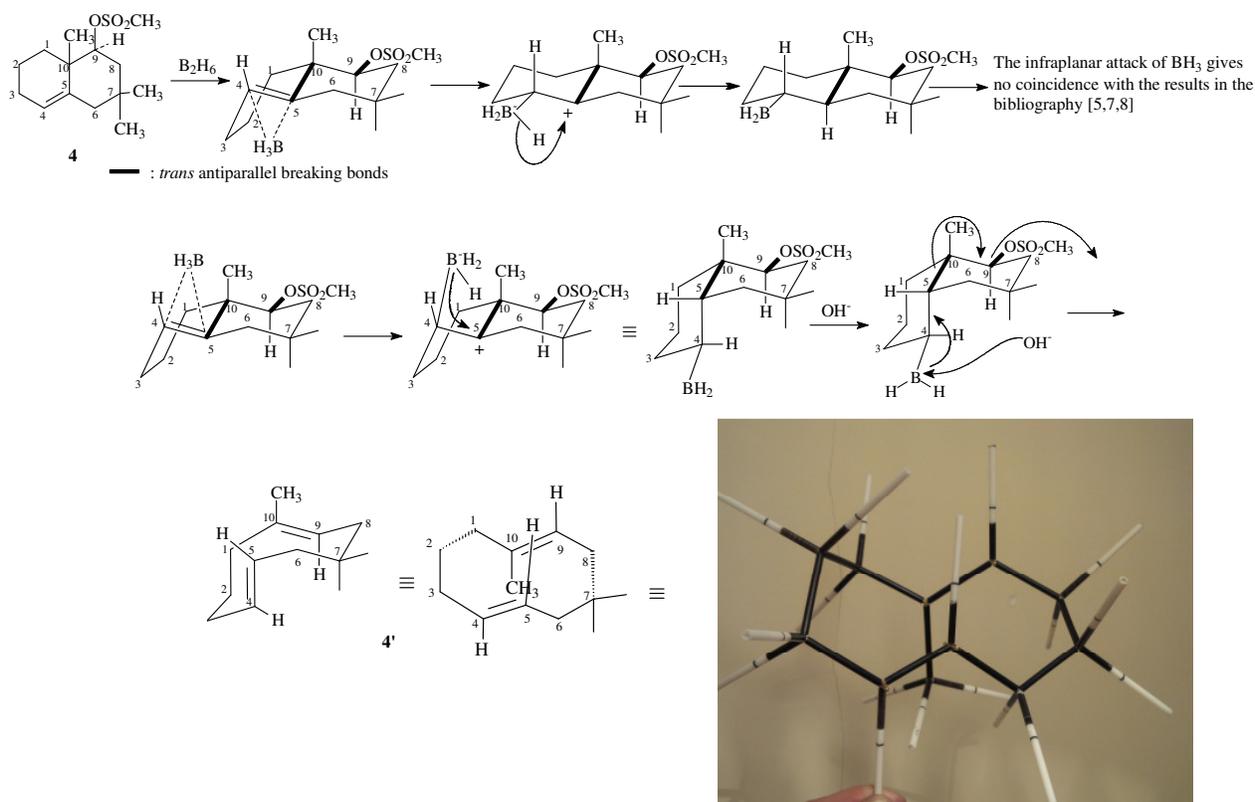


Figure 4. Extended fragmentation reaction for the preparation of cyclodecadienes. Reviewed by W. Carruthers [5]; mechanistic views

Some important remarks regarding Figures 2-4 include the fact that structures signaled as 1', 2' and 4' are designed according to the framework molecular models employed and shown in photographs. These models forced the current conformers named as 1', 2' and 4'.

Another application of fragmentation can be observed in the bridged-bicyclic compound 5 to obtain compound 6 [5,9,10]. This synthesis produces the correct relative orientation of the substituents in both rings, the all as reviewed by W. Carruthers [5]; see Figure 5; the corresponding mechanistic analysis is shown in Figure 6.

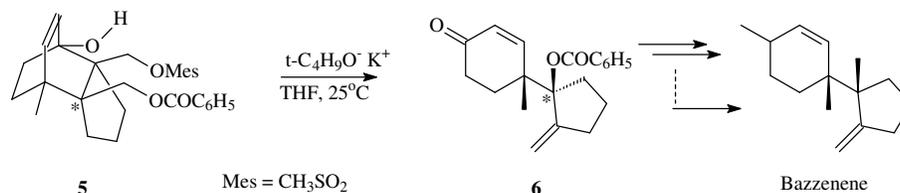


Figure 5. Fragmentation of the bridged-bicyclic compound 5 to obtain compound 6. Reviewed by W. Carruthers [5]

Figure 6 reveals, thanks to the application of molecular models, that the stereochemistry at the chiral centre (*) in compound 6, defined as "β" for the benzoate substituent in Figure 5, is erroneous [5]. The molecular model on the down photograph in Figure 6 clearly exhibits the stereochemistry for the benzoate substituent of 6 as "α". In this scheme the intermediate 5' is submitted to a free rotation around the inter-rings bond resulting in a "α" stereochemistry for the benzoate substituent at the chiral centre (*) contrarily to what is signalled in the reference reviewed by W. Carruthers [5].

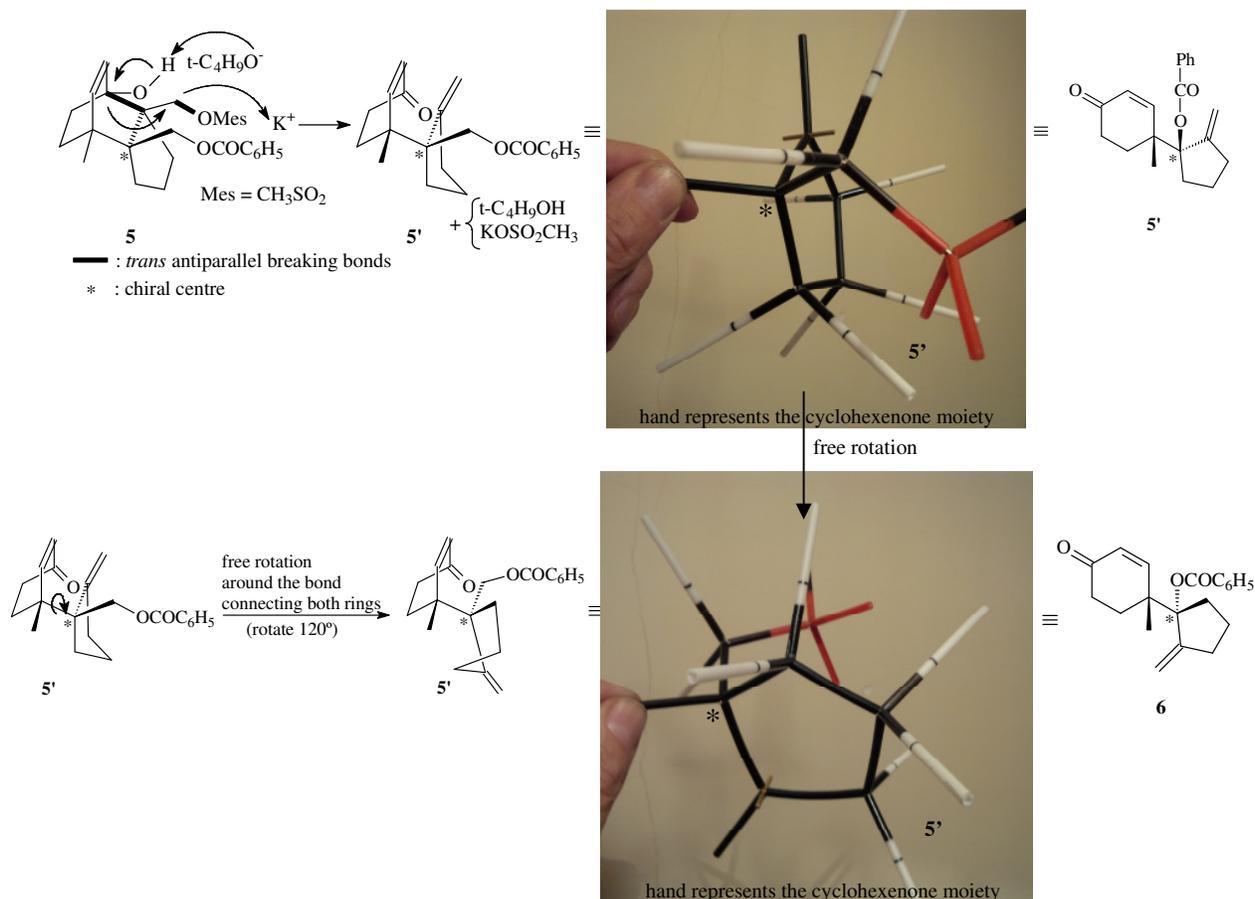


Figure 6. Fragmentation of the bridged-bicyclic compound 5 to obtain compound 6. Mechanistic view and analysis

In another application we find the example of the double fragmentation of the acetal tosylate 7 triggered by loss of carbon dioxide from the carboxylate anion to obtain the macrolide 8 [5,11]. All these reactions so far described are based on a sole principle: the breaking bonds are *trans* antiparallel. In 7, the bond C¹⁰-C⁵ is antiperiplanar (*trans* antiparallel) to the equatorial tosylate and so are to the equatorial electron pair *sp*³ axes of the acetal function (9). In the acetal function (9), the O⁹-C⁸ bond is also antiperiplanar to the carboxylate (Figure 7). See the mechanism in Figure 8.

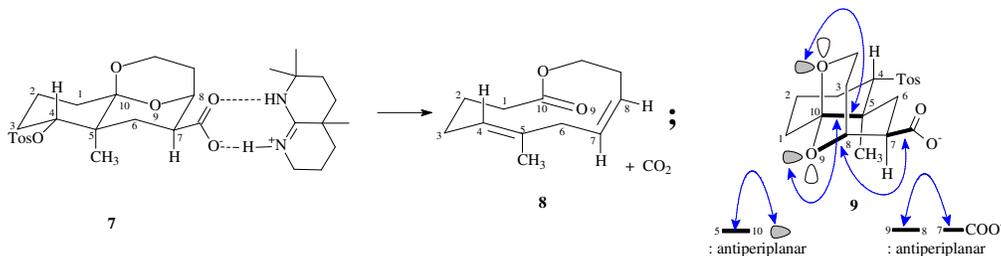


Figure 7. Fragmentation of the acetal function 7 into macrolide. Reviewed by W. Carruthers [5].

The fact of the antiperiplanar disposition of bonds in decalin-type cyclic compounds permit to predict in a feasible way the breaking of these bonds, (if disposed in such a way), and therefore to predict a prospective alkene.

Since the molecular models coincide with the alkene's stereochemistry of Figure 8 (structure 8), then, it has been demonstrated that the present approach to the synthesis of alkenes by fragmentation of cyclic structures of the decalin-type, is a trustable synthetic method in the prediction of stereochemistry of prospective alkenes.

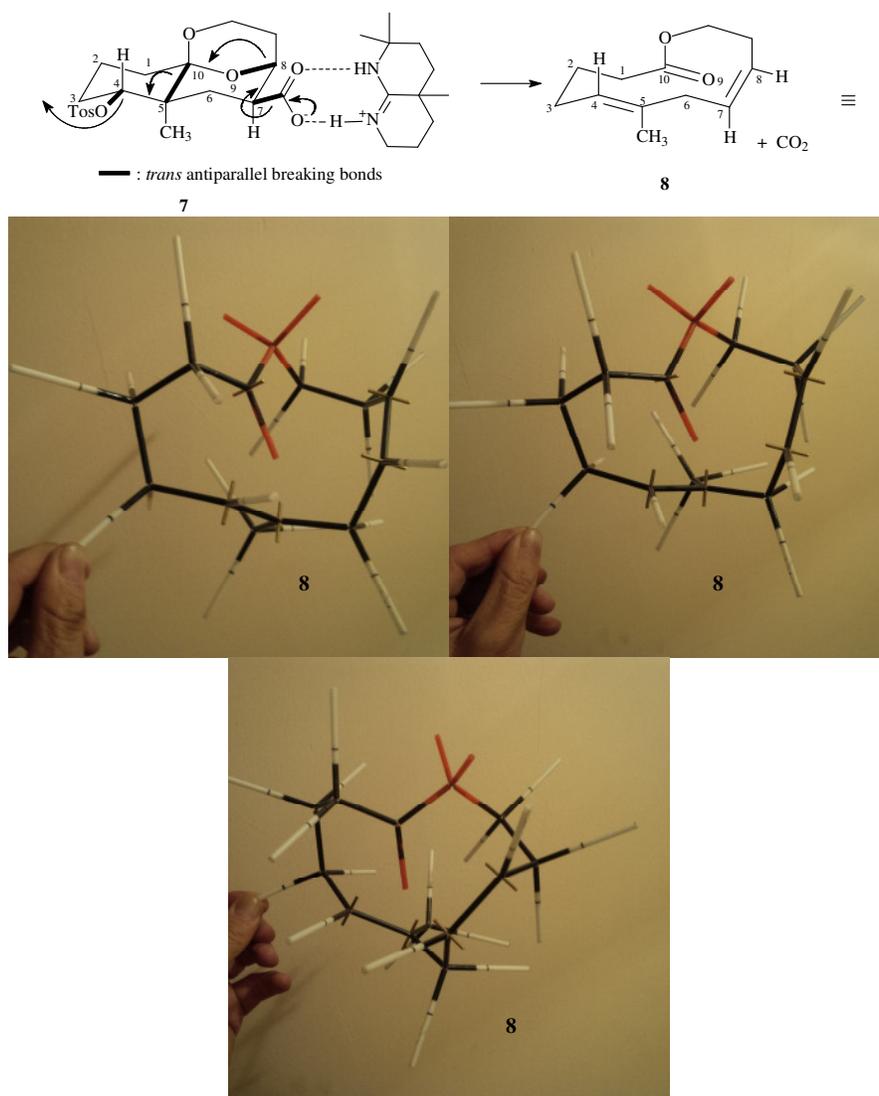


Figure 8. Fragmentation of the acetal function **7** into macrolide **8**. Mechanistic views

Fragmentation is also applied in the generation of acyclic alkenes using cyclic compounds as precursors. The definition of the geometry of alkene can be derived from the stereochemistry in the cyclic precursor [5]. *Exempli gratia*, the ketone **12** which is intermediate in the synthesis of the juvenile hormone was made stereospecifically through the application of two fragmentation steps [5,12], see Figure 9. The intermediate compounds **10** and **11**, possess such a geometry that allow the readily fragmentation at each step [5,12].

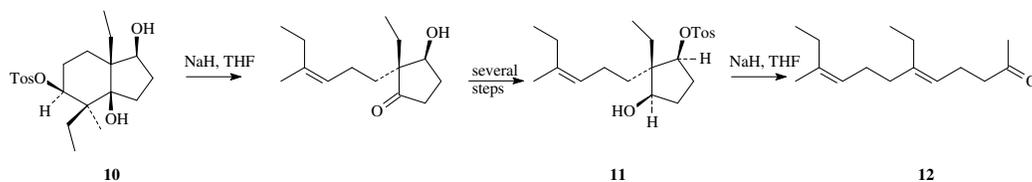


Figure 9. Two successive fragmentation steps in the synthesis of acyclic alkenes from cyclic compounds. Reviewed by W. Carruthers [5].

The mechanistic views of this synthesis are shown in Figure 10.

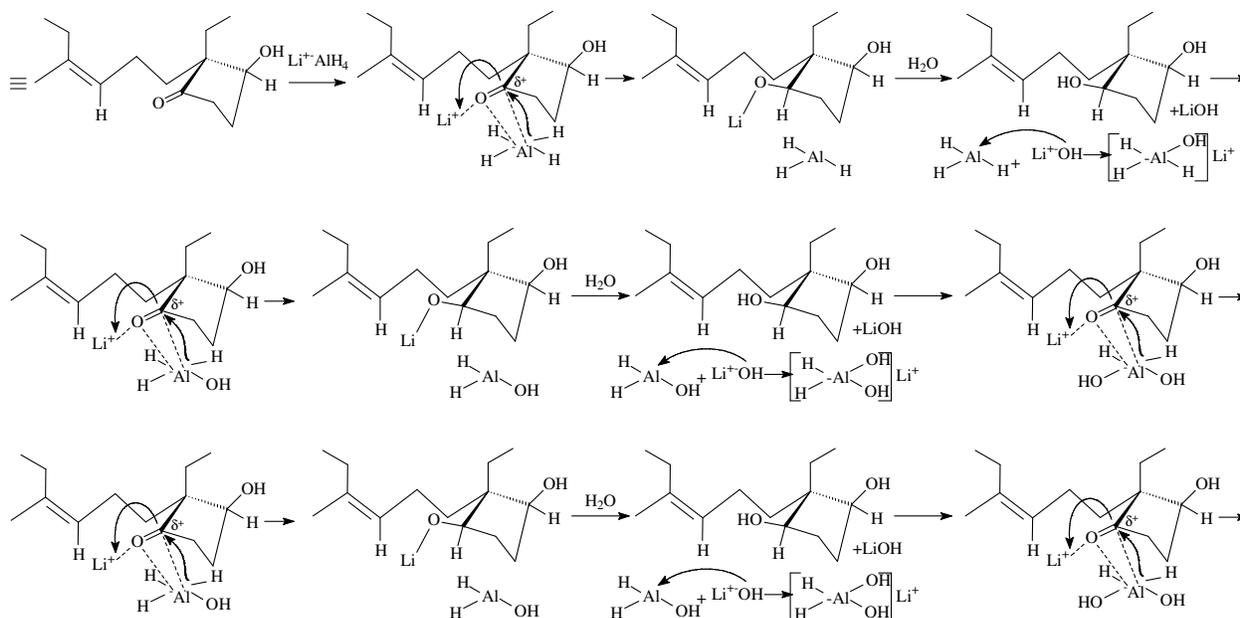
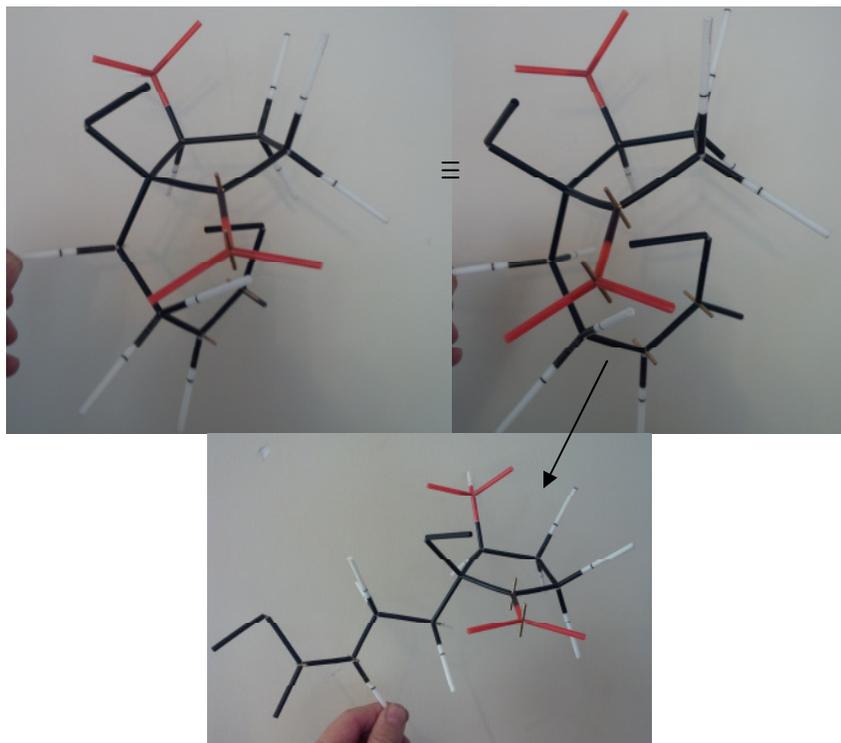
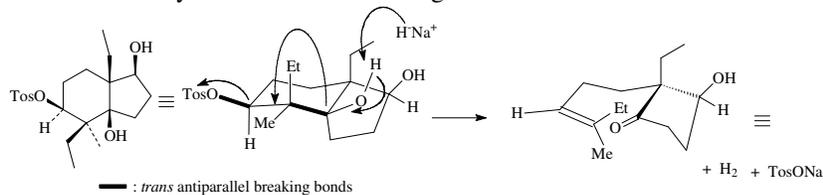


Figure 10. Two successive fragmentation steps in the synthesis of acyclic alkenes from cyclic compounds. Mechanistic views.

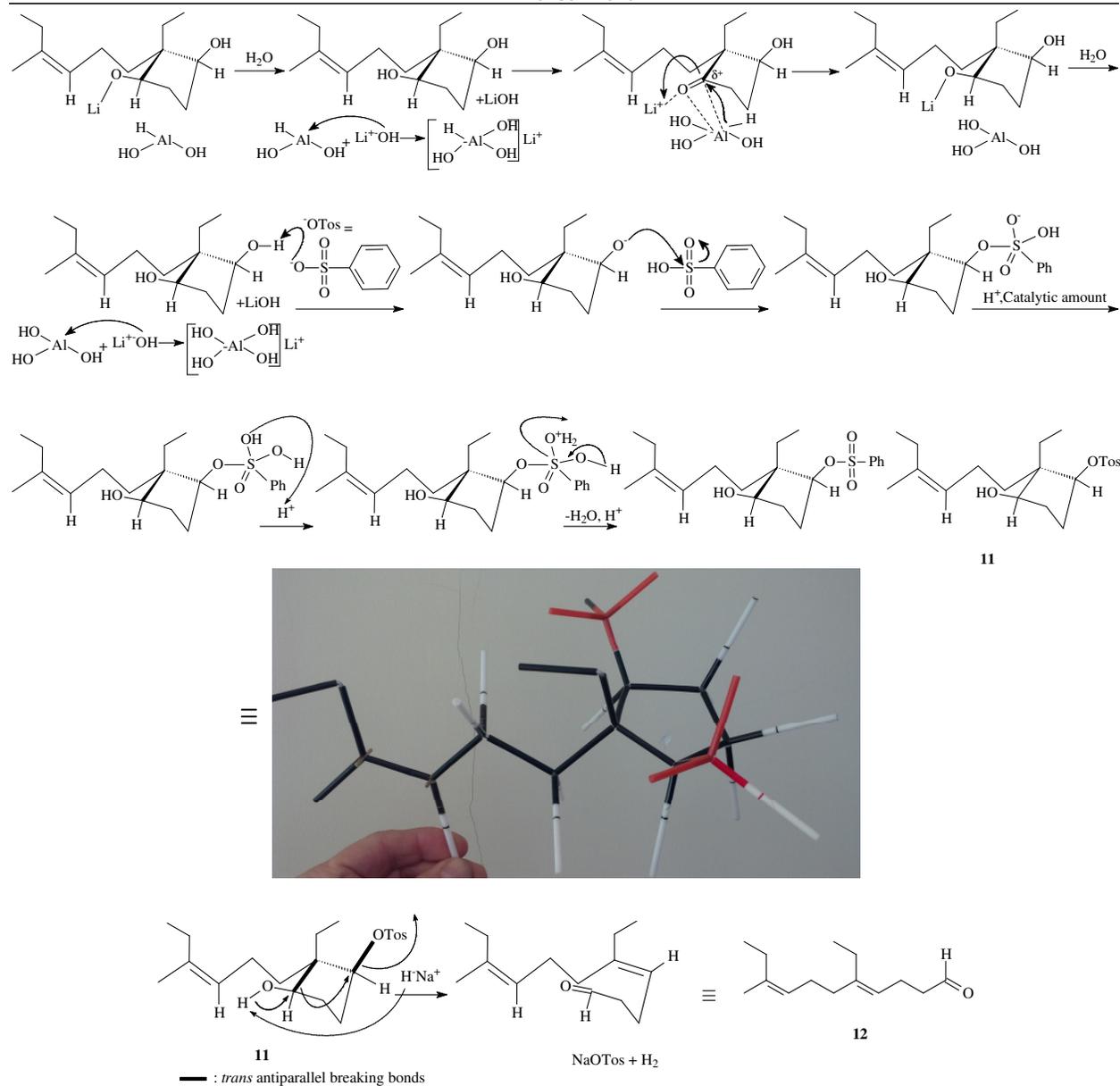


Figure 10(Cont.). Two successive fragmentation steps in the synthesis of acyclic alkenes from cyclic compounds. Mechanistic views.

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