The Dimerisation of Methallyl Alcohol. A Case Study of Novel Asynchronicity in the Ene Reaction

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The dimerisation of the potassium alkoxide of methallyl alcohol to give mainly lactols (**3**) may be rationalised in terms of a redox system incorporating a stepwise ene reaction in which hydride transfer precedes carbon–carbon bond formation.

In recent years, the Alder ene reaction has become an increasingly important weapon in the armoury of the synthetic chemist, both in the intermolecular[1] and intramolecular[2] modes. From the classical mechanistic standpoint, it is generally agreed[1] that the concerted reaction involves a highly asynchronous transition state featuring a well developed carbon–carbon bond prior to a relatively late proton transfer towards the incipient carbocation as illustrated in Figure 1(a) (Z = electron withdrawing group).

We reasoned however, that use of an allylic alkoxide as the ene component in such a reaction could lead to a reversal of asynchronicity as shown in Figure 1(b), whereby, at the limit, a stepwise mechanism involving hydride transfer followed by Michael addition of the resultant carbanion to the α,β-unsaturated carbonyl component may be considered.[3] The regiochemical outcome of such a reaction would also be the reverse of that normally encountered in use of an allylic alcohol with an electron deficient enophile.[4] Of paramount thermodynamic importance is the fact that allylic assistance to bond breaking is reinforced by the alkoxide anion effect,[5] which is now routinely used in a number of pericyclic processes and calculated to decrease the homolytic bond dissociation energy by some 17 kcal mol^{-1} (1 kcal = 4.184 kJ) as compared to the parent alcohol.[6] To the best of our knowledge ene reactions of this type have not previously been recognised in the chemical literature.

In the first instance, we were particularly intrigued by an isolated report[7] that reaction of methallyl alcohol (**1**) with an aqueous solution of sodium hydroxide in a steel autoclave at 200 °C furnished the dicarboxylic acid (**2**). Although no satisfactory mechanistic rationale was presented for this process, it seemed to us that the crucial intermolecular reaction to form the observed carbon skeleton could be represented as shown in Scheme 1 using the allylic alkoxide anion as the ene component. We therefore confirmed this experiment in our laboratory with isolation of the dicarboxylic acid (**2**) in 20% yield.

In order to obviate the intervention of hydroxide anion as a

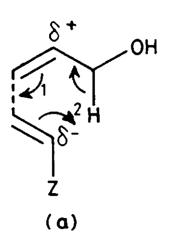
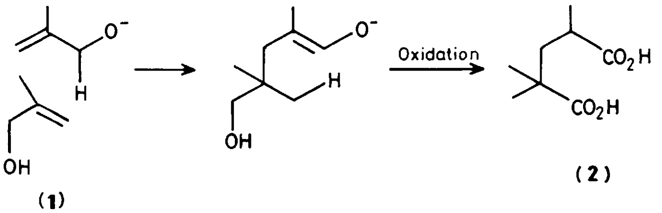
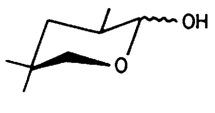


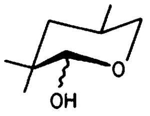
Figure 1



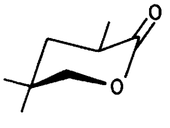
Scheme 1



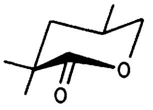
(3)



(4)



(5)

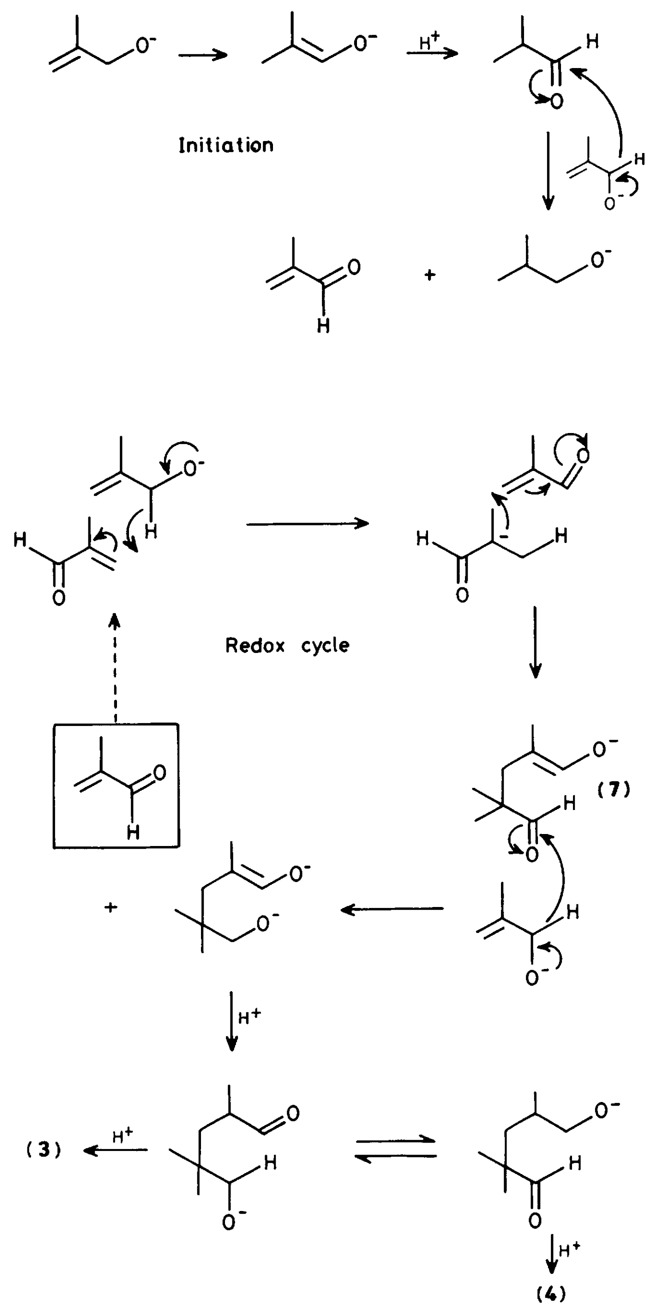


(6)

nucleophile, we subsequently studied the reaction of the parent potassium alkoxide of methallyl alcohol, generated by reaction with potassium hydride (0.9 to 1.0 equiv.) in diglyme. Work up of the reaction after 9 h at 120 °C led to the isolation of a stereoisomeric mixture of lactols (**3**) in excellent yield (75%). The regioisomeric lactols (**4**) were also formed as a minor component in this reaction. These were further characterised by oxidation with aqueous bromine to give the corresponding lactones (**5**) and (**6**).

Our attention was then focused on the enophilic component of the reaction. Attempted condensation of potassium methallyl alkoxide with cyclohexene, even under extremely vigorous conditions, led after work-up only to the lactones (**5**) and (**6**) and to a hydrocarbon mixture whose mass spectrum indicated that cyclohexene had undergone no less than four consecutive ene reactions with itself. No crossed product was detected in this reaction, clearly indicating that the simple unactivated carbon–carbon double bond of methallyl alcohol was an unlikely partner as an enophile in formation of lactols (**3**).

Accordingly, a g.l.c. examination of the early stages of the self dimerisation reaction was undertaken and revealed the presence of methacrolein, isobutyraldehyde, and isobutyl alcohol. The formation of methacrolein and isobutyl alcohol is readily understood by a process involving hydride transfer from the allylic alkoxide anion to isobutyraldehyde, the latter compound in turn being derived *via* isomerisation of the same allylic alkoxide and protonation. Some precedent for the base



Scheme 2

induced isomerisation of allylic alcohols to aldehydes has recently been adduced by Hoffmann,[8] although we do not consider that the dianion mechanism invoked is operative in this case. The most probable source of protons to give a small amount of a free carbonyl compound is methallyl alcohol itself, since measurement of hydrogen evolution during alkoxide anion formation with potassium hydride indicated incomplete reaction.

On the basis of these observations, the essential features of a possible redox cycle initiated by hydride transfer to isobutyraldehyde can therefore be constructed as shown in Scheme 2. From the electronic viewpoint, use of methacrolein as the active enophile is clearly more satisfactory [*cf.* Figure 1(b)]. The formation of the major regioisomeric lactols (**3**) consequently involves preferential reduction of the nonenolisable aldehyde moiety in the initial ene adduct (**7**) by hydride transfer from the alkoxide anion of methallyl alcohol with concomitant regeneration of a molecule of methacrolein. The minor lactols (**4**) can be rationalised by competing intramolecular hydride transfer from the ring opened form of the major regioisomer. Although a variety of other possible hydride transfers may also occur during reaction, the net result is a redox stable system leading to dimerisation of methallyl alcohol.

While the present study has been argued in terms of hydride transfer reactions, the exact timing of the bond changes can also be presented in terms either of hydrogen atom abstraction from the allylic alkoxide followed by biradical coupling, or of one electron transfer followed by hydrogen atom capture, as has recently been shown in the case of a Cannizzaro reaction.[9] The observed regioselectivity of the dimerisation nevertheless provides strong presumptive evidence that formation of a new carbon–hydrogen bond precedes carbon–carbon bond formation.

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