A Lewis Acid Catalysed Diels–Alder Reaction with Inverse Electron Demand; an Alternative Synthesis of α-Damascone

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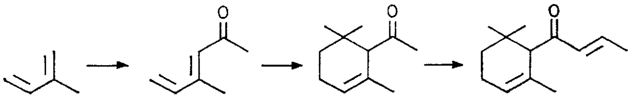
Summary α-Damascone has been synthesised from isoprene by acetylation, acid catalysed Diels–Alder reaction of the resulting 4-methylhexa-3,5-dien-2-one with isobutylene, and final aldol condensation with acetaldehyde.

Lewis acid catalysis of Diels–Alder reactions with inverse electron demand has been reported[1] only in the rather special case of tetraphenylcyclopentadienone with ethylene. We describe the catalysed Diels–Alder reaction between 4-methylhexa-3,5-dien-2-one[2] (**1**) and 2-methylprop-1-ene (isobutylene) to give the adduct (**2**). The adduct (**2**) was subsequently converted into α-damascone (**3**), a natural product[3] with important fragrance and flavour properties.

Dienone (**1**) was conveniently prepared by acylation[4] of isoprene with acetyl chloride and stannic chloride catalyst at −60°. 6-Chloro-4-methylhex-4-en-2-one, obtained as the only acylation product,† was dehydrochlorinated with diethylaniline to give dienone (**1**) as a mixture of *cis*- and *trans*-isomers (20:80) in *ca.* 30% yield based on acetyl chloride.

2-Methylprop-1-ene was passed through a solution of dienone (**1**) (1·0 mol) and aluminium chloride (0·9 mol) in methylene chloride at room temperature. In 4 h 90% of the dienone (**1**) had reacted and, after column chromatography, addition products were obtained in 60% yield based on (**1**). Products (**2**), (**4**)—(**7**) were separated in the ratios 20:55:15:6:4 respectively.‡ The structure of vinyl ether (**4**) was confirmed by Büchi and Pickenhagen who recently reported[5] that it was also the major product from cyclisation of *cis*- and *trans*-4,8-dimethylnona-3,7-dien-2-one in sulphuric acid. [We had found that with boron trifluoride in benzene the main product from this dienone was (**2**).]

The products can be explained through the zwitterion intermediate (**8**) which either closes to form adduct (**2**) or (more favourably) loses a proton and cyclises to give (**4**)—(**7**). The possibility of formation of (**2**) by a one-step mechanism cannot be excluded at present.



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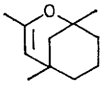

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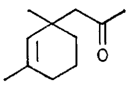

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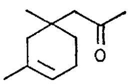

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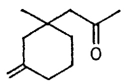

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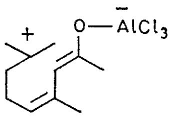

(8)

Adduct (**2**) was treated with *N*-methylanilinomagnesium bromide[6] and then condensed with acetaldehyde. Elimination of water from the intermediate aldol with sodium acetate in acetic anhydride gave α-damascone in good yield.[7]

(*Received*, 9*th July* 1973; *Com.* 970.)

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† Applications of this stereospecific reaction will be published later.

‡ Pure *trans*-dienone (**1**) isomerised under the reaction conditions to give a mixture of *cis*- and *trans*-isomers (20:80).

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