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VILSMEIER FORMYLATION OF CONJUGATED TRIENES.
A convenient synthesis of dehydrocitral.

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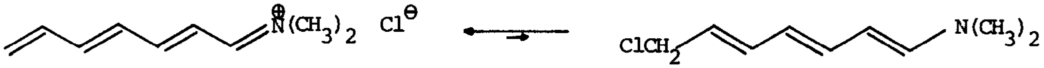
Formylation of alkenes by means of the Vilsmeier reaction has not found general application. Only in some special cases can double bonds be made to react e.g. in simple olefins such as isobutene[1] or in alicyclic compounds containing an exocyclic double bond[2]. Even then polyformylation is often observed, depending on the environment of the double bond.

The application to dienes is limited to some special systems such as cyclohexadienes[3a-c] and cyclopentadienes[4a,b]. Little attention has been paid to the formylation of trienes[5a-c] and we therefore thought it worth-while to study the formylation of a number of trienes in order to get an insight in their reactivity (Table I).

The parent compound 1,3,5-hexatriene (1), proves to be sufficiently activated for formylation, but it gives the corresponding heptatrienal only in low yield (25%). It is difficult to stop the reaction after the introduction of one formyl group. This may seem surprising because the initially formed iminium salt is hardly expected to be vulnerable for formylation. However, the iminium salt is presumably in equilibrium with the ω-chloro poly-unsaturated enamine, which is highly susceptable to formylation.



Introduction of a methyl substituent at position two in 1,3,5-hexatriene (cf. table I, compound 2) greatly enhances its reactivity and the corresponding aldehyde, 3-methyl-2,4,6-heptatrienal can be isolated in a yield of 65%.

The regiospecificity of the reaction i.e. predominant formylation at position one (not six), is in accordance with expected stabilities of the charged intermediates.

The same applies to the formylation of 2,4-dimethyl-1,3,5-hexatriene (3) and 2,3,5-trimethyl-1,3,5-hexatriene (4). In the formylation of the trimethyl derivative 4 intermediates may undergo cyclisation as can be seen from the formation of 2% of 2-methyl-4-isopropenylbenzaldehyde, essentially the product of a twofold formylation.

7 7

sec,sec,sec C^+ (10%) prim,tert,tert C^+ (55%)

8 8

tert,sec,sec C^+ (30%) prim,tert,tert C^+ (40%)

Subscripts indicate nature of positive carbons (prim,sec,tert.) in canonical structures; yields of formylation products are also indicated (cf. Table I).

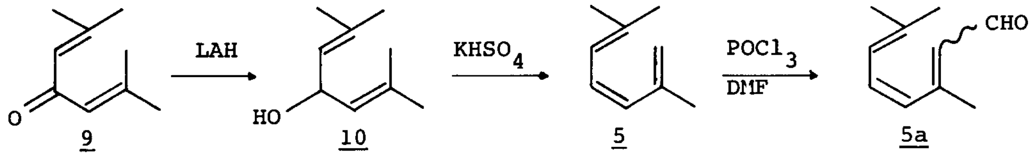
Scheme I

The usefulness of the reaction is illustrated in its application to triene 5, easily obtained from commercially available phorone (2,6-dimethyl-2,5-heptadien-4-one). This provides a new and simple route to 3,7-dimethyl-2,4,6-octatrien-1-al (dehydrocitral) as is depicted in Scheme II.

Up till now this (unstable) natural compound was synthesized by self-condensation of 3-methyl-2-buten-1-al[7a,b] but this could not be reproduced according to a recent paper[6].

Reduction of phorone (9) with lithiumaluminiumhydride and subsequent dehydration of the corresponding alcohol (10) gave 2,6-dimethyl-1,3,5,-heptatriene (5) in an overall yield of 85%; b.p. 72°/30 mm (Lit.[9] 54°/15 mm).

Formylation of this triene with the Vilsmeier reagent obtained from phosphoryl chloride and dimethylformamide (1:5) afforded in a yield of 80% dehydrocitral (5a) as a mixture of the 2Z/2E stereoisomers; b.p. 100-105°/1 mm; Lit.[8a] 57-60/0.05 mm).



9 10 5 5a

Scheme II

Formylation of 3,7-dimethyl-2,4,6-octatriene (6) (allo-ocimene) gave in less satisfactory yield (30%) a mixture of ZE and EE 2,3,7-trimethyl-2,4,6-octatrien-1-al with the concomitant formation of at least 20% of α,β,4-trimethyl-3,5-diformylcinnamaldehyde.

The formation of this fourfold formylated reaction product, initiated by abstraction of a proton from the initially formed iminium salt (11) is depicted in Scheme III.

It should be noted that although in these cases the formylation is regiospecific, a rather complicated reaction mixture is obtained because of the formation of four stereoisomers (ZZ, ZE, EZ and EE).

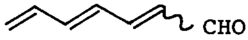
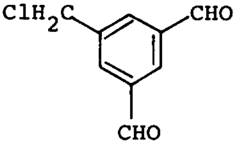
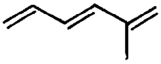
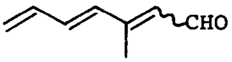
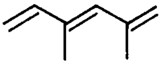
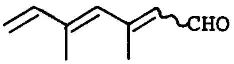
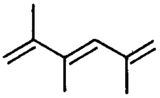
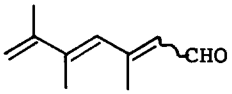
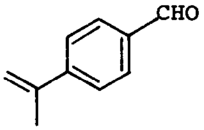
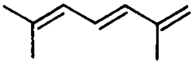
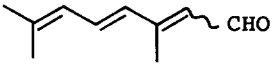
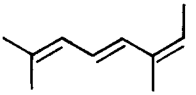
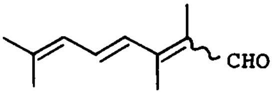
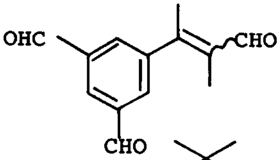
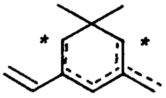
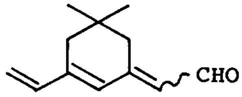
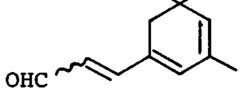
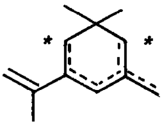
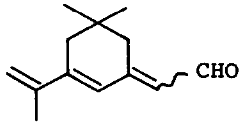
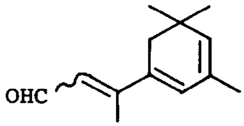
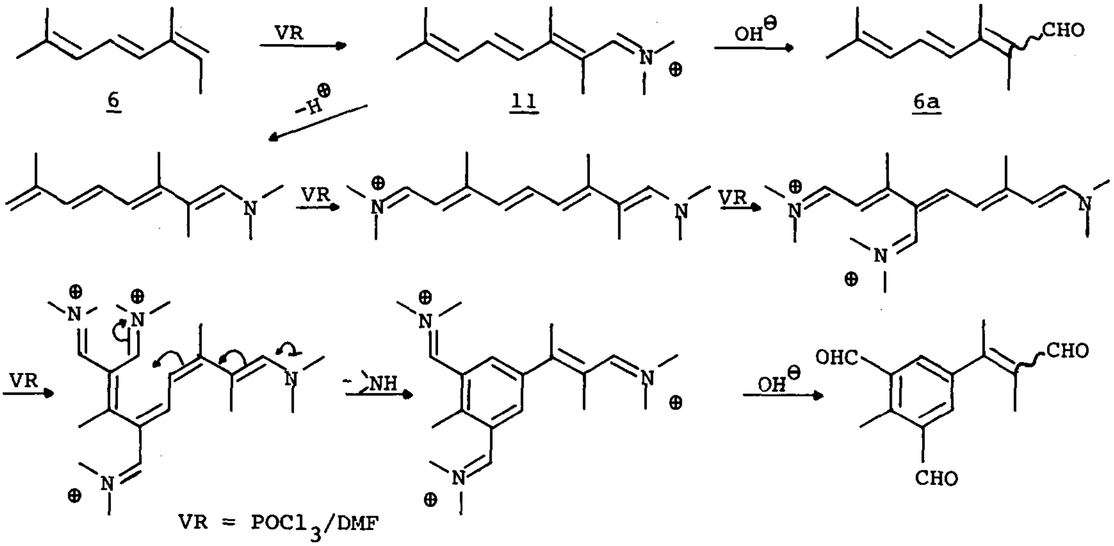
Entry	Starting material	Main product	By product	Yield (%)	
1				25	25
2				65	
3				70	
4				67	2
5				80	
6				30	20
7				55	10
8				40	30

Table I

Complications can also arise if the unsaturated starting materials undergo isomerisations prior to formylation partly for steric reasons. This is observed in the Vilsmeier reaction of trienes 7 and 8, where positions marked with an asterisk are inaccessible[3,6] and a methyl group is involved in the isomerisation. Its C-atom is the main point of attack by the Vilsmeier reagent, because this leads to a relatively stabilized charged intermediate. There is also some attack at the other end of the conjugated chain, but the resulting intermediate is less stabilized - as can be seen by considering canonical structures (Scheme I) - and consequently yields remain low.



Scheme III

The difference between the trienes 5 and 6 amounts to one (terminal) methyl group. This extra methyl group in 6 increases the reactivity of the unsaturated system. On the other hand a methylene group, as present in 5, is usually far more reactive than a more substituted double bond. As a consequence more drastic conditions, which favour polyformylation, are needed for 6 to ensure formylation.

In conclusion we believe that, apart from a few specific exceptions, the Vilsmeier formylation is a convenient method for the synthesis of trienals.

Acknowledgement.

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