Lewis Acid Catalyzed Additions to Unsaturated Fatty Compounds* II: Alkylaluminium Halide Catalyzed Ene Reactions of Unsaturated Fatty Compounds and Formaldehyde**

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We are presenting our results on the alkylaluminium halide catalyzed ene addition of formaldehyde to readily available unsaturated fatty compounds to give primary homoallylic alcohols. The reaction of oleic acid and 10-undecenoic acid with formaldehyde gives (*E*)-9(10)-(hydroxymethyl)octadec-10(8)-enoic acid and 12-hydroxydodec-9-enoic acid, respectively, in high yields. Formaldehyde can be added also to oleyl alcohol to give the very interesting diol (*E*)-9(10)-(hydroxymethyl)oxtadec-10(8)-en-1-ol. Me_2AlCl and EtAl-sesquichloride are the most suitable catalysts for these reactions. The addition of formaldehyde to methyl oleate and methyl 10-undecenoate, respectively, to give the corresponding ene products is catalyzed by $EtAlCl_2$.

Lewis-Säure katalysierte Additionen an ungesättigte Fettstoffe II: Alkylaluminiumhalogenid katalysierte En-Reaktionen von ungesättigten Fettstoffen und Formaldehyd

Wir stellen unsere Ergebnisse der alkylaluminiumhalogenid katalysierten En-Addition von Formaldehyd an ungesättigte Fettstoffe vor. Die Produkte dieser Reaktionen sind primäre Homoallylalkohole. Die Umsetzung von Ölsäure und 10-Undecensäure mit Formaldehyd ergeben die (*E*)-9(10)-(Hydroxymethyl)octadec-10(8)-ensäure bzw. die 12-Hydroxydodec-9-ensäure in guten Ausbeuten. Durch Addition von Formaldehyd an Oleylalkohol kann das interessante Diol, (*E*)-9(10)-(Hydroxymethyl)octadec-10(8)-en-1-ol dargestellt werden. Me_2AlCl und EtAl-sesquichlorid sind die am besten geeigneten Katalysatoren für die genannten Reaktionen. Die Addition von Formaldehyd an Ölsäure- und 10-Undecensäuremethylester zu den entsprechenden En-Produkten erfolgt unter Katalyse von $EtAlCl_2$.

Introduction

The reaction of an alkene having an allylic hydrogen ("ene") with a compound containing a double or triple bond ("enophile") to form a new C,C-bond with migration of the ene double bond and 1,5-hydrogen shift is referred to as the ene reaction (Fig. 1)[1–3]. Ene reactions are carried out under thermal conditions or by use of Lewis acids such as $SnCl_4$, $AlCl_3$, $TiCl_4$ or alkylaluminium halides as catalysts[2].

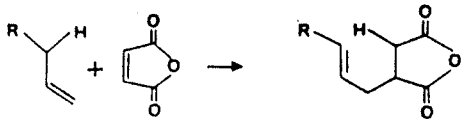

Fig. 1. Ene reaction of an alkene and maleic anhydride

The ene reaction of carbonyl compounds with alkenes is a potentially valuable route to homoallylic alcohols. Formaldehyde reacts thermally with alkenes at 180 °C. Optimal yields are often obtained when acetic acid – acetic anhydride is the solvent[4,5]. In Lewis acid catalyzed reactions good yields of ene-type-products are obtained with alkenes which can give a tertiary carbenium ion[6,7].

Snider et al.[8–11] found that dimethylaluminium chloride (Me_2AlCl) is a useful catalyst for ene reactions of aliphatic and aromatic aldehydes and leads to improved yields of ene adducts from formaldehyde. Me_2AlCl is a mild Lewis acid and a proton scavenger. Proton initiated rearrangements do not occur, since the alcohol-Lewis acid complex formed in the ene reaction reacts rapidly to give methane and non-acidic aluminium alkoxide (Fig. 2).

We have been interested in the application of the alkylaluminium halide catalyzed ene addition of formaldehyde to unsaturated fatty compounds, e.g. oleic acid, 10-undecenoic acid, the respective esters, oleyl alcohol and 10-undecenol.

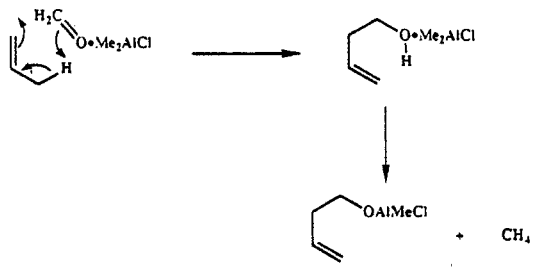

Fig. 2. Me_2AlCl-catalyzed ene reaction with formaldehyde as enophile

Results

The Me_2AlCl-catalyzed reaction of oleic acid and paraformaldehyde gives after a reaction time of 2 h the ene

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adduct in an isolated yield of 73%, a mixture of the (*E*)-9(10)-(hydroxymethyl)octadec-10(8)-enoic-acids (Fig. 3).

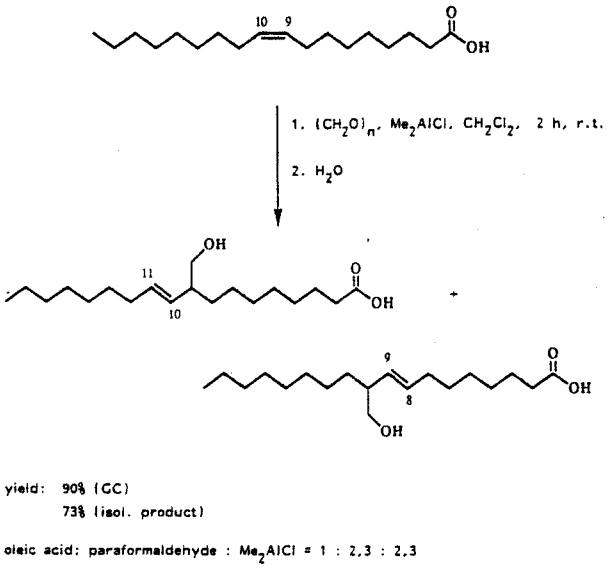

Fig. 3. Me_2AlCl-catalyzed ene reaction of oleic acid and formaldehyde

Because of steric hindrance in the ene reaction of *cis*-alkenes the regioisomers are formed with high selectivity as (*E*)-adducts[11]. A two fold excess of Me_2AlCl is necessary because of the acid-base reaction of Me_2AlCl and oleic acid to give methane and aluminium salt. To examine the regioselectivity the ene product was hydrogenated and reduced by $LiAlH_4$ via diol and ditosylate to give the respective saturated alkane. The EI-mass spectrum (Fig. 4) exhibits the characteristic signals of 9-methyloctadecane m/z = 140/141 and m/z = 154/155 at the branch point of the hydrocarbon chain. Thus, the addition of formaldehyde takes place exclusively to positions C-9 and C-10 of the oleic acid. The ethylaluminium sesquichloride ($Et_3Al_2Cl_3$)-catalyzed addition of paraformaldehyde to oleic acid gives approximately the same yield of ene products.

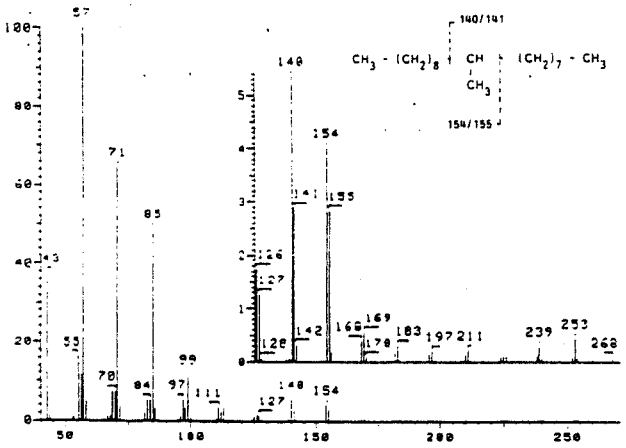

Fig. 4. Regioselectivity of the addition of formaldehyde to oleic acid. The addition product was hydrogenated and reduced to give the respective saturated alkane. The EI-mass spectrum is identical with the mass spectrum of 9-methyloctadecane

Another unsaturated fatty acid we used in our investigations was 10-undecenoic acid. The Me_2AlCl- or $Et_3Al_2Cl_3$-catalyzed addition of paraformaldehyde gives with high regioselectivity the ene adduct, 12-hydroxydodec-9-enoic acid. The ratio of [(*E*)]/[(Z)]-isomers is 4 : 1 (Fig. 5).

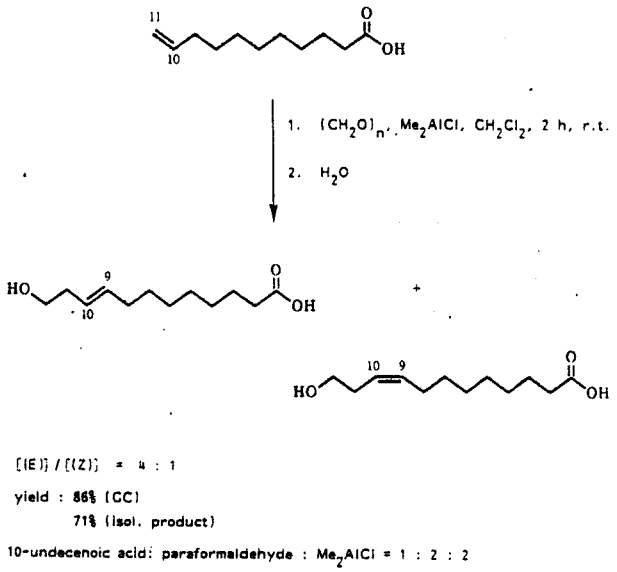

Fig. 5. Me_2AlCl-catalyzed ene reaction of 10-undecenoic acid and formaldehyde

Furthermore, formaldehyde can be added to unsaturated fatty alcohols as oleyl alcohol and 10-undecenol. *Snider* and *Phillips*[11] described the alkylaluminium halide catalyzed reaction of unsaturated alcohols and formaldehyde to give the corresponding unsaturated diols. The $EtAlCl_2$-catalyzed addition of formaldehyde to 5-hexen-1-ol gave nearly the double amount (59%) of ene adduct as the Me_2AlCl-catalyzed reaction (32%). In contrast, we found that the reaction of oleyl alcohol and formaldehyde catalyzed by $EtAlCl_2$ gives only some unidentified products but no ene adduct. However, the Me_2AlCl-catalyzed addition of formaldehyde to oleyl alcohol gives the expected unsaturated diol (Fig. 6). The mixture of the regioisomers, the 9(10)-(hydroxymethyl)octadec-10(8)-en-1-ol, is obtained with high stereoselectivity as (*E*)-adducts. The addition of formaldehyde to oleyl alcohol shows the same regioselectivity as the addition to oleic acid. The introduction of the hydroxymethylgroup occurs to position C-9 and C-10 of the mole-

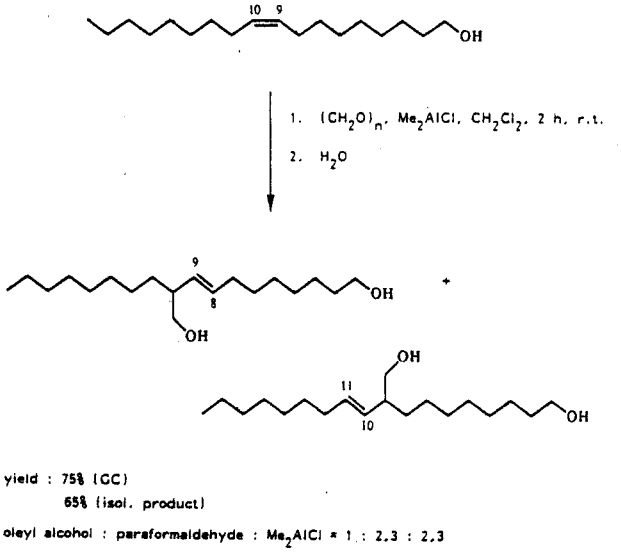

Fig. 6. Me_2AlCl-catalyzed ene reaction of oleyl alcohol and formaldehyde

cule chain. The $Et_3Al_2Cl_3$-catalyzed addition of formaldehyde to oleyl alcohol gives approximately the same yield of ene products.

While additions of formaldehyde to unsaturated acids and alcohols give good yields of ene adducts with Me_2AlCl or $Et_3Al_2Cl_3$ it is necessary to use $EtAlCl_2$, a stronger Lewis acid, for additions of formaldehyde to the respective esters. In $EtAlCl_2$-catalyzed reactions formaldehyde is added to methyl 10-undecenoate and to methyl oleate in yields of 52 % and 63 %, respectively. If Me_2AlCl is used as catalyst the yields of ene adducts are less than 10 %.

Conclusion

The alkylaluminium halide catalyzed ene addition of unsaturated fatty compounds and formaldehyde is a suitable reaction to synthesize fatty compounds with the functionality of primary homoallylic alcohols. With Me_2AlCl and $Et_3Al_2Cl_3$ as catalysts formaldehyde is added to unsaturated fatty acids and fatty alcohols in good yields. $EtAlCl_2$ has to be used in ene reactions of the respective esters and formaldehyde.

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