Lewis Acid Induced Additions to Unsaturated Fatty Compounds* III: Alkylaluminium Halide Induced Friedel-Crafts Acylations of Unsaturated Fatty Compounds**

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Alkylaluminium halide induced Friedel-Crafts acylations of unsaturated fatty compounds with acyl chlorides give the corresponding β,γ-unsaturated ketones. Acylation of oleic acid and 10-undecenoic acid with acetyl chloride yields (*E*)-9(10)-acetyloctadec-10(8)-enoic acid and 12-oxo-tridec-9-enoic acid, respectively. Acylation of 10-undecenoic acid with heptanoyl chloride followed by $NaBH_4$-reduction gives ricinelaidic acid. The very interesting β,γ-unsaturated ketodicarboxylic acid (*E*)-9(10)-(1-oxo-3-carboxy-propyl)octadec-10(8)-enoic acid is obtained by acylation of oleic acid with succinic anhydride.

Lewis-Säure induzierte Additionen an ungesättigte Fettstoffe III: Alkylaluminiumhalogenid induzierte Friedel-Crafts Acylierungen von ungesättigten Fettstoffen

Mittels Alkylaluminiumhalogenid induzierter Friedel-Crafts Acylierungen können aus ungesättigten Fettstoffen die entsprechenden β,γ-ungesättigten Ketone dargestellt werden. Die Ethylaluminiumdichlorid($EtAlCl_2$)-induzierte Acylierung von Ölsäure bzw. 10-Undecensäure mit Acetylchlorid ergibt (*E*)-9(10)-Acetyloctadec-10(8)-ensäure bzw. 12-Oxo-tridec-9-ensäure. Acylierung von 10-Undecensäure mit Heptanoylchlorid und anschließende Reduktion mit $NaBH_4$ gibt Ricinelaidinsäure. Ein sehr interessantes Produkt mit hoher Funktionalität wird durch Acylierung von Ölsäure mit Bernsteinsäureanhydrid erhalten, die β,γ-ungesättigte Ketodicarbonsäure (*E*)-9(10)-(1-Oxo-3-carboxy-propyl)octadec-10(8)-ensäure.

Introduction

Unsaturated fatty compounds can be functionalized by Lewis acid induced additions to the C,C-double bond. Alkylaluminium halide induced ene reactions of unsaturated fatty compounds and formaldehyde give primary homoallylic alcohols[1].

Another reaction to introduce functionality to an alkene is the Friedel-Crafts acylation[2, 3]. This reaction induced by Lewis acids such as $AlCl_3$, $SnCl_4$ or $ZnCl_2$ often leads to a mixture of products (Fig. 1)[4]. The main products are β,γ-unsaturated ketones, α,β-unsaturated ketones and β-chloro ketones.

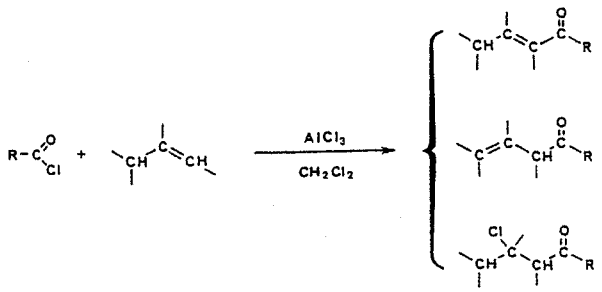

Fig. 1. Friedel-Crafts acylation of an alkene with an acyl chloride[4]

Snider and *Jackson*[5] found that $EtAlCl_2$-induced Friedel-Crafts acylations of alkenes with acetyl chloride give the corresponding β,γ-unsaturated ketones in good yields (53–73 %). The mechanism of the acylation is explained by *Snider* and *Jackson* as shown in Fig. 2. The intermediate cation (I) undergoes a 1,5-proton shift of the allylic hydrogen to a protonated β,γ-unsaturated ketone – Lewis acid complex (II) which immediately loses ethane to give the β,γ-unsaturated ketone (III). The minor formation of the β-chloro ketone (IV) takes place by an intermolecular chloride transfer. The acylations were carried out with cyclic and aliphatic alkenes. However, the reaction has not been applied to olefines with functional groups e. g. unsaturated alcohols or acids.

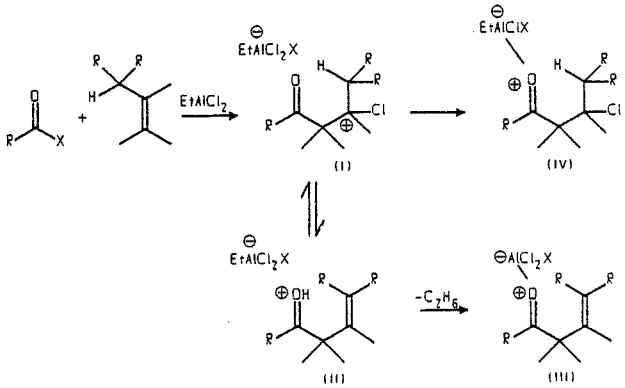

Fig. 2. Mechanism of the $EtAlCl_2$-induced Friedel-Crafts acylation of an alkene with an acyl chloride[5]

We have been interested in the Friedel-Crafts acylation of unsaturated fatty compounds e. g. oleic acid, 10-undecenoic acid, the respective esters and alcohols with acyl chlorides and cyclic anhydrides to give linear and branched long chain fatty compounds with a β,γ-unsaturated keto functionality.

Results

The reaction of oleic acid with acetyl chloride and $EtAlCl_2$ (1:1:2) in dichloromethane gave after a reaction time of two hours at room temperature a 1:1 mixture of regioisomers of the β,γ-unsaturated ketocarboxylic acids (*E*)-9-acetyl-octadec-10-enoic acid and (*E*)-10-acetyloctadec-8-enoic acid in an isolated yield of 55 % (Fig. 3). The reaction required a two fold excess of the Lewis acid because of the acid-base reaction of $EtAlCl_2$

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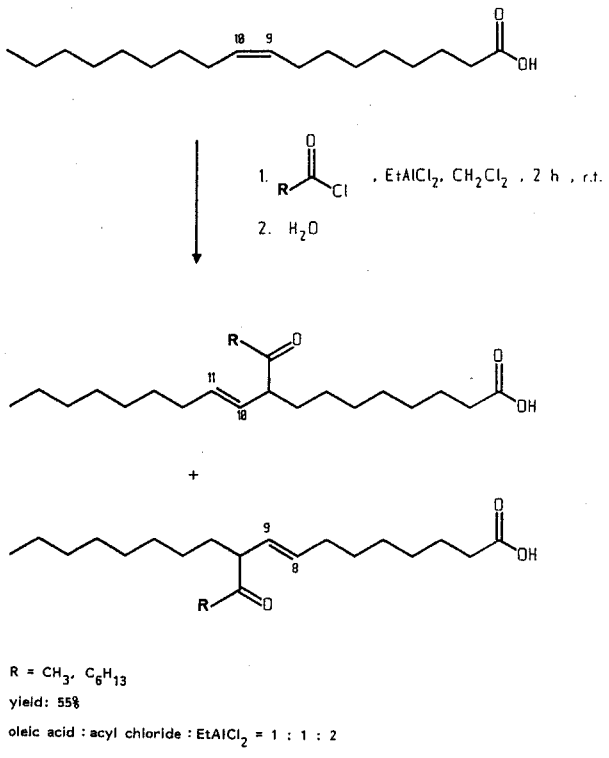

Fig. 3. $EtAlCl_2$-induced Friedel-Crafts acylation of oleic acid

and oleic acid to give ethane and aluminium carboxylate. To examine the regioselectivity of the reaction the acylation product was hydrogenated. The mass spectrum of the saturated ketocarboxylic acids exhibits the characteristic signals at the branch point of the hydrocarbon chain of the two regioisomers (Fig. 4). The acylation of oleic acid with acetyl chloride takes place exclusively to positions C-9 and C-10. The regioisomers were identified as pure (*E*)-adducts.

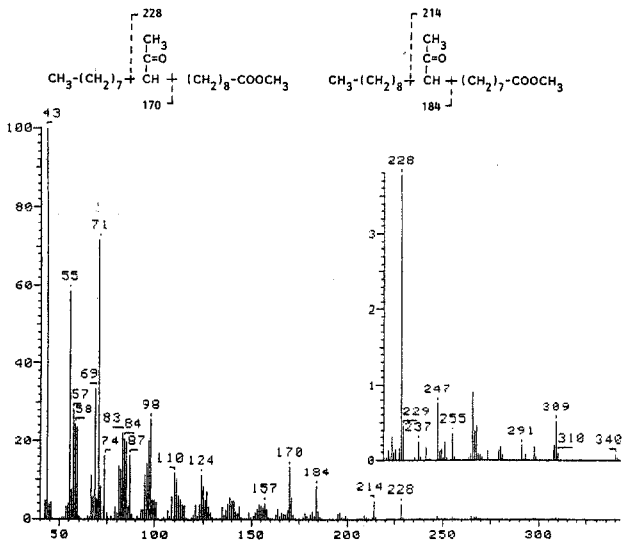

Fig. 4. Regioselectivity of the acetylation of oleic acid. EI-mass spectrum of the hydrogenated addition product methyl 9(10)-acetyloctadecanoate. The characteristic fragmentation pattern (Mc Lafferty rearrangement) is given in the formula scheme.

The respective acylation of 10-undecenoic acid with acetyl chloride yielded with high regioselectivity the β,γ-unsaturated ketocarboxylic acid 12-oxotridec-9-enoic acid (isolated yield: 50%, Fig. 5). The ratio of the (*E*)/(*Z*)-isomers was 3.2:1. The observed stereochemistry is in agreement with the results of *Snider* and *Jackson*[5] as well as the formation of β-chloro ketones as minor products (GC:6–11%).

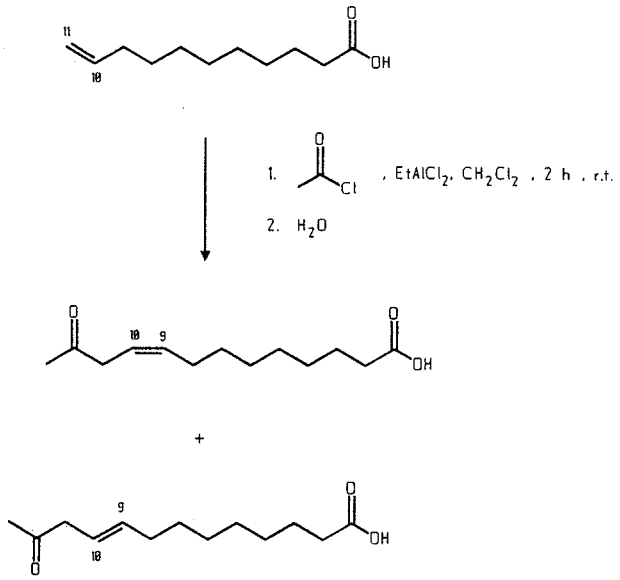

Fig. 5. $EtAlCl_2$-induced Friedel-Crafts acylation of 10-undecenoic acid with acetyl chloride

The acetylation of oleic acid and 10-undecenoic acid could be carried out also with ethylaluminiumsesquichloride ($Et_3Al_2Cl_3$), a milder Lewis acid. The yields of the corresponding β,γ-unsaturated ketones were lower compared to the $EtAlCl_2$-induced reactions (GC: 39% and 34%, respectively).

The acylation of methyl oleate with acetyl chloride could be carried out under the same reaction conditions as the acylation of the free acid. The product methyl (*E*)-9(10)-acetyloctadec-10(8)-enoate was purified by "Kugelrohr" distillation and isolated in a yield of 25%. Furthermore, we carried out the Friedel-Crafts acylation of 10-undecenoic acid with heptanoyl chloride to give regioselectively 12-oxo-octadec-9-enoic acid (GC: 72%) as a (*E*)/(*Z*)-mixture (Fig. 6). After crystallisation of the product from petrolether/ether = 4:1 the pure (*E*)-adduct was obtained (m.p. 55°–57°C, yield: 48%). Reduction of the carbonyl group of the unsaturated ketocarboxylic acid with $NaBH_4$ gave the racemate of (*E*)-12-hydroxy-9-octadecenoic acid (ricinelaidic acid), a natural substance. *Snider* and *Phillips*[6] described the synthesis of ricinelaidic acid by an $EtAlCl_2$-induced ene reaction of 10-undecenoic acid and heptanal. The ene reaction yielded 41% of a 4:1 mixture of ricinelaidic acid and ricinoleic acid.

(*E*)-9(10)-(1-oxo-heptyl)octadec-10(8)-enoic acid was obtained by addition of heptanoyl chloride to oleic acid

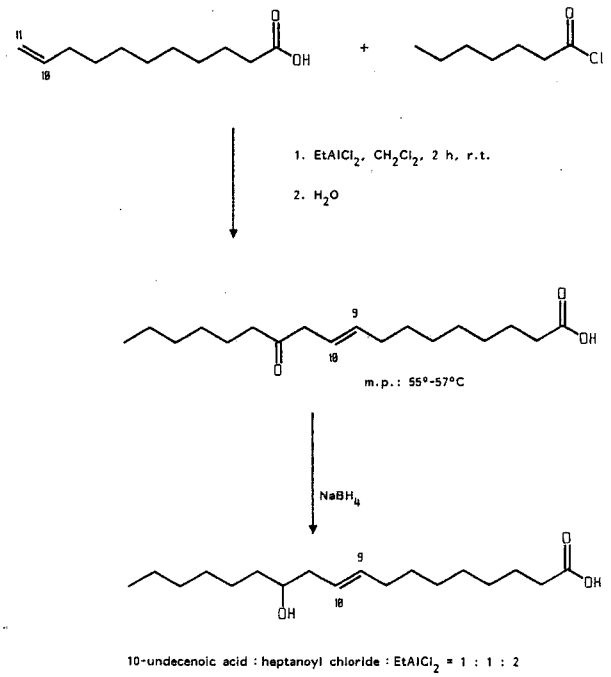

Fig. 6. Synthesis of *rac*-ricinelaidic acid

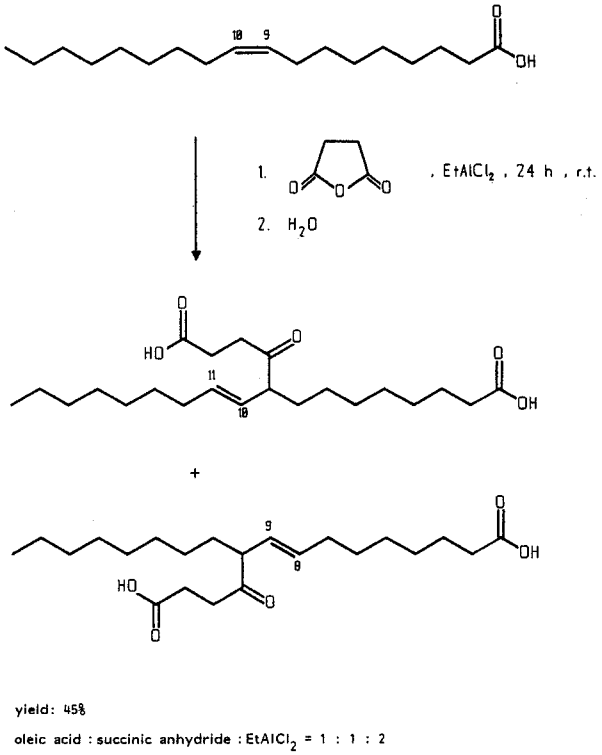

Fig. 7. $EtAlCl_2$-induced acylation of oleic acid with succinic anhydride

in an isolated yield of 45 %. The product was a 1:1 mixture of the two regioisomers.

Furthermore, the Friedel-Crafts acylation of unsaturated fatty acids can be carried out with cyclic anhydrides. *Snider* and *Jackson*[5] described the $EtAlCl_2$-induced acylation of 1-methyl-cyclohexene with succinic anhydride. The corresponding β,γ-unsaturated ketocarboxylic acid was obtained in a yield of 20 %. The acylation of unsaturated fatty acids with succinic anhydride should give very intersting products. Two functional groups, a carbonyl and a carboxyl group are introduced to the molecule chain of the fatty acid.

The reaction of oleic acid with succinic anhydride and $EtAlCl_2$ (1:1:2) gave after a reaction time of 24 h at room temperature the β,γ-unsaturated ketodicarboxylic acid (*E*)-9(10) - (1-oxo-3-carboxy-propyl)octadec-10(8) -enoic acid in a yield of 45 % (Fig. 7). Hydrogenation gave the saturated ketodicarboxylic acid which could be crystallized from petrolether/ether = 4:1 (m.p. 45–47 °C). The acylation of 10-undecenoic acid with succinic anhydride gave the β,γ-unsaturated ketocarboxylic acid 4-oxo-pentadec-6-endioic acid. After crystallisation from ether the pure (*E*)-adduct (m.p. 90–92 °C) was obtained in a yield of 50 %.

Another unsaturated fatty compound we used in our investigations was oleyl alcohol. The $EtAlCl_2$-induced acylation was carried out with acetyl chloride (Fig. 8). The product (*E*)-9(10)-acetyloctadec-10(8)-en-1-ol was obtained in a 60 % yield of a 1:1 mixture of the regioisomers. To prevent an acylation of the hydroxy function it is neccessary to add the acylation agent to a mixture of oleyl alcohol and the Lewis acid while the general procedure is carried out by adding the Lewis acid to a solution of the fatty compound and the acylating agent in dichloromethane.

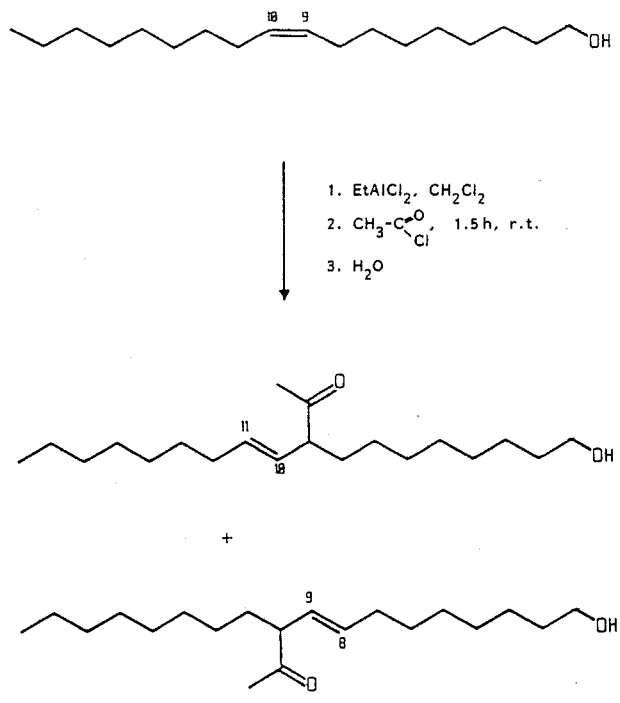

Fig. 8. $EtAlCl_2$-induced acylation of oleyl alcohol with acetyl chloride

Conclusion

The alkylaluminium halide induced Friedel-Crafts acylation of unsaturated fatty compounds and acyl chlorides give the corresponding β,γ-unsaturated ketones. Very interesting products are obtained by the acylation of unsaturated fatty acids and succinic anhydride. By this reaction a carbonyl and a carboxyl function can be introduced to the molecule chain of the fatty compound.

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Acknowledgments

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