Isomerizations

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Direct Conversion of Linoleic Acid over Silver Catalysts in the Presence of H_2: An Unusual Way towards Conjugated Linoleic Acids

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Dedicated to Professor Gerhard Zimmermann
on the occasion of his 75th birthday

In the search for anticarcinogenic substances towards the end of the 1980s, isomers of linoleic acid were discovered in beef and dairy products and proved to be potential mutagen

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inhibitors.[1,2] Owing to the conjugated double bonds present in these isomers, they were called CLAs (conjugated linoleic acids). Food that is modified by the addition of CLAs (so-called functional foods) offers specific benefits and advantages for human health.[3] Although functional food has been at the center of traditional Chinese medicine for over 2000 years, the amount of research has only increased since the physiological benefits CLAs were proved. Most of this research has been in the field of food chemistry and is particularly anchored in a framework program of the European Union.[4,5] These studies have shown that CLAs exhibit a variety of positive qualities. Besides their anticarcinogenic and antioxidative qualities, they also influence the fat and muscle content in the body and display antiarteriosclerotic qualities. The latest theories attribute these qualities to the 9-*cis*,11-*trans* and the 10-*trans*,12-*cis* isomer.[6–10] The influence of the other CLA isomers on these qualities are largely unknown.

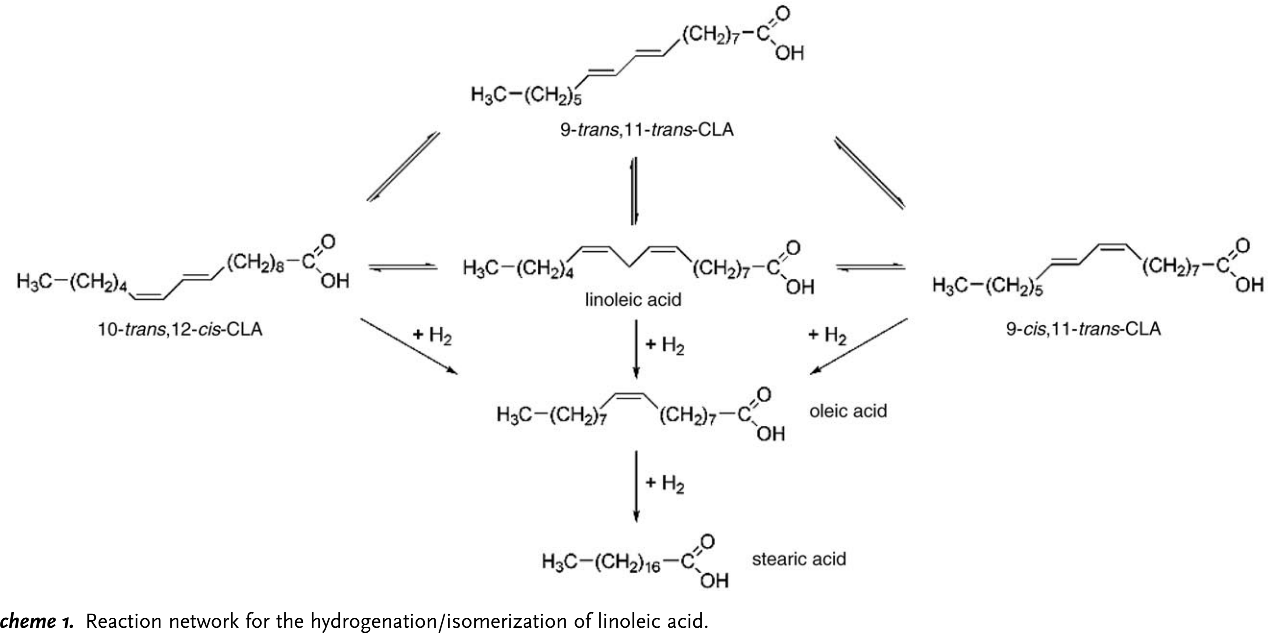
The established and industrial approach to the production of CLA is isomerization under alkaline conditions, which converts linoleic acids and their alkyl esters with alkali bases or potassium alkoxides into CLAs.[11] Subsequent neutralization with acid—typically phosphoric acid—is necessary. The alkali bases, solvents (e.g. DMSO and propylene glycol), and phosphoric acid are disadvantageous from an ecological and economic point of view. The enzyme-catalyzed production of CLA is known from biochemistry;[12] in nature, this process occurs in the rumen of cattle by means of *Butyrivibrio fibrisolvens*.[13,14] Homogeneous catalysts such as [{RhCl-(C_8H_{14})$_2$}$_2$] and [RhCl(PPh_3)$_3$] have also been applied in the isomerization of soybean oil.[15]

Very little work has been carried out on the production of CLA under heterogeneous catalysis, in which the problem of catalyst separation is avoided. This is due to the fact that the CLA have only received attention in the last few years as a result of investigations in the pharmaceutical field. On the other hand, direct CLA production is a very complex and difficult process. It is easy to find a catalyst that hydrogenates linoleic acid directly to stearic acid. In contrast, the search for a heterogeneous catalyst that favors selective isomerization to the physiologically important 9-*cis*,11-*trans* and 10-*trans*,12-*cis*-CLAs has proved to be much more challenging (Scheme 1).

In experiments described in the literature with heterogeneous ruthenium catalysts supported on Al_2O_3 and carbon, the catalyst was first covered with hydrogen, and linoleic acid was subsequently converted into CLA under nitrogen.[16] In order to produce CLA at all, this two-step reaction is necessary owing to the catalyst properties and the subsequent reactions competing with the desired isomerization. On the one hand, the excellent hydrogenation qualities of ruthenium catalysts results in the complete and rapid conversion of linoleic acid under hydrogen to give to stearic acid via oleic acid. On the other hand, it is clear that only a small quantity of hydrogen is required for the isomerization of linoleic acid into CLAs. It is therefore a fine line between the high activity of the catalyst, but under formation of unwanted hydrogenation products (oleic acid, stearic acid), and an increased selectivity towards CLAs controlled by the surface concentration of hydrogen over the catalyst.

Although we first achieved good results with ruthenium catalysts (Ru/C, Ru/Al_2O_3) in agreement with literature reports,[16] the two-step reaction (chemisorptive preadsorption of hydrogen onto the Ru catalyst followed by deactivation and chemical reaction in the semi-batch-mode under N_2) was a constant point of criticism in our considerations. The use of typical hydrogenation metal catalysts (e.g. Ni) promised no improvement, as was already discussed amply in the literature.[16c]

We describe herein a completely new and highly selective method for the synthesis of CLAs over heterogeneous silver catalysts and in the constant presence of hydrogen. According



Scheme 1. Reaction network for the hydrogenation/isomerization of linoleic acid.

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to the literature, silver is the metal with the lowest hydrogen-binding energy; experimental results and DFT calculations, although for Ag single crystals, showed weakly bound hydrogen on Ag.[17,18] Moreover, our work in the field of selective hydrogenation of polyunsaturated organic substances shows a much lower C=C hydrogenation activity over silver.[19] This reactivity is the exact prerequisite of the reaction network, which calls for a suppression of the parallel and/or consecutive hydrogenations to oleic acid and stearic acid. During isomerization experiments with silver catalysts carried out in the same way as those with ruthenium catalysts (i.e. under nitrogen after preactivation of the catalyst with hydrogen), we did not observe any conversions, as expected. As the success of the reaction depends on the surface coverage by hydrogen, as mentioned above, it seemed reasonable in the case of a metal such as silver to change the reaction procedure and to convert linoleic acid in the semi-batch-mode under hydrogen. At first, the catalyst was preactivated with hydrogen as in the case of the Ru catalysts.

We achieved surprisingly good results with respect to the direct synthesis of CLA (Table 1). Despite the simple reaction procedure under hydrogen, linoleic acid underwent 90% conversion on average after 90 min over Ag/SiO_2 using different grain fractions. The selectivity towards CLAs reached values between 60 and 67%. This shows at the same time that the particle size does not exhibit a noticeable influence on the catalytic properties. Therefore, there is no evidence of mass transport limitation in the examined area of ≤ 500 μm. The formation of the 9-*trans*,11-*trans* isomer was preferred at high conversions. The linoleic acid conversion increased with the reaction temperature, thus the physiologically important 9-*cis*,11-*trans*- and 10-*trans*,12-*cis* isomers were always the main components of the products. Furthermore, it was observed that the selectivity towards the hydrogenation products oleic acid and stearic acid decreased with decreasing substrate/catalyst mass ratio. Consequently, a desirable practical result is the increase in isomerization/hydrogenation ratio. From the selectivity–conversion data, CLA yields of up to 60% can be calculated, depending on the reaction conditions applied. Furthermore, the conversion of linoleic acid was carried out without previous contact of the Ag catalyst with hydrogen; this occurred primarily at the beginning of the reaction by switching from nitrogen to H_2. These experiments delivered the same degrees of conversion and selectivity as those with preactivation.

To understand the different effects of hydrogen on the Ru catalyst (hydrogenation to stearic and oleic acid) and the Ag catalyst (isomerization to 9-*cis*,11-*trans*- and 10-*trans*,12-*cis*-CLA), calorimetric experiments of H_2 adsorption were carried out with these catalysts. As seen in Figure 1a, at first an irreversible hydrogen adsorption occurs at the ruthenium catalyst. A reversible adsorption can be recognized only beyond the appearance of a saturation point (after the sixth pulse). The adsorption heat of the hydrogen determined from the calorimetric experiments has been estimated to about 90 kJ mol^{-1} from which a Ru−H bond strength of approximately 260 kJ mol^{-1} can be calculated.[20] On the silver catalyst (Figure 1B) only reversible hydrogen adsorption appears; an irreversible chemisorption could not be verified.[21] Therefore, we can distinguish between strongly adsorbed hydrogen on ruthenium and weakly adsorbed hydrogen in the case of the silver catalyst.[22] These findings suggest that the differences in the reactivity/selectivity patterns (hydrogenation activity on Ru versus isomerization activity on Ag) are based on differences in the hydrogen adsorption behavior of the active metal catalyst. It is clear that the weakly bound hydrogen plays a key role in the selective isomerization of conjugated double bonds (to CLA). A very similar situation is present in the case of the control of the intramolecular selectivity with respect to the hydrogenation of conjugated C=C−C=O double bonds.[19] With weakly chemisorbed hydrogen, a discrimination of the hydrogenation of the C=O- in contrast to the C=C-bond is possible; the latter is hardly hydrogenated by the weakly bonded hydrogen.[19,23] For the conversion of linoleic acid in the presence of H_2, an addition–elimination mechanism according to Horiuti–Polanyi[16g,20] is assumed, which is typical for the isomerization of C=C-double bonds in alkenes and alkadienes (Scheme 2). According to this mechanism, the selectivity of the reaction is decided by the type of reaction of the half-hydrogenated

Table 1: Catalytic properties of Ag/SiO_2 in the conversion of linoleic acid.[a]

Conditions	X_{LS} [%]	$S_{9\text{-}cis,11\text{-}trans}$ [%]	$S_{10\text{-}trans,12\text{-}cis}$ [%]	$S_{9\text{-}trans,11\text{-}trans}$ [%]	$S_{hydr.}$[e] [%]	S_{NP}[f] [%]	Σ_{CLA}[g] [%]	CLA/Hydr.
Variation of catalyst particle size:[b]								
< 63 μm	90	15	13	32	19	21	60	3.2
63–200 μm	91	20	14	33	17	16	67	3.9
200–500 μm	86	20	14	33	20	13	67	3.4
Variation of the temperature:[c]								
383 K	35	25	19	15	31	10	59	1.9
398 K	44	29	19	13	33	6	61	1.8
438 K	69	35	26	20	12	7	81	6.8
Variation of the substrate/catalyst mass ratio:[d]								
2	16	7	7	14	61	11	28	0.5
0.5	38	29	20	24	27	–	73	2.7
0.24	86	20	13	32	19	16	65	3.4

[a] $t = 90$ min; X_{LS}=conversion; S_i=selectivity. [b] $T = 438$ K, $m_{cat} = 0.8$ g. [c] $m_{cat} = 0.8$ g, $d_{cat} = 200$–500 μm. [d] $T = 438$ K, $d_{cat} = 200$–500 μm. [e] Selectivity towards hydrogenation products (oleic acid + stearic acid). [f] Unidentified products. [g] Sum of CLAs. Hydr.=hydrogenation.

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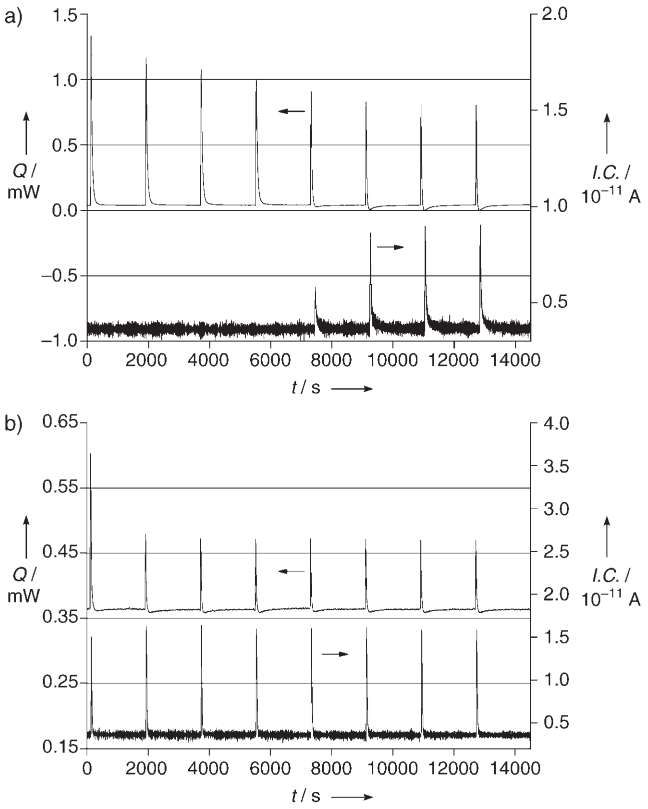
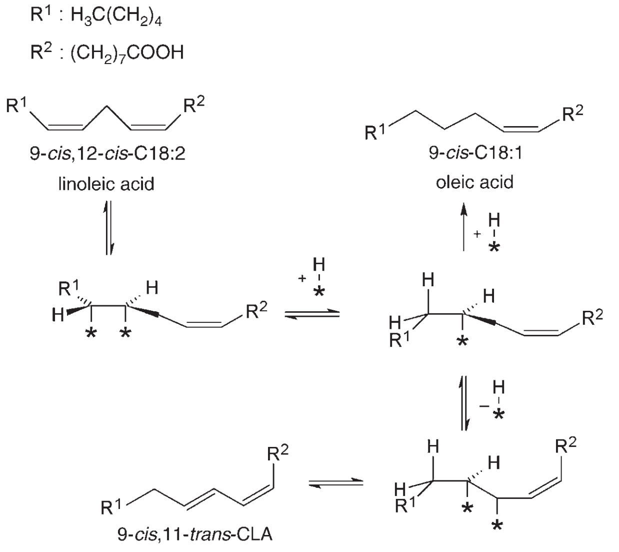


Figure 1. Results of calorimetric measurements of H_2 adsorption over Ru/C (a) and Ag/SiO_2 (b) catalysts in the presence of H_2 ($T_{ads} = 293$ K (a), 423 K (b)). The heat flow of the DSC (left ordinate) and the H_2 signal of the mass spectrometer (right ordinate) are shown. DSC = differential scanning calorimeter.



Scheme 2. Horiuti–Polanyi mechanism for the hydrogenation/isomerization of linoleic acid: weakly bonded hydrogen (on Ag) causes the desired CLA formation through an addition/elimination mechanism, whereas strongly bonded hydrogen (on Ru) causes the formation of oleic acid through consecutive H addition.

intermediate: addition of a further chemisorbed hydrogen atom under hydrogenation to give undesired oleic acid in the case of catalysts with high affinity to hydrogen chemisorption (Ru) versus elimination of a hydrogen atom with desired CLA formation in the case of weakly bonded hydrogen (Ag). Investigations are currently underway to examine the activation/adsorption of hydrogen on silver catalysts, which is rather unusual and is in contrast to the oxygen chemisorption known from oxidation catalysis, but comparable with gold catalysts.[24] Transient experiments with a Ag/SiO_2 catalyst preconditioned with H_2 in a TAP (temporal analysis of products) reactor and subsequent D_2 pulses revealed the formation of H–D and, thus, that H_2 dissociation must occur. This is not noticed over pure silver or SiO_2.[25]

The results presented herein show not only a direct route to CLAs but also a completely new method for the isomerization of (conjugated) double bonds. The prospects for the isomerization of linoleic acid to CLA in the presence of hydrogen and silver catalysts are obvious. After optimization of important catalyst properties (e.g. support material, silver particle size, and metal loading) the high CLA selectivity and yield as well as the simple reaction procedure in the presence of hydrogen permit the assignment to a continuous operation coupled with simple catalyst separation. Despite the high CLA selectivity, the product spectrum has to be further improved with respect to potential use in functional food. In particular, the fraction of 9-*trans*,11-*trans*-CLA must be decreased. Fundamentally, nothing should stand in the way of applying the presented principle of direct conversion of linoleic acid into CLAs over silver catalysts in the presence of H_2 as an alternative for the alkaline isomerization.

Experimental Section

General: The experiments were carried out in a 250-mL four-necked quartz-glass reactor, which was equipped with a reflux condenser, a drip funnel, a thermometer, a stirrer bar, and a gas-inlet tube. A magnetic stirrer with an oil bath was used as for heating and stirring. The Ag/SiO_2 catalyst was synthesized by incipient wetness impregnation from silver lactate (Fluka 85210) and SiO_2 (Alfa Aesar, "large pore") (Ag-content via ICP-OES: 7.7 wt %). The catalyst was dried at 353 K and reduced at 598 K under H_2 flow. A TEM examination (Philips CM 200 UT) resulted in an average Ag particle size of 14 nm. The Ru/C catalyst was a commercial product of Fluka (Ru content: 5 wt %). The calorimetric measurements of H_2 adsorption were carried out with a DSC 111 (Setaram) with mass spectrometer (Pfeiffer Vakuum) coupled to a pulse apparatus.

Example of an isomerization experiment: The catalyst ($m_{cat} =$ 800 mg, grain fraction $d_{cat} = 200$–500 µm) was introduced into the reactor, and the mixture of linoleic acid (Aldrich, purity > 99 %) and *n*-decane was placed in the dropping funnel ($V = 70$ mL, $c_{LA} =$ 0.01 molL^{-1}). Nitrogen (100 mLmin^{-1}) was flushed through the apparatus for 15 min to create an inert atmosphere and for degassing the linoleic acid/*n*-decane mixture. The catalyst was then activated under hydrogen flow (100 mLmin^{-1}) for 1.5 h (including heating time) at 438 K. The linoleic acid/*n*-decane mixture was then added to the catalyst; this represents the starting time of the reaction ($t = 0$). The reaction mixture was kept at a reaction temperature of 438 K under permanent stirring (1100 rpm). Hydrogen (100 mLmin^{-1}) was flushed through the mixture as reaction gas. Subsequent analysis was performed by means of temperature-programmed capillary gas chromatography (with FID) through an Agilent HP-5 column ($l =$ 25 m, $d_i = 0.20$ mm, $t_f = 0.11$ mm), carried out according to the literature.[16b] Heptadecanoic acid was used as an internal GC standard. The samples were concentrated in a heating block and silylated with bis(trimethylsilyl)trifluoroacetamide (BSTFA) (80 μL) and trimethylchlorosilane (TMCS) (40 μL). Details of the analysis as well as a chromatogram example can be found in the Supporting Information.

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