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Conjugation of linoleic acid over a hydrogen pre-activated heterogeneous catalyst†

Andreas Bernas,[a] Narendra Kumar,[a] Päivi Mäki-Arvela,[a] Ensio Laine,[b] Bjarne Holmbom,[c] Tapio Salmi[a] and Dmitry Yu. Murzin*[a]

[a] *Laboratory of Industrial Chemistry, Process Chemistry Group, Åbo Akademi University, FIN-20500 Åbo/Turku, Finland. E-mail: dmurzin@abo.fi; Fax: +358 2 215 4479; Tel: +358 2 215 4985*

[b] *Laboratory of Industrial Physics, Department of Physics, University of Turku, Åbo/Turku, Finland*

[c] *Laboratory of Wood Chemistry, Process Chemistry Group, Åbo Akademi University, Åbo/Turku, Finland*

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Development of a new heterogeneous catalytic pathway for isomerization of linoleic acid to conjugated linoleic acids at mild reaction conditions over Ni/H-MCM-41 in a soluted system.

Conjugated linoleic acids (CLA), first positively identified in 1987 as potential mutagen inhibitors,[1] are being marketed as a panacea that has the capability of reducing or eliminating cancer, preventing heart diseases, improving immune function and altering body composition in order to treat obesity or build lean body mass.[2] Conjugated linoleic acids is a collective term describing the positional and geometric conjugated dienoic isomers of linoleic acid. Linoleic acid ($C_{18:2}$), has double bonds located on carbons 9 and 12, both in the *cis* configuration, whereas CLA has either the *cis* or *trans* configuration or both located along the carbon chain. CLA is naturally present in meat and diary products, especially those from ruminant sources where it is synthesized from linoleic acid by rumen bacteria. The total content of CLA in food varies, but the *cis*-9, *trans*-11 isomer has been found to be the predominant form.[3] Studies have concluded that the *cis*-9, *trans*-11 isomer is responsible for the anticarcinogenic effects of CLA. It has also been concluded that the *trans*-10, *cis*-12 isomer produces the changes in body composition. Structures of linoleic acid, *cis*-9, *trans*-11-CLA, and *trans*-10, *cis*-12-CLA are presented in Fig. 1.

CLA can be prepared by homogeneous isomerization of linoleic acid under alkaline conditions. The homogeneous catalysts tris(triphenylphosphine) chlororhodium[4] and arene chromiumcarbonyl complexes[5] enable lower reaction temperatures than 180–200 °C, which are necessary for non-catalyzed systems, but these catalysts are difficult to separate and not environmentally friendly. The main disadvantage in alkali isomerization of linoleic acid is the use of excess of strong basic potassium hydroxide or sodium methoxide.[6]

Instead a heterogeneous catalyst could be used, which is easy to filter and re-use, but reactions with carboxylic acids over heterogeneous catalysts are difficult to perform. The double bond migration reactions over supported noble metal catalysts reported in the literature consider the isomerization of methyl linoleate[7] (the ester of linoleic acid) in solvents which are supposed to hydrogen transfer agents.

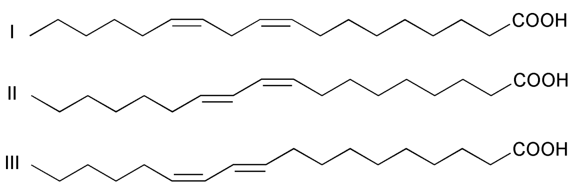

Fig. 1 Structures of linoleic acid and CLA isomers. I, *cis*-9, *cis*-12-octadecadienoic acid; II, *cis*-9, *trans*-11-octadecadienoic acid; III, *trans*-10, *cis*-12-octadecadienoic acid.

The use of linoleic acid as a raw material is an attractive alternative and in this study a novel pathway for isomerization of linoleic acid is developed. Preliminary isomerization experiments‡ at 120 °C under a nitrogen atmosphere in 1-octanol over a commercial catalyst (50 mg 5 wt% Ru/C), resulted in 89% selectivity for conjugation. However, the total converted amount of linoleic acid after 6 h was only 11%. Polymerization or cracking reactions of fatty acids were not detected at these reaction conditions.

Experiments under a hydrogen atmosphere over the same catalyst resulted in hydrogenated products. Isomerization of linoleic acid to CLA and hydrogenation of linoleic acid to mono-unsaturated acids (oleic acid, elaidic acid, *cis*-vaccenic acid and *trans*-vaccenic acid) were two competing reactions. It was also concluded that hydrogenation of linoleic acid proceeds consecutively *via* mono-unsaturated acids to stearic acid (n-octadecanoic acid).

The isomerization reaction in a nitrogen atmosphere was dramatically enhanced when the catalyst was pre-activated with hydrogen, otherwise using the same reaction conditions. In this case the reaction rate was slower, but the selectivity for conjugation was higher than the selectivity for hydrogenation and only a small trace of stearic acid was present. The conversion and the selectivity for conjugation at 6 h were 46% and 72%, respectively.

The isomerization and hydrogenation reactions are influenced by the concentration of chemisorbed hydrogen. If the hydrogen concentration in the solvent is high, the concentration of hydrogen chemisorbed sites on the catalyst surface will also have a high value. This increases the hydrogenation rate. If the concentration of chemisorbed hydrogen on the other hand is low, double bond migration is preferred over hydrogenation.

5 wt% Ni/H-MCM-41§ pre-activated at 180 °C in hydrogen was tested in comparison. The reaction was carried out at 120 °C in both 1-octanol and n-decane in order to evaluate the effects of a slightly protic and a non-polar solvent. For 1-octanol, the conversion and the selectivity for conjugation were only 17% and 13%, respectively. When n-decane was used as a solvent, the conversion and the selectivity for conjugation were 65% and 71%, respectively. The isomer distribution was 32% *trans*-9, *trans*-11-CLA, 11% *cis*-9, *trans*-11-CLA, 3% *trans*-10, *cis*-12-CLA, 2% *cis*-9, *cis*-11-CLA and the remaining 52% unknown conjugated dienoic isomers. The overall reaction rate was high in the beginning of the reaction but decreased with the conversion. The selectivity for conjugation was increasing with the conversion. After 1 h the concentrations of the fatty acids were reaching approximately constant values, influenced not only by the total amount of chemisorbed hydrogen generated in the catalyst pre-activation, but also reaction conditions, possible catalyst deactivation, availability of active vacant sites on the catalyst surface, and competitive adsorption between linoleic acid, solvent and reaction products. When all hydrogen pre-adsorbed on the catalyst surface is consumed, the consumption rate of linoleic acid is limited to hydrogen derived from the solvent. The concentrations of chemisorbed hydrogen and an adsorbed key intermediate on the catalyst surface have a

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† Electronic supplementary information (ESI) available: XRD measurements. See http://www.rsc.org/suppdata/cc/b2/b201722a/

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Table 1 Activity and selectivity data on Ni/H-MCM-41 for isomerization of linoleic acid

Solvent	Reaction temperature (°C)	Metal loading (wt-%)	Catalyst quantity (mg)	Particle size (μm)	Catalyst reduction	[a]Conversion (%)	[b]Conjugation (%)	[c]Hydrogenation (%)	[d]S_C	[e]S_H	[f]Initial overall reaction rate (10^{-7} mol s^{-1} g^{-1})
n-Decane	120	5	200	0–180	no	56	40	16	0.71	0.29	3.764
n-Decane	120	5	200	0–180	yes	51	37	15	0.71	0.29	3.167
n-Decane	120	5	200	45–63	yes	34	25	9	0.73	0.27	1.387
n-Decane	120	0	200	45–63	yes	22	16	6	0.71	0.29	0.881
n-Decane	120	15	200	45–63	yes	64	45	19	0.70	0.30	3.863
n-Decane	120	5	400	0–180	yes	73	43	30	0.59	0.41	3.625
n-Decane	100	5	200	0–180	yes	22	15	7	0.70	0.30	0.990
n-Decane	80	5	200	0–180	yes	11	7	4	0.64	0.36	0.597
1-Octanol	120	5	200	0–180	yes	17	2	15	0.13	0.87	1.387

[a] All percentages refer to mole percentages. [b] Includes all CLA isomers. [c] Includes both mono-unsaturated acids and stearic acids. [d] Selectivity for conjugation: S_C = conjugation/total conversion. [e] Selectivity for hydrogenation: S_H = hydrogenation/total conversion. [f] Based on total converted amount of linoleic acid after 60 min and catalyst mass. Conditions: Raw material: 200 mg linoleic acid, solvent quantity: 70 ml, stirring rate: 800 rpm, reaction time: 6 h.

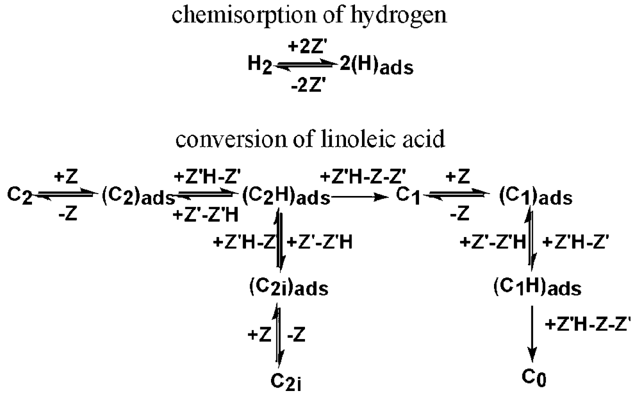

Fig. 2 Schematic representation of a possible reaction network. Z, Z′, Z′H, C_2, C_{2i}, C_1, C_0, C_2H and C_1H denote active vacant surface sites for chemisorption of organic molecule and hydrogen, hydrogen chemisorbed site, linoleic acid, CLA, monoenoic acids, stearic acid, half-hydrogenated intermediate species derived from di- and monoenoic acids respectively. $(C_i)_{ads}$ denotes chemisorbed organic molecule *i*, *etc.*

definite influence on catalytic activity and selectivities toward conjugation and hydrogenated products through a complex connection. A decrease of the hydrogen concentration favors isomerization but also reduces the conversion; a compromise has to be made.

Activity and selectivity data on Ni/H-MCM-41 are presented in Table 1. The total conversion is affected by reaction temperature, catalyst metal loading, catalyst quantity, catalyst particle size and nature of the solvent. No changes in the selectivities for specific CLA isomers were detected by varying these parameters. Selectivities for conjugation and hydrogenation on the other hand are affected only by catalyst quantity and nature of the solvent. Also selectivities for specific CLA isomers are affected by the nature of the solvent, n-decane showed for example higher selectivity for *trans*-9, *cis*-11-CLA than 1-octanol.

As illustrated in Fig. 2, after initial pre-activation of catalyst under hydrogen pressure, linoleic acid is chemisorbed on the surface of the metal or on the surface of the support material for the case with no metal loading. Thereafter a hydrogen atom derived from a hydrogen chemisorbed site is added to the chemisorbed acid to give a chemisorbed half-hydrogenated intermediate. If the hydrogen coverage on the catalyst surface is low (as at the end of the reaction when isomerization is preferred over hydrogenation), hydrogen abstraction by the metal takes place from an adjacent carbon atom. This could lead to a double bond migration depending on which carbon atom the hydrogen is abstracted from. Thereafter the chemisorbed product is desorbed from the surface of the catalyst metal or the support material. If the coverage of hydrogen on the other hand is high (as in the beginning of the reaction when hydrogenation is preferred over isomerization), a second hydrogen atom is added to the chemisorbed half-hydrogenated intermediate, leading to a hydrogenated product. It is assumed that hydrogenation and double bond migration is through the Horiuti-Polanyi mechanism.[8]

In summary, we have described a novel pathway for synthesis of CLA. This is the first report on the isomerization reaction of linoleic acid over a heterogeneous catalyst.

Notes and references

‡ *Catalytic experiment*: 200 mg of linoleic acid was mixed with 70 ml of a solvent (initial concentration: 0.010 mol dm^{-3}). The catalyst was charged into a jacket heated 200 ml stirred batch reactor operating at 1 atm, which was provided with a reflux condenser. The catalyst was pre-activated in flowing hydrogen at 180 °C. Thereafter the liquid phase containing linoleic acid and the solvent was fed into the reactor and the reaction time was initialized to zero. *Analytical procedure*: The samples were silylated and analyzed by a temperature programmed gas chromatography. The temperature program was 150 °C (0.5 min) 7 °C min^{-1} 230 °C, 230 °C 10 °C min^{-1} 290 °C (10 min). Peaks corresponding to CLA were identified by injecting authentic samples. Peak identities were verified by analysis with a gas chromatograph-mass spectrometer (GC-MS) applying same GC conditions.

§ *Catalyst synthesis and characterization methods*: Na-MCM-41 mesoporous molecular sieve was synthesized using a method described elsewhere[9] with some modifications. The sample was dried and calcined at 550 °C. The Na-MCM-41 was ion-exchanged with 1 M NH_4Cl solution. The H-MCM-41 was obtained by calcination of NH_4-MCM-41 at 550 °C. H-MCM-41 was modified with Ni by incipient wetness impregnation using an aqueous solution of nickel nitrate. The Ni/H-MCM-41 catalyst was calcined at 450 °C. Ni was reduced at 450 °C under flowing hydrogen. The catalytic material was characterized X-ray fluorescence (Siemens SRS 303), hydrogen TPD (Autochem 2910, Micrometrics), and BET (Sorptometer 1900, Carlo Erba Instruments) techniques. XRD (Philips PW 1800) measurements confirmed that the synthesized mesoporous material had MCM-41 structure.

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