Catalytic double bond isomerization / functionalization of fatty acids

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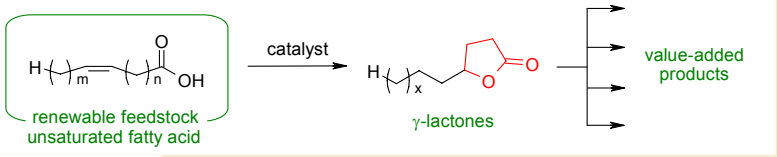
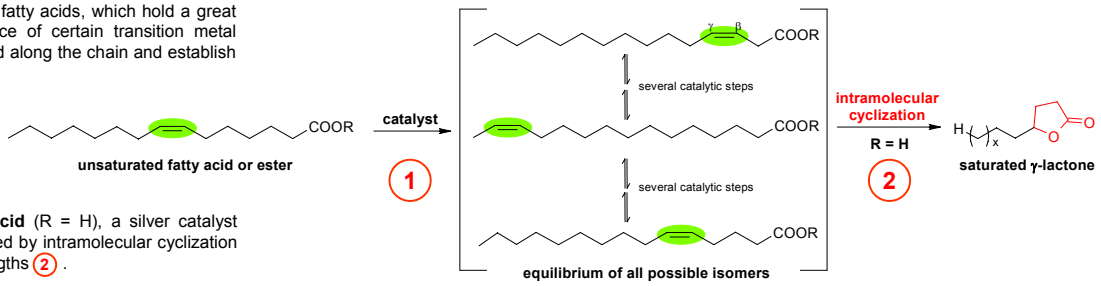


A new concept for the catalytic one-pot isomerization-functionalization of unsaturated fatty acids is presented. The catalyst establishes a rapidly interconverting equilibrium of double bond isomers, and at the same time facilitates the regioselective intramolecular conversion to long-chain lactones.

Double bond migration as the initiating step in functionalization reactions

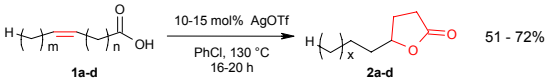
We approached the development of new transformations by exploiting the mobility of the double bond within unsaturated fatty acids, which hold a great potential for derivatization [1]. In the presence of certain transition metal catalysts, it is possible to move the double bond along the chain and establish a fast equilibrium of positional isomers (1).



If the unsaturated substrate is a **free fatty acid** (R = H), a silver catalyst mediates the double bond isomerization followed by intramolecular cyclization to furnish aliphatic lactones of various chain lengths (2).

Silver-catalyzed isomerization-lactonization

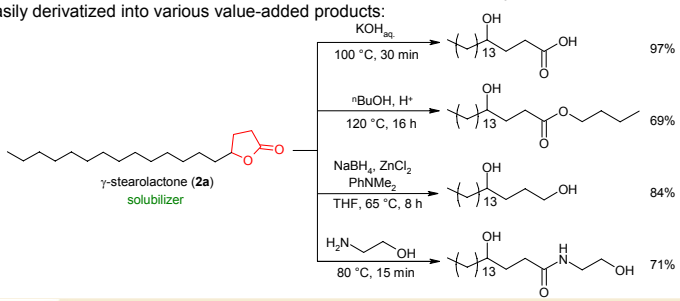
Direct lactonization protocols starting from fatty acids are rare and usually involve large quantities of corrosive and hazardous mediators like H_2SO_4 or $HClO_4$ [2]. Contrarily, our reaction methodology offers the catalytic use of a non-toxic, easy-to-handle silver salt [3].



Unsaturated fatty acids of variable length and double bond position are smoothly converted:

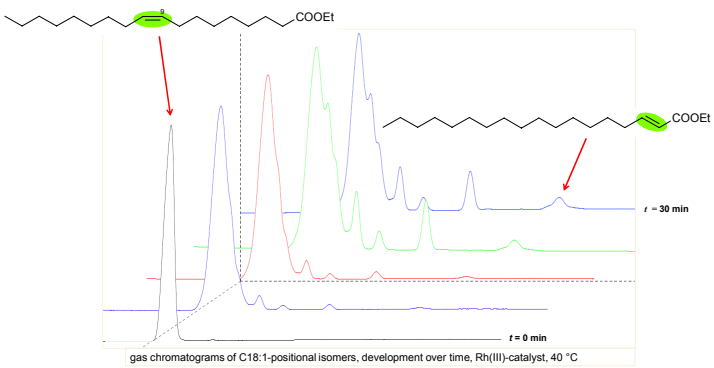
Entry	Fatty Acid		m	n	Mol% Cat. γ-Lactone		x	Yield (%)
1	**Oleic (18:1)**	**1a**	8	7	10	**2a**	12	51
2	**Undecylenic (11:1)**	**1b**	0	9	15	**2b**	5	72
3	**Palmitoleic (16:1)**	**1c**	6	7	15	**2c**	10	57
4	**(*5Z*)-Dodecenoic (12:1)**	**1d**	6	3	15	**2d**	6	66

The new protocol allows the preparative-scale synthesis of the C_{18}-lactone **2a**, which was easily derivatized into various value-added products:



Monitoring the isomerization equilibrium

We wanted to extend our concept to unsaturated fatty esters and therefore searched for suitable catalysts. Using a rhodium(III) system, **ethyl oleate** was quickly equilibrated into a mixture of isomers. So far, this was only possible at elevated temperatures with stoichiometric amounts of metal carbonyls [4]. We followed the development of the equilibrium by means of GC [5]:



gas chromatograms of C18:1-positional isomers, development over time, Rh(III)-catalyst, 40 °C

To further proof the capability of the catalyst, we could show by GC and NMR that **ethyl 2-octadecenoate** is equilibrated into the same distribution of isomers as ethyl oleate.

With this catalyst we are currently exploring new reactions with double bond shift as initiating step.

Literature and further reading (see also www.chemie.uni-kl.de/goossen)

[1] a) M. A. R. Meier, J. O. Metzger, U. S. Schubert, *Chem Soc. Rev.* **2007**, *36*, 1788. b) J. O. Metzger, *Eur. J. Lipid Sci. Technol.* **2009**, *111*, 865. c) Metzger, J. O. et al. *Angew. Chem. Int. Ed.* **2000**, *39*, 2206.
[2] a) J. S. Showell, D. Swern, W. R. Noble, *J. Org. Chem.* **1968**, *33*, 2697. b) A. Granata, F. Sauriol, A. S. Perlin, *Can. J. Chem.* **1994**, *72*, 1684. c) R. Stern, G. Hillion, *Patent FR 1987/2623499*.
[3] a) L. J. Gooßen, D. M. Ohlmann, M. Dierker, *Green Chem.* **2010**, *2*, 197. b) L. J. Gooßen, D. M. Ohlmann, T. Löhl, M. Dierker, *European Patent* (**2009**).
[4] a) R. Laï, E. Ucciani, M. Naudet, *Bull. Soc. Chim. Fr.* **1969**, *3*, 793. b) K.-C. Shih, R. J. Angelici, *J. Org. Chem.* **1996**, *61*, 7784.
[5] L. J. Gooßen, D. M. Ohlmann, *unpublished results*.

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