Benign by Design as an Important Building Block of Green and Sustainable Chemistry-The Example of Small Molecules

Prof. Dr. Klaus Kümmerer

LEUPHANA
UNIVERSITÄT LÜNEBURG

Bildquelle: UBA 2011







$S = k \bullet \ln W$

A smart person solves a problem.

A wise person avoids it.

Attributed to Albert Einstein

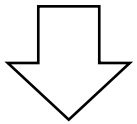
What Is the Problem ?

Persistence

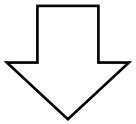
Non-toxic Environment:
Avoiding Persistance

Chemical

Fast and complete mineralization in the environment

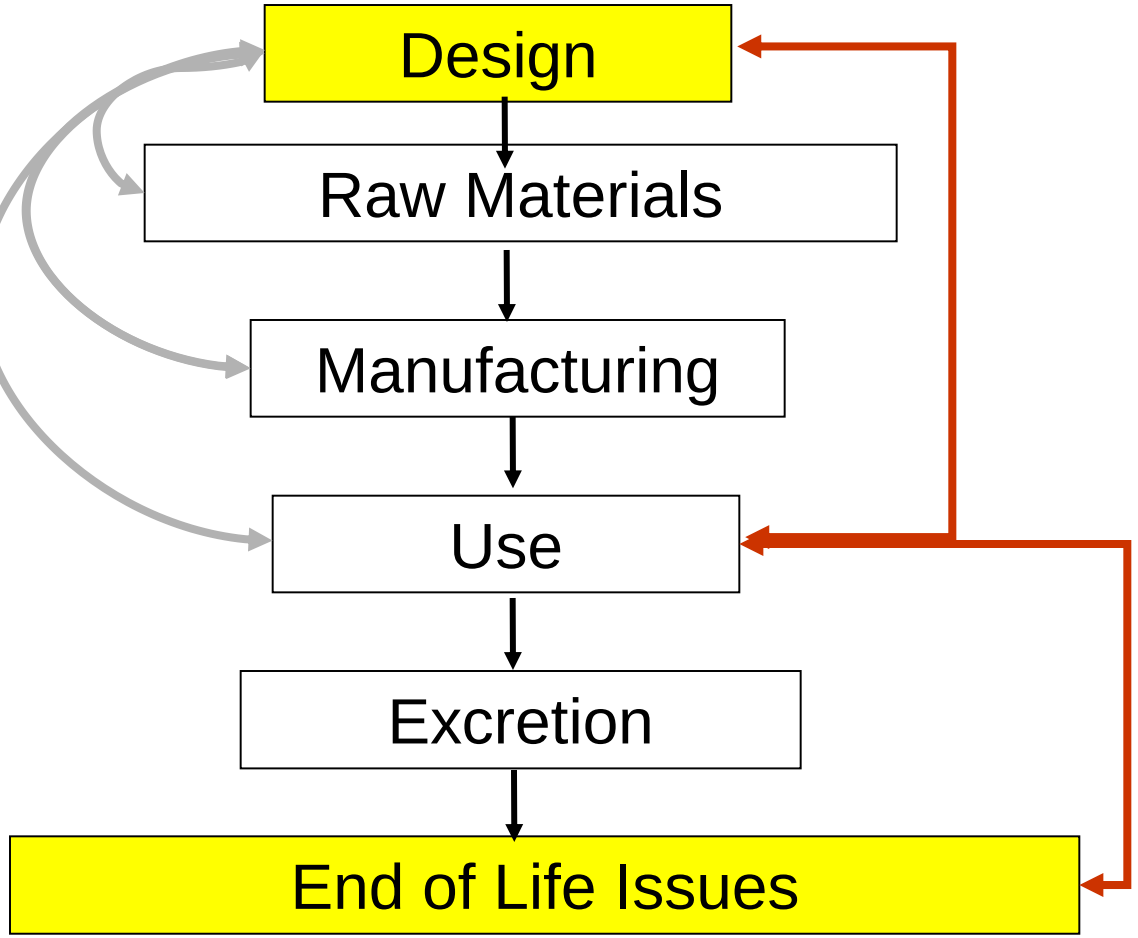


No Exposition



No Effect

Summary:
Life Cycle of Chemicals, Materials and Products

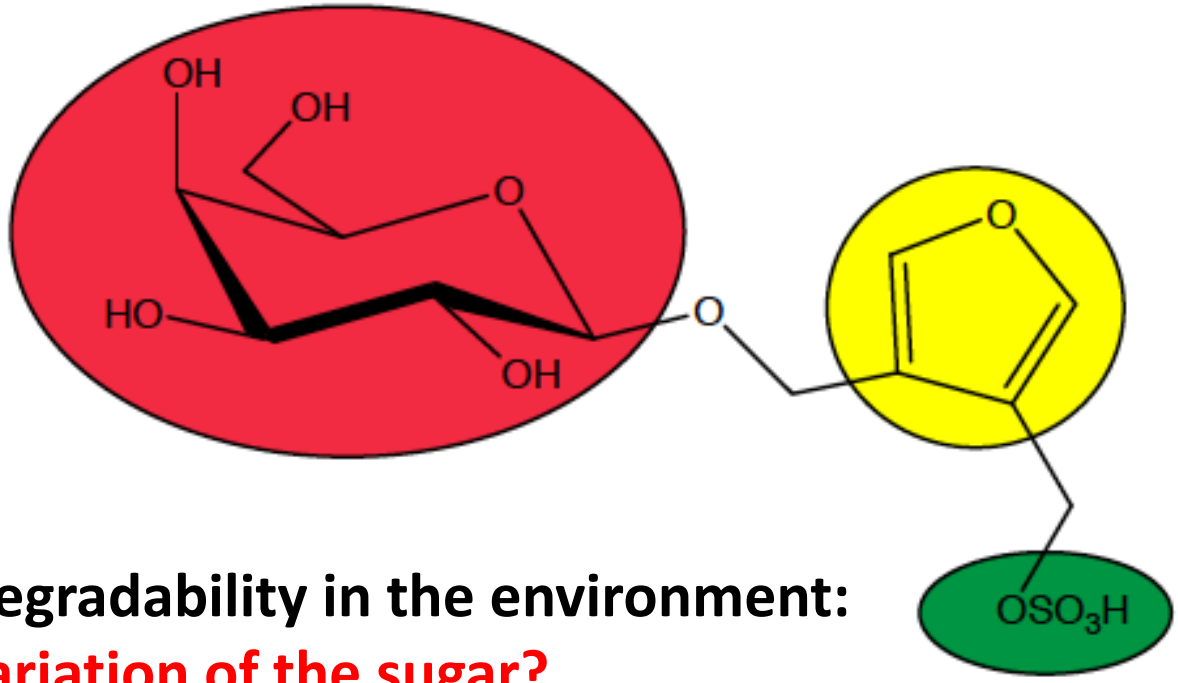


The end already always in mind!

Benign – by Design

📖 Kümmerer, K. (2007) Green Chemistry 9, 899-907, modified

De Novo-Design
Systematic Structure Variation of a New Leadstructure



Efficacy and biodegradability in the environment:

- **Improved by variation of the sugar?**
- **Improved by variation of substituents at the furan ring?**
- **Improved by variation of the aromatic ring?**

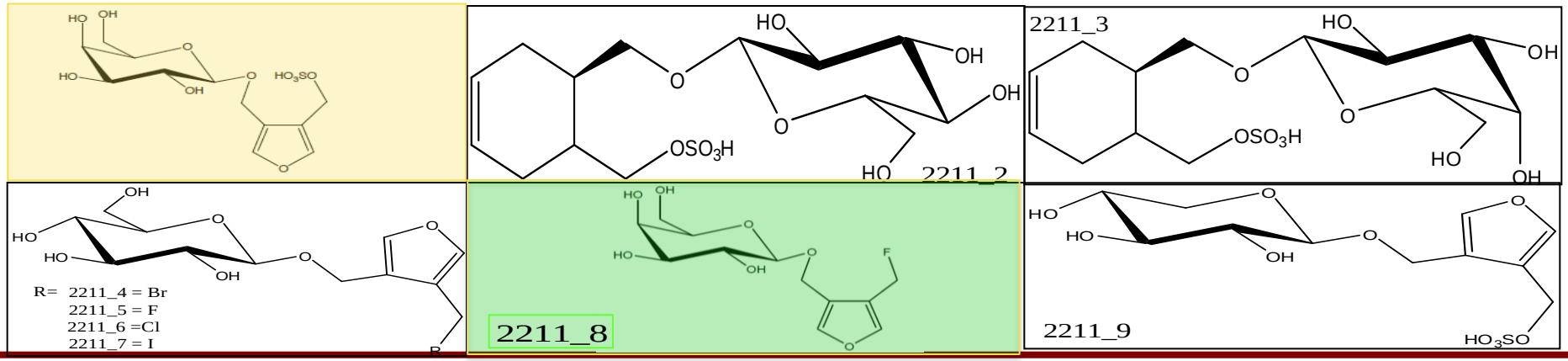
📖 Kümmerer K, Frei E, Marano G, in preparation

De-Novo Design-Systematic Structure Variation

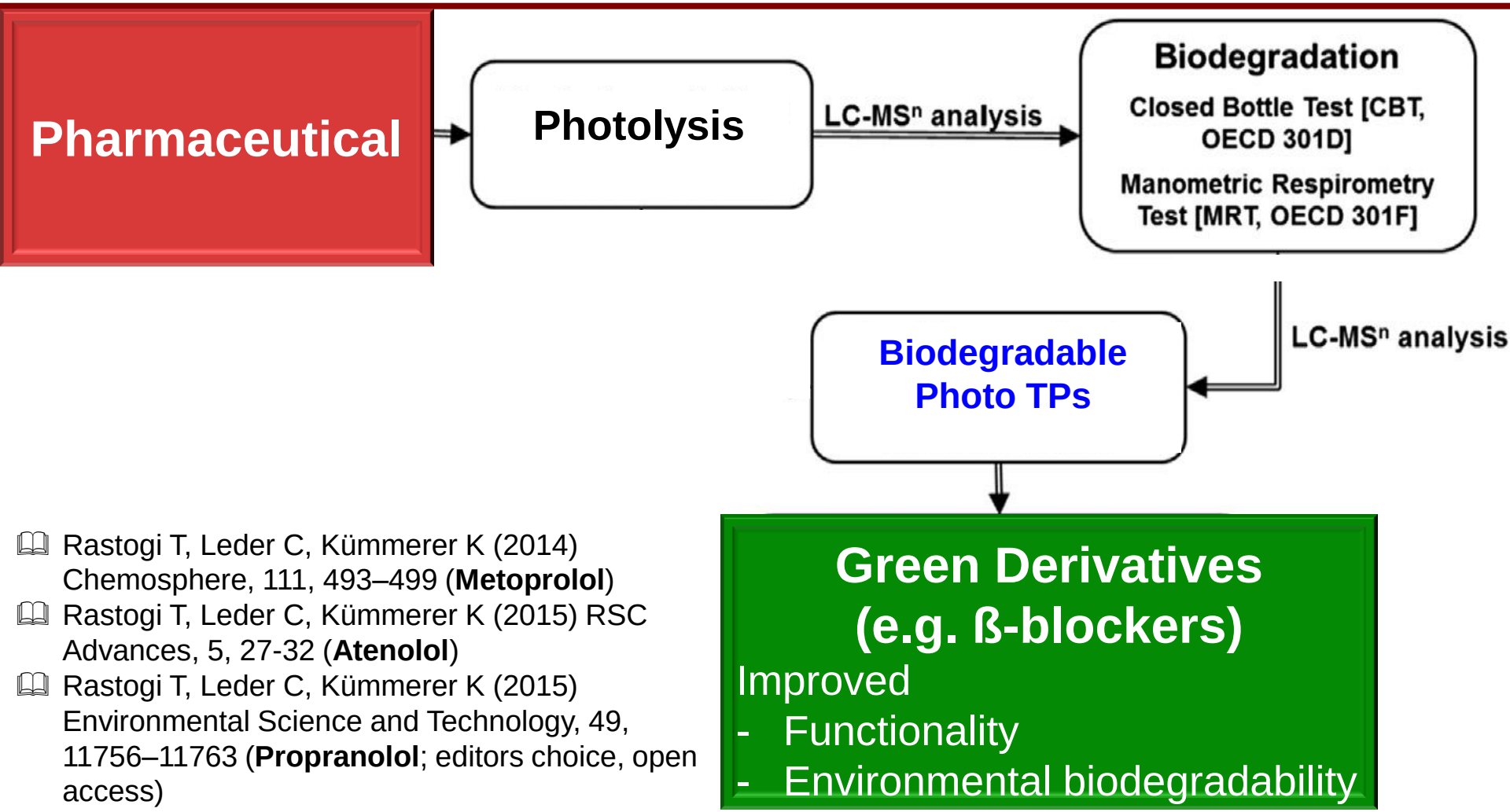
gefördert durch DBU Deutsche Bundesstiftung Umwelt www.dbu.de

📖 Marano G. et al. EP 2 474 552 A1

Structure ID	Log Kow	Effect threshold (rel. units)	Biodegradation [%] (CBT)
GSF (D-Gal)	-2.1	1	19
2211_2 (Glu ,Cyclohex)	-1.8	> 1	37
2211_3 (Gal, Cyclohex)	-1.8	> 1	37
2211_4 (Glu-Br)	-0.5	> 1	14
2211_5 (Glu-F)	-0.9	> 1	14
2211_6 (Glu-Cl)	-0.7	> 1	14
2211_7 (Glu-I)	-0.5	> 1	14
2211_8 (Gal-F)	-2.0	<0,01	37
2211_9 (Desoxyglu)	-1.5	> 1	31



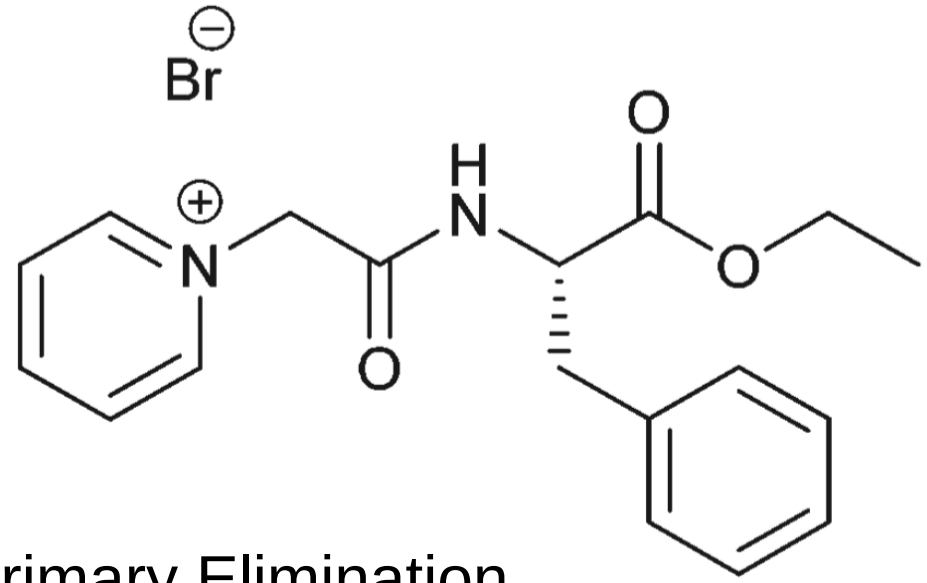
“Non-Targeted” Re-Design



- Rastogi T, Leder C, Kümmerer K (2014) Chemosphere, 111, 493–499 (**Metoprolol**)
- Rastogi T, Leder C, Kümmerer K (2015) RSC Advances, 5, 27-32 (**Atenolol**)
- Rastogi T, Leder C, Kümmerer K (2015) Environmental Science and Technology, 49, 11756–11763 (**Propranolol**; editors choice, open access)

Targeted Re-Design

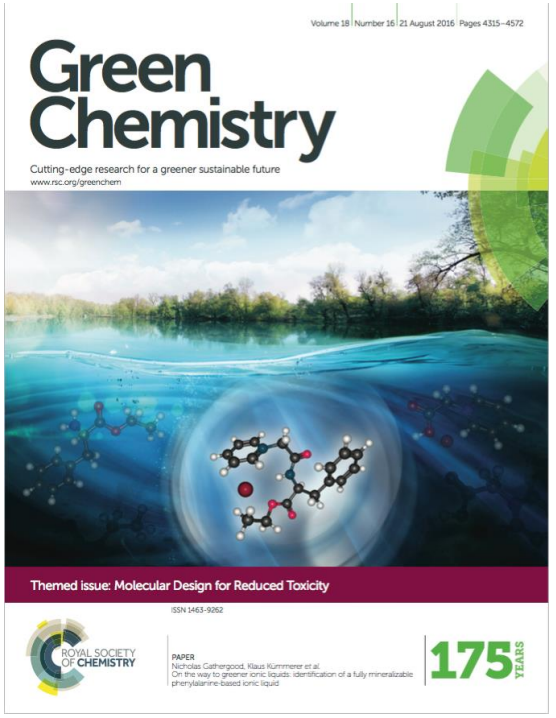
Biodegradabale Pyridinium Substituted Phenylalanine Derived Ionic Liquid



Primary Elimination

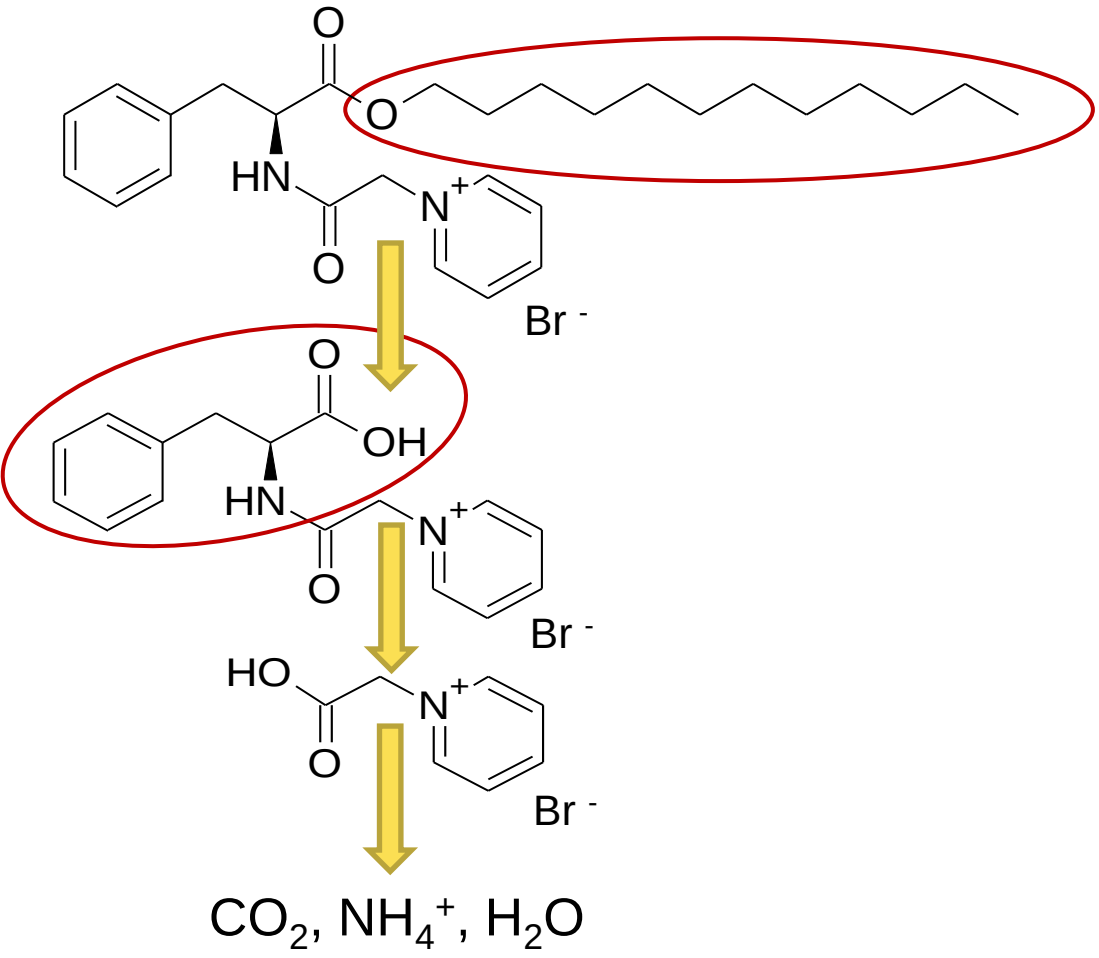
Closed Bottle test (OECD 301D):

- 73 % ± 0.7 % (28d)
- 100 % ± 0.0 % (40d)
- No transformation products (LC-MS)



📖 Haiß, ... Gathergood, Kümmerer et al. (2016) Green Chem 18, 4361-4373

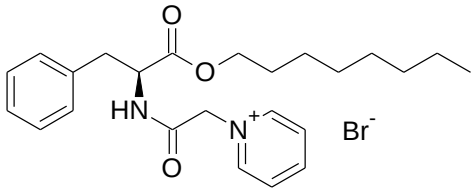
Breakdown Pathway



1. Loss of alkyl chain (ß-oxidation?)
2. Loss of phenylalanin
3. Loss of pyridinium acetic acid
4. Full mineralisation?

📖 **Haiß, ..., Gathergood, Kümmerer et al. 2016, Green Chemistry 18, 4315-4572; Haiß, ..., Gathergood, Kümmerer et al. , manuscript in preparation**

Structure Biodegradability Relationships (1)

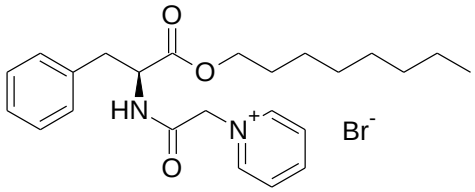


Phenylalanine-Pyridinium-Ils

Full mineralisation if ≤ C_8 (>28 days in CBT)

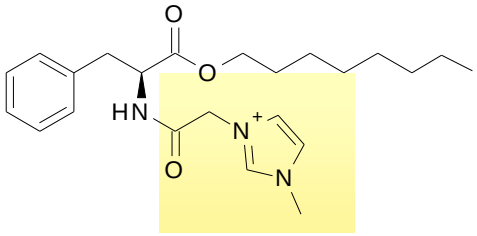
Haiß et al. 2016, Green Chemistry 18, 4315-4572
Haiß et al., publication in preparation

Structure Biodegradability Relationships (3)



Phenylalanine-Pyridinium-Ils

Full mineralisation if ≤ C_8 (>28 days in CBT)

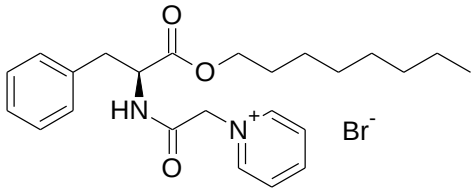


Phenylalanine-Imidazolium-ILs

Break-down ends with a propably persistent fragment
(1-carboxymethyl)-3-methyl-imidazol-3-ium)

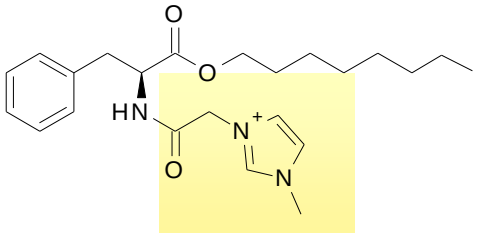
📖 **Haiß et al. 2016, Green Chemistry 18, 4315-4572**
📖 **Haiß et al., publication in preparation**

Structure Biodegradability Relationships (4)



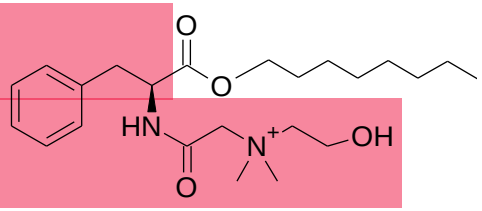
Phenylalanine-Pyridinium-Ils

Full mineralisation if ≤ C_8 (>28 days in CBT)



Phenylalanine-Imidazolium-ILs

Break-down ends with a propably persistent fragment
(1-carboxymethyl)-3-methyl-imidazol-3-ium)

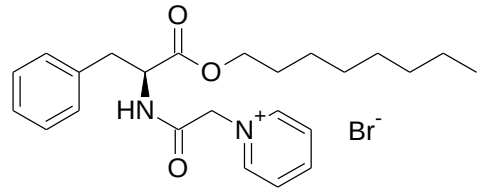


Phenylalanine-Cholinium-ILs

Break-down ends after alkyl chain cleavage with a persistant fragment

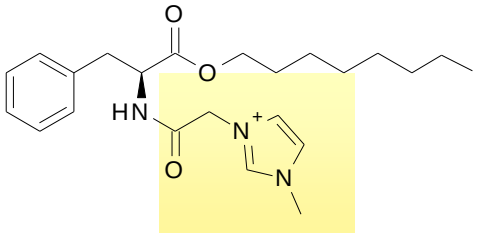
🕮 **Haiß et al. 2016, Green Chemistry 18, 4315-4572**
🕮 **Haiß et al., publication in preparation**

Recommendation



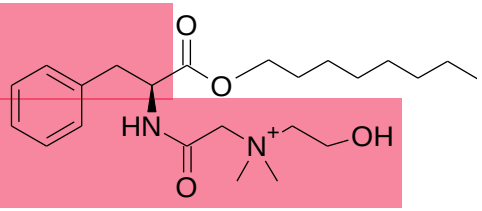
Phenylalanine-Pyridinium-Ils

Full mineralisation if ≤ C_8 (>28 days in CBT)



Phenylalanine-Imidazolium-ILs

Break-down ends with a propably persistent fragment
(1-carboxymethyl)-3-methyl-imidazol-3-ium)



Phenylalanine-Cholinium-ILs

Break-down ends after alkyl chain cleavage with a persistant fragment

Use Phenylalanine derived Pyridinium-ILs with an linear alkyl chain up to C_8

Haiß et al. 2016, Green Chemistry 18, 4315-4572
Haiß et al., publication in preparation

Conclusions

- Fully environmentally biodegradable chemicals and pharmaceuticals reduce micro pollutants **inherently**
- Environmentally benign design **is feasible**
- Structure biodegradability relationships allow for a **targeted selection of compounds**

LEUPHANA
UNIVERSITÄT LÜNEBURG

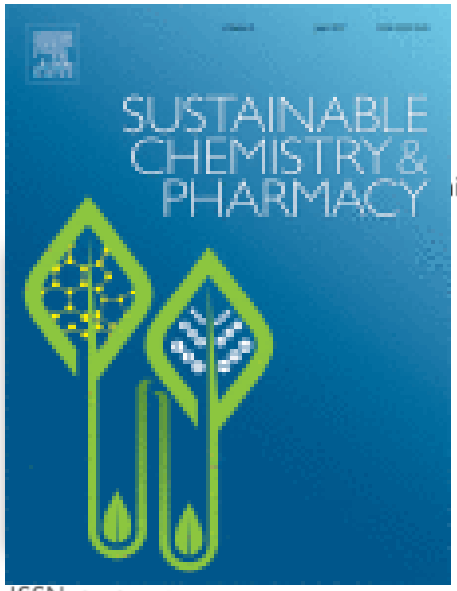
ISC3

S³C

3rd Summer School on Sustainable Chemistry for Sustainable Development

Sustainable Chemistry and Electronic Goods

24th September – 29th September 2017
at Leuphana University, Lüneburg



ISSN: 2352-5541

Submit Your Paper

View Articles

Guide for Authors

Abstracting/ Indexing

Sustainable Chemistry and Pharmacy

> Supports Open Access

Editor-in-Chief: Klaus Kümmerer

> View Editorial Board

Sustainable Chemistry and Pharmacy is an interdisciplinary and transdisciplinary journal. It publishes research that is related to chemistry and pharmacy on the one hand and sustainability on the other one in a forward oriented manner.

As such it will publish in the following areas given that a clear...

Read more

Most Downloaded | Recent Articles | Most Cited | Open Access Articles

Experimental and chemometric strategies for the development of Green

Abstracting and Indexing

Chemical Abstracts

Scopus

ISI Emerging Sources Citation Index (ESCI)

Cite Score: > 60% of journals of respective areas