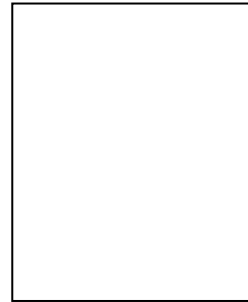


## Integration of fermentation and crystallisation to produce carboxylic acids

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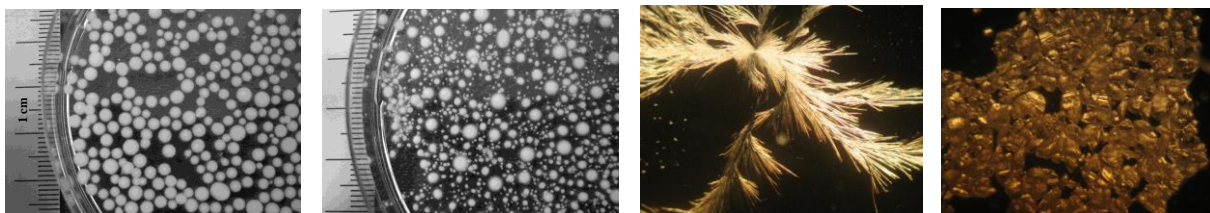


### Description

In this study, product recovery applying crystallisation techniques was studied for two organic acids: 7-aminodeacetoxycephalosporanic acid (7-ADCA) and in particular fumaric acid.

The production of fumaric acid was done using *Rhizopus oryzae*. Delay of pH control during the fermentation until a low pH has been reached at the end of the batch cycle did not affect fermentation productivities and allows the fermentation unit to be integrated with product crystallisation without pH shifting. Solubility studies of fumaric acids and its sodium salts showed that the integration should be performed in a pH range of 2.5 – 3.5 in order to get only fumaric acid crystals and avoid the crystallisation of one of the sodium fumarate salts. Integration of fumaric acid production by fermentation and cooling crystallisation was proven to work in an experimental set-up. Consumption of neutralising agent is reduced as compared to the base case system, which uses sulphuric acid to precipitate the fumaric acid out of the fermentation broth thus reducing the associated production of waste salts.

As a side line, integration of fermentative production and enzymatic deacylation of adipyl-7-aminodeacetoxycephalosporanic acid in one reactor was proposed, to produce 7-ADCA crystals directly from glucose.



*Pellets of R. oryzae and crystals of fumaric acid*

### Dissertation

C.A. Roa Engel, Integration of fermentation and crystallisation to produce carboxylic acids, PhD thesis, Delft University of Technology, 2010 <http://resolver.tudelft.nl/uuid:0518e010-08f9-40c0-a731-e7edfe379c2d>

### Publications from the dissertation

1. C.A. Roa Engel, A.J.J. Straathof, T.W. Zijlmans, W.M. van Gulik and L.A.M. van der Wielen, Fumaric acid production by fermentation, [Appl. Microbiol. Biotechnol. 78 \(2008\) 379-389](#).

2. C.A. Roa Engel, A.J.J. Straathof, W.M. van Gulik, E.J.A.X. van de Sandt, T. van der Does, and L.A.M. van der Wielen, Conceptual process design of integrated fermentation, deacylation and crystallisation in the production of  $\beta$ -lactam antibiotics, [Ind. Eng. Chem. Res. 48 \(2009\) 4352-4364.](#)
  3. C.A. Roa Engel, W.M. van Gulik, L. Marang, L.A.M. van der Wielen and A.J.J. Straathof, Development of a low pH fermentation strategy for fumaric acid production by *Rhizopus oryzae*, [Enzyme Microb. Technol. 48 \(2011\) 39-47.](#)
  4. C.A. Roa Engel, J. ter Horst, M. Pieterse, L.A.M. van der Wielen and A.J.J. Straathof, Controlling crystallisation in fermentation processes: The solubility of fumaric acid and its monosodium salt, [Ind. Eng. Chem. Res. 52 \(2013\) 9454-9460.](#)
  5. C.A. Roa Engel, M. Pieterse, L.A.M. van der Wielen and A.J.J. Straathof, Integration of fermentation and crystallisation in the production of fumaric acid, submitted for publication.
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