Doctoral Thesis

Hydrogenation of aliphatic nitriles over nickel catalysts modified by formaldehyde

Author(s):
Novi, Roc

Publication Date:
2004

Permanent Link:
https://doi.org/10.3929/ethz-a-004877494

Rights / License:
In Copyright - Non-Commercial Use Permitted
Hydrogenation of Aliphatic Nitriles over Nickel Catalysts Modified by Formaldehyde

A dissertation submitted to the
SWISS FEDERAL INSTITUTE OF TECHNOLOGY ZURICH
for the degree of

Doctor of natural sciences

presented by

ROC NOVI

Dipl. Chem. ETH
born on 15. October 1977
citizen of Vignogn GR

accepted on the recommendation of
Prof. Dr. P. Rys, examiner
Prof. Dr. M. Morbidelli, co-examiner

Zürich 2004
I wish to express my sincere gratitude to...

...Prof. Dr. P. Rys, who gave me the chance to work on this project. I am very grateful to him for many discussions and his continuous support.

...Prof. Dr. M. Morbidelli for accepting co-examination of this doctoral thesis.

...Dr. F. Rössler for the possibility to perform the experiments in Kaiseraugst, the scientific support and the discussions. His confidence in my work was very supporting and encouraging.

...Dr. A. Rössler and B. Sägesser for the numerous discussions, tips and advices.

...my colleagues of the Rys group, especially Dr. F. Antognoli, Dr. E. Dedeoglu, Dr. A. J. Klaus, Dr. M. Mösche, Dr. A. Rössler, D. Schoch and Dr. P. Skrabal.

...the members of the hydrogenation team in Kaiseraugst, H. Bruder, B. Close, A. Dodane, H. Lehmann, T. Müller, A. Saaler, B. Sägesser, R. Santillo, P. Schmidt, G. Weisser and C. Zürcher for the good team work.

...the members of the analytical groups in Kaiseraugst and Zürich H. Kleissner, Dr. G. Schiefer and Dr. P. Skrabal for the coaching and measurements they performed.

...M. Bäbler, L. Brändli, M. Bucher, S. Diezi, M. Günther, J. Fischesser, P. Müller and S. Sasso for the discussions and practical advice.
...my friends, D. Günther, I. Netzer, M. A. Plaz and J. W. Solèr for their friendship and moral support apart from the work.

...my parents, my grandparents as well as my brother and sister for their support during all these years of education.

...the company F. Hoffmann-La Roche for the financial support of this project as well as the possibility to perform the experiments in its laboratory in Kaiseraugst.
# Table of contents

1 Abstract ........................................................................................................... 1

2 Zusammenfassung ............................................................................................. 3

3 Introduction .................................................................................................... 5
  3.1 Overview ..................................................................................................... 5
  3.2 Aim and scope of this thesis ....................................................................... 7
  3.3 List of abbreviations and symbols ................................................................ 8
  3.4 List of substances ...................................................................................... 9

4 Theoretical section ........................................................................................ 13
  4.1 Hydrogenation of nitriles ......................................................................... 13
    4.1.1 General aspects .................................................................................. 13
    4.1.2 Hydrogenation of nitriles to amines ............................................... 13
    4.1.3 Hydrogenation of nitriles to aldehydes .......................................... 15
    4.1.4 Hydrogenation of nitriles to hydrocarbons ................................... 16
    4.1.5 Hydrogenation and cyclisation ....................................................... 16
  4.2 Mechanistic considerations of nitrile hydrogenation ............................... 17
    4.2.1 Historic development ...................................................................... 17
    4.2.2 Models for the formation of side products ..................................... 23
    4.2.3 Influence of reaction parameters on nitrile hydrogenation .......... 25
  4.3 Reversible reactions of amines .................................................................. 27
  4.4 Raney nickel ............................................................................................. 30
    4.4.1 Preparation methods ......................................................................... 30
    4.4.2 Industrial applications ...................................................................... 31
    4.4.3 Variation of the properties of Raney nickel ..................................... 32
    4.4.4 Adsorption of nitriles and their hydrogenation intermediates ....... 33
    4.4.5 Inhibition/poisoning of the catalyst ............................................... 35
    4.4.6 Acid sites ......................................................................................... 36

5 Hydrogenation of butyronitrile ................................................................... 39
  5.1 Reaction system ......................................................................................... 39
5.2 Thermodynamic aspects ................................................................. 45
5.3 Aspects of mass and heat transport ............................................... 45
5.4 Influence of reaction parameters on nitrile hydrogenation .............. 47
  5.4.1 Influence of the overall pressure ............................................. 48
  5.4.2 Influence of the temperature ................................................. 50
  5.4.3 Influence of the ratio of catalyst to substrate ......................... 54
  5.4.4 Recycling of the catalyst ..................................................... 57
  5.4.5 Influence of additives ......................................................... 59
5.5 Influence of washing/modification procedures ............................... 60
  5.5.1 Influence of washing procedures with different solvents .......... 60
  5.5.2 Influence of the modification by formaldehyde ....................... 63
5.6 Reversibility of the hydrogenation steps ...................................... 68
  5.6.1 Disproportionation of butylamine ......................................... 68
  5.6.2 Influence of reaction parameters on the disproportionation of butylamine ......................................................... 70
  5.6.3 Dibutylimine as starting material ......................................... 72
5.7 Discussion .................................................................................... 73
  5.7.1 The bifunctional catalytic hydrogenation and its reversibility .......... 73
  5.7.2 Influence of various reaction parameters on the selectivity ....... 74

6 Modification of nickel catalysts by formaldehyde .............................. 77
6.1 General remarks ........................................................................... 77
6.2 Influence of the treatment with different solvents on the properties of the catalyst ......................................................... 79
  6.2.1 Reduction potential ............................................................. 79
  6.2.2 Adsorption of an indicator .................................................... 80
6.3 Modification of Raney nickel by various formaldehyde concentrations .................................................................................. 81
  6.3.1 Analysis of the modifying solution ....................................... 81
  6.3.2 Properties of the modified catalysts ..................................... 84
6.4 Modification of various amounts of Raney nickel at constant modification strength ................................................................. 85
  6.4.1 Analysis of the modifying solution ....................................... 85
  6.4.2 Properties of the modified catalysts ..................................... 87
6.5 Modification of nickel-on-carrier ................................................. 89
6.6 Discussion .................................................................................. 89

7 Effect of formaldehyde modified nickel catalysts on other chemical systems ... 91
7.1 Hydrogenation of crotonaldehyde .................................................. 91
  7.1.1 General remarks .................................................................. 91
  7.1.2 Test for a possible gas-liquid transfer limitation for hydrogen ........................................... 93
  7.1.3 Influence of the formaldehyde modification of Raney nickel on the hydrogenation of crotonaldehyde ........................................... 94
  7.1.4 Influence of the formaldehyde modification of nickel-on-carrier on the hydrogenation of crotonaldehyde ........................................... 96
7.2 Hydrogenation of 1-bromo-4-nitrobenzene .................................. 97
  7.2.1 General aspects .................................................................. 97
  7.2.2 Test for a possible gas-liquid transfer limitation for hydrogen ........................................... 98
  7.2.3 Influence of the modification on selectivity and reaction rates .................................................................................. 99
7.3 Hydrogenation of levodione ....................................................... 101
  7.3.1 General remarks .................................................................. 101
  7.3.2 Test for a possible gas-liquid transfer limitation for hydrogen ........................................... 101
  7.3.3 Influence of the modification on selectivity and hydrogenation rate ........................................... 102
7.4 Discussion .................................................................................. 103

8 Conclusions and outlook .................................................................. 105

9 Experimental .................................................................................. 107
  9.1 Apparatus .................................................................................. 107
    9.1.1 Description of the 500 ml steel hydrogenator ......................... 107
    9.1.2 200 ml glass hydrogenator .................................................. 109
    9.1.3 100 ml low pressure hydrogenation apparatus ...................... 109
    9.1.4 Lab Shaker ........................................................................ 110
    9.1.5 Modification and washing apparatus ..................................... 110
    9.1.6 Gas chromatograph .............................................................. 110
  9.2 Methods .................................................................................... 111
9.2.1 Hydrogenation of butyronitrile ........................................ 111
9.2.2 Reversibility experiments in the 35 ml screening autoclave 111
9.2.3 Hydrogenation of crotonaldehyde ..................................... 112
9.2.4 Hydrogenation of 1-bromo-4-nitrobenzene ....................... 112
9.2.5 Hydrogenation of levodione ........................................... 113
9.2.6 Description of the sampling procedure .............................. 113
9.2.7 Neutralisation with water .............................................. 114
9.2.8 Neutralisation with methanol ......................................... 114
9.2.9 Neutralisation with tetrahydrofurane ............................... 114
9.2.10 Modification with formaldehyde ................................... 114

9.3 Analytics ........................................................................ 115
9.3.1 Determination of butyronitrile, butylamine, dibutylamine and dibutylimine with a GC method using an internal standard ......................................................... 115
9.3.2 Determination of crotonaldehyde, crotylalkohol, butanal and butanol with a GC method using an internal standard ................................................... 116
9.3.3 Determination of 1-bromo-4-nitrobenzene, 1-bromo-4-aminobenzene and aniline ........................................................ 118
9.3.4 Determination of levodione and actinol ............................ 119
9.3.5 Methanol determination in aqueous medium with a headspace GC method using an external standard .................... 120
9.3.6 Formaldehyde determination in aqueous medium with an HPLC method using an external standard .......................... 121
9.3.7 Synthesis of dibutylimine as a standard for GC measurements ................................................................. 122

9.4 Identification of by-products ............................................. 123
9.4.1 N-Butylbutanamide ....................................................... 123
9.4.2 N,N-Dibutylbutyramidine ............................................. 123
9.4.3 1,1-Diethoxybutane ..................................................... 124

9.5 Characterisation of the catalyst ........................................... 124
9.5.1 The reduction potential ................................................. 124
9.5.2 Adsorption of an indicator ............................................. 125
9.5.3 Dissolution in acidic medium ......................................... 125

9.6 Chemicals ..................................................................... 125
Chapter 1

Abstract

In the present work the liquid phase hydrogenation of aliphatic nitriles as well as an industrially applicable modification procedure for hydrogenation catalysts [1] producing higher yields of primary amines were investigated.

In a first part, by using Raney nickel as catalyst and butyronitrile as a model substance the influence of the gas-liquid hydrogen transfer limitation and several reaction parameters, such as the temperature, the hydrogen pressure, the ratio of catalyst to substrate, the recyclability of the catalyst and various additives on the hydrogenation selectivity were investigated. The influence of these parameters is discussed with a semi-quantitative macro-kinetic model presented within this thesis. Furthermore, the reversibility of the reaction steps that characterise the hydrogenation system was investigated with an intermediate product as starting material.

A new, economically interesting and easily applicable method to rise the selectivity towards primary amines is the modification of nickel catalysts by formaldehyde. Several parameters of this modification process were investigated, because the desired higher selectivity is also accompanied by an undesired loss of activity during the hydrogenation. In particular the amount of formaldehyde used to treat the catalyst and the amount of catalyst at a constant formaldehyde concentration were explored. The nickel leaching during the modification as well as during the hydrogenation was shown to be also an economically relevant factor, if a modified catalyst is used in an industrial process.

The effect of the modified catalysts on other chemical systems was screened by employing the following hydrogenation systems: the hydrogenation of an \(\alpha,\beta\)-unsaturated aldehyde, the hydrogenation of a halogenated nitroarene and the enantioselective hydrogenation of a cyclic
dione. The modification by formaldehyde was not beneficial in the tested cases as the selectivities were not enhanced. On the contrary, a decrease in activity was observed with the modified catalysts.
Zusammenfassung

Im Rahmen der vorliegenden Arbeit wurden die Hydrierung von aliphatischen Nitrilen in flüssiger Phase sowie ein industriell anwendbarer Prozess zur Modifizierung von Hydrierkatalysatoren [1], welcher höhere Ausbeuten an primären Aminen liefert, untersucht.


Die Einwirkung der modifizierten Katalysatoren auf andere chemische Systeme wurde ebenfalls evaluiert. Hierbei wurden die modifizierten
Katalysatoren auch bei der Hydrierung von α,β-ungesättigten Aldehyden, halogenierten Nitroaromaten und Dialdehyden getestet. Es stellte sich heraus, dass die Formaldehyd-Modifizierung für diese Systeme keinen Vorteil in Form einer Selektivitätssteigerung bringt: Es konnte lediglich ein Aktivitätsverlust beobachtet werden.
3.1 Overview

The catalytic hydrogenation of nitriles leads to a mixture of primary, secondary and tertiary amines, amides and alcohols. The economic efficiency of this catalytic reaction to the primary amines is influenced mainly by the by-products mentioned above. Further research is, therefore, necessary to determine an optimal selective hydrogenation for each nitrile. Formation of the by-products can be minimized by using a suitable catalyst, by modification of the catalyst, or by additives such as ammonia or alcohols. The most important catalyst for this system is Raney nickel and its modifications, but the exact mechanism, especially the intrinsic selectivity determining step, is presently unknown. The aim of this work is, therefore, to obtain a deeper understanding of the mechanism and to achieve an optimization of the process.

The selectivity obtained during nitrile hydrogenation is determined by a strong interaction of two catalytic functions, the acid and the hydrogenation sites. This is shown in the following reaction scheme (Figure 3-1). The ratio of and the distance between the acid and the hydrogenation sites determine the ratio of the reaction constants \( k_{H4}/k_{C5} \), and therefore the formation of by-products (secondary and tertiary amines). It can be assumed that the reaction pathway via \( k_{H3} \), \( k_{H4} \) is kinetically favoured towards the reaction pathway via \( k_{H1} \), \( k_{H2} \). Thus, a minimal number of acid catalytic sites is favoured.
Fig. 3-1: Bifunctional mechanism for the hydrogenation of nitriles.
3.2 Aim and scope of this thesis

The aim of this work is to investigate the mechanism presented in Chapter 3.1 and to ultimately confirm or reject its feasibility. Therefore, investigations on the following parameters have been performed:

- catalyst
- catalyst modification
- hydrogen pressure
- additives
- temperature
- solvent

In addition, a recently patented modification of hydrogenation catalysts by formaldehyde, which leads to better selectivities towards the primary amines if aromatic nitriles are hydrogenated, is tested for aliphatic nitriles. The completely unknown mechanism of this modification has also to be investigated.
3.3 List of abbreviations and symbols

Table 3-1: List of abbreviations and symbols.

<table>
<thead>
<tr>
<th>Abbreviation</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>actinol</td>
<td>(4R,6R)-4-hydroxy-2,2,6-trimethylcyclohexanone</td>
</tr>
<tr>
<td>BA</td>
<td>butylamine</td>
</tr>
<tr>
<td>BN</td>
<td>butyronitrile</td>
</tr>
<tr>
<td>BI</td>
<td>butylimine</td>
</tr>
<tr>
<td>cat</td>
<td>catalyst</td>
</tr>
<tr>
<td>Damide</td>
<td>dibutylamide, N-butylbutanamide</td>
</tr>
<tr>
<td>DBA</td>
<td>dibutylamine</td>
</tr>
<tr>
<td>DBD</td>
<td>dibutylamidine</td>
</tr>
<tr>
<td>DBDH⁺</td>
<td>protonated dibutylamidine</td>
</tr>
<tr>
<td>DBI</td>
<td>dibutylimine, dibutylazomethine</td>
</tr>
<tr>
<td>EDS</td>
<td>1,2-bis(2-hydroxyethylthio)ethane</td>
</tr>
<tr>
<td>ESTD</td>
<td>external standard</td>
</tr>
<tr>
<td>FAME C8</td>
<td>n-caprylic acid methyl ester</td>
</tr>
<tr>
<td>FID</td>
<td>flame ionisation detector</td>
</tr>
<tr>
<td>ISTD</td>
<td>internal standard</td>
</tr>
<tr>
<td>levodione</td>
<td>(6R)-2,2,6-trimethylcyclohexa-1,4-dione</td>
</tr>
<tr>
<td>MeOH</td>
<td>methanol</td>
</tr>
<tr>
<td>RaNi</td>
<td><em>Raney</em> nickel</td>
</tr>
<tr>
<td>Tamidine</td>
<td>tributylamidine, N,N-dibutylbutyramidine</td>
</tr>
<tr>
<td>TBA</td>
<td>tributylamine</td>
</tr>
<tr>
<td>TFA</td>
<td>trifluoro acetic acid</td>
</tr>
<tr>
<td>THF</td>
<td>tetrahydrofuran</td>
</tr>
<tr>
<td>C</td>
<td>concentration</td>
</tr>
<tr>
<td>exp</td>
<td>experiment</td>
</tr>
</tbody>
</table>
Table 3-1: List of abbreviations and symbols.

<table>
<thead>
<tr>
<th>Symbol</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>G</td>
<td>gas phase</td>
</tr>
<tr>
<td>$k_x$</td>
<td>rate constant of the reaction $x$</td>
</tr>
<tr>
<td>L</td>
<td>liquid phase</td>
</tr>
<tr>
<td>$P(H_2)$</td>
<td>hydrogen pressure</td>
</tr>
<tr>
<td>$P(NH_3)$</td>
<td>ammonia pressure</td>
</tr>
<tr>
<td>$r$</td>
<td>distance</td>
</tr>
<tr>
<td>$r_0$</td>
<td>initial reaction rate</td>
</tr>
<tr>
<td>$\sigma$</td>
<td>standard deviation</td>
</tr>
<tr>
<td>rel. $\sigma$</td>
<td>relative standard deviation</td>
</tr>
<tr>
<td>S</td>
<td>solid phase</td>
</tr>
<tr>
<td>T</td>
<td>temperature</td>
</tr>
</tbody>
</table>

3.4 List of substances

Table 3-2: List of substances.

4-aminoazobenzene

4-amino-5-cyano-2-methoxy-pyrimidine pynitrile
<table>
<thead>
<tr>
<th>Substance</th>
<th>Chemical Structure</th>
</tr>
</thead>
<tbody>
<tr>
<td>Aniline</td>
<td><img src="image" alt="Aniline" /></td>
</tr>
<tr>
<td>1,2-bis(2-hydroxyethylthio)ethane</td>
<td><img src="image" alt="" /></td>
</tr>
<tr>
<td>1-bromo-4-aminobenzene</td>
<td><img src="image" alt="1-bromo-4-aminobenzene" /></td>
</tr>
<tr>
<td>1-bromo-4-nitrobenzene</td>
<td><img src="image" alt="1-bromo-4-nitrobenzene" /></td>
</tr>
<tr>
<td>Butanol</td>
<td><img src="image" alt="Butanol" /></td>
</tr>
<tr>
<td>Butyraldehyde</td>
<td><img src="image" alt="Butyraldehyde" /></td>
</tr>
<tr>
<td>Butylamine</td>
<td><img src="image" alt="Butylamine" /></td>
</tr>
<tr>
<td>Butylimine</td>
<td><img src="image" alt="Butylimine" /></td>
</tr>
<tr>
<td>Butyronitrile</td>
<td><img src="image" alt="Butyronitrile" /></td>
</tr>
<tr>
<td>n-Caprylic acid methyl ester</td>
<td><img src="image" alt="n-Caprylic acid methyl ester" /></td>
</tr>
<tr>
<td>Chemical Structure</td>
<td>Name</td>
</tr>
<tr>
<td>--------------------</td>
<td>-----------------------------</td>
</tr>
<tr>
<td><img src="image" alt="crotonaldehyde" /></td>
<td>crotonaldehyde</td>
</tr>
<tr>
<td><img src="image" alt="crotylalkohol" /></td>
<td>crotylalkohol</td>
</tr>
<tr>
<td><img src="image" alt="dibutylamide" /></td>
<td>dibutylamide</td>
</tr>
<tr>
<td><img src="image" alt="dibutylamidine" /></td>
<td>dibutylamidine</td>
</tr>
<tr>
<td><img src="image" alt="protonated dibutylamidine" /></td>
<td>protonated dibutylamidine</td>
</tr>
<tr>
<td><img src="image" alt="dibutylamine" /></td>
<td>dibutylamine</td>
</tr>
<tr>
<td><img src="image" alt="N,N-dibutylbutyramidine" /></td>
<td>N,N-dibutylbutyramidine</td>
</tr>
<tr>
<td><img src="image" alt="tributylamidine" /></td>
<td>tributylamidine</td>
</tr>
<tr>
<td><img src="image" alt="Tamidine" /></td>
<td>Tamidine</td>
</tr>
</tbody>
</table>
Table 3-2: List of substances.

|(4R,6R)-4-hydroxy-2,2,6-trimethylcyclohexanone\(\begin{array}{c}
\text{HO} \\
\text{R} \\
\text{R}
\end{array}\) & actinol \\
|pyridine & \\
|tributylamine & \\
|(6R)-2,2,6-trimethylcyclohexa-1,4-dione\(\begin{array}{c}
\text{R} \\
\text{R}
\end{array}\) & levodione|
4.1 Hydrogenation of nitriles

4.1.1 General aspects

The reduction of organic substances with molecular hydrogen in the presence of solid contact substances is based on heterogeneous catalysis. Because the substances do not react with hydrogen under standard conditions, the reaction occurs exclusively on the contact surface. Different processes, which depend on the adsorption of reaction partners on the catalyst, and which are not understood in detail, determine the selectivity of such reactions. Consequently, the result of the reduction often depends on the catalyst and the chosen conditions.

4.1.2 Hydrogenation of nitriles to amines

The hydrogenation of nitriles is one of the main methods used in industrial chemistry for the synthesis of primary amines. The product is always a mixture of primary, secondary and tertiary amines. The selectivity of this catalytic reaction depends on several factors: The nature of the catalyst (metal and support), the addition of ammonia, the temperature and the solvent used [2-4]. This was impressively demonstrated in the case of butyronitrile (Figure 4-1) [5].

To control the selectivity towards the primary amine, the following methods are proposed in the literature [6]:

Fig. 4-1: Selectivities of butyronitrile hydrogenation using different catalysts, conditions and solvents [5].

- **Hydrogenation in acid solution:** The produced amines are converted into salts and thereby deactivated for a further reaction to higher substituted amines.

- **Hydrogenation under acylating conditions:** In reactions with acetic anhydride or methyl formate the primary amines are converted into amides, which subsequently can be hydrolysed.

- **Hydrogenation in presence of ammonia:** Reactions that produce secondary and tertiary amines by the cleavage of ammonia are inhibited in the presence of ammonia.

In industrial nitrile hydrogenation the addition of ammonia is the method of choice, which has no great disadvantages and produces considerable higher selectivities towards the primary amine. A new, industrially applicable method to increase the selectivity to primary amines is to modify the catalyst by formaldehyde (see Chapter 4.4.3).
4.1.3 Hydrogenation of nitriles to aldehydes

The hydrogenation of nitriles produces aldimines as intermediates. Therefore, in principle it is possible to synthesize aldehydes via the partial hydrogenation of nitriles and the subsequent hydrolysis of the produced aldimines. This conversion is only successful with γ- and δ-hydroxynitriles, because the cyclisation of the corresponding aldimines to the saturated 2-aminotetrahydrofuranes and -pyranes is faster than the further hydrogenation (Figure 4-2) [7, 8].

Fig. 4-2: Hydrogenation and cyclisation of a hydroxynitrile [6, 8].

Based on these fundamentals, in sugar chemistry a process for chain prolongation was developed. Hydrogen cyanide is added and the intermediate is partially hydrogenated and subsequently hydrolysed.

The conditions for an intramolecular stabilisation do not exist in most aliphatic and aromatic aldimines. Nevertheless, the nitrile hydrogenation can be stopped after the uptake of one mole equivalent hydrogen if suitable basic compounds are added and the secondary imine is produced. In general, the more stable the formed secondary imines are, the higher is the conversion.

Aldehydes can be produced from the secondary imines according to two processes:

- **Hydrolysis:** Short heating with diluted mineral acids in alcohol or acetic acid. The azomethines are split into aldehydes and the salts of the released amines.
• **Displacement**: Aldehydes which produce more stable secondary imines displace the other aldehydes.

Another possibility, the direct hydrogenation of nitriles to aldehydes in acidic medium, was investigated by Möltgen and Tinapp [9]. High selectivities were obtained with Raney nickel as catalyst in acid solutions.

### 4.1.4 Hydrogenation of nitriles to hydrocarbons

With a mixed catalyst of nickel- and copper(II)-oxide (3:2) on silicic acid, nitriles can be converted to hydrocarbons, e.g. p-aminobenzonitrile to p-toluidine (80%) or cinnamic acid nitrile to propylbenzol (90%) [4, 6]. For this conversion, the catalyst is prehydrogenated at 300°C and subsequently a mixture of nitrile and hydrogen is added at similar temperatures. This transformation is also possible with a molybdenum sulphide catalyst [6].

### 4.1.5 Hydrogenation and cyclisation

Cyclisations occur in catalytic hydrogenations if a functional group is produced that can react with a second functional group located in suitable distance. One of the best known examples is the reduction of γ-hydroxyl-acids to γ-lactones. Schiff bases or primary amines in molecules containing a second interacting group, such as ketones, esters, acids, amides, olefins and various heterocyclic rings can be hydrogenated into cyclic amines [2, 3]. A second nitrogen group can also lead to cyclic amines via the hydrogenolysis of ammonia. Halogen atoms in the γ- or δ-position favour cyclisations to pyrrolines or piperidines.

Cyclisations are not limited to catalytic hydrogenation, but can also occur during organic reductions. Because the favourable conditions for cyclisations are not identical to the conditions for hydrogenation, the cyclisation sometimes occurs when the reaction mixture is recovered. In some cases, the cyclisation can be either suppressed or enforced in presence of large quantities of ammonia or acylating solvent, respectively [2, 3, 6].
4.2 Mechanistic considerations of nitrile hydrogenation

4.2.1 Historic development

In the literature results are generally discussed according to a mechanism proposed by Braun et al. [10] in 1923, based on a competition between heterogeneous hydrogenations and homogeneous condensations (Figure 4-3, Figure 4-4).

![Chemical structures](image)

**Fig. 4-3:** Hydrogenation of the nitrile, producing the intermediate imine which is further hydrogenated to the primary amine.

With his experiments Braun et al. [10] could exclude the reaction pathway to the secondary amine via the aldehyde intermediate formed by the reaction of aldimine with water.

![Chemical structures](image)

**Fig. 4-4:** Mechanism proposed by Braun et al. [10] for the reaction towards the secondary amine.
Two possible intermediates (Figure 4-4) were proposed, the 1-aminoamine (route A) and the secondary imine (route B). After the reaction of the nitrile with one mole equivalent of hydrogen, the aldime is produced, which can then react with hydrogen to produce a primary amine. As soon as both the aldime and the primary amine are present, they react to form the *Schiff* base by condensation to the 1-aminoamine and splitting of ammonia. The *Schiff* base can then be hydrogenated to the secondary amine (route B). Alternatively, the amine and the aldime can react to form the 1-aminoamine, which can be hydrogenolysed to the secondary amine (route A).

In 1967, Greenfield [11] presented a similar scheme for the formation of the tertiary amine (Figure 4-5). The aldime reacts with the secondary amine to produce the 1-aminotrialkylamine, which is hydrogenolysed to the tertiary amine (route A). Greenfield also proposed the alternative reaction path via the intermediate of the enamine (route B).

In 1986, Volf and Pasek [12] summarised the hydrogenation in a scheme and pointed out that there exist two types of reactions: Typical hydrogenations (A, B, E and H) and acid-base catalysed condensations (C, D, F and G, Figure 4-6).
In 1992, *Dallons et al.* [13] postulated a mechanism for the formation of by-products in which a semi-hydrogenated intermediate adsorbed on the catalyst reacts with a primary or a secondary amine. The resulting 1-aminoalkylamine or 1-aminodialkylamine reacts further to the secondary imine or the tertiary enamine (*Figure 4-7*).

Non-hydrogenating active sites (acid sites) are responsible for the adsorption of the amine on the catalyst. Obviously, the support has a great
influence on the selectivity. The adsorption of primary and secondary amines as well as ammonia is enabled by the acid sites. Dallons et al. proposed that acid sites on the support give a high selectivity in favour of the primary amines because these amines are adsorbed on the sites that are not neighbouring the hydrogenation sites. The formation of by-products is therefore suppressed.

A fundamentally different mechanism was formulated by Verhaak et al. [14-16] (Figure 4-8). The hydrogenation of acetonitrile in the gas phase was investigated using various acid nickel catalysts. The acidity of the catalysts was successfully decreased by modifying the reaction temperature and by the addition of potassium as a promoter to achieve a higher selectivity towards the primary amine. The quantity and strengths of the acid sites were determined by temperature programmed desorption (TPD) of ammonia, and a linear correlation was found between the selectivity and the quantity of the acid sites.

In this mechanism, the imine produced during the hydrogenation can either be further hydrogenated to a primary amine or desorb from the catalyst (Figure 4-8). If the imine readsorbs on acid sites, the acid-catalysed

![Diagram](image.png)

**Fig. 4-8:** Mechanism proposed by Verhaak et al. [14-16] in which side reactions to secondary and tertiary amines are catalysed by acid sites on the catalyst.
side reactions occur (Figure 4-9) forming azomethine and enamine. These substances then migrate back to the hydrogenation sites through the gas phase and are hydrogenated to secondary or tertiary amines.

\[
\text{NH}_2, \text{NH}_2, \text{NH}_2, \text{NH}_2
\]

\[
\text{R'} - \text{H} - \text{NH}_2, \text{NH}_2
\]

\[
\text{R'} - \text{H} - \text{NH}_2, \text{NH}_2
\]

\[
\text{NH}_3, \text{NH}_3, \text{NH}_3
\]

\[
\text{Vc/R}
\]

Fig. 4-9: Condensation reactions on the acid sites of the catalyst: I Chemisorbed primary imine on the acid sites and its resonance structures, II reactions of the primary imine to produce the secondary imine or the 1-aminooamine [16].

Huang and Sachtler [17-22] presented a mechanism based on deuterium exchange experiments. Acetonitrile was hydrogenated with D$_2$ in the presence of a ruthenium catalyst to produce CHD$_2$CN and CH$_3$CD$_2$NH$_2$ (Eq. 4.1). Deuterated acetonitrile (CD$_3$CN) was hydrogenated with H$_2$ to produce CD$_3$CH$_2$ND$_2$ and CDH$_2$CN (Eq. 4.2).

\[
2 \text{CH}_3\text{CN} + 2 \text{D}_2 \rightarrow \text{CHD}_2\text{CN} + \text{CH}_3\text{CD}_2\text{NH}_2 \quad \text{Eq. 4.1}
\]
Based on these experiments, Huang and Sachtler formulated a mechanism without an imine intermediate but instead with the formation of intermediates that are chemisorbed by double bonds on the catalyst (Figure 4-10). According to Huang et al. [18] and Rode et al. [23], acid sites on the catalyst surface have no influence on the selectivity towards the primary amine. This conclusion is based on two ideas [18]:

- Secondary and tertiary amines are also formed on catalysts on neutral supports.
- Acid sites on a catalyst are neutralised in strongly basic media.

Coq et al. [24] postulated a mechanism (Figure 4-11) which includes the side reactions and does not exclude Huang and Sachtler’s [22] mechanism. The mechanism of Verhaak et al. [14] is also not excluded. The side reactions that lead to the secondary and tertiary amines can take place on acid sites or on hydrogenation sites of the catalyst. A mechanism for the condensations on the hydrogenation sites was postulated (Figure 4-11), in which a primary amine reacts with the chemisorbed carbene E, or alternatively the chemisorbed intermediates D and E condense.
Fig. 4-11: Mechanism for the hydrogenation proposed by Coq et al. [24].

4.2.2 Models for the formation of side products

Nucleophilic attack on the imine carbon: Addition of water to the double bond of the imine, forming an aldehyde via the aminole intermediate (hydrolysis of the imine). This aldehyde then condenses with amines to secondary imines that are hydrogenated to the corresponding amines (Figure 4-12) [25, 26].

Fig. 4-12: Formation of by-products: Side reaction with water, forming the secondary amine [26].
*Nucleophilic attack on the cyano carbon:* Nucleophiles (water, alcohols and amines) can attack the nitrile group (*Figure 4-13*).

![Diagram](image)

*Fig. 4-13:* Formation of by-products: Nucleophilic attack on the cyano carbon [26].

*Insertion reactions:* Insertion of the nitrile on chemisorbed intermediates and by-products (*Figure 4-14*).

*Electron transfer and C-C coupling reaction:* One electron transfers from the nitrile to the metallic catalyst, forming an iminoradical that can dimerize (*Figure 4-15*).

Obviously, the reactions to hydrocarbons (at high temperatures) and the cyclisation reactions (Chapter 4.1.4 and Chapter 4.1.5) can also diminish the yields of primary amines.
4.2.3 Influence of reaction parameters on nitrile hydrogenation

Influence of ammonia

The effect of ammonia on the selectivity was first investigated by Braun et al. [10]. All authors describe a higher selectivity towards the primary amine if ammonia is added to the reaction mixture, but the reason of this effect is unknown. Another unexplained effect is that the reaction rates are higher if ammonia is added up to a certain ammonia concentration and are then again lowered [27]. Several explanations were put forward:
• Ammonia influences the equilibrium between the amine, the imine and the azomethine (Figure 4-16) [28].

\[
R\text{-CH}_2\text{-NH}_2 + R\text{-CH} = NH \xrightarrow{-\text{NH}_3} R\text{-N} = CH \xrightarrow{+\text{NH}_3} R\text{-CH}_2\text{-NH}_2
\]

Fig. 4-16: Equilibrium of amine, imine, azomethine and ammonia [28].

• Ammonia reacts with the primary imine to produce the 1-aminoamine, which is hydrogenolysed to form the primary amine (Figure 4-17) [29].

\[
R\text{-CH} = NH \xrightarrow{+\text{NH}_3} R\text{-CH}_2\text{-NH}_2 \xrightarrow{+\text{H}_2} R\text{-CH}_2\text{-NH}_2
\]

Fig. 4-17: Addition of ammonia to the double bond of the imine and hydrogenolysis of the 1-aminoamine [29].

• Ammonia poisons the acid sites of the catalyst, inhibiting the acid-catalysed side reactions [16].
• Ammonia modifies the electronic properties of the catalyst, preventing the unwanted side reactions.

A similar positive effect on the selectivity can be observed if alkali hydroxides are added to the reaction mixture [30, 31].

Influence of the solvent
Besson et al. [32] investigated the effect of various solvents on the selectivity and the activity by comparing the polarity of the solvent with the selectivity towards the primary amine. It was found that the more polar the solvent, the higher the selectivity. In addition, the activity in different alcohols was investigated, and it was found that the reaction rate increased
as the number of C-atoms in the alcohol increased. The solubility of hydrogen in the solvent also influences the hydrogenation reaction.

**Influence of the temperature**

Generally, the selectivity decreases as the temperature increases [26]. Degischer [27] found that within the range 60-140°C the selectivity increased linearly with increasing temperature. At temperatures above 160°C, the selectivity decreased with increasing temperature. This change may be due to different activation energies at higher temperatures (kinetic control) or a shift towards equilibrium at higher temperatures (thermodynamic control).

**Influence of the hydrogen pressure**

A higher hydrogen pressure causes a higher reaction rate. Furthermore, a higher pressure, in general, leads also to a higher selectivity. However, if Raney nickel is employed, a higher hydrogen pressure surprisingly yields a lower selectivity towards the primary amine [26].

**Influence of the catalyst**

The main influence on selectivity and activity is based on the metal catalyst and its support. Often similar selectivities and activities are observed in the liquid and the gas phase hydrogenation.

### 4.3 Reversible reactions of amines

The synthesis of secondary and tertiary amines starting from primary amines was described by Nicodemus and Schmidt [33] in 1930. Ethylamine and butylamine reacted at temperatures of about 220°C to the corresponding secondary amines using a catalyst produced by coating cobalt carbonate onto pumice stone. Selectivities of 76-78% towards the secondary amine were observed at conversions of 65-70%. 1936 Herold and Smykal [34] reported on the preparation of primary amines from secondary
and tertiary amines and ammonia. At temperatures of 300-450°C, using an excess of ammonia and catalysts such as alumina gel, activated carbon, aluminium oxide, reduced nickel catalysts, yields up to 66% were achieved. A commercially interesting application is the production of hexamethylene-diamine starting from azepane, that was patented by Reppe and Bauer [35] (Figure 4-18). In the presence of hydrogen, ammonia and a nickel or cobalt catalyst azepane is converted to hexamethylenediamine "in good yields" in the liquid phase at temperatures of 140-220°C. This reaction is of interest because azepane is produced as a by-product during the hydrogenation of adiponitrile. Also, the production of hexamethylenediamine from the corresponding dimer and ammonia is an interesting reaction since the dimer is another by-product of the adiponitrile hydrogenation (Figure 4-18).

The reverse reaction, the cyclisation of hexamethylenediamine, was also investigated [36], and azepane was obtained at conversions of 84% in the gas phase at temperatures of 350-380°C using chromium and vanadium oxide catalysts. Nowadays, the production of secondary amines starting with primary amines is one of the standard methods in the laboratory [37-40].

**Fig. 4-18:** Production of hexamethylenediamine starting from azepane (I) and the corresponding secondary amine (II).
In 1993/94 Verhaak et al. [14-16] proposed a mechanism for the hydrogenation of amines. Their attention focussed on the acid sites on the catalyst and their role in the production of higher substituted amines as by-products *(vide Chapter 4.2.1, Figure 4-8 and Figure 4-9)*.

In another publication, the disproportionation of the propylamine in the gas phase using a continuous flow reactor, hydrogen and hydrogenation catalysts was investigated [41]. The production rate of dipropylamine formation decreased with increasing hydrogen pressure. If the reaction was run without hydrogen, the conversion to the secondary amine was decreased and dipropylimine as well as propylimine were obtained as main products *(Figure 4-19)*. The reaction rates depend on the acid sites on the catalyst.

![Chemical structures](image)

*Fig. 4-19:* Production of dipropylamine B (in the presence of hydrogen), or dipropylimine C and propylimine D (in the absence of hydrogen) [41].

A mechanism was proposed in which the disproportionation is divided into four reaction steps *(Figure 4-20)*: a dehydrogenation followed by an acid catalysed condensation and finally the hydrogenolysis of the amino-amine produced.

This reaction mechanism is supported by the fact that the number of the acid sites determined by temperature programmed desorption of ammonia...
correlates with the conversion of propylamine in the disproportionation experiments (Figure 4-8).

Fig. 4-20: Reaction sequence for the disproportionation of primary amines proposed by Verhaak et al. [41].

4.4 Raney nickel

4.4.1 Preparation methods

Since the work of Sabatier [42] nickel is known as a good hydrogenation catalyst. To enlarge the reaction surface, the metal was dispersed on inorganic supports. Another way to increase the activity was discovered by Raney [43] in 1925. His patent describes a process to remove Si from a NiSi-alloy with alkaline solutions. NiAl intermetallic components showed a higher activity than those of Si [44]. The investigation of Raney nickel is interesting due to its complex skeletal structure and its wide range of application in organic synthesis. Raney nickel is often used in industry, e.g., in the catalytic hydrogenation of adiponitrile to hexamethylenediamine, or in the hydrogenation of benzene to cyclohexane.
Raney nickel is prepared by leaching the Al in a NiAl-alloy with a sodium or potassium hydroxide solution in accordance with Eq. 4.3 [45, 46]. If the alkaline hydroxide is not used in large excess (20-30% NaOH or 30-40% KOH), the aluminate formed is deposited as bayerite on the catalyst (Eq. 4.4).

\[
2 \text{Al} + 2 \text{OH}^- + 2 \text{H}_2\text{O} \rightleftharpoons 2 \text{AlO}_2^- + 3 \text{H}_2 \quad \text{Eq. 4.3}
\]

\[
2 \text{AlO}_2^- + 4 \text{H}_2\text{O} \rightleftharpoons \text{Al}_2\text{O}_3 \times 3\text{H}_2\text{O} + 2\text{OH}^- \quad \text{Eq. 4.4}
\]

There are three methods that can be used to manufacture Raney nickel. In the first method, the nickel particles are slowly added to an alkaline solution. In the second method, the solution is slowly added to the alloy in a neutral suspension. In both cases, it is important that the reaction is controlled. If aluminium has to be removed quantitatively, the nickel particles must be added slowly to an alkaline solution. When no further hydrogen is evolved, the reaction mixture is heated in concentrated alkali solution.

The concentration of the leach decreases with conversion, so that the suspension must be decanted several times, and the lye replaced. The fresh Raney nickel is stored in a 1 M sodium hydroxide solution. To minimize variations in the properties of the catalyst, all samples should be taken from the same batch.

4.4.2 Industrial applications

Raney nickel is a heterogeneous catalyst often used, with many applications in hydrogenation reactions [47-49], especially in the hydrogenation of nitriles to primary amines which are used in polymerization reactions. This is due to the good selectivity and the cheap price of the metal compared to other metals used in hydrogenation processes. Another field of application is the hydrogenation of aromatic nitro compounds [50], of C-C double bonds and even as a substitute for the Lindlar catalyst (Table 4-1).
Table 4-1: Examples for the applications of *Raney* nickel in industrial processes [47-49].

<table>
<thead>
<tr>
<th>reaction functional group</th>
<th>substrate</th>
<th>product</th>
<th>application</th>
</tr>
</thead>
<tbody>
<tr>
<td>hydrogenation nitro</td>
<td>2,4-dinitrotoluene</td>
<td>2,4-diaminotoluene</td>
<td>polyurethanes</td>
</tr>
<tr>
<td>hydrogenation diene</td>
<td>1,5,9-cyclododecatriene</td>
<td>cyclododecane</td>
<td>polyesters from nylon-6,12</td>
</tr>
<tr>
<td>hydrogenation ketone</td>
<td>C_{10}-C_{13}-3-ketoacid</td>
<td>C_{10}-C_{13}-3-hydroxyacid</td>
<td>pharma products</td>
</tr>
<tr>
<td>hydrogenation aldehyde</td>
<td>2-ethylhexanal</td>
<td>2-ethylhexanol</td>
<td>plasticiser</td>
</tr>
<tr>
<td>hydrogenation nitrile</td>
<td>stearonitrile</td>
<td>stearylamine</td>
<td>plasticiser</td>
</tr>
<tr>
<td>hydrogenation dinitrile</td>
<td>adiponitrile</td>
<td>hexamethylenediamine</td>
<td>nylon-6,6</td>
</tr>
<tr>
<td>hydrogenation alkyne</td>
<td>1,4-butynediol</td>
<td>1,4-butanediol</td>
<td>THF</td>
</tr>
<tr>
<td>hydrogenation aromatic</td>
<td>benzene</td>
<td>cyclohexene</td>
<td>polyamides</td>
</tr>
<tr>
<td>hydrogenation aromatic</td>
<td>phenol</td>
<td>cyclohexanol</td>
<td>polyamides</td>
</tr>
<tr>
<td>aminolysis alcohol</td>
<td>1,6-hexanediol</td>
<td>hexamethylenediamine</td>
<td>nylon-6,6</td>
</tr>
<tr>
<td>alkylation amine</td>
<td>dodecylamine</td>
<td>dimethyldecylamine</td>
<td>surfactants</td>
</tr>
</tbody>
</table>

4.4.3 Variation of the properties of *Raney* nickel

Various methods were tested to obtain more selective catalysts for different processes, mainly in the hydrogenation of nitriles and of aromatic nitro compounds. There, the main parameters are the metal composition
(ratio of nickel/aluminium) [50-52], the strength of the basic treatment, the
doping with other metals [53-55], the process parameters during the
production process (e.g. quenching the parent alloy in cold water [56-58])
and the modifying additives such as lithium hydroxide [31], morpholine
[59], copper acetate [60], formamidine salts [61] or vanadium salts [62]. A
recently published patent of Degischer and Rössler [1] is presenting the
advantages of a catalyst modified by formaldehyde in the hydrogenation of
nitriles. A yield of 96.4% was obtained if ‘pynitrile’ (4-amino-5-cyano-2-
methoxypryrimidine) was hydrogenated using a commercially obtainable
Raney nickel. The selectivity was increased to 99.6% if the catalyst was
treated with a 1% formaldehyde solution prior to the hydrogenation
reaction. Similar effects on the selectivity were found if instead of
formaldehyde carbon monoxide (98.8% primary amine) or acetaldehyde
(97.3% primary amine) were used to modify the catalyst [63]. Further
experiments with benzonitrile as a model substance are presented in
Figure 4-21. The disadvantage of such a modification is the loss of activity,
which is leading to a higher catalyst load in industrial processes [64].

In addition, experiments with Raney cobalt and nickel-on-carrier
catalysts were patented. Again, the modification by formaldehyde has a
positive effect on the selectivity towards the primary amine. The selectivity
for the primary amine increased from 96.8% to 98.1% if a nickel-on-carrier
was modified using formaldehyde, and from 96.8% to 99.1% if a Raney
cobalt catalyst was modified.

4.4.4 Adsorption of nitriles and their hydrogenation intermediates

Recently, great efforts have been made to describe the adsorption of
hydrogen as well as of other substances involved in the catalytic
hydrogenation of nitriles. Semi-empirical studies, molecular modellings,
studies on metalorganic substances as well as spectroscopic data (high
resolution electron energy loss vibrational spectroscopy: HREELS) were
reported [26, 65-69]. De Bellefon and Fouilloux [26] summarised the
chemisorbed species in a scheme as shown in Figure 4-22.
Because not only the knowledge of the interaction between nitriles and their hydrogenation intermediates with the catalyst is important to understand the hydrogenation, Blyholder and Neff [70] investigated the adsorption properties of solvents, such as methanol, ethanol, diethyl ether and water using a nickel-on-siliciumoxide catalyst. The adsorbed species were observed with infrared spectroscopy. It was found that methanol reacts at a temperature of 20°C and produces chemisorbed CO on the catalyst surface. Ethanol reacts in the same way, so that in addition to the infrared band of CO also bands of CH$_3$ and CH$_2$ were detected. Ni-CH$_3$, Ni-CH$_2$-CH$_3$ and Ni-O-CH$_2$-CH$_3$ are supposed to be chemisorbed at the surface. Neither water nor diethyl ether chemisorbed or reacted with the surface.

From these experiments Blyholder and Neff [70] concluded that carbon monoxide is the only species that is chemisorbed on nickel surfaces. The
reaction pathway of alcohols leading to CO produces aldehyde or ketone as intermediates. Initially, the alcohol is dehydrogenated before the C-C and the C-H bonds are broken and CO and other fragments are produced. Diethyl ether does not react with nickel surfaces as it can not dehydrogenate a hydroxyl group. The dehydrogenation of alcohols on Raney nickel was also reported by Besson et al. [25].

4.4.5 Inhibition/poisoning of the catalyst

Every process, chemical or physical, that reduces the activity of a catalyst can be classified as deactivation. In most cases, especially in complex reactions or when using complex catalysts, a change in activity is accompanied by changes in selectivity. A change in selectivity can be achieved using poisons or inhibitors. The following processes are important [71, 72]:

- Irreversible adsorption of an inhibitor at the surface or reaction of an inhibitor with the catalyst surface.
• Competitive reversible adsorption of a poison on the surface.
• Poison induced restructuring of the surface.
• Physical or chemical blocking of the pores.

With the example of a hydrocracking reaction, Penchev et al. [73] demonstrated that the selectivity can be changed using different poisons (thiophene poisons the metallic sites, pyridine the acid sites).

In the case of Raney nickel acetonitrile desorbs at temperatures above 75°C, while more strongly adsorbed nitrile fragments or molecules desorb at temperatures above 180°C. The decomposition of acetonitrile forms two carbon compounds that deactivate the catalyst. McCarty and Wise [74] and Kock et al. [75] identified the adsorbed species as α-carbon and nickel carbide. These compounds can be hydrogenated at temperatures above 200°C, thereby restoring the catalyst’s activity. Thus, the deactivation of the catalyst during the hydrogenation of acetonitrile can be prevented by applying high hydrogen pressures [24, 76].

4.4.6 Acid sites

The influence of acid sites on the selectivity of the hydrogenation of nitriles is still disputed. Verhaak et al. [14-16] described the influence of acid sites present during the hydrogenation of nitriles on the selectivity and the catalyst activity using nickel on a silicon and magnesium support. These acid sites are formed during the synthesis of the catalyst and are ascribed to the support. Their amount and strength were determined by the temperature programmed desorption (TPD) of ammonia.

Increasing the number of acid sites leads to higher reaction rates and a decreased selectivity. These observations were confirmed by Cabello et al. [28] and Dung et al. [77].

Other authors [12, 17-22] did not confirm the influence of acid sites and point out that the selectivity is influenced only by the metal used and by the reaction conditions.

Aluminiumoxide is one of the most commonly used support materials in heterogeneous catalysis. Examples are Pt-Re/Al₂O₃ (reforming) and Co-Mo/Al₂O₃ (dehydrosulfonation). This support is thermally stable and
allows an appropriate distribution of catalytically active compounds. However, as aluminium oxide is not an inert support, many reactions are catalysed by it, e.g. double bond migrations, E/Z isomerisations of olefins and H/D exchange in hydrocarbons.

Knözinger [78] determined the acid sites via the infrared adsorption of CO and measuring the stretching vibrations of C-O and O-H bonds, which depend on the bond strength (Figure 4-23). CO is also chemisorbed by Lewis acid sites via $\sigma$-bond and $\pi$-rebond. Knözinger determined the oxidation state and the coordination number of cations on the surface and the relative bond strengths of metal-CO bonds. In addition, acid site sequences were determined for hydroxyl groups on the surfaces.

\[
\text{M—O—H—CO}
\]

Fig. 4-23: Chemisorption of CO on surface hydroxyl groups [78].
Chapter 5

Hydrogenation of butyronitrile

5.1 Reaction system

The hydrogenation of butyronitrile leads to butylamine as main product if Raney nickel is used as hydrogenation catalyst. A scheme of the reaction is given in Figure 5-1. The hydrogenation experiments were made in a 500 ml steel hydrogenator (see Chapter 9.1.1) according to the procedure described in Chapter 9.2.1. The reversibility experiments presented in Chapter 5.6 were made in the 500 ml steel hydrogenator or in 35 ml screening autoclaves (see Chapter 9.1.4) according to the procedure described in Chapter 9.2.2. Two different catalysts were used, Raney nickel B 113 Z, batch 20018989 from Degussa-Hüls AG and nickel-on-carrier Ni 1404 P, lot H-99 form Engelhard.

Always when dibutylimine is mentioned, this means, that this is the amount of dibutylimine measured by gas chromatographic analysis or reaction rates extrapolated from gas chromatographic measured values. However, one must keep in mind that it is possible, that other substances as 1-amino amines, amidines or imines react in the injector and the column of the gas chromatograph (at temperatures of 250°C) and then appear as dibutylimine in the gas chromatographic spectrum.

Next to dibutylamine, tributylamine was observed as by-product. Dibutylamide and the tertiary amidine were also formed in the reaction mixture (Figure 5-2).

The product distribution of the hydrogenation is expressed in [mass-%], the reaction rates in [mmol/s] or in [mmol/s*kg catalyst]. The indicated pressure ascribes to the overall pressure, used during the reaction.
Fig. 5-1: Hydrogenation of butyronitrile (BN) to the desired primary amine (BA) and the secondary amine (DBA) over butylimine (not observed by GC) and dibutylimine (DBI) as intermediate.
In order to follow through a well structured discussion of the influence of various reaction parameters on the rate and the selectivity of the hydrogenation of nitriles, first a simple semi-quantitative macro-kinetic model is presented. The basis for the derivation of the kinetic equations is the mechanism depicted in Figure 5-1. For the sake of simplicity it is assumed that the rates of the individual hydrogenation steps are of the x-th order with respect to the partial pressure of hydrogen. Furthermore, based on the experimental data it can be assumed, that for the concentrations of the intermediates BI, DBDH+ and DBD the steady-state approximation of Bodenstein [79] can be applied.

The differential selectivity ratio (d[BA]/d[DBA]) is given by (Eq. 5.3):

\[
\frac{d[BA]}{dt} = k_2 p_{H_2}^x [BI] \quad \text{Eq. 5.1}
\]

\[
\frac{d[DBA]}{dt} = k_5 p_{H_2}^x [DBI] \quad \text{Eq. 5.2}
\]

\[
\frac{d[BA]}{d[DBA]} = \frac{k_2 [BI]}{k_5 [DBI]} \quad \text{Eq. 5.3}
\]
The ratio $[\text{BI}]/[\text{DBI}]$ can be evaluated from the following equations (Eq. 5.5-Eq. 5.8):

\[
\frac{d[\text{BI}]}{dt} = k_1[\text{BN}]p_{(H_2)}^x - [\text{BI}](k_{-1} + k_2p_{(H_2)}^x + k_3[\text{BA}][H^+]) + k_{-3}[\text{DBD}^-] 
\]

Eq. 5.4

\[
\frac{d[\text{DBD}^-]}{dt} = k_3[\text{BI}][\text{BA}][H^+] + k_4[\text{DBI}][H^+]p_{(NH_3)} - (k_4 + k_{-3})[\text{DBD}^-] 
\]

Eq. 5.5

As the protolytic side equilibrium between $\text{DBD}^+$ and $\text{DBD}^-$ is assumed to be much faster than all the other partial reaction steps, it can be neglected for the formulation of the kinetic equations. From the equations (Eq. 5.4) and (Eq. 5.5) the equations (Eq. 5.6) and (Eq. 5.7), respectively follow:

\[
[\text{BI}] = \frac{k_1[\text{BN}]p_{(H_2)}^x + k_{-3}[\text{DBD}^-]}{k_{-1} + k_2p_{(H_2)}^x + k_3([\text{BA}][H^+])} - \frac{d[\text{BI}]}{dt} 
\]

Eq. 5.6

\[
[\text{DBD}^-] = \frac{k_3[\text{BI}][\text{BA}][H^+] + k_4[\text{DBI}][H^+]p_{(NH_3)} - d[\text{DBD}^-]}{k_4 + k_{-3}} 
\]

Eq. 5.7

If the steady-state approximation of Bodenstein [79] applies for the intermediates $\text{BI}$, $\text{DBD}^+$ and $\text{DBD}^-$, i.e. if

\[
\left| \frac{d[\text{BI}]}{dt} \right| \ll k_1[\text{BN}]p_{(H_2)}^x + k_{-3}[\text{DBAD}] 
\]

and

\[
\left| \frac{d[\text{DBD}^-]}{dt} \right| \ll k_3[\text{BI}][\text{BA}][H^+] + k_4[\text{DBI}][H^+]p_{(NH_3)} 
\]
It follows:

\[
[B1] = \frac{k_{-3}(k_1[BN]p^x_{(H_2)} + k_{-4}[DBI][H^+][p_{(NH_3)}] + k_{1}k_{3}k_{4}[BA][H^+])}{(k_{-3} + k_{4})(k_{1} + k_{2}p^x_{(H_2)}) + k_{3}k_{4}[BA][H^+]} \quad \text{Eq. 5.8}
\]

and thus

\[
\frac{[B1]}{[DBI]} = \frac{1}{k_4} \left( \frac{k_{-3} + k_{4}}{k_4} \right) \left( k_{-1} + k_{2}p^x_{(H_2)} \right) + k_{3}[BA][H^+] \quad \text{Eq. 5.9}
\]

From the equations (Eq. 5.3) and (Eq. 5.9), the differential selectivity (Eq. 5.10) follows:

\[
\frac{d[BA]}{d[DBA]} = \frac{k_2}{k_4k_5} \frac{(k_{-3} + k_{4})k_1[BN]p^x_{(H_2)} + \frac{1}{[DBI]} + k_{-3}k_{4}[H^+][p_{(NH_3)}]}{(\frac{k_{-3} + k_{4}}{k_4})(k_{-1} + k_{2}p^x_{(H_2)}) + k_{3}[BA][H^+]} \quad \text{Eq. 5.10}
\]

Equation (Eq. 5.10) reveals a very diversified and complex influence of the selectivity on the various reaction parameters. A given reaction parameter, such as e.g. the partial pressure of hydrogen, can either increase or decrease the selectivity with respect to the desired butylamine, depending on the relative rates of the individual reaction steps. This diversity shall be exemplified by the following few cases:

**Case I**: \(k_2p^x_{(H_2)} \gg k_{-1} ; k_{-3} \gg k_4 ; k_{-4}[H^+][p_{(NH_3)}] \gg k_1[BN]p^x_{(H_2)} \gg \frac{1}{[DBI]}\)

\[
\frac{d[BA]}{d[DBA]} = \frac{k_2k_{-3}}{k_5} \frac{k_{-4}[H^+][p_{(NH_3)}]}{k_{-3}k_{2}p^x_{(H_2)} + k_{3}k_{4}[BA][H^+]} \quad \text{Eq. 5.11}
\]

**Case II**: \(k_2p^x_{(H_2)} \ll k_{-1} ; k_{-3} \gg k_4 ; k_{-4}[H^+][p_{(NH_3)}] \gg k_1[BN]p^x_{(H_2)} \gg \frac{1}{[DBI]}\)
\[
\frac{d[BA]}{d[DBA]} = \frac{k_2 k_{-3} k_{-4}[H^+]p_{(NH_3)}}{k_5 k_{-3} k_{-1} + k_3 k_4[BA][H^+]} \quad \text{Eq. 5.12}
\]

\text{Case III: } k_2 p_{(H_2)}^x k_{-1} ; k_{-3} \ll k_4 ; k_{-3} k_{-4}[H^+]p_{(NH_3)} \ll k_1 k_4 [BN]p_{(H_2)}^x \frac{1}{[DBI]}

\[
\frac{d[BA]}{d[DBA]} = \frac{k_2 k_{-3} k_4[H^+]p_{(NH_3)}}{k_4 k_5 k_{26[PA]}^x k_3[BA][H^+]} \quad \text{Eq. 5.13}
\]

\text{Case IV: } k_2 p_{(H_2)}^x \ll k_{-1} ; k_{-3} \ll k_4 ; k_{-3} k_{-4}[H^+]p_{(NH_3)} \ll k_1 k_4 [BN]p_{(H_2)}^x \frac{1}{[DBI]}

\[
\frac{d[BA]}{d[DBA]} = \frac{k_2 k_{-3} k_4[H^+]p_{(NH_3)}}{k_4 k_5 k_{-1} + k_3[BA][H^+]} \quad \text{Eq. 5.14}
\]

\text{Case V: } k_2 p_{(H_2)}^x \ll k_{-1} ; k_{-3} \ll k_4 ; k_{-4}[H^+]p_{(NH_3)} \ll k_1 [BN]p_{(H_2)}^x \frac{1}{[DBI]}

\[
\frac{d[BA]}{d[DBA]} = \frac{k_2 k_{-3} k_1[BN]p_{(H_2)}^x}{k_5 k_{-3} k_{26[PA]}^x k_3[BA][H^+]} \quad \text{Eq. 5.15}
\]

\text{Case VI: } k_2 p_{(H_2)}^x \ll k_{-1} ; k_{-3} \ll k_4 ; k_{-4}[H^+]p_{(NH_3)} \ll k_1 [BN]p_{(H_2)}^x \frac{1}{[DBI]}

\[
\frac{d[BA]}{d[DBA]} = \frac{k_2 k_{-3} k_1[BN]p_{(H_2)}^x}{k_5 k_{-3} k_{-1} + k_3 k_4[BA][H^+]} \quad \text{Eq. 5.16}
\]
5.2 Thermodynamic aspects

A profound investigation of the thermodynamic equilibrium of the hydrogenation of butylamine within a temperature range of 25 to 150°C and a hydrogen pressure range of 1 to 20 MPa partial pressure of hydrogen was made by Chojecki [80] using HSC Chemistry software. The best thermodynamic selectivity was calculated at high hydrogen pressures and low temperatures (75% butylamine at 20 MPa hydrogen and 298 K). The thermodynamic selectivity decreased dramatically at lower hydrogen pressures, while temperature had only a small influence.

5.3 Aspects of mass and heat transport

The kinetics of multiphase reactions are not only influenced by the chemical kinetic but also by the rate of mass and heat transfer. The investigated system presented in this study is a three phase hydrogenation consisting of gaseous hydrogen, liquid substrate and a solid catalyst. Mass transfer of
hydrogen from the gaseous phase into the liquid phase as well as that of hydrogen and the substrate (A) from the liquid phase to the surface of the catalyst can significantly influence the kinetics of the individual reaction steps, and thereby, also the selectivity of the overall hydrogenation process (Figure 5-3).

**Fig. 5-3:** Model of a three phase mass transport: Mass transport from the gaseous into the liquid phase and from the liquid phase to the surface of the catalyst. $C_{ij}$: concentration of reagent i in phase j. i:H$_2$ = hydrogen, i:A = substrate A; a,b,c: diffusional boundary layers.

Heat transfer from the surface of the catalyst to the liquid phase can also influence the selectivity. This can occur if the reaction rates are much faster than the heat transfer. In the case of a highly exothermic reaction such as the hydrogenation of nitriles, the temperature on the surface of the catalyst is higher than the measured temperature in the bulk liquid phase (Figure 5-4). This, in turn, increases the local hydrogenation rate which than increases the local temperature even further (run away). A different temperature effect on
5.4 Influence of reaction parameters on nitrile hydrogenation

The influence of the different reaction parameters on the initial differential selectivity, the product distribution and the activity of the catalysts are discussed in this Chapter. The product distribution (as yield butylamine after full conversion) is plotted versus the initial differential selectivity (calculated by dividing the initial production rate of butylamine $d[BA]/dt$ by the initial production rate of dibutylamine $d[DBA]/dt$) in Figure 5-5. It seems quite evident that an interdependence of these parameters exists and that with increasing values of the initial differential selectivity the yield of butylamine approaches a maximum limiting value which is definitely lower than 100%.
5.4.1 Influence of the overall pressure

The influence of the overall pressure on the product distribution, initial rates and initial differential selectivity was investigated for 240 g BN, 3.75 g RaNi, 100°C, and 1000 rpm in a range from 1 to 6 MPa. The results are summarised in Figure 5-6, Figure 5-7 and Figure 5-8. The selectivity towards the primary amine is decreasing with higher partial pressures of hydrogen. Such a selectivity behavior is predicted by the approximate equation (Eq. 5.10), mainly for the special cases I and III. The maximum amount of the intermediate dibutylimine is almost independent of the hydrogen pressure. The initial rates are rising using higher pressures.

The large scattering range of the measured initial reaction rates is due to technical problems with the cascade regulation of the temperature. When large amounts of hydrogen are pressed into the reactor, the temperature is decreasing due to the cold gas. This is compensated by the temperature regulation. If the reaction is then started, the reactor is heated from outside as well as from inside by the exothermic reaction. The temperature controlling cascade regulation is compensating this trend and starts to cool.
Fig. 5-6: Influence of the overall pressure on the product distribution. Reaction conditions: 240 g BN, 3.75 g RaNi, 100°C and 1000 rpm.

Fig. 5-7: Influence of the overall pressure on the initial reaction rates. Reaction conditions: 240 g BN, 3.75 g RaNi, 100°C and 1000 rpm.
However, due to a heat transfer delay the cooling is not fast enough. As a consequence, a certain thermal runaway occurs. Thus, the difference between the measured and the effective reaction temperature amounts in some cases up to 10°C. This in turn has a massive effect on the initial rates.

5.4.2 Influence of the temperature

The influence of the temperature on the product distribution, the initial rates and the initial differential selectivity was investigated in a range of 60-120°C using standard conditions (240 g BN, 3.75 g RaNi, 1 MPa, 1000 rpm). The results are presented in Figure 5-9, Figure 5-10 and Figure 5-11. The increase in selectivity towards butylamine can be explained by the lower activation energy for the hydrogenation to dibutylamine. Activation energies were determined using a “quasi” Arrhenius plot (Figure 5-12). The conditions of 240 g BN, 100°C, 1MPa and 1000 rpm are near the gas-liquid hydrogen transfer limitation so that the experiments (and
Fig. 5-9: Influence of the temperature on the product distribution. Reaction conditions: 240 g BN, 3.75 g RaNi, 1 MPa and 1000 rpm.

Fig. 5-10: Influence of the temperature on the initial rates of butyronitrile hydrogenation. Reaction conditions: 240 g BN, 3.75 g RaNi, 1 MPa and 1000 rpm
Fig. 5-11: Influence of the temperature on the initial differential selectivity. Reaction conditions: 240 g BN, 3.75 g RaNi, 1 MPa and 1000 rpm.

Fig. 5-12: “Quasi” Arrhenius plot obtained from the initial reaction rates $r_0$ (see Figure 5-10).
Table 5-1: Activation energies determined from the "quasi" Arrhenius plot by linear fit.

<table>
<thead>
<tr>
<th>rates $r_0$</th>
<th>temperature range</th>
<th>activation energy</th>
<th>error (±)</th>
</tr>
</thead>
<tbody>
<tr>
<td>/ [see Figure 5-12]</td>
<td>/ [°C]</td>
<td>/ [kJ/mol]</td>
<td>/ [kJ/mol]</td>
</tr>
<tr>
<td>$-d[BN]/dt$</td>
<td>60-100</td>
<td>48.9</td>
<td>2.2</td>
</tr>
<tr>
<td>$-d[BN]/dt$</td>
<td>100-120</td>
<td>26.9</td>
<td>1.8</td>
</tr>
<tr>
<td>$d[BA]/dt$</td>
<td>60-100</td>
<td>50.7</td>
<td>1.8</td>
</tr>
<tr>
<td>$d[BA]/dt$</td>
<td>100-120</td>
<td>23.8</td>
<td>2.7</td>
</tr>
<tr>
<td>$d[DBI]/dt$</td>
<td>60-80</td>
<td>63.4</td>
<td>2.5</td>
</tr>
<tr>
<td>$d[DBI]/dt$</td>
<td>80-120</td>
<td>37.9</td>
<td>0.6</td>
</tr>
<tr>
<td>$d[DBA]/dt$</td>
<td>60-80</td>
<td>39.5</td>
<td>0.9</td>
</tr>
<tr>
<td>$d[DBA]/dt$</td>
<td>80-120</td>
<td>15.8</td>
<td>2.2</td>
</tr>
</tbody>
</table>

specially the reaction rates) using temperatures above 100°C are mainly influenced by this limitation. The ln(-$d[BN]/dt$) versus 1/T data show a kink in the linear correlation at a value of 0.00268 (100°C). The linear fit in the range of 60 to 100°C gives an activation energy of 49 kJ/mol, above 100 °C an activation energy of about 27 kJ/mol. Interesting data points were obtained for the production rates of dibutylimine and dibutylamine. A sharp break at the linear plot at 0.00283 (corresponding to 80°C) can be observed. An explanation for these sharp breaks in the linear plots can be given either by a diffusion limitation of the reagents to the corresponding hydrogenation or acid sites, respectively, or by a change of the rate determining steps (see Chapter 5.3). As the activation energy is approximately half as large at high temperatures than at low temperatures the explanation of a diffusion limitation is more probable. A summary of the obtained activation energies is given in Table 5-1.
5.4.3 Influence of the ratio of catalyst to substrate

The influence of the catalyst to substrate ratio on the product distribution, the initial rates and the initial differential selectivity was investigated to exclude a gas-liquid transport limitation for hydrogen. The following reaction parameters were chosen: 240 g BN, 100°C, 1 MPa and 1000 rpm. The catalyst amount was varied from 1.25 g to 20 g (0.5-8.3% catalyst). The results are plotted in Figure 5-13, Figure 5-14 and Figure 5-15. The selectivity towards the primary amine is rising using larger amounts of catalyst. This may be due to catalyst deactivation (see Chapter 5.4.4). The initial reaction rates are rising linearly with the catalyst amount until 5 g catalyst. This is an indication that the hydrogen concentration in the liquid phase is constant and no mass transfer limitation exists for hydrogen within this range. Above a catalyst amount of 5 g the reaction rates approach a

![Graph showing product distribution using different amounts of catalyst. Reaction conditions: 240 g BN, 100°C, 1 MPa and 1000 rpm. Selectivity towards the primary amine is rising using larger amounts of catalyst. This may be due to catalyst deactivation (see Chapter 5.4.4). The initial reaction rates are rising linearly with the catalyst amount until 5 g catalyst. This is an indication that the hydrogen concentration in the liquid phase is constant and no mass transfer limitation exists for hydrogen within this range. Above a catalyst amount of 5 g the reaction rates approach a]
Fig. 5-14: Initial differential selectivity using different amounts of catalyst. Reaction conditions: 240 g BN, 100°C, 1 MPa and 1000 rpm.

Fig. 5-15: Initial reaction rates using different amounts of catalyst. Reaction conditions: 240 g BN, 100°C, 1 MPa and 1000 rpm.
limiting value. This limit is given by the rate of hydrogen transfer to the catalyst surface (see Chapter 5.3).

An explanation for the increasing selectivity towards butylamine using higher catalyst loadings can be twofold: With an increasing amount of catalyst per reaction volume the hydrogenation rate increases and thus also the local temperature due to the exothermic reaction. This in turn accelerates the reaction even more (runaway) and thus decreases the local hydrogen concentration at the catalyst surface. These local temperature and hydrogen concentration gradients are the larger the higher the catalyst concentration is. The stirring is not efficient enough to cancel out these gradients. As a consequence, a larger amount of catalyst per reaction volume decreases the local hydrogen concentration and increases the local temperature. Both effects result in an increase in selectivity towards butylamine.

Such a selectivity behavior is predicted by the approximate equation (Eq. 5.10), mainly for the special cases I and III.

If the stirrer speed is risen from 1000 rpm to 1500 rpm the reaction rates rose only slightly whereas the selectivity did not change. These results are shown in Table 5-2 (the conditions were: 240 g BN, 3.75 g RaNi, 100°C and 1 MPa). This is a second indication that no gas liquid transfer limitation for hydrogen exists at the following conditions: 240 g BN, 3.75 g RaNi, 100°C, 1 MPa and 1000 rpm. An important note is, that this conditions are near the gas-liquid transfer limitation for hydrogen.

### Table 5-2: Selectivity and reaction rates at different stirrer speed. Reaction conditions: 240 g BN, 3.75 g RaNi, 100°C and 1 MPa.

<table>
<thead>
<tr>
<th>stirrer speed</th>
<th>[BA]</th>
<th>[DBA]</th>
<th>[max. DBI]</th>
<th>-d[BN]/dt</th>
<th>d[BA]/dt</th>
</tr>
</thead>
<tbody>
<tr>
<td>/ [rpm]</td>
<td>[mass-%]</td>
<td>[mass-%]</td>
<td>[mass-%]</td>
<td>[mmol/(s*kg)]</td>
<td>[mmol/(s*kg)]</td>
</tr>
<tr>
<td>1000</td>
<td>88.6</td>
<td>11.0</td>
<td>9.95</td>
<td>118</td>
<td>83</td>
</tr>
<tr>
<td>1500</td>
<td>88.7</td>
<td>10.6</td>
<td>10.6</td>
<td>131</td>
<td>87</td>
</tr>
</tbody>
</table>
5.4.4 Recycling of the catalyst

Experiments to investigate the catalyst deactivation were carried out at the following conditions: 240 g BN, 3.75 g RaNi, 100°C, 1 MPa and 1000 rpm. The results are presented in Figure 5-16, Figure 5-17, Figure 5-18. The selectivity towards the primary amine as well as the activity and the initial differential selectivity are decreasing. In both cases, the decrease is large from the first to the second cycle and small in the following cycles. Due to this decrease in activity it follows that the local gradients of temperature and hydrogen concentration are becoming less and less pronounced (see Chapter 5.3). Following what has been said in Chapter 5.4.3 about the effects of these local gradients one must expect a decrease in selectivity with increasing the catalyst cycles. Such a selectivity behavior is predicted by the approximate equation (Eq. 5.10) mainly for the special cases II and IV.
Fig. 5-17: Initial rates of butyronitrile hydrogenation recycling the same catalysts four times. Reaction conditions: 240 g BN, 3.75 g RaNi, 100°C, 1 MPa and 1000 rpm.

Fig. 5-18: Initial differential selectivity recycling the same catalysts four times. Reaction conditions: 240 g BN, 3.75 g RaNi, 100°C, 1 MPa and 1000 rpm.
5.4.5 Influence of additives

The influence of additives on the selectivity and activity was investigated using standard conditions (240 g BN, 3.75 g RaNi, 100 °C, 1 MPa, 1000 rpm). The results are presented in Figure 5-19 and Figure 5-20. The following additives were tested: EDS, pyridine and ammonia. If EDS is used, the reaction rate as well as the selectivity towards butylamine are decreasing. EDS is known as a poison for hydrogenation catalysts. An explanation for this results is, that EDS is poisoning the hydrogenation sites of the catalyst and thereby slowing down the hydrogenation (-d[BN]/dt and d[BA]/dt). Because EDS does not poison the acid sites, the side reactions (BI → DBI) are not slowed down and the measured selectivity towards butylamine is lowered. Addition of pyridine does neither change the selectivity nor the reaction rates significantly. If ammonia is added, the selectivity towards butylamine is increased. The hydrogenation reactions are

![Graph showing product distribution](Image)

**Fig. 5-19:** Influence of additives on the product distribution. Reaction conditions: 240 g BN, 3.75 g RaNi, 100 °C, 1 MPa and 1000 rpm.
Fig. 5-20: Influence of additives on the initial rates of butyronitrile hydrogenation. Reaction conditions: 240 g BN, 3.75 g RaNi, 100 °C, 1 MPa and 1000 rpm.

slowed down, but not as dramatically as the side reactions (BI → DBI). The maximum intermediate concentration of dibutylimine is reduced too. Explanations for this behavior are given in Chapter 4.2.3.

5.5 Influence of washing/modification procedures

5.5.1 Influence of washing procedures with different solvents

In order to describe the changes of catalyst properties brought about by various washing procedures, the washed catalysts were tested using the butyronitrile hydrogenation reaction. Thereby, standard conditions were used: 240 g BN, 3.75 g RaNi, 100 °C, 1 MPa, 1000 rpm. The results are plotted in Figure 5-21 and Figure 5-22. The water treatment does neither change the selectivity towards the primary amine nor the reaction rates.
Fig. 5-21: Influence of the washing procedure on the product distribution. Reaction conditions: 240 g BN, 3.75 g RaNi, 100 °C, 1 MPa and 1000 rpm.

Fig. 5-22: Influence of the washing procedure on the initial rates of butyronitrile hydrogenation. Reaction conditions: 240 g BN, 3.75 g RaNi, 100 °C, 1 MPa and 1000 rpm.
Washing the fresh catalyst with methanol or modify it using formaldehyde is dramatically decreasing (by a factor of 10) the reaction rates. The selectivity towards butylamine is also decreasing. This is not in agreement with a published patent of Degischer and Rössler. An explanation for this behavior is that at the given conditions, the hydrogenation rates are so slow, that the formation of secondary amine from butylamine already present in the reaction mixture is lowering the yield of butylamine.

The influence of the washing procedure was also investigated under conditions of gas-liquid transfer limitation for hydrogen (compare Chapter 5.4.3). The following conditions were used: 240 g BN, 15 g RaNi, 100°C, 1 MPa and 1000 rpm. The results are plotted in Figure 5-23 and

![Figure 5-23](image)

*Fig. 5-23*: Influence of the modification on the product distribution at conditions of a hydrogen transfer limitation. Reaction conditions: 240 g BN, 15 g RaNi, 100°C, 1 MPa and 1000 rpm.

*Figure 5-24*. Again the water washing does not change the selectivity and only a small change in the reaction rates was measured. The reaction rates for the methanol washed and the formaldehyde modified catalyst decrease
Fig. 5-24: Influence of the modification on the initial rates of butyronitrile hydrogenation at conditions of a hydrogen transfer limitation. Reaction conditions: 240 g BN, 15 g RaNi, 100 °C, 1 MPa and 1000 rpm.

again, but the decrease is not as dramatically as if no hydrogen transfer limitation exists, or in other words, the reaction rates using the unmodified catalyst are slowed down because of the hydrogen transfer limitation. As expected, the selectivity towards the primary amine is rising due to the local hydrogen concentration (see Chapter 5.4.1) if high amounts of catalyst are used.

5.5.2 Influence of the modification by formaldehyde

The influence of the strength of the formaldehyde treatment (compare Chapter 6) was investigated using the conditions outside the transfer limitation region for hydrogen. The selectivity towards butylamine was higher if a low concentration of formaldehyde was used to modify the catalyst (from 88.6 mass-% to 93.3 mass-%, compare Figure 5-25). The hydrogenation rates decrease dramatically, so that if higher formaldehyde concentrations are used to modify the catalyst, the hydrogenation reactions
are so slow, that the dimerisation can compete successfully the hydrogenation (Table 5-3 and Figure 5-26). In Figure 5-26 the relative initial reaction rates that were calculated by dividing the initial rates obtained with the modified catalyst by the initial rates of the unmodified catalyst are compared for various modification procedures. The reaction leading to DBI (d[DBI]/dt) is somewhat stronger decelerated than the reactions leading to butylamine.

Figure 5-27 reveals that the measured data points for the modified catalysts do not fit the correlation between the yield butylamine versus the initial differential selectivity for the unmodified catalysts shown in Figure 5-5. Thus, the improved selectivity behavior of the modified catalyst can not be solely explained by mass and heat transport limitation effects.

If modified nickel-on-carrier is used at the same conditions, again a rise in selectivity is observed (Figure 5-28). The benefit of the modification (from 84.1 mass-% to 92.1 mass-%) is even more impressive as in the case of Raney nickel. Decreased hydrogenation rates were observed again, if the
catalyst was modified (Table 5-4 and Figure 5-29). Plotting the relative initial reaction rates again shows a stronger deceleration of the reaction leading to dibutylimine.

Table 5-3: Influence of the modification strength on the initial reaction rates. Reaction conditions: 240 g BN, 3.75 g RaNi, 100°C, 1 MPa and 1000 rpm.

<table>
<thead>
<tr>
<th>modification</th>
<th>$-\frac{d[BN]}{dt}$ / [mmol/(s*kg)]</th>
<th>$\frac{d[BA]}{dt}$ / [mmol/(s*kg)]</th>
<th>$\frac{d[DBA]}{dt}$ / [mmol/(s*kg)]</th>
<th>$\frac{d[DBI]}{dt}$ / [mmol/(s*kg)]</th>
</tr>
</thead>
<tbody>
<tr>
<td>unmodified</td>
<td>118.656</td>
<td>82.612</td>
<td>3.199</td>
<td>14.258</td>
</tr>
<tr>
<td>1% CH$_2$O</td>
<td>82.262</td>
<td>59.926</td>
<td>2.322</td>
<td>8.194</td>
</tr>
<tr>
<td>2% CH$_2$O</td>
<td>42.310</td>
<td>31.967</td>
<td>1.034</td>
<td>3.633</td>
</tr>
<tr>
<td>3.5% CH$_2$O</td>
<td>18.743</td>
<td>13.771</td>
<td>0.455</td>
<td>1.835</td>
</tr>
<tr>
<td>5% CH$_2$O</td>
<td>12.233</td>
<td>8.806</td>
<td>0.314</td>
<td>1.276</td>
</tr>
</tbody>
</table>

Fig. 5-26: Influence of the formaldehyde modification of Raney nickel on the relative initial reaction rates. Reaction conditions: 240 g BN, 3.75 g RaNi, 100°C, 1 MPa and 1000 rpm.
Fig. 5-27: Initial differential selectivity versus product distribution (yield butylamine).

Fig. 5-28: Influence of the formaldehyde modification of nickel-on-carrier on the product distribution. Reaction conditions: 240 g BN, 10 g nickel-on-carrier, 100°C, 1 MPa and 1000 rpm.
Table 5-4: Influence of the formaldehyde modification of nickel-on-carrier on the initial reaction rates. Reaction conditions: 240 g BN, 10 g nickel-on-carrier, 100°C, 1 MPa and 1000 rpm.

<table>
<thead>
<tr>
<th>modification</th>
<th>-d[BN]/dt / [mmol/(s*kg)]</th>
<th>d[BA]/dt / [mmol/(s*kg)]</th>
<th>d[DBA]/dt / [mmol/(s*kg)]</th>
<th>d[DBI]/dt / [mmol/(s*kg)]</th>
</tr>
</thead>
<tbody>
<tr>
<td>unmodified</td>
<td>30.605</td>
<td>15.979</td>
<td>1.430</td>
<td>6.219</td>
</tr>
<tr>
<td>2.5% CH₂O</td>
<td>14.867</td>
<td>10.673</td>
<td>0.448</td>
<td>1.542</td>
</tr>
<tr>
<td>5% CH₂O</td>
<td>8.810</td>
<td>5.734</td>
<td>0.256</td>
<td>1.256</td>
</tr>
</tbody>
</table>

Fig. 5-29: Influence of the formaldehyde modification of nickel-on-carrier on the relative initial reaction rates. Reaction conditions: 240 g BN, 10 g nickel-on-carrier, 100°C, 1 MPa and 1000 rpm.
5.6 Reversibility of the hydrogenation steps

5.6.1 Disproportionation of butylamine

To investigate the reversibility of the hydrogenation steps, experiments using butylamine and dibutylimine as starting materials were carried out. In a first experiment, the conditions were identical with those used as standard conditions to hydrogenate butyronitrile (254 g BA, 24 g RaNi, 100 °C, 1 MPa, and 1000 rpm). The reaction profile is shown in Figure 5-30. The first derivation of the concentration profile results in the disproportionation rates of the primary amine at a given concentration. Using this experiment, the reversibility of the hydrogenation reaction leading from the primary amine to the secondary amine is proved. This experiment also shows that the amount of the primary amine obtained by the catalytic hydrogenation of

Fig. 5-30: Reaction profile using butylamine as starting material. Reaction conditions: 254 g BA, 24 g RaNi, 100 °C, 1 MPa and 1000 rpm.
butyronitrile with *Raney* nickel is mainly determined by the kinetics and not by the thermodynamics (equilibrium) of the process. This fact may also explain the obtained low selectivity of the third cycle when the recycling of the catalyst was investigated (*Figure 5-16*) or the low selectivity of the catalyst modified by 5% formaldehyde. If the hydrogenation is to slow, *i.e.* if the reaction time is to high, the obtained selectivity towards butylamine is not the maximum possible one (kinetic) but strives towards the much lower thermodynamically determined product distribution. This is shown in *Figure 5-31*.

![Graph showing the composition over time](image)

*Fig. 5-31:* Hydrogenation of butyronitrile (not stopped after full conversion). Reaction conditions: 240 g BN, 3.75 g RaNi, 100 °C, 1 MPa and 1000 rpm.

A second experiment was performed, using dibutylamine as starting material. 240 g DBA, 20 g RaNi and 30 g NH₃ were placed in the reactor. The stirrer speed was set at 1000 rpm and the temperature was 100°C. No reaction was observed, after 5000 min. The explanation for this behavior is, that the dibutylamine could not make sufficient contact with the catalytic surface of the wet catalyst.
5.6.2 Influence of reaction parameters on the disproportionation of butylamine

The influence of the temperature and the hydrogen pressure was investigated using the 35 ml reactors (see Chapter 9.1.4) and the procedure described in Chapter 9.2.2. The reactors were charged with high catalyst loadings, and the hydrogen was pressed into the reactor before heating. The pressure during the reaction was not recorded. It is evident, that the temperature has a great influence on the disproportionation rate (Figure 5-32).

![Diagram showing the influence of temperature on the disproportionation rate of butylamine.](image)

**Fig. 5-32:** Influence of the temperature on the disproportionation rate of butylamine. Reaction conditions: 20 g BA, 2 g RaNi, 280 min.\(^{-1}\) without hydrogen.

The hydrogen pressure also influences the disproportionation rate. Higher hydrogen pressures decrease the reaction to the secondary amine (Figure 5-33). A dehydrogenation of butylamine as the first step in the disproportionation mechanism could be an explanation for this behavior [41].

As mentioned above, a faster disproportionation of butylamine can decrease the high yield obtained under kinetic controlled conditions. This
Fig. 5-33: Influence of the hydrogen pressure on the disproportionation of butylamine. Reaction conditions: 20 g BA, 2 g RaNi, 120°C and 280 min$^{-1}$.

Fig. 5-34: Influence of the catalyst modification on the disproportionation of butylamine. Reaction conditions: 20 g BA, 2 g RaNi, 120°C and 280 min$^{-1}$. 
argumentation was also used to explain the lower selectivity, if a catalyst, modified by 5% formaldehyde was used. The influence of the catalyst modification by formaldehyde on the disproportionation rate is shown Figure 5-34.

5.6.3 Dibutylimine as starting material

Dibutylimine was synthesised from butylamine and butyraldehyde using an excess of butylamine. 174 g of the obtained solution, containing 69.5% dibutylimine (0.95 mol), 12.4% butylamine and 18.1% side products from the synthesis was used for the disproportionation study. The reaction conditions were: 3.79 g RaNi, 20 g NH₃ (1.18 mol), 100°C, 2 MPa, 1000 rpm. During the heating period dibutylimine already disappears and butyronitrile and butylamine are produced. This experiment shows that the hydrogenation of butyronitrile is reversible too. A second result is, that the

![Reaction profile using dibutylimine as starting material. Reaction conditions: 174 g DBI, 3.75 g RaNi, 20 g ammonia, 100°C, 2 MPa and 1000 rpm](image-url)
amount of dibutylimine is not decisively influencing the selectivity of this reaction, or in other words: the reaction rates transforming dibutylimine, butylamine and butylimine to the state of equilibrium are faster than the reaction rate of the hydrogenation of butylimine leading to butylamine (Figure 5-35).

5.7 Discussion

5.7.1 The bifunctional catalytic hydrogenation and its reversibility

The mechanism presented in Chapter 3.1 (Figure 3-1) postulates, that the selectivity of the hydrogenation of nitriles depends on two catalytic functions, an acidic and a hydrogenation function. The ratio and the distance between these two functions is assumed to determine the ratio of the reaction constants $k_{H4}/k_{C5}$ (in Figure 3-1) and therefore the yield of primary amine. Furthermore, the maximum produced amount of dibutylimine was observed to be higher than the produced amount of dibutylamine at full conversion, so that a reaction path from dibutylimine to butylamine is highly probable (see Figure 5-9, Figure 5-13 and Figure 5-31). From the experiments using dibutylimine and ammonia as starting material it is obvious, that high selectivities towards the primary amine can be obtained, even if the condensation products are already present in the reaction mixture. This leads to the conclusion, that dibutylimine is in a fast equilibrium with ammonia and a species that can be hydrogenated to the primary amine. In such disproportionation experiments with the butylamine or the condensation by-products as starting materials butyronitrile as intermediate is detected. This reveals the reversibility of the hydrogenation as well as the condensation steps. Depending on the reaction conditions applied, such reversible reaction systems can exhibit, as two extremes, a kinetically or a thermodynamically determined product distribution. The catalytic hydrogenation of the aliphatic butyronitrile is obviously such a reaction system with butylamine as the kinetically controlled product. Thus,
in order to optimize the selectivity towards butylamine, the reaction must be well monitored over time and immediately stopped after conversion has been completed. If the reaction proceeds beyond this time the butylamine disproportionates and the reaction strives towards a product distribution determined by the equilibrium. This, however, is unfavourable for a selective production of butylamine.

5.7.2 Influence of various reaction parameters on the selectivity

First attempts to get a qualitative understanding of the influence of various reaction parameters on the selectivity towards the desired primary amine failed due to the complexity of the hydrogenation system. Therefore, a simple semi-quantitative macro-kinetic model has been derived, with the help of which the complex selectivity behavior of the explored reaction system could more easily be characterised. For the sake of simplicity the rate constants of the adsorption and desorption steps of the various reaction components to and from the catalyst surface, respectively, has in each case been incorporated into the overall rate constant of the corresponding reaction step. The explanation of the effects of various reaction parameters such as the gas-liquid transfer limitation of hydrogen, the overall pressure, the temperature, the amount and recycling of catalyst and the presence of various additives on the yield of the desired butylamine led to the conclusion that all measured parameter effects can be explained if the following question can be answered: “What influence do the changes of the various reaction parameters exert on the local gradients of temperature and hydrogen concentration near the catalyst surface?” It has been shown (Chapter 5.4) that the selectivity towards butylamine increases if the local temperature increases (Chapter 5.4.2) or if the local hydrogen concentration decreases (Chapter 5.4.1). This can be rationalised with the help of the “quasi” Arrhenius plot (Figure 5-12) and the equation for the differential selectivity (Eq. 5.10) taking also into account aspects of mass and heat transfer effects (Chapter 5.3). The more these local gradients change by changing the reaction parameters the lower the influence on the selectivity
becomes. Therefore, the most favourable selectivity towards butylamine can be expected, if highly active catalysts are used and as a consequence, a temperature and mass diffusion limitation becomes dominant causing high local gradients.
Chapter 6

Modification of nickel catalysts by formaldehyde

6.1 General remarks

The modification mechanism of nickel or cobalt catalysts by formaldehyde is still unknown. The interaction of formaldehyde and/or products of its decomposition or polymerisation with the catalyst, produces a catalyst with different properties, thereby producing higher selectivities towards the primary amines, if nitriles are hydrogenated [1, 63, 64, 81]. One explanation for the interaction of formaldehyde and the nickel catalyst is a disproportionation of formaldehyde to methanol and carbon monoxide (Eq. 6.1).

\[
2 \text{CH}_2\text{O} \rightarrow \text{CH}_3\text{OH} + \text{CO} \quad \text{Eq. 6.1}
\]

The formed methanol desorbs from the catalyst while carbon monoxide is still adsorbed on the catalysts surface as Ni\text{\textsubscript{y}}(CO)\text{\textsubscript{y}}. This mechanism would be in agreement with reported results, where the interaction of formaldehyde with Ni(110) surfaces was investigated at low temperatures (95 K) by Richter and Ho [82]. Formaldehyde reacts on the catalysts surface, producing a mixed CH\textsubscript{3}O and CO adlayer on the surface (Eq. 6.2).

\[
\text{CH}_2\text{O} + \text{CH}_2\text{O} \rightarrow \text{CH}_3\text{O}(a) + \text{CO}(a) + \text{H}(a) \quad \text{Eq. 6.2}
\]

The adsorbed species that arised due to the adsorption and thermal processing of CH\textsubscript{2}O on Ni(110) were summarised in Eq. 6.3-Eq. 6.7. Mixed
paraformaldehyde and solid H$_2$CO multilayers were formed at high formaldehyde exposures.

\[
\text{CH}_2\text{O}(g) \rightarrow \text{CO}(a) + 2 \text{H}(a) \quad \text{Eq. 6.3}
\]

\[
2 \text{CH}_2\text{O}(g) \rightarrow \text{CH}_3\text{O}(a) + \text{CO}(a) + \text{H}(a) \quad \text{Eq. 6.4}
\]

\[
n \text{CH}_2\text{O}(g) \rightarrow (\text{CH}_2\text{O})_n(a) \quad \text{Eq. 6.5}
\]

\[
(\text{CH}_2\text{O})_n(a) \rightarrow \text{HCOO}(a) + \text{CH}_3\text{O}(a) + \text{CO}(a) + \text{H}(a) + \text{CH}_x(a) + \text{CH}_2\text{O}(g) \quad \text{Eq. 6.6}
\]

\[
\text{CH}_3\text{O}(a) \rightarrow \text{CO}(a) + 3 \text{H}(a) \quad \text{Eq. 6.7}
\]

If the catalyst was heated after the formaldehyde treatment, methanol desorbed from the catalyst at temperatures of about -10°C, carbon monoxide desorbed at temperatures above 174°C.

Newton and Dodge [83] investigated the equilibrium constants between carbon monoxide, hydrogen, formaldehyde and methanol (Eq. 6.8 and Eq. 6.9).

\[
\text{CO} + \text{H}_2 \leftrightarrow \text{CH}_2\text{O} \quad \text{Eq. 6.8}
\]

\[
\text{CH}_2\text{O} + \text{H}_2 \leftrightarrow \text{CH}_3\text{OH} \quad \text{Eq. 6.9}
\]

The scope of their work was to investigate, if it is possible to produce formaldehyde by hydrogenation of carbon monoxide. One of the results was, that nickel catalysts promote the decomposition of formaldehyde into carbon monoxide and hydrogen. At 200°C and 0.1 MPa the equilibrium constants were $K_1 = 2.30 \times 10^{-5}$ (Eq. 6.8) and $K_2 = 1800$ (Eq. 6.9). The conclusion was, that the production of formaldehyde from carbon monoxide by hydrogenation is not feasible at any reasonable temperature or pressure.

Several investigations concerning the chemisorption of CO on different Ni surfaces were recently made [84-87]. Especially the adsorption mode
was investigated, thereby two species were observed: Bridged CO and on-top or terminal CO. Both species coexist and are in an equilibrium depending on pressure (surface coverage) and temperature. The desorption temperature is in the range of 170°C.

The washing operations as well as the formaldehyde treatment were made in a three-neck sulfonation flask (see Chapter 9.1.5) as described in Chapter 9.2.7-9.2.10.

Modification experiments were usually made, using the procedures of Degischer and Rössler [1, 63]. A 5% formaldehyde modification of a Raney catalyst means, that X g Raney nickel are modified by 2X g of an aqueous solution containing 5% formaldehyde (normal procedure: 50 g Raney nickel in 100 g aqueous solution, that contains 5 g formaldehyde).

Methanol (by headspace-GC), formaldehyde (by HPLC) and the nickel concentration (by XRF) were determined in the aqueous modification solution after a modification time of 30 min.

6.2 Influence of the treatment with different solvents on the properties of the catalyst

6.2.1 Reduction potential

The standard reduction potential of fresh, water washed, alcohol and formaldehyde modified catalysts was measured as described in Chapter 9.5.1. The potential of the fresh and the water washed catalyst is in a range of -0.6 V indicating that the water washing does not change the properties of the catalyst. This observation is in agreement with the results of the nitrile hydrogenation (see Figure 5-19 and Figure 5-20). The potential of the methanol, ethanol and formaldehyde modified catalyst is in a range of -0.3 V, indicating that these substances do change the catalysts properties. In addition, if the fresh catalyst was washed with water or methanol, no nickel was found in the washing solutions.
6.2.2 Adsorption of an indicator

In order to get some information about the influence of the modification treatments on the acid sites activity the adsorption capacity for 4-aminoazobenzene was determined for fresh, water washed, methanol and formaldehyde modified catalysts as described in Chapter 9.5.2. Four measurements were carried out. Figure 6-2 reveals that the acid activity of the catalysts does depend on the modification treatment applied. However, no simple correlation between these measurements and the selectivity data was found.

Fig. 6-1: Standard reduction potential of fresh and modified catalysts determined with a combined gold electrode.
6.3 Modification of Raney nickel by various formaldehyde concentrations

6.3.1 Analysis of the modifying solution

Different formaldehyde concentrations were used (1%, 2%, 3.5%, 5% and 7% in water), while the mass of catalyst and the mass of the aqueous solution were not varied (50 g wet Raney nickel and 100 g solution). The methanol, formaldehyde (which was not converted during the modification) and residual formaldehyde amounts are plotted in Figure 6-3. At low formaldehyde concentrations, formaldehyde disappears completely, at higher concentrations not all formaldehyde is consumed. A remarkable result is, that the amount of methanol corresponds to the half amount of the consumed formaldehyde at low modification concentration (Table 6-1). In this table, the mass balance of the modification procedure is given, as well as the division of methanol found by the residual mass in [mmol CH₂O] that was not found. At low concentrations, the stoichiometry of methanol and
Fig. 6-3: Amount of methanol, formaldehyde and residual mass in the modifying solution at various modification conditions. Reaction conditions: 50 g Raney nickel modified in total 100 g aqueous solution.

Table 6-1: Mass balance of the catalyst modification by various formaldehyde concentrations. Initial formaldehyde, not converted formaldehyde and methanol determined in the modification solution and the residual mass (volume: 100 ml).

<table>
<thead>
<tr>
<th>initial CH$_2$O</th>
<th>CH$_2$O measured / [mmol]</th>
<th>MeOH measured / [mmol]</th>
<th>residual MeOH / [mmol]</th>
<th>MeOH/residual CH$_2$O / [-]</th>
<th>hydrogen needed to produce MeOH / [ml/g cat]</th>
</tr>
</thead>
<tbody>
<tr>
<td>33.9</td>
<td>0.0</td>
<td>17.0</td>
<td>17.0</td>
<td>1.00</td>
<td>7.6</td>
</tr>
<tr>
<td>68.0</td>
<td>0.0</td>
<td>29.4</td>
<td>38.6</td>
<td>0.76</td>
<td>13.2</td>
</tr>
<tr>
<td>118.1</td>
<td>5.9</td>
<td>51.6</td>
<td>60.7</td>
<td>0.85</td>
<td>23.1</td>
</tr>
<tr>
<td>169.2</td>
<td>11.7</td>
<td>87.3</td>
<td>70.2</td>
<td>1.24</td>
<td>39.5</td>
</tr>
<tr>
<td>237.0</td>
<td>66.4</td>
<td>87.6</td>
<td>83.0</td>
<td>1.06</td>
<td>39.2</td>
</tr>
</tbody>
</table>
residual mass is 1, indicating that formaldehyde reacts according Eq. 6.1 to methanol and carbon monoxide. The last row of the table, describes the hydrogen, that would be needed to produce the measured methanol from formaldehyde by direct hydrogenation. This value was 39 ml hydrogen per g catalyst at high modification concentrations. Literature values for the hydrogen content stored on Raney nickel are about 20 ml/g, so that not enough hydrogen is stored on the catalyst to produce the methanol measured in the modification solution [45].

The nickel concentration in the liquid phase after modification is shown in Figure 6-4. The higher the formaldehyde concentration is, the higher is the nickel amount removed from the catalyst. There exists almost a linear correlation between the modification concentration and the leached nickel.

![Graph](image.png)

**Fig. 6-4:** Concentration of leached nickel in the modifying solution determined by XRF. Reaction conditions: 50 g Raney nickel in total 50 g aqueous solution.
6.3.2 Properties of the modified catalysts

The standard reduction potential of the modified catalysts are presented in Figure 6-5. The potential is higher, if the catalyst is modified by formaldehyde. A value of -0.35 V is obtained for catalyst, treated by high formaldehyde concentrations.

The stability against acidic attack is shown in Figure 6-6. The fresh catalyst is completely dissolved in hydrochloric solution, while the 7.5% formaldehyde modified catalyst at these conditions is stable and almost releases no hydrogen.

Fig. 6-5: Standard reduction potential of Raney nickel modified by various formaldehyde concentrations determined with a combined gold electrode.
6.4 Modification of various amounts of Raney nickel at constant modification strength

6.4.1 Analysis of the modifying solution

Different catalyst amounts (12.5 g, 25 g, 37.5 g, 50 g, 75 g and 100 g) were used while the formaldehyde concentration and the mass of the aqueous solution were constant (113 g of a 4.5% formaldehyde solution). The methanol and residual formaldehyde amounts are plotted in Figure 6-7. The amount of disappeared formaldehyde, that is not found as methanol in the liquid phase is plotted as residual mass. At low catalyst amounts, not all the formaldehyde reacts. At higher catalyst amounts, all formaldehyde disappears. The same calculation as in Chapter 6.3 was made again and the results are listed in Table 6-2. At high catalyst masses (low formaldehyde concentration / catalyst ratio), the stoichiometry between methanol found in
Fig. 6-7: Amount of methanol, formaldehyde and residual mass found in the modifying solution. Reaction conditions: 113 g of an aqueous solution containing 4.5% formaldehyde.

Table 6-2: Mass balance of the catalyst modification by various catalyst amounts. Mass of catalyst used, not converted formaldehyde and methanol determined in the modification solution and the residual mass (initial formaldehyde amount 169.2 mmol, volume: 113 ml).

<table>
<thead>
<tr>
<th>catalyst amount / [g]</th>
<th>CH$_2$O measured / [mmol]</th>
<th>MeOH measured / [mmol]</th>
<th>residual / [mmol CH$_2$O]</th>
<th>MeOH/residual / [-]</th>
<th>hydrogen needed to produce MeOH / [ml/g cat]</th>
</tr>
</thead>
<tbody>
<tr>
<td>12.5</td>
<td>119.2</td>
<td>14.2</td>
<td>35.9</td>
<td>0.39</td>
<td>25.1</td>
</tr>
<tr>
<td>25</td>
<td>92.9</td>
<td>30.8</td>
<td>45.4</td>
<td>0.68</td>
<td>27.2</td>
</tr>
<tr>
<td>37.5</td>
<td>47.7</td>
<td>55.1</td>
<td>66.5</td>
<td>0.83</td>
<td>33.0</td>
</tr>
<tr>
<td>50</td>
<td>49.6</td>
<td>57.2</td>
<td>62.6</td>
<td>0.91</td>
<td>25.5</td>
</tr>
<tr>
<td>75</td>
<td>0</td>
<td>86.5</td>
<td>82.7</td>
<td>1.05</td>
<td>25.84</td>
</tr>
<tr>
<td>100</td>
<td>0</td>
<td>86.9</td>
<td>82.5</td>
<td>1.05</td>
<td>19.5</td>
</tr>
</tbody>
</table>
the solution and residual mass is almost 1, at low amounts of catalyst, the stoichiometry is far from 1.

The nickel concentration in the liquid phase after modification is shown in Figure 6-8. The more catalyst being present in the modifying system, the more nickel is leached from the catalyst.

![Graph showing concentration of leached nickel](image)

**Fig. 6-8:** Concentration of leached nickel in the modifying solution determined by XRF. Reaction conditions: 113 g of an aqueous solution containing 4.5% formaldehyde modifying various amounts of catalyst.

### 6.4.2 Properties of the modified catalysts

The standard reduction potential of the modified catalysts is plotted in Figure 6-9. The amount of hydrogen which is released if the catalyst is attacked by hydrochloric acid is shown in Figure 6-10. If the formaldehyde modification is carried out with small amounts of catalyst the released hydrogen remains the same.
Fig. 6-9: Standard reduction potential of various catalyst amounts modified by a 4.5% formaldehyde solution.

Fig. 6-10: Hydrogen evolved from differently modified catalysts after treatment with hydrochloric acid. Reaction conditions: 1 g Raney nickel dissolved in 70 g of a 10% hydrochloric acid.
6.5 Modification of nickel-on-carrier

The modification procedure was not only investigated using Raney catalysts, but also using a nickel-on-carrier as hydrogenation catalyst. If the catalyst was modified by a 5% formaldehyde solution (169 mmol formaldehyde), not all formaldehyde was consumed (Table 6-3). If unmodified catalyst is washed with water, no nickel is leached from the catalyst (< 10 ppm). However, if the catalyst was modified by formaldehyde, a concentration of 463 ppm nickel was found in the modification solution.

Table 6-3: Mass balance of the modification of nickel-on-carrier. Mass of catalyst used, formaldehyde and methanol determined in the modification solution and the residual mass.

<table>
<thead>
<tr>
<th>catalyst amount / [g]</th>
<th>CH$_2$O measured / [mmol]</th>
<th>MeOH measured / [mmol]</th>
<th>residual MeOH / [mmol CH$_2$O]</th>
<th>MeOH/ residual</th>
<th>hydrogen needed to produce MeOH / [ml / g cat]</th>
</tr>
</thead>
<tbody>
<tr>
<td>50</td>
<td>113.3</td>
<td>19.8</td>
<td>36.0</td>
<td>0.55</td>
<td>8.8</td>
</tr>
</tbody>
</table>

6.6 Discussion

The first conclusion which can be drawn from modification experiments with formaldehyde is that changes of the catalyst properties due to water washing operations before and after the modification by formaldehyde can be excluded.

Up to 50% of the formaldehyde used to modify the catalyst can be found as methanol in the solution. If modification conditions were used whereby more than 50 g catalyst amount and a formaldehyde concentration of 1 mass-% were applied almost exactly 50% were found as methanol. This is an indication that the reaction of formaldehyde to methanol together with
an adsorbed species occurs. The catalyst does not store enough hydrogen to hydrogenate formaldehyde to the produced amount methanol. Therefore, this additional hydrogen has to be taken from somewhere else presumably from formaldehyde itself or from the solvent. These facts are strong indications that formaldehyde reacts according to Eq. 6.1 at low concentrations of formaldehyde and high amounts of catalyst. The production of chemisorbed carbon monoxide would also explain the effect of other modifiers, such as acetaldehyde, benzaldehyde, carbon dioxide, acetone and carbon monoxide itself that were described in the patent [1]. From all these modifiers, carbon monoxide could be produced on the surface of the catalyst.

The effect of chemisorbed carbon monoxide on the hydrogenation of nitriles could be explained by stereochemical restrictions. Carbon monoxide blocks metal sites on the catalyst, so that larger substrates (dialkylimines) can not adsorb as easily as smaller substrates (alkylimines). Tributylamidine was observed as by-product if modified catalysts were used to hydrogenate butyronitrile. One explanation for the formation of this product, is that this large molecule can not be hydrogenated to tributylamine at the chosen conditions because of stereochemical reasons.

Large amounts of nickel can be found in the modification solution, an important fact, if modifications have to be made on a larger scale. The minimization of this nickel leaching during the modification procedure and also during the hydrogenation reaction is evidently important for the preparation of large amounts of catalyst.

The catalysts treated by high formaldehyde concentrations are almost stable in hydrochloric acid, while a fresh catalyst is completely dissolved in a short time.
Chapter 7

Effect of formaldehyde modified nickel catalysts on other chemical systems

Formaldehyde modified nickel catalysts have revealed an unexpected and positive selectivity effect on the hydrogenation of nitriles (Chapter 5.5). The exact reason for this observation is not yet known and its investigation shall be the aim of future research studies. In order to examine whether these new catalysts also bring about such selectivity effects in other well known hydrogenation processes, in this Chapter some typical hydrogenations were screened.

7.1 Hydrogenation of crotonaldehyde

7.1.1 General remarks

The hydrogenation of $\alpha,\beta$-unsaturated aldehydes is still a challenging field of investigation. The desired $\alpha,\beta$-unsaturated alcohol is not the thermodynamic product, and therefore, the saturated aldehyde is preferably formed. A change of the selectivity has to be achieved by a change of the reaction rate constants of the competitive reactions and of the competitive adsorption constants of the components. The catalytic system that produces the highest selectivities are Pt/TiO$_2$, Pt/SiO$_2$, doped by different transition metals or modifiers [88-91]. Selectivities up to 50% were achieved if crotonaldehyde was hydrogenated in ethanol. NiPt/SiO$_2$ catalysts were also tested, but produced only small amounts of the desired alcohol [92].
Selectivities up to 85% towards the unsaturated alcohol can be achieved using bimetallic Ag/SiO₂ catalysts [93, 94] or Ru/SiO₂ catalysts [95, 96].

Investigations on the influence of the catalyst modification on the hydrogenation of α,β-unsaturated aldehydes were performed in a system of crotonaldehyde and ethanol as solvent. A scheme of the reaction system is given in *Figure 7-1*. E/Z crotonaldehyde reacts to butanal over butanal or over E/Z crotylalkohol as intermediate.

![Reaction Scheme](image)

**Fig. 7-1:** Hydrogenation of E/Z crotonaldehyde to butanol over the intermediates butanal or E/Z crotylalkohol.

Experiments were made in a 500 ml steel hydrogenator (see Chapter 9.1.1) according the procedure described in Chapter 9.2.3, and samples were taken according the procedure in Chapter 9.2.6. 1,1-diethoxybutane was observed as by-product (*Figure 7-2*) or even as main product, in cases that Raney nickel was modified by formaldehyde. This product is formed in an acid catalysed side reaction via the semiacetal by addition of the solvent and subsequent dehydration [90].
Fig. 7-2: 1,1-diethoxybutane was formed as by-product, if crotonaldehyde was hydrogenated.

7.1.2 Test for a possible gas-liquid transfer limitation for hydrogen

To investigate whether a gas-liquid transfer limitation for hydrogen exists at the chosen reaction conditions, the amount of catalyst was doubled (40 g E/Z crotonaldehyde, 200 g ethanol, 30°C, 1 MPa overall pressure and 1000 rpm). As can be seen in Table 7-1 and Figure 7-3 the reaction rate increases as the catalyst amount was raised, so that a transfer limitation can be excluded.

Table 7-1: Influence of the catalyst amount on the initial reaction rates, if E/Z crotonaldehyde is hydrogenated. Reaction conditions: 40 g E/Z crotonaldehyde, 200 g ethanol, 30°C, 1 MPa and 1000 rpm.

<table>
<thead>
<tr>
<th>catalyst amount / [g]</th>
<th>initial disappearance rate of crotonaldehyde / [mmol/s]</th>
<th>initial production rate of butanol / [mmol/s]</th>
</tr>
</thead>
<tbody>
<tr>
<td>2</td>
<td>0.193</td>
<td>0.0024</td>
</tr>
<tr>
<td>4</td>
<td>0.395</td>
<td>0.0049</td>
</tr>
</tbody>
</table>
7.1.3 Influence of the formaldehyde modification of Raney nickel on the hydrogenation of crotonaldehyde

Modification of Raney nickel with formaldehyde leads to a lower disappearance rate of crotonaldehyde and a lower production rate for butanol (*Figure 7-4* and *Figure 7-5*). Butanal is the only observed intermediate, no crotylalkohol was observed during the reaction. If the catalyst is modified using a 5% formaldehyde solution, condensations take place and 1,1-diethoxybutane is observed as main product.
Fig. 7-4: Influence of the modification strength of the catalyst on the crotonaldehyde disappearance rate. Reaction conditions: 40 g crotonaldehyde, 2 g RaNi, 30°C, 1 MPa and 1000 rpm.

Fig. 7-5: Influence of the modification strength of the catalyst on the product distribution and formation rate. Reaction conditions: 40 g crotonaldehyde, 2 g RaNi, 30°C, 1 MPa and 1000 rpm.
7.1.4 Influence of the formaldehyde modification of nickel-on-carrier on the hydrogenation of crotonaldehyde

The influence of the modification by formaldehyde on the selectivity and activity was also investigated using a nickel-on-carrier catalyst. The behavior of the system was as in the case of Raney nickel (Figure 7-6). The modification lowers the hydrogenation rate of crotonaldehyde if formaldehyde concentrations above ca. 2.5% for the modification were used. No 1,1-diethoxybutane was observed as by-product using this catalyst.

Fig. 7-6: Influence of the modification of a nickel-on-carrier catalyst on the reaction rates. Reaction conditions: 40 g crotonaldehyde, 4 g nickel-on-carrier, 30°C, 1 MPa and 1000 rpm.
7.2 Hydrogenation of 1-bromo-4-nitrobenzene

7.2.1 General aspects

Several possibilities exist to reduce nitroaromatic compounds. The Béchamps-reduction, the reduction using other metals than iron, the reduction by sulphides, electrochemical reductions or the reduction using hydrazine [97].

The hydrogenation of nitroarenes, especially of halide substituted arenes using Raney nickel as catalyst is of industrial interest [98]. One of the problems thereby is the dehalogenation of the substrate or product. Therefore, there was some hope that the newly discovered formaldehyde

![Reaction scheme](image-url)
modified catalyst might prevent the undesired dehalogenation. The hydrogenation of a halide substituted nitroarene was investigated using the substrate 1-bromo-4-nitrobenzene. A reaction scheme is given in Figure 7-7. The experiments were made in a 200 ml glass hydrogenator (Chapter 9.1.2) according the procedure described in Chapter 9.2.4. After a modification procedure the catalyst was washed three times with tetrahydrofuran (Chapter 9.2.9). The reaction conditions were: 0.5 g Raney nickel, 10 g 1-bromo-4-nitrobenzene, 90 g THF, 50°C, 0.5 MPa and 1500 rpm.

7.2.2 Test for a possible gas-liquid transfer limitation for hydrogen

To check whether an influence of the gas-liquid transfer limitation for hydrogen exists, the hydrogenation rate was doubled by using twice the amount of the catalyst (Table 7-2). This is an indication that no limitation for hydrogen exists. In addition, if the catalyst was not washed with tetrahydrofuran, no reproducible reaction rates were obtained.

<table>
<thead>
<tr>
<th>Raneynickel initial hydrogen</th>
<th>initial hydrogenation rate</th>
<th>1-bromo-4-aminobenzene</th>
<th>aniline</th>
</tr>
</thead>
<tbody>
<tr>
<td>amount / [g]</td>
<td>uptake / [mmol/s]</td>
<td>/ [mmol/(s*kg)]</td>
<td>/ [mass-%]</td>
</tr>
<tr>
<td>0.48</td>
<td>0.011</td>
<td>22.2</td>
<td>99.3</td>
</tr>
<tr>
<td>1.00</td>
<td>0.028</td>
<td>28.0</td>
<td>98.5</td>
</tr>
</tbody>
</table>
7.2.3 Influence of the modification on selectivity and reaction rates

The selectivity towards 1-bromo-4-aminobenzene is lower if the catalyst is modified by formaldehyde and higher again, at high modification concentrations of formaldehyde (Figure 7-8). A systematic prevention of the dehalogenation was not observed. A loss of activity was observed, as it is demonstrated in Figure 7-9 and Table 7-3.

![Graph showing the influence of modification on selectivity and reaction rates]

**Fig. 7-8:** Influence of the modification of Raney nickel by formaldehyde on the hydrogenation of 1-bromo-4-nitrobenzene. Reaction conditions: 10 g 1-bromo-4-nitrobenzene, 90 g THF, 60°C. 0.5 MPa and 1500 rpm.
Fig. 7-9: Hydrogen uptake (from a 37.5 ml storage vessel thermostated at 25°C) of modified Raney nickel. Reaction conditions: 10 g 1-bromo-4-nitrobenzene, 90 g THF, 60°C. 0.5 MPa and 1500 rpm.

Table 7-3: Summary of the influence of formaldehyde modified Raney catalysts on the initial hydrogenation rate and the selectivity towards 1-bromo-4-aminobenzene.

<table>
<thead>
<tr>
<th>modification</th>
<th>initial hydrogenation rate / [-]</th>
<th>1-bromo-4-aminobenzene / [mass-%]</th>
<th>aniline / [mass-%]</th>
</tr>
</thead>
<tbody>
<tr>
<td>unmodified</td>
<td>22.2</td>
<td>99.3</td>
<td>0.7</td>
</tr>
<tr>
<td>1% CH₂O</td>
<td>11.5</td>
<td>98.5</td>
<td>0.5</td>
</tr>
<tr>
<td>2% CH₂O</td>
<td>7.8</td>
<td>98.4</td>
<td>1.6</td>
</tr>
<tr>
<td>3.5% CH₂O</td>
<td>7.5</td>
<td>98.6</td>
<td>1.4</td>
</tr>
<tr>
<td>5% CH₂O</td>
<td>4.8</td>
<td>99.4</td>
<td>0.6</td>
</tr>
</tbody>
</table>
7.3 Hydrogenation of levodione

7.3.1 General remarks

The low pressure hydrogenation of levodione ((6R)-2,2,6-trimethylcyclohexa-1,4-dione) to actinol ((4R,6R)-4-hydroxy-2,2,6-trimethylcyclohexanone) is an important industrial process. Thereby, the R,R isomer is the desired product [99, 100]. A scheme of the reaction is given in Figure 7-10.

![Reaction scheme for the hydrogenation of levodione to R,R- or R,S-actinol.](image)

The reaction was carried out in a 100 ml three-neck sulphonation flask (Chapter 9.1.3) according the described procedure in Chapter 9.2.5. The catalyst was washed three times with methanol (Chapter 9.2.8) before the reaction was started. The reaction conditions were: 10 g levodione, 50 g MeOH, 25°C, 0.11 MPa and 600 rpm.

7.3.2 Test for a possible gas-liquid transfer limitation for hydrogen

To check a possible influence of a transfer limitation on the hydrogenation rate, the hydrogen uptake was monitored for two different catalyst amounts (4 and 6 g Raney nickel). The reaction conditions were: 10 g levodione, 50 g methanol, 25°C, 0.11 MPa and 600 rpm. The initial hydrogen uptake was 0.071 bar/(min*g) (4 g catalyst) and 0.10 bar/(min*g) (6 g catalyst), respectively. Thus, a gas-liquid transfer limitation for hydrogen can be
excluded, as the rate is linearly proportional to the amount of the catalyst used.

7.3.3 Influence of the modification on selectivity and hydrogenation rate

The influence of a modification by formaldehyde on the selectivity towards the desired isomer and the hydrogenation rate was investigated using unmodified and differently modified Raney catalysts. The influence on the hydrogen uptake is plotted in Figure 7-11. The formaldehyde modified catalysts have less activity than the unmodified. The selectivity towards the desired R, R-actinol is shown in Figure 7-12. A higher selectivity towards
Selectivity of the hydrogenation of levodione using differently modified Raney catalysts. Reaction conditions: 10 g levodione, 4 g catalyst, 50 g MeOH, 25°C, 0.11 MPa and 600 rpm.

R,R-actinol was not observed. The reported selectivity of 80-85% R,R-actinol [99] could not be confirmed, even not if fresh catalysts were used. The distribution of R,R-actinol and R,S-actinol is about 1:1. The possible isomerisation of the hydrogenation products, can be explained either by the sodium hydroxide present in the catalyst or by residual acid in the levodione. Both, acid as well as base, catalyse the isomerisation of the product.

7.4 Discussion

The hydrogenation of other substances than nitriles was performed to find other potential applications for formaldehyde treated nickel catalysts. These systems were screened without a profound study of the reaction mechanism.
The modification of nickel catalysts by formaldehyde has no benefit with respect to a selective hydrogenation of crotonaldehyde. The desired crotylalkohol is not preferentially produced using the modified catalyst. The modification only lowers the hydrogenation rates and causes undesired by-products formed by condensation reactions on the catalyst.

If a halogenated nitrobenzene is hydrogenated, a modification by formaldehyde does not systematically inhibit the dehalogenation. However, a decrease in activity was observed.

The hydrogenation of levodione using formaldehyde treated catalysts does not improve the yield to the desired R,R-actinol. Only a decreased activity was observed.

Summing up, until now no other hydrogenations than that of nitriles were found for which a modification of the nickel catalysts by formaldehyde has been beneficial.
Chapter 8

Conclusions and outlook

The modification of Raney nickel by formaldehyde leads to higher selectivities towards the primary amines, also in cases that aliphatic nitriles are hydrogenated. Up to 50% of the formaldehyde used to modify the catalyst were found as methanol in the modification solution. A possible explanation for this behavior is that formaldehyde disproportionates at the catalyst to methanol and chemisorbed carbon monoxide.

If amines have to be produced from nitriles at large scale, several points have to be thoroughly considered to produce high selectivities:

• The reaction time until the hydrogenation is finished has to be known, so that the reaction mixture can be cooled immediately after full conversion (kinetically controlled product distribution) to avoid disproportionation reactions, that lower the selectivity (thermodynamically controlled product distribution).

• Low hydrogen pressures favour the production of primary amines, thus a hydrogenation in the gas-liquid transfer limitation for hydrogen (high catalyst loadings) may be favorable.

• The modification of catalysts by formaldehyde offers a new way to increase the selectivity towards primary amines, especially in cases that aromatic nitriles are hydrogenated. In order to find the optimal modification concentration investigations have to be performed because desired higher selectivities are also accompanied by undesired lower reaction rates.

• An optimal temperature has to be found, because high temperatures lead to higher selectivities towards primary amines (higher activation energy of the hydrogenation to the primary amine than of the hydrogenation to the secondary amine), but disproportionation reactions leading to the
product distribution determined by the thermodynamic equilibrium can lower the selectivity at high temperatures [27].
Experimental

9.1 Apparatus

9.1.1 Description of the 500 ml steel hydrogenator

Hydrogenations of butylamine and crotonaldehyde were carried out in a 500 ml hardening vessel (built by F. Hoffmann-La Roche, Figure 9-1). The apparatus is designed to withstand a maximum pressure of 10 MPa and a maximal temperature of 200°C. The autoclave is equipped with a four-bladed agitator that can be rotated at rates between 10 and 2000 rpm.

The reactor can be operated at temperatures between 20 and 200°C. The heating is electrical and cooling is achieved using cooling water at 15°C.

The autoclave consists of a reaction vessel and a cap, both made of rust-resistant steel (W. No. 1.4435). A silverseal and 8 screws ensure tightness. The cap has 7 boreholes (Figure 9-2), and within a central bore for the agitator shaft (1). Hydrogen is introduced from the side via the cap. Samples can be taken via valve 4 (Nova Swiss).

Liquid or gaseous starting products are added via valve 7 (Nova Swiss). The temperature is measured with a type PT100 sensor (range: -100 to 400°C, precision: ±0.33%) manufactured by Rotax. This sensor is positioned in borehole 2. The temperature is controlled by cascade regulation.

The pressure in the autoclave is measured with a piezometer PA-23 100 (range: 0.1 to 10 MPa, precision: ±0.05 MPa) manufactured by Rotax (8). The pressure in the hydrogen storage vessel is measured using a piezometer PA-23 200 (range: 0.1 to 20 MPa, precision ±0.1 MPa) also manufactured by Rotax. A bursting disk (Sitec) is also installed (bursting pressure: 11 MPa)
Fig. 9-1: Hydrogenation apparatus.

±10%) in the cap (9). The autoclave pressure can be released by a valve (3, Sitec). Nitrogen is fed to the autoclave via valve 6 (Nova Swiss). The remaining holes (5 and 7) were not used and were therefore fitted with blind flanges.
9.1.2 200 ml glass hydrogenator

A 200 ml glass hydrogenation vessel from Büchi AG (max. pressure 1 MPa, max. temperature 200°C) was mounted on an apparatus containing a Büchi Cyclo 075 stirrer (max. speed 3000 rpm), a PA-23 10 piezometer (Rotax, range 0.1 to 1 MPa), a PT 100 B (Rotax, -100 to 400°C, ±0.33%) and a bursting disk (Sitek, 1 MPa bursting pressure). Two hydrogen storages, thermostated at 25°C with a Lauda E 100 thermostat, were used (5 ml and 50 ml, total hydrogen storage volume inclusive pipes: 73.5 ml) during the reaction. The glass hydrogenator was thermostated with a Lauda E 200 thermostat. The reaction data were stored in a Eurotherm Chessel 4100 G.

9.1.3 100 ml low pressure hydrogenation apparatus

A three-neck sulphonation flask, equipped with a glass thermometer and a gas inlet (inlet of argon, hydrogen and pressure release on the same pipe) was mounted on a stirrer system (the third hole was fitted with a blind flange). A Julabo PC/4 thermostat was used to control the reaction.
temperature. The hydrogen uptake was monitored by a W+W recorder 312 from Kontron AG attached to a piezometer in the storage vessel. A bursting disk (Sitek) was installed with a bursting pressure of 0.07 MPa.

9.1.4 Lab Shaker

A Lab Shaker from Kühner AG with 35 ml hydrogenation reactors (built by F. Hoffmann-La Roche) was used to perform the reversibility experiments. These autoclaves were equipped with a bursting disk (30 MPa) and a valve. A shaking frequency of 280 min⁻¹ on 25 mm was applied.

9.1.5 Modification and washing apparatus

Modification and washing procedures were carried out in a three-neck sulphonation flask, equipped with a nitrogen intake and an outlet connected to a bubble counter. A glass stirrer driven by a motor was installed in the central grinding. If the catalyst was modified, a dropping funnel was installed in the last vent, otherwise this vent was provided with a blind plug.

9.1.6 Gas chromatograph

An HP 6890 Series GC System with an HP 7683 Series Injector autosampler was used. A flame ionisation detector was used for normal measurements. An HP 5973 Mass Selective Detector was used for gas chromatography with mass spectroscopic detection. HP ChemStation software, version Rev.A. 06.03 [509] was used to control and analyse the measurements. By aid of this program an analysis method was developed [101-103].
9.2 Methods

9.2.1 Hydrogenation of butyronitrile

240 g (3 mol) butyronitrile were placed in the 500 ml steel autoclave (Chapter 9.1.1) before the catalyst (if Raney nickel was used, the catalyst was added as wet paste) was added. The autoclave was sealed and purged three times with 0.55 MPa nitrogen. The reactor was then heated while the content was stirred slowly (600 rpm). Once the reaction temperature had been reached, the stirrer was turned off and hydrogen was pressed into the autoclave. The reaction was initiated by turning on the stirrer. Samples were taken during the hydrogenation (Chapter 9.2.6).

After the reaction was completed, the reaction vessel was cooled to room temperature, the pressure released and the vessel purged three times with 0.55 MPa nitrogen. The reaction mixture was sucked off by a vacuum pump and then filtered. The autoclave and the filtering apparatus were purged with methanol. To clean the autoclave, the vessel was filled with methanol which then was boiled at 80°C for 15 min.

The Raney nickel was disposed into a special nickel waste jar and the reaction mixture in a solvent waste jar.

9.2.2 Reversibility experiments in the 35 ml screening autoclave

20 g butylamine (0.27 mol) were placed in a 35 ml screening hydrogenator before 2 g of wet Raney nickel catalyst were added. The hydrogenator was then closed and purged three times with 4.2 barg nitrogen. Ammonia or hydrogen were then added via the valve on the autoclave. The autoclave was placed in the Lab Shaker and heated to reaction temperature while being shaken at 280 min⁻¹.

After a defined reaction time the screening hydrogenator was placed in a cooling block (copper block cooled by water), the pressure was released, the reactors were again purged three times with 4.2 barg nitrogen and then
opened. The content of the reactors was flushed out with methanol. The reaction mixture was then filtered and analysed.

9.2.3 Hydrogenation of crotonaldehyde

40 g (0.57 mol) butyronitrile and 200 g ethanol were placed in the 500 ml steel autoclave (Chapter 9.1.1) before the catalyst (if Raney nickel was used, the catalyst was added as wet paste) was added. The autoclave was sealed and purged three times with 0.55 MPa nitrogen. The reactor was then heated while the content was stirred slowly (600 rpm). Once the reaction temperature had been reached, the stirrer was turned off and hydrogen was pressed into the autoclave. The reaction was initiated by turning on the stirrer. Samples were taken during the hydrogenation (Chapter 9.2.6).

After completion of the reaction, the reaction vessel was cooled to room temperature, the pressure released and the vessel purged three times with 0.55 MPa nitrogen. The reaction mixture was sucked off with a vacuum pump and then filtered. The autoclave and the filtering apparatus were purged with ethanol. To clean the autoclave, the vessel was filled with ethanol which then was boiled at 80 °C for 15 min.

The Raney nickel was disposed into a special nickel waste jar and the reaction mixture in a solvent waste jar.

9.2.4 Hydrogenation of 1-bromo-4-nitrobenzene

10 g (50 mmol) 1-bromo-4-nitrobenzene and 100 g tetrahydrofurane were placed in the 200 ml glass autoclave (Chapter 9.1.2) before the catalyst was added as a wet paste. The autoclave was sealed and purged three times with 0.3 MPa nitrogen. The reactor was then heated while the contents were stirred slowly (600 rpm). Once the reaction temperature had been reached, the stirrer was turned off and hydrogen was pressed into the autoclave. The reaction was initiated by turning on the stirrer.

After completion of the reaction, the reaction vessel was cooled to room temperature, the pressure released and the vessel purged three times with
0.3 MPa nitrogen. The reaction mixture was sucked off with a vacuum pump and then filtered. The autoclave and the filtering apparatus were finally purged with tetrahydrofurane.

The Raney nickel was disposed into a special nickel waste jar and the reaction mixture in a solvent waste jar.

9.2.5 Hydrogenation of levodione

10 g (65 mmol) levodione ((6R)-2,2,6-trimethylcyclohexa-1,4-dione) and 50 g methanol were placed in a 100 ml three-neck sulphonation flask (Chapter 9.1.3) before the catalyst was added as a wet paste. The flask was installed on the hydrogenation equipment, evacuated and purged three times with 0.11 MPa argon. The reactor was then heated while the contents were stirred slowly (600 rpm). Once the reaction temperature had been reached, the stirrer was turned off and hydrogen was pressed into the autoclave. Then, the reaction was started by turning the stirrer on again.

After the reaction was completed, the reaction vessel was cooled to room temperature, the pressure released and the vessel evacuated and purged three times with 0.11 MPa argon. The reaction mixture was sucked off with a vacuum pump and then filtered. To clean the autoclave and the filtering apparatus they were purged with methanol.

The Raney nickel was disposed into a special nickel waste jar and the reaction mixture in a solvent waste jar.

9.2.6 Description of the sampling procedure

Samples were taken with a steel capillary with 1 mm inner diameter and a 2 μm frit (dead volume: 0.5 ml). Because sometimes the reaction temperatures were higher than the boiling temperatures of the substances, the samples were collected in a test tube with solvent (methanol or ethanol in the case of butyronitrile or crotonaldehyde, respectively). These test tubes were cooled in a Dewar vessel containing dry ice and ethanol. Initially, 2 ml of the reaction mixture were rejected before 1 ml was collected and analysed.
9.2.7 Neutralisation with water

50 g Raney nickel were suspended in 100 ml distilled water in a three-neck sulphonation flask. The flask was purged three times with argon before the suspension was stirred for 30 min. The catalyst was then allowed to settle before the solvent was decanted. This procedure was repeated three times with distilled water. The neutralised catalyst was stored in distilled water.

9.2.8 Neutralisation with methanol

50 g Raney nickel were suspended in 100 ml distilled water in a three-neck sulphonation flask. The flask was purged three times with argon before the suspension was stirred for 30 min. The catalyst was then allowed to settle before the solvent was decanted. This procedure was first carried out once with distilled water and then three times with methanol. The neutralised catalyst was stored in methanol.

9.2.9 Neutralisation with tetrahydrofurane

50 g Raney nickel were suspended in 100 ml distilled water in a three-neck sulphonation flask. The flask was purged three times with argon before the suspension was stirred for 30 min. The catalyst was then allowed to settle before the solvent was decanted. This procedure was first carried out once with distilled water and then three times with tetrahydrofurane. The neutralised catalyst was stored in tetrahydrofurane.

9.2.10 Modification with formaldehyde

50 g Raney nickel were suspended in 100 ml distilled water in a three-neck sulphonation flask. The flask was purged three times with argon before 13 ml of a solution of 35% formaldehyde were added slowly. The suspension was stirred for 30 min. The catalyst was then allowed to settle before the solvent was decanted. The catalyst was washed three times with
30 ml distilled water (in accordance with Chapter 9.2.7), and the modified catalyst was stored in methanol.

9.3 Analytics

9.3.1 Determination of butyronitrile, butylamine, dibutylamine and dibutylimine with a GC method using an internal standard

GC conditions

<table>
<thead>
<tr>
<th>apparatus</th>
<th>HP 6890 gas chromatograph with split injector and FID</th>
</tr>
</thead>
<tbody>
<tr>
<td>HP 7863 autosampler</td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>column</th>
<th>stationary phase</th>
<th>Rtx-5 Amine</th>
</tr>
</thead>
<tbody>
<tr>
<td>length x ID</td>
<td>30 m x 0.32 mm, film 1.0 μm</td>
<td></td>
</tr>
<tr>
<td>column material</td>
<td>5% diphenyl- 95% dimethyl polysiloxane</td>
<td></td>
</tr>
<tr>
<td>manufacturer</td>
<td>Restek Corporation</td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>carrier gas</th>
<th>helium</th>
</tr>
</thead>
<tbody>
<tr>
<td>pressure</td>
<td>75 kPa</td>
</tr>
<tr>
<td>total flow</td>
<td>112 ml/min</td>
</tr>
<tr>
<td>split ratio</td>
<td>50:1</td>
</tr>
</tbody>
</table>

| column temperature | 65°C(0 min), 3°C/min, 80°C(0 min), 20°C/min, 280°C(0 min) |
| injector temperature | 250°C |
| detector temperature | 250°C |
| injection volume | 1μl |

Sample preparation

ISTD solution 5 g n-caprylic acid methyl ester were diluted in 1 l methanol.
calibration solution  5-10 mg of reference substances were weighted in a sample vial before 1 ml internal standard solution was added.

sample solution  15 μl of the collected sample were diluted in 1 ml internal standard solution.

analysis time  15.0 min
retention times  butylamine  2.5 min
                 butyronitrile  2.9 min
                 dibutylimine  7.4 min
                 dibutylamine  8.0 min
                 ISTD  10.1 min
                 tributylamine  10.6 min

Remarks
Calibrations were performed using four different concentrations of the substances to be analysed.

9.3.2 Determination of crotonaldehyde, crotylalkohol, butanal and butanol with a GC method using an internal standard

GC conditions
apparatus  HP 6890 gas chromatograph with split injector and FID
           HP 7863 autosampler

column  stationary phase  Stabilwax
length x ID  30 m x 0.32 mm, film 0.25 μm
column material  Carbowax-PEG
manufacturer  Restek Corporation
carrier gas: helium
pressure: 75 kPa
total flow: 127 ml/min
split ratio: 50:1

column temperature: 40°C (5 min), 3°C/ min, 70°C (0 min), 15°C/ min, 240°C (3.6 min)
injector temperature: 240°C
detector temperature: 240°C
injection volume: 1 μl

Sample preparation
ISTD solution: 5 g n-caprylic acid methyl ester were diluted in 1 l ethanol.
calibration solution: 5-10 mg of reference substances were weighted in a sample vial before 1 ml internal standard solution was added.
sample solution: 100 μl were diluted in 1 ml internal standard solution.

analysis time: 30.0 min
retention times:
- butanal: 2.4 min
- crotonaldehyde E: 4.9 min
- crotonaldehyde Z: 5.0 min
- butanol: 8.5 min
- crotylalkohol E: 11.7 min
- crotylalkohol Z: 12.9 min
- ISTD: 17.8 min

Remarks
Crotonaldehyde and crotylalkohol were calibrated and measured as the sum of the E and Z isomers. Four samples of different concentrations were used for calibration.
9.3.3 Determination of 1-bromo-4-nitrobenzene, 1-bromo-4-aminobenzene and aniline

**GC conditions**

- **apparatus**: HP 6890 gas chromatograph with split injector and FID
  HP 7863 autosampler

- **column**: stationary phase *DB-5HT*
  length x ID 15 m x 0.25 mm, film 0.1 μm
  column material 5% diphenyl - 95% dimethyl polysiloxane
  manufacturer J&W Scientific

- **carrier gas**: helium
  pressure 57 kPa
  total flow 33 ml/min
  split ratio 25:1

- **column temperature**: 60°C(0min), 10°C/min, 250°C(0min)
- **injector temperature**: 250°C
- **detector temperature**: 250°C
- **injection volume**: 1μl

**Sample preparation**

- **sample solution**: 500 μl of the filtrated reaction mixture were diluted with 500 μl THF.

- **analysis time**: 19.0 min
- **retention times**: aniline 1.9 min
  1-bromo-4-nitrobenzene 2.9 min
  1-bromo-4-aminobenzene 5.2 min
9.3.4 Determination of levodione and actinol

**GC conditions**

**apparatus**  
*HP 6890* gas chromatograph with  
split injector and FID  
*HP 7863* autosampler

**column**  
stationary phase  
*HP-5*  
length x ID  
30 m x 0.32 mm, film 0.25 μm  
column material  
5% diphenyl - 95% dimethyl polysiloxane  
manufacturer  
*Hewlett Packard*

**carrier gas**  
helium  
pressure  
total flow  
79 ml/min  
split ratio  
50:1

**column temperature**  
50°C(0min), 10°C/min, 150°C(3min)

**injector temperature**  
250°C

**detector temperature**  
300°C

**injection volume**  
1μl

**Sample preparation**

**sample solution**  
100 μl of the filtrated reaction solution were diluted with 900 μl methanol

**analysis time**  
13.0 min

**retention times**  
levodione  
8.8 min  
(R,S)-actinol  
9.8 min  
(R,R)-actinol  
9.9 min
9.3.5 Methanol determination in aqueous medium with a headspace GC method using an external standard

**GC conditions**

**apparatus**    
*Agilent 6890N* gas chromatograph with FID  
*PE HS 40 XL* headspace autosampler

**column**  
stationary phase: *DB-1*  
length x ID: 30 m x 0.32 mm, film 5 μm  
column material: 100% dimethyl polysiloxane  
manufacturer: *J&W Scientific*

**carrier gas**    
nitrogen  
pressure: 20 psi  
splitless

**column temperature**    
40°C(3min), 10°C/min, 150°C(2min)

**transfer temperature**    
100°C

**injector temperature**    
140°C

**detector temperature**    
300°C

**injection time**    
0.08s

**Sample preparation**

**calibration solution**    
a solution of 100 μl MeOH in 1000 ml water was prepared as ESTD, 1 ml of this solution was placed in the HS autosampler.

**sample solution**    
the aqueous modification solution was diluted 1:10 with water before 100 mg were again diluted in 1 ml water and then placed in the HS autosampler.

**analysis time**    
16.0 min

**retention times**    
methanol  
1.6 min
9.3.6 Formaldehyde determination in aqueous medium with an HPLC method using an external standard

HPLC conditions

apparatus \textit{HP 1050} HPLC with UV detector

column \text{stationary phase} \textit{Supelcosil LC-18}

length x ID 250 mm x 4.6 mm, film 5 μm

manufacturer \textit{Supelco}

solvent acetonitrile : water 60 : 40

flow 1.5 ml/min

detection wavelength 360 nm

injection volume 2 μl

Sample preparation

derivatization solution 2.37 g (8 mmol) 2,4-dinitrophenylhydrazine were dissolved in 100 ml THF.

derivatization 5 ml of the derivatization solution were tared, before 30 mg of the sample were added. 1 drop of conc. hydrochloric acid was added and the sample was stored for 1 hour at 50°C. 1 ml of the warm derivatized solution was diluted with 10 ml acetonitrile and then analysed.

calibration solution a solution containing 5% formaldehyde was derivatized and then used as ESTD.

analysis time 20.0 min

retention times 2,4-dinitrophenylhydrazone 3.8 min
9.3.7 Synthesis of dibutylimine as a standard for GC measurements

Butylamine condenses with butyraldehyde to produce the *Schiff base* (Figure 9-3) [104, 105].

![Figure 9-3](image)

**Fig. 9-3:** Condensation of butylamine and butyraldehyde [104].

34.6 g (506 mmol) butyraldehyde in 56 g toluene were placed in a three-neck sulphonation flask before 36.8 g (504 mmol) butylamine were added slowly via a dropping funnel. The solution was heated to 66°C and water was produced. After one hour the aqueous phase was separated off and the organic phase was distilled.

The same conversion was also made on a smaller scale (calibration samples for gas chromatographic analysis) and on a larger scale (to produce azomethine as starting material for the hydrogenation), in both cases without solvent and using an excess of butylamine. This conversion is quantitative, no butyraldehyde was detected after the reaction.

The condensation of dibutylamine and butyraldehyde is slower than the one of butylamine and butyraldehyde, but using the same conversion, tributyleneamine could be produced. This was not done because tributyleneamine was not detected during the hydrogenation of butyronitrile in the reaction mixture.
9.4 Identification of by-products

9.4.1 N-Butylbutanamide

Initially, a reaction mixture, containing 4 mass-% N-butylbutanamide was concentrated and distilled under vacuum. The obtained sample was purified by chromatography using ethyl acetate/light petroleum (50 : 50) as eluent to yield the pure compound. A *DPX 400* NMR spectrometer (400 MHz $^1$H, 75 MHz $^{13}$C) was used to measure the nuclear magnetic resonance spectra; $\delta_{\text{H}}$(CDCl$_3$) 0.92 (3H, t, $J=8.0$, CH$_3$), 0.95 (3H, t, $J=8.2$, CH$_3$), 1.34 (2H, m, CH$_2$CH$_2$CH$_2$NH), 1.48 (2H, m, CH$_2$CH$_2$NH), 1.66 (2H, sext, $J=7.5$ CH$_2$CH$_2$CO), 2.15 (2H, t, $J=7.4$, CH$_2$CO), 3.25 (2H, q, $J=6.7$, CH$_2$NH), 5.67 (1H, s, NH); $\delta_{\text{C}}$(CDCl$_3$) 14.1 (2CH$_3$), 19.6 (CH$_2$CH$_2$CO), 20.4 (CH$_2$CH$_2$CH$_2$N), 32.1 (CH$_2$CH$_2$N), 39.2 (CH$_2$CO), 39.6 (CH$_2$N) and 173.4 (CO). A mass spectrum was measured using a GC-MS system (*5973 Mass Selective Detector*); m/z 143 (M$^+$, 19%), 128 (C$_7$H$_{14}$NO$^+$, 23), 115 (29), 101 (25), 100 (C$_5$H$_{10}$NO$^+$, 57), 88 (20), 86 (C$_4$H$_8$NO$^+$, 19), 73 (52), 71 (C$_4$H$_7$O$^+$, 90), 57 (C$_4$H$_5^+$, 35), 44 (62), 43 (C$_3$H$_7^+$, 95), 41 (60) and 30 (C$_2$H$_6^+$, 100). These results are in accordance with published data [106].

9.4.2 N,N-Dibutyldutyramidine

The reaction mixture containing about 7 mass-% N,N-dibutyldutyramidine was concentrated to a small volume and then distilled *in vacuo*. A sample of 15 mass-% N-butylbutanamide and 85 mass-% N,N-dibutyldutyramidine was obtained. An *AV 500* NMR spectrometer (500 MHz $^1$H, 125 MHz $^{13}$C, 36 MHz $^{14}$N (ref. nitromethane)) was used to measure the nuclear magnetic resonance spectra; $\delta_{\text{H}}$(CDCl$_3$) 0.94 (6H, t, $J=7.4$, CH$_3$CH$_2$CH$_2$CH$_2$N), 1.09 (3H, t, $J=7.4$ CH$_3$CH$_2$CH$_2$C), 1.37 (4H, m, CH$_2$CH$_2$CH$_2$N), 1.63 (6H, m, CH$_2$CH$_2$N, CH$_2$CH$_2$C), 2.34 (2H, m, CH$_2$C), 3.19 (4H, t, $J=7.5$ CH$_2$N), 7.29 (1H, s, NH); $\delta_{\text{C}}$(CDCl$_3$) 13.6 (2 CH$_3$CH$_2$CH$_2$CH$_2$N), 14.1 (CH$_3$CH$_2$CH$_2$C) 19.7 (2 CH$_2$CH$_2$CH$_2$N), 20.0 (2 CH$_2$CH$_2$N), 27.5 (CH$_2$CH$_2$C), 31.8 (CH$_2$C), 43.3 (2 CH$_2$N), 137.6 (CNH); $\delta_{\text{N}}$(CDCl$_3$, 300K)
-165, line width 90, -280, line width 75; δN(CDC13, 333K) -230 line width 175; δN(TFA/dioxane, 300K) -260, line width 125. An NMR literature reference for aromatic amidines is given in [107]. A mass spectrum was measured using a GC-MS system (5973 Mass Selective Detector); m/z 198 (M+, 20%), 183 (C11H23N2+, 24), 169 (C10H21N2+, 29), 155 (C9H19N2+, 17), 141 (C8H17N2+, 17), 127 (C8H17N+, 45), 113 (16), 99 (15), 85 (15), 84 (78), 72 (C4H10N+, 26), 70 (C4H8N+, 100), 57 (C4H9+, 17), 43 (C3H7+, 24), 41 (33) and 29 (C2H5+, 23).

9.4.3 1,1-Diethoxybutane

A mass spectrum was measured using a GC-MS system (5973 Mass Selective Detector); m/z 103 (C5H11O2+, 100%), 101 (C6H13O+, 85), 75 (50), 73 (M2+, 40), 55 (48), 47 (38), 43 (C3H7O+, 16) and 29 (C2H5O+, 14).

9.5 Characterisation of the catalyst

9.5.1 The reduction potential

The reduction potential of Raney nickel was measured with two different combined gold electrodes with an integrated Ag/AgCl reference, model 6.0413.100, manufactured by Metrohm. The measurement was monitored by a Metrohm pH-meter 691. The electrodes were calibrated with Metrohm redox standard 6.2306.020 (U=250±5 mV). When the redox potential was measured, the electrodes were placed directly on the solid catalyst. The values obtained were converted into the standard reduction potentials relative to the Pt/H2-electrode.
9.5.2 Adsorption of an indicator

0.01-0.02 g of wet Raney nickel were placed in a 100 ml volumetric flask before 100 ml of a $10^{-4}$ M 4-aminoazobenzene solution were added. The solution was allowed to stand for 4 weeks, before the concentration of 4-aminoazobenzene was measured with an UVIKON 720 LC UV-VIS absorption spectrometer. From the difference in concentration the amount of the adsorbed indicator was calculated.

9.5.3 Dissolution in acidic medium

1 g of wet Raney nickel was placed in a three-neck sulphonation flask before 50 g water were added. With a dropping funnel 32 ml of hydrochloric acid (35%) were slowly added while the content of the flask was stirred with a magnetic stirrer. The released gas was measured with a measuring cylinder that was filled with water inversely placed in a water containing vessel.

9.6 Chemicals

The chemicals used, their suppliers and purity grades are listed in Table 9-1.

Table 9-1: Purity values and suppliers of the chemicals used

<table>
<thead>
<tr>
<th>Substance</th>
<th>Supplier</th>
<th>Purity grade</th>
</tr>
</thead>
<tbody>
<tr>
<td>4-aminoazobenzene</td>
<td>Merck</td>
<td>for synthesis &gt; 98% (HClO₄)</td>
</tr>
<tr>
<td>aniline</td>
<td>Fluka</td>
<td>puriss. p. a. &gt; 99.5% (GC)</td>
</tr>
<tr>
<td>1,2-bis(2-hydroxyethylthio)ethane (EDS)</td>
<td>F. Hoffmann-La Roche</td>
<td>Lot No. 28611</td>
</tr>
<tr>
<td>1-bromo-4-nitrobenzene</td>
<td>Fluka</td>
<td>puriss. p. a. &gt; 98% (GC)</td>
</tr>
<tr>
<td>butanol</td>
<td>Fluka</td>
<td>puriss. p. a. &gt; 99.5% (GC)</td>
</tr>
</tbody>
</table>
Table 9-1: Purity values and suppliers of the chemicals used

<table>
<thead>
<tr>
<th>Substance</th>
<th>Supplier</th>
<th>Purity grade</th>
</tr>
</thead>
<tbody>
<tr>
<td>butyraldehyde</td>
<td>Fluka</td>
<td>purum &gt; 97% (GC)</td>
</tr>
<tr>
<td>butylamine</td>
<td>Fluka</td>
<td>purum &gt; 98% (GC)</td>
</tr>
<tr>
<td>butyronitrile</td>
<td>Fluka</td>
<td>purum &gt; 99% (GC)</td>
</tr>
<tr>
<td>n-caprylic acid methyl ester</td>
<td>Fluka</td>
<td>puriss &gt; 99% (GC)</td>
</tr>
<tr>
<td>crotonaldehyde (E + Z)</td>
<td>Fluka</td>
<td>purum &gt; 98% (GC)</td>
</tr>
<tr>
<td>crotylalkohol (E + Z)</td>
<td>Fluka</td>
<td>purum &gt; 97% (GC)</td>
</tr>
<tr>
<td>dibutylamine</td>
<td>Fluka</td>
<td>puriss. &gt; 99% (GC)</td>
</tr>
<tr>
<td>ethanol</td>
<td>Merck</td>
<td>p. a.</td>
</tr>
<tr>
<td>formaldehyde solution</td>
<td>Merck</td>
<td>extra pure 35%</td>
</tr>
<tr>
<td>formaldehyde solution</td>
<td>Fluka</td>
<td>puriss. p. a. ACS free of acids</td>
</tr>
<tr>
<td>hydrochloric acid 25%</td>
<td>Merck</td>
<td>GR for analysis</td>
</tr>
<tr>
<td>levodione</td>
<td>F. Hoffmann-La Roche</td>
<td>Lot No. 32716-a8</td>
</tr>
<tr>
<td>methanol</td>
<td>Merck</td>
<td>p. a.</td>
</tr>
<tr>
<td>methanol</td>
<td>F. Hoffmann-La Roche</td>
<td>tech.</td>
</tr>
<tr>
<td>nickel-on-carrier</td>
<td>Engelhard</td>
<td>Ni 1404 P, Lot H-99</td>
</tr>
<tr>
<td>pyridine</td>
<td>Fluka</td>
<td>p. a. &gt; 99.8% (GC)</td>
</tr>
<tr>
<td>tetrahydrofurane</td>
<td>Fluka</td>
<td>puriss. p. a. &gt; 99.5% (GC)</td>
</tr>
<tr>
<td>toluene</td>
<td>Fluka</td>
<td>puriss. p. a. &gt; 99.5% (GC)</td>
</tr>
<tr>
<td>tributylamine</td>
<td>Fluka</td>
<td>puriss. p. a. &gt; 99% (GC)</td>
</tr>
<tr>
<td>argon</td>
<td>Carbagas</td>
<td>99.995%</td>
</tr>
<tr>
<td>nitrogen</td>
<td>Carbagas</td>
<td>99.995%</td>
</tr>
<tr>
<td>hydrogen</td>
<td>Carbagas</td>
<td>99.995%</td>
</tr>
<tr>
<td>Raney nickel</td>
<td>Degussa-Hülls AG</td>
<td>Type B113 Z, Batch 20018989</td>
</tr>
</tbody>
</table>
9.7 Calculation of selectivity and reaction rates

In every experiment samples were taken after 10, 20, 30, 40, 50, 60, 75, 90, 105, 120, 150, 180 min and, if necessary, every further hour. With aid of these samples reaction profiles were drawn (an example is given in Figure 9-4) and the selectivity and the initial reaction rates were calculated.

![Figure 9-4](image)

**Fig. 9-4:** Typical reaction profile for the hydrogenation of butyronitrile. Reaction conditions: 240 g BN, 3.75 g RaNi, 100°C, 1 MPa overall pressure, 1000 rpm.

The selectivities of the substances were calculated with the following equation (Eq. 9.1):

\[
\text{selectivity}(x) = \frac{\text{mass of component } x}{\text{total mass}} \tag{Eq. 9.1}
\]
Initially, to calculate the initial reaction rates, polynomials of second order were fitted to the data in a range of 0 to 50% butyronitrile conversion. The reaction rates were then obtained from the first derivatisation of the fitted function at the point of zero butyronitrile conversion (origin). The obtained values /[mass-%/min] were converted to molar rates, and these were divided by the mass of charged catalyst in order to obtain the molar rates per mass catalyst and second (/[mmol/kg*s]).

9.8 Error analysis

9.8.1 Precision of a gas chromatographic analysis

The precision of an analysis by gas chromatography was measured with a calibration sample. Five measurements were carried out (Table 9-2). The relative standard deviation was 1.2% in the worst case.

<table>
<thead>
<tr>
<th>substance</th>
<th>mean  / [mass-%]</th>
<th>$\sigma$ / [mass-%]</th>
<th>rel. $\sigma$ / [%]</th>
</tr>
</thead>
<tbody>
<tr>
<td>butylamine</td>
<td>18.55</td>
<td>0.15</td>
<td>0.81</td>
</tr>
<tr>
<td>butyronitrile</td>
<td>40.48</td>
<td>0.44</td>
<td>1.09</td>
</tr>
<tr>
<td>dibutylamine</td>
<td>30.17</td>
<td>0.36</td>
<td>1.19</td>
</tr>
<tr>
<td>tributylamine</td>
<td>10.81</td>
<td>0.09</td>
<td>0.84</td>
</tr>
</tbody>
</table>
9.8.2 Precision of a sample analysed with gas chromatography

The precision of the sampling procedure with gas chromatography was measured in experiment 5 (conditions: 240 g BN, 15 g methanol washed RaNi, 100°C, 1 MPa, 1000 rpm) after a reaction time of 120 min. Five samples were taken and analysed (Table 9-3).

<table>
<thead>
<tr>
<th>substances</th>
<th>mean / [mass-%]</th>
<th>σ / [mass-%]</th>
<th>rel. σ / [%]</th>
</tr>
</thead>
<tbody>
<tr>
<td>butylamine</td>
<td>64.14</td>
<td>0.27</td>
<td>0.42</td>
</tr>
<tr>
<td>butyronitrile</td>
<td>20.87</td>
<td>0.49</td>
<td>2.33</td>
</tr>
<tr>
<td>dibutylamine</td>
<td>6.52</td>
<td>0.14</td>
<td>2.14</td>
</tr>
<tr>
<td>dibutylimine</td>
<td>8.46</td>
<td>0.21</td>
<td>2.52</td>
</tr>
</tbody>
</table>

The relative standard deviation was 2.6% in the worst case. It must be noted that the sampling procedure for five samples lasted 3 min and that during this time the reaction was running. This value is in an expected range and is comparable to literature values of about 2% [27].

Concerning the accuracy of the measurement the following has to be mentioned: To calculate the relative concentrations, all compounds in the sample were determined in [mg] and divided by the total mass. Compounds not calibrated were considered using a relative response factor of 1.0 relative to the internal standard. A systematic error is therefore made when calculating the total mass and of course in the concentrations of the components. This error depends on the concentration of substances that are not calibrated. Two not calibrated compounds were detected: dibutylamide and tributylamidine.
9.8.3 Precision of the selectivity and the reaction rates

The precision of the selectivity and the reaction rates was measured by repeating an experiment twice (Table 9-4 and Table 9-5). Different calibrations of the gas chromatograph were used and the time periods between the experiments were several months. The conditions were: 240 g BN, 15 g RaNi, 100°C, 1 MPa hydrogen, 1000 rpm.

Table 9-4: Precision of the selectivity of the hydrogenation of butyronitrile. Reaction conditions: 240 g butyronitrile, 15 g RaNi, 100°C, 1 MPa, and 1000 rpm.

<table>
<thead>
<tr>
<th></th>
<th>BA [mass-%]</th>
<th>DBA [mass-%]</th>
<th>Tamidine [mass-%]</th>
<th>max. DBI [mass-%]</th>
</tr>
</thead>
<tbody>
<tr>
<td>exp 1</td>
<td>90.98</td>
<td>8.50</td>
<td>0.53</td>
<td>10.80</td>
</tr>
<tr>
<td>exp 2</td>
<td>90.73</td>
<td>8.84</td>
<td>0.43</td>
<td>9.73</td>
</tr>
<tr>
<td>exp 3</td>
<td>91.13</td>
<td>8.07</td>
<td>0.61</td>
<td>10.46</td>
</tr>
<tr>
<td>mean</td>
<td>90.95</td>
<td>8.47</td>
<td>0.52</td>
<td>10.33</td>
</tr>
<tr>
<td>std.</td>
<td>0.20</td>
<td>0.38</td>
<td>0.09</td>
<td>0.55</td>
</tr>
</tbody>
</table>

Table 9-5: Precision of the initial reaction rates. Reaction conditions: 240 g butyronitrile, 15 g RaNi, 100°C, 1 MPa, and 1000 rpm.

<table>
<thead>
<tr>
<th></th>
<th>d[BN]/dt [mmol/kg*s]</th>
<th>d[BA]/dt [mmol/kg*s]</th>
<th>d[DBA]/dt [mmol/kg*s]</th>
<th>d[DBI]/dt [mmol/kg*s]</th>
</tr>
</thead>
<tbody>
<tr>
<td>exp 1</td>
<td>65.7</td>
<td>46.6</td>
<td>1.40</td>
<td>7.97</td>
</tr>
<tr>
<td>exp 2</td>
<td>60.7</td>
<td>43.6</td>
<td>1.16</td>
<td>7.35</td>
</tr>
<tr>
<td>exp 3</td>
<td>67.0</td>
<td>48.7</td>
<td>0.97</td>
<td>8.17</td>
</tr>
<tr>
<td>mean</td>
<td>64.5</td>
<td>46.3</td>
<td>1.18</td>
<td>7.83</td>
</tr>
<tr>
<td>std.</td>
<td>3.3</td>
<td>2.5</td>
<td>0.21</td>
<td>0.43</td>
</tr>
</tbody>
</table>
Chapter 10

Literature


11.1 Curriculum vitae

name: Roc Novi

date of birth: 15.10.1977

citizen: Vignogn GR

Education

1984-1990 primary school in Savognin
1990-1992 secondary school in Savognin
1992-1997 gymnasium at the EMS in Schiers
1997-2001 diploma education in chemistry at the Swiss Federal Institute of Technology in Zürich
2001-2004 Ph.D. thesis at the Swiss Federal Institute of Technology in Zürich and the F. Hoffmann-La Roche (VFCR) in Kaiseraugst
11.2 Conference contributions
