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Technology development in nicotinate production

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Abstract

An overview is given of the developments in nicotinate technology over the past 10–15 years. In particular the developments of the areas of the starting materials, reaction technology and of the working-up to the final product are considered. Attention is paid both to niacin (nicotinic acid) and niacinamide (nicotinamide).

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Keywords: Niacin; Nicotinic acid; Niacinamide; Nicotinamide; Nicotinate technology

1. Introduction

1.1. The importance of niacin

Co-enzyme I (nicotinamide-adenine dinucleotide NAD) and co-enzyme II (nicotinamide-adenine dinucleotide phosphate NADP) are required by all living cells. They enable both the conversion of carbohydrates into energy as well as the metabolism of proteins and fats. Both nicotinamide and nicotinic acid are building blocks for these co-enzymes. The common name for vitamin B3 is niacin, and strictly speaking, refers only to nicotinic acid (Fig. 1).

Since the human body produces neither nicotinic acid nor the amide, it is dependent on intake via foodstuffs. After the recognition of the importance of niacin, the number of deaths due to the vitamin deficiency disease pellagra dropped in the US from over 7500 to 70 in the years from 1929 to 1956 (E. Kodicek, *Nutr. Dieta* 4, 109 (1962) – taken from [1]). Although niacin is found in a bound form naturally in wheat, yeast and pork and beef liver, the majority of niacin today is produced synthetically by chemical oxidation or ammoxidation of alkyl pyridines. To demonstrate the economic significance of this, in 1995 world-wide a total of 22,000 metric tonnes of niacin (14,000 t) and niacinamide (8000 t) were produced. The

major producers in 1995 included Lonza, Reilly-Degussa (Vitachem JV), Nepera and Yuki Gosei [2].

A review has been recently compiled on the preparations and applications of nicotinic acid and nicotinamide, including most recent developments in the treatment of schizophrenia, diabetes, auto-immune diseases and cholesterol-related diseases and in cosmetic skin care [3].

1.2. Scope of article

This article attempts to overview the progress in production methods and manufacture of the nicotinates within the last 10–15 years. Under nicotinates are understood nicotinic acid and the corresponding acid amide. No attempt is made to review related compounds such as hydroxy-nicotinic acid or the esters of nicotinic acid, all of which have industrial significance. The article can fundamentally be divided into three parts:

- type and manufacture of raw materials (picoline, methyl-ethyl-pyridine),
- methods of conversion of raw materials into cyanopyridine or nicotinic acid,
- methods of conversion or work-up to final product.

2. Raw materials

Pyridine bases such as 3-picoline and 2-methyl-5-ethylpyridine are traditionally manufactured by the Chichibabin

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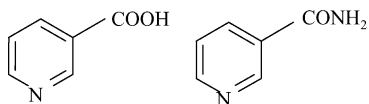


Fig. 1. Nicotinic acid (niacin) and nicotinamide (niacinamide).

reaction, where a mixture of aldehydes or ketones is reacted with ammonia. Thus formaldehyde, acetaldehyde and ammonia react in the gas-phase to produce a mixture of pyridine and 3-picoline. By choosing the appropriate aldehyde or ketone, the catalyst and the phase (liquid or gas-phase), the composition of the mixture can be varied at will, depending on the desired end product [4]. In the gas-phase silica alumina catalysts are often used, and in the liquid-phase acid catalysts based on phosphoric or acetic acid are employed. In the 1990s, Reilly patented MFI- and BEA-based zeolite catalyst compositions for ammonia-aldehyde conversions to pyridine, picolines, and alkyl pyridines [30].

From the chemical standpoint, 3-picoline is the ideal starting-material for nicotinic acid or amide: the methyl group can be selectively and readily oxidised to the carboxyl derivative with few side-products or pollutants. High selectivity coupled with the low molecular weight ratio (1:1.3) compared to the end-products make picoline an attractive industrial starting-material for the production of nicotinic derivatives.

3-Picoline is obtained, typically in a 1:2 ratio along with the main product pyridine, by the gas-phase reaction of acetaldehyde, formaldehyde and ammonia [4]. The lack of selectivity of this reaction to either pyridine or picoline has hitherto meant that the economy of the major product (pyridine) has determined the price and availability of picoline. Thus producers of pyridine have been able to control the quantity and prices of picoline on the market. This situation has led to the search for alternative feedstock and manufacturing processes for picoline.

2-Methyl-5-ethyl-pyridine (MEP) is used as a starting-material for the high temperature and pressure liquid-phase oxidation with nitric acid. The reasons for this apparently unlikely choice of starting-material are many. MEP can be relatively made in the liquid-phase from acetaldehyde and ammonia selectively (around 70%) compared to picoline (20–40%) from the traditional picoline/pyridine process. It is thus considerably cheaper to produce than picoline. The reaction of MEP with nitric acid is also surprisingly selective (>80%). The resulting nitric oxide gases are recycled and reacted with air and water to reconstitute nitric acid. This process has been utilised for nearly 40 years by Lonza for producing niacin.

The disadvantages of the process include the obvious problems involved with handling nitric acid at elevated temperatures and pressure, together with a complex work-up system to ensure the desired quality, appearance and physical properties of the final product. Additionally, from the ecological standpoint, the intrinsic loss of two carbon

atoms as carbon dioxide makes the use of MEP in future processes unattractive.

As mentioned above, the bulk of picoline is produced today by the condensation of acetaldehyde, formaldehyde and ammonia in the gas-phase, which simultaneously produces large quantities of pyridine. A selective and suitable alternative method starting from these or similar simple molecules has yet to be developed. Given the thermodynamic properties of the molecules and reactions involved, it does not seem likely to expect a completely selective process for 3-picoline following this strategy.

Nevertheless, a viable alternative for manufacturing picoline has been found; namely the condensation of the molecule 2-methylpentanediamine (MPDA) to methylpiperidine, followed by the dehydrogenation to 3-picoline (Fig. 2). 2-Methylglutaronitrile (MGN) is the major side-product in the adiponitrile process and, as such, a readily available starting-material (~105,000 mtpa). It is readily hydrogenated to MPDA.

Although this route has the similar fundamental weakness as the traditional process of being coupled to another product (adiponitrile), the foreseeable future of nylon 6,6 and the route to its manufacture (hydrogen cyanide addition to butadiene) seem assured for the next 10–20 years or so. Several advantages are apparent in this route.

1. The 3-picoline produced has a very high isomeric purity.
2. Picoline is produced from MPDA in a 2-stage catalytic process which is practically energetically neutral: an endothermic (ring closure) and an exothermic (dehydrogenation) reaction.
3. Ammonia is liberated during the ring closure which is then incorporated in the subsequent ammoxidation process, so there is practically no ammonia waste and no net ammonia consumption.
4. Utilisation of a waste-product (2-methylglutaronitrile) can be used as a co-monomer in the production of other polyamides, but the end-product niacin has an intrinsically much higher value).

Several companies have described processes for producing nicotinate precursors utilising 2-methylglutaronitrile or its hydrogenated product MPDA [5–8]. The Lonza process utilises Al oxide and/or Si oxide catalysts (e.g., zeolites) in the cyclization step to 3-methylpiperidine and a catalytic dehydrogenation to 3-picoline in the second step. The Mitsubishi process hydrogenates MGN directly to 3-methylpiperidine with a rhodium catalyst in the presence of ammonia. The presence of ammonia prevents the formation of polyamines, which otherwise would poison the rhodium catalyst. Reilly have taken this idea one step further and have devised a method for producing 3-cyanopyridine in significant yields directly from MPDA [7,8] Reilly employed both fixed and fluidised bed reactors to accomplish this, using a combination of vanadium and silica/alumina catalysts typical for both types of reaction. In

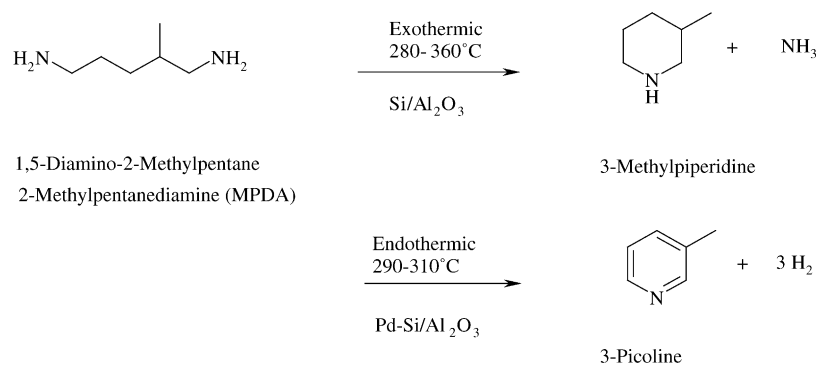


Fig. 2. Alternative process for picoline manufacture.

182 the early 1990s, Reilly started the commercial conversion of
 183 MPDA/3-methylpiperidine to 3-picoline [30].

184 3. Conversion to niacin

185 3.1. Gas-phase ammoxidation of picoline to cyanopyridine

186 The gas-phase ammoxidation of 3-picoline to 3-cyano-
 187 pyridine followed by a hydrolysis either to nicotinamide or
 188 nicotinic acid are commercial processes, and for the
 189 production of nicotinamide, represents the most logical
 190 and direct route via 3-picoline (Fig. 3). The ammoxidation
 191 reaction has received much attention in the past 15 years,
 192 both in industry [9–18] and from academic institutions in
 193 Europe [19], Asia [20] and India [21–27].

194 3.2. Catalysts employed in ammoxidation

195 Virtually all of the catalysts employed for the ammox-
 196 idation reaction contain vanadium as the key component.
 197 Vanadium oxide has long proven to be most effective metal
 198 oxide for both ammoxidation and oxidation in the gas-phase.
 199 The progress in catalyst design described in the literature has
 200 been limited to variation and optimisation of the composi-
 201 tion, particularly promoters. Promoters include elements
 202 from practically the whole of the periodic table, although the
 203 more common promoters are usually restricted to group 5
 204 and first row transition and alkaline metals. The mechanism
 205 of promoters is still poorly understood, especially in the light

of the fact that catalysts of very simple chemical
 composition have been shown to perform just as satisfactori-
 rily as more complex recipes [12,13]. Supports vary widely,
 too, although oxides of silicon, aluminium, titanium and
 zirconium are the ones most commonly utilised. The role of
 supports is generally to provide a medium on which the
 active component can be efficiently dispersed, as well as
 providing mechanical stability to the catalyst. The impor-
 tance of the physical properties of the catalyst cannot be
 overemphasised. Particle size, particle shape, pore size, pore
 distribution, surface area, mechanical integrity, attrition
 resistance are all key factors which have to be balanced in
 order to obtain a satisfactory catalyst. Reaction conditions
 such as temperature, gas flow and composition, as well as
 picoline feed, generally have to be tailored to the individual
 catalyst.

The VPO type catalyst of catalyst used in the maleic
 anhydride process has also been reported to give satisfactory
 results in the ammoxidation reaction [27].

225 3.3. Reactor technology

226 Most installations appear to be based on fixed-bed
 227 technology, i.e., the catalyst is packed into a tubular reactor
 228 and the hot reaction vapours are passed over the static bed.
 229 However, Reilly have been utilising fluidised-bed technol-
 230 ogy for the past 50 years. Reilly commercialized the
 231 pyridine-β-picoline production in 1952 using fluid-bed
 232 reactor technology at its Indianapolis facility. This was a
 233 result of pioneering work of Cislak and Wheeler [28,29].

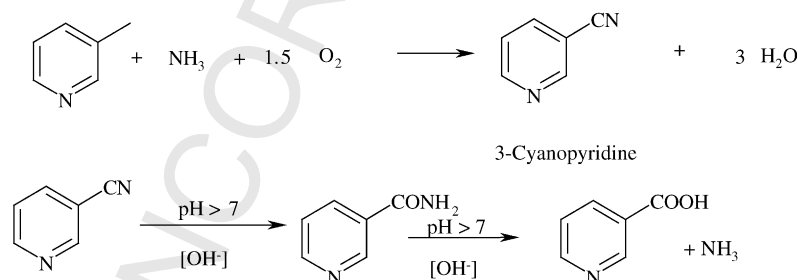


Fig. 3. Ammoxidation of 3-picoline and hydrolysis of cyanopyridine to niacinamide and niacin.

234 This may have been one of the earliest cases of fluid-bed
235 reactor technology being applied to the commercial
236 production of chemicals. The original feed was acety-
237 lene–formaldehyde, but this was eventually replaced by
238 acetaldehyde–formaldehyde mixtures.

239 In 1960, Reilly commercialized the 3-picoline to 3-
240 cyanopyridine ammoxidation reaction using fluid-bed
241 reactor technology; again a result of Cislak and Wheeler's
242 efforts. Also in the 1960s, Reilly operated a 3-cyanopyr-
243 idine-to-niacin plant. Both pyridine and ammoxidation units
244 went through a series of scale-ups from the 1970s to present
245 day [30].

246 In the late 1990s, Lonza started up a fixed-bed plant in
247 Guangzhou, China to produce nominally 3000 mtpa
248 niacinamide using ammoxidation technology and starting
249 from MPDA. This unique process utilises no fewer than six
250 different catalysts for conversion of MPDA through to
251 niacinamide, including waste-gas treatment [11]. In terms of
252 green technology [31], this process is a tribute to today's
253 ecological and economic demands.

254 3.4. Gas-phase oxidation of picoline to nicotinic acid

255 In the past, 3-picoline has been oxidised with stoichio-
256 metric or excess quantities of chemical oxidising agents,
257 such as permanganate, nitric acid, or chromic acid. The
258 ecological aspects of this are considered in detail elsewhere
259 [31]. The most logical and direct method of producing
260 nicotinic acid is to oxidise 3-picoline with air. In fact, the
261 direct gas-phase oxidation of 3-picoline using vanadium
262 oxide catalysts has been known for over 60 years [32], but it
263 is only in the last 15 years or so that serious efforts have been
264 made to develop a commercial process. The reasons for this
265 are undoubtedly based on the considerable difficulties
266 involved in obtaining a selective and efficient reaction in the
267 gas-phase. In the absence of ammonia, the direct oxidation
268 reaction proceeds slower than the ammoxidation and in
269 contrast to the latter, an intermediate – 3-pyridinecarbalde-
270 hyde – can be observed. The competitive total oxidation
271 reaction of both the intermediate and picoline to oxides of
272 carbon can severely reduce the selectivity (Fig. 4). In
273 addition, nicotinic acid is less stable than 3-cyanopyridine
274 and decarboxylates readily at temperatures normally
275 encountered in the gas-phase reaction. Nicotinic acid also
276 de-sublimes at temperatures below 200 °C and thus can
277 create plugging difficulties in the equipment.

278 Since 3-cyanopyridine can be fairly selectively hydro-
279 lysed to niacinamide, which in itself is considered equivalent
280 if not even in some cases preferable to nicotinic acid, it is
281 hardly surprising that niacinamide has been up to now the
282 preferred end product starting from picoline.

283 Nevertheless, both the Borekov Institute in Siberia [33]
284 and Lonza [34] have developed pilot processes for the
285 manufacture of niacin based on the catalytic gas-phase
286 oxidation of picoline. The processes differ predominantly in
287 the method of removing niacin from the process. Whereas
288 Borekov utilise a de-sublimation procedure, Lonza's
289 patented technology is based on spray-drying of a highly
290 concentrated solution of ammonium nicotinate. This meth-
291 od takes advantage of the fact that under Lonza's reac-
292 tion conditions, ammonia is produced as a side-product
293 rather than hydrogen cyanide in the total or deep oxidation
294 (Fig. 4).

295 The “green” advantages of the process can be
296 summarised as follows:

- 297 1. Use of air as oxidant instead of stoichiometric quantities
298 of chemical oxidising agents. 300
- 299 2. Use of catalysts to promote reaction. 300
- 300 3. Reaction carried out at atmospheric pressure. 303
- 301 4. Gas-phase reaction means that catalyst does not have to
302 be recovered from solution. 303
- 303 5. Energy from exothermic reaction can be recovered. 309
- 304 6. Few unit operations. 300
- 305 7. The only solvent used is water. 303
- 306 8. Ammonia is recycled. 303
- 307 9. Waste is minimised by a highly selective reaction. 303
- 308 10. Conversion is high, leading to an efficient use of
309 equipment, energy and material. 320
- 310 11. Throughput is acceptable for a commercial process. 322

312 The reaction has also been studied elsewhere and high
313 yields have been obtained under laboratory conditions. P-
314 atents have been submitted by Degussa and Hölderich at
315 Aachen [35], and by industries in Asia [36,37]. The appa-
316 rently simple catalyst system of V-Ti oxides has been shown
317 to be efficient and very selective, although an alternative
318 system using a mixture of vanadia, titanium, chromium,
319 antimony and samarium oxides on an alumina support is
320 described in the Chinese patent. Vanadium chromate [37]
321 leads to modest yields. 322

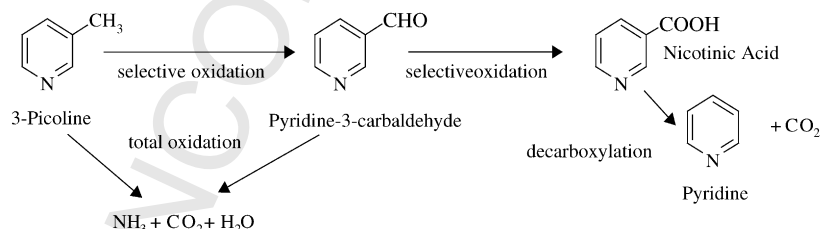


Fig. 4. Reactions in the gas-phase oxidation of picoline to nicotinic acid.

333 3.5. Liquid-phase oxidation of 3-picoline with oxygen

334 Picoline can be selectively oxidised with air in the liquid-
335 phase to niacin [38]. A catalyst combination such as cobalt
336 and manganese acetate and/or bromide is usually used in an
337 acetic acid medium, and the air-oxidation takes place under
338 elevated temperatures and pressures. The disadvantages of
339 this process are the following:

- 340 1. The product must be efficiently and cleanly separated
341 form the reaction solution. In practice the two goals run
342 contrary to each other; if the product is clean, then non-
343 negligible quantities remain in solution and vice-versa.
- 344 2. In practice, additional cleaning and/or processing steps
345 are necessary to ensure the desired purity and physical
346 properties of the product.
- 347 3. The mother-liquor contains metallic catalysts which must
348 be recycled if the process is to be efficient. Recycling
349 of the reaction solution (mother-liquor) usually entails
350 considerable effort in working-up and cleaning (the spent
351 solution contains water, tars and/or high boilers and
352 of course the metal catalyst salts in addition to acetic
353 acid).

354 In spite of these inherent difficulties, several companies
355 have developed processes based on the catalytic liquid-
356 phase oxidation. Most of these companies are Japanese, such
357 as Daicel [39,40], Mitsubishi [41–44], Nissan [45,46], but
358 also Reilly in the US practiced liquid-phase oxidation of 3-
359 picoline to niacin on a commercial scale in the 1970s [30].

360 An interesting development is Daicel's use of *N*-
361 hydroxyphthalimide together with cobalt and manganese
362 acetate. This leads to very pure nicotinic acid (>99%) with a
363 selectivity of 80%. However, neither the fate nor the
364 consumption of the expensive *N*-hydroxyphthalimide is
365 clear in this process.

366 Mitsubishi remain with the traditional use of cobalt and
367 manganese acetates and bromide, but overcome the problem
368 of bromide contamination in the end-product by hydro-
369 genation of the reaction product with Pd/C. Optimisation of
370 this process by Mitsubishi leads to reported yields of over
371 90%, and less than 30 ppm bromide in the end product.
372 Although recycling was reported, it is not clear how many
373 cycles can be effected without having to work-up the mother
374 liquors, nor is it clear whether nicotinic acid can be
375 quantitatively removed from the recycled liquors. If
376 decarboxylation to pyridine can be suppressed, then this
377 latter point may not be too critical.

378 Nissan have also developed a very efficient process with
379 conversion at 98% and selectivity at 97%. Nissan use a
380 catalyst cocktail of cobalt and manganese acetate, sodium
381 bromide and hydrochloric acid in acetic acid. Hastelloy
382 reactors are necessary to resist corrosion.

383 A further development of Nissan is described where use
384 of the solvent is waived, thus avoiding corrosion. An 80%
385 conversion is reported using this variant. Whether this

ingenious development can be converted to a technical or
commercial process remains to be seen.

334 3.6. Ammoxidation and direct oxidation of methyl ethyl
335 pyridine (MEP) 336

337 As mentioned above, the intrinsic loss of two carbon
338 atoms as carbon dioxide during the conversion to nicotinic
339 acid or amide makes the use of MEP in future processes
340 unattractive. Nonetheless, because the starting-material is
341 relatively inexpensive compared to picoline, efforts have
342 been made to develop catalytic gas-phase processes [13,47].
343 The above-mentioned loss of two carbon atoms as carbon
344 dioxide means that the reaction enthalpy to nicotinic acid is
345 three times higher than that of picoline, so that there is a heat
346 transfer problem which limits the throughput of MEP. The
347 selectivity of both direct oxidation and ammoxidation is
348 considerably lower than that of picoline, so that the gas-
349 phase process hardly seems a likely alternative to either
350 oxidation or ammoxidation.

351 3.7. Electrochemical oxidation 352

353 Quite good chemical selectivity (80%) and electrical
354 efficiency (up to 90%) have been achieved in the laboratory
355 with the oxidation of 3-picoline using lead cells [48,49], but
356 there are considerable practical difficulties involved in this
357 approach. With a lead anode, corrosion occurred in an alkyl
358 pyridine oxidation corresponding to 0.3 mol lead/mol
359 product [50]. Other work using a Pb–Ag anode reports
360 better corrosion resistance [51]. For nicotinic acid it was
361 calculated that for the above conditions about 11 MW h of
362 electrical power are necessary to produce 1 t of nicotinic
363 acid from picoline. The present cost of electricity, at least in
364 Europe, makes this an expensive oxidising agent.

365 An indirect chemical/electrochemical oxidation of pico-
366 line by manganese dioxide was developed in the lab, in
367 which the latter is reduced to manganese sulphate [50]. The
368 electrochemical oxidation of this back to MnO₂ is quite
369 efficient, but the process requires stoichiometric quantities
370 of the oxidising material, for example 3 mol MnO₂/mol
371 picoline or 9 mol MnO₂/mol MEP, to effect the desired
372 reaction. Both the present technical and economic factors for
373 the direct anodic oxidation as well as the indirect method
374 using manganese oxide relegate these methods to scientific
375 curiosities.

376 4. Conversion or work-up 377

378 4.1. Chemical hydrolysis of 3-cyanopyridine 379

380 The market demands and expects a constant nicotinate
381 quality in both purity and form. Clearly, a key factor in the
382 commercial production of either niacinamide or niacin is the
383 purification and formulation process following the main
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441 reaction. In the case of niacinamide, the reaction product is
442 3-cyanopyridine, which first has to be selectively hydro-
443 lysed. The hydrolysis is usually carried out in the presence of
444 a strongly basic catalyst, which unavoidably generates some
445 nicotinate salt. This has to be removed if pure niacinamide is
446 desired. Both Reilly [52–54] and Degussa [55–57] describe
447 processes involving strong bases and subsequent purification
448 using ion-exchangers. Recently catalysts based on supported
449 manganese dioxide and alkali or alkaline earth oxides have
450 been developed which also efficiently promote the hydro-
451 lysis [58].

452 4.2. *Enzymatic hydrolysis of 3-cyanopyridine*

453 From the above it will be seen that one drawback of the
454 chemical hydrolysis is that inevitably some nicotinate salt is
455 produced due to over-hydrolysis of cyanopyridine. Nitto
456 discovered that it is possible to selectively hydrolyse nitriles
457 to amides enzymatically and then developed this to include
458 hydrolysing 3-cyanopyridine to niacinamide [59,60]. The
459 bacterium *Rhodococcus* is astonishingly active and selective
460 even at high concentrations of starting-material. Further
461 developments have been made in this direction by BASF
462 [61] and Lonza [62]. The latter have incorporated this
463 technology into their patented niacinamide process in China
464 [11]. This has the advantage over the chemical hydrolysis in
465 that the reaction is completely selective and the concentrated
466 solution of niacinamide may be directly transformed into a
467 pharmaceutical-quality free-flowing material by spray-
468 drying. Thus there are no mother-liquors and no side-
469 products, which need to be eliminated.

470 4.3. *Formulation of end product*

471 Niacin and niacinamide in their natural crystalline form
472 are not free-flowing materials and show a tendency to
473 coalesce to form large clumps (caking). This property is not
474 acceptable when accurate dosing of material is required for
475 GMP feed and food formulations. Thus it has been of
476 paramount importance for industry to overcome this
477 problem and create a free-flowing product, but without
478 any additional foreign material present. Mechanical treat-
479 ments such as granulation and compacting are standard
480 methods for achieving the desired rheological properties.

481 Degussa developed a crystallisation process to give large
482 nicotinic acid crystals. This involves the total hydrolysis of
483 3-cyanopyridine with a strong base [63]. Since the crystal
484 size of nicotinic acid depends on the concentration (which is
485 low at temperatures under 100 °C), the process is carried out
486 at elevated pressures and temperatures to ensure sufficiently
487 high concentrations.

488 Recently Degussa [64] have also patented a process to
489 produce free-flowing niacinamide by cooling droplets of
490 molten product in an inert atmosphere.

491 As mentioned above, Boreskov's process incorporates a
492 de-sublimation of nicotinic acid out of the gas-stream. This

method exploits the physical properties of nicotinic acid and
functions well [65]. Subsequent re-crystallisation and
formulation stages are however probably necessary to
ensure adequate purity.

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A different approach has been taken by Lonza [34] and
Nippon Soda [66]. Both methods utilise the decomposition
of ammonium nicotinate at elevated temperatures. Lonza
convert highly concentrated solutions of ammonium
nicotinate to pure nicotinic acid by spray-drying, which
also ensures a free-flowing material. Nippon treated the
ammonium salt of several acids, including nicotinic, in high-
boiling ethers at elevated temperatures, whereupon ammo-
nia is split off.

5. Conclusions and outlook

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In the past 15 years or so there has been no real dramatic
change in the fundamental methods of manufacturing
nicotinates on an industrial scale.

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Nevertheless, there have been significant developments
both in the niacinamide technology and in niacin itself. What
is apparent is the increasing awareness of economic and
ecological factors, which are determined by the limitations
of the technologies. Thus the gas-phase ammoxidation of 3-
picoline is the preferred route to niacinamide, because it is
the most cost-effective, efficient and environmentally
friendly process presently available.

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Picoline itself is now also industrially produced starting
from MGN or MPDA, and is no longer the Cinderella of the
pyridine process.

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In the conversion of cyanopyridine to niacinamide, the
enzymatic hydrolysis is a new development, which offers
several advantages over the established chemical alternative.

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Liquid-phase oxidation of picoline has received
considerable attention in the past 10 years or so and
excellent yields have been obtained. Nevertheless, the
problems with the mother-liquors, catalyst recycling and/
or regeneration, together with the purity and form of the
end-product are considerable and at best the process
represents a compromise solution to a cost-effective and
environmentally acceptable production. The bulk of niacin
is still produced using the liquid-phase oxidation of MEP
with nitric acid.

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As yet there are no known direct gas-phase processes
producing commercial quantities of niacin. Niacin produced
via ammoxidation has to be hydrolysed using stoichiometric
quantities of base, which in turn leads to considerable waste
production. Direct oxidation processes, which have been
developed on a lab and pilot scale have yet to be proven on a
larger scale. The reaction technology of the direct oxidation
of picoline is intrinsically considerably less robust when
compared to ammoxidation. The future challenge is to
develop a commercial process, which is robust, simple and
capable of producing niacin of an acceptable quality for the
market.

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 550 processes.

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