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Efficient and Scaleable Methods for ω-Functionalized Nonanoic Acids: Development of a Novel Process for Azelaic and 9-Aminononanoic Acids (Nylon-6,9 and Nylon-9 Precursors)

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Abstract:

A new, convergent synthesis and process of the title open-chain C-9 compounds, valuable monomers for preparation of polyamides with specific properties, are discussed. Starting from relatively inexpensive raw materials, for example, cyclohexanone and activated C-3 olefins, the method provides polymer grade ω-functionalized nonanoic acids. An improved protocol for cyanoethylation or carbalkoxyethylation of cyclohexanone in the presence of a catalytic amount of primary or secondary amines gave 3-(2-oxo-cyclohexane) propanecarboxylic acid derivatives 1 in high yield. Cyclohexaneperoxycarboxylic acid (CHPCA) is introduced as highly efficient reagent in Baeyer−Villiger rearrangement of 1. Pyrolysis of 2 (EWG = CN) afforded under optimized conditions 3 in high yield and regioisomeric purity, otherwise a mixture of three unsaturated isomeric ω-cyano nonenoic acids is obtained. Partial hydrogenation of unsaturated acids 3 allowed isolation of saturated long-chain difunctionalized acids 4. Hydrolysis of 4 led to 1,9-nonanedicarboxylic acid (azelaic acid) 5, whereas its hydrogenation at elevated pressure gave 9-aminononanoic acid 6. Alternatively, a practical four-step syntehsis of 5 via isolable 7-substituted oxepan-2-one (EWG = COOMe) 2 has been designed and experimentated. The versatile position of 3-(2-oxo-cyclohexane) propanecarboxylic acid derivatives 1 as raw materials for Fine Chemicals is also discussed.

Introduction

Altough polymer synthesis is almost completely atom-efficient, monomer synthesis cannot be expected to be so perfect. Because monomers are produced in such large amounts, every effort has been made to maximize their yield and purity. Remarkable success has been achieved in creating high-purity, polymerization-grade monomers in enormous volumes. The concept of atom economy for organic reactions proposed by B. Trost teaches that, for economical and ecological reasons, organic synthesis should be atom-efficient; in other words, all reagents used should end up in the final product. Ideally, there would be no waste streams, and maximum use would be made of available resources. Addition and cycloaddition reactions of organic molecules are the most representative pathways to realize this concept.[1]

The versatility of linear polyamides in the manufacture of various products ranging from synthetic textiles to electronic components, from packaging film to structural elements induced a large and continuous interest for more efficient synthesis of suitable monomers of their manufacturing.[2]

The polyamides 6 and 6,6 are the most popular as well as their monomers, caprolactam, adipic acid and hexamethylenediamine, which are important products of the petrochemical industry.

Polyamides from long-chain amino acids in which the polar groups are separated by at least four methylene groups can yield materials that form fibers with superior properties. Long-chain polyamides have found “niche” applications requested by specific physicomechanical characteristics of the polymer. The consumptions of long-chain polyamides in the past decade were around 100 000 mt/year at the growth rate of 8% per year. The past decade prices ranged from the \$7.3/kg of nylon-6,12 to the \$10.6/kg of nylon-11.

Long-chain nylons are characterized by a ratio between methylenic and amidic groups higher than nylon-6 and -6,6. That enhances all polyethylene-like properties, as low water absorption, dimensional stability under different conditions of humidity, impact strengths, good behavior at low temperatures, low density, low softening points, and lower hydrolysis sensitivity, while some properties of polyamide are maintained, like high melting points, good aesthetic properties, good processability, and resistance to hydrocarbon solvents.

This set of properties allows the use of long-chain nylons in applications forbidden for nylon-6 and -6,6 types, despite their higher prices. As a consequence, nylon-11 and -12 are particularly attractive as engineering polymers, and for special technical applications, where the improved mechanical properties, such as toughness, flexional strengths, abrasion resistance, and dimensional stability are highly desirable for the manufacture of precision engineering components.

Looking to the long-chain polyamides, those based on the C-9 chain seem to have interesting properties. The ratio between methylene groups, conferring hydrophobicity to the polymer and amide groups, giving hydrophilic properties,

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is still high, and therefore water is absorbed in moderate amounts. Their melting points, depending on the chain length, are still too high to afford high operation temperature of derived polymer. The above physical properties induce a dimensional stability and use in the manufacturing of precision components.

Nylon-9 was commercialized in the former Soviet Union. It was made there by the polycondensation of 9-aminonopelargonic acid and went under the trade name "Pelargon".

The most important monomers of long-chain polyamides are the ω-amino acids, their corresponding lactams, or the ω-dicarboxylic acids and ω-diamines. Industrial applications have found for example, 11-aminoundecanoic acid for nylon-11, laurolactam for nylon-12, hexamethylenediamine and azelaic or sebacic acids as comonomers for nylon-6,9 and nylon-6,10, respectively.

The main C-9 monomers are 1,9-nonanedioic acid (azelaic acid) and 9-aminononanoic acids (9-aminopelargonic acid). ω-Functionalized nonanoic acids have been the subject of active preparative investigations as they are important monomers and comonomers for polyamides with specific properties and applications[2] and are also used as raw materials for complex ester oils and lubricants[4] as principal components in alkyd resin preparation[5] or as pharmaceutical intermediates.[6]

Synthetic Approaches to Acid Monomers. Odd-numbered carbon acids are rare in nature and in industrial chemistry. Azelaic and pelargonic are the most accessible. As an interesting characteristic it appears that odd-numbered carbon acids are more surface active than are those with an even number.

Even the most simple non-α-amino carboxylic acids, for example, (3-amino propanoic acid-β-alanine-4-aminobutanoic acid, also known as γ-aminobutyric acid (GABA), 5-aminopentanoic acid, known as δ-aminovaleric acid (DAVA), are important compounds. The synthetic approaches to non-α-amino acids basically relay on functional group exchange strategy and substituent refunctionalization of cyclic precursors[3]

The commercial-scale manufacture of the above ω-amino or alkanoic acids falls into two logical approaches.

The first one is of **fragmentation type**: long-chain compounds can be fragmented and simultaneously functionalized to difunctionalized compounds. The raw materials are generally derived from agriculture. Synthesis of 11-aminoundecanoic and sebacic acids from castor oil and the synthesis of azelaic acid from tallow oil via oleic acid by ozonolysis are examples of this approach.

The second approach is of **convergent type**: the alkane chain is built up from low molecular weight fragments starting from inexpensive petrochemical raw materials. Synthesis of laurolactam starting from cyclododecatriene obtained by the butadiene trimerization is a good example of this approach.

Azelaic Acid. The class representative, 1,9-nonanedioic acid is produced commercially by the ozone oxidation of oleic acid (Henkel−Emery process),[7] and it is the preferred aliphatic dicarboxylic acid for preparation and modification of high molecular weight polymers.[4] Oleic acid may be cleaved at the double bond by treatment with ozone from an electrical discharge. Ozonolysis gives a mixture of crude 8-carboxyoctanealdehyde and pelargonic aldehyde. The next step is the oxidation of aldehydes to pelargonic and azelaic acids as well as other oxidation products. The process ends with several clean up operations.

Reported Routes to 9-Aminononanoic Acid (and Nylon-9). Although 9-aminononanoic acid is a compound which has been known for a century,[8] very few routes were available (and only at high cost) until now for its commercial production. On a laboratory scale, the preparation and purification of 9-aminononanoic acid is complicated and difficult.[11] Laboratory methods starting either from ω-halogenated[9a] or from ω-nitro derivatives[9b] have been studied; however, neither precursor is easily available. Flaschentrager[12] prepared 9-aminononanoic acid by performing the Hoffmann degradation reaction on sebacic acid. Reductive ozonolysis, reductive ammination, and ammonolysis of olefins from soybean oil[10a−f,19] (Scheme 1) and methods that

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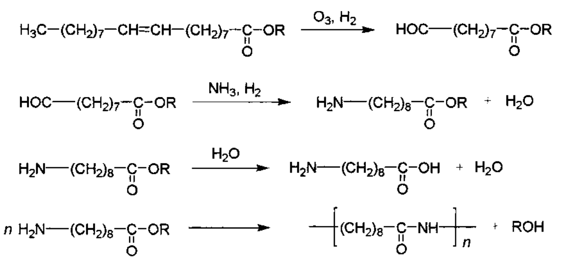
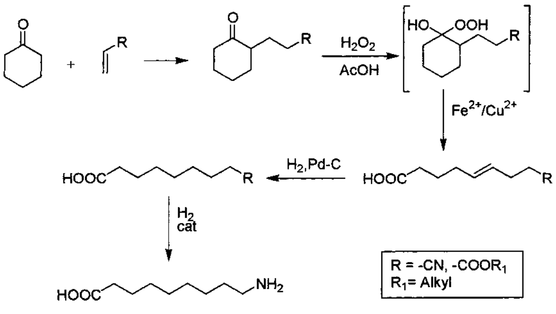
Scheme 1. **Ozonolysis and reductive amination route to nylon-9**



Scheme 2. **Redox-radicalic route to 9-aminononanoic acid**



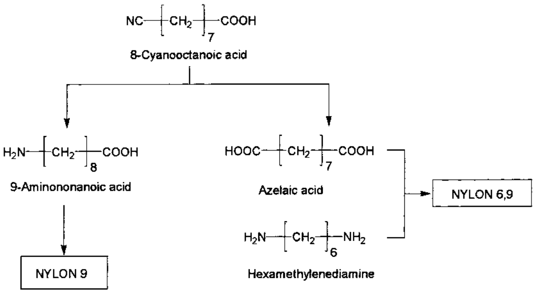
imply either elongation (e.g., telomerization[17,18] or shortening of the chain length have been also published.[10g,13−16]

Results and Discussion

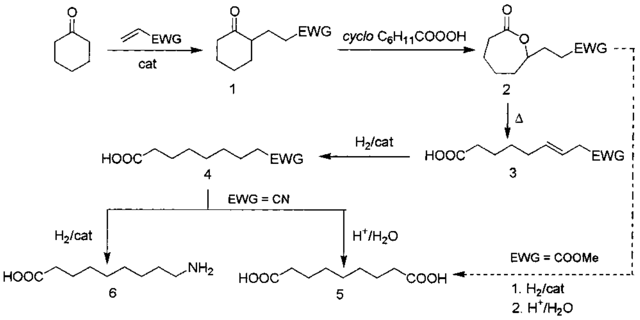
Minisci and co-workers proposed a convergent route to azelaic and 9-aminononanoic acid, starting from cyclohexanone and acrylonitrile.[21] The intermediate addition product, 3-(2-oxocyclohexane)propionitrile can be oxidized by hydrogen peroxide and Fe^{2+}/Cu^{2+} salts as catalyst to give 8-cyanooctenoic acid (Scheme 2). Further conversion of nitrile group by hydogenation or hydrolysis led to the desired product. The above reaction sequence presents important economical advantages and easy access to the raw materials. This “discovery method” has been extensively examined in our laboratory to find a scalable route to the amino acid. Unfortunately, the method as originally reported failed to be developed as: (i) the hydrogen peroxide oxidation was not selective, and a complex mixture of hydroxy acids was formed from hydroperoxide intermediates; (ii) the work up to isolate the oxidation intermediate was complicated, and we did not succeed to recover it from the aqueous medium; (iii) a high amount of catalyst salts was necessary, and therefore much work had to be done to solve mixing problems.

Improving the selectivity of the oxidation step was therefore the entrance key to a scalable process. This new versatile process is able to produce both monomers of **nylon-9** and **nylon-6,9**, for example, azelaic acid (or its esters) and 9-aminononanoic acid (or its esters), through the new key intermediate 8-cyanooctanoic acid (Scheme 3).

Scheme 3. **Nylon-9 and nylon-9,9 monomers**



Scheme 4. **Chemistry of the new process**



We now report the five-step synthesis of two ω-functionalized derivatives of nonanoic acid, starting from easily available C-6 and C-3 synthons (Scheme 4).

Starting from an isolable and pure cyclic precursor, the corresponding lactone, we were able to find a route to the difunctionalized saturated linear compounds. The lactone cyclic precursor was easily accessible by a convergent process, for example, by a coupled Stork addition and Baeyer−Villiger rearrangement. The initial steps are notably improved as compared to the described procedures, and the whole method is operable on the large scale.

Cyclohexanone Alkylation by Electophilic Olefins. Numerous investigators have found that the base-catalyzed Michael addition of acrylonitrile to active hydrogen compounds leads to the formation of polycyanoethylated derivatives as the main reaction products. The requirement for a strongly basic catalyst (such as sodium methoxide) precludes the use of reactants having base-sensitive functional groups and can result in side reaction such as aldol condensations. The reactions are, moreover, strongly exothermic, thus necessitating special precautions for removing the reaction heat when the reactions are carried out on a technical scale.

Excellent alternatives to base-catalyzed condensation of electrophilic olefins with cyclanones having active hydrogen atoms are: (a) Stork’s procedure using tertiary enamines,[22] and (b) Michael-type α-alkylation using imine derivatives reacting as their secondary enamine tautomers[23]

However, until now, literature concerning the one-step catalytic enamine alkylation of cycloalkanones is still limited.[24] The reported methods,[25a−f] required a two-step

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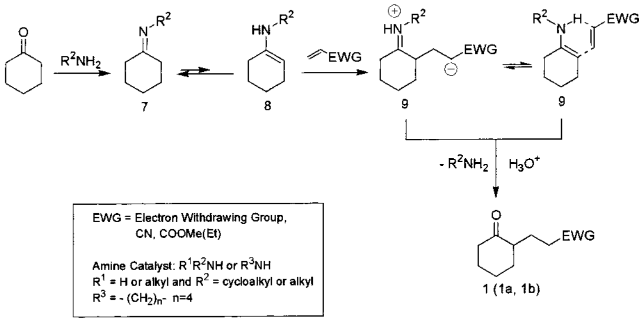
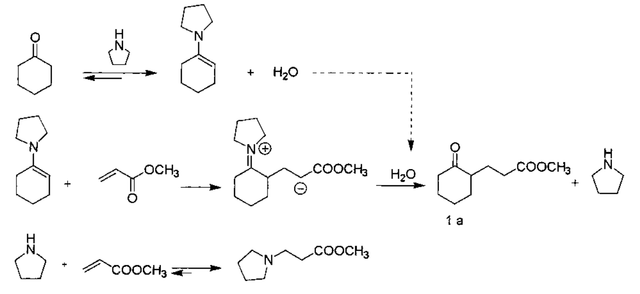
Scheme 5. **Michael-type monoalkylation of cyclohexanone**



Scheme 6. **Catalytic alkylation of cyclohexanone by methyl acrylate in the presence of pyrrolidine**



reaction involving enamine formation with equimolecular quantities of amine and hydrolysis of C-alkylated imine, respectively.

By our method,$^{26a-e}$ the α-alkylation of cyclohexanone by acrylonitrile was carried out in the presence of cyclohexylamine/acetic acid as a catalytic system, at 130 °C. GC−MS monitoring of reaction progress at 60−90 °C revealed the very selective formation of **1** via intermediary imine compounds **7** and **9** (Scheme 5). In the final stage formation of *N*,*N*-di(*β*-cyanoethyl)cyclohexylamine has been also observed.

High yields (92−95%) and selectivities of 3-(2-oxocyclohexane)propanoic acid alkyl esters (**1a, 1b**) have been obtained when pyrrolidine was used as catalyst and with methyl or ethyl acrylate as the olefins (Scheme 6).

Moreover, we observed that using a recycled distillation fraction containing controlled amount of water, cyclohexanone and *N*-alkylated pyrrolidine [e.g., alkyl (Me or Et) 3-(*N*-pyrrolidino) propionate], and neutral pH, high yields (94%) of *δ*-ketoesters **1a** or **1b** were obtained. Pyrrolidine or alkyl (Me or Et) 3-(*N*-pyrrolidino) propionates have been used as catalysts to prepare compounds **1a** or **1b**, according to the method described for **1**. Crude product was isolated by distillation in a vacuum, and the fraction containing water, cyclohexanone, and *N*-alkylated pyrrolidine was recycled.

Development of the process involved significant improvements regarding suppression of cyclohexanone self-aldol condensation, olefin polymerization, and amine alkylation by the olefin.

The catalytic variant of Michael-type imine alkylation has the advantage that it can also be performed in continuous mode, which comprises running the reaction in two stages, first at 70−80°, then at 130 °C. Cyclohexanone, acrylonitrile, and the catalyst (molar ratio 2:1:0.15) were simultaneously fed into the first reactor at 70−80 °C. Then the reaction mixture was continuously transferred into a continuous stirred tank reactor, preheated at 130°, residence time of 2 h, thus allowing nearly quantitative conversion of the olefin and yield of isolated *δ*-keto nitrile **1** of 92%. Continuous distillation of the reaction mixture afforded separation of the main product stream, a recycle stream containing the catalyst, and the purge.

Baeyer−Villiger Oxidation. Regioselective Baeyer−Villiger rearrangement of **1** was best performed using an *n*-hexane solution of cyclohexaneperoxycarboxylic acid (CHPCA).

CHPCA is an oxidising agent recently developed in our laboratory.^{26a,d} It has the advantage over short-chain aliphatic peracids to be substantially immiscible with water, less shock-sensitive, and nondeflagrating. CHPCA can be produced more cheaply than many other known peracids that already have wide applications in preparative and industrial organic chemistry. Organic solutions of CHPCA are safer on both small- and large-scale operations. We prepared solutions of CHPCA in *n*-hexane, cyclohexane, or cyclohexanecarboxylic acid (CHCA) by a modified Swern procedure^{26d,27} avoiding dangerous isolation of the solid product. The loss of available oxygen content of a 1 M solution of CHPCA in cyclohexanecarboxylic acid was less than 2% after 48 h at 50 °C.

CHPCA offered significant advantages in the process scale up. It can be produced in situ from the commercially available parent acid, which is recycled, and hydrogen peroxide, avoiding hazardous storage and handling (shipment). CHPCA/CHCA couple shows interesting oxidation behavior. The parent acid, CHCA, has melting point of 28 °C and is therefore liquid at temperatures slightly above ambient; it can be simultaneously used as reagent and solvent of peracid. It is immiscible with water, and consequently it can be prepared in biphasic system, and the peracid can be recovered in the organic phase by simple phase separation. Azeotropic distillation at low temperature and pressure affords the preparation of anhydrous peracid organic solution.

The peracid preparation has been scaled up in a continuous process, and the peracid stream has the operating concentration below 20%. The active oxygen content was continuously monitored to ensure the reaction and processing outside the detonable area.

The main reaction product, 7-(*β*-cyanoethyl)oxepan-2-one, **2a** (Scheme 7) is slightly soluble in an *n*-hexane solution of

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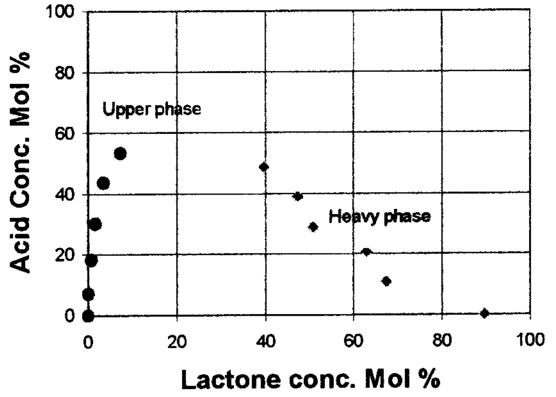
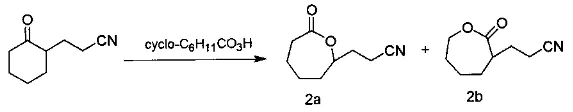


Figure 1. **Liquid−liquid equilibrium of the *n*-hexane−CHCA-7 cyanoethylcaprolactone at 50 °C.**

Scheme 7. **Regioselectivity of Baeyer−Villiger rearrangement**



cyclohexanecarboxylic acid. This behavior facilitated its separation from the reaction mixture (Figure 1), affording significant advantage, that is to use *n*-hexane solutions of cyclohexaneperoxycarboxylic acid in Baeyer−Villiger reaction.

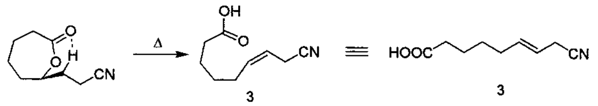
The scaled Baeyer−Villiger step was carried out at 50 °C, that is the temperature of peracid synthesis. Therefore, during the process, the peracid temperature and concentration are kept constant, enhancing thus the plant safety operation. Quantitative peracid conversion is achieved in a plug-flow reactor and with residence time of a few hours.

As CHCA is completely soluble in *n*-hexane, separation of lactone is possible by hexane counter-flow extraction, applying mild separation conditions, without heating or evaporation/concentration. The last operations would represent hazardous points in the process in the case of th wrong operation of the Baeyer−Villiger reactor. All of these considerations are incorporated in the plant process.

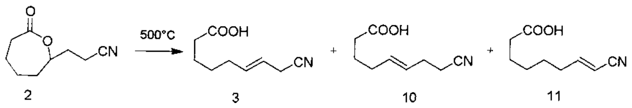
Lactone Pyrolytic Ring Opening. Synthesis of Unsaturated Acids. Unsaturated *ω*-functionalized nonanoic acids are precursors of corresponding saturated chain carboxylic acids. Their facile hydrogenation affords the synthesis of a 9-carbon atom straight-chain structure, difficult to build through carbon−carbon homologation pathways or starting from the common available organic synthons. Formation of the open-chain C-9 intermediate was completed by pyrolytic ring opening of lactone at 550−600 °C, and according to the reaction thermodynamics, a residence time of a few seconds is sufficient to cleanly and quantitatively convert the lactone.[26b−e]

Surprisingly, the pyrolytic reaction proceeded with higher regioselectivity at more elevated temperatures than at the lower ones: at 600 °C, 92% of 8-cyano-6-octenoic acid was formed, (Scheme 8), whereas at 550 °C, a mixture 2:1:1 of three olefinic *ω*-cyanooctenoic acids was obtained (Scheme 9). This product distribution was revealed by GC−MS and confirmed by oxidative cleavage of **3, 10**, and **11** to hexandioic, pentandioic, and heptandioic acid, respectively (Bayer test).

Scheme 8. **Pyrolysis of 7-(*β*-cyanoethyl)oxepan-2-one**



Scheme 9. **Pyrolysis of 7-(*β*-cyanoethyl)oxepan-2-one at lower temperature**



As regarding the process, the three unsaturated acids are all useful precursors of saturated chain carboxylic acid. Increased selectivity with temperature can be explained by prevalent ionic, surface-catalysed pyrolysis at lower temperatures and pure gas-phase thermal pyrolysis at higher temperatures. The lower-temperature conditions are known to increase the surface-catalyzed carbocation formation that rearranges into other structurally similar, more stable carbocations,[28] whereas gas-phase pyrolysis follows a pericyclic mechanism,[29] and in our case leads to **3** as the only product.

Although the reaction is known, no preparative applications are reported according to our knowledge in the caprolactone family.

The main difficulty of the scale-up was the cyanolactone transfer in the gas phase. In fact heating the lactone at the boiling point induced an extensive polymerization. To avoid the lactone loss, the vaporization (nebulization) has to be realized in very short time at pyrolytic temperature. This stage of the process has been realized on pilot scale by “on-column” feeding of the liquid lactone into the pyrolysis tube reactor flushed by nitrogen flow through a suitably designed dispersion system of dropping liquid into the gas phase. This stage of reaction has been the determining step of the scale-up.

A purpose-built vertical furnace-reactor equipped with a pyrolysis metal tube having an inner spinning-carrier device was used. Nitrogen was passed through the lactone **2**, previously melted, and then the lactone was added dropwise at the rate of 0.5 g/min through the pyrolysis tube preheated at 600 °C. A pale-yellow pyrolysate was formed. To isolate pure **3**, pyrolysate was washed with base and acid, extracted and fractionally distilled; 8-cyano-6-octenoic acid, **3** was obtained in 92% yield, bp 155 °C/0.05 Torr; its titration indicated the presence of 95% of titratable carboxylic acid (mixture of *cis/trans* isomers).

An alternative procedure for the lactone opening is the nucleophilic cleavage by various methods and reagents (Scheme 10). All of the methods above add new steps to the process and increase the costs.

Lactone cleavage can be also performed batchwise, with hydrogen gas and catalyst under pressure (Scheme 11). In the case of lactone-ester a mixture of azelaic acid methyl esters and acid itself is obtained in a very clean process which has not been yet scaled up.

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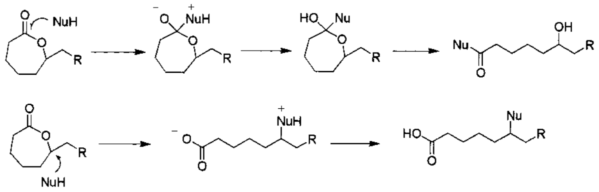
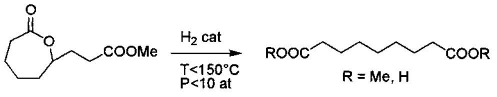
(28) Wertz, D. H.; Allinger, N. L. *J. Org. Chem.* **1977**, *42*, 698.

(29) Bailey, W. J.; Bird, C. N. *J. Org. Chem.* **1977**, *42*, 3895.

Scheme 10. **Nucleophilic cleavage of substituted caprolactones**



Scheme 11. **Hydrogen cleavage of 7-(β-cyanoethyl)oxepan-2-one**



Use of hydrogen as carrier gas and of a suitable hydrogenation catalyst to directly obtain 8-cyanooctanoic acid are the likely improvements in the nitrile-lactone opening.

Experimental work on hydrogenation of unsaturated cyanoacids has been carried out using traditional conditions, for example, batch reactor and Pd−C as catalyst. Low-pressure catalytic hydrogenation of unsaturated carboxylic acid **3** yields 8-cyanoctanoic acid **4**. Compound **3** was hydrogenated with H_2 at 50 °C and 8-at, using toluene as solvent and 5% Pd−C as catalyst. After filtration and solvent evaporation (90%) of pale yellow oil was recovered. It contained 99% of titratable 8-cyanooctanoic acid. Pure **4** has bp 150 °C/0.05 Torr.[26b−e]

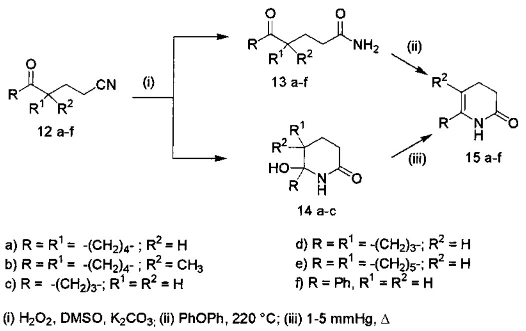
In the final steps either hydrolysis to **5** or hydrogenation to **6** was performed; under optimized conditions both reactions proceed with ~90% yield.[26b−e] Final hydrogenation of saturated cyanoacid to obtain 9-aminononanoic acid was performed as follows: compound **4** was hydrogenated at 55 °C and 80 atm in ammonia-saturated ethyl alcohol, over Raney-Ni. Cooling, filtration, and recrystallization from hot water afforded (90%) of 9-aminononanoic acid, mp 191−192 °C. Polymer grade 9-aminonononanoic acid (mp 192−193 °C) was obtained by recrystallization of amino acid barium salt from hot water and then recovering the amino acid by treatment with “dry ice” CO_2.

1,9-Nonanedioic acid was obtained by hydrolysis of **4** at 100 °C in concentrated H_2SO_4. After the mixture cooled, the solid product was separated by filtration. Washing and recrystallization from water afforded (90%) of 1,9-nonandioic acid **6**, mp 107−108 °C.

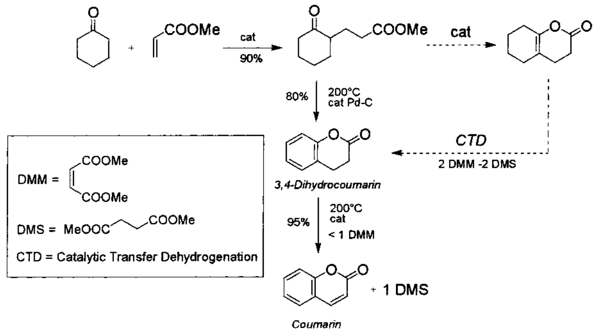
Versatility of 3-(2-oxocyclohexane) Propanoic Acid Derivatives. δ-Keto-derivatives of 3-substituted propanoic acid are useful intermediates in the synthesis of fine chemicals. Selective monoalkylation of cyclohexanone by acrylic acid derivatives afforded the study of intramolecular cyclization of the above compounds.

3,4-Dihydro-2-pyridones (ene-lactams) are versatile intermediates for the synthesis of piperidine and hydroquinoline ring system. Katritzky’s procedure for the oxidative hydration of nitriles to amides by basic hydrogen peroxide in DMSO may be efficiently applied to the synthesis of 3,4-dihydro-2-pyridones (15a−f) from cyanoethylated ketones (12a−f) (Scheme 12).[30]

Scheme 12. **Synthesis of 3,4-dihydro-2-pyridones**



Scheme 13. **Synthesis of coumarin from 3-(2-oxocyclohexyl)propanoic acid methyl ester**



Intramolecular cyclization of 3-(2-oxocyclohexyl)propanoic acid esters to ene-lactones opened a very interesting preparative route to coumarin and its hydrogenated precursor, 3,4-dihydrobenzopyran-2-one (dihydrocoumarin).[31] A pilot-scale process including alkylation of cyclohexanone by methyl acrylate and dehydrogenation of ene-lactone under catalytic hydrogen transfer conditions by various hydrogen acceptors (e.g., dimethyl maleate) has been developed (Scheme 13).

Conclusions

In summary, an efficient route to ω-functionalized derivatives of nonanoic acid has been developed. The initial two steps can be performed also in a continuous manner. The first one is characterized by the catalytic variant of the Michael-type imine alkylation of cyclohexanone, and the second by the use of cyclohexaneperoxycarboxylic acid as a new regioselective Baeyer−Villiger reagent. In the final steps controlled pyrolysis of 7-(β-cyanoethyl)oxepan-2-one affords unsaturated ω-cyanooctenoic acid, a key intermediate which is converted to the saturated chain corresponding acid and then to 9-aminononanoic and azelaic acids, both valuable C-9 monomers.

Azelaic acid has a well-consolidated commercial position. 9-Aminononanoic acid, on the contrary, has not found until now a suitable process to compete with other nylon monomers. The comparative evaluation of the new manufacturing process would require a detailed cost-performance

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(30) Citterio, A.; Carnevali, E.; Farina, A.; Meille, V.; Stefano, A.; Cotarca, L. *Org. Prep. Proced. Int.* **1997**, *29(4)*, 465.

(31) Alini, S.; Cotarca, L.; Delogu, P. U.S. Patent 5,872,265, 1997; Cotarca, L.; Clauti, G.; Delogu, P.; Nardelli, A.; Nero, A. I.; Alini, S.; Bianchini, R.; Sguassero, S. ICOS-12, 1998, Venice, Italy.

analysis of the nylon-9 polymer versus other long-chain polyamides. This is outside of the scope of this paper.

The new process uses easily available and stably priced petrochemical raw materials. Cyclohexanone and acrylonitrile are basic raw materials in the polymeric materials arena. Hydrogen peroxide is becoming more and more a “commodity” with favorable and less hazardous industrial applications. Cyclohexanecarboxylic acid is the more problematic raw material being available only from only one company even through it is manufactured at 20 thousand mt/levels for many years. CHCA is continuously recycled in the process, and therefore losses can be limited by a careful plant design. The unit operations are all of standard type, with liquid or gas flows and solid final products. Only the pyrolysis reactor remains with outstanding design problems.

The new process has a high atom economy and produces only a low volume of easily treated waste. The only important byproduct is ammonia, which is, eliminated as ammonium sulfate (∼0.7 kg/kg of azelaic acid) a common large byproduct of petrochemical industry where a single process (e.g., caprolactam manufacture) coproduces amounts such as millions of mt/y.

The process starting from oleic acid has more unfavorable mass balances. One ton of tallow oil produces an average amount of 270 kg of long-chain acids, half of them being represented by oleic acid. A small part of the other coproducts are useful to agricultural or industrial applications; the other one is treated.

In the oleic acid process, beside the pelargonic acid, a huge amount of low molecular weight acids sludge and water-soluble acids are produced. The synthesis starting from natural raw materials looks much more problematic with respect to the route starting from low-price petrochemical raw materials, and the atom economy is very low.

Experimental Section

3-(2-oxocyclohexyl) Propanenitrile (1). A mixture of cyclohexanone (20.7 g, 210 mmol), cyclohexylamine (1.5 g, 15 mmol), acetic acid (0.16 g, 2.5 mmol), and 4-methoxyphenol (0.17 g, 1.4 mmol) was heated at 70−80 °C. Acrylonitrile (5.55 g, 105 mmol) was dropwise added, heating the reaction mixture without reflux at 130 °C for 2 h. The product was then distilled in a vacuum. Obtained was 14 g of 3-(2-oxocyclohexyl)-propanenitrile, bp 114−115 °C/4 mmHg. The second crop (∼1 g) was obtained on heating on a steam bath with dilute hydrochloric acid for 30 min, followed by separation of the oil by extraction in benzene, evaporation of the solvent, and distillation in a vacuum. The yield of **1** thus amounts to 95%.

3-(2-oxocyclohexyl)-propanoic Acid Alkyl Esters (1a, 1b). Pyrrolidine or alkyl (Me or Et) 3-(*N*-pyrrolidino) propionates have been used as catalysts to prepare compounds **1a** or **1b**, according to the method described for **1**. Crude product was isolated by distillation in a vacuum, and the fraction containing water, cyclohexanone, and *N*-alkylated pyrrolidine was recycled. Obtained was 18.3 g (94%) of 3-(2-oxocyclohexyl)-propanoic acid methyl ester (**1a**) or 19.7 g (94%) of 3-(2-oxocyclohexyl)-propanoic acid ethyl ester **1b**.

Cyclohexaneperoxycarboxylic Acid. *A. Batchwise Method*. Cyclohexanecarboxylic acid (12.8 g, purified by crystallization of commercial product, from *n*-hexane/diethyl ether, mp 43−44 °C) was dissolved in methanesulphonic acid (64 g), and hydrogen peroxide (13 mL, 70% in water) was added dropwise at −5 to 0 °C over 1 h. Stirring was continued for additional 2.5 h at the same temperature, and then a water−ice mixture (200 mL) was added at such a rate that the temperature never exceeded +5 °C. The dilute reaction mixture was rapidly extracted with cold ether (2 × 100 mL), and extracts were washed with cold saturated ammonium sulfate solution (3 × 50 mL) and then with 100 mL of cold water. The ether solution was dried over anhydrous magnesium sulfate and kept in a refrigerator. Vacuum evaporation of filtrate below 10 °C afforded an oily residue, which slowly crystallized at 0 °C, to yield cyclohexaneperoxycarboxylic acid (82%), white crystalline solid, 11.8 g, mp ∼0 °C; peroxide oxygen: calcd 11.10%, found 11.25%. Purity of peracid is >95% (0.1 N NaOH titration) when freshly prepared. It quickly decomposed in the pure solid state, at ambient temperature, but contrarywise, it was stable for weeks when dissolved in organic solvents such as *n*-hexane, cyclohexane, or cyclohexanecarboxylic acid, at room temperature. We did not succeed in recrystallyzation of crude product.

Warning! Violent decomposition occurred in our laboratory when the solid CHPCA was deposited at ambient temperature.

B. Continuous Method. To produce solutions of “equilibrium” concentration of CHPCA in a biphasic water−*n*-hexane system, 1.75 mol/h of 50% hydrogen peroxide, 1.85 mol/h *n*-hexane solution of cyclohexanecarboxylic acid, and 385 mL of continuously recycled 45% sulfuric acid were fed into a laboratory glass continuously stirred tank reactor at 50−70 °C and slightly reduced pressure. The residence time was 3 h. CHPCA content in the efluent organic solution (usually 17−19%) was controlled by the rate of azeotropic water removal. Conversion of hydrogen peroxide was of over 60%, and selectivity of CHPCA formation was 50−55%. Anhydrification and acidity removal afforded a solution ready for use in Baeyer−Villiger rearrangement.

7-(β-Cyanoethyl)oxepan-2-one (2). 3-(2-oxocyclohexyl)-propanenitrile **1**, (15.1 g, 100 mmol) was heated at 40 °C, then cyclohexaneperoxycarboxylic acid (53 g of a hexane solution containing 15.8 g (109 mmol) of peracid) was added dropwise, under stirring, over 1.5 h. The reaction required cooling during the addition of peracid to maintain the temperature at 45−50 °C. After an additional 2 h of stirring, determination of peracid indicated 96% conversion. After the mixture cooled, two well-separated organic phases were formed. The lower layer containing 7-(β-cyanoethyl)oxepan-2-one, **2**, was concentrated under reduced pressure to remove *n*-hexane and cyclohexanecarboxylic acid. Lactone can be isolated either by short-path distillation or by continuous extraction of cyclohexanecarboxylic acid with *n*-hexane. On crystallization from ethyl acetate and methyl-*tert*-butyl ether 15.3 g (yield of 92%) of pure **2**, mp 34−36 °C, was obtained.

8-Cyano-6-octenoic Acid (3). A purpose-built vertical furnace equipped with a pyrolysis metal tube having an inner spinning-carrier device was used. Nitrogen was bubbled for a few minutes through the melted lactone **2** to be pyrolyzed, and then 0.24 mol of lactone was added dropwise at the rate of 0.5 g/min through the pyrolysis tube preheated at 600 °C. A pale-yellow pyrolysate was formed. To isolate pure **3**, pyrolysate was base- and acid-washed, extracted, and fractionally distilled; 8-cyano-6-octenoic acid, **3** was obtained in 92% yield, bp 155 °C/0.05 Torr; its titration indicated the presence of 95% of titrable carboxylic acid (mixture of *cis/trans* isomers).

Working at temperatures of 500−550 °C, mixtures of regioisomers **3**, **10**, and **11** were obtained in the ratio 2:1:1. Their structures were assigned by oxidative cleavage of double bond (Baeyer test)[25] and by GC−MS identification of the resulted dicarboxylic acids. Partial, low-pressure hydrogenation of this mixture, as described below for **3**, afforded saturated acid **4** with >98% purity.

8-Cyanooctanoic Acid (4). Compound **3** (38 g, 220 mmol) was hydrogenated in toluene (370 mL), at 50 °C and 8 atm of hydrogen, in the presence of 1.8 g Pd/C (5%). After filtration and solvent evaporation 35 g (90%) of pale yellow oil was recovered. It contained 99% of titratable 8-cyano-octanoic acid. Pure **4** has bp 150 °C/0.05 Torr.

1,9-Nonanedioic Acid (5). Compound **4** (5.5 g, 32 mmol) was hydrolyzed for 6 h at 100 °C in H_2SO_4 concentrated (10 mL). After the mixture cooled, the solid product was separated by filtration. Washing and recrystallization from water afforded 5.5 g (90%) of 1,9-nonandioic acid (**5**), mp 107−108 °C.

9-Aminononanoic Acid (6). Compound **4** (23 g, 134.5 mmol) was hydrogenated at 55 °C and 80 atm in 380 mL of ammonia saturated ethyl alcohol, over 2.2 g of Raney-Ni. Cooling, then filtration, and recrystallization from hot water afforded 21 g (90.2%) of 9-aminononanoic acid, mp 191−192 °C. Polymer grade 9-aminonononanoic acid (mp 192−193 °C) was obtained by recrystallization of amino acid barium salt from hot water and then recovering the amino acid by treatment with “dry ice” CO_2.

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