ORGANIC CHEMISTRY

FRONTIERS

Accepted Manuscript

Volume 6 | Number 1 | 7 January 2019

ORGANIC CHEMISTRY

FRONTIERS

CCS CHINESE CHEMICAL SOCIETY

rsc.li/frontiers-organic

CCS CHINESE CHEMICAL SOCIETY 中国化学会

SIOC 1950

ROYAL SOCIETY OF CHEMISTRY

rsc.li/frontiers-organic

Organic Chemistry Frontiers

Method

Combination of the structural components of amino acids with fatty acids: Access to an unknown class of "fatty" α-amino acids by palladium-catalyzed amidocarbonylation

Mohammed Asadpour,[a†] Edson Leonardo Scarpa de Souza,[a, b†] and Anke Spannenberg,[a] Carlos Roque Duarte Correia,[b] Helfried Neumann,[a] and Matthias Beller.[a*]

A new class of amino acids, so-called fatty amino acids, which integrate the typical structural motif of another important type of natural products, fatty acids, is presented. Applying the palladium-catalyzed amidocarbonylation, diverse new N-acyl fatty amino acids are synthesized in one step in 100% atom-efficient manner. Utilizing small amounts (0.5 mol%) of simple commercial Pd(OAc)$_2$ the desired products can be synthesized in good to high yields in up to multi-g-scale. The shown products represent a combination of two essential classes of natural products and provides new bio-based building blocks with potential for many applications.

Introduction

α-Amino acids and their derivatives are a prerequisite for life on earth.[1-10] Apart from their manifold biological functions in humans, animals, and plants, they find numerous applications in diverse fields ranging from nutrition and pharmaceuticals up to cosmetics. Another class of essential biomolecules are fatty acids, which are aliphatic monocarboxylic acids with longer linear, partially unsaturated carbon chains. Esters of fatty acids with glycerol are found in all natural fats and oils and represent an important renewable feedstock highly relevant for the chemical industry.[11-14]

Due to their importance, α-amino acids and fatty acids have been studied in detail by chemists, biologists, and many other scientists for more than a hundred years, and a large number of derivatives have been synthesized for numerous applications.[15-23] Although both biochemically essential classes of compounds occur in all living organisms, surprisingly there are no "hybrid" molecules in nature, e.g. amino acids with longer (unsaturated) aliphatic chains in α-position. Clearly, such extended alkyl groups will determine the hydrophobicity of the respective amino acid. In fact, hydrophobic interactions play a dominant role in stabilizing protein structures. Why has evolution avoided such chemical compounds? To answer this and to study the properties of "fatty" amino acids it is important to provide synthetic methodologies, which allow a convenient and general preparation of such compounds. Very surprisingly, such derivatives (with alkyl chains >C9) have not been synthesized to the best of our knowledge (Figure 1). Therefore, we set out to develop an efficient and environmentally friendly protocol to

make such molecules conveniently available on a g-scale for further studies. A straightforward route to synthesize natural and unnatural N-acyl amino acids is the so called amidocarbonylation of aldehydes (Figure 2a).[24] This one pot, three component reaction makes use of aldehydes, amides, and carbon monoxide in the presence of a suitable metal catalyst. Amidocarbonylations are generally catalyzed by cobalt and palladium complexes. As they are 100% atom-economical and use readily available substrates, they are also interesting from an ecological and economic point of view.
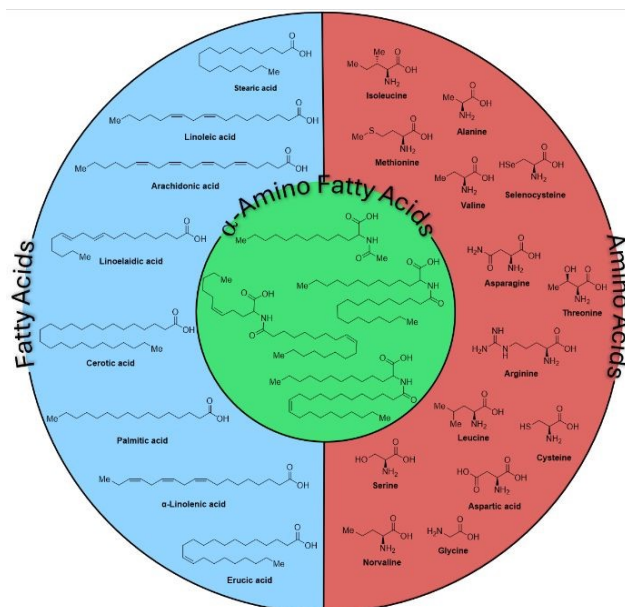
Figure 1. "Fatty" a-amino acids: A new class of compounds.

Originally in 1971, Wakamatsu reported the use of cobalt carbonyl complexes for this transformation.[25] Later, researchers at Hoechst developed a palladium-catalysed variant, which works at milder reaction conditions.[26] Interestingly, homogeneous[27-30] and heterogeneous[31-34] palladium catalysts have been applied in the latter and related cases.

a. Leibniz-Institut für Katalyse e.V., Albert-Einstein-Straße 29a, 18059 Rostock, Germany.
b. Institute of Chemistry, University of Campinas, Josué de Castro, 10384-612, Campinas, São Paulo, Brazil.

Organic Chemistry Frontiers Accepted Manuscript

Method

The carbonylation of fatty aldehydes with CO in the presence of amides should in principle lead to unnatural long-chain amino acids, which also exhibit interesting amphiphilic (surface-active) properties.[35-37] At this point, it is worth mentioning that the synthesis of new (bio-)surfactants with a hydrophilic head and a hydrophobic tail, gained increasing attention in recent years,[38-40] *e.g.* as part of modern vaccines.[41]

Against this background, we report here the first synthesis of a new class of unnatural amino acids. More specifically, we show that a variety of α-fatty amino acid derivatives are readily accessible by a palladium-catalysed amidocarbonylation reaction of the corresponding aldehydes in very good yields and selectively (Figure 2b).
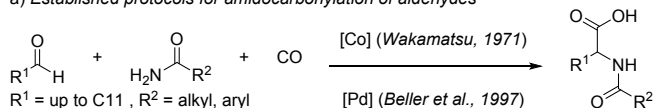
a) *Established protocols for amidocarbonylation of aldehydes*

b) *This work*

Extension of the methodology allows the synthesis of an un-known class of α-amino acids with many potential applications.

22 examples, up to 90% yield

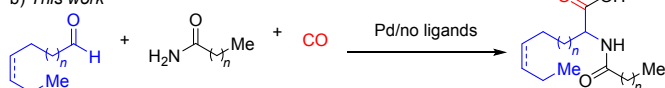**Figure 2.** Amidocarbonylation of aldehydes and amides.

Results and discussion

We commenced our studies using commercially available dodecanal **1a** and acetamide **2a** as model substrates in the presence of 1 mol% Pd(OAc)$_2$, 1 mol% H$_2$SO$_4$, 35 mol% LiBr in *N*-methyl-2-pyrrolidone (NMP) as solvent at 100°C under 60 bars of CO. Similar reaction conditions have been reported by some of us in developmental studies of the palladium-catalysed amidocarbonylation.[24] Gratifying, the desired product was obtained in quantitative yield under these conditions.

To identify crucial reaction parameters some variations of the metal precursor, temperature, pressure, additives, and solvent were made (Figure 3). Notably, in all these experiments a 1:1 ratio of amide and aldehyde was used, which is most economic and avoids additional waste formation. Among the different palladium precursors Pd(acac)$_2$ and Pd(OAc)$_2$ provided **3a** in quantitative yield, while Pd$_2$dba$_3$ and PdBr$_2$ gave lower product yield. Utilizing different solvents in the reaction furnished the product **3a** in lower yield compared to NMP. In general, high product yields were obtained at lower CO pressure (20 bar) and lower temperature (60°C). Decreasing the amount of catalyst proved to be viable and with only 0.1 mol% Pd(OAc)$_2$ 80% yield of **3a** was achieved. Furthermore, high catalyst turnover numbers (TON >2000) in this transformation could be realized. From a mechanistic point of view, it is interesting that the reaction is quite sensitive to the amount of LiBr (35 mol%). As discussed below (see Figure 5.), the formation of the α-bromo-*N*-alkylamide seems to be crucial for the product formation. In agreement with this assumption, the replacement of LiBr by LiCl
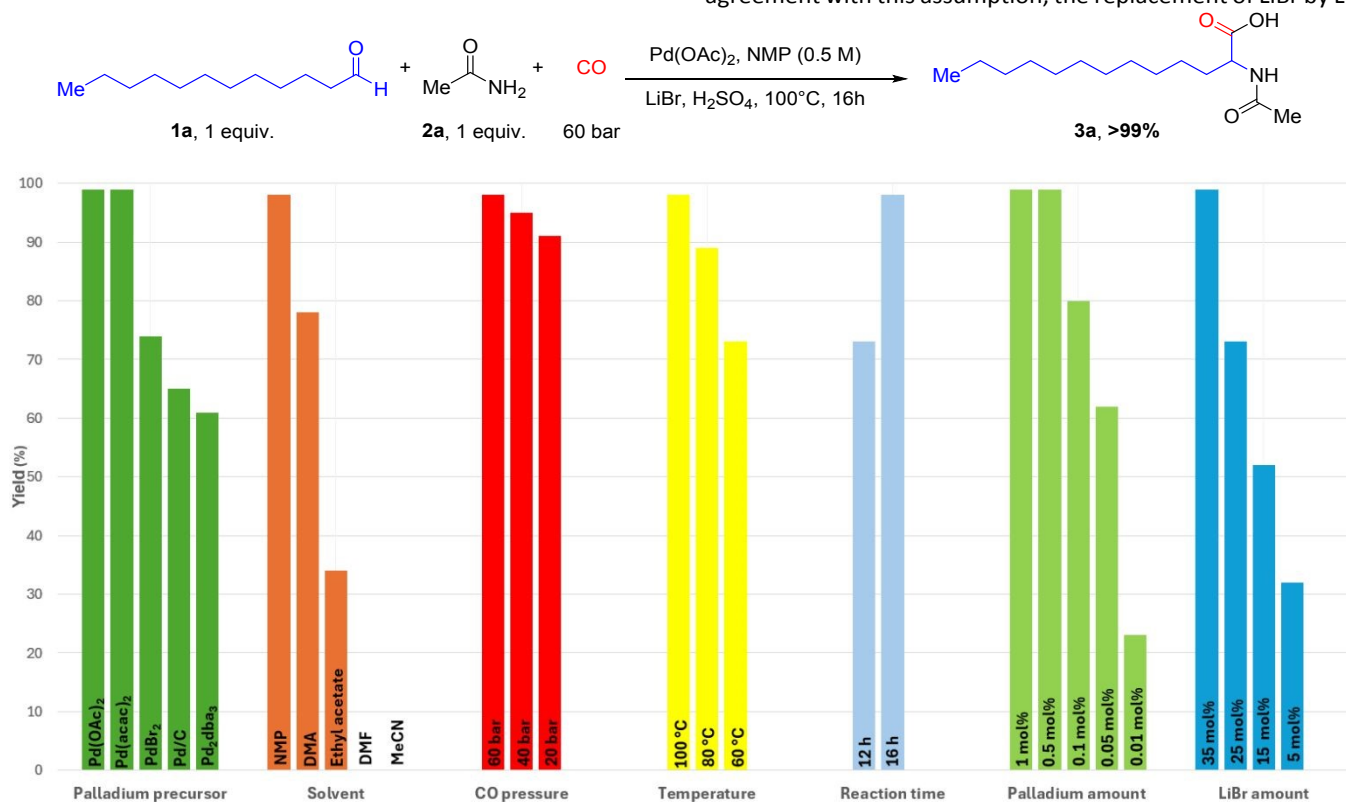

Figure 3. Palladium-catalysed amidocarbonylation of dodecanal with acetamide: Variation of reaction conditions. Reactions were conducted on 0.5 mmol scale and yields were determined by ^{1}H-NMR analysis using 3,5-bis(trifluoromethyl)bromobenzene as an internal standard.

Journal Name

resulted in a lower yield of **3a**. To better understand the amidocarbonylation of dodecanal, a kinetic profile of the model system was created under the optimized conditions. For this purpose, reactions were interrupted at precise moments and the crude reaction mixture was analysed. Already after 1 hour reaction time, 60 % of product **3a** was formed in addition to 40% of unreacted aldehyde **1a** (Figure 4 and Table S1, entry 2), showing the fast process. Interestingly, after 6 hours there was no more aldehyde **1a** nor amide **2a** observed, but the product yield still increased in the following 10 h until a nearly quantitative yield of **3a** was obtained (Table S1, entry 5). It is worth mentioning that aldehyde and amide showed the same rate of consumption in the reaction and no intermediates could be observed. Adding new substrates and co-catalysts after 16 hours led to the formation of additional 40% of 3a indicating that the catalyst was still "alive".
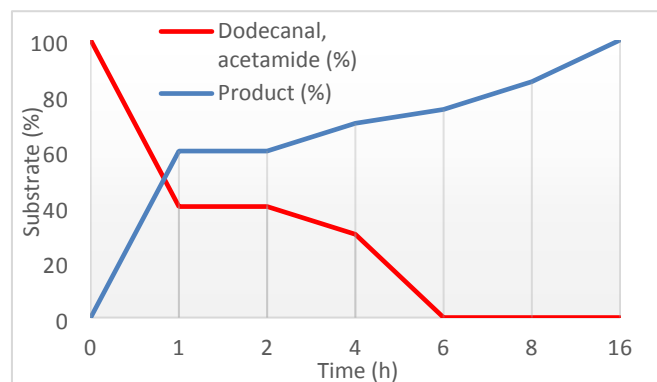

Figure 4. Consumption of dodecanal and acetamide, and formation of product 3a hour by hour.
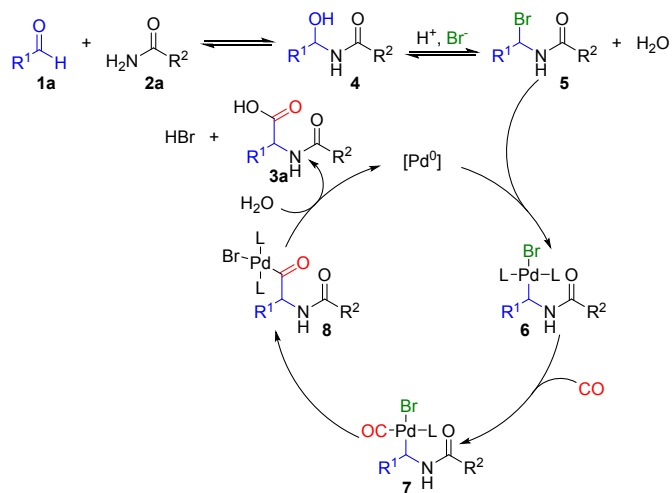

Figure 5. Proposed mechanism for the Pd-catalyzed amidocarbonylation of aldehydes.

Performing the model reaction under standard conditions but without CO showed significant conversion of dodecanal and acetamide; however, apart from an aldol condensation by-product no other product was observed by GC-MS (see ESI for details). All these control experiments agree with the previously postulated mechanism for the Pd catalyzed amidocarbonylation of aldehyde (Figure 5).[26] The process starts with the condensation between the aldehyde **1a** and the amide **2a**, resulting in the intermediate **4**. Then, due to acidic conditions, protonation of the hydroxy group and further replacement by a bromide anion leads to intermediate **5**, which is in equilibrium with **4**. Then, oxidative addition of Pd[0] species to intermediate **5** starts the catalytic cycle and leads to **6**. Next, CO coordinates to the stabilized Pd[+2] intermediate furnishing **7**. After ligand exchange, the desired product is formed by reductive elimination and the active Pd[0] species is restored to start again the catalytic cycle.

To showcase the possibility to provide multi gram-scale amounts of this novel class of compounds, *e.g.* for biological studies, we carried out upscaling experiments. As expected, product **3a** could be easily isolated in around 8 g after filtration, solvent removal, and extraction without the necessity of column chromatography. Then, we started to prepare a variety of *N*-acyl amino acids with longer alkyl chains and investigated the scope of the reaction (Figure 7). Firstly, we performed reactions of the model aldehyde dodecanal **1a** with different amides. Applying *n*-alkyl amides, such as acetamide **2a**, butanamide **2b**, and stearamide **2c** provided the corresponding products **3a**, **3b**, and **3c** in good to high yields (84%, 90% and 78%, respectively). Similarly, cyclohexanecarboxamide **2g** led to the desired product **3g** in 75% yield. In humans, it is well known that saturated fatty acids have undesired biological properties. In contrast, unsaturated fatty acids have several health benefits, including potentially reducing the risk of heart disease. Hence, we tested unsaturated amides containing isolated double bonds in the alkyl chain, like oleamide **2d** and erucamide **2e**. To our delight, the reaction system is well tolerant towards olefins and the respective products **3d-e** were furnished in good yields (68% and 71%). These latter results are noteworthy, as Pd-catalysed double bond isomerization or olefin carbonylation reactions could be expected. We also performed the reaction with the industrially relevant methacrylamide containing a conjugated double bond, and the product **3f** was obtained in 55% yield. For the first time this substrate has been applied in amidocarbonlations and it was also possible to obtain suitable crystals for SC-XRD and its structure could be confirmed (Figure 6, see ESI for details).[42]
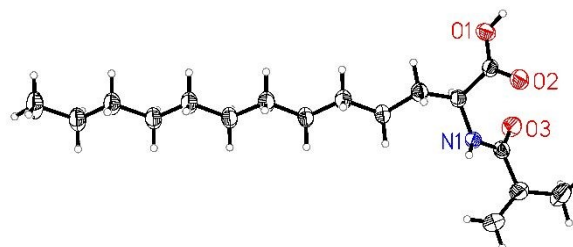

Figure 6. Molecular structure of 3f. Displacement ellipsoids correspond to 50% probability.
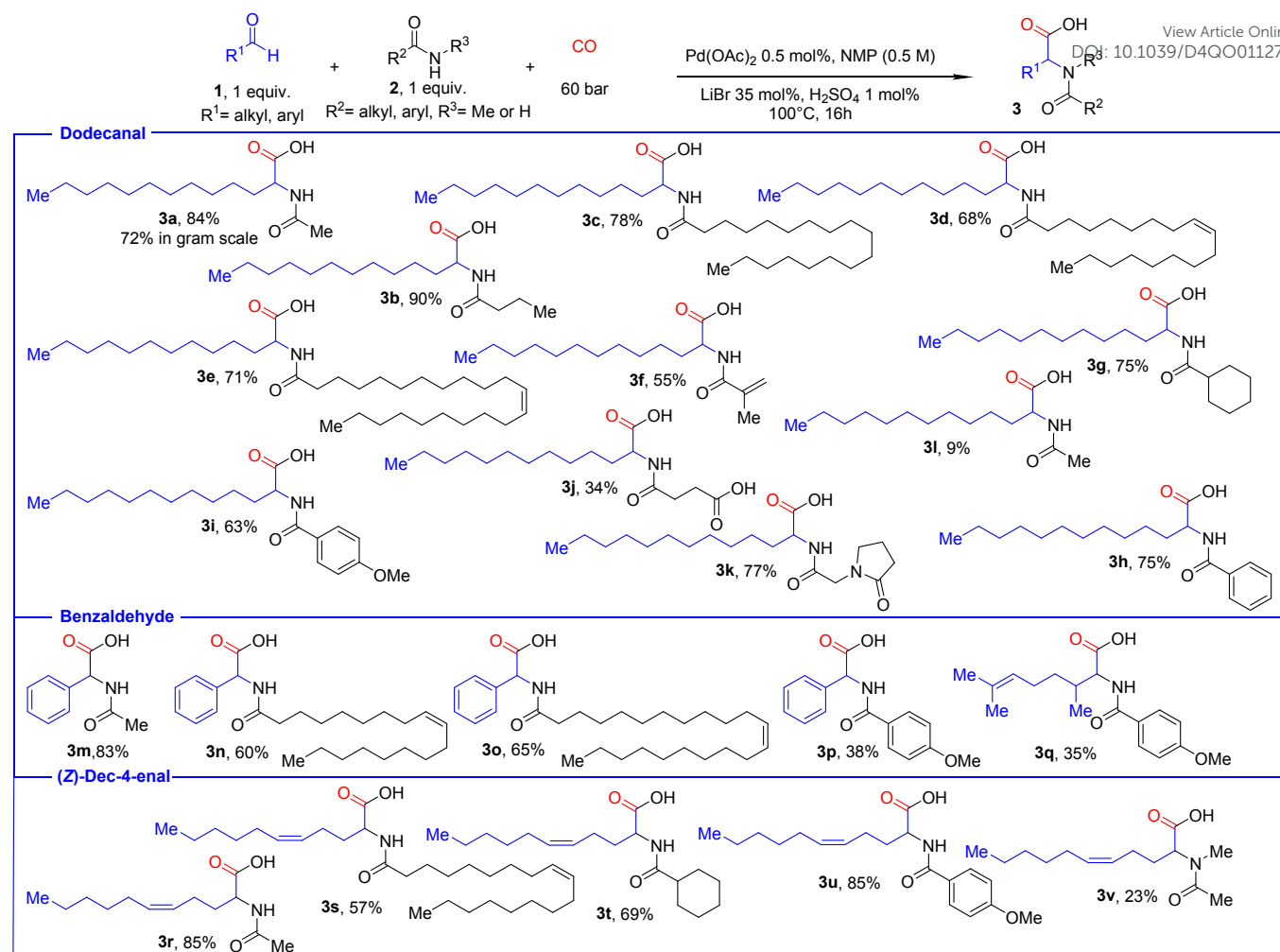
Method

Figure 7. Synthesis of diverse *N*-acyl fatty α-amino acids. Reaction conditions: Pd(OAc)₂ (0.5 mol%), aldehyde (0.5 mmol, 1 equiv), amide (0.5 mmol, 1 equiv), LiBr (35 mol%) and H₂SO₄ (1 mol%) in NMP (1 mL), CO (60 bar), 100°C, 16 h. Isolated yields from 0.5 mmol scale reactions.

Next, we turned our attention to the reaction of dodecanal with aromatic amides bearing different substituents. The parent benzamide 2h gave the respective *N*-aryl-fatty amino acid **3h** in 75% yield, while more electron-rich 4-methoxybenzamide **2i** provided the desired product **3i** in 63%. Amides containing other functional groups, such as carboxylic acid and cyclic amide, were also tolerated, and respective **3j** and **3k** products were isolated in 34% and 77%. However, *N*-methyl acetamide **2l** showed only low reactivity under these optimized conditions. As expected, aromatic aldehydes furnished the desired products **3p-m** in 38-83% yield. Furthermore, other unsaturated aldehydes can be utilized to provide novel amino acids in one step. As an example, (*Z*)-dec-4-enal **1r** reacted smoothly with acetamide **2r** to afford product **3r** in 85% yield, while the product **3s** from reaction with oleamide **2d** was obtained in 57%. In addition, cyclohexanecarboxamide and 4-methoxybenz-amide furnished the respective products **3t** and **3u** in 69% and 85% yield, respectively. Applying 2,6-dimethylhept-5-enal, a fragrance aldehyde also known as melonal **1q** was obtained in 35% yield.

Apart from all these examples, other functionalized aldehydes including geranial, vanillin, 5-hydroxymethylfurfural (HMF), furfural, and syringaldehyde were tested. Unfortunately, under the standard reaction conditions in these cases no desired product was formed and unwanted side-reactions such as oligomerization occurred.

Procedure and Characterization

An 8 mL vial equipped with a stir bar was charged with Pd(OAc)₂ (0.5 mol%), aldehyde (0.5 mmol, 1 equiv), amide (0.5 mmol, 1 equiv), LiBr (35 mol%) and H₂SO₄ (1 mol%) in NMP (1 mL). The reactional mixture was stirred under 60 bar CO at 100°C for 16 h. After this time, the crude was filtered through a small pad of Celite® with EtOAc and it was concentrated under reduced pressure. Then, NMP was removed from the crude with distillation (1 mbar, 68°C) and proceeded extraction methods or column chromatography.

ARTICLE

Conclusions

In summary, we have developed a protocol for the synthesis of an overlooked class of α-amino acid derivatives. It is very surprising that amino acids with long (unsaturated) alkyl chains in α-position have never been described or found in living organism or plants although another important class of biomolecules, fatty acids, contain such structural units. We believe it will be interesting to study the biological function of such amino acids, and modified peptides or proteins. Therefore, it is necessary to provide synthetic protocols for their synthesis. We show that the known palladium-catalysed amidocarbonylation can be easily utilized to prepare a variety of so-called fatty amino acids in an 100% atom-efficient manner in the presence of low catalyst amounts.

All the obtained products have previously not been synthesized and present an interesting class of compounds, which combine two essential classes of natural products. Integrating such novel amino acids allows preparing peptides and proteins with many potentially biological functions as hydrophobic residues from amino acids contribute significantly to receptor activation, G protein coupling, and oligomerization processes. In addition, their physical properties as surfactants makes this synthetic protocol interesting for several applications in chemistry and biology. Finally, it is worthwhile mentioning that the developed procedure can be combined with subsequent enzyme-catalysed kinetic resolution, which should allow for a straightforward two step synthesis of the respective amino acid enantiomers.[42]

Data availability

The data supporting this article have been included as part of the Supplementary Information.

Acknowledgements

References

1   B. E. Sleebs, T. Van Nguyen, A. B. Hughes, Recent Advances in Stereoselective Synthesis and Application of β-Amino Acids, *Org. Prep. Proced. Int.* 2000, **41**, 429-478.

2   R. Zhang, C. Zhang, J. Tan, Y. He, D. Zhuo, J. Zhang, Z. Luo, Q. Li, J. Yao, C. Ke, C. Tang, Y. Ye, S. He, X. Sheng, C. Liao, Enzymatic Synthesis of Noncanonical α-Amino Acids Containing γ-Tertiary Alcohols, *Angew. Chem. Int. Ed.* 2024, **136**, e202318550.

3   D. S. Prendes, F. Papp, N. Sankaran, R. Sivendran, F. Beyer, C. Merten, L. J. Gooßen, Enantioselective Synthesis of Arylglycines via Pd-Catalyzed Coupling of Schöllkopf Bis-Lactim Ethers with Aryl Chlorides, *Angew. Chem. Int. Ed.* 2023, **62**, e202309868.

4   M. Lubberink, W. Finnigan, C. Schnepel, C. R Baldwin, N. J. Turner S. L. Flitsch, One-Step Biocatalytic Synthesis of Sustainable Surfactants bySelective Amide Bond Formation, *Angew. Chem. Int. Ed.* 2022, **61**, e202205054.

5   D. Gördes, H. Neumann, A. J. von Wangelin, C. Fischer, K. Drauz, H. Krimmer, M. Beller, The Amidocarbonylation of Aldehydes, *Adv. Synth. Catal.* 2003, **345**, 510-516.

6   Y. Zhang, J. Vanderghinste, J. Wang, S. Das, Challenges and recent advancements in the synthesis of α,α-disubstituted α-amino acids, *Nat. Commun.* 2024, **15**, 1474.

7   F. J. A. Troyano, K. Merkens, K. Anwar, A. Gómez-Suárez, Radical-Based Synthesis and Modification of Amino Acids, *Angew. Chem. Int. Ed.* 2021, **60**, 1098-1115.

8   C. Najera, J. M. Sansano, Catalytic asymmetric synthesis of alpha-amino acids, *Chem. Rev.* 2007, **107**, 4584-4671.

9   C. J. Moreno, K. Hernández, S. J. Charnok, S. Gittings, M. Bolte, J. Joglar, J. Bujons, T. Parella, P. Clapés, Synthesis of γ-Hydroxy-α-amino Acid Derivatives by Enzymatic Tandem Aldol Addition-Transamination Reactions, *ACS Catal.* 2021, **11**, 4660-4669.

10 Y. Matsumoto, J. Sawamura, Y. Murata, T. Nishikata, R. Yazaki, T. Ohshima, Amino Acid Schiff Base Bearing Benzophenone Imine As a Platform for Highly Congested Unnatural α-Amino Acid Synthesis, *J. Am. Chem. Soc.* 2020, **142**, 8498-8505.

11 A. S. Elgharbawy, W. Sadik, O. M. Sadek, M. A. Kasaby. *J. Chil, A REVIEW ON BIODIESEL FEEDSTOCKS AND PRODUCTION TECHNOLOGIES, Chem. Soc.* 2021, **66**, 5098-5109.

12 G. M. Mathew, D. Raina, V. Narisetty, V. Kumar, S. Saran, A. Pugazhendi, R. Sindhu, A. Pandey, P. Binod, Recent advances in biodiesel production: Challenges and solutions, *Sci. Total. Env.* 2021, **794**, 148751.

13 W. Muramatsu, C. Manthena, E. Nakashima, H. Yamamoto, Peptide Bond-Forming Reaction via Amino Acid Silyl Esters: New Catalytic Reactivity of an Aminosilane, *ACS Catal.* 2020, **10**, 9594-9603.

14 N. Tanaka, J. L. Zhu, O. L. Valencia, C. R. Schull, K. A. Scheidt. *J, Cooperative Carbene Photocatalysis for β-Amino Ester Synthesis, Am. Chem. Soc.* 2023, **145**, 24486-24492.

15 M. U. Ahmad, Fatty acids: Chemistry, synthesis, and applications. (Elsevier, 2017).

16 J. Guo, L. Sun, F. Zhang, B. Sun, B. Xu, Y. Zhou, Progress in synthesis, properties and application of amino acid surfactants, *Chem. Phys. Lett.* 2022, **794**, 139499.

17 A. Vik, T. V. Hansen, Synthetic manipulations of polyunsaturated fatty acids as a convenient strategy for the synthesis of bioactive compounds, *Org. Biomol. Chem.* 2018, **16**, 9319-9333.

18 O. G. Mountanea, D. Limnios, M. G. Kokotou, A. Bourboula, G. Kokotos, Asymmetric Synthesis of Saturated Hydroxy Fatty Acids and Fatty Acid Esters of Hydroxy Fatty Acids, *Eur. J. Org. Chem.* 2019, **2019**, 2010-2019.

19 A. F. Noisier, M. A. Brimble, C-H functionalization in the synthesis of amino acids and peptides, *Chem. Rev.* 2014, **114**, 8775-8806.

20 J. A. Avendaño-Villarreal, F. G. Delolo, A. V. Granato, E. V. Gusevskaya, E. N. dos Santos, The first one-pot metathesis–hydroformylation procedure: a straight synthesis of 2-arylpropanals from renewable 1-propenylbenzenes, *ChemCatChem* 2023, **15**, e202201186.

21 S. H. Park, S. Lee, Selective Synthesis of (Z)- and (E)-β-Fluoro-α,β-Unsaturated Amides Using Palladium-Catalyzed Aminocarbonylation, *Org. Lett.* 2023, **25**, 6925-6930.

22 T. J. Fulton, A. Q. Cusumano, E. J. Alexy, Y. E. Du, H. Zhang, K. N. Houk, B. M. Stoltz, Global Diastereoconvergence in the Ireland-Claisen Rearrangement of Isomeric Enolates:

Method

Synthesis of Tetrasubstituted *α*-Amino Acids, *J. Am. Chem. Soc.* 2020, **142**, 21938-21947.

23 W. Guo, Y. Luo, H. H.-Y. Sung, I. D. Williams, P. Li, J. Sun, Chiral Phosphoric Acid Catalyzed Enantioselective Synthesis of α-Tertiary Amino Ketones from Sulfonium Ylides, *J. Am. Chem. Soc.* 2020, **142**, 14384-14390.

24 M. Beller, M. Ecker, Amidocarbonylation—An Efficient Route to Amino Acid Derivatives, *Angew. Chem. Int. Ed*. 2000, **39**, 1010-1027.

25 H. Wakamatsu, J. Uda, N. Yamakami, Synthesis of N-acyl amino-acids by a carbonylation reaction, *Chem. Commun*. 1971, 1540-1540.

26 M. Beller, M. Eckert, F. Vollmüller, S. Bogdanovic, H. Geissler, Palladium-Catalyzed Amidocarbonylation—A New, Efficient Synthesis of N-Acyl Amino Acid, *Angew. Chem. Int. Ed.* 1997, **36**, 1494-1496.

27 Y. Ge, F. Ye, J. Yang, A. Spannenberg, R. Jackstell, M. Beller, Palladium-Catalyzed Domino Aminocarbonylation of Alkynols: Direct and Selective Synthesis of Itaconimides, *JACS Au.* 2021, **1**, 1257-1265.

28 J. S. Quesnel, B. A. Arndtsen, Transition-metal-catalyzed multicomponent coupling reactions with imines and carbon monoxide, *Pure Appl. Chem.* 2013, **85**, 377-384.

29 G. M. Torres et al. Palladium-catalyzed, multicomponent approach to β-lactams via aryl halide carbonylation, *J. Org. Chem*. 2016, **81**, 12106-12115.

30 M. Li, S. Li, D. Chen, F. Gao, Y. Qiu, X. Wang, Z. Quan, Y. Liang, Regioselective C–H Active Carbonylation via 1,4-Palladium Migration, *Org. Lett.* 2023, **25**, 2761-2766.

31 S. Hancker, S. Kreft, H. Neumann, M. Beller, Synthesis of N-Lauroyl Sarcosine by Amidocarbonylation: Comparing Homogeneous and Heterogeneous Palladium Catalysts, *Org. Process Res. Dev.* 2017, **21**, 2045-2051.

32 R. Akiyama, T. Sagae, M. Sugiura, S. Kobayashi, Efficient synthesis of N-acyl-α-amino acids via polymer incarcerated palladium-catalyzed amidocarbonylation, *J. Organomet. Chem.* 2004, **689**, 3806-3809.

33 A. Hamasaki, X. Liu, M. Tokunaga, Amidocarbonylation of Aldehydes Utilizing Cobalt Oxide-supported Gold Nanoparticles as a Heterogeneous Catalyst, *Chem. Lett.* 2008, **37**, 1292-1293.

34 T. T. Dang, Y. Zhu, J. S. Y. Ngiam, S. C. Ghosh, A. Chen, A. M. Seayad, Palladium Nanoparticles Supported on ZIF-8 As an Efficient Heterogeneous Catalyst for Aminocarbonylation, *ACS Catal.* 2013, **3**, 1406-1410.

35 M. Connor, C. W. Vaughan, R. J. Vandenberg, N-Acyl amino acids and N-acyl neurotransmitter conjugates: neuromodulators and probes for new drug targets, *Br. J. Pharmacol*. 2010, **160**, 1857-1871.

36 L. Hanuš, E. Shohami, I. Bab, R. Mechoulam, N-Acyl amino acids and their impact on biological processes, *Biofactors* 2014, **40**, 381-388.

37 D. K. F. Santos, R. D. Rufino, J. M. Luna, V. A. Santos, L. A. Sarubbo, Open AccessReview

38 Biosurfactants: Multifunctional Biomolecules of the 21st Century, *Int J Mol Sci.* 2016, **17**, 401.

39 C. E. Drakontis, S. Amin, Biosurfactants: Formulations, properties, and applications, *Curr. Opin. Colloid Interface Sci.* 2020, **48**, 77-90.

40 D. G. Almeida, R. C. F. S. Silva, J. M. Luna, R. D. Rufino, V. A. Santos, I. M. Banat, L. A. Sarubbo, Biosurfactants: Promising Molecules for Petroleum Biotechnology Advances, *Front Microbiol*. 2016, **7**, 1718.

41 A. Hinzmann, S. S. Druhmann, H. Gröger, Synthesis of Bifunctional Molecules for the Production of Polymers Based on Unsaturated Fatty Acids as Bioderived Raw Materials, *Sustain. Chem.* 2020, **1**, 18.

42 M. L. Smith, S. Gandolfi, P. M. Coshall, P. K. Rahman, Biosurfactants: a Covid-19 perspective, Front Microbiol, 2020, **11**, 1341.

43 H. K. Chenault, J. Dahmer, G. M. Whitesides, Kinetic resolution of unnatural and rarely occurring amino acids: enantioselective hydrolysis of N-acyl amino acids catalyzed by acylase I, *J. Am. Chem. Soc*. 1989, **111**, 6354-6364.

Data availability

The data supporting this article have been included as part of the Supplementary Information.