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Original scientific paper

Esters and amides of hexanoic acid substituted with tertiary amino group in terminal position and their activity as transdermal permeation enhancers

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Abstract: Series of alkyl esters of 6-(diethylamino)-, 6-(pyrrolidin-1-yl)-, 6-(piperidin-1-yl) and 6-(morpholin-4-yl)hexanoic acids and alkylamides of 6-(dimethylamino)-, 6-(piperidin-1-yl) and 6-(morpholin-4-yl)hexanoic acids, containing 8–12 carbon atoms in the alkyl chain, were prepared by methods of classical organic synthesis. The appropriate secondary amine was alkylated with ethyl 6-bromohexanoate to give ester of ω-substituted hexanoic acid, except of ethyl 6-(dimethylamino)hexanoate (**1**), which was prepared by Eschweiler–Clarke methylation of 6-aminohexanoic acid followed by direct esterification with ethanol. The resulted esters of ω-substituted hexanoic acids underwent direct transesterification with long chain alkanols to yield the desired amino esters, or they were treated with long-chain alkylamines to prepare secondary amides of the appropriate heterocyclic hexanoic acids. These products were *in vitro* tested on their activity as transdermal permeation enhancers on the strips of the excised human skin with theophylline as the model permeant. The activity was evaluated using parameter enhancement ratio (*ER*), defined as the ratio between the overall amount of the permeant passing through the skin with the tested enhancer and that without tested substance. Decyl 6-(pyrrolidin-1-yl)hexanoate (**9**) with $ER = 30$ showed the highest activity. The enhancing effects of the esters were generally better than those of the amides.

Keywords: transdermal permeation enhancers; ω-amino acid derivatives.

INTRODUCTION

Transdermal permeation enhancers (TPEs) are special pharmaceutical excipients, which enable or facilitate the passage of various drugs through the skin

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barrier to the blood circulation, thereby enabling their systemic effect. Together with antimicrobial preservatives and antioxidants, they belong to a narrow group of excipients which can be characterized by their own enumerable activities. Only a few drugs with high lipophilicity, such as steroids, nitrates, some opioid analgesics (fentanyl) and several alkaloids (*e.g.*, nicotine or scopolamine), are capable of penetrating through the skin by themselves. For this reason TPEs constitute important ingredients of transdermal application systems, which are popular because of their benefits and used not only in human, but more recently also in veterinary therapy.[1] They can provide steady-state plasma concentrations of drugs and long-term therapy from a single dose, avoid the hepatic first-pass metabolism associated with oral administration and allow easy termination of drug input. The role of chemical TPEs is to reversibly alter the barrier properties of the *stratum corneum* (SC), which is the outermost layer of skin, by disruption of the membrane structures or by maximizing drug solubility within the skin.[2]

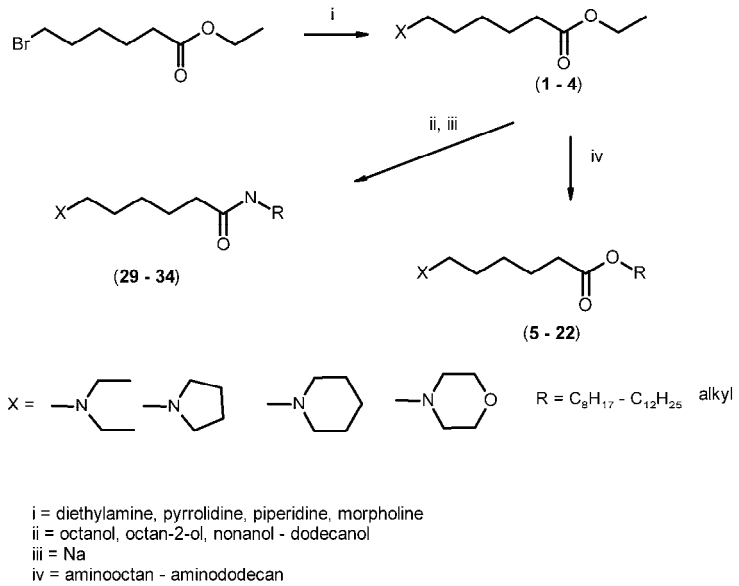
Compounds used or tested as TPEs constitute a very diverse group of structures. Various derivatives of amino acids occupy among them a comparatively important position. Previously, a series of long chain alkyl esters of 6-(dimethylamino)hexanoic acid with a linear alkyl chain having 8 to 12 carbon atoms were prepared.[3] The distance of 5 carbon atoms between the terminal amino group and the carboxyl as well as the range of lengths of alkyl chains were selected based on previous experiences. The older results demonstrated that alkyl esters of ω-amino acids have their optimum transdermal permeation enhancing effect for linear octyl to dodecyl groups, that branching of an alkyl chain essentially lowers the activity,[4] and that derivatives of 6-aminohexanoic acid are significantly more potent than those with another number of carbon atoms in the acyl chain.[5] It was found that these compounds showed high enhancement activity of transdermal permeation of theophylline as a model permeant of "moderate lipophilicity". The highest effect was obtained with dodecyl 6-(dimethylamino)hexanoate (DDAK) with an enhancement ratio (*ER*) of nearly 80. Such a significant activity was rationalized based on the higher basicity of the tertiary amino group of this compound.[3] It is also supposed this increase of activity must be connected with an essentially higher toxicity due to high stability against enzymatic hydrolysis. For this reason, this type of structural modification temporarily became of marginal interest. More recently, the above-mentioned DDAK was shown to be an effective enhancer of percutaneous permeation of adefovir[6] and hydrocortisone. Surprisingly, DDAK was demonstrated to be rapidly metabolized by porcine esterase with $t_{1/2}$ = 17.2 min and displayed low acute toxicity. It also showed reversibility of action on treated skin expressed as electrical resistance (impedance) at 120 kHz, which during 3 h after treatment with DDAK dropped to 20 % of its initial value and after removal of the enhancer slowly increased.[7] These results returned our interest to the field of enhancers with a tertiary amino group. The

aim of this preliminary pilot study was to determine the influence of expansion of the dimethylamino group into either an open diethylamino group or a closed saturated heterocyclic ring, *i.e.*, pyrrolidine, piperidine or morpholine, on permeation enhancement activity. Simultaneously, the effect of substitution of the ester group with an amide moiety could also be evaluated.

RESULTS

Synthesis of compounds and determination of their activity

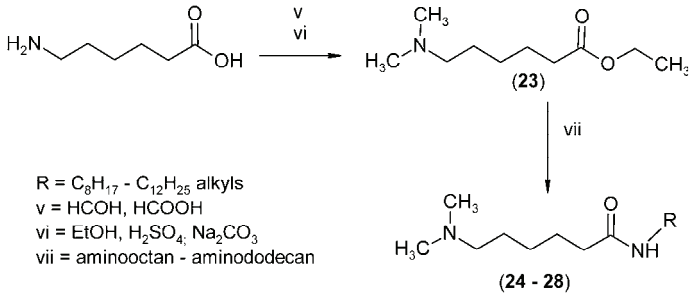
Long-chain alkyl esters of 6-aminohexanoic acids with a tertiary amino group. Ethyl esters of 6-(diethylamino)hexanoic, 6-(pyrrolidin-1-yl)hexanoic, 6-(piperidin-1-yl)hexanoic and 6-(morpholin-4-yl)hexanoic acids were prepared by direct alkylation of the appropriate secondary amine with ethyl 6-bromohexanoate. Their transesterification with an appropriate long-chain alkanol catalyzed with *in situ* prepared sodium alcoholate under the simultaneous distilling off of the arising ethanol according to Franke *et al.*[8] led to octyl to dodecyl esters of these ω-amino acids (Scheme 1).



Scheme 1. Procedure of the synthesis of alkyl esters and *N*-alkylamides of 6-(diethylamino)hexanoic, 6-(pyrrolidin-1-yl)hexanoic, 6-(piperidin-1-yl)hexanoic and 6-(morpholin-4-yl)hexanoic acids.

Long chain alkyl amides of 6-(dimethylamino)hexanoic acid. Eschweiler–Clarke methylation of 6-aminohexanoic acid with formaldehyde and formic acid according to Fusco *et al.*[9] (the detailed description of the reaction procedure is given in the literature[3]) gave 6-(dimethylamino)hexanoic acid, which was di-

rectly esterified with ethanol. The resulting ethyl-6-(dimethylamino)hexanoate was heated with an appropriate aminoalkane to yield the corresponding alkylamide of 6-(dimethylamino)hexanoic acid (Scheme 2).



Scheme 2. Procedure of the synthesis of *N*-alkyl-6-dimethylaminohexanamides (**24**–**28**).

Long chain alkyl amides of N,N-*disubstituted 6-aminohexanoic acids.* Octyl to dodecyl amides of 6-(diethylamino)hexanoic, 6-(pyrrolidin-1-yl)hexanoic, 6-(piperidin-1-yl)hexanoic and 6-(morpholin-4-yl)hexanoic acids were synthesized similarly by heating of the appropriate aminoalkane with an ω-substituted ethyl hexanoate under the simultaneous distilling off of the arising ethanol (Scheme 1).

All products were isolated and purified either by distillation under reduced pressure or by crystallization from a suitable system of solvents, or only by sorption filtration through an alumina column. The identities of all the compounds were confirmed by their IR, ^{1}H- and ^{13}C-NMR-spectra and by elemental analysis.

Analytical and spectral data of the synthesized compounds

The complete analytical and spectral data of the synthesized compounds can be found in the electronic version of the paper as Supplementary material (http://www.shd.org.rs/JSCS/), from the office of the Serbian Chemical Society upon request (JSCS@shd.org.rs) or from the corresponding author upon request.

Evaluation of the activity of the synthesized compounds and their results

Testing of the transdermal permeation enhancing activity was performed *in vitro* on strips of excised human skin with theophylline, thought to be a drug of "middle lipophilicity", as a model penetrant in the system of liberation cells according to Franz[10] from a propylene glycol medium. Due to capacity utilization of the testing workplace, only one or several members of each homologous series underwent the evaluation procedure. The final results of the testing are presented as values of the enhancement ratio (*ER*), defined simply as the ratio between the overall amount of the permeant which passed through the skin with tested enhancer and that without the tested substance. These values are given in Table I.

TABLE I. Values of the enhancement ratio (*ER*) of the prepared and related compounds (X-$(CH_2)_5$CO-Y-R)

Compd.	X	Y	R	*ER*	Compd.	X	Y	R	*ER*
DDAK	$(CH_3)_2N$–	–O–	C_8H_{17}	82.4±19.0[a]	**17**		–O–	$C_{12}H_{25}$	2.0±0.4
	$(CH_3)_2N$–	–O–	2-C_8H_{17}	–	**18**		–O–	C_8H_{17}	–
	$(CH_3)_2N$–	–O–	C_9H_{19}	89.3±11.0[a]	**19**		–O–	C_9H_{19}	–
	$(CH_3)_2N$–	–O–	$C_{10}H_{21}$	104.5±11.0[a]	**20**		–O–	$C_{10}H_{21}$	15.0±2.9
	$(CH_3)_2N$–	–O–	$C_{11}H_{23}$	118.3±19.0[a]	**21**		–O–	$C_{11}H_{23}$	–
	$(CH_3)_2N$–	–O–	$C_{12}H_{25}$	79.7±19.0[a]	**22**		–O–	$C_{12}H_{25}$	–
5	$(C_2H_5)_2N$–	–O–	C_8H_{17}	–	**24**	$(CH_3)_2N$–	–NH–	C_8H_{17}	11.2±2.2
6	$(C_2H_5)_2N$–	–O–	$C_{10}H_{21}$	10.0±2.3	**25**	$(CH_3)_2N$–	–NH–	2-C_8H_{17}	–
7	$(C_2H_5)_2N$–	–O–	$C_{12}H_{25}$	–	**26**	$(CH_3)_2N$–	–NH–	C_9H_{19}	1.9±0.4
8		–O–	C_8H_{17}	–	**27**	$(CH_3)_2N$–	–NH–	$C_{10}H_{21}$	11.6±2.2
9		–O–	$C_{10}H_{21}$	30.0±5.1	**28**[b]	$(CH_3)_2N$–	–NH–	$C_{12}H_{25}$	9.9±2.0
10		–O–	$C_{11}H_{23}$	–	**29**		–NH–	$C_{10}H_{21}$	–
11		–O–	$C_{12}H_{25}$	11.2±2.1	**30**		–NH–	$C_{12}H_{25}$	5.0±1.1
12		–O–	C_8H_{17}	6.0±1.1	**31**		–NH–	C_8H_{17}	–
13		–O–	2-C_8H_{17}	–	**32**		–NH–	C_9H_{19}	–
14		–O–	C_9H_{19}	–	**33**		–NH–	$C_{10}H_{21}$	–
15		–O–	$C_{10}H_{21}$	5.6±1.1	**34**		–NH–	$C_{12}H_{25}$	5.0±1.1
16		–O–	$C_{11}H_{23}$	3.0±0.6					

[a]Values taken from the literature;[3] [b]mentioned in patents[14,15]

DISCUSSION

The results of the determination of the percutaneous permeation enhancing activity of the prepared compounds showed that substitution of ester moiety with the isosteric amide group led to significant activity loss. This fact is probably not only due to a decrease of the overall lipophilicity of such amides in comparison to the isosteric esters, but more to the presence of an additional hydrogen bond donor site in the CONH moiety and possibly also to the higher melting points of the amides (*e.g.*, m.p. 48–49 °C for 6-(dimethylamino)*N*-dodecyl-hexanamide (**28**), while the isosteric dodecyl 6-dimethylaminohexanoate is a liquid at room temperature). These changes of the physicochemical properties could lead to a higher phase transition temperature of the lipid bilayers of cell membranes of SC of a skin treated with an appropriate amide in comparison with that of a skin treated with the isosteric ester, partially due to the lower SC uptake of the amidic enhancer (comp.[13,14]). In addition, an exchange of the terminal dimethylamino group with any other tertiary amino function, either acyclic diethylamino group, or five- to six-membered saturated basic rings, caused a decrease in the activity. Differences between the enhancing effect of the esters of 6-(piperidin-1-yl)hexanoic acid and the isosteric esters of 6-(morpholin-4-yl)hexanoic acid (the *ER* values of the decyl esters **15** and **20** are 5.6 and 15.0, respectively) suggest that not only the bulkiness of the basic substituent at the terminal position of the chain of hexanoic acid itself, but also its lipophilicity and/or the presence of additional hydrogen bond acceptor site (ethereal oxygen of the morpholine ring) could influence the activity (comp.[15]). However, also the influence of the different basicity of both heterocyclic substituents cannot be excluded (the pK_a of *N*-alkylpiperidines ranges between 9 and 10, while the pK_a of *N*-alkylmorpholines varies from 7 to 8). The overall basicity optimum could be found at a pK_a slightly under 9, which is the value of the most potent 6-(dimethylamino)-hexanoic acid derivative (pK_a of 6-(dimethylamino)*N*-dodecyl-hexanamide (**28**) is 8.8[11]). As far as the alkyl chain length is concerned, the alkyls with 10 and 12 carbon atoms of both prepared esters and amides seem to be more advantageous than those with 8, 9 or 11 carbon atoms, but more data are required for a more concrete statement. In general, the structural changes realized in this study led to compounds with reduced activities.

EXPERIMENTAL

General

The ^{1}H- and ^{13}C-NMR spectra were obtained using a Varian Mercury 300 MHz or Varian Gemini 200 MHz FT-NMR spectrometer in deuterated chloroform or dimethyl sulfoxide. The IR spectra were measured on a Nicolet Impact FTIR spectrometer. Melting points were determined on a Boetius apparatus Nagema (Rapido Wägetechnik, Radebeul, Germany) and are uncorrected. Elemental analyses (C, H, N, O) were performed on a Perkin–Elmer 2400 CHNS/O analyzer. All the presented reaction yields are preparative. Determination of trans-

dermal permeation enhancing activity was performed on the set of cells according to Franz[10] manufactured in the workshops of the Faculty of Pharmacy of the Charles University in Hradec Králové, Czech Republic. The HPLC analyses were performed on the chromatographic system consisting of the isocratic pump LCP 4001(Ecom, Prague, Czech Republic), injector LCI 30 (Laboratorni pristroje, Prague, Czech Republic), column LiChroCart 125-4 (LiChrospher 100, RP 18, 5 μm, Merck, Darmstadt, Germany), an SP 8440 UV detector (Spectra Physics) and the integrating software CSW 1.7 (Data Apex, Prague, Czech Republic), the mixture methanol:water 1:1 was used as the mobile phase at a flow rate 1 ml/min. The effluent was monitored at 272 nm. The retention time of theophylline was 2.70±0.02 min.

*Synthesis of esters of 6-(diethylamino)hexanoic acid (**1**, **5–7**), 6-(pyrrolidin-1-yl)hexanoic acid (**2**,**8–11**), 6-(piperidin-1-yl)hexanoic acid (**3**, **12–17**) and 6-(morpholin-4-yl)hexanoic acid (**4**,**18–22**)*

A mixture of 0.500 mol (112 g) of ethyl 6-bromohexanoate and 1.5 mol of the appropriate secondary amine was refluxed under stirring for 24 h. After cooling, the reaction mixture was diluted with 100 ml of diethyl ether and left in a refrigerator until crystals of hydrobromide of the appropriate secondary amine formed. This salt was filtered off, the diethyl ether was evaporated and the residue was distilled under reduced pressure. A reduced pressure distillation of the reaction mixture after alkylation of pyrrolidine with ethyl 6-bromohexanoate also gave a small amount of 1,6-bis(pyrrolidin-1-yl)hexan-1-one (**2a**) as a by-product, probably originating by the direct aminolysis of ethyl 6-(pyrrolidin-1-yl)hexanoate with pyrrolidine.

A solution of 0.020 mol of (**1**), (**2**) (**3**) or (**4**) and 0.10 mol of an appropriate alkanol was heated to 90 °C and then 0.010 mol of sodium was dissolved in it. This mixture was heated to boiling and kept boiling under continuous distilling off of the formed ethanol through a 10 cm long Vigreux column for 6 h. The unreacted alkanol was then distilled off, the liquid residue was diluted with 4.0 ml of 0.50 M aqueous acetic acid, and this mixture was vigorously stirred and then extracted with 3×20 ml of diethyl ether. The combined ethereal extracts were dried with sodium sulfate, the diethyl ether was evaporated and the pure long-chain alkyl ester was obtained by distillation of the liquid residue under reduced pressure.

Alkylamides of 6-(dimethylamino)hexanoic acid

A mixture of 20 mmol ethyl 6-(dimethylamino)hexanoate (**23**), prepared by Eschweiler–Clarke reductive methylation followed by direct esterification with ethanol,[3] and 22 mmol of an appropriate aminoalkane, was heated under stirring at 180 °C for 2.5 h. After cooling, the reaction mixture was distilled under reduced pressure to remove both unreacted **23** and alkylamine and to isolate the desired alkyl amide (**24**–**27**). *N*-Decyl-6-(dimethylamino)hexanamide (**27**), which spontaneously solidified at room temperature after it had been isolated by distillation, was additionally recrystallized from hexane. 6-(dimethylamino)*N*-dodecyl-hexanamide (**28**) could not be isolated by distillation under reduced pressure due to its to high boiling temperature, for this reason it was isolated by recrystallization of the residue after dodecylamine and **23** had been distilled off.

Alkylamides of 6-(piperidin-1-yl)hexanoic acid and 6-(morpholin-4-yl)hexanoic acid

A mixture of 0.020 mol of **3** or **4** and 0.022 mol of an alkylamine was heated to a temperature near to the boiling point of the amine for 4 h, then the mixture was distilled under reduced pressure, or it was dissolved in hexane and left to crystallize in a refrigerator to give the corresponding alkylamide.

Evaluation of the activity of the prepared compounds

Testing of transdermal permeation enhancing activity of the prepared compounds was performed by the same manner as was previously described for alkyl esters of 6-(dimethylamino)hexanoic acid.[3]

CONCLUSIONS

32 novel long-chain alkyl esters and *N*-alkylamides of 6-aminohexanoic acids with an acyclic or cyclic tertiary amino group and with alkyl chains in the range from octyl to dodecyl were prepared (compound **28**, 6-(dimethylamino) *N*-dodecyl-hexanamide, which was previously patented in different contexts,[11,12] was also prepared as a member of the homologous series). Thirteen of the prepared compounds were tested on their transdermal permeation enhancement activity *in vitro* using excised human skin with theophylline as the model permeant. All the evaluated substances showed an enhancing effect. The highest activity, characterized by $ER = 30$ was exhibited by compound **9**, *i.e.*, decyl 6-(pyrrolidin-1-yl)-hexanoate. In general, the esters were more potent than the amides. Comparison of the activities of the tested compounds, including the previously prepared alkyl 6-(dimethylamino)hexanoates,[3] suggested that increasing bulkiness of the terminal basic substituent leads to a decrease of the activity and, in addition, a basicity optimum exists in region of pK_a slightly under 9.

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ИЗВОД

ЕСТРИ И АМИДИ ХЕКСАНСКЕ КИСЕЛИНЕ СУПСТИТУИСАНИ ТЕРЦИЈАРНОМ АМИНО ГРУПОМ У ТЕРМИНАЛНОМ ПОЛОЖАЈУ И ЊИХОВА АКТИВНОСТ У ПОВЕЋАЊУ ТРАНСДЕРМАЛНЕ ПРОПУСТЉИВОСТИ

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Серија алкил естара 6-(диетиламино)-, 6-(пиролидин-1-ил)-, 6-(пиперидин-1-ил) и 6-(морфолин-4-ил)хексанских киселина и алкиламида 6-(диметиламино)-, 6-(пиперидин-1-ил) и 6-(морфолин-4-ил)хексанских киселина, који садрже 8–12 угљеникових атома у алкил-низу, добијена је класичним органским синтезама. Одговарајући секундарни амин алкилован је етил-6-бромхексаноатом (**1**) да би се добио естар ω-супституисане хексанске киселине, осим етил-6-(диметиламино)хексаноата, који је добијен Ешвајлер–Кларковим (Eschweiler–Clarke) метиловањем праћеним директном естерификацијом са етанолом. Добијени естри ω-супституисане хексанске киселине подвргнути су директној трансестерификацији са алкохолима дугачког низа да би се добили жељени амино естри, или су третирани алкиламинима са дугачким низом да би се добили секундарни амиди одговарајућих хетероцикличних хексанских киселина. Активност ових прозвода у повећању трансдермалне пропустљивости тестирана је *in vitro* на узорцима људске коже, са теофилином као моделом пропустљивости. За

оцену активности коришћен је параметар односа пропустљивости (*ER*), дефинисан као однос укупне количине супстанце која пролази кроз кожу уз присуство испитиваних једињења и без њих. Децил-6-(пиролидин-1-ил)хексаноат (**9**) са *ER* = 30 показао је највећу активност. Ефекти естара у повећању пропустљивости били су, генерално, бољи него ефекти амида.

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Supplementary material

SUPPLEMENTARY MATERIAL TO

Esters and amides of hexanoic acid substituted with tertiary amino group in terminal position and their activity as transdermal permeation enhancers

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*Ethyl 6-(diethylamino)hexanoate (**1**).* Yield 50 % ; b.p. 104–109 °C at 0.7–0.9 kPa (137–140 °C at 1.86 kPa[16]). IR ($CHCl_3$, cm^{-1}): 2973, 2838, 1727, 1466, 1375, 1300, 1270. ^{1}H-NMR (300 MHz, $CDCl_3$, δ / ppm): 4.13 (2H, *q*, *J* = 14.5, 7.4 Hz, $CH_3C\mathbf{H}_2O$), 2.49 (4H, *q*, *J* = 14.0, 6.9 Hz, $(CH_3C\mathbf{H}_2)_2N$), 2.40 (2H, *t*, *J* = = 7.2 Hz, CH_2CO), 2.30 (2H, *t*, *J* = 7.5 Hz, NCH_2 acyl), 1.70–1.58 (2H, *m*, CH_2 acyl), 1.52–1.38 (2H, *m*, CH_2 acyl), 1.36–1.20 (5H, *m*, CH_2 acyl + $C\mathbf{H}_3CH_2O$), 1.00 (6H, *t*, *J* = 6.5 Hz, $(C\mathbf{H}_3CH_2)_2N$). ^{13}C-NMR (75 MHz, δ / ppm): 173.45 (CO), 60.07 (OCH_2), 52.70 (CH_2N acyl), 46.80 ($(CH_2)_2N$), 34.28 ($\mathbf{C}H_2CO$), 27.22 ($\mathbf{C}H_2CH_2N$), 26.73 ($\mathbf{C}H_2(CH_2)_2CO$), 24.95 ($\mathbf{C}H_2CH_2CO$), 14.25 ($\mathbf{C}H_3CH_2O$) 11.68 (($\mathbf{C}H_3CH_2)_2N$).

*Ethyl 6-(pyrrolidin-1-yl)hexanoate (**2**).* Yield 53 %; b.p. 106–112 °C at 0.5–0.6 kPa (143–146°C at 2.0 kPa[16]). IR ($CHCl_3$, cm^{-1}): 2965, 2938, 2880, 2865, 2800, 1727, 1464, 1375, 1301, 1271. ^{1}H-NMR (200 MHz, $CDCl_3$, δ / ppm): 4.11 (2H, *q*, *J* = 14.3, 7.3 Hz, OCH_2), 2.55–2.36 (6H, *m*, $(CH_2)_3N$), 2.29 (2H, *t*, *J* = = 7.51 Hz, CH_2CO), 1.82–1.30 (10H, *m*, $5CH_2$), 1.24 (3H, *t*, *J* = 7.1 Hz, CH_3). ^{13}C-NMR (50 MHz, δ / ppm): 173.67 (CO), 60.10 (OCH_2) 56.40 (NCH_2 acyl), 54.18 (($CH_2)_2N$ pyrr.), 34.30 ($\mathbf{C}H_2CO$), 28.65 (CH_2), 27.25 (CH_2), 24.92 (CH_2), 23.43 (CH_2), 14.20 (CH_3).

*1,6-Bis(pyrrolidin-1-yl)hexan-1-one (**2a**), a side product.* Yield 3 % ; b.p. 178–183 °C at 0.06–0.08 kPa; Anal. Calcd. for $C_{14}H_{26}N_2O$: C, 70.54; H, 10.99; N, 11.75; O, 6.71 %. Found: C, 70.61; H, 11.05; N, 11.69; O, 6.80 %. IR ($CHCl_3$,

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cm^{-1}): 2973, 2936, 2879, 2800, 1624, 1448, 1343, 1328, 1294, 1270, 1252. ^{1}H-NMR (200 MHz, $CDCl_3$, δ / ppm): 3.40 (4H, *qi*, 2 CH_2); 2.58–2.37 (6H, *m*, $(CH_2)_3N$) acyl); 2.24 (2H, *t*, J = 7.5 Hz, CH_2CO), 2.00–1.15 (14H, *m*, 7 CH_2). ^{13}C-NMR (50 MHz, δ / ppm): 171.55 (CO), 56.43 (NCH_2 acyl), 54.16 ($(CH_2)_2N$ pyrr-acyl), 46.50 (CON($\mathbf{C}H_2)_2$), 45.48 (CH_2), 34.63 ($\mathbf{C}H_2CO$), 28.81 (CH_2), 27.55 (CH_2), 26.06 (CH_2), 24.77 (CH_2), 24.33 (CH_2), 23.38 (CH_2).

*Ethyl 6-(piperidin-1-yl)hexanoate (**3**)*. Yield 55 %, b.p. 120–124 °C at 0.13 kPa (114–115 °C at 0.11 kPa [17]). IR ($CHCl_3$, cm^{-1}): 2938, 2865, 2800, 1727, 1464, 1375, 1271. ^{1}H-NMR (200 MHz, $CDCl_3$, δ / ppm): 4.11 (2H, *q*, J = 14.3, 7.3 Hz, OCH_2) 2.43–2.20 (4H, *m*, NCH_2 + CH_2CN acyl), 2.3 (4H, *4t*, J = 7.0 Hz, 2 CH_2N piperid.), 1.77–1.30 (12H, *m*, β+γ CH_2 piperid. + β+γ+δ CH_2 acyl), 1.24 (3H, *t*, J = 7.1 Hz, CH_3). ^{13}C-NMR (50 MHz, δ / ppm): 173.67 (CO), 60.10 (OCH_2), 59.35 (NCH_2 acyl), 54.63 (($CH_2)_2N$ piperid), 34.33 ($\mathbf{C}H_2CO$), 27.33 ($NCH_2\mathbf{C}H_2$), 26.04 (CH_2), 25.02 ($\mathbf{C}H_2CH_2CO$), 14.20 (CH_3).

*Ethyl 6-(morpholin-4-yl)hexanoate (**4**)*. Yield: 82 %; b.p. 120–123 °C at 0.4 kPa (140–144 °C at 0.53 kPa,[18] 150–153 °C at 0.53 kPa[19]). IR ($CHCl_3$, cm^{-1}): 2941, 2863, 1727, 1458, 1375, 1256. ^{1}H-NMR (300 MHz, $CDCl_3$, δ / ppm): 4.11 (2H, *q*, J = 14.4, 7.5 Hz, $CH_3C\mathbf{H}_2O$), 3.70 (4H, *t*, J = 4.7 Hz, $O(C\mathbf{H}_2CH_2)_2N$), 2.40 (4H, *t*, J = 4.4 Hz, $O(CH_2C\mathbf{H}_2)_2N$), 2.35–2.25 (4H, *m*, CH_2CO + NCH_2 acyl), 1.73–1.41 (6H, *m*, $(3CH_2)$), 0.87 (3H, *t*, J = 6.7 Hz, CH_3). ^{13}C-NMR (75 MHz, $CDCl_3$, δ / ppm): 173.28 (CO), 66.82 (($CH_2)_2O$ morph.), 60.04 ($\mathbf{C}H_2OCO$), 58.74 (CH_2N acyl), 53.64 (($CH_2)_2N$ morph.), 34.15 ($\mathbf{C}H_2CO$), 26.93 ($\mathbf{C}H_2CH_2N$ acyl), 26.16 ($\mathbf{C}H_2(CH_2)_2CO$), 24.79 ($\mathbf{C}H_2CH_2CO$), 14.21 (CH_3).

*Octyl 6-(diethylamino)hexanoate (**5**)*. Yield 67 %; b.p. 134–138 °C at 0.035 kPa; Anal. Calcd. for $C_{18}H_{37}NO_2$: C, 72.19; H, 12.45; N, 4.68; O, 10.68 %. Found: C, 72.25; H, 12.35; N, 4.59; O, 10.80 %. IR ($CHCl_3$, cm^{-1}): 2930, 2856, 1727, 1465, 1378, 1271. ^{1}H-NMR (300 MHz, $CDCl_3$, δ / ppm): 4.04 (2H, *t*, J = 6.9 Hz, OCH_2), 2.50 (4H, *q*, J = 7.1, 14.3 Hz, $(CH_3C\mathbf{H}_2)_2N$), 2.36 (2H, *t*, J = 7.7 Hz, $NC\mathbf{H}_2CH_2$), 2.29 (2H, *t*, J = 7.6 Hz, CH_2CO), 1.68–1.25 (18H, *m*, 9 CH_2), 0.99 (6H, *t*, J = 7.1 Hz, $(C\mathbf{H}_3CH_2)_2N$), 0.87 (3H, *t*, J = 6.7 Hz, CH_3 octyl). ^{13}C-NMR (75 MHz, δ / ppm): 174.12 (CO), 64.66 (OCH_2), 52.98 (NCH_2), 47.07 (($CH_3\mathbf{C}H_2)_2N$), 34.58 ($\mathbf{C}H_2CO$), 32.01 (CH_2), 29.44 ($\mathbf{C}H_2CO$), 29.41 ($\mathbf{C}H_2CO$), 28.86 ($\mathbf{C}H_2CO$), 27.48 ($\mathbf{C}H_2CO$), 26.94 ($\mathbf{C}H_2CO$), 26.16 ($\mathbf{C}H_2CO$), 25.23 (CH_2CO), 22.65 ($\mathbf{C}H_2CH_3$ octyl), 14.32 (CH_3 octyl). 11.87 (($\mathbf{C}H_3CH_2)_2N$).

*Decyl 6-(diethylamino)hexanoate (**6**)*. Yield 52 %; b.p. 154–158 °C at 0.018 kPa. Anal. calcd. for $C_{20}H_{41}NO_2$: C, 73.34; H, 12.62; N, 4.28; O, 9.77 %. Found: C, 73.25; H, 12.54; N, 4.17; O, 9.66 %. IR ($CHCl_3$, cm^{-1}): 2933, 2859, 1727, 1458, 1378, 1270. ^{1}H-NMR (300 MHz, $CDCl_3$, δ / ppm): 4.05 (2H, *t*, J = 6.8 Hz, OCH_2), 2.51 (4H, *q*, J = 7.1, 14.3 Hz, $(CH_3C\mathbf{H}_2)_2N$), 2.37 (2H, *t*, J = 7.7 Hz, $NC\mathbf{H}_2CH_2$), 2.29 (2H, *t*, J = 7.6 Hz, CH_2CO), 1.69–1.23 (20H, *m*, 10 CH_2), 0.99 (6H, *t*, J = 7.1 Hz, $(C\mathbf{H}_3CH_2)_2N$), 0.87 (3H, *t*, J = 6.7 Hz, CH_3 decyl). ^{13}C-NMR

(75 MHz, δ / ppm): 173.91 (CO), 64.48 (OCH_2), 52.69 (NCH_2), 46.80 (($CH_3\mathbf{C}H_2)_2N$), 29.31 (C H_2), 29.22 (CH_2), 28.59 (CH_2), 27.21 (CH_2); 26.66 (CH_2), 25.89 (CH_2), 24.96 (CH_2), 22.65 (CH_2), 14.15 (CH_3 decyl), 11.59 (($\mathbf{C}H_3CH_2)_2N$).

*Dodecyl 6-(diethylamino)hexanoate (**7**)*. Yield: 52 %; b.p. 162–166 at 0.02 kPa. Anal. Calcd. for $C_{22}H_{45}NO_2$: C, 74.31; H, 12.76; N, 3.94; O, 9.0 %. Found: C, 74.27; H, 12.64; N, 4.02; O, 8.92 %. IR ($CHCl_3$, cm^{-1}): 2931, 2859, 1727, 1465, 1378, 1270. ^{1}H-NMR (300 MHz, $CDCl_3$, δ / ppm): 4.03 (2H, *t*, *J* = 6.7 Hz, OCH_2), 2.50 (4H, *q*, *J* = 14.3, 7.1 Hz, ($CH_3C\mathbf{H}_2)_2N$), 2.38 (2H, *t*, *J* = 7.6 Hz, $NC\mathbf{H}_2CH_2$), 2.30 (2H, *t*, *J* = 7.6 Hz, CH_2CO), 1.63–1.56 (2H, *m*, $OCH_2C\mathbf{H}_2$), 1.49–1.35 (2H, *m*, CH_2), 1.32–1.24 (18H, *m*, 9 CH_2), 0.99 (6H, *t*, *J* = 7.1 Hz, ($C\mathbf{H}_3CH_2)_2N$), 0.88 (3H, *t*, *J* = 6.7 Hz, CH_3 dodecyl). ^{13}C-NMR (75 MHz, δ / / ppm): 173.83 (CO), 64.38 (OCH_2), 52.69 (NCH_2), 46.79 (($CH_3\mathbf{C}H_2)_2N$), 34.30 ($\mathbf{C}H_2CO$), 29.60 (CH_2), 29.59 (CH_2), 29.54 (CH_2), 29.49 (CH_2), 29.31 (CH_2), 29.22 (CH_2), 28.59 (CH_2), 27.21 (CH_2), 26.66 (CH_2), 25.89 (CH_2), 24.96 ($\mathbf{C}H_2CH_2CO$), 22.65 ($\mathbf{C}H_2CH_3$ dodecyl), 14.08 (CH_3 dodecyl), 11.59 (($\mathbf{C}H_3CH_2)_2N$).

*Octyl 6-(pyrrolidin-1-yl)hexanoate (**8**)*. Yield: 71 %; b.p. 127–136 °C at 0.03 kPa. Anal. Calcd. for $C_{18}H_{35}NO_2$: C, 72.68; H, 11.86; N, 4.71; O, 10.76 %. Found: C, 72.56; H, 11.92; N, 4.61; O, 10.82 %. IR ($CHCl_3$, cm^{-1}): 2930, 2858, 2801, 1724, 1466, 1352, 1270. ^{1}H-NMR (300 MHz, $CDCl_3$, δ / ppm): 4.04 (2H, *t*, *J* = 6.7 Hz, OCH_2), 2.51–2.35 (6H, *m*, $(CH_2)_2N$ pyrr. + NCH_2 acyl), 2.30 (2H, *t*, *J* = 7.5 Hz, CH_2CO), 1.79–1.73 (4H, *m*, 2 CH_2), 1.69–1.46 (6H, *m*, 3 CH_2), 1.40–1.19 (14H, *m*, 7 CH_2), 0.87 (3H, *t*, *J* = 6.9 Hz, CH_3). ^{13}C-NMR (75 MHz, δ / ppm): 173.59 (CO), 64.40 (OCH_2), 56.40 (NCH_2 acyl), 54.20 ($(CH_2)_2N$ pyrr.), 34.30 ($\mathbf{C}H_2CO$), 31.79 ($\mathbf{C}H_2CH_2CH_3$), 29.22 (CH_2 alkyl), 29.20 (CH_2 alkyl), 28.80 ($OCH_2\mathbf{C}H_2$), 28.66 (NCH_2CH_2 acyl), 27.29 ($\mathbf{C}H_2(CH_2)_2CO$), 25.95 ($O(CH_2)_2\mathbf{C}H_2$), 24.99 ($\mathbf{C}H_2CH_2CO$), 23.40 (($\mathbf{C}H_2)_2CH_2N$ pyrr., *i.e.*, 2 βCH_2 pyrr.), 22.66 ($\mathbf{C}H_2CH_3$), 14.13 (CH_3).

*Decyl 6-(pyrrolidin-1-yl)hexanoate (**9**)*. Yield: 62 %; b.p.150–155 °C at 0.02 kPa. Anal. Calcd. for $C_{20}H_{39}NO_2$: C, 73.79; H, 12.08; N, 4.30; O, 9.83 %. Found: C, 73.67; H, 12.15; N, 4.21; O, 9.91 %. IR ($CHCl_3$, cm^{-1}): 2929, 2858, 2800, 1724, 1467, 1353, 1272. ^{1}H-NMR (300 MHz, $CDCl_3$, δ / ppm): 4.07 (2H, *t*, *J* = 6.8 Hz, OCH_2), 2.51–2.34 (6H, *m*, $(CH_2)_2N$ pyrr.+ NCH_2 acyl), 2.29 (2H, *t*, *J* = 7.5 Hz, CH_2CO), 1.79–1.73 (4H, *m*, 2 CH_2), 1.68–1.45 (6H, *m*, 3 CH_2), 1.41–1.16 (16H, *m*, 8 CH_2), 0.87 (3H, *t*, *J* = 6.7 Hz, CH_3). ^{13}C-NMR (75 MHz, δ / ppm): 173.61 (CO), 64.40 (OCH_2), 56.42 (NCH_2 acyl), 54.21($(CH_2)_2N$ pyrr.), 34.33 ($\mathbf{C}H_2CO$), 31.92 ($\mathbf{C}H_2CH_2CH_3$), 29.66 (CH_2 alkyl), 29.62 (CH_2 alkyl), 29.57 (CH_2 alkyl), 29.35 (CH_2 alkyl), 29.29 (CH_2 alkyl), 28.79 ($OCH_2\mathbf{C}H_2$), 28.68 ($NCH_2\mathbf{C}H_2$ acyl), 27.31 ($\mathbf{C}H_2(CH_2)_2CO$), 25.98 ($O(CH_2)_2\mathbf{C}H_2$), 25.01 ($\mathbf{C}H_2CH_2CO$), 23.42 (($\mathbf{C}H_2)_2CH_2N$ pyrr., *i.e.*, 2 βCH_2 pyrr.), 22.73 ($\mathbf{C}H_2CH_3$), 14.18 (CH_3).

*Undecyl 6-(pyrrolidin-1-yl)hexanoate (**10**)*. Yield: 66 %; b.p. 169–170 °C at 0.04 kPa. IR (CHCl$_3$, cm^{-1}): 2928, 2856, 2801, 1724, 1466, 1352, 1275; ^{1}H-NMR (300 MHz, CDCl$_3$, δ / ppm): 4.04 (2H, *t*, *J* = 6.8 Hz, OCH$_2$), 2.51–2.35 (*m*, 6H, (CH$_2$)$_2$N pyrr.+ NCH$_2$ acyl), 2.29 (2H, *t*, *J* = 7.5 Hz, CH$_2$CO), 1.81–1.71 (4H, *m*, 2 CH$_2$), 1.69–1.47 (6H, *m*, 3 CH$_2$); 1.40–1.18 (18H, *m*, 9 CH$_2$), 0.87 (3H, *t*, *J* = 6.6 Hz, CH$_3$). ^{13}C-NMR (75 MHz, δ / ppm): 173.57 (CO), 64.37 (OCH$_2$), 56.40 (NCH$_2$ acyl); 54.21 ((CH$_2$)$_2$N pyrr.), 34.30 (**C**H$_2$CO), 31.92 (**C**H$_2$CH$_2$CH$_3$); 29.62 (CH$_2$ alkyl); 29.60 (CH$_2$ alkyl), 29.55 (CH$_2$ alkyl), 29.35 (CH$_2$ alkyl), 29.28 (CH$_2$ alkyl), 28.81 (OCH$_2$**C**H$_2$), 28.66 (NCH$_2$**C**H$_2$ acyl), 27.29 (**C**H$_2$(CH$_2$)$_2$CO), 25.96 (O(CH$_2$)$_2$**C**H$_2$), 25.00 (**C**H$_2$CH$_2$CO), 23.41 ((**C**H$_2$)$_2$CH$_2$N pyrr., *i.e.*, 2 βCH$_2$ pyrr.), 22.71 (**C**H$_2$CH$_3$), 14.17 (CH$_3$).

*Dodecyl 6-(pyrrolidin-1-yl)hexanoate (**11**)*. Yield 49 %; b.p. 182–183 °C at 0.04 kPa. Anal. Calcd. for C$_{22}$H$_{43}$NO$_2$: C, 74.73; H, 12.26; N, 3.96; O, 9.05 %. Found: C, 74.68; H, 12.35; N, 3.89; O, 9.11 %. IR (CHCl$_3$, cm^{-1}): 2928, 2856, 2801, 1724, 1466, 1352, 1275. ^{1}H-NMR (300 MHz, CDCl$_3$, δ / ppm): 4.04 (2H, *t*, *J* = 6.8 Hz, OCH$_2$), 2.52–2.37 (6H, *m*, (CH$_2$)$_2$N pyrr. + NCH$_2$ acyl), 2.30 (2H, *t*, *J* = 7.4 Hz, CH$_2$CO), 1.81–1.71 (4H, *m*, 2 CH$_2$), 1.70–1.46 (6H, *m*, 3 CH$_2$), 1.42–1.17 (20H, *m*, 10 CH$_2$), 0.87 (3H, *t*, *J* = 6.8 Hz, CH$_3$). ^{13}C-NMR (75 MHz, δ / ppm): 173.61 (CO). 64.40 (OCH$_2$), 56.42 (NCH$_2$ acyl), 54.22 (CH$_2$)$_2$N pyrr.), 34.33 (**C**H$_2$CO), 31.95 (**C**H$_2$CH$_2$CH$_3$), 29.69 (CH$_2$ alkyl), 29.67 (CH$_2$ alkyl), 29.62 (CH$_2$ alkyl), 29.57 (CH$_2$ alkyl), 29.39 (CH$_2$ alkyl), 29.30 (CH$_2$ alkyl), 28.81 (OCH$_2$CH$_2$), 28.69 (NCH$_2$CH$_2$ acyl), 27.32 (CH$_2$(CH$_2$)$_2$CO), 25.98 (O(CH$_2$)$_2$CH$_2$), 25.02 (**C**H$_2$CH$_2$CO), 23.43 ((**C**H$_2$)$_2$CH$_2$N pyrr., *i.e.*, 2 βCH$_2$ pyrr.), 22.74 (**C**H$_2$CH$_3$), 14.19 (CH$_3$).

*Octyl 6-(piperidin-1-yl)hexanoate (**12**)*. Yield: 62 %; b.p.163 °C at 0.04–0.05 kPa; Anal. Calcd. for C$_{19}$H$_{37}$NO$_2$: C, 73.26; H, 11.97; N, 4.50; O, 10.27 %. Found: C, 73.18; H, 12.05; N, 4.43; O, 10.39 %. IR (CHCl$_3$, cm^{-1}): 2934, 2858, 1724, 1469, 1456, 1378, 1271, 1258. ^{1}H-NMR (300 MHz, CDCl$_3$, δ / ppm): 4.04 (2H, *t*, *J* = 6.5 Hz, OCH$_2$), 2.41–2.20 (8H, *m*, (4 CH$_2$), 1.69–1.37 (12H, *m*, 6 CH$_2$), 1.36–1.20 (12H, *m*, 6 CH$_2$), 0.88 (3H, *t*, *J* = 6.8 Hz, CH$_3$). ^{13}C-NMR (75 MHz, CDCl$_3$, δ / ppm): 173.61 (CO); 64.39 (OCH$_2$), 59.35 (NCH$_2$ acyl), 54.63 ((CH$_2$)$_2$N piperid.), 34.33 (**C**H$_2$CO), 31.81 (CH$_2$); 29.25 (CH$_2$) 29.22 (CH$_2$), 28.67 (CH$_2$), 27.33 (NCH$_2$**C**H$_2$), 26.68 (CH$_2$); 26.04 (CH$_2$), 25.97 (CH$_2$), 25.02 (**C**H$_2$CH$_2$CO), 24.54 (CH$_2$), 22.68 (**C**H$_2$CH$_3$); 14.15 (CH$_3$).

*2-Octyl 6-(piperidin-1-yl)hexanoate (**13**)*. Yield: 68 %; pale yellow oil. Anal. Calcd. for C$_{19}$H$_{37}$NO$_2$: C, 73.26; H, 11.97; N, 4.50; O, 10.27 %. Found: C, 73.21; H, 12.08; N, 4.41; O, 10.34 %. IR (CHCl$_3$, cm^{-1}): 2936, 2858, 1725, 1469, 1456, 1378, 1271, 1257. ^{1}H-NMR (300 MHz, CDCl$_3$, δ / ppm): 4.98–4.82 (1H, *m*, OCH), 2.43–2.20 (8H, *m*, 4 CH$_2$) 1.69–1.37 (12H, *m*, 6 CH$_2$), 1.36–1.13 (13H, *m*, 5 CH$_2$ + CHC**H**$_3$), 0.87 (3H, *t*, *J* = 6.80 Hz, terminal CH$_3$). ^{13}C-NMR (75 MHz, CDCl$_3$, δ / ppm) 173.17 (CO), 70.71 (OCH), 59.37 (NCH$_2$ acyl), 54.63

((CH$_2$)$_2$N piperid.), 35.9 6 (OCH **C**H$_2$), 34.69 (**C**H$_2$CO), 31.78 (CH $_2$), 29.14 (CH$_2$), 27.32 (NCH$_2$**C**H$_2$), 26.70 (CH$_2$), 26.04 (CH$_2$), 25.41 (OCHCH$_2$**C**H$_2$), 25.10 (**C**H$_2$CH$_2$CO), 24.54 (**C**H$_2$(CH$_2$)$_2$ piperid.), 22.6 2 (**C**H$_2$CH$_3$), 20.06 (OCH**C**H$_3$), 14.13 (CH$_2$**C**H$_3$).

Nonyl 6-(piperidin-1-yl)hexanoate ***(14)***. Yield: 47 %; pale y ellow oil. Anal. Calcd. for $C_{20}H_{39}NO_2$: C, 73.79; H, 12.08; N, 4.30; O, 9.83 %. Found: C, 73.69; H, 12.15; N, 4.24; O, 9.94 %. IR (CHCl$_3$, cm^{-1}): 2934, 2857, 1724, 1468, 1456, 1378, 1271, 1257. ^{1}H-NMR (300 MHz, CDCl$_3$, δ / ppm): 4.03 (2H, *t*, *J* = 6.7 Hz, OCH$_2$), 2.41–2.21 (8H, *m*, 4 CH$_2$), 1.70–1.18 (26H, *m*, 13 CH$_2$), 0.86 (3H, *t*, *J* = = 6.7 Hz, CH $_3$). ^{13}C-NMR (75 MHz, CDCl $_3$, δ / ppm): 173.81 (CO), 64. 38 (OCH$_2$), 59.30 (NCH$_2$ acyl), 54.57 ((CH $_2$)$_2$N p iperid.), 34.25 (**C**H$_2$CO), 31.80 (CH$_2$), 29.43 (CH$_2$), 29.20 (CH$_2$), 29.19 (CH$_2$), 28.58 (CH$_2$), 27.24 (CH$_2$), 26.56 (CH$_2$), 25.91 (CH $_2$), 25.88 (CH $_2$), 24.92 (**C**H$_2$CH$_2$CO), 24.42 (*C*H$_2$), 22.61 (**C**H$_2$CH$_3$), 14.06 (CH$_3$).

Decyl 6-(piperidin-1-yl)hexanoate ***(15)***. Yield: 55 % ; pale yellow oil. Anal. Calcd. for $C_{21}H_{41}NO_2$: C, 74.28; H, 12.17; N, 4.13; O, 9.42 %. Found: C, 74.18; H, 12.25; N, 4.07; O, 9.5 3 %. IR (CHCl$_3$ cm^{-1}): 2931, 285 7, 1724, 1468, 1456, 1378, 1271, 1258. ^{1}H-NMR (300 MHz, CDCl$_3$, δ / ppm): 4.04 (2H, *t*, *J* = 6.7 Hz, OCH$_2$), 2.38–2.30 (4H, *m*, 2 CH $_2$), 2.26 (2H, *t*, *J* = 7.7 Hz, CH $_2$CO), 1.67–1.48 (10H, *m*, 5 CH $_2$), 1.35–1 .24 (20H, *m*, 10 CH $_2$), 0.87 (3H, *t*, *J* = 6.7 Hz, CH $_3$). ^{13}C-NMR (75 MHz, CDCl$_3$, δ / ppm): 173.86 (CO), 64.41 (OCH$_2$), 59.36 (NCH$_2$ acyl), 54.62 ((CH$_2$)$_2$N piperid.), 3 4.29 (**C**H$_2$CO), 31. 89 (CH $_2$), 29. 62 (CH $_2$), 29.61 (CH$_2$), 29.55 (CH$_2$), 29.51 (CH$_2$), 29.33 (CH$_2$), 29.24 (**C**H$_2$); 28.61 (CH$_2$), 27.27 (CH $_2$), 26.62 (CH $_2$), 25.97 (CH $_2$), 25.91 (CH$_2$), 24.95 (**C**H$_2$CH$_2$CO), 24.47 (CH$_2$), 22.66 (**C**H$_2$CH$_3$), 14.10 (CH$_3$).

Undecyl 6-(piperidin-1-yl)hexanoate ***(16)***. Yield 53 %; pale yellow oil. Anal. Calcd. for $C_{22}H_{43}NO_2$: C, 74.73; H, 12.26; N, 3.96; O, 9.05 %. Found: C, 74.68; H, 12.35; N, 3.88; O, 9.12 %. IR (CHCl$_3$, cm^{-1}): 2927. 2856, 1724, 1468, 1457, 1378, 1271, 1258. ^{1}H-NMR (300 MHz, CDCl$_3$, δ / ppm): 4.04 (2H, *t*, *J* = 6.7 Hz, OCH$_2$), 2.40–2.24 (8H, *m*, 4 CH$_2$), 1.68–1.25 (30H, *m*, 15 CH$_2$), 0.87 (3H, *t*, *J* = = 6.6 Hz, CH $_3$). ^{13}C-NMR (75 MHz, CDCl $_3$, δ / ppm): 174.11 (CO), 64. 67 (OCH$_2$), 59.57 (NCH $_2$ acyl), 54.8 4 ((CH $_2$)$_2$N piperid.), 34. 54 (**C**H$_2$CO), 32.14 (CH$_2$), 31.82 (CH$_2$), 29.84 (CH$_2$); 29.81 (CH$_2$), 29.76 (CH$_2$), 29.57 (CH$_2$), 29.49 (CH$_2$), 28.87 (CH$_2$), 27.52 (CH$_2$), 26.83 (CH$_2$), 26.18 (CH$_2$), 25.20 (CH$_2$), 24.69 (CH$_2$), 22.89 (**C**H$_2$CH$_3$); 14.36 (CH$_3$).

Dodecyl 6-(piperidin-1-yl)hexanoate ***(17)***. Yield: 7 8 % ; pale yellow oil . Anal. Calcd. for $C_{23}H_{45}NO_2$: C, 75.15; H, 12.34; N, 3.81; O, 8.70 %. Found: C, 75.08; H, 12.42; N, 3.75; O, 8.79 %. IR (CHCl$_3$, cm^{-1}): 2930, 2856, 1724, 1468, 1457, 1378, 1271, 1258; ^{1}H-NMR (300 MHz, CDCl$_3$, δ / pp m): 4.05 (2H, *t*, *J* = = 6.7 Hz, OCH $_2$), 2.40–2.24 (8H, *m*, 4 CH$_2$), 1.69–1.26 (32H, *m*, 16 CH$_2$), 0.88 (3H, *t*, *J* = 6.6 Hz, CH $_3$). ^{13}C-NMR (75 MHz, CDC l$_3$, δ / pp m): 173.86 (CO),

64.41 (OCH_2), 59.36 (NCH_2 acyl), 54.62 ($(CH_2)_2N$ piperid.), 34.29 ($\mathbf{C}H_2CO$), 31.89 (CH_2), 29.62 (CH_2), 29.61 (CH_2), 29.55 (CH_2), 29.51 (CH_2), 29.33(CH_2), 29.23 (CH_2), 28.61 (CH_2), 27.27 ($NCH_2\mathbf{C}H_2$ acyl), 26.62 (CH_2), 25.97 (CH_2), 25.91 (CH_2), 24.95 ($\mathbf{C}H_2CH_2CO$), 24.47 (CH_2), 22.66 ($\mathbf{C}H_2CH_3$), 14.10 (CH_3).

*Octyl 6-(morpholin-4-yl)hexanoate (**18**)*. Yield: 58 %, b.p. 161–163 °C at 0.04–0.05 kPa. Anal. Calcd. for $C_{18}H_{35}NO_3$: C, 68.97; H, 11.25; N, 4.47; O, 15.31 %. Found: C, 69.08; H, 11.33; N, 4.38; O, 15.39 %. IR ($CHCl_3$, cm^{-1}): 2930, 2859, 1724, 1468, 1373, 1287, 1258. ^{1}H-NMR (300 MHz, $CDCl_3$, δ / ppm): 4.04 (2H, *t*, J = 6.7 Hz, OCH_2 alkyl), 3.70 (4H, *t*, J = 4.6 Hz, $O(C\mathbf{H}_2CH_2)_2N$), 2.41 (4H, *t*, $O(CH_2C\mathbf{H}_2)_2N$), 2.30–2.26 (4H, *m*, CH_2CO + NCH_2 acyl), 1.73–1.41 (6H, *m*, 3 CH_2), 1.40–1.18 (12H, *m*, 6 CH_2), 0.87 (3H, *t*, J = 6.8 Hz, CH_3). ^{13}C-
-NMR (75 MHz, $CDCl_3$, δ / ppm): 173.53 (CO), 66.93 ($(CH_2)_2O$ morph.), 64.41 (OCH_2), 58.86 (NCH_2 acyl), 53.74 ($(CH_2)_2N$ morph.), 34.28 ($\mathbf{C}H_2CO$), 31.79 ($\mathbf{C}H_2CH_2CH_3$), 29.23 (CH_2), 29.21 (CH_2), 28.66 ($OCH_2\mathbf{C}H_2$), 27.05 ($NCH_2\mathbf{C}H_2$ acyl), 26.26 ($\mathbf{C}H_2(CH_2)_2CO$), 25.95 ($O(CH_2)_2\mathbf{C}H_2$), 24.93 ($\mathbf{C}H_2CH_2CO$), 22.67 ($\mathbf{C}H_2CH_3$), 14.15 (CH_3).

*Nonyl 6-(morpholin-4-yl)hexanoate (**19**)*. Yield 56 %; b.p. 175–179 °C at 0.04–0.06 kPa. Anal. Calcd. for $C_{19}H_{37}NO_3$: C, 69.68; H, 11.39; N, 4.28; O, 14.66 %. Found: C, 69.78; H, 11.43; N, 4.19; O, 14.69 %. IR ($CHCl_3$, cm^{-1}): 2928, 2858, 1725, 1467, 1375, 1287, 1259. ^{1}H-NMR (300MHz, $CDCl_3$, δ / ppm): 4.15–3.95 (2H, *m*, OCH_2), 3.70 (4H, *t*, J = 6.8 Hz, $O(C\mathbf{H}_2CH_2)_2N$), 2.41 (4H, *t*, J = 4.5 Hz, $O(CH_2C\mathbf{H}_2)_2N$), 2.34–2.24 (4H, *m*, CH_2CO + NCH_2 acyl), 1.70–1.43 (6H, *m*, 3 CH_2), 1.39–1.19 (14H, *m*, 7 CH_2), 0.87 (3H, *t*, J = 6.8 Hz, CH_3). ^{13}C-NMR (75 MHz, $CDCl_3$, δ / ppm): 173.52 (CO), 66.94 ($(CH_2)_2O$ morph.), 64.41 (OCH_2), 58.87 (NCH_2 acyl), 53.75 ($(CH_2)_2N$ morph.), 34.28 ($\mathbf{C}H_2CO$), 31.91 ($CH_2CH_2CH_3$), 29.55 (CH_2), 29.33 (CH_2), 29.27 (CH_2), 28.66 (OCH_2CH_2), 27.05 ($NCH_2\mathbf{C}H_2$ acyl), 26.27 ($\mathbf{C}H_2(CH_2)_2CO$), 25.96 ($O(CH_2)_2\mathbf{C}H_2$), 24.94 ($\mathbf{C}H_2CH_2CO$), 22.71 ($\mathbf{C}H_2CH_3$), 14.17 (CH_3).

*Decyl 6-(morpholin-4-yl)hexanoate (**20**)*. Yield 48 %; b.p. 150 °C at 0.02 kPa. Anal. Calcd. for $C_{20}H_{39}NO_3$: C, 70.33; H, 11.51; N, 4.10; O, 14.05 %. Found: C, 70.44; H, 11.63; N, 4.08; O, 14.11 %. IR ($CHCl_3$, cm^{-1}): 2929, 2857, 1724, 1467, 1375, 1287, 1258. ^{1}H-NMR (300 MHz, $CDCl_3$, δ / ppm): 4.05 (2H, *t*, J = 6.7 Hz, OCH_2), 3.71 (4H, *t*, J = 5.0 Hz, $O(C\mathbf{H}_2CH_2)_2N$), 2.42 (4H, *t*, J = = 4.5 Hz, $O(CH_2C\mathbf{H}_2)_2N$), 2.35–2.27 (4H, *m*, CH_2CO + NCH_2 acyl), 1.72–1.44 (6H, *m*, 3 CH_2), 1.42–1.17 (16H, *m*, 8 CH_2), 0.87 (3H, *t*, J = 6.7 Hz, CH_3). ^{13}C-
-NMR (75 MHz, $CDCl_3$, δ / ppm): 173.52 (CO), 66.93 ($(CH_2)_2O$ morph.), 64.41 (OCH_2), 58.85 (NCH_2 acyl), 53.74 ($(CH_2)_2N$ morph.), 34.26 ($\mathbf{C}H_2CO$), 31.86 ($\mathbf{C}H_2CH_2CH_3$), 29.50 (CH_2), 29.44 (CH_2), 29.27 (CH_2), 29.25 (CH_2), 28.66 ($OCH_2\mathbf{C}H_2$), 27.04 ($NCH_2\mathbf{C}H_2$ acyl), 26.26 ($\mathbf{C}H_2(CH_2)_2CO$), 25.95 ($O(CH_2)_2\mathbf{C}H_2$), 24.93 ($\mathbf{C}H_2CH_2CO$), 22.69 ($\mathbf{C}H_2CH_3$), 14.16 (CH_3).

*Undecyl 6-(morpholin-4-yl)hexanoate (**21**)*. Yield 43 %; b.p. 180 °C at 0.055 kPa. Anal. C alcd. for $C_{21}H_{41}NO_3$: C, 70.94; H, 11.62; N, 3.94; O, 13.50 %. Found: C, 71.08; H, 11.73; N, 3.82; O, 13.59 %. IR ($CHCl_3$, cm^{-1}): 2928, 2857, 1725, 1467, 1375, 1287, 1259. ^{1}H-NMR (300 MHz, $CDCl_3$, δ / ppm): 4.07 (2H, *t*, *J* = 6.8 Hz, OCH_2), 3.71 (4H, *t*, *J* = 4.9 Hz, $O(CH_2CH_2)_2N$), 2.41 (4H, *t*, *J* = = 5.7 Hz, $O(CH_2CH_2)_2N$), 2.35–2.23 (4H, *m*, CH_2CO + NCH_2 acyl), 1.73–1.42 (6H, *m*, 3 CH_2), 1.40–1.15 (18H, *m*, 9 CH_2), 0.86 (3H, *t*, *J* = 7.0 Hz, CH_3). ^{13}C--NMR (75 MHz, $CDCl_3$, δ / ppm): 173.48 (CO), 66.92 (($CH_2)_2$O morph.), 64.38 (OCH_2), 58.81 (NCH_2 acyl), 53.73 (($CH_2)_2$N morph.), 34.25 (CH_2CO), 31.91 ($CH_2CH_2CH_3$), 29.69 (CH_2), 29.61 (CH_2), 29.52 (CH_2), 29.36 ($O(CH_2)_3CH_2$), 29.26 ($CH_2(CH_2)_2CH_3$), 28.64 (OCH_2CH_2), 27.03 (NCH_2CH_2 acyl), 26.22 ($CH_2(CH_2)_2CO$), 25.94 ($O(CH_2)_2CH_2$), 24.98 (CH_2CH_2CO), 22.73 (CH_2CH_3), 14.18 (CH_3).

*Dodecyl 6-(morpholin-4-yl)hexanoate (**22**)*. Yield 29 %; b.p. 178–182 °C at 0.03 kPa. Anal. Calcd. for $C_{22}H_{43}NO_3$: C, 71.5; H, 11.73; N, 3.79; O, 12.99 %. Found: C, 71.58; H, 11.81; N, 3.65; O, 13.09 %. IR ($CHCl_3$, cm^{-1}): 2927, 2856, 1724, 1467, 1374, 1287, 1257. ^{1}H-NMR (300 MHz, $CDCl_3$, δ / ppm): 4.05 (2H, *t*, *J* = 6.8 Hz, OCH_2), 3.71 (4H, *t*, *J* = 4.9 Hz, $O(CH_2CH_2)_2N$), 2.42 (4H, *t*, *J* = = 4.4 Hz, $O(CH_2CH_2)_2N$), 2.35–2.27 (4H, *m*, CH_2CO + NCH_2 acyl), 1.73–1.43 (6H, *m*, 3 CH_2), 1.41–1.19 (20H, *m*, 10 CH_2), 0.88 (3H, *t*, *J* = 6.7 Hz, CH_3). ^{13}C--NMR (75 MHz, $CDCl_3$, δ / ppm): 173.47 (CO), 66.92 (($CH_2)_2$O morph.), 64.38 (OCH_2), 58.84 (NCH_2 acyl), 53.73 (($CH_2)_2$N morph.), 34.25 (CH_2CO), 31.91 ($CH_2CH_2CH_3$), 29.65 (CH_2), 29.64 (CH_2), 29.58 (CH_2), 29.54 (CH_2), 29.36 ($O(CH_2)_3CH_2$), 29.26 ($CH_2(CH_2)_2CH_3$), 28.65 (OCH_2CH_2), 27.03 (NCH_2CH_2 acyl), 26.26 ($CH_2(CH_2)_2CO$), 25.94 ($O(CH_2)_2CH_2$), 24.92 (CH_2CH_2CO), 22.70 (CH_2CH_3), 14.16 (CH_3).

*6-(Dimethylamino)-N-octyl-hexanamide (**24**)*. Yield: 77 % ; b.p.: 152 °C at 0.4 kPa. Anal. Calcd. for $C_{16}H_{34}N_2O$: C, 71.06; H, 12.67; N, 10.36; O, 5.92 %. Found: C, 71.12; H, 12.75; N, 10.54; O, 6.01 % . IR (KBr, cm^{-1}): 3449, 2930, 2859, 1660, 1518, 1467, 1378. ^{1}H-NMR (300 MHz, $CDCl_3$, δ / ppm): 5.60 (1H, *s*, CONH), 3.21 (2H, *q*, *J* = 7.0, 13.1 Hz, CH_2), 2.25–2.12 (10H, *m*, $(CH_3)_2N$ + 2 CH_2), 1.68–1.58 (2H, *m*, CH_2) 1.48–1.41 (4H, *m*, 2 CH_2), 1.36–1.25 (12H, *m*, 6 CH_2), 0.88 (3H, *t*, *J* = 6.7 Hz, CH_3 octyl). ^{13}C-NMR (75 MHz, $CDCl_3$, δ / ppm): 172.83 (CO), 59.52 (($CH_3)_2NCH_2$), 45.56 (($CH_3)_2$N), 39.46 ($CONHCH_2$), 36.74 (CH_2), 31.74 (CH_2), 29.65 (CH_2), 29.22 (CH_2), 29.17 (CH_2), 27.38 (CH_2), 26.98 (CH_2), 26.89 (CH_2), 25.60 (CH_2), 22.59 (CH_2), 14.05 (CH_3).

*6-(Dimethylamino)-N-(1-methylheptyl)-hexanamide (**25**)*. Yield: 54 %; b.p.: 176–178 °C at 0.6–0.8 kPa. Anal. Calcd. for $C_{16}H_{34}N_2O$: C, 71.06; H, 12.67; N, 10.36; O, 5.92 %. Found: C, 71.10; H, 12.73; N, 10.45; O, 5.87 %. IR (KBr, cm^{-1}): 3436, 2931, 2860, 1656, 1511, 1466, 1379. ^{1}H-NMR (300 MHz, $CDCl_3$, δ / / ppm): 5.31 (1H, *d*, *J* = 8.8 Hz, CONH), 4.08–3.88 (1H, *m*, $NHCH(CH_3)CH_2$),

2.32–2.20 (8H, *m*, $(CH_3)_2N + CH_2$), 2.15 (2H, *t*, *J* = 7.3 Hz, CH_2CO), 1.73–1.35 (16H, *m*, 8 CH_2), 1.11 (3H, *d*, *J* = 6.6 Hz, $NHCH(C\mathbf{H}_3)CH_2$), 0.88 (3H, *t*, *J* = 6.4 Hz, CH_3 terminal). ^{13}C-NMR (75 MHz, $CDCl_3$, δ / ppm): 172.05 (CO), 59.57 ($(CH_3)_2N\mathbf{C}H_2$), 45.38 ($CONH\mathbf{C}H$), 45.08 ($(CH_3)_2N$), 37.05 ($CONHCH(CH_3)\mathbf{C}H_2$), 36.94 ($\mathbf{C}H_2CO$), 31.75 ($CH_2$), 29.14 ($CH_2$), 27.34 ($CH_2$), 27.00 ($CH_2$), 25.97 ($CH_2$), 25.67 ($CH_2$), 22.53 ($CH_2$), 21.02 ($CONHCH(\mathbf{C}H_3)CH_2$), 13.97 ($CH_3$ terminal).

6-(Dimethylamino)-N-*nonyl-hexanamide* (***26***). Yield 59 %; b.p. 211–212 °C at 0.7–0.8 kPa. Anal. Calcd. for $C_{17}H_{36}N_2O$: C, 71.77; H, 12.76; N, 9.85; O, 5.62 %. Found: C, 71.70; H, 12.81; N, 9.91; O, 5.55 %. IR (KBr, cm^{-1}): 3449, 2930, 2858, 1660, 1518, 1467, 1378. ^{1}H-NMR (300 MHz, $CDCl_3$, δ / ppm): 5.64 (1H, *s*, CONH); 3.21 (2H, *q*, *J* = 7.0, 13.1 Hz, CH_2), 2.24–2.11 (10H, *m*, $(CH_3)_2N + 2$ CH_2), 1.67–1.57 (2H, *m*, CH_2), 1.50–1.42 (4H, *m*, 2 CH_2), 1.40–1.23 (14H, *m*, 7 CH_2), 0.85 (3H, *t*, *J* = 6.7 Hz, CH_3 nonyl). ^{13}C-NMR (75 MHz, $CDCl_3$, δ / ppm): 173.10 (CO), 59.78 ($(CH_3)_2N\mathbf{C}H_2$); 45.71 ($(CH_3)_2N$) 39.72 ($CONH\mathbf{C}H_2$), 36.98 (CH_2), 32.07 (CH_2), 29.91 (CH_2), 29.73 (CH_2), 29.53 (CH_2), 29.46 (CH_2), 27.64 (CH_2), 27.24 (CH_2), 27.16 (CH_2), 25.87 (CH_2), 22.87 (CH_2), 14.33 (CH_3).

6-(Dimethylamino)-N-*decyl-hexanamide* (***27***). Yield 69 %; colorless powder, m.p. 36–40 °C, b.p. 173–175 °C at 0.03 kPa. Anal. Calcd. for $C_{18}H_{38}N_2O$: C, 72.42; H, 12.83; N, 9.38; O, 5.36 %. Found: C, 72.35; H, 12.81; N, 9.45; O, 5.28 %. IR (KBr, cm^{-1}): 3449, 2928, 2856, 1660, 1518, 1467, 1378. ^{1}H-NMR (300 MHz, $CDCl_3$, δ / ppm): 5.60 (1H, *s*, (CONH), 3.21 (2H, *q*, *J* = 7.0, 13.2 Hz, CH_2), 2.26–2.13 (10H, *m*, $((CH_3)_2N + 2\ CH_2)$, 1.67–1.57 (2H, *m*, CH_2), 1.49–1.40 (4H, *m*, 2 CH_2), 1.38–1.21 (16H *m*, 8 CH_2), 0.87 (3H, *t*, *J* = 6.7 Hz, CH_3 decyl). ^{13}C--NMR (75 MHz, $CDCl_3$, δ / ppm): 172.82 (CO), 59.51 ($(CH_3)_2N\mathbf{C}H_2$) 45.45 ($(CH_3)_2N$), 39.46 ($CONH\mathbf{C}H_2$), 36.74 ($\mathbf{C}H_2CO$), 29.05 (CH_2), 29.12 (CH_2), 29.27 (CH_2), 29.48 (CH_2), 27.37 (CH_2), 26.97 (CH_2), 26.90 (CH_2), 25.60 (CH_2), 22.64 (CH_2), 14.09 (CH_3).

6-(Dimethylamino)-N-dodecyl-hexanamide (***28***). Yield 40 %; colorless powder, m.p. 48–49 °C (48–50 °C).[12] IR (KBr, cm^{-1}): 3449, 2927, 2856, 1660, 1518, 1467, 1377. ^{1}H-NMR (300 MHz, $CDCl_3$, δ / ppm): 5.57 (1H *s*, (CONH), 3.21 (2H, *q*, *J* = 7.0, 13.1, CH_2), 2.25–2.12 (10H, *m*, $(CH_3)_2N + 2\ CH_2$), 1.68–1.58 (2H, *m*, CH_2), 1.51–1.36 (2H, *m*, CH_2), 1.35–1.23 (22H, *m*, 11 CH_2), 0.86 (3H, *t*, *J* = 6.6 Hz, CH_3 dodecyl). ^{13}C-NMR (75 MHz, $CDCl_3$, δ / ppm): 172.82 (CO), 59.51 ($(CH_3)_2N\mathbf{C}H_2$), 45.45 ($(CH_3)_2N$), 39.46 ($CONH\mathbf{C}H_2$), 36.74 ($\mathbf{C}H_2CO$) 31.87 (CH_2), 29.65 (CH_2), 29.61 (CH_2), 29.59 (CH_2), 29.58 (CH_2), 29.55 (CH_2), 29.31 (CH_2), 29.27 (CH_2), 27.37 (CH_2), 26.97 (CH_2), 26.90 (CH_2), 25.60 (CH_2), 22.64 (CH_2), 14.09 (CH_3).

N-*Decyl-6-(piperidin-1-yl)hexanamide* (***29***). Yield: 40 %; colorless powder, m.p. 36–40 °C. Anal. Calcd. for $C_{21}H_{42}N_2O$: C, 74.5; H, 12.5; N, 8.27; O, 4.73 %. Found: C, 74.39; H, 12.53; N, 8.38; O, 4.61 %. IR ($CHCl_3$, cm^{-1}): 3450, 2930,

2856, 1660, 1518, 1468, 1377. ^{1}H-NMR (300 MHz, $CDCl_3$, δ / ppm): 5.51 (1H, *s*, NH), 3.24 –3.17 (2H, *q*, CH_2), 2.33 (4H, *s*, 2 CH_2), 2.25 (2H, *t*, J = 7.7 Hz, NCH_2), 2.14 (2H, *t*, J = 7.6 Hz, CH_2CO), 1.68–1.23 (28H, *m*, 14 CH_2), 0.86 (3H, *t*, J = 6.6 Hz, CH_3). ^{13}C-NMR (75 MHz, $CDCl_3$, δ / ppm): 172.84 (CO), 59.34 ($CH_2(CH_2CH_2)_2N$), 54.61 (NCH_2 acyl), 39.45 (CONH**C**H_2), 36.74 (**C**H_2CO), 31.84 ($CONHCH_2$**C**H_2), 29.65 (CH_2), 29.50 (CH_2), 29.27 (CH_2), 27.30 (CH_2), 26.89 (CH_2), 26.63 (CH_2), 25.95 (CH_2), 25.70 (CH_2), 24.44 (CH_2), 22.64 (**C**H_2CH_3), 14.08 (CH_3).

N-*Dodecyl-6-(piperidin-1-yl)hexanamide* ***(30)***. Yield: 38 %; colorless powder, m.p. 45–49 °C. Anal. Calcd. for $C_{23}H_{46}N_2O$: C, 75.35; H, 12.65; N, 7.64; O, 4.36 %. Found: C, 75.28; H, 12.73; N, 7.74; O, 4.29 %. IR ($CHCl_3$, cm^{-1}): 3449, 2931, 2856, 1660, 1518, 1468, 1377. ^{1}H-NMR (300 MHz, $CDCl_3$, δ / ppm): 5.50 (1H, *s*, NH), 3.24 –3.18 (2H, *q*, CH_2), 2.33 (4H, *s*, 2 CH_2), 2.26 (2H, *t*, J = 7.8 Hz, NCH_2), 2.14 (2H, *t*, J = 7.6 Hz, CH_2CO), 1.68–1.24 (32H, *m*, 16 CH_2), 0.86 (3H, *t*, J = 6.7 Hz, CH_3). ^{13}C-NMR (75 MHz, $CDCl_3$, δ / ppm): 172.83 (CO), 59.35 ($CH_2(CH_2$**C**$H_2)_2N$), 54.62 (NCH_2 acyl), 39.46 (CONH**C**H_2), 36.76 (**C**H_2CO), 31.88 ($CONHCH_2$**C**H_2), 29.66 (CH_2), 29.61 (CH_2), 29.60 (CH_2), 29.55 (CH_2), 29.52 (CH_2), 29.31 (CH_2), 29.28 (CH_2), 27.30 (CH_2), 26.90 (CH_2), 26.64 (CH_2), 25.96 (CH_2), 25.70 (CH_2), 24.45 (CH_2), 22.65 (**C**H_2CH_3), 14.10 (CH_3).

6-(Morpholin-4-yl)-N-*octyl-hexanamide* ***(31)***. Yield 28 % ; b.p. 225–230 °C at 0.2 kPa. Anal. Calcd. for $C_{18}H_{36}N_2O_2$: C, 69.18; H, 11.61; N, 8.96; O, 10.24 %. Found: C , 69.28; H, 11.73; N, 9.04; O, 10.29 %. IR ($CHCl_3$, cm^{-1}): 3449, 2930, 2857, 1660, 1518, 1467, 1459, 1373. ^{1}H-NMR (300 MHz, $CDCl_3$, δ / / ppm): 5.58 (1H, *s*, CONH), 3.72 (4H, *t*, O(C**H**$_2CH_2)_2N$), 3.20 (2H, *q*, J = 7.2, 12.8 Hz, CH_2), 2.39 (4H, *t*, J = 4.5 Hz, O(CH_2C**H**$_2)_2N$), 2.32 (2H, *t*, J = 7.7 Hz, NCH_2 acyl), 2.13 (2H, *t*, J = 7.6 Hz, CH_2CO), 1.70–1.55 (2H, *m*, C**H**$_2CH_2CO$), 1.52–1.41 (4H, *m*, 2 CH_2), 1.38–1.25 (12H, *m*, 6 CH_2), 0.88 (3H, *t*, J = 6.7 Hz, CH_3). ^{13}C-NMR (75 MHz, $CDCl_3$, δ / ppm): 172.72 (CO), 66.75 ($O(CH_2CH_2)_2N$), 58.80 (NCH_2 acyl), 53.54 ($O(CH_2CH_2)_2N$), 39.44 (CONH**C**H_2), 36.55 (**C**H_2CO), 31.82 (CH_2), 29.71 (CH_2), 29.48 (CH_2), 29.28 (CH_2), 27.11 (CH_2), 26.86 (CH_2), 26.19 (CH_2), 25.63 (CH_2), 22.60 (CH_2), 14.05 (CH_3).

6-(Morpholin-4-yl)-N-*nonyl-hexanamide* ***(32)***. Yield 41 %; colorless powder, m.p. 41–47 °C, b.p. 201–203 °C at 0.05 kPa. Anal. Calcd. for $C_{19}H_{38}N_2O_2$: C, 69.89; H, 11.73; N, 8.58; O, 9.80 %. Found: C, 69.95; H, 11.83; N, 8.64 ; O, 9.91 %. IR ($CHCl_3$, cm^{-1}): 3449, 2930, 2858, 1661, 1518,1467, 1459, 1375. ^{1}H--NMR (300 MHz, $CDCl_3$, δ / ppm): 5.45 (1H, *s*, CONH), 3.70 (4H, *t*, J = 4.7 Hz, O(C**H**$_2CH_2)_2N$), 3.21 (2H , *q*, J = 7.1, 12.9, CH_2), 2.40 (4H, *t*, J = 4.4 Hz, O(CH_2C**H**$_2)_2N$), 2.31 (2H, *t*, J = 7.7 Hz, NCH_2 acyl), 2.14 (2H, *t*, J = 7.6 Hz, CH_2CO), 1.69–1.59 (2H, *m*, C**H**$_2CH_2CO$), 1.54–1.44 (4H, *m*, 2 CH_2), 1.37–1.24 (14H, *m*, 7 CH_2), 0.86 (3H, *t*, J = 6.7 Hz, CH_3). ^{13}C-NMR (75MHz, $CDCl_3$, δ /

/ ppm): 172.73 (CO), 6 6.95 (O(**C**$H_2CH_2)_2$N), 5 8.88 (NCH $_2$ acy l), 53.73 (O(CH_2**C**$H_2)_2$N), 39.46 (CONH**C**H_2), 36.73 (**C**H_2CO), 31.81 (CH_2), 29.65 (CH_2), 29.47 (CH_2), 29.26 (CH_2), 29.20 (CH_2), 27.11 (CH_2), 26.88 (CH_2), 26.27 (CH_2), 25.65 (CH_2), 22.62 (**C**H_2CH_3), 14.08 (CH_3).

N-*Decyl-6-(morpholin-4-yl)hexanamide* (***33***). Yield 44 %; colorless powder, m.p. 45–48 °C. Anal. Calcd. for $C_{20}H_{40}N_2O_2$: C, 70.54; H, 11.84; N, 8.23; O, 9.40 %. Found: C, 70.65; H, 11.75; N, 8.14; O, 9.51 %. IR (CHCl $_3$, cm^{-1}): 3449, 2930, 2857, 1660, 1518, 1467, 1459, 1378. ^{1}H-NMR (300 MHz, $CDCl_3$, δ / / ppm): 5.45 (1H, *s*, CONH), 3.70 (4H, *t*, *J* = 4.7 Hz, O(C**H**$_2$$CH_2)_2$N), 3.21 (2H, *q*, *J* = 7.1, 12.9 Hz, CH_2), 2.40 (4H, *t*, *J* = 4.4 Hz, O($CH_2CH_2)_2$N), 2.31 (2H, *t*, *J* = 7.7 Hz, NCH_2 acyl), 2.14 (2H, *t*, *J* = 7.6 Hz, CH_2CO), 1.69–1.59 (2H, *m*, C**H**$_2$$CH_2$CO), 1.54–1.44 (4H, *m*, 2 CH_2), 1.37–1.24 (14H, *m*, 7 CH_2), 0.86 (3H, *t*, *J* = 6.7 Hz, C H_3). ^{13}C-NMR (75 MHz, $CDCl_3$, δ / ppm): 172.72 (CO), 66.74 (O(**C**$H_2CH_2)_2$N), 58.76 (NCH $_2$ acyl), 53.60 (O(CH_2**C**$H_2)_2$N), 39.43 (CONH**C**H_2), 36.60 (**C**H_2CO), 31.80 (C H_2), 29.59 (CH_2), 29.47 (CH_2), 29.46 (CH_2), 29.43 (CH_2), 29.22 (CH_2), 26.98 (CH_2), 26.85 (CH_2), 26.05 (CH_2), 25.55 (CH_2), 22.59 (**C**H_2CH_3), 14.04 (CH_3).

N-*Dodecyl-6-(morpholin-4-yl)hexanamide* (***34***). Yield 50 %; colorless powder, m.p. 48–53 °C. Anal. Calcd. for $C_{22}H_{44}N_2O_2$: C, 71.69; H, 12.03; N, 7.6; O, 8.68 %. Found: C, 71.58; H, 11.93; N, 7.54; O, 8.71 %. IR ($CHCl_3$, cm^{-1}): 3449, 2930, 2858, 1660, 1518, 1467, 1459, 1376. ^{1}H-NMR (300 MHz, $CDCl_3$, δ / ppm): 5.56 (1H, *s*, CONH), 3.77 (4H, *t*, *J* = 4.6 Hz, O(C **H**$_2$$CH_2)_2$N), 3.22 (2H, *q*, *J* = = 13.2 Hz, 6.6 Hz, CH_2), 2.43 (4H, *t*, *J* = 7.5 Hz, O(CH_2C**H**$_2)_2$N), 2.34 (2H, *t*, *J* = = 4.6 Hz, NCH_2 acyl), 2.17 (2H, *t*, *J* = 7.51 Hz, CH_2CO), 1.65–1.12 (26H, *m*, 13 CH_2), 0.87 (3H, *t*, *J* = 6.42, CH_3). ^{13}C-NMR (75 MHz, $CDCl_3$, δ / ppm): 172.70 (CO), 66.43 (O(**C**$H_2CH_2)_2$N), 58.65 (NCH_2 acyl), 53.49 (O(CH_2**C**$H_2)_2$N), 39.55 (CONH**C**H_2), 36.55 (**C**H_2CO), 31.88 (CH_2), 29.69 (CH_2), 29.59 (CH_2), 29.55 (CH_2), 29.30 (CH_2), 29.01 (CH_2), 28.93 (CH_2), 27.82 (CH_2), 26.93 (CH_2), 26.56 (CH_2), 25.64 (CH_2), 25.43 (CH_2), 22.64 (**C**H_2CH_3), 14.03 (CH_3).