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Revisiting capsaicin and nonivamide: Their analogs exert strong inhibitory activity against cholinesterases☆

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ABSTRACT

The scientific community has long been interested in capsaicin, and the extensive hunt for AChE and BChE enzyme inhibitors is still ongoing. In this investigation analogs of capsaicin, such as the pharmaceutical nonivamide, which is preferred in clinical settings for the topical treatment of pain, were explored in the search for appropriate inhibitors. Thus, to test their inhibitory effect on AChE and BChE, we synthesized a short series of derivatives derived from vanillylamide. Consequently, it was discovered that compounds **12**, **34**, and **35**, which have K_i values in the sub-micromolar concentration range, are especially effective inhibitors. Compound **12** demonstrated dual mixed-type (competitive/uncompetitive) inhibitory activity for both enzymes; compound **34** showed selective mixed-type inhibitory activity for AChE, and compound **35** was found to have selective uncompetitive activity for AChE.

1. Introduction

Alzheimer's disease (AD) represents the predominant form of senile dementia, projected to affect approximately 153 million individuals by the year 2050. The current therapeutic repertoire for AD encompasses two distinct modalities: a recently introduced antibody-based treatment, albeit hampered by substantial side effects affecting up to 30 % of recipients, and several drugs mitigating symptomatic expression while decelerating cognitive decline for a limited duration, none of which qualify as disease-modifying agents [1–13].

Cholinesterase inhibitors address the central cholinergic deficiency observed in AD patients by impeding the activity of acetylcholinesterase, an enzyme responsible for cleaving acetylcholine (ACh) into choline and acetate within the brain. The diminished ACh levels in the brains of AD patients justify the use of AChE inhibitors for symptomatic relief. While AChE levels in the brain remain relatively constant throughout the progression of AD, butyrylcholinesterase (BChE) activity undergoes a marked 180 % increase and is also localized within neuritic plaques [1–13]. Inhibitors of cholinesterases are also used off-label to treat or at least to ameliorate the symptoms of Lewy body [14] and vascular dementia [15]. They might also influence gait speed and step/stride variability of patients suffering from Parkinson's disease [16–20].

Capsaicin (**A**, Fig. 1) serves as a primary bioactive constituent in red hot chili peppers, primarily employed in clinical settings for pain management [21–25] due to its capacity to scavenge reactive oxygen species [26]. Recent findings have highlighted the identification of dual inhibitors targeting acetylcholinesterase (AChE) and butyrylcholinesterase (BChE) through the combination of the cholinesterase inhibitor huprine Y and the antioxidant capsaicin (**B**, Fig. 1) [27]. When utilized as a singular component, capsaicin exhibited inactivity against both AChE and BChE.

On the other hand, capsaicin has been reported to reduce AD-associated tau change in the hippocampus of type-2 diabetic rats, and to reduce brain amyloid-beta generation, too [28]. Moreover, it has been described that the consumption of red pepper might be an effective intervention for preventing age-related memory deficits [29], but some other data indicated that higher chili intake is possibly associated with cognitive decline in adults of both genders. However, very recent studies found, that capsaicin analogs were found to anti-oxidant and neuro-protective agents [30–37].

Nonivamide (**C**, also known as pseudocapsain) acts as an analgetic especially in combination with another drug, nicoboxil (**D**). Quite recently, Zhang et al. [38] showed nonivamide to be able to protect model cells from Alzheimer's disease related damage, and even more recently, capsaicin-tacrine hybrids were able to act as multi-target

☆ Dedicated to Professor Karl Wonisch on the occasion of his 80th birthday; ad multos annos!.

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agents for the treatment of AD [39]. Interestingly, nonivamide and analogs thereof have never been investigated for their potential to act as inhibitors of cholinesterases.

2. Results and discussion

In previous investigations, we demonstrated the inhibitory properties of derivatives derived from cinnamic acid [40], (α,β)-unsaturated fatty acids [41], or caffeic acid [42] against cholinesterases. Building upon these studies, our focus shifted to the synthesis and biological assessment of compounds derived from vanillylamine (Scheme 1). The reaction of carboxylic acids with oxalyl chloride generated acid chlorides *in situ*, which, upon reaction with vanillylamine, yielded amides **1**, **3**,**5**,**7**,**9**,**11**,**13**,**15**,**17**,**19**,**21**,**23**,**25**,**27**,**29**, and **31**. Concurrently, byproducts **2**,**4**,**6**,**8**,**10**,**12**,**14**,**16**,**18**,**20**,**22**,**24**,**26**,**28**,**30**,**32** emerged from an additional acylation of vanillylamine at its hydroxyl group.

The reaction (Scheme 2) involving divanillylamine and nonanoic acid chloride produced a mixture of **33**, **34** and **35**; these compounds were easily separated by chromatography. Divanillylamine occurs as a trace impurity in vanillylamine; consequently, the formation of byproducts derived from divanillylamine are observed in the industrial production of nonivamide. Similarly, from the reaction involving vanillylamine and 2-methyl-octanoic acid, **36** and **37** were obtained. 2-Methyl-octanoic acid is also often found as an impurity to nonanoic acid in the synthesis of nonivamide thus leading to the formation of an isomer of nonivamide consequently then observed as trace impurity in the final pharmaceutical nonivamide preparations.

Compounds **1**–**37** were screened for their inhibitory activity employing *ee*AChE and *eq*BChE; the results from these assays are compiled in Tables 1–3 and Figs. 2–4.

As a result, for the amides, their ability to inhibit AChE increases more-or-less with the chain length of the carboxylic acid moiety reaching a maximum of 98.9 % inhibition with compound **23** holding a hexadecanoyl moiety. Extending the carbon chain length diminishes the inhibitory effect. For double acylated products the highest inhibition was observed for compounds **10** (a nonanoate) and **12** (a decanoate), and 98.8 and 99 % inhibition of AChE were determined. Only **12** was also a strong inhibitor for BChE, thus making this compound an interesting candidate for further biological exploration. As far as the divanillyl-derived compounds **33**–**35** are concerned: Thereby only **34** and **35** are excellent dual inhibitors for both enzymes, while **33** is a better inhibitor for BChE (86.8 % inhibition) than for AChE (18.5 %). Nonivamide analogue **36** is only a weak inhibitor for both enzymes while **37** holds strong inhibitory activity for AChE (98.3 %) but shows only moderate inhibition for BChE (42.5 %). For comparison, for reference compound galantamine 85.6 % inhibition were determined for AChE and 46.9 % for BChE.

Kinetic measurements were performed on the best inhibitors of AChE and BChE to determine the corresponding inhibition constants K_i and to obtain information on the possible mechanism of inhibition. The corresponding data are summarized in Table 4 and presented graphically in Figs. 5–7 (Dixon and Cornish-Bowden plots).

Compound **12** proved to be a mixed-type inhibitor (competitive and uncompetitive) for both AChE and BChE. In contrast to this finding, compound **35** is not only a selective inhibitor for AChE but other than **12**, **35** also inhibits the enzyme AChE in an uncompetitive manner, i.e. the inhibitor binds only to the enzyme-substrate complex and has no interaction with the free enzyme.

Our results are in excellent agreement with very recent findings showing extracts of capsaicin and dihydrocapsaicin as inhibitors of AChE; thereby, both compounds acted as mixed-type inhibitors [43]. These findings support previous reports describing capsaicin as an inhibitor for both AChE and BChE; thereby inhibition rates of about 63–75 % have been measured [44]. As pointed out by L. Blaikie et al. [45] and M. Scipioni [46] this makes vanillin derivates in general of increased interest as multi-targeted therapeutics for the treatment of Alzheimer's disease.

3. Conclusion

The intensive search for inhibitors of the enzymes AChE and BChE continues unabated; thereby, capsaicin has also been the focus of scientific interest for many years. In the search for suitable inhibitors, we turned our attention to analogs of capsaicin, i.e. the pharmaceutical drug nonivamide preferentially used in clinical settings for pain management, and we synthesized a small series of derivatives derived from vanillylamide to eventually test their inhibitory effect on AChE and BChE. As a result, compounds **12**, **34** and **35** were found to be particularly good inhibitors holding K_i values in the sub-micro-molar concentration range. Thereby, compound **12** proved to be a dual mixed-type inhibitor (competitive/uncompetitive) for both enzymes, **34** was a selective mixed-type inhibitor for AChE, while **35** was identified as a selective uncompetitive inhibitor for AChE.

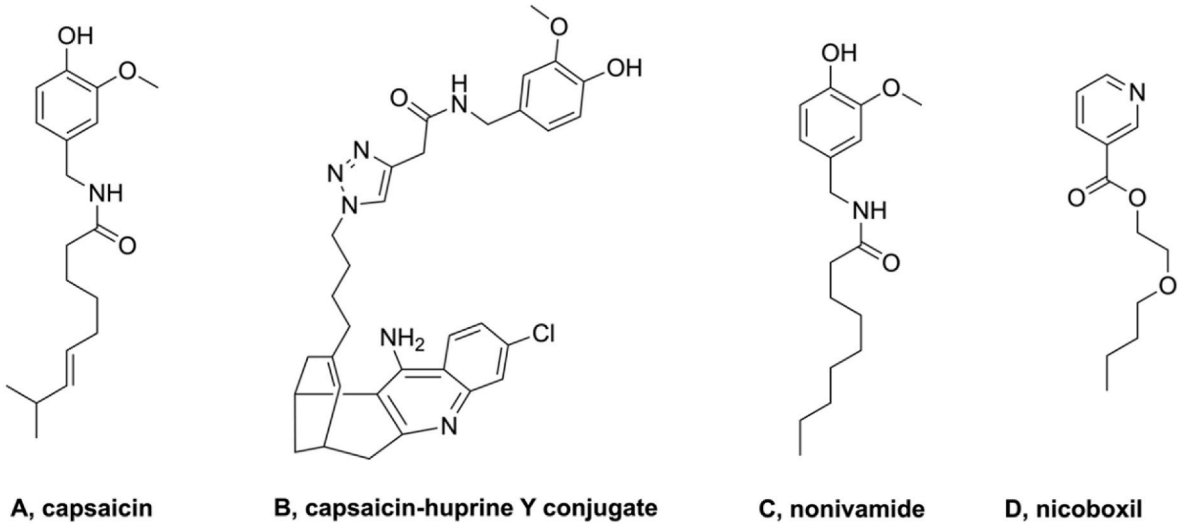
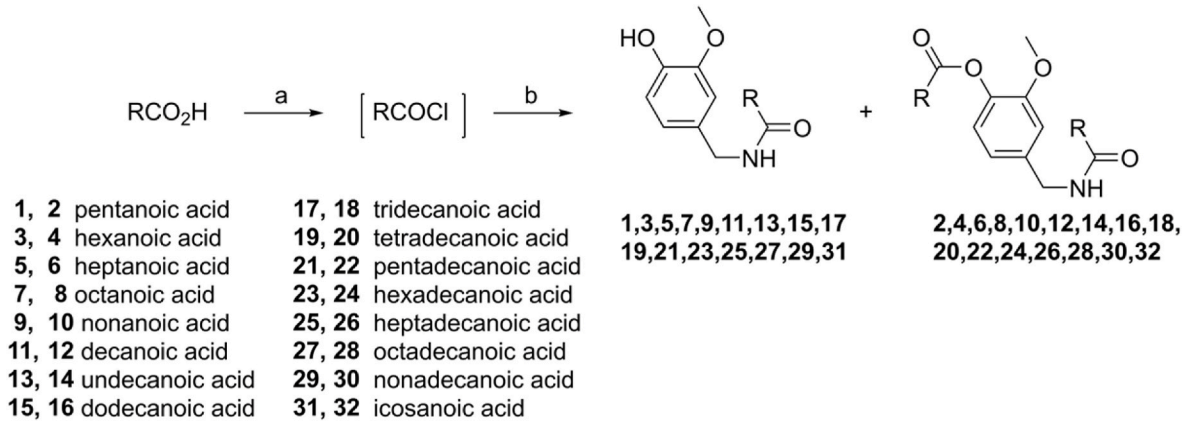
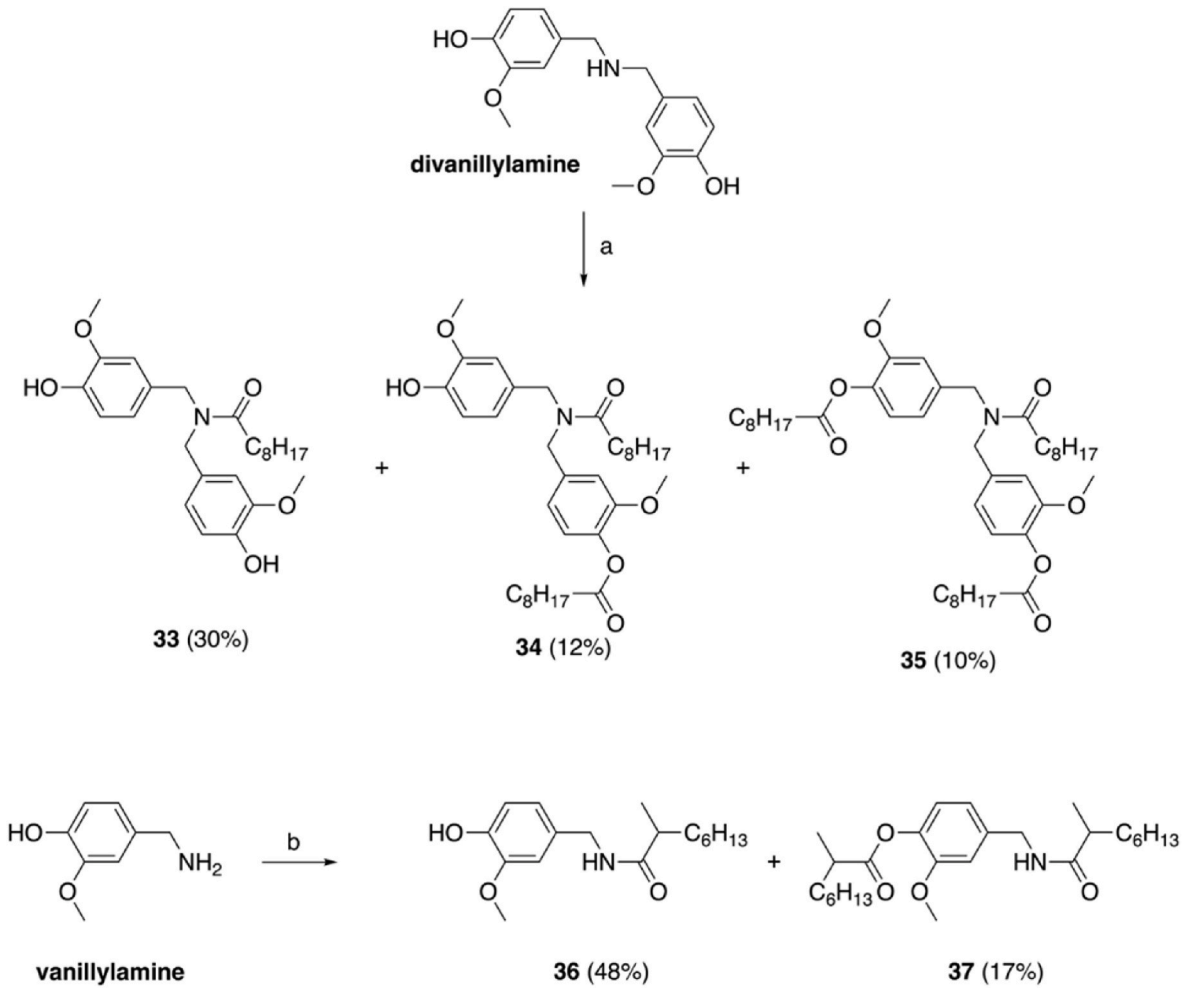


Fig. 1. Structure of capsaicin (**A**) and a capsaicin-huperin Y conjugate (**B**), the latter holding significant cholinesterase inhibitory activity; structure of analgetic nonivamide (**C**) and nicoboxil (**D**).



Scheme 1. Synthesis of vanillylamides and di-acylation products: a) $(COCl)_2$, DMF (cat), DCM; b) vanillylamine, DCM, 5 h, 20 °C.



Scheme 2. Synthesis of **33**–**37**; reactions and conditions: a) nonanoic acid, $(COCl)_2$, DMF (cat), DCM, then divanillylamine, 5 h 20 °C; b) 2-methyl-octanoic acid, $(COCl)_2$, DMF (cat), DCM, then vanillylamine, 5 h, 20 °C.

4. Experimental

4.1. General

NMR spectra were recorded using the Varian spectrometers (Darmstadt, Germany) DD2 and VNMRS (400 and 500 MHz, respectively). MS spectra were taken on a Advion expression^{L} CMS mass spectrometer (Ithaca, NY, USA; positive ion polarity mode, solvent: methanol, solvent flow: 0.2 mL/min, spray voltage: 5.17 kV, source voltage: 77 V, APCI corona discharge: 4.2 μA, capillary temperature: 250 °C, capillary voltage: 180 V, sheath gas: N2). Thin-layer chromatography was performed on pre-coated silica gel plates supplied by Macherey-Nagel (Düren, Germany). IR spectra were recorded on a Spectrum 1000 FT-IR-spectrometer from PerkinElmer (Rodgau, Germany). The UV/Vis-spectra were recorded on a Lambda 14 spectrometer from PerkinElmer (Rodgau, Germany); optical rotations were measured at 20 °C

Table 1
Inhibition of *ee*AChE and *eq*BChE (concentration of the inhibitor: 10 μM) by vanillylamides; all experiments were performed as triplicates each as a technical triplicate; galantamine (**GA**) was used as a positive standard.

Compound	Inhibition AChE [%]	Inhibition BChE [%]
1	<5	<5
3	<5	<5
5	<5	<5
7	<5	<5
9	22.4 ± 0.5	<5
11	15.8 ± 0.6	19.8 ± 1.6
13	<10	16.5 ± 0.5
15	<10	<10
17	14.8 ± 0.5	<10
19	51.2 ± 1.5	40.9 ± 1.9
21	87.5 ± 0.5	64.3 ± 2.5
23	98.9 ± 0.2	22.5 ± 0.4
25	71.1 ± 0.1	12.1 ± 0.6
27	41.2 ± 0.1	<5
29	24.5 ± 0.1	<5
31	<5	<5
GA	85.6 ± 0.1	46.9 ± 0.9

Table 2
Inhibition of *ee*AChE and *eq*BChE (concentration of the inhibitor: 10 μM) by esterified vanillylamides; all experiments were performed as triplicates each as a technical triplicate.

Compound	Inhibition AChE [%]	Inhibition BChE [%]
2	16.7 ± 1.7	<10
4	<10	13.8 ± 1.3
6	<10	<10
8	52.4 ± 0.6	16.9 ± 1.0
10	98.8 ± 0.5	44.8 ± 1.5
12	99.0 ± 0.1	98.2 ± 0.4
14	92.8 ± 0.1	48.3 ± 0.8
16	66.4 ± 1.0	41.3 ± 1.1
18	32.1 ± 0.1	28.6 ± 1.8
20	25.1 ± 1.1	22.1 ± 0.6
22	<5	<5
24	<5	<5
26	<10	<10
28	<10	<5
30	<10	<5
32	<10	<10

Table 3
Inhibition of AChE and BChE (concentration of the inhibitor: 10 μM) by vanillylamides derived from divanillylamine and 2-methyl-octanoic acid, respectively; all experiments were performed as triplicates.

Compound	Inhibition AChE [%]	Inhibition BChE [%]
33	18.5 ± 1.3	86.8 ± 0.2
34	99.1 ± 0.1	88.5 ± 0.9
35	99.4 ± 0.1	94.5 ± 0.8
36	23.7 ± 1.4	<5
37	98.3 ± 0.3	42.5 ± 0.7

using a JASCO-P2000 instrument (JASCO Germany GmbH, Pfungstadt, Germany) The melting points were determined using the Leica hot stage microscope Galen III (Leica Biosystems, Nussloch, Germany). Microanalyses were performed with an Elementar Vario EL (CHNS) instrument (Elementar Analysensysteme GmbH, Elementar-Straße 1, D-63505, Langenselbold, Germany).

Reactions using air- or moisture-sensitive reagents were carried out under argon atmosphere in dried glassware. All dry solvents were distilled over respective drying agents, and triethylamine was stored over potassium hydroxide. Chemicals and solvents were obtained from local vendors and used as received.

Enzymatic assays were performed as previously reported [40–42]. The absorbance was measured with a 96 well plate reader from BMG Labtech (BMG Labtech GmbH, Ortenberg, Germany).

4.2. Syntheses

4.2.1. General procedure (GP)

To a solution of the carboxylic acid (1.25 equiv.) in dry DCM (25 mL), DMF (cat.) and oxalyl chloride (4 equiv.) were added, and the reaction mixture was stirred until the evolution of gases had ceased (about 1 h). The volatiles were removed under reduced pressure, and the residue was re-dissolved in dry THF, and the volatiles were removed again under reduced pressure. This procedure was repeated two times. The *in situ* generated acyl chloride was dissolved in dry DCM (25 mL), and added dropwise to a solution of (di)vanillylamine (1 equiv.) in dry DCM (25 mL). After stirring for 5h at room temperature, followed by usual aqueous work-up and column chromatography, products were obtained.

4.2.2. N-[(4-Hydroxy-3-methoxy)benzyl]pentanamide (1) [93094-25-8] and 2-methoxy-4-[(pentanoylamino)methyl]phenyl pentanoate (2)

Following GP from vanillylamine (400 mg, 2.63 mmol) and pentanoic acid (400 mg, 3.95 mmol), **1** [47–53] (80 mg, 25 %) and **2** (120 mg, 28 %) were obtained.

Data for **1**: colorless oil; R_F = 0.21 (SiO_2, hexanes/EtOAc, 6:4); UV–Vis (MeOH): λ_{max} (log ε) = 228 nm (3.56), 280 nm (3.21); IR (ATR): ν = 3552w, 3284m, 2957m, 2933m, 2872m, 1634s, 1464m, 1272vs, 1124s, 1034s, 734 m cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.26 (s, 1H, NH), 6.96 (d, J = 8.0 Hz, 1H, 3-H), 6.88 (d, J = 1.9 Hz, 1H, 6-H), 6.82 (*dd*, J = 8.1, 1.9 Hz, 1H, 4-H), 5.89 (s, 1H, OH), 4.40 (d, J = 4.6 Hz, 2H, 7-H), 3.80 (s, 3H, 8-H), 2.25–2.20 (t, J = 7.5 Hz, 2H, 10-H), 1.79–1.70 (m, 2H, 11-H), 1.51–1.40 (m, 2H, 12-H), 0.96 (m, 3H, 13-H) ppm; ^{13}C NMR (101 MHz, $CDCl_3$): δ = 171.9 (C-9), 151.3 (C-1), 139.2 (C-2), 137.2 (C-5), 122.9 (C-4), 120.0 (C-3), 112.2 (C-6), 55.9 (C-8), 43.4 (C-7), 33.7 (C-10), 27.8 (C-12), 22.4 (C-11), 13.7 (C-13) ppm; MS (ESI, MeOH/$CHCl_3$, 4:1): *m/z* (%) = 102 (100 %, $[M+Na]^+$); anal. calcd for $C_{13}H_{19}NO_3$ (237.3): C 65.80, H 8.07, N 5.90; found: C 65.59, H 8.31, N 5.77.

Data for **2**: R_F = 0.37 (SiO_2, hexanes/EtOAc, 6:4); UV–Vis (MeOH): λ_{max} (log ε) = 278 nm (3.52); IR (ATR): ν = 3312m, 2959m, 2933w, 2872w, 1748s, 1643s, 1466m, 1273s, 1150vs, 1123s, 1036s, 729 m cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$): δ = 6.96 (d, J = 8.0 Hz, 1H, 3-H), 6.89 (d, J = 1.9 Hz, 1H, 6-H), 6.83 (*dd*, J = 8.0, 1.8 Hz, 1H, 4-H), 5.79 (s, 1H, NH), 4.40 (d, J = 5.1 Hz, 2H, 7-H), 3.80 (s, 3H, 8-H), 2.57 (t, J = 7.5 Hz, 2H, 15-H), 2.22 (t, J = 7.6 Hz, 2H, 10-H), 1.79–1.70 (m, 2H, 16-H), 1.69–1.59 (m, 2H, 11-H), 1.50–1.41 (m, 2H, 18-H), 1.41–1.31 (m, 2H, 12-H), 0.96 (t, J = 7.4 Hz, 3H, 19-H), 0.92 (t, J = 7.3 Hz, 3H, 13-H) ppm; ^{13}C NMR (101 MHz, $CDCl_3$): δ = 173.0 (C-14), 171.9 (C-9), 151.3 (C-1), 139.2 (C-2), 137.2 (C-5), 122.9 (C-4), 120.0 (C-3), 112.2 (C-6), 55.9 (C-8), 43.5 (C-7), 36.5 (C-10), 33.7 (C-15), 27.8 (C-11), 27.0 (C-16), 22.4 (C-12), 22.2 (C-18), 13.8 (C-13), 13.7 (C-19) ppm; MS (ESI, MeOH/$CHCl_3$, 4:1): *m/z* (%) = 344 (100 %, $[M+Na]^+$); anal. calcd for $C_{18}H_{27}NO_4$ (321.42): C 67.26, H 8.47, N 4.36; found: C 66.98, H 8.65, N 4.13.

4.2.3. N-[(4-Hydroxy-3-methoxy)benzyl]hexanamide (3) [58570-67-5] and 2-methoxy-4-[(hexanoylamino)methyl]phenyl hexanoate (4)

Following GP from vanillylamine (400 mg, 2.63 mmol) and hexanoic acid (458 mg, 3.95 mmol), **3** [54–57] (90 mg, 27 %) and **4** (80 mg, 25 %) were obtained.

Data for **3**: colorless oil (lit. [55]: m.p. 49–49.5 °C); R_F = 0.06 (SiO_2, hexanes/EtOAc, 7:3); UV–Vis (MeOH): λ_{max} (log ε) = 229 nm (3.63), 281 nm (3.22); IR (ATR): ν = 3552w, 3287w, 2930m, 2870w, 1638s, 1430s, 1273s, 1124s, 1034s, 737 m cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$): δ = 6.81 (d, J = 8.0 Hz, 1H, 3-H), 6.75 (d, J = 1.9 Hz, 1H, 6-H), 6.69 (*dd*, J = 8.0, 1.9 Hz, 1H, 4-H), 6.10 (s, 1H, NH), 4.29 (d, J = 5.5 Hz, 2H, 7-H), 3.80 (s, 3H, 8-H), 2.16 (d, J = 7.8 Hz, 2H, 10-H), 1.66–1.57 (m, 2H, 11-H), 1.32–1.20 (m, 4H, 12-H, 13-H), 0.85 (d, J = 6.9 Hz, 3H, 14-H)

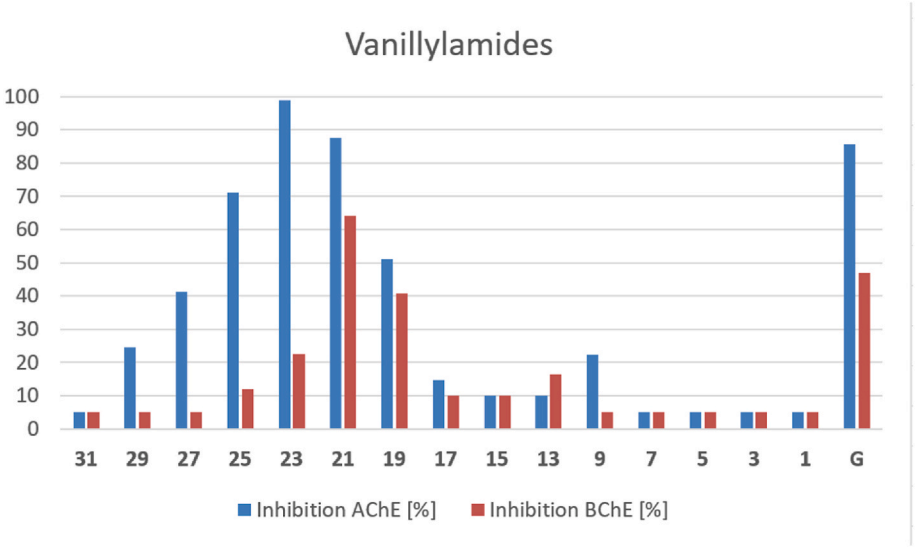


Fig. 2. Inhibition of AChE and BChE by vanillylamides (concentration of inhibitor 10 μM).

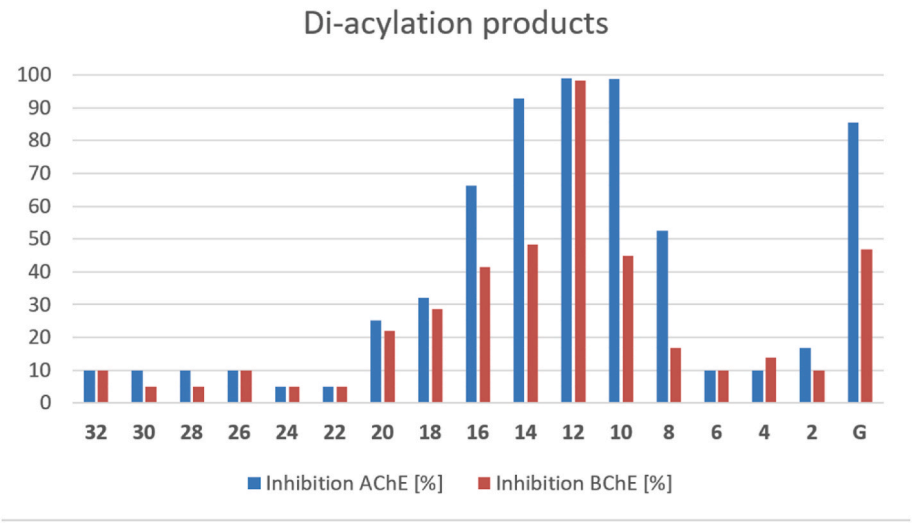


Fig. 3. Inhibition of AChE and BChE by esterified vanillylamides (concentration of inhibitor 10 mM).

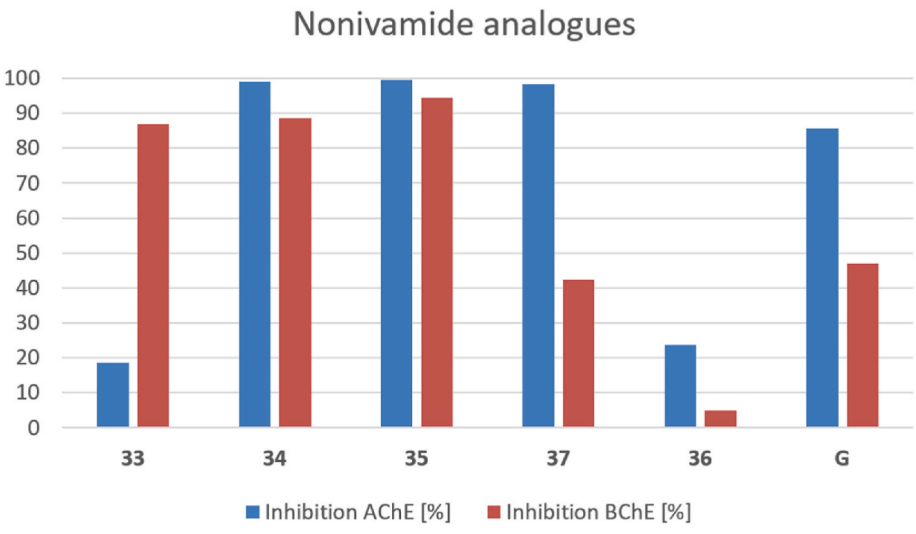


Fig. 4. Inhibition of AChE and BChE by analogs of nonivamide **33**–**37** (concentration of inhibitor 10 μM).

Table 4
Determination of inhibition constants (in μM) for compounds **12**, **34** and **35** and the enzymes AChE and BChE; n.m. not measured due to solubility problems under the conditions of the assay; values represent the mean values of triplicate measuring each performed as triplicate.

Compound	AChE, K_i	AChE, K_i'	BChE, K_i	BChE, K_i'
12	0.32 ± 0.03	0.61 ± 0.05	0.29 ± 0.03	0.19 ± 0.05
34	2.0 ± 0.07	5.5 ± 0.19	n.m.	n.m.
35	–	0.96 ± 0.04	n.m.	n.m.

ppm; ^{13}C NMR (101 MHz, $CDCl_3$): δ = 173.4 (C-9), 146.9 (C-1), 145.2 (C-2), 130.2 (C-5), 120.6 (C-4), 114.5 (C-3), 110.8 (C-6), 55.8 (C-8), 43.4 (C-7), 36.6 (C-10), 31.4 (C-12), 25.5 (C-11), 22.3 (C-13), 13.9 (C-14) ppm; MS (ESI, MeOH/$CHCl_3$, 4:1): *m/z* (%) = 274 (100 %, $[M+Na]^+$); anal. calcd for $C_{14}H_{21}NO_3$ (251.3): C 66.91, H 8.42, N 5.57; found: C 66.75, H 8.72, N 5.34.

Data for **4**: white solid; m.p. 105 °C; R_F = 0.22 (SiO_2, hexanes/EtOAc, 7:3); UV–Vis (MeOH): λ_{max} (log ε) = 229 nm (3.41), 280 nm (3.18); IR (ATR): ν = 3303m, 2959m, 2932m, 2873w, 1713s, 1643s, 1465m, 1271s, 1154m, 1121m, 1040m, 731 m cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$): δ = 6.84 (d, *J* = 8.0 Hz, 1H, 3-H), 6.75 (d, *J* = 1.9 Hz, 1H, 4-H), 6.72 (*dd*, *J* = 8.0, 1.9 Hz, 1H, 6-H), 6.54 (s, 1H, NH), 4.41–4.25 (m, 2H, 7-H), 3.86 (s, 3H, 8-H), 3.41 (t, *J* = 7.4 Hz, 2H, 16-H), 2.56–2.49 (m, 2H, 10-H), 1.89–1.76 (m, 2H, 17-H), 1.59–1.49 (m, 2H, 11-H), 1.36–1.18 (m, 8H, 12-H, 13-H, 18-H, 19-H), 0.91–0.83 (m, 6H, 14-H, 20-H) ppm; ^{13}C NMR (101 MHz, $CDCl_3$): δ = 210.1 (C-15), 168.6 (C-9), 146.7 (C-1), 145.1 (C-2), 130.0 (C-5), 120.6 (C-4), 114.4 (C-3), 110.4 (C-6), 60.7 (C-8), 55.9 (C-7), 43.5 (C-10), 42.8 (C-16), 31.2 (C-12), 30.8 (C-18), 29.6 (C-11), 22.9 (C-17), 22.4 (C-13), 22.4 (C-19), 13.8 (C-14), 13.7 (C-20) ppm; MS (ESI, MeOH/$CHCl_3$, 4:1): *m/z* (%) = 372 (100 %, $[M+Na]^+$); anal. calcd for $C_{20}H_{31}NO_4$ (349.47): C 68.74, H 8.94, N 4.01; found: C

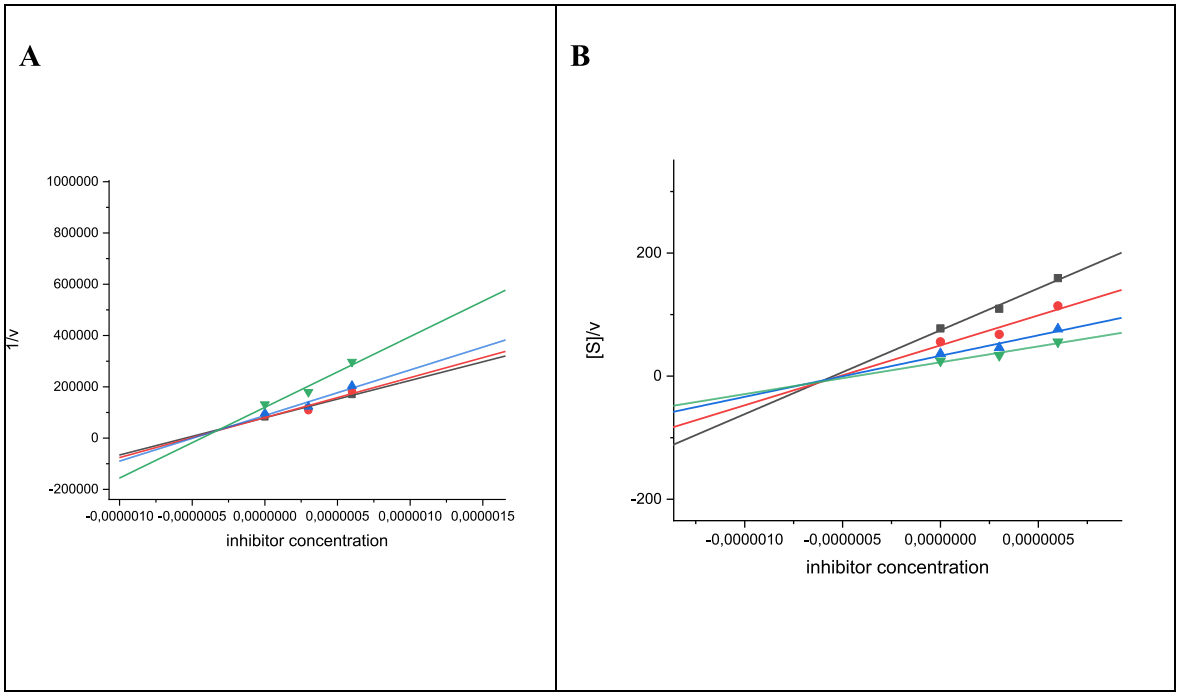


Fig. 5. Dixon (A) and Cornish-Bowden plot (B) for **12** and AChE.

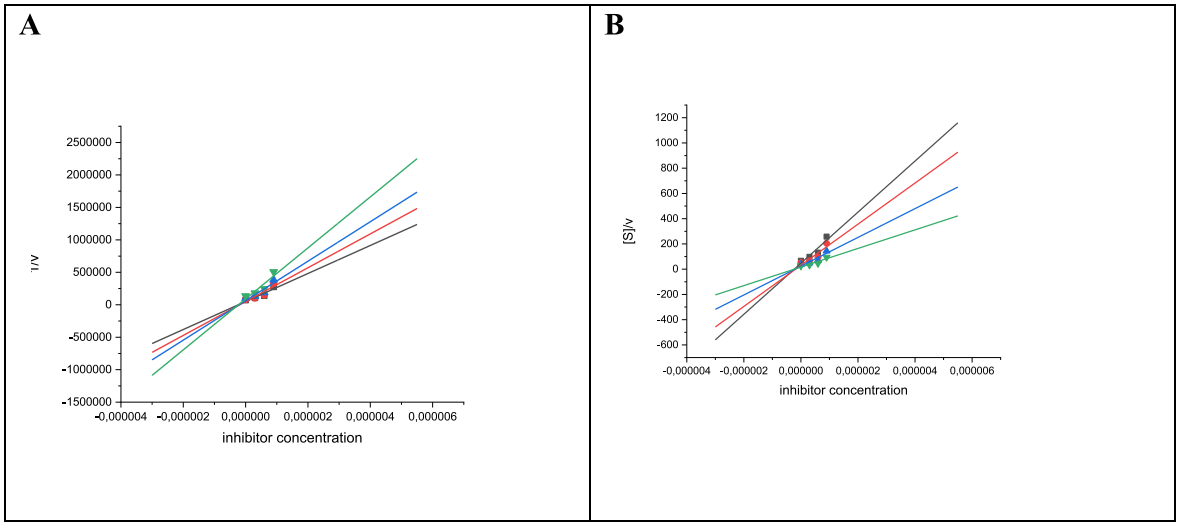


Fig. 6. Dixon (A) and Cornish-Bowden plot (B) for **12** and BChE.

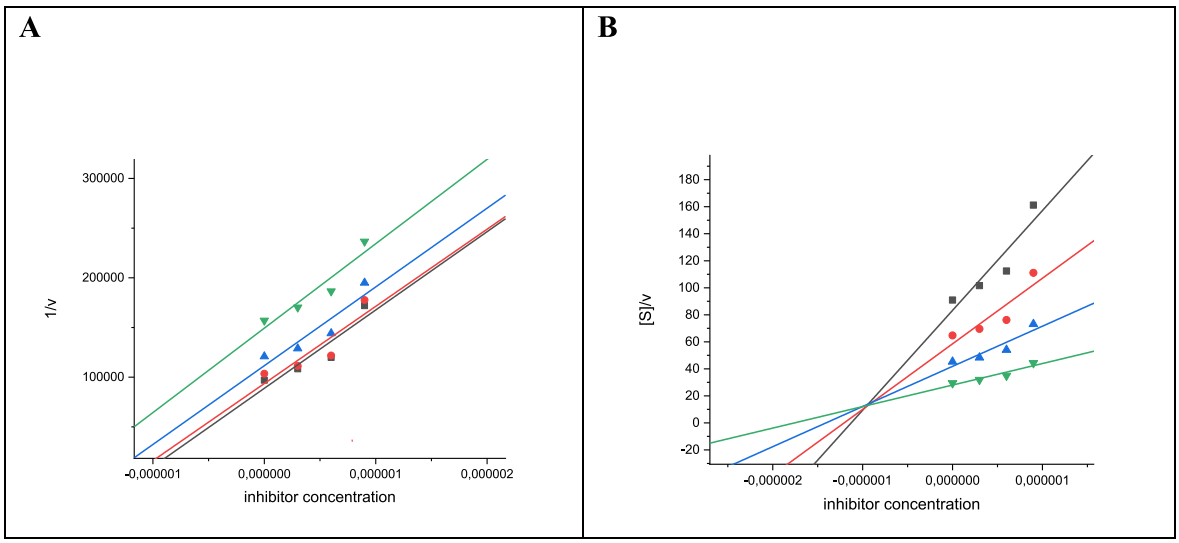


Fig. 7. Dixon (A) and Cornish-Bowden plot (B) for **35** and AChE.

68.48, H 9.15, N 3.76.

4.2.4. N-[(4-Hydroxy-3-methoxy)benzyl]heptanamide (5) [89575-10-0] and 2-methoxy-4-[(heptanoylamino)methyl]phenyl heptanoate (6)

Following GP from vanillylamine (400 mg, 2.63 mmol) and heptanoic acid (513 mg, 3.95 mmol), **5** [58–60] (110 mg, 31 %) and **6** (280 mg, 56 %) were obtained.

Data for **5**: colorless oil (lit. [60]: m.p. 61 °C); R_F = 0.46 (SiO_2, hexanes/EtOAc, 6:4); UV–Vis (MeOH): λ_{max} (log ε) = 229 nm (3.70), 280 nm (3.34); IR (ATR): ν = 3550w, 2931m, 1640s, 1438s, 1271s, 1128s, 1030s, 735 m cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$): δ = 6.86 (d, J = 8.0 Hz, 1H, 3-H), 6.81 (d, J = 1.9 Hz, 1H, 6-H), 6.76 (*dd*, J = 8.1, 1.9 Hz, 1H, 4-H), 5.79 (s, 1H, 8-H), 4.35 (d, J = 5.5 Hz, 2H, 7-H), 3.87 (s, 3H, 8-H), 2.20 (t, 2H, 10-H), 1.69–1.61 (m, 2H, 11-H), 1.37–1.23 (m, 6H, 12-H, 13-H, 14-H), 0.87 (t, 3H, 15-H) ppm; ^{13}C NMR (126 MHz, $CDCl_3$): δ = 173.0 (C-9), 146.7 (C-1), 145.2 (C-2), 130.3 (C-5), 120.8 (C-4), 114.4 (C-3), 110.7 (C-6), 55.9 (C-8), 43.5 (C-7), 36.8 (C-10), 31.5 (C-12), 29.0 (C-13), 25.8 (C-11), 22.5 (C-14), 14.0 (C-15) ppm; MS (ESI, MeOH/$CHCl_3$, 4:1): *m/z* (%) = 288 (100 %, $[M+Na]^+$); anal. calcd for $C_{13}H_{19}NO_3$ (237.3): C 65.80, H 8.07, N 5.90; found: 65.70, H 8.33, N 5.68.

Data for **6**: white solid; m.p. 65 °C; R_F = 0.67 (SiO_2, hexanes/EtOAc, 6:4); UV–Vis (MeOH): λ_{max} (log ε) = 278 nm (3,64); IR (ATR): ν = 3312w, 2957w, 2925m, 2872w, 1747s, 1642s, 1467m, 1276s, 1154vs, 1124s, 1036m, 730 m cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$): δ = 6.95 (d, J = 8.0 Hz, 1H, 3-H), 6.88 (d, J = 1.9 Hz, 1H, 6-H), 6.82 (*dd*, J = 8.0, 1.8 Hz, 1H, 4-H), 5.91 (s, 1H, NH), 4.39 (d, J = 5.0 Hz, 2H, 7-H), 3.79 (s, 3H, 8-H), 2.56 (t, J = 7.5 Hz, 2H, 17-H), 2.21 (t, J = 7.6 Hz, 2H, 10-H), 1.81–1.69 (m, 2H, 18-H), 1.69–1.60 (m, 2H, 11-H), 1.47–1.37 (m, 2H, 20-H), 1.37–1.22 (m, 10H, 12-H, 13-H, 14-H, 19-H, 21-H), 0.93–0.84 (m, 6H, 15-H, 22-H) ppm; ^{13}C NMR (101 MHz, $CDCl_3$): δ = 173.1 (C-16), 172.0 (C-9), 151.3 (C-1), 139.2 (C-2), 137.2 (C-5), 122.8 (C-4), 120.0 (C-3), 112.2 (C-6), 55.8 (C-8), 43.4 (C-7), 36.7 (C-10), 34.0 (C-17), 31.5 (C-13), 31.4 (C-20), 29.0 (C-12), 28.7 (C-19), 25.7 (C-11), 25.0 (C-18), 22.5 (C-14), 22.5 (C-21), 14.0 (C-15), 14.0 (C-22) ppm; MS (ESI, MeOH/$CHCl_3$, 4:1): *m/z* (%) = 400 (100 %, $[M+Na]^+$); anal. calcd for $C_{22}H_{35}NO_4$ (377.53): C 69.99, H 9.35, N 3.71; found: C 69.67, H 3.92, N 3.46.

4.2.5. N-[(4-Hydroxy-3-methoxy)benzyl]octanamide(7) [58493-47-3] and 2-methoxy-4-[(octanoylamino)methyl]phenyl octanoate (8)

Following GP from vanillylamine (400 mg, 2.63 mmol) and octanoic anhydride (1006 mg, 3.95 mmol), **7** [61–65] (170 mg, 46 %) and **8** (300 mg, 56 %) were obtained.

Data for **8**: colorless oil (lit. [55]: m.p. 44.5 °C); R_F = 0.44 (SiO_2, hexanes/EtOAc, 6:4); UV–Vis (MeOH): λ_{max} (log ε) = 229 nm (4.42), 281 nm (4.04); IR (ATR): ν = 3552w, 3286w, 2926m, 2855m, 1639s, 1430m, 1273s, 1123s, 1034s, 722 m cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$): δ = 6.83 (d, J = 8.0 Hz, 1H, 3-H), 6.78 (d, J = 1.9 Hz, 1H, 6-H), 6.73 (*dd*, J = 8.0, 1.9 Hz, 1H, 4-H), 5.95 (s, 1H, NH), 4.32 (d, J = 5.3 Hz, 2H, 7-H), 3.84 (s, 3H, 8-H), 2.19 (t, 2H, 10-H), 1.69–1.57 (m, 2H, 11-H), 1.33–1.19 (m, 8H, 12-H, 13-H, 14-H, 15-H), 0.88–0.83 (m, 3H, 16-H) ppm; ^{13}C NMR (101 MHz, $CDCl_3$): δ = 173.1 (C-9), 146.7 (C-1), 145.2 (C-2), 130.2 (C-5), 120.8 (C-4), 114.4 (C-3), 110.7 (C-6), 55.9 (C-8), 43.6 (C-7), 36.7 (C-10), 31.7 (C-14), 29.2 (C-12), 29.0 (C-13), 25.8 (C-11), 22.6 (C-15), 14.0 (C-16) ppm; MS (ESI, MeOH/$CHCl_3$, 4:1): *m/z* (%) = 304 (100 %, $[M+Na]^+$); anal. calcd for $C_{16}H_{25}NO_3$ (279.38): C 68.79, H 9.02, N 5.01; found: C 68.51, H 9.34, N 4.76.

Data for **8**: white solid; m.p. 72 °C; R_F = 0.88 (SiO_2, hexanes/EtOAc, 6:4); UV–Vis (MeOH): λ_{max} (log ε) = 279 nm (3.49); IR (ATR): ν = 3309w, 2955m, 2921m, 2852m, 1747s, 1642s, 1466m, 1276s, 1154vs, 1124s, 1036m, 725 m cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$): δ = 6.94 (d, J = 8.0 Hz, 1H, 3-H), 6.87 (d, J = 1.9 Hz, 1H, 6-H), 6.81 (*dd*, J = 8.0, 1.9 Hz, 1H, 4-H), 5.95 (s, 1H, NH), 4.38 (d, J = 5.4 Hz, 2H, 7-H), 3.78 (s, 3H, 8-H), 2.55 (t, J = 7.5 Hz, 2H, 18-H), 2.20 (t, 2H, 10-H), 1.79–1.69 (m, 2H, 19-H), 1.68–1.59 (m, 2H, 11-H), 1.48–1.19 (m, 16H, 12-H, 13-H, 14-H, 15-H, 20-H, 21-H, 22-H, 23-H), 0.92–0.83 (m, 6H, 16-H, 24-H) ppm; ^{13}C NMR (101 MHz, $CDCl_3$): δ = 173.2 (C-17), 172.0 (C-9), 151.2 (C-1), 139.2 (C-2), 137.2, 122.8 (C-4), 120.0 (C-3), 112.1 (C-6), 55.8 (C-8), 43.4 (C-7), 36.7 (C-18), 34.0 (C-10), 31.7 (C-22), 31.7 (C-14), 29.3 (C-12, 20), 29.0 (C-13, 21), 28.9 (C-19), 25.8 (C-11), 25.0 (C-23), 22.6 (C-15), 14.0 (C-24), 14.0 (C-16) ppm; MS (ESI, MeOH/$CHCl_3$, 4:1): *m/z* (%) = 428 (100 %, $[M+Na]^+$); anal. calcd for $C_{24}H_{39}NO_4$ (405.58): C 71.07, H 9.69, N 3.45; found: 70.86, H 9.90, N 3.13.

N-[(4-Hydroxy-3-methoxy)benzyl]nonanamide (**9**) [2444−46−4] and 2-methoxy-4-[(nonanoylamino)methyl]phenyl nonanoate (**10**) [2727060-97-9]

Following GP from vanillylamine (1000 mg, 2.63 mmol) and nonanoic acid (1240 mg, 5.90 mmol), **9** [66,67] (740 mg, 77 %) and **10** (520 mg, 36 %) were obtained.

Data for **9**: white solid; m.p. 48 °C (lit. [66]: 52 °C); R_F = 0.65 (SiO_2, hexanes/EtOAc, 4:6); UV–Vis (MeOH): λ_{max} (log ε) = 229 nm (3.82), 280 nm (3.44); IR (ATR): ν = 3287w, 2925m, 2854w, 1640m, 1601w, 1514s, 1464m, 1431m, 1376w, 1273s, 1237m, 1154m, 1123m, 1035m, 851w, 796w, 722w, 636w, 557w cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$): δ = 6.85 (d, J = 8.0 Hz, 1H, 3-H), 6.80 (d, J = 1.9 Hz, 1H, 6-H), 6.75 (*dd*, J =

8.0, 1.7 Hz, 1H, 4-H), 5.84 (s, 1H, NH), 4.35 (d, J = 4.3 Hz, 2H, 7-H), 3.87 (s, 3H, 8-H), 2.21 (t, J = 7.6 Hz, 2H, 10-H), 1.70–1.60 (m, 2H, 11-H), 1.36–1.20 (m, 11H, 12-H, 13-H, 14-H, 15-H, 16-H), 0.87 (t, J = 6.9 Hz, 3H, 17-H) ppm; ^{13}C NMR (126 MHz, $CDCl_3$): δ = 173.2 (C-9), 146.7 (C-5), 145.2 (C-4), 130.2 (C-1), 120.8 (C-2), 114.4 (C-3), 110.7 (C-6), 55.9 (C-8), 43.6 (C-7), 36.7 (C-10), 31.8 (C-15), 29.3 (C-11, C-13), 29.1 (C-14), 25.8 (C-12), 22.6 (C-16), 14.0 (C-17) ppm; MS (ESI, MeOH/$CHCl_3$, 4:1): m/z (%) = 292 (100 %, $[M - H]^-$); anal. calcd for $C_{17}H_{27}NO_3$ (293.41): C 69.59, H 9.28, N 4.77; found: C 69.43, H 9.41, N 4.47.

Data for **10**: white solid; m.p. 75 °C; R_F = 0.8 (SiO_2, hexanes/EtOAc, 4:6); UV–Vis (MeOH): λ_{max} (log ε) = 274 nm (3.37); IR (ATR): ν = 3309w, 2920m, 2851w, 1747m, 1642m, 1606w, 1548m, 1514m, 1467w, 1419w, 1378w, 1290w, 1276m, 1200w, 1155s, 1124m, 1036m, 946w, 876w, 822w, 751w, 722 m cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$): δ = 6.97 (d, J = 8.0 Hz, 1H, 3-H), 6.89 (s, 1H, 6-H), 6.84 (d, J = 8.0 Hz, 1H, 4-H), 5.76 (s, 1H, NH), 4.44–4.36 (m, 2H, 7-H), 3.80 (s, 3H, 8-H), 2.56 (t, J = 7.5 Hz, 2H, 19-H), 2.22 (t, J = 8.1 Hz, 2H, 10-H), 1.81–1.71 (m, 2H, 20-H), 1.71–1.18 (m, 22H, 11-H, 12-H, 13-H, 14-H, 15-H, 16-H, 21-H, 22-H, 23-H, 24-H), 0.94–0.82 (m, 6H, 17-H, 26-H) ppm; ^{13}C NMR (101 MHz, $CDCl_3$): δ = 173.3 (C-9), 172.1 (C-18), 151.5 (C-6), 139.4 (C-1), 123.1 (C-3), 120.2 (C-2), 112.4 (C-5), 56.1 (C-8), 43.7 (C-7), 37.0 (C-10), 34.2 (C-19), 32.0 (C-24), 32.0 (C-15), 29.5 (C-21), 29.5 (C-12), 29.4 (C-14), 29.4 (C-23), 29.2 (C-13), 29.2 (C-22), 26.0 (C-11), 25.2 (C-20), 22.8 (C-25), 22.8 (C-16), 14.2 (C-17), 14.2 (C-26) ppm; MS (ESI, MeOH/$CHCl_3$, 4:1): m/z (%) = 432 (100 %, $[M - H]^-$); anal. calcd for $C_{26}H_{43}NO_4$ (433.63): C 72.02, H 10.00, N 3.23; found: C 71.78, H 10.27, N 2.96.

4.2.6. N-[(4-Hydroxy-3-methoxy)benzyl]decanamide (**11**) [31078-36-1] and 2-methoxy-4-[(decanoylamino)methyl]phenyl decanoate (**12**)

Following GP from vanillylamine (400 mg, 2.63 mmol) and decanoic acid (679 mg, 3.95 mmol), **11** [68,69] (185 mg, 45 %) and **12** (451 mg, 74 %) were obtained.

Data for **11**: white solid; m.p. 57 °C (lit. [57]: m.p. 48–50 °C); R_F = 0.16 (SiO_2, hexanes/EtOAc, 6:4); UV–Vis (MeOH): λ_{max} (log ε) = 230 nm (4,02), 280 nm (3,65); IR (ATR): ν = 3484w, 3304m, 2921s, 2850m, 1635s, 1429m, 1275s, 1122s, 1039m, 720 m cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$): δ = 6.85 (d, J = 8.0 Hz, 1H, 3-H), 6.80 (d, 1H, 6-H), 6.75 (*dd*, J = 8.0, 1.4 Hz, 1H, 4-H), 5.84 (s, 1H, NH), 4.34 (d, J = 4.0 Hz, 2H, 7-H), 3.87 (s, 3H, 8-H), 2.20 (t, J = 7.5 Hz, 2H, 10-H), 1.70–1.58 (m, 2H, 11-H), 1.34–1.20 (m, 12H, 12-H, 13-H, 14-H, 15-H, 16-H, 17-H), 0.87 (t, J = 6.8 Hz, 3H, 18-H) ppm; ^{13}C NMR (126 MHz, $CDCl_3$): δ = 173.1 (C-9), 146.7 (C-1), 145.2 (C-2), 130.3 (C-5), 120.8 (C-4), 114.4 (C-3), 110.8 (C-6), 56.0 (C-8), 43.6 (C-7), 36.9 (C-10), 31.8 (C-16), 29.4 (C-12), 29.3 (C-15), 29.3 (C-13), 29.2 (C-14), 25.8 (C-11), 22.6 (C-17), 14.1 (C-18) ppm; MS (ESI, MeOH/$CHCl_3$, 4:1): m/z (%) = 331 (100 %, $[M+Na]^+$); anal. calcd for $C_{18}H_{29}NO_3$ (307.43): C 70.32, H 9.51, N 4.56; found: C 70.05, H 9.83, N 4.33.

Data for **12**: white solid; m.p. 99 °C; R_F = 0.70 (SiO_2, hexanes/EtOAc, 6:4); UV–Vis (MeOH): λ_{max} (log ε) = 272 nm (3.81); IR (ATR): ν = 3287m, 2951m, 2918s, 2851m, 1716s, 1645s, 1467m, 1246vs, 1151m, 1122m, 1028s, 726 s cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$): δ = 6.85 (d, J = 8.0 Hz, 1H, 3-H), 6.75 (d, J = 1.9 Hz, 1H, 6-H), 6.72 (*dd*, J = 8.0, 1.9 Hz, 1H, 4-H), 6.52 (s, 1H, NH), 4.42–4.25 (m, 2H, 7-H), 3.86 (s, 3H, 8-H), 3.42 (t, J = 7.4 Hz, 2H, 20-H), 2.53 (*t*, J = 7.2, 5.7 Hz, 2H, 10-H), 1.87–1.75 (m, 2H, 21-H), 1.58–1.48 (m, 2H, 11-H), 1.32–1.20 (m, 24H, 12-H, 13-H, 14-H, 15-H, 16-H, 17-H, 22-H, 23-H, 24-H, 25-H, 26-H, 27-H), 0.87 (m, 6H, 18-H, 28-H) ppm; ^{13}C NMR (101 MHz, $CDCl_3$): δ = 210.2 (C-19), 168.5 (C-9), 146.6 (C-1), 145.1 (C-2), 130.0 (C-5), 120.6 (C-4), 114.4 (C-3), 110.4 (C-6), 60.7, 55.9, 43.5 (C-7), 42.9 (C-10), 31.8 (C-20), 31.8 (C-16), 31.2 (C-26), 29.4 (C-12), 29.3 (C-22), 29.3 (C-13), 29.3 (C-23), 29.2 (C-14, C-24), 29.1 (C-15, C-25), 29.0 (C-11), 27.5 (C-21), 23.3, 22.6 (C-17), 22.6 (C-27), 14.1 (C-18, C-28) ppm; MS (ESI, MeOH/$CHCl_3$, 4:1): m/z (%) = 460 (100 %, $[M - H]^-$); anal. calcd for $C_{28}H_{47}NO_4$ (461.69): C 72.84, H 10.26, N 3.03; found: C 72.67, H 9.93, N 2.80.

4.2.7. N-[(4-Hydroxy-3-methoxy)benzyl]undecanamide (**13**) [47311-59-1] and 22-methoxy-4-[(undecanoylamino)methyl]phenyl undecanoate (**14**)

Following GP from vanillylamine (400 mg, 2.63 mmol) and undecanoic acid (734 mg, 3.95 mmol), **13** [70] (100 mg, 23 %) and **14** (350 mg, 54 %) were obtained.

Data for **13**: white solid; m.p. 62 °C (lit. [70]: m.p. 51 °C); R_F = 0.24 (SiO_2, hexanes/EtOAc, 6:4); UV–Vis (MeOH): λ_{max} (log ε) = 229 nm (3.96), 281 nm (3.57); IR (ATR): ν = 3485w, 3302m, 2920s, 2848m, 1635s, 1430m, 1276s, 1122s, 1040m, 720 s cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$): δ = 6.86 (d, J = 8.0 Hz, 1H, 3-H), 6.81 (d, J = 1.9 Hz, 1H, 6-H), 6.75 (*dd*, J = 8.0, 1.8 Hz, 1H, 4-H), 5.79 (s, 1H, NH), 4.35 (d, J = 4.5 Hz, 2H, 7-H), 3.87 (s, 3H, 8-H), 2.21 (t, J = 7.6 Hz, 2H, 10-H), 1.70–1.58 (m, 2H, 11-H), 1.37–1.19 (m, 14H, 12-H, 13-H, 14-H, 15-H, 16-H, 17-H, 18-H), 0.87 (t, J = 6.9 Hz, 3H, 19-H) ppm; ^{13}C NMR (101 MHz, $CDCl_3$): δ = 173.0 (C-9), 146.7 (C-1), 145.1 (C-2), 130.3 (C-5), 120.8 (C-4), 114.3 (C-3), 110.7 (C-6), 55.9 (C-8), 43.6 (C-7), 36.8 (C-10), 31.9 (C-16), 29.5 (C-12), 29.5 (C-13), 29.3 (C-14), 29.3 (C-15), 29.3 (C-17), 25.8 (C-11), 22.6 (C-18), 14.1 (C-19) ppm; MS (ESI, MeOH/$CHCl_3$, 4:1): m/z (%) = 344 (100 %, $[M+Na]^+$); anal. calcd for $C_{19}H_{31}NO_3$ (321.46): C 70.99, H 9.72, N 4.36; found: C 70.77, H 9.98, N 4.12.

Data for **14**: white solid; m.p. 84 °C; R_F = 0.64 (SiO_2, hexanes/EtOAc, 6:4); UV–Vis (MeOH): λ_{max} (log ε) = 279 nm (3.32); IR (ATR): ν = 3309m, 2954m, 2918s, 2850m, 1745s, 1648s, 1469m, 1277m, 1154vs, 1126m, 1029m, 719 s cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$): δ = 6.96 (d, J = 8.0 Hz, 1H, 3-H), 6.89 (d, J = 1.9 Hz, 1H, 6-H), 6.83 (*d*, J = 8.0, 1.8 Hz, 1H, 4-H), 5.85 (s, 1H, NH), 4.40 (d, J = 4.8 Hz, 2H, 7-H), 3.80 (s, 3H, 8-H), 2.56 (t, J = 7.5 Hz, 2H, 21-H), 2.22 (t, J = 7.6 Hz, 2H, 10-H), 1.80–1.71 (m, 2H, 22-H), 1.69–1.60 (m, 2H, 11-H), 1.47–1.37 (m, 2H, 24-H), 1.37–1.21 (m, 26H, 12-H, 13-H, 14-H, 15-H, 16-H, 17-H, 18-H, 23-H, 25-H, 26-H, 27-H, 28-H, 29-H), 0.92–0.84 (m, 6H, 19-H, 30-H) ppm; ^{13}C NMR (101 MHz, $CDCl_3$): δ = 173.1 (C-20), 172.0 (C-9), 151.3 (C-1), 139.2 (C-2), 137.2 (C-5), 122.9 (C-4), 120.0 (C-3), 112.2 (C-6), 55.9 (C-8), 43.5 (C-7), 36.7 (C-10), 34.0 (C-21), 31.9 (C-17), 31.9 (C-28), 29.5 (C-12, C-23), 29.5 (C-14), 29.5 (C-25), 29.3 (C-15), 29.3 (C-26), 29.3 (C-16), 29.3 (C-27), 29.3 (C-13), 29.0 (C-24), 25.8 (C-11), 25.0 (C-22), 22.7 (C-18, C-29), 14.1 (C-19, C-30) ppm; MS (ESI, MeOH/$CHCl_3$, 4:1): m/z (%) = 513 (100 %, $[M+Na]^+$); anal. calcd for $C_{30}H_{51}NO_4$ (489.74): C 73.58, H 10.50, N 2.86; found: C 73.33, H 10.84, N 2.57.

4.2.8. N-[(4-Hydroxy-3-methoxy)benzyl]dodecanamide (**15**) [69693-11-4] and 2-methoxy-4-[(dodecanoylamino)methyl]phenyl dodecanoate (**16**) [101831-70-3]

Following GP from vanillylamine (400 mg, 2.63 mmol) and dodecanoic acid (790 mg, 3.95 mmol), **15** (170 mg, 38 %) and **16** (400 mg, 59 %) were obtained.

Data for **15** white solid; m.p. 77 °C (lit. [55]: m.p. 67.0–67.5 °C); R_F = 0.25 (SiO_2, hexanes/EtOAc, 6:4); UV–Vis (MeOH): λ_{max} (log ε) = 231 nm (3.84), 278 nm (3.23); IR (ATR): ν = 3488w, 3298m, 2919s, 2849m, 1636s, 1463m, 1274s, 1122s, 1039m, 720 m cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$): δ = 6.87 (d, J = 8.0 Hz, 1H, 3-H), 6.81 (d, J = 1.9 Hz, 1H, 6-H), 6.77 (*dd*, J = 8.1, 1.9 Hz, 1H, 4-H), 5.73 (s, 1H, NH), 4.36 (d, J = 5.4 Hz, 2H, 7-H), 3.88 (s, 3H, 8-H), 2.21 (t, 2H, 10-H), 1.69–1.62 (m, 2H, 11-H), 1.35–1.22 (m, 16H, 12-H, 13-H, 14-H, 15-H, 16-H, 17-H, 18-H, 19-H), 0.89 (t, J = 7.0 Hz, 3H, 20-H) ppm; ^{13}C NMR (101 MHz, $CDCl_3$): δ = 173.0 (C-9), 146.7 (C-1), 145.1 (C-2), 130.3 (C-5), 120.8 (C-4), 114.4 (C-3), 110.7 (C-6), 77.3, 77.0, 76.7, 55.9 (C-8), 43.6 (C-7), 36.8 (C-10), 31.9 (C-18), 29.6 (C-12), 29.5 (C-14), 29.3 (C-16), 29.3 (C-13, 15, 17), 25.8 (C-11), 22.7 (C-19), 14.1 (C-20) ppm; MS (ESI, MeOH/$CHCl_3$, 4:1): m/z (%) = 358 (100 %, $[M+Na]^+$); anal. calcd for $C_{20}H_{33}NO_3$ (335.49): C 71.60, H 9.92, N 4.18; found: C 71.46, H 10.18, N 3.83.

Data for **16**: white solid; m.p. 84 °C; R_F = 0.64 (SiO_2, hexanes/EtOAc, 6:4); UV–Vis (MeOH): λ_{max} (log ε) = 279 nm (3.29); IR (ATR): ν =

3310m, 2956m, 2918s, 2850s, 1754s, 1648s, 1468s, 1267s, 1153vs, 1126m, 1029m, 719 s cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): $\delta = 6.95$ (d, 1H, 3-H), 6.88 (d, $J = 1.9$ Hz, 1H, 6-H), 6.82 (*d*, $J = 8.0$, 1.9 Hz, 1H, 4-H), 5.87 (s, 1H, NH), 4.39 (d, 2H, 7-H), 3.79 (d, $J = 1.5$ Hz, 3H, 8-H), 2.55 (t, $J = 7.5$ Hz, 2H, 22-H), 2.20 (t, $J = 7.6$ Hz, 2H, 10-H), 1.80–1.70 (m, 2H, 23-H), 1.69–1.59 (m, 2H, 11-H), 1.46–1.36 (m, 2H, 25-H), 1.36–1.20 (m, 30H, 12-H, 13-H, 14-H, 15-H, 16-H, 17-H, 18-H, 19-H, 24-H, 26-H, 27-H, 28-H, 29-H, 30-H, 31-H), 0.87 (m, 6H, 20-H, 32-H) ppm; ^{13}C NMR (101 MHz, $CDCl_3$): $\delta = 173.1$ (C-21), 172.0 (C-9), 151.3 (C-1), 139.2 (C-2), 137.2 (C-5), 122.9 (C-4), 120.0 (C-3), 112.2 (C-6), 55.9 (C-8), 43.5 (C-7), 36.7 (C-10), 34.0 (C-22), 31.9 (C-18, C-30), 29.6 (C-14, C-26), 29.6 (C-16, C-28), 29.5 (C-12), 29.5 (C-24), 29.3 (C-17, C-29), 29.3 (C-15), 29.3 (C-27), 29.3 (C-13), 29.0 (C-25), 25.8 (C-11), 25.0 (C-23), 22.7 (C-19, C-31), 14.1 (C-20, C-32) ppm; MS (ESI, MeOH/$CHCl_3$, 4:1): *m/z* (%) = 540 (100 %, $[M+Na]^+$); anal. calcd for $C_{32}H_{55}NO_4$ (517.80): C 74.23, H 10.71, N 2.71; found: C 73.96, H 10.98, N 2.45.

4.2.9. N-[(4-Hydroxy-3-methoxy)benzyl]tridecanamide (17) [1215175-51-1] and 2-methoxy-4-[(tridecanoylamino)methyl]phenyl tridecanoate (18)

Following GP from vanillylamine (400 mg, 2.63 mmol) and tridecanoic acid (845 mg, 3.95 mmol), **17** (243 mg, 53 %) and **18** (310 mg, 43 %) were obtained.

Data for **17**: white solid; m.p. 71 °C; $R_F = 0.11$ (SiO_2, hexanes/EtOAc, 7:3); UV–Vis (MeOH): λ_{max} (log ε) = 230 nm (3.88), 281 nm (3.52); IR (ATR): ν = 3487w, 3306m, 2919s, 2848m, 1635s, 1466m, 1277s, 1122m, 1040m, 720 m cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): $\delta = 6.85$ (d, $J = 8.0$ Hz, 1H, 3-H), 6.80 (d, $J = 1.9$ Hz, 1H, 6-H), 6.75 (*dd*, $J = 8.0$, 1.9 Hz, 1H, 4-H), 5.80 (s, 1H, NH), 4.34 (d, $J = 5.2$ Hz, 2H, 7-H), 3.86 (s, 3H, 8-H), 2.20 (t, $J = 7.6$ Hz, 2H, 10-H), 1.68–1.59 (m, 2H, 11-H), 1.35–1.21 (m, 18H, 12-H, 13-H, 14-H, 15-H, 16-H, 17-H, 18-H, 19-H, 20-H), 0.86 (t, 3H, 21-H) ppm; ^{13}C NMR (101 MHz, $CDCl_3$): $\delta = 173.0$ (C-9), 146.7 (C-1), 145.1 (C-2), 130.3 (C-5), 120.8 (C-4), 114.4 (C-3), 110.7 (C-6), 55.9 (C-8), 43.5 (C-7), 36.8 (C-10), 31.9 (C-19), 29.6 (C-12), 29.6 (C-14), 29.6 (C-18), 29.5 (C-17), 29.3 (C-16), 29.3 (C-15), 29.3 (C-13), 25.8 (C-11), 22.7 (C-20), 14.1 (C-21) ppm; MS (ESI, MeOH/$CHCl_3$, 4:1): *m/z* (%) = 373 (100 %, $[M+Na]^+$); anal. calcd for $C_{21}H_{35}NO_3$ (349.52): C 72.17, H 10.09, N 4.01; found: C 71.81, H 10.36, N 3.76.

Data for **18**: m.p. 79 °C; $R_F = 0.24$ (SiO_2, hexanes/EtOAc, 7:3); UV–Vis (MeOH): λ_{max} (log ε) = 279 nm (3.09); IR (ATR): ν = 3309m, 2954m, 2917vs, 2849s, 1745m, 1648s, 1469s, 1277m, 1153vs, 1126m, 1028m, 718 s cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): $\delta = 6.95$ (d, $J = 8.0$ Hz, 1H, 3-H), 6.88 (d, $J = 1.9$ Hz, 1H, 6-H), 6.83 (*dd*, $J = 8.0$, 1.9 Hz, 1H, 4-H), 5.79 (t, $J = 5.7$ Hz, 1H, NH), 4.40 (d, $J = 5.3$ Hz, 2H, 7-H), 3.80 (s, 3H, 8-H), 2.56 (t, $J = 7.5$ Hz, 2H, 23-H), 2.25–2.16 (m, 2H, 10-H), 1.80–1.70 (m, 2H, 24-H), 1.70–1.59 (m, 2H, 11-H), 1.47–1.36 (m, 2H, 26-H), 1.36–1.21 (m, 34H), 0.88 (t, $J = 6.7$ Hz, 6H, 21-H, 34-H) ppm; ^{13}C NMR (101 MHz, $CDCl_3$): $\delta = 173.1$ (C-22), 172.0 (C-9), 151.3 (C-1), 139.2 (C-2), 137.2 (C-5), 122.9 (C-4), 120.0 (C-3), 112.2 (C-6), 55.8 (C-8), 43.4 (C-7), 36.8 (C-10), 34.0 (C-23), 31.9 (C-19, C-32), 29.6 (C-17, C-30), 29.6 (C-16, C-18, C-29, C-31), 29.6 (C-12, C-25), 29.5 (C-14, C-27), 29.3 (C-15), 29.3 (C-28), 29.3 (C-13), 29.0 (C-26), 25.8 (C-11), 25.0 (C-24), 22.7 (C-20, C-33), 14.1 (C-21, C-34) ppm; MS (ESI, MeOH/$CHCl_3$, 4:1): *m/z* (%) = 569 (100 %, $[M+Na]^+$); anal. calcd for $C_{34}H_{59}NO_4$ (545.85): C 74.81, H 10.90, N 2.57; found: C 74.55, H 11.06, N 2.39.

4.2.10. N-[(4-Hydroxy-3-methoxy)benzyl]tetradecanamide (19) [69693-12-5] and 2-methoxy-4-[(tetradecanoylamino)methyl]phenyl tetradecanoate (20)

Following GP from vanillylamine (400 mg, 2.63 mmol) and tetradecanoic acid (900 mg, 3.95 mmol), **19** [71] (160 mg, 33 %) and **20** (358 mg, 47 %) were obtained.

Data for **19**: white solid; m.p. 76 °C (lit. [57]: m.p. 76–78 °C); R_F = 0.13 (SiO_2, hexanes/EtOAc, 7:3); UV–Vis (MeOH): λ_{max} (log ε) = 229 nm (4.01), 280 nm (3.65); IR (ATR): ν = 3486w, 3306m, 2918vs, 2849s, 1635s, 1466m, 1276s, 1122m, 1040m, 719 s cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): $\delta = 6.85$ (d, $J = 8.0$ Hz, 1H, 3-H), 6.80 (d, $J = 1.9$ Hz, 1H, 6-H), 6.75 (*dd*, $J = 8.0$, 1.9 Hz, 1H, 4-H), 5.83 (s, 1H, NH), 4.34 (d, $J = 4.7$ Hz, 2H, 7-H), 3.87 (s, 3H, 8-H), 2.20 (t, $J = 7.6$ Hz, 2H, 10-H), 1.70–1.59 (m, 2H, 11-H), 1.35–1.22 (m, 20H, 12-H, 13-H, 14-H, 15-H, 16-H, 17-H, 18-H, 19-H, 20-H, 21-H), 0.90–0.85 (m, 3H, 22-H) ppm; ^{13}C NMR (101 MHz, $CDCl_3$): δ = 173.0 (C-9), 146.7 (C-1), 145.1 (C-2), 130.3 (C-5), 120.8 (C-4), 114.4 (C-3), 110.7 (C-6), 55.9 (C-8), 43.6 (C-10), 36.8 (C-20), 31.9 (C-12), 29.6 (C-13), 29.6 (C-14), 29.6 (C-15), 29.5 (C-16), 29.3 (C-19), 29.3 (C-17), 29.3 (C-18), 25.8 (C-11), 22.7 (C-21), 14.1 (C-22)ppm; MS (ESI, MeOH/$CHCl_3$, 4:1): *m/z* (%) = 386 (100 %, $[M+Na]^+$); anal. calcd for $C_{22}H_{37}NO_3$ (363.54): C 72.69, H 10.26, N 3.85; found: C 72.54, H 10.51, N 3.61.

Data for **20**: white solid; m.p. 87 °C; $R_F = 0.28$ (SiO_2, hexanes/EtOAc, 7:3); UV–Vis (MeOH): λ_{max} (log ε) = 279 nm (3.16); IR (ATR): ν = 3311m, 2956w, 2917vs, 2849s, 1745m, 1648s, 1470s, 1277m, 1152vs, 1125m, 1029m, 718 s cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): $\delta = 6.95$ (d, $J = 8.0$ Hz, 1H, 3-H), 6.91–6.86 (m, 1H, 6-H), 6.82 (*dd*, $J = 8.0$, 1.5 Hz, 1H, 4-H), 5.85 (s, 1H, NH), 4.40 (d, $J = 4.3$ Hz, 2H, 7-H), 3.80 (s, 3H, 8-H), 2.56 (t, $J = 7.5$ Hz, 2H, 24-H), 2.21 (t, $J = 7.5$ Hz, 2H, 10-H), 1.82–1.70 (m, 2H, 25-H), 1.69–1.59 (m, 2H, 11-H), 1.47–1.37 (m, 2H, 27-H), 1.37–1.18 (m, 38H, 12-H, 13-H, 14-H, 15-H, 16-H, 17-H, 18-H, 19-H, 20-H, 21-H, 26-H, 28-H, 29-H, 30-H, 31-H, 32-H, 33-H, 34-H, 35-H), 0.88 (t, $J = 6.7$ Hz, 7H, 22-H, 36-H) ppm; ^{13}C NMR (101 MHz, $CDCl_3$): $\delta = 173.0$ (C-23), 171.9 (C-9), 151.3 (C-1), 139.2 (C-2), 137.2 (C-5), 122.9 (C-4), 120.0 (C-3), 112.2 (C-6), 55.9 (C-8), 43.5 (C-7), 36.8 (C-10), 34.0 (C-24), 31.9 (C-20, C-34), 29.7 (C-18, C-32), 29.6 (C-16, C-17, C-30, C-31), 29.6 (C-12, C-26), 29.5 (C-14), 29.5 (C-28), 29.3 (C-15, C-19, C-29, C-33), 29.3 (C-13), 29.0 (C-27), 25.8 (C-11), 25.0 (C-25), 22.7 (C-21, C-35), 14.1 (C-22, C-36) ppm; MS (ESI, MeOH/$CHCl_3$, 4:1): *m/z* (%) = 596 (100 %, $[M+Na]^+$); anal. calcd for $C_{36}H_{63}NO_4$ (573.90): C 75.34, H 11.07, N 2.44; found: C 75.01, H 11.35, N 2.08.

4.2.11. N-[(4-Hydroxy-3-methoxy)benzyl]pentadecanamide (21) and 2-methoxy-4-[(pentadecanoylamino)methyl]phenyl pentadecanoate (22)

Following GP from vanillylamine (400 mg, 2.63 mmol) and pentadecnoic acid (955 mg, 3.95 mmol), **21** (250 mg, 48 %) and **22** (210 mg, 26 %) were obtained.

Data for **21**: white solid; m.p. 79 °C; $R_F = 0.11$ (SiO_2, hexanes/EtOAc, 7:3); UV–Vis (MeOH): λ_{max} (log ε) = 230 nm (3.88), 280 nm (3.52); IR (ATR): ν = 3487w, 3305m, 2918vs, 2848s, 1635s, 1467m, 1276s, 1123m 1040m, 719 s cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): $\delta = 6.85$ (d, $J = 8.0$ Hz, 1H, 3-H), 6.80 (d, $J = 1.9$ Hz, 1H, 6-H), 6.75 (*dd*, $J = 8.0$, 1.8 Hz, 1H, 4-H), 5.82 (s, 1H, NH), 4.35 (d, $J = 4.5$ Hz, 2H, 7-H), 3.87 (s, 3H, 8-H), 2.21 (t, $J = 7.6$ Hz, 2H, 10-H), 1.72–1.56 (m, 2H, 11-H), 1.38–1.17 (m, 22H, 12-H, 13-H, 14-H, 15-H, 16-H, 17-H, 18-H, 19-H, 20-H, 21-H, 22-H), 0.88 (t, $J = 6.8$ Hz, 3H, 23-H) ppm; ^{13}C NMR (126 MHz, $CDCl_3$): δ = 173.0 (C-9), 146.7 (C-1), 145.2 (C-2), 130.3 (C-5), 120.8 (C-4), 114.4 (C-3), 110.7 (C-6), 55.9 (C-8), 43.6 (C-7), 36.8 (C-10), 31.9 (C-21), 29.7 (C-12), 29.7 (C-13), 29.6 (C-15, 16, 17), 29.6 (C-18), 29.5 (C-19), 29.3 (C-20), 29.3 (C-14), 25.8 (C-11), 22.7 (C-22), 14.1 (C-23) ppm; MS (ESI, MeOH/$CHCl_3$, 4:1): *m/z* (%) = 400 (100 %, $[M+Na]^+$); anal. calcd for $C_{23}H_{39}NO_3$ (377.57): C 73.17, H 10.41, N 3.71; found: C 72.86, H 10.19, N 3.50.

Data for **22**: white solid; m.p. 80 °C; $R_F = 0.75$ (SiO_2, hexanes/EtOAc, 6:4); UV–Vis (MeOH): λ_{max} (log ε) = 273 nm (3.11), 279 nm (3.13); IR (ATR): ν = 3308m, 2954m, 2916vs, 2849s, 1745m, 1648s, 1470m, 1277m, 1153s, 1125m, 1029m, 718 s cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): $\delta = 6.96$ (d, $J = 8.0$ Hz, 1H, 3-H), 6.89 (d, $J = 1.9$ Hz, 1H, 6-H), 6.83 (*dd*, $J = 8.1$, 1.9 Hz, 1H, 4-H), 5.74 (t, $J = 5.7$ Hz, 1H, NH), 4.41 (d, $J = 5.4$ Hz, 2H, 7-H), 3.80 (s, 3H, 8-H), 2.56 (t, $J = 7.5$ Hz, 2H, 25-H), 2.40–2.24 (m, 2H, 10-H), 2.26–2.15 (m, 2H, 26-H), 1.81–1.70 (m, 2H, 11-H), 1.69–1.58 (m, 2H, 13-H), 1.48–1.36 (m, 2H, 28-H), 1.36–1.17 (m, 36H, 12-H, 14-H, 15-H, 16-H, 17-H, 18-H, 19-H, 20-H, 21-H, 27-H, 29-H, 30-H, 31-H, 32-H, 33-H, 34-H, 35-H, 36-H), 1.00–0.76 (m, 10H, 22-H, 23-H, 37-H, 38-H) ppm; ^{13}C NMR (101 MHz, $CDCl_3$): $\delta = 173.1$ (C-24),

172.0 (C-9), 151.3 (C-1), 139.2 (C-2), 137.1 (C-5), 122.9 (C-4), 120.0 (C-3), 112.2 (C-6), 55.9 (C-8), 43.5 (C-7), 36.8 (C-10), 34.0 (C-25), 31.9 (C-21, C-36), 29.7 (C-12, C-14, C-18, C-27, C-29, C-33), 29.7 (C-30), 29.6 (C-15, C-16, C-17, C-19, C-31, C-32, C-34), 29.3 (C-13, C-20, C-28, C-35), 25.8 (C-11), 25.0 (C-26), 22.7 (C-22, C-37), 14.1 (C-23, C-38) ppm; MS (ESI, MeOH/$CHCl_3$, 4:1): *m/z* (%) = 625 (100 %, $[M+Na]^+$); anal. calcd for $C_{38}H_{67}NO_4$ (601.96): C 75.82, H 11.22, N 2.33; found: 75.64, H 11.53, N 2.19.

4.2.12. *N-[(4-Hydroxy-3-methoxy)benzyl]hexadecanamide **(23)** [69693-13-6] and 2-methoxy-4-[(hexadecanoylamino)methyl]phenyl hexadecanoate **(24)** [2512225-49-7]*

Following GP from vanillylamine (400 mg, 2.63 mmol) and hexadecanoic acid (1044 mg, 3.95 mmol), **23** [72,73] (320 mg, 31 %) and **24** (490 mg, 30 %) were obtained.

Data for **23**: white solid; m.p. 80 °C; R_F = 0.12 (SiO_2, hexanes/EtOAc, 7:3); UV–Vis (MeOH): λ_{max} (log ε) = 279 nm (3.65); IR (ATR): ν = 3311w, 2955w, 2916vs, 2871w, 2849s, 1745m, 1648s, 1605w, 1552m, 1517m, 1470m, 1452w, 1442w, 1423w, 1414w, 1377w, 1356w, 1308w, 1290m, 1277m, 1260w, 1250w, 1231w, 1204w, 1195w, 1153s, 1125m, 1029m, 823w, 751w, 718 m cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ = 6.84 (d, *J* = 8.0 Hz, 1H, 3-H), 6.75 (d, *J* = 1.9 Hz, 1H, 6-H), 6.72 (*dd*, *J* = 8.0, 2.0 Hz, 1H, 4-H), 5.62 (s, 1H, NH), 4.42–4.24 (m, 2H, 7-H), 3.86 (s, 3H, 8-H), 2.55–2.48 (m, 2H, 10-H), 1.80 (t, *J* = 7.6 Hz, 2H, 11-H), 1.42–1.12 (m, 24H, 12-H, 13-H, 14-H, 15-H, 16-H, 17-H, 18-H, 19-H, 20-H, 21-H, 22-H, 23-H), 0.92–0.82 (m, 3H, 24-H) ppm; ^{13}C NMR (101 MHz, $CDCl_3$): δ = 168.5 (C-9), 146.6 (C-1), 145.1 (C-2), 130.0 (C-5), 120.6 (C-4), 114.4 (C-3), 110.4 (C-6), 60.8, 55.9 (C-8), 43.5 (C-7), 42.9, 31.9 (C-10), 31.2 (C-22), 29.7 (C-12), 29.6 (C-21), 29.6 (C-20), 29.5 (C-13), 29.4 (C-19), 29.4 (C-14), 29.3 (C-15), 29.3 (C-18), 29.0 (C-17), 27.5 (C-16), 23.3 (C-11), 22.7 (C-23), 14.1 (C-24) ppm; MS (ESI, MeOH/$CHCl_3$, 4:1): *m/z* (%) = 390 (100 %, $[M-H]^-$); anal. calcd for $C_{24}H_{41}NO_3$ (391.60): C 73.61, H 10.55, N 3.58; found: C 73.44, H 10.75, N 3.41.

Data for **24**: m.p. 92 °C; R_F = 0.45 (SiO_2, hexanes/EtOAc, 7:3); UV–Vis (MeOH): λ_{max} (log ε) = 280 nm (3.34); IR (ATR): ν = 3279w, 2952w, 2917vs, 2849s, 1715m, 1644m, 1615w, 1544m, 1515s, 1467m, 1456m, 1435m, 1403w, 1376w, 1344w, 1319w, 1301w, 1271s, 1247s, 1228m, 1213m, 1192w, 1151m, 1139w, 1122m, 1075w, 1029m, 815w, 799m, 719m, 683m, 622w, 562w, 547w, 531w, 520w, 505w cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ = 6.95 (d, *J* = 8.0 Hz, 1H, 3-H), 6.88 (d, *J* = 1.9 Hz, 1H, 6-H), 6.82 (*dd*, *J* = 8.0, 1.9 Hz, 1H, 4-H), 5.75 (t, *J* = 5.7 Hz, 1H, NH), 4.40 (d, *J* = 5.7 Hz, 2H, 7-H), 3.79 (s, 3H, 8-H), 2.56 (t, *J* = 7.5 Hz, 2H, 26-H), 2.23–2.15 (m, 2H, 10-H), 1.81–1.70 (m, 2H, 27-H), 1.69–1.58 (m, 2H, 11-H), 1.49–1.18 (m, 48H, CH_2), 0.92–0.81 (m, 6H, 24-H, 40-H) ppm; ^{13}C NMR (101 MHz, $CDCl_3$): δ = 172.9 (C-25), 171.9 (C-9), 151.3 (C-1), 139.2 (C-2), 137.3 (C-5), 122.9 (C-4), 120.0 (C-3), 112.2 (C-6), 55.8 (C-8), 43.4 (C-7), 36.8 (C-10), 34.0 (C-26), 31.9 (C-22, C-38), 29.7–29.0 (*C*H_2), 25.8 (C-11), 25.0 (C-27), 22.7 (C-23, C-39), 14.1 (C-24, C-40) ppm; MS (ESI, MeOH/$CHCl_3$, 4:1): *m/z* (%) = 665 (100 %, $[M+Na]^+$); anal. calcd for $C_{40}H_{71}NO_4$ (630.01): C 76.26, H 11.36, N 2.22; found: C 75.97, H 11.56, N 1.96.

4.2.13. *N-[(4-Hydroxy-3-methoxy)benzyl]heptadecanamide **(25)** and 2-methoxy-4-[(heptadecanoylamino)methyl]phenyl heptadecanoate **(26)***

Following GP from vanillylamine (400 mg, 2.63 mmol) and heptadecanoic acid (1102 mg, 3.95 mmol), **25** (345 mg, 32 %) and **26** (515 mg, 30 %) were obtained.

Data for **25**: white solid; m.p. 84 °C; R_F = 0.15 (SiO_2, hexanes/EtOAc, 7:3); UV–Vis (MeOH): λ_{max} (log ε) = 281 nm (3.11); IR (ATR): ν = 3303w, 2953w, 2917vs, 2849s, 1649m, 1635s, 1607w, 1550m, 1518vs, 1467m, 1438m, 1430m, 1415m, 1381w, 1349w, 1277s, 1259m, 1245m, 1237m, 1225m, 1204m, 1187m, 1175m, 1153m, 1123m, 1039m, 1021m, 821w, 799m, 733m, 719s, 702m, 673w, 635m, 579m, 563 m cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ = 6.85 (d, *J* = 8.0 Hz, 1H, 3-H), 6.79 (d, *J* = 2.0 Hz, 1H, 6-H), 6.74 (*dd*, *J* = 8.0, 2.0 Hz, 1H, 4-H), 5.73–5.66 (m, 1H, NH), 4.34 (d, *J* = 5.5 Hz, 2H, 7-H), 3.86 (s, 3H, 8-H), 2.18 (t, *J* = 7.4 Hz, 2H, 10-H), 1.67–1.56 (m, 2H, 11-H), 1.24 (d, *J* = 3.2 Hz, 26H, CH_2), 0.91–0.80 (m, 3H, 25-H) ppm; ^{13}C NMR (101 MHz, $CDCl_3$): δ = 172.9 (C-9), 146.7 (C-1), 145.1 (C-2), 130.4 (C-5), 120.8 (C-4), 114.3 (C-3), 110.7 (C-6), 55.9 (C-8), 43.5 (C-7), 36.8 (C-10), 31.9 (C-23), 29.7–29.3 (*C*H_2), 25.8 (C-11), 22.7 (C-24), 14.1 (C-25) ppm; MS (ESI, MeOH/$CHCl_3$, 4:1): *m/z* (%) = 404 (100 %, $[M-H]^-$); anal. calcd for $C_{25}H_{43}NO_3$ (405.62): C 74.03, H 10.69, N 3.45; found:

Data for **26**: m.p. 94 °C; R_F = 0.45 (SiO_2, hexanes/EtOAc, 7:3); UV–Vis (MeOH): λ_{max} (log ε) = 280 nm (3.14); IR (ATR): ν = 2917vs, 2850s, 1715m, 1644m, 1544m, 1515s, 1467m, 1457m, 1435m, 1377w, 1341w, 1271m, 1247m, 1229m, 1213m, 1151m, 1139w, 1122m, 1029m, 815w, 798m, 718m, 683w, 623w, 562w, 547w cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$): δ = 6.84 (d, *J* = 8.0 Hz, 1H, 3-H), 6.75 (d, *J* = 1.9 Hz, 1H, 6-H), 6.72 (*dd*, *J* = 8.0, 2.0 Hz, 1H, 4-H), 5.69–5.58 (m, 1H, NH), 4.38–4.27 (m, 2H, 7-H), 3.86 (s, 3H, 8-H), 2.65–2.43 (m, 2H, 27-H), 1.88–1.65 (m, 2H, 10-H), 1.43–1.14 (m, 56H, CH_2), 0.95–0.81 (m, 6H, 25-H, 42-H) ppm; ^{13}C NMR (101 MHz, $CDCl_3$): δ = 173.7 (C-26), 168.5 (C-9), 146.6 (C-1), 145.1 (C-2), 130.0 (C-5), 120.6 (C-4), 114.4 (C-3), 110.4 (C-6), 55.9 (C-8), 43.5 (C-7), 31.9 (C-10), 31.2 (C-27), 29.7–27.5 (*C*H_2), 23.3 (C-40), 22.7 (C-23), 14.1 (C-25, C-42) ppm; MS (ESI, MeOH/$CHCl_3$, 4:1): *m/z* (%) = 680 (100 %, $[M+Na]^+$); anal. calcd for $C_{42}H_{75}NO_4$ (658.07): C 76.66, H 11.49, N 2.13; found: C 76.35, H 11.70, N 1.97.

4.2.14. *N-[(4-Hydroxy-3-methoxy)benzyl]octadecanamide **(27)** [58493-50-8] and 2-methoxy-4-[(octadecanoylamino)methyl]phenyl octadecanoate **(28)***

Following GP from vanillylamine (400 mg, 2.63 mmol) and octadecanoic acid (1158 mg, 3.95 mmol), **27** [74,75] (495 mg, 45 %) and **28** (590 mg, 34 %) were obtained.

Data for **27**: white solid; m.p. 84 °C (lit. [57]: m.p. 93–95 °C); R_F = 0.10 (SiO_2, hexanes/EtOAc, 7:3); UV–Vis (MeOH): λ_{max} (log ε) = 280 nm (3.28); IR (ATR): ν = 3305w, 2954w, 2917vs, 2871w, 2849s, 1649m, 1635s, 1608w, 1550m, 1519s, 1468m, 1438m, 1430m, 1416w, 1382w, 1349w, 1277s, 1256m, 1251m, 1237m, 1223m, 1202m, 1186m, 1164m, 1154m, 1123m, 1039m, 1021m, 822w, 799m, 733m, 719m, 673w, 635m, 579m, 563m, 550w, 514w, cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ = 6.85 (d, *J* = 8.0 Hz, 1H, 3-H), 6.79 (d, *J* = 1.9 Hz, 1H, 6-H), 6.74 (*dd*, *J* = 8.0, 2.0 Hz, 1H, 4-H), 5.69 (t, *J* = 5.9 Hz, 1H, NH), 4.34 (d, *J* = 5.6 Hz, 2H, 7-H), 3.86 (s, 3H, 8-H), 2.24–2.11 (m, 2H, 10-H), 1.66–1.58 (m, 2H, 11-H), 1.44–1.11 (m, 28H, CH_2), 0.87 (t, *J* = 6.7 Hz, 3H, 26-H) ppm; ^{13}C NMR (101 MHz, $CDCl_3$): δ = 172.9 (C-9), 146.7 (C-1), 145.1 (C-2), 130.4 (C-5), 120.8 (C-4), 114.4 (C-3), 110.7 (C-6), 55.9 (C-8), 43.5 (C-7), 31.9 (C-10), 29.7 (C-24), 29.7–29.0 (*C*H_2), 25.8 (C-25), 22.7 (C-11), 14.1 (C-26) ppm; MS (ESI, MeOH/$CHCl_3$, 4:1): *m/z* (%) = 418 (100 %, $[M-H]^-$); anal. calcd for $C_{26}H_{45}NO_3$ (419.65): C 74.42, H 10.81, N 3.34; found: C 74.25, H 11.03, N 3.16.

Data for **28**: white solid; 94 °C; R_F = 0.49 (SiO_2, hexanes/EtOAc, 7:3); UV–Vis (MeOH): λ_{max} (log ε) = 228 nm (3.62), 277 nm (3.34); IR (ATR): ν = 3310w, 2955w, 2916vs, 2872w, 2849s, 1745m, 1648m, 1605w, 1552m, 1517m, 1470m, 1453w, 1442w, 1422w, 1415w, 1377w, 1307w, 1291m, 1277m, 1259m, 1242w, 1224w, 1204m, 1191w, 1153s, 1125m, 1029m, 822w, 751w, 718 m cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ = 6.95 (d, *J* = 8.0 Hz, 1H, 3-H), 6.88 (d, *J* = 1.9 Hz, 1H, 6-H), 6.82 (*dd*, *J* = 8.1, 1.8 Hz, 1H, 4-H), 5.73–5.65 (m, 1H, NH), 4.40 (d, *J* = 5.3 Hz, 2H, 7-H), 3.80 (s, 3H, 8-H), 2.56 (t, *J* = 7.5 Hz, 2H, 10-H), 2.20 (t, *J* = 7.6 Hz, 2H, 28-H), 1.78–1.70 (m, 2H, 11-H), 1.71–1.56 (m, 2H, 29-H), 1.36–1.16 (m, 56H, CH_2), 0.93–0.84 (m, 6H, 26-H, 44-H) ppm; ^{13}C NMR (101 MHz, $CDCl_3$): δ = 173.0 (C-27), 171.9 (C-9), 151.3 (C-1), 139.2 (C-2), 137.2 (C-5), 122.9 (C-4), 120.0 (C-3), 112.2 (C-6), 55.9 (C-8), 43.5 (C-7), 36.8 (C-10), 34.0 (C-28), 31.9 (C-24, C-42), 29.7–29.0 (*C*H_2), 25.8 (C-11), 25.0 (C-29), 22.7 (C-25, C-43), 14.1 (C-26, C-44) ppm; MS (ESI, MeOH/$CHCl_3$, 4:1): *m/z* (%) = 709 (100 %, $[M+Na]^+$); anal. calcd for $C_{44}H_{79}NO_4$ (686.12): C 77.03, H 11.61, N 2.04; found: C 76.76, H 11.95, N 1.84.

*4.2.15. N-[(4-Hydroxy-3-methoxy)benzyl]nonadecanamide **(29)** and 2-methoxy-4-[(nonadecanoylamino)methyl]phenyl nonadecanoate **(30)***

Following GP from vanillylamine (400 mg, 2.63 mmol) and nonadecanoic acid (1215 mg, 3.95 mmol), **29** (580 mg, 51 %) and **30** (595 mg, 34 %) were obtained.

Data for **29**: white solid; m.p. 92 °C; $R_F = 0.18$ (SiO_2, hexanes/EtOAc, 7:3); UV–Vis (MeOH): λ_{max} (log ε) = 229 nm (3.72), 280 nm (3.41); IR (ATR): ν = 3305w, 2917vs, 2849s, 1648m, 1635s, 1551m, 1519s, 1468m, 1438m, 1430m, 1415w, 1347w, 1277s, 1251m, 1236m, 1220m, 1201m, 1185m, 1175w, 1154m, 1123m, 1040m, 1021m, 799m, 733m, 719m, 702w, 672w, 635m, 579m, 563 m cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$): δ = 6.86 (d, J = 8.0 Hz, 1H, 6-H), 6.80 (d, J = 1.9 Hz, 1H, 3-H), 6.76 (*dd*, J = 8.1, 1.9 Hz, 1H, 4-H), 5.76–5.64 (m, 1H, NH), 4.35 (d, J = 5.4 Hz, 2H, 7-H), 3.87 (s, 3H, 8-H), 2.22–2.15 (m, 2H, 10-H), 1.69–1.58 (m, 2H, 11-H), 1.25 (d, J = 4.2 Hz, 30H, CH_2), 0.88 (t, J = 6.9 Hz, 3H, 27-H) ppm; ^{13}C NMR (126 MHz, $CDCl_3$): δ = 172.9 (C-9), 146.7 (C-1), 145.1 (C-2), 130.4 (C-5), 120.8 (C-4), 114.3 (C-3), 110.7 (C-6), 55.9 (C-8), 43.5 (C-7), 36.8 (C-10), 31.9 (C-25), 29.7–29.3 (CH_2), 25.8 (C-26), 22.7 (C-11), 14.1 (C-27) ppm; MS (ESI, MeOH/$CHCl_3$, 4:1): *m/z* (%) = 432 (100 %, $[M - H]^-$); anal. calcd for $C_{27}H_{47}NO_3$ (433.68): C 74.78, H 10.92, N 3.23; found: C 74.56, H 11.11, N 2.96.

Data for **30**: white solid; m.p. 97 °C; $R_F = 0.55$ (SiO_2, hexanes/EtOAc, 7:3); UV–Vis (MeOH): λ_{max} (log ε) = 229 nm (3.82), 278 nm (3.54); IR (ATR): ν = 3307w, 2955w, 2916vs, 2849s, 1745m, 1648m, 1605w, 1555m, 1518m, 1471s, 1453w, 1443w, 1423w, 1414w, 1305w, 1289m, 1277m, 1256m, 1222w, 1204m, 1190m, 1153s, 1125m, 1046w, 1038m, 1029m, 819w, 750w, 733m, 717 s cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$): δ = 6.96 (d, J = 7.9 Hz, 1H, 3-H), 6.89 (d, J = 1.9 Hz, 1H, 6-H), 6.83 (*dd*, J = 8.0, 1.7 Hz, 1H, 4-H), 5.75–5.61 (m, 1H, NH), 4.41 (d, J = 5.0 Hz, 2H, 7-H), 3.80 (s, 3H, 8-H), 2.56 (t, J = 7.5 Hz, 2H, 10-H), 2.20 (t, J = 7.6 Hz, 2H, 29-H), 1.78–1.72 (m, 2H, 11-H), 1.68–1.61 (m, 2H, 30-H), 1.43–1.18 (m, 60H, CH_2), 0.91–0.83 (m, 6H, 27-H, 46-H) ppm; ^{13}C NMR (126 MHz, $CDCl_3$): δ = 172.9 (C-28), 171.9 (C-9), 151.3 (C-1), 139.2 (C-2), 137.2 (C-5), 122.9 (C-4), 120.0 (C-3), 112.2 (C-6), 55.9 (C-8), 43.5 (C-7), 36.8 (C-27), 34.0 (C-29), 31.9 (C-25, C-44), 29.7–29.1 (CH_2), 25.8 (C-11), 25.0 (C-30), 22.7 (C-26, C-45), 14.1 (C-46) ppm; MS (ESI, MeOH/$CHCl_3$, 4:1): *m/z* (%) = 737 (100 %, $[M+Na]^+$); anal. calcd for $C_{46}H_{83}NO_4$ (714.17), C 77.36, H 11.71, N 1.96; found.

*4.2.16. N-[(4-Hydroxy-3-methoxy)benzyl]icosanamide **(31)** [152919-36-3] and 2-methoxy-4-[(icosanoylamino)methyl]phenyl icosanoate **(32)***

Following GP from vanillylamine (400 mg, 2.63 mmol) and icosanoic acid (1230 mg, 3.95 mmol), **31** (120 mg, 20 %) and **32** (550 mg, 56 %) were obtained.

Data for **31**: white solid; m.p. 94 °C; $R_F = 0.38$ (SiO_2, hexanes/EtOAc, 6:4); UV–Vis (MeOH): λ_{max} (log ε) = 230 nm (3.19), 279 nm (2.83); IR (ATR): ν = 3499w, 3310w, 2916vs, 2849s, 1635m, 1471m, 1278m, 1125m, 1029w, 718 m cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ = 6.96 (d, J = 8.0 Hz, 1H, 3-H), 6.89 (d, J = 1.9 Hz, 1H, 6-H), 6.81 (*dd*, J = 5.4, 1.9 Hz, 1H, 4-H), 5.84–5.63 (m, 1H, NH), 4.41 (d, J = 5.2 Hz, 2H, 7-H), 3.80 (s, 3H, 8-H), 2.56 (t, J = 7.5 Hz, 2H, 10-H), 2.20 (*td*, J = 7.6, 4.5 Hz, 2H, 11-H), 1.75 (*p*, J = 7.5 Hz, 2H, 12-H), 1.69–1.58 (m, 2H, 14-H), 1.44–1.36 (m, 2H, 27-H), 1.35–1.21 (m, 26H, CH_2), 0.90–0.84 (m, 3H, 28-H) ppm; ^{13}C NMR (101 MHz, $CDCl_3$): δ = 137.2 (C-9), 122.9 (C-1), 120.8 (C-2), 120.0 (C-5), 114.3 (C-4), 112.2 (C-3), 110.7 (C-6), 77.3, 77.0, 76.7, 55.9 (C-8), 43.5 (C-7), 34.0 (C-10), 31.9 (C-26), 29.7–29.1 (CH_2), 25.8 (C-14), 25.0 (C-11), 22.7 (C-27), 14.1 (C-28) ppm; MS (ESI, MeOH/$CHCl_3$, 4:1): *m/z* (%) = 446 (100 %, $[M - H]^-$); anal. calcd for $C_{28}H_{49}NO_3$ (447.70): C 75.12, H 11.03, N 3.13; found: C 74.85. H 11.37, N 2.98.

Data for **32**: white solid; m.p. 80 °C; $R_F = 0.75$ (SiO_2, hexanes/EtOAc, 6:4); UV–Vis (MeOH): λ_{max} (log ε) = 279 nm (2.79); IR (ATR): ν = 3310m, 2956m, 2916vs, 2849s, 1745m, 1648m, 1471s, 1277m, 1153s, 1125m, 1029m, 717 m cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ = 6.96 (d, J = 7.8 Hz, 1H, 3-H), 6.89 (s, 1H, 6-H), 6.83 (d, J = 7.9 Hz, 1H, 4-H), 5.81–5.76 (m, 1H, NH), 4.43–4.39 (m, 2H, 7-H), 3.80 (s, 3H, 8-H), 2.56 (t, J = 7.5 Hz, 2H, 30-H), 2.29–2.12 (m, 2H, 10-H), 1.85–1.69 (m, 2H, 31-H), 1.69–1.60 (m, 2H, 11-H), 1.50–1.11 (m, 64H, CH_2), 0.88 (t, J = 6.7 Hz, 6H, 28-H, 48-H) ppm; ^{13}C NMR (101 MHz, $CDCl_3$): δ = 173.3 (C-29), 172.1 (C-9), 151.4 (C-1), 139.4 (C-2), 137.3 (C-5), 123.0 (C-4), 120.2 (C-3), 112.4 (C-6), 77.5, 77.2, 76.8, 56.1 (C-8), 43.7 (C-7), 37.0 (C-10), 34.2 (C-30), 32.1 (C-26, 46), 29.8–29.2 (CH_2), 26.0 (C-11), 25.2 (C-31), 22.8 (C-27, 47), 14.3 (C-28, 48) ppm; MS (ESI, MeOH/$CHCl_3$, 4:1): *m/z* (%) = 764 (100 %, $[M+Na]^+$); anal. calcd for $C_{48}H_{87}NO_4$ (742.23): C 77.68, H 11.82, N 1.89; found: CC 77.50, H 12.07, N 1.64.

*4.2.17. N,N-bis(4-hydroxy-3-methoxybenzyl)nonanamide **(33)**, 4-{[4-hydroxy-3-methoxybenzyl)(nonanoyl)amino]methyl}-2-methoxyphenyl nonanoate **(34)** and (nonanoylimino) bis(methylene-2-methoxy-4,1-phenylene) dinonanoate **(35)***

Following GP from divanillylamine (400 mg, 1.39 mmol) and nonanoic acid (440 mg, 2.80 mmol), **33** (180 mg, 30 %), **34** (95 mg, 12 %) and **35** (100 mg, 10 %) were obtained.

Data for **33**: colorless oil; $R_F = 0.55$ (hexanes/EtOAc, 5:5); UV–Vis (MeOH): λ_{max} (log ε) = 231 nm (4.13), 282 nm (3.79); IR (ATR): ν = 3296br, 2925m, 2854w, 1614m, 1598m, 1512s, 1463m, 1423m, 1353w, 1271s, 1237s, 1207s, 1152m, 1122s, 1033s, 798w, 749m, 722w, 560 m cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ = 6.95–6.50 (m, 6H, 3-H, 4-H, 6-H), 4.44 (d, J = 54.6 Hz, 4H, 7-H), 3.83 (s, 6H, 8-H), 2.42 (t, J = 7.5 Hz, 2H, 10-H), 1.73–1.68 (m, 2H, 11-H), 1.36–1.21 (m, 10H, 12-H, 13-H, 14-H, 15-H, 16-H), 0.87 (t, J = 6.8 Hz, 3H, 17-H) ppm; ^{13}C NMR (101 MHz, $CDCl_3$): δ = 174.0 (C-9), 146.9 (C-1), 145.2 (C-2), 129.7 (C-5), 128.5, 121.7 (C-4), 119.6, 114.8 (C-3), 111.3 (C-6), 109.0, 56.1 (C-8), 49.9 (C-7), 33.5 (C-10), 32.0 (C-15), 29.6 (C-13), 29.5 (C-14), 29.3 (C-12), 25.8 (C-11), 22.8 (C-16), 14.2 (C-17) ppm; MS (ESI, MeOH/$CHCl_3$, 4:1): *m/z* (%) = 430 (100 %, $[M+H]^+$); anal. calcd for $C_{25}H_{35}NO_5$ (429.56): C 69.90, H 8.21, N 3.26; found: 69.67, H 8.40, N 3.01.

Data for **34**: colorless oil; $R_F = 0.65$ (hexanes/EtOAc, 5:5); UV–Vis (MeOH): λ_{max} (log ε) = 280 nm (3.66); IR (ATR): ν = 2954m, 2924s, 2854m, 1761m, 1605m, 1510s, 1464s, 1416s, 1377m, 1348m, 1273s, 1239s, 1201s, 1142vs, 1121vs, 1034s, 936w, 817m, 798m, 744m, 723m, 663w, 559m, 464w, 437w, 433w, 427w, 419w, 408w, 717s, 463 m cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ = 7.02–6.53 (m, 6H, 3-H, 4-H, 6-H, 11-H, 12-H, 14-H), 5.80 (d, J = 22.9 Hz, 1H, OH), 4.53 (d, J = 10.3 Hz, 2H, 7-H), 4.39 (d, J = 13.7 Hz, 2H, 15-H), 3.82 (d, J = 1.4 Hz, 3H, 16-H), 3.75 (d, J = 1.4 Hz, 3H, 8-H), 2.63–2.50 (m, 2H, 27-H), 2.50–2.32 (m, 2H, 18-H), 1.79–1.65 (m, 4H, 19-H, 28-H), 1.46–1.17 (m, 20H, CH_2), 0.92–0.81 (m, 6H, 25-H, 34-H) ppm; ^{13}C NMR (101 MHz, $CDCl_3$): δ = 173.9 (C-26), 171.9 (C-17), 151.3 (C-9), 147.1 (C-1), 145.2 (C-2), 139.2 (C-10), 136.4 (C-13), 129.4 (C-5), 123.2 (C-4), 122.6 (C-12), 121.5 (C-11), 114.7 (C-3), 112.6 (C-14), 110.2 (C-6), 55.9 (C-16), 55.8 (C-8), 50.0 (C-15), 47.9 (C-7), 34.0 (C-27), 33.3 (C-18), 31.8 (C-23, 32), 29.5–29.0 (CH_2), 25.6 (C-19), 25.0 (C-28), 22.6 (C-24, C-33), 14.0 (C-25, C-34) ppm; MS (ESI, MeOH/$CHCl_3$, 4:1): *m/z* (%) = 592 (100 %, $[M+Na]^+$); anal. calcd for $C_{34}H_{51}NO_6$ (569.78): C 71.67, H 9.02, N 2.46; found: C 71.54, H 9.35, N 2.11.

Data for **35**: colorless oil; $R_F = 0.8$ (hexanes/EtOAc, 5:5); UV–Vis (MeOH): λ_{max} (log ε) = 274 nm (3.60); IR (ATR): ν = 2956m, 2920vs, 2870m, 2853s, 1748s, 1711s, 1652vs, 1607m, 1512s, 1467s, 1442m, 1414vs, 1378w, 1347m, 1284vs, 1262s, 1234m, 1223m, 1199s, 1179s, 1151vs, 1117vs, 1105m, 1092m, 1077w, 1032s, 968w, 952w, 935m, 920m, 909m, 892w, 850m, 834m, 818m, 793w, 755w, 719m, 672w, 651w, 585w cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ = 7.10–6.62 (m, 6H, 3-H, 4-H, 6-H, 11-H, 12-H, 14-H), 4.57 (s, 2H, 7-H), 4.43 (s, 2H, 15-H), 3.77 (s, 6H, 8-H, 16-H), 2.74–2.26 (m, 6H, 18-H, 27-H, 36-H), 1.85–1.54 (m, 6H, 19-H, 28-H, 37-H), 1.44–1.17 (m, 30H, CH_2), 0.95–0.76 (m, 9H, 25-H, 34-H, 43-H) ppm; ^{13}C NMR (101 MHz, $CDCl_3$): δ = 179.3 (C-26), 174.0 (C-35), 171.9 (C-17), 151.6 (C-1), 151.3 (C-9), 139.2 (C-2, C-10), 136.2 (C-5), 135.2 (C-13), 123.2 (C-4), 122.7 (C-12), 120.5 (C-3), 118.3 (C-11), 112.6 (C-6), 110.2 (C-14), 55.9 (C-8), 55.8 (C-16), 49.8 (C-7), 48.0 (C-15), 34.0–22.6 (CH_2), 14.0 (C-25, C-34, C-43)

ppm; MS (ESI, MeOH/$CHCl_3$, 4:1): *m/z* (%) = 733 (100 %, $[M+Na]^+$); anal. calcd for $C_{43}H_{67}NO_7$ (710.01): C 72.74, H 9.51, N 1.97; found: C 72.46, H 9.80, N 1.67.

*4.2.18. N-[(4-Hydroxy-3-methoxyphenyl)methyl]-2-methyloctanamide (**36**) and 4-{[(2-methyloctanoyl)amino]methyl}-2-(methyloxy)phenyl 2-methyloctanoate (**37**)*

Following GP from vanillylamine (1935 mg, 12.66 mmol) and 2-methyloctanoic acid (1000 mg, 6.33 mmol), **36** (890 mg, 48 %) and **37** (470 mg, 17 %) were obtained.

Data for **36**: white solid; m.p. 79–80 °C; R_F = 0.28 (SiO_2, hexanes/EtOAc, 4:6); UV–Vis (MeOH): λ_{max} (log ε) = 230 nm (3.85), 281 nm (3.47); IR (ATR): ν = 3359m, 2922m, 2853m, 1633m, 1592m, 1525s, 1464m, 1428w, 1370m, 1285m, 1253s, 1210s, 1152m, 1135s, 1038m, 851m, 828m, 733m, 657m, 554 m cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ = 6.83 (d, J = 8.0 Hz, 1H, 3-H), 6.78 (d, J = 1.9 Hz, 1H, 6-H), 6.72 (*dd*, J = 8.0, 1.9 Hz, 1H, 4-H), 5.98 (t, J = 5.5 Hz, 1H, NH), 5.78–4.79 (m, 1H, OH), 4.40–4.26 (m, 2H, 7-H), 3.83 (s, 3H, 8-H), 2.20 (m, 1H, 10-H), 1.70–1.59 (m, 1H, 11-H_b), 1.42–1.32 (m, 1H, 11-H_a), 1.25 (m, 8H, 12-H, 13-H, 14-H, 15-H), 1.13 (d, J = 6.8 Hz, 3H, 17-H), 0.85 (t, J = 7.0 Hz, 3H, 16-H) ppm; ^{13}C NMR (101 MHz, $CDCl_3$): δ = 176.8 (C-9), 146.9 (C-1), 145.2 (C-2), 130.5 (C-5), 120.7 (C-4), 114.5 (C-3), 110.7 (C-6), 56.0 (C-8), 43.5 (C-7), 41.7 (C-10), 34.5 (C-11), 31.8 (C-14), 29.4 (C-13), 27.6 (C-12), 22.7 (C-15), 18.0 (C-17), 14.1 (C-16) ppm; MS (ESI, MeOH/$CHCl_3$, 4:1): *m/z* (%) = 292 (100 %, $[M-H]^-$); anal. calcd for $C_{17}H_{27}NO_3$ (293.41): C 69.59, H 9.28, N 4.77; found: C 69.32, H 9.54, N 4.58.

Data for **37**: white solid; m.p. 81–82 °C; R_F = 0.55 (SiO_2, hexanes/EtOAc, 4:6); UV–Vis (MeOH): λ_{max} (log ε) = 274 nm (3.21); IR (ATR): ν = 3307m, 2957m, 2924m, 1854m, 1746s, 1641s, 1606m, 1550m, 1515m, 1465m, 1355w, 1290m, 1276m, 1158s, 1140s, 1122s, 1036s, 941w, 865w, 811w, 745m, 721m, 705m, 646w, 554w cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ = 6.94 (d, J = 8.0 Hz, 1H, 4-H), 6.88 (d, J = 1.9 Hz, 1H, 6-H), 6.82 (*dd*, J = 8.0, 1.9 Hz, 1H, 3-H), 6.10–5.99 (m, 1H, NH), 4.47–4.38 (m, 2H, 7-H), 3.78 (s, 3H, 8-H), 2.78–2.62 (m, 1H, 19-H), 2.33–2.18 (m, 1H, 10-H), 1.87–1.75 (m, 1H, 20-H_b), 1.73–1.63 (m, 1H, 11-H_b), 1.59–1.48 (m, 1H, 20-H_a), 1.46–1.37 (m, 2H, 11-H_a, 21-H_b), 1.29 (d, J = 7.0 Hz, 3H, 26-H), 1.37–1.21 (m, 15H, 12-H, 13-H, 14-H, 15-H, 21-H_a, 22-H, 23-H, 24-H), 1.17 (d, J = 6.9 Hz, 3H, 17-H), 0.91–0.84 (m, 6H, 16-H, 25-H) ppm; ^{13}C NMR (101 MHz, $CDCl_3$): δ = 177.1 (C-9), 175.1 (C-18), 151.5 (C-1), 139.5 (C-2), 137.2 (C-5), 123.0 (C-4), 120.1 (C-3), 112.2 (C-6), 77.5, 77.4, 77.2, 76.8, 55.9 (C-8), 43.6 (C-7), 41.7 (C-10), 39.7 (C-19), 39.6, 34.5 (C-11), 34.0 (C-20), 31.9 (C-23), 31.9 (C-14), 29.4 (C-13), 29.4 (C-22), 27.6 (C-12), 27.2 (C-21), 22.8 (C-15), 22.7 (C-24), 18.0 (C-17), 17.3 (C-26), 14.2 (C-25), 14.2 (C-16) ppm; MS (ESI, MeOH/$CHCl_3$, 4:1): *m/z* (%) = 432 (100 %, $[M-H]^-$); anal. calcd for $C_{26}H_{43}NO_4$ (433.63): C 72.02, H 10.00, N 3.23; found: C 71, 74, H 10.29, N 3.02.

CRediT authorship contribution statement

Niels V. Heise: Writing – review & editing, Writing – original draft, Investigation. **Jeremy Quast:** Writing – review & editing, Writing – original draft, Investigation. **René Csuk:** Writing – review & editing, Writing – original draft, Validation, Supervision, Investigation, Conceptualization.

Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

Data availability

No data was used for the research described in the article.

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