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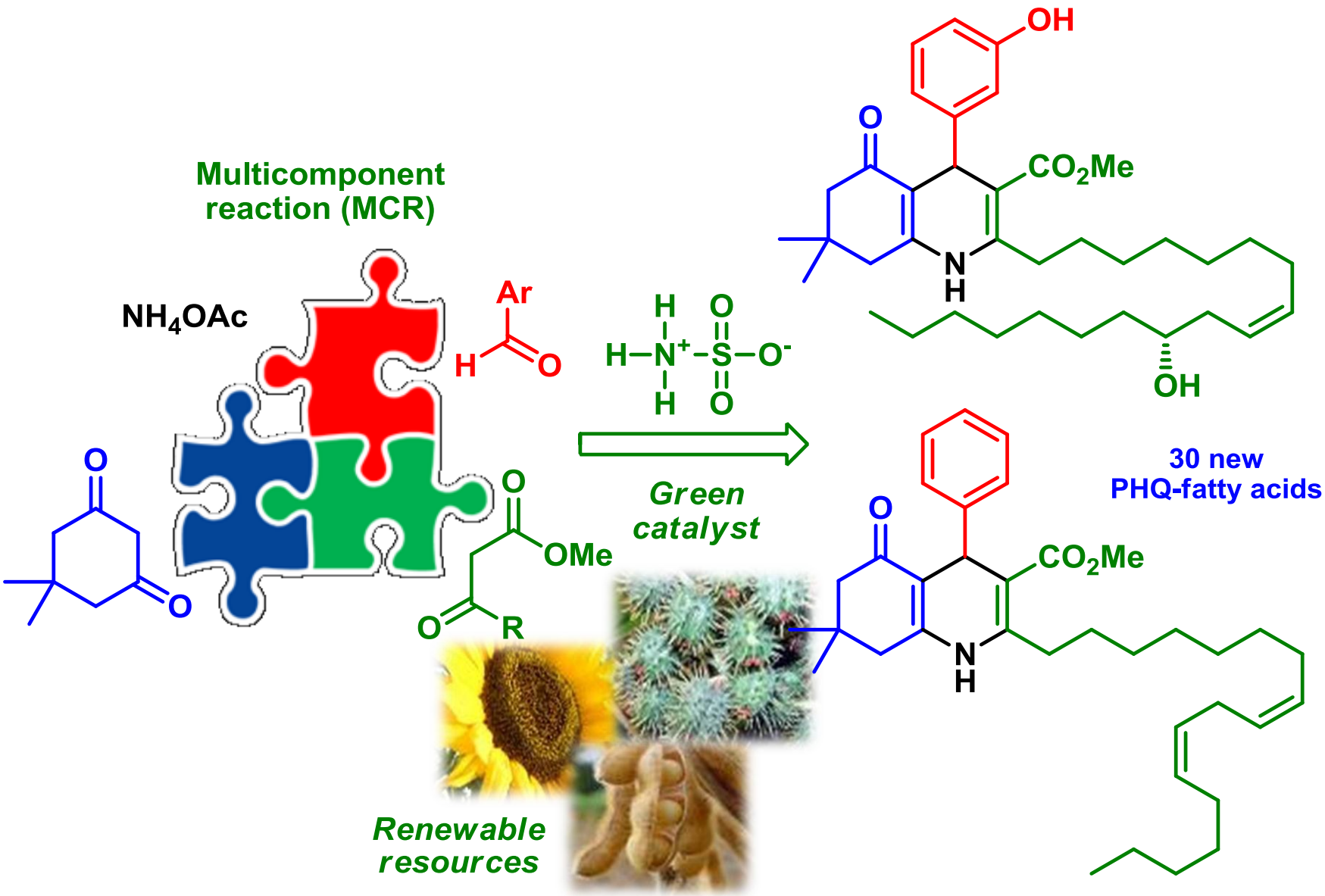

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Multicomponent synthesis of novel hybrid PHQ-fatty acids

H. D. Fontecha-Tarazona[a], R. C. Brinkerhoff[a], P. M. de Oliveira[a], S. B. Rosa[a], D. C. Flores[a], C. Da R. Montes D'Oca[b], D. Russowsky[b] and M. G. Montes D'Oca.*[a]

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Multicomponent reactions as methods for green synthesis are important pathways for obtaining of pharmacological compounds. In this work, an efficient synthesis of new fatty Hantzsch derivative compounds using a four-component reaction is described. We demonstrate for the first time a fatty acid polyhydroquinoline (hybrid PHQ-fatty acids) synthesis from renewable resources containing C16 and C18 saturated and unsaturated fatty chains, including the ricinoleic acid (12-hydroxy-9-*cis*-octadecenoic acid), the major constituent of castor oil. The experimental results demonstrate that the best value for charging the sulfamic acid was 20 mol% and that thirty new hybrids PHQ-fatty acids were synthesised in good yields.

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† Electronic supplementary information (ESI) available: [^{1}H and ^{13}C NMR analysis for all products]. See DOI:

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Introduction

Multicomponent reactions (MCRs)[1] combine at least three reactants in one pot to generate a product containing most of the atoms of the starting materials. According to Orru *et al.* their atom economy, efficiency, mild conditions, high convergence and concomitant step economy in combination with their general compatibility with green solvents would justify a central place in the toolbox of sustainable synthetic methodologies.[1a] MCRs, such as the Biginelli[2] or Hantzsch[3] reactions, provide access to a wide variety of important compounds. The Hantzsch reaction is a prominent MCR that produces an interesting class of nitrogen-based heterocycles, the 1,4-dihydropyridines (1,4-DHPs). 1,4-DHPs such as nifedipine (**1**) and others derivatives are well known as calcium channel blockers and have emerged as one of the most important class of drugs for the treatment of hypertension (Figure 1).[4] This class of compounds shows a range of biological properties, such as antituberculosis, antiviral, antileishmanial, antitrypanosomal, and anticancer activities.[4-8]

According to the literature, photoactive 2-(2'-hydroxyphenyl)benzoxazole-1,4-dihydropyridine (HBO-DHP) dyads were obtained by a multicomponent Hantzsch reaction using a fluorescent aldehyde, a 1,3-dicarbonylic compound and ammonium acetate. The novel fluorescent compounds were obtained as stable solids with absorption in the UV region and emission in the blue-green region.[9]

Polyhydroquinolines (**2**, PHQs, Figure 1) are the unsymmetrical derivatives of 1,4-dihydropyridines, and many methodologies are reported for their synthesis.[10] In recent years, much consideration has been given to the synthesis of polyhydroquinoline compounds due to their broad therapeutic and pharmacological significance.[11] Overall, these compounds exhibit different medicinal functions, acting as antimalarial, antibacterial, and antitubercular agents, and screening hypoglycemic and antidyslipidemic with impressive cytotoxic activity, which make them potential targets for a wide variety of applications.[12-14]

The method for synthesis of PHQs involves a multicomponent Hantzsch reaction of an aldehyde with cyclic 1,3-diketone, ethyl acetoacetate, and ammonia acetate in an acid catalyst.[4,15] Alternatively, the Hantzsch reaction for the synthesis of polyhydroquinolines was recently studied using crosslinked poly (AMPS-co-AA),[16] magnetic Fe_3O_4 nanoparticles,[17] Brönsted ionic liquid,[18] $[TBA]_2[W_6O_{19}]$,[19] visible light irradiation in ethyl-L-lactate-water,[20] microwave irradiation,[21] organocatalysts,[22] ZnO-beta zeolite,[23] *p*-TSA[24] and vanadium dodecylamino phosphate.[25] However, these methods suffer from drawbacks, such as the use of complex metal catalysts, the use of expensive reagents, difficult workup, corrosion problems, effluent pollution and non-recoverable catalysts.

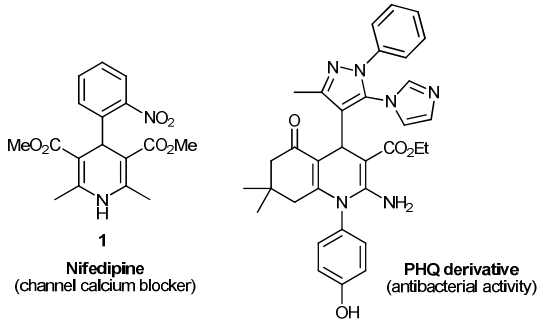


Figure 1. Synthetic bioactive Hantzsch adducts.

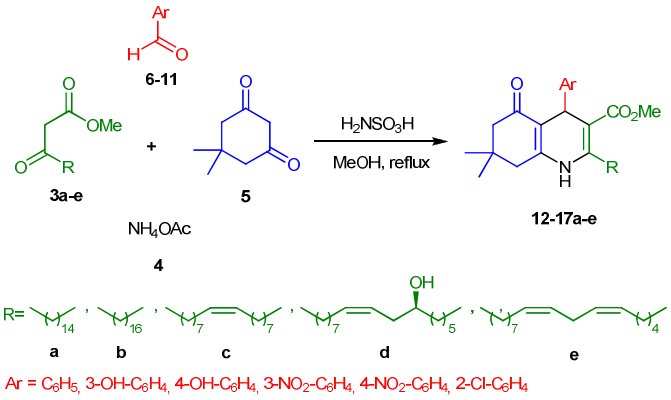
Therefore, the use of an efficient, cost effective, and environmentally benign protocol for the synthesis of PHQs could overcome these drawbacks. In this regard, sulfamic acid (H_2NSO_3H) has attracted great interest due to its low toxicity, ease of handling, low cost, relative stability, non-volatility, non-hygroscopic nature, non-corrosive nature and high performance as a green catalyst in organic synthesis.[26-29] Sulfamic acid and methanol, as an organic reaction promoter system, was proven to have remarkable efficiency due a synergistic effect of sulfamic acid in zwitterionic form in methanol, as demonstrated in the synthesis of quinoxalines,[30] benzimidazole derivatives[31] and 2,3-dihydroquinazolinones.[32] According to the literature, an efficient approach to 1,4-dihydropyridines containing novel substituted pyrazole involved the synthesis via a three-component reaction of pyrazolyl aldehyde, β-ketoester, and ammonium acetate under sulfamic acid catalysis.[33]

Hybrid drugs and multifunctional drugs have recently gained much attention.[34, 35] The goal of developing such hybrid drugs is to create a new chemical entity that is able to modulate biological processes as well as one with completely new activity or multiple, combined activities.

Recently, we described the first synthesis of fatty acid analogues of dihydropyrimidinones (hybrids DHPM-fatty acids) derived from renewable resources using the Biginelli multicomponent protocol.[35] The antiproliferative activity was evaluated against two glioma cell lines (C6 rat and U-138-MG human). The DHPM-fatty acids reduced glioma cell viability. These results suggested that the

hybrids DHPMs derived respectively from palmitic and oleic acids represent promising candidates for the treatment of glioma.

In a continuation of our studies aimed at devising the synthesis of new compounds from renewable resources[35-39] and the development of greener approaches for the synthesis of hybrid compounds, we report here a convenient synthesis of new hybrids of fatty acids polyhydroquinolines (PHQ-fatty acids). In addition, this work investigated for the first time the synthesis of 30 new PHQ-fatty acids **12-17a-e** 2-substituted from palmitic (C16:0), stearic (C18:0), oleic (*cis*-C18:1), linoleic (*cis, cis*-C18:2) and ricinoleic (*cis*-C18:1, 12-OH) acids. The PHQ-fatty acids **12-17a-e** were synthesised through a one-pot four-component reaction of fatty *β*-ketoester **3a-e**, different aromatic aldehydes **6-11**, dimedone (**5**) and ammonium acetate (**4**) using sulfamic acid (H_2NSO_3H) catalyst in methanol (Scheme 1).

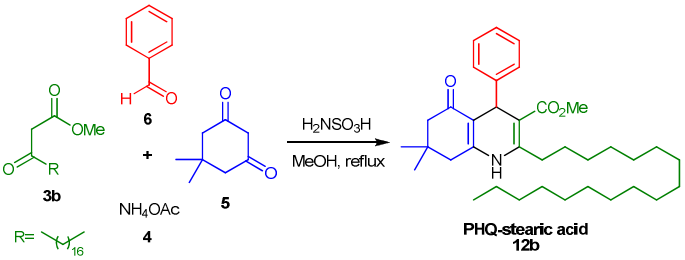


Scheme 1. Synthesis of novel PHQs-fatty acids **12-17a-e** via a Hantzsch four-component reaction using a green catalyst.

Results and discussion

The synthesis of fatty *β*-ketoester **3a-e** was realised in according to previous work.[40] To optimise the multicomponent reaction conditions, a set of experiments was realised using stearic *β*-ketoester **3b** as a model and sulfamic acid as the catalyst. Initially, polyhydroquinoline **12b** was synthesised by reaction of **3b**, benzaldehyde (**6**), dimedone (**5**) and ammonium acetate (**4**) in the presence of 20 mol% of H_2NSO_3H in methanol at reflux (Scheme 2). However, in this experimental condition, the TLC of the reaction mixture revealed the presence of starting material after four hours and the **12b** was isolated in a poor yield (Table 1, entry 1). Afterwards, the synthesis of polyhydroquinoline **12b** was investigated under different experimental conditions, such as reaction time and catalysis loading (Table 1).

The reactions were performed for different times and were also monitored using TLC every 4 hours. After 24 hours of reaction in 20 mol% of sulfamic acid, the lack of presence of the starting reagents was observed. In this case, polyhydroquinoline **12b** was purified by column chromatography and isolated at a good yield (Table 1, entry 3). In the first set of experiments (Table 1, entries 1-4), for the same amount catalyst, the time was found to be a determining factor in the yield of product formed, with increasing the time enabling an improvement in the product yield. In addition, the efficiency of sulfamic acid was evaluated. The amounts of catalyst loading were varied: 5, 10, or 30 mol% (Table 1, entries 5-7). These experiments demonstrate that the best value for charging the sulfamic acid was 20% and that the higher percentage of catalysts did not produce higher yields.



Scheme 2. Synthesis of the PHQ-stearic acid derivative **12b** catalysed by H_2NSO_3H.

Table 1. Synthesis of **12b** under different experimental conditions.

Entry	H_2NSO_3H (mol%)	Time (h)	12b, Yield (%)
1	20%	4	31
2	20%	12	51
3	20%	24	83
4	20%	36	80
5	5%	24	48
6	10%	24	55
7	30%	24	81

Next, the efficiency of the protocol was evaluated using different aromatic aldehydes - with donor and electron withdrawing groups - and different families of fatty acid chains as reagents.

The design of the PHQ derivatives was based on the natural availability of the fatty acids derived from renewable resources containing C16 and C18, i.e., saturated and unsaturated, fatty chains. In addition, the derivative from ricinoleic acid (12-hydroxy-9-*cis*-octadecenoic acid), which is the major constituent (80%–90%) of castor oil (*Ricinus comunnis*)[41] and is an uncommon fatty acid that contains a double bond and a hydroxyl group, was synthesised. Recently, ricinoleic acid has been used for the synthesis of different kinds of polymers, dendrimers and polyamides using the Passerini and Ugi multicomponent reactions.[42-44]

Thus, the hybrid PHQ-fatty acids **12-17a-e** were synthesised in good yields from the respective *β*-ketoesters **3a-e** (Scheme 1, Table 2). The products **12-17a-e** were purified using column

chromatography and characterised by the usual spectroscopic methods, including infrared (IR) spectroscopy, in addition to proton (^{1}H NMR) and carbon (^{13}C NMR) nuclear magnetic resonance and CHN elemental analysis.

Next, the partition coefficients (Clog P), as a measure of lipophilicity, from the new PHQs-fatty acids were investigated. The lipophilicity is a physicochemical parameter, which plays an important role in biological activity and drug design.

Thus, the Clog P values of the PHQs-fatty acids **12-17a-e** were calculated to provide an estimate of their lipophilicity. The results demonstrated that the increased lipophilicity (Clog P = 5.9–10.34) compared to the Clog P values of correspondent PHQs (Clog P = 1–3.04) are not fatty derivatives. The lipophilicities of PHQ-fatty acids are indicative of compounds with poor water solubility and high lipophilicity.

Previously, we reported the synthesis of new fatty acid isoniazid (INH-fatty acids) and demonstrated that the fatty acid chain is of fundamental importance to biological activity, most likely facilitating the permeability of INH-fatty acids in bacterial cells, suggesting that the increased lipophilicity of isoniazid plays an important role in its antimycobacterial activity.[36] Among the tested derivatives, INH derived from palmitic acid could represent a prototype of a new anti-TB drug because it exhibited good MIC values against all the studied strains.

Conclusions

In summary, we developed a simple and efficient procedure for the synthesis of several new fatty acid polyhydroquinolines (PHQ-fatty acids) via four-component condensation of fatty β–ketoesters, aldehydes, dimedone and ammonium acetate using sulfamic acid as an inexpensive and nontoxic catalyst along a greener pathway.

Finally, the synthesis using a green catalyst, along with the use of a renewable feedstock with a directed synthesis for obtaining the compounds with high complexity and value, targeting the pharmacological use, demonstrate the high potential of the approach in both environmental protection and in synthetic chemistry. The biological analyses of these new compounds are currently in progress.

Experimental

Apparatus and Chemistry

The fatty acids and sulfamic acid (98 wt.%) were supplied by Aldrich Chemical Co., and the methanol was supplied by Merck. The ricinoleic acid (*cis*-C18:1,12-OH) was obtained from castor oil or via castor oil biodiesel hydrolysis.[36] The other reagents were purchased from Aldrich Chemical Co. and used without further purification. All organic solvents used for the synthesis were of analytical grade. Column chromatography was performed using a Silica Gel 60 A (ACROS Organics, 0.035–0.070 mesh). The reactions were monitored using thin-layer chromatography (TLC) performed with plates containing silica gel (Merck 60GF245), and the spots were visualised using iodine. Yields refer to chromatographically and spectroscopically homogeneous materials. The melting points were obtained on a Fisatom 430D apparatus and are uncorrected. Infrared (IR) spectra were measured on a Schimadzu PRESTIGIE-21 FT-IR spectrophotometer. The NMR spectra were recorded using a Varian VNMRS 300 spectrometer (^{1}H at 300 MHz and ^{13}C at 75.5 MHz) in deuterochloroform ($CDCl_3$) as the solvent. The chemical shift data are reported in units of δ (ppm) downfield from tetramethylsilane (TMS), which was used as an internal standard. The coupling constants (^3J) are reported in Hz and refer to apparent peak multiplicities. CHN elemental analysis was used to ascertain the purity (> 95%) of all compounds for which biological data was determined and was performed using a CHN 2400 elemental analyser (Universidade de São Paulo, Brazil).

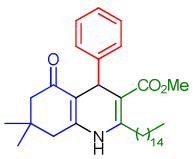
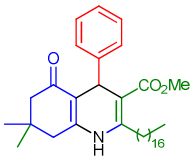
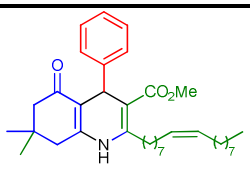
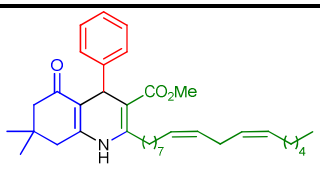
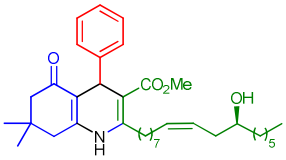
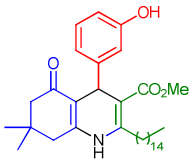
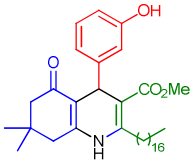
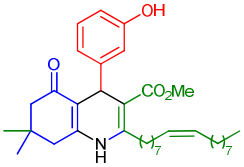
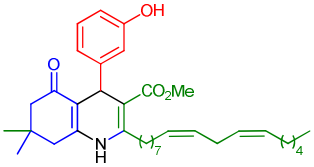
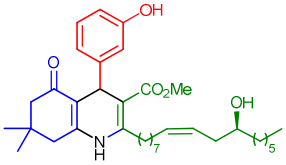
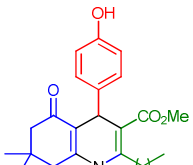
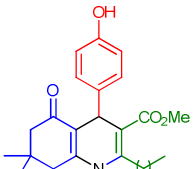
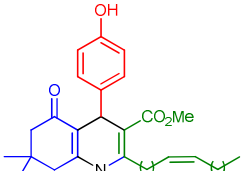
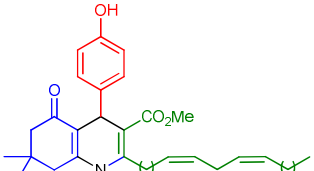
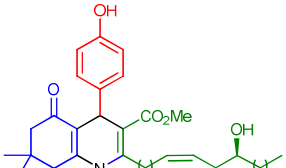
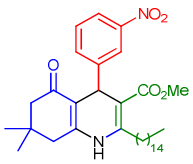
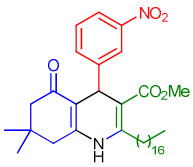
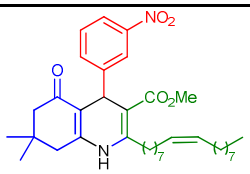
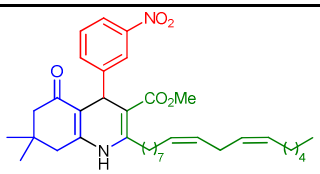
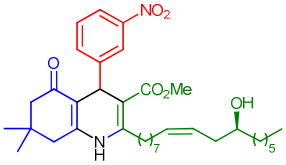
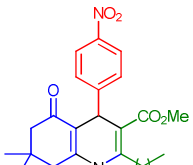
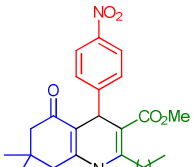
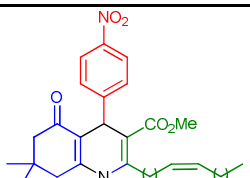
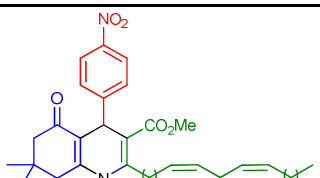
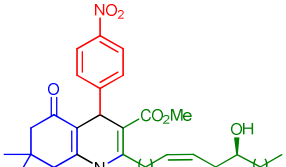
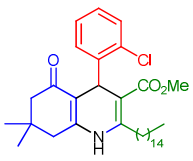
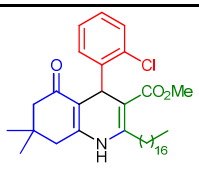
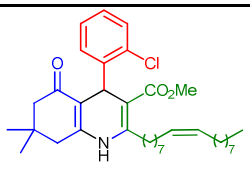
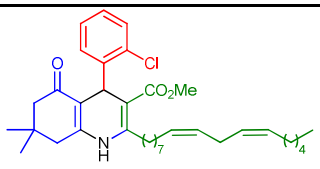
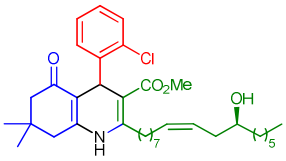
Synthesis

General procedure for the synthesis of fatty polyhydroquinoline derivatives 12-17a-e

Fatty β-ketoester **3a-e** (1 mmol), aromatic aldehydes **6-11** (1 mmol), dimedone (**5**, 1 mmol), ammonium acetate (**4**, 1.5 mmol), and sulfamic acid (0.2 mmol) in 10 mL methanol were charged around the bottom flask. Next, the reaction mixture was stirred and refluxed at 80 °C for 24 hours. The reaction was monitored using TLC by taking hexane:ethyl acetate (60:40) proportion. After completion of the reaction the solvent was removed by reduced pressure, and the residue obtained was purified by flash column chromatography on a silica gel, with the eluent of hexane/ethyl acetate (75:25), to yield fatty polyhydroquinolines **12-17a-e**.

Methyl-7,7-dimethyl-5-oxo-2-pentadecyl-4-phenyl 1,4,5,6,7,8-hexahydroquinoline-3-carboxylate (12a). Yellow solid. Yield: 72%. M.p.: 104–106 °C; IR (film, ν_{max} cm^{-1}): 696, 835, 914, 1072, 1213, 1305, 1386, 1490, 1606, 1708, 2357, 2848, 2922, 3080, 3190, 3265; ^{1}H NMR ($CDCl_3$, 300 MHz): δ (ppm) 7.25 – 6.98 (m, 5H, Ph), 6.19 (s, 1H, NH), 5.00 (s, 1H, CH), 3.53 (s, 3H, O-CH_3), 2.81 – 2.55 (m, 2H, 2CH_2), 2.32 – 2.03 (m, 4H, 2CH_2), 1.66 – 1.46 (m, 2H, CH_2), 1.18 (s, 24H, 12CH_2), 0.99 (s, 3H, CH_3), 0.87 (s, 3H, CH_3), 0.80 (t, J = 6 Hz, 3H, CH_3). ^{13}C NMR ($CDCl_3$, 75 MHz): δ (ppm) 195.4, 167.5, 162.2, 148.0, 146.8, 127.7, 127.4, 126.0, 112.1, 105.2, 53.7, 52.1, 51.0, 47.4, 41.2, 36.8, 33.8, 32.6, 32.5, 32.4, 31.9, 29.7, 29.6, 29.6, 29.5, 29.4, 29.1, 28.6, 28.2, 27.1, 25.6, 24.9, 22.7, 14.1. Anal. Calcd. (%) for $C_{34}H_{51}NO_3$: C, 78.26; H, 9.85; N, 2.68; Found: C, 77.58; H, 10.17; N, 2.90.

Table 2. Structural scope of the synthesised fatty 2-substituted polyhydroquinolines **12-17a-e**.[a]

PHQs-palmitic acid	PHQs-stearic acid	PHQs-oleic acid	PHQs-linoleic acid	PHQs-ricinoleic acid
 **12a, 72%**	 **12b, 83%**	 **12c, 77%**	 **12d, 79%**	 **12e, 73%**
 **13a, 81%**	 **13b, 74%**	 **13c, 80%**	 **13d, 77%**	 **13e, 75%**
 **14a, 75%**	 **14b, 76%**	 **14c, 80%**	 **14d, 75%**	 **14e, 78%**
 **15a, 73%**	 **15b, 75%**	 **15c,73%**	 **15d, 77%**	 **15e, 74%**
 **16a, 70%**	 **16b, 74%**	 **16c, 70%**	 **16d, 71%**	 **16e, 75%**
 **17a, 75%**	 **17b, 85%**	 **17c, 82%**	 **17d, 86%**	 **17e, 71%**

[a] Reaction conditions: fatty β-ketoester **3a-e** (1 mmol), aldehyde **6-11** (1 mmol), dimedone (**5**, 1 mmol) and ammonium acetate (**4**, 1.5 mmol); catalyst: H_2NSO_3H (0.2 mmol); reflux in methanol.

RSC Advances

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Methyl-2-heptadecyl-7,7-dimethyl-5-oxo-4-phenyl-1,4,5,6,7,8-hexahydroquinoline-3-carboxylate (12b): Yellow solid. Yield: 83%. M.p.: 110–112 °C. IR (film, ν_{max} cm^{-1}): 696, 835, 914, 1072, 1213, 1305, 1386, 1490, 1606, 1708, 2357, 2848, 2922, 3080, 3190, 3265; ^{1}H NMR ($CDCl_3$, 300 MHz): δ (ppm) 7.25 – 6.98 (m, 5H, Ph), 6.25 (s, 1H, NH), 5.01 (s, 1H, CH), 3.53 (s, 3H, O-CH_3), 2.82 – 2.56 (m, 2H, CH_2), 2.31 – 2.03 (m, 4H, $2CH_2$), 1.69 – 1.47 (m, 2H, CH_2), 1.18 (m, 28H, $14CH_2$), 0.99 (s, 3H, CH_3), 0.83 (s, 3H, CH_3), 0.81 (t, ^3J = 6 Hz, 3H, CH_3). ^{13}C NMR ($CDCl_3$, 75 MHz): δ (ppm) 196.2, 168.2, 165.6, 149.4, 147.6, 128.6, 128.4, 126.6, 112.4, 105.6, 51.6, 51.4, 49.7, 41.6, 36.9, 34.6, 33.3, 32.6, 30.4, 30.3, 30.2, 30.0, 29.4, 27.7, 26.2, 25.6, 23.3, 14.8. Found: C, 78.6; H, 10.3; N, 2.4. Anal. Calcd. (%) for $C_{36}H_{55}NO_3$: C, 78.64; H, 10.08; N, 2.55; Found: C, 78.55; H, 10.33; N, 2.43.

Methyl-2-[(*Z*)-heptadec-8-en-1-yl]-7,7-dimethyl-5-oxo-4-phenyl-1,4,5,6,7,8-hexahydroquinoline-3-carboxylate (12c): Yellow solid. Yield: 77%. M.p.: 89-91 °C. IR (film, ν_{max} cm^{-1}): 696, 1070, 1219, 1384, 1498, 1606, 1708, 2358, 2852, 2926, 3080, 3209, 3275; ^{1}H NMR ($CDCl_3$, 300 MHz): δ (ppm) 7.34 – 7.06 (m, 5H, Ph), 6.42 (s, 1H, NH), 5.43 – 5.29 (m, 2H, 2CH), 5.09 (s, 1H, CH), 3.61 (s, 3H, O-CH_3), 2.89 – 2.63 (m, 2H, CH_2), 2.39 – 2.12 (m, 4H, $2CH_2$), 2.05 – 1.99 (m, 4H, $2CH_2$), 1.69 – 1.54 (m, 2H, CH_2), 1.28 (m, 20H, $10CH_2$), 1.07 (s, 3H, CH_3), 0.92 (s, 3H, CH_3), 0.89 (t, ^3J = 6 Hz, 3H, CH_3). ^{13}C NMR ($CDCl_3$, 75 MHz): δ (ppm) 195.6, 167.5, 149.2, 148.6, 146.8, 130.0, 129.7, 128.0, 127.7, 126.0, 111.8, 105.4, 51.0, 50.5, 41.5, 41.0, 36.3, 32.7, 29.8, 29.6, (2C), 29.3, (2C), 28.9, 27.2, (2C), 27.0, 23.5, 22.7, 14.1. Anal. Calcd. (%) for $C_{36}H_{53}NO_3$: C, 78.93; H, 9.75; N, 2.56; Found: C, 77.16; H, 10.04; N, 2.42.

Methyl-2-[(8*Z*,11*Z*)-heptadeca-8,11-dien-1-yl]-7,7-dimethyl-5-oxo-4-phenyl-1,4,5,6,7,8-hexahydroquinoline-3-carboxylate (12d): Yellow solid. Yield: 79%. M.p.: 88-90 °C. IR (film, ν_{max} cm^{-1}): 696, 837, 1070, 1147, 1219, 1386, 1498, 1604, 1707, 1938, 2854, 2927, 3080, 3205, 3277; ^{1}H NMR ($CDCl_3$, 300 MHz): δ (ppm) 7.32 – 7.05 (m, 5H, Ph), 6.62 (s, 1H, NH), 5.44 – 5.27 (m, 4H, 4CH), 5.07 (s, 1H, CH), 3.60 (s, 3H, O-CH_3), 2.89 – 2.62 (m, 4H, $2CH_2$), 2.37 – 2.11 (m, 4H, $2CH_2$), 2.09 – 2.00 (m, 4H, $2CH_2$), 1.67 – 1.54 (m, 2H, CH_2), 1.31 (m, 14H, $7CH_2$), 1.06 (s, 3H, CH_3), 0.91 (s, 3H, CH_3), 0.88 (t, ^3J = 6 Hz, 3H, CH_3). ^{13}C NMR ($CDCl_3$, 75 MHz): δ (ppm) 195.5, 167.5, 164.9, 148.4, 146.8, 130.2, 130.0, 127.9, 127.7, 127.2, 126.0, 111.9, 105.1, 53.5, 52.2, 51.0, 50.6, 41.0, 36.2, 32.6, 32.5, 31.4, 29.6 (2C), 29.2(2C), 28.1, 27.1, 27.0, 25.6 (2C), 22.5, 14.0. Anal. Calcd. (%) for $C_{36}H_{51}NO_3$: C, 79.22; H, 9.42; N, 2.57; Found: C, 76.04; H, 9.76; N, 2.31.

Methyl-2-[(*S*)-(*Z*)-11-hydroxyheptadec-8-en-1-yl]-7,7-dimethyl-5-oxo-4-phenyl-1,4,5,6,7,8-hexahydroquinoline-3-carboxylate (12e): Yellow solid. Yield. 73%. M.p.: 76-78 °C. IR (film, ν_{max} cm^{-1}): 696, 839, 1070, 1219, 1384, 1489, 1602, 1707, 2358, 2852, 2926, 3080, 3205, 3278, 3493; ^{1}H NMR ($CDCl_3$, 300 MHz): δ (ppm) 7.29 – 7.25 (m, 2H, Ph), 7.21 – 7.16 (m, 2H, Ph), 7.11 – 7.06 (m, 1H, Ph), 6.20 (s, 1H, NH), 5.62 – 5.52 (m, 1H, CH), 5.44 – 5.35 (m, 1H, CH), 5.06 (s, 1H, CH), 3.65 – 3.57 (m, 1H, CH), 3.59 (s, 3H, O-CH_3), 2.83 – 2.78 (m, 1H, C$\underline{H}_2$), 2.67 – 2.65 (m, 1H, C$\underline{H}_2$), 2.36 – 2.20 (m, 6H, $3CH_2$), 2.17 – 2.04 (m, 2H, CH_2), 1.77 – 1.70 (m, 2H, CH_2), 1.64 – 1.55 (m, 2H, CH_2), 1.51 – 1.43 (m, 2H, CH_2), 1.28 – 1.31 (m, 14H, $7CH_2$), 1.06 (s, 3H, CH_3), 0.90 (s, 3H, CH_3), 0.87 (t, ^3J = 6 Hz, 3H, CH_3). ^{13}C NMR ($CDCl_3$, 75 MHz): δ (ppm) 195.5, 167.5, 164.9, 148.4, 146.8, 133.5, 127.9, 127.7, 126.0, 125.2, 112.0, 105.1, 71.5, 51.0, 50.6, 41.1, 36.8, 36.2, 35.3, 32.5, 31.8, 29.3, 28.5, 27.0, 25.7, 22.6, 14.1. Anal. Calcd. (%) for $C_{36}H_{53}NO_4$: C, 76.69; H, 9.47; N, 2.48; Found: C, 76.03; H, 8.45; N, 2.17.

Methyl-4-(3-hydroxyphenyl)-7,7-dimethyl-5-oxo-2-pentadecyl-1,4,5,6,7,8-hexahydroquinoline-3-carboxylate (13a). Yellow solid. Yield 81%. M.p.: 81-83°C. IR (film, ν_{max} cm^{-1}): 696, 783, 871, 1026, 1072, 1217, 1386, 1487, 1587, 1708, 1915, 2852, 2924, 3076, 3203, 3304, 3429; ^{1}H NMR ($CDCl_3$, 300 MHz): δ (ppm) 7.05 – 6.98 (m, 2H, Ph), 6.91 (s, 1H, OH), 6.80 (d, ^3J = 7.9 Hz, 1H, Ph), 6.60 (d, ^3J = 7.9 Hz, 1H, Ph), 5.05 (s, 1H, CH), 3.62 (s, 3H, O-CH_3), 2.80 – 2.62 (m, 2H, $2CH_2$), 2.32 – 2.12 (m, 4H, $2CH_2$), 1.65 – 1.53 (m, 2H, CH_2), 1.45 – 1.20 (m, 24H, $12CH_2$), 1.01 (s, 3H, CH_3), 0.88 (s, 3H, CH_3), 0.87 (t, ^3J = 6 Hz, 3H, CH_3). ^{13}C NMR ($CDCl_3$, 75 MHz): δ (ppm) 196.6, 168.1, 156.3, 150.3, 149.0, 148.2, 129.1, 119.5, 114.8, 113.5, 111.4, 104.9, 51.2, 50.5, 40.7, 36.2, 32.7, 31.9, 29.7, (2C), 29.5,(2C), 29.2, 28.8, 27.2, 22.7, 14.1. Anal. Calcd. (%) for $C_{34}H_{51}NO_4$: C, 75.94; H, 9.56; N, 2.60; Found: C, 74.84; H, 9.74; N, 2.46.

Methyl-2-heptadecyl-4-(3-hydroxyphenyl)-7,7-dimethyl-5-oxo-1,4,5,6,7,8-hexahydroquinoline-3-carboxylate (13b): Yellow solid. Yield: 74%. M.p.: 110-112 °C. IR (film, ν_{max} cm^{-1}): 696, 785, 871, 935, 1072, 1219, 1386, 1487, 1587, 1707, 1915, 2607, 2850, 2924, 3080, 3190, 3305; ^{1}H NMR ($CDCl_3$, 300 MHz): δ (ppm) 7.06 – 7.02 (m, 2H, Ph), 6.97 (s, 1H, OH), 6.84 (d, ^3J = 7.9 Hz, 1H, Ph), 6.61 (d, ^3J = 7.9 Hz, 1H, Ph), 5.09 (s, 1H, CH), 3.64 (s, 3H, O-CH_3), 2.81 – 2.57 (m, 2H, CH_2), 2.31 – 2.11 (m, 4H, $2CH_2$), 1.69 – 1.45 (m, 2H, CH_2), 1.35 – 1.20 (m, 28H,

14CH_2), 1.01 (s, 3H, CH_3), 0.90 (s, 3H, CH_3), 0.89 (t, ^3J = 6 Hz, 3H, CH_3). ^{13}C NMR ($CDCl_3$, 75 MHz): δ (ppm) 196.4, 168.0, 164.9, 156.2, 148.9, 148.1, 129.1, 119.4, 114.8, 113.2, 111.4, 104.8, 51.2, 50.5, 40.7, 36.1, 32.6, 31.9, 29.7, 29.4, 29.3, 29.2, 28.7, 27.1(2C)/, 22.6, 14.1. Anal. Calcd. (%) for $C_{36}H_{55}NO_4$: C, 76.42; H, 9.80; N, 2.48; Found: C, 75.84; H, 10.54; N, 2.42.

Methyl-2-[(*Z*)-heptadec-8-en-1-yl]-4-(3-hydroxyphenyl)-7,7-dimethyl-5-oxo-1,4,5,6,7,8-hexahydroquinoline-3-carboxylate (13c): Yellow solid. Yield: 80%. M.p.: 91-93 °C. IR (film, ν_{max} cm^{-1}): 603, 698, 779, 881, 1068, 1219, 1388, 1483, 1579, 1707, 1840, 1919, 2852, 2924, 3292; ^{1}H NMR ($CDCl_3$, 300 MHz): δ (ppm) 7.07 – 7.00 (m, 2H, Ph), 6.94 (s, 1H, OH), 6.82 (d, ^3J = 7.3 Hz, 1H, Ph), 6.76 (s, 1H, NH), 6.60 (d, ^3J = 10.5 Hz, 1H, Ph), 5.42 – 5.29 (m, 2H, 2CH), 5.08 (s, 1H, CH), 3.63 (s, 3H, O-CH_3), 2.80 – 2.63 (m, 2H, CH_2), 2.31 – 2.10 (m, 4H, 2CH_2), 2.07 – 1.96 (m, 4H, 2CH_2), 1.67 – 1.53 (m, 2H, CH_2), 1.39 – 1.20 (m, 20H, 10CH_2), 1.03 (s, 3H, CH_3), 0.90 (s, 3H, CH_3), 0.88 (t, ^3J = 6 Hz, 3H, CH_3). ^{13}C NMR ($CDCl_3$, 75 MHz): δ (ppm) 196.4, 167.8, 156.1, 148.6, 148.0, 130.0, 129.8, 129.2, 119.3, 114.9, 113.5, 111.3, 105.5, 51.3, 50.1, 40.9, 36.1, 32.7, 31.9, 29.8, 29.7, 29.6, 29.4, 29.3, 29.3, 29.2, 28.7, 27.3, 27.2, 22.7, 14.2. Anal. Calcd. (%) for $C_{36}H_{53}NO_4$: C, 76.69; H, 9.47; N, 2.48; Found: C, 76.15; H, 9.98; N, 2.22.

Methyl-2-[(8*Z*,11*Z*)-heptadeca-8,11-dien-1-yl]-4-(3-hydroxyphenyl)-7,7-dimethyl-5-oxo-1,4,5,6,7,8-hexahydroquinoline-3-carboxylate (13d): Yellow solid. Yield 77%. M.p.: 88-90 °C. IR (film, ν_{max} cm^{-1}): 698, 785, 873, 1072, 1219, 1386, 1487, 1589, 1707, 1734, 1840, 1919, 2854, 2927, 3298, 3498; ^{1}H NMR ($CDCl_3$, 300 MHz): δ (ppm) 7.05 – 7.00 (m, 2H, Ph), 6.92 (s, 1H, OH), 6.81 (s, 1H, NH) 6.79 (m, 1H, Ph), 6.60 (d, *J* = 10.3 Hz, 1H, Ph), 5.44 – 5.26 (m, 4H, 4CH), 5.06 (s, 1H, CH), 3.62 (s, 3H, O-CH_3), 2.85 – 2.65 (m, 4H, 2CH_2), 2.32 – 2.12 (m, 4H, 2CH_2), 2.09 – 1.99 (m, 4H, 2CH_2), 1.66 – 1.52 (m, 2H, CH_2), 1.28 (m, 14H, 7CH_2), 1.43 – 1.20 (m, 3H, CH_3), 0.89 (s, 3H, CH_3), 0.88 (t, ^3J = 6 Hz, 3H, CH_3). ^{13}C NMR ($CDCl_3$, 75 MHz): δ (ppm) 196.3, 167.7, 164.9, 155.9, 148.4, 148.2, 130.2, 130.0, 129.1, 128.0, 127.8, 119.5, 114.9, 114.5, 113.3, 111.6, 105.1, 53.4, 52.5, 51.2, 50.4, 40.9, 36.0, 32.7, 31.5, 29.6, 29.1, 28.6, 27.2, 25.6, 22.5, 14.1. Anal. Calcd. (%) for $C_{36}H_{51}NO_4$: C, 76.97; H, 9.15; N, 2.47; Found: C, 74.53; H, 9.48; N, 1.99.

Methyl-2-[(*S*)-(*Z*)-11-hydroxyheptadec-8-en-1-yl]-4-(3-hydroxyphenyl)-7,7-dimethyl-5-oxo-1,4,5,6,7,8-hexahydroquinoline-3-carboxylate (13e): Yellow solid. Yield: 75%. M.p.: 93-95 °C. IR (film, ν_{max} cm^{-1}): 696, 837, 1070, 1170, 1217, 1276, 1309, 1485, 1601, 1707, 1938, 2854, 2929, 3082, 3293; ^{1}H RMN ($CDCl_3$, 300 MHz): δ (ppm) 7.09 – 7.05 (m, 1H, Ph), 6.88 – 6.83 (m, 2H, Ph), 6.60 (d, ^3J = 10.3 Hz, 1H, Ph), 6.29 (s, 1H, NH), 5.62 – 5.56 (m, 1H, CH), 5.46 – 5.39 (m, 1H, CH), 5.09 (s, 1H, CH), 3.69 – 3.66 (m, 1H, CH), 3.63 (s, 3H, O-CH_3), 2.86 – 2.75 (m, 1H, C$\underline{H}_2$), 2.68 – 2.60 (m, 1H, C$\underline{H}_2$), 2.35 – 2.28 (m, 6H, 3CH_2), 2.24 – 2.20 (m, 2H, CH_2), 1.70 – 1.64 (m, 4H, 2CH_2), 1.52 – 1.49 (m, 2H, CH_2), 1.30 – 1.28 (m, 14H, 7CH_2), 1.08 (s, 3H, CH_3), 0.94 (s, 3H, CH_3), 0.90 (t, ^3J = 6 Hz, 3H, CH_3). ^{13}C NMR ($CDCl_3$, 75 MHz): δ (ppm) 195.5, 167.5, 164.9, 148.4, 146.8, 133.5, 127.9, 127.7, 126.0, 125.2, 112.0, 105.1, 71.5, 51.0, 50.6, 41.1, 36.8, 36.2, 35.3, 32.5, 31.8, 29.3, 28.5, 27.0, 25.7, 22.6, 14.1. Anal. Calcd. (%) for $C_{36}H_{53}NO_5$: C, 74.57; H, 9.21; N, 2.42; Found: C, 74.68; H, 8.47; N, 2.14.

Methyl-4-(4-hydroxyphenyl)-7,7-dimethyl-5-oxo-2-pentadecyl-1,4,5,6,7,8-hexahydroquinoline-3-carboxylate (14a): Yellow solid. Yield: 75%. M.p.: 71-73 °C. IR (film, ν_{max} cm^{-1}): 696, 783, 871, 1026, 1072, 1217, 1386, 1487, 1587, 1708, 1915, 2852, 2924, 3076, 3203, 3304, 3429; ^{1}H NMR ($CDCl_3$, 300 MHz): δ (ppm) 7.98 (s, 1H, NH), 7.25 (s, 1H, OH), 7.09 (d, ^3J = 8.3 Hz, 2H, Ph), 6.59 (d, ^3J = 8.3 Hz, 2H, Ph), 4.99 (s, 1H, CH), 3.61 (s, 3H, O-CH_3), 2.77 – 2.71 (m, 2H, 2CH_2), 2.31 – 2.10 (m, 4H, 2CH_2), 1.70 – 1.51 (m, 2H, CH_2), 1.40 – 1.20 (m, 24H, 12CH_2), 0.99 (s, 3H, CH_3), 0.92 (s, 3H, CH_3), 0.87 (t, ^3J = 6 Hz, 3H, CH_3). ^{13}C NMR ($CDCl_3$, 75 MHz): δ (ppm) 196.7, 167.9, 154.6, 150.3, 148.4, 138.5, 129.5, 129.3, 128.0, 127.3, 115.8, 114.3, 111.7, 111.6, 105.1, 52.1, 51.3, 50.6, 40.6, 36.4, 36.0, 34.8, 32.5, 31.8, 30.6, 30.4, 29.6, 29.5, 29.3, 28.7, 27.8, 26.8, 22.6, 14.0. Anal. Calcd. (%) for $C_{34}H_{51}NO_4$: C, 74.94; H, 9.56; N, 2.60; Found: C, 75.42; H, 9.90; N, 2.37.

Methyl-2-heptadecyl-4-(4-hydroxyphenyl)-7,7-dimethyl-5-oxo-1,4,5,6,7,8-hexahydroquinoline-3-carboxylate (14b): Yellow solid. Yield: 76%. M.p.: 72-74 °C. IR (film, ν_{max} cm^{-1}): 696, 785, 871, 935, 1072, 1219, 1386, 1487, 1587, 1707, 1915, 2607, 2850, 2924, 3080, 3190, 3305; ^{1}H NMR ($CDCl_3$, 300 MHz): δ (ppm) 7.10 (d, ^3J = 8.8 Hz, 2H, Ph), 6.59 (d, ^3J = 8.6 Hz, 2H, Ph), 6.49 (s, 1H, NH), 5.00 (s, 1H, CH), 3.62 (s, 3H, O-CH_3), 2.75 (t, ^3J = 7.9 Hz, 2H, CH_2), 2.33 – 2.15 (m, 4H, 2CH_2), 1.67 – 1.57 (m, 2H, CH_2), 1.38 – 1.27 (m, 28H, 14CH_2), 1.05 (s, 3H, CH_3), 0.92 (s, 3H, CH_3), 0.90 (t, ^3J = 6 Hz, 3H, CH_3). ^{13}C NMR ($CDCl_3$, 75 MHz): δ (ppm) 196.5, 167.8, 154.6, 149.2, 148.0, 138.6, 128.8, 115.1, 112.2, 105.8, 51.1, 50.6, 41.0, 35.5, 32.7, 32.5, 31.9, 29.7, 29.6, 29.5, 29.4, 29.3, 28.7, 27.0, 22.7, 14.1. Anal. Calcd. (%) for $C_{36}H_{55}NO_4$: C, 76.42; H, 9.80; N, 2.48; Found: C, 75.71; H, 10.21; N, 2.33.

Methyl-2-[(*Z*)-heptadec-8-en-1-yl)]-4-(4-hydroxyphenyl)-7,7-dimethyl-5-oxo-1,4,5,6,7,8-hexahydroquinoline-3-carboxylate (14c): Yellow solid. Yield: 80%. M.p.: 76-78 °C. IR (film, ν_{max} cm^{-1}): 603, 698, 779, 881, 1068, 1219, 1388, 1483, 1579, 1707, 1840, 1919, 2852, 2924, 3292; ^{1}H NMR ($CDCl_3$, 300 MHz): δ (ppm) 7.09 (d, ^3J = 8.6 Hz, 2H, Ph), 6.59 (d, ^3J = 8.3 Hz, 2H, Ph), 5.41 – 5.30 (m, 2H, 2CH), 5.00 (s, 1H, CH), 3.61 (s, 3H, O-CH_3), 2.79 – 2.72 (m, 2H, CH_2), 2.33 – 2.13 (m, 4H, 2CH_2), 2.05 – 2.00 (m, 4H, 2CH_2), 1.67 – 1.57 (m, 2H, CH_2), 1.45 – 1.25 (m, 20H, 10CH_2), 1.04 (s, 3H, CH_3), 0.92 (s, 3H, CH_3), 0.90 (t, ^3J = 6 Hz, 3H, CH_3). ^{13}C NMR ($CDCl_3$, 75 MHz): δ (ppm) 196.6, 167.9, 154.6, 149.5, 148.1, 138.6, 130.3, 130.0, 129.8, 128.8, 115.2, 112.1, 105.8, 51.1, 50.6, 41.0, 35.1, 32.7, 32.5, 31.9, 31.5, 29.8,

29.7, 29.5, 29.4, 29.3, 28.7, 27.2, 27.0, 22.7, 14.4. Anal. Calcd. (%) for $C_{36}H_{53}NO_4$: C, 76.69; H, 9.47; N, 2.48; Found: C, 75.94; H, 9.54; N, 2.41.

Methyl-2-[(8*Z*,11*Z*)-heptadeca-8,11-dien-1-yl]-4-(4-hydroxyphenyl)-7,7-dimethyl-5-oxo-1,4,5,6,7,8-hexahydroquinoline-3-carboxylate (14d): Yellow solid. Yield: 75%. M.p.: 62-64 °C; IR (film, ν_{max} cm^{-1}): 698, 785, 873, 1073, 1219, 1384, 1486, 1611, 1703, 2885, 2928, 2964, 3011, 3222, 3303; ^{1}H NMR ($CDCl_3$, 300 MHz): δ (ppm) 7.10 (d, ^3J = 8.6 Hz, 2H, Ph), 6.60 (d, ^3J = 8.6 Hz, 2H, Ph), 6.50 (s, 1H, NH), 5.44 – 5.30 (m, 4H, 4CH), 4.99 (s, 1H, CH), 3.62 (s, 3H, O-CH_3), 2.81 – 2.72 (m, 4H, 2CH_2), 2.33 – 2.14 (m, 8H, 4CH_2), 2.09 – 2.04 (m, 4H, 2CH_2), 1.65 – 1.57 (m, 2H, CH_2), 1.45 – 1.32 (m, 10H, 5CH_2), 1.04 (s, 3H, CH_3), 0.93 (s, 3H, CH_3), 0.90 (t, ^3J = 6 Hz, 3H, CH_3). ^{13}C NMR ($CDCl_3$, 75 MHz): δ (ppm) 196.5, 167.8, 165.0, 154.5, 149.3, 147.9, 138.6, 131.0, 129.4, 128.1, 127.9, 127.2, 127.1, 127.0, 115.9, 114.3, 112.07, 105.9, 105.8, 52.2, 51.4, 50.7, 49.9, 36.1, 35.9, 32.7, 31.5, 29.6, 29.3, 29.2, 28.6, 27.3, 26.9, 25.6, 22.5, 14.1. Anal. Calcd. (%) for $C_{36}H_{51}NO_4$: C, 76.97; H, 9.15; N, 2.49; Found: C, 73.11; H, 8.87; N, 2.17.

Methyl-2-[(*S*)-(*Z*)-11-hydroxyheptadec-8-en-1-yl]-4-(4-hydroxyphenyl)-7,7-dimethyl-5-oxo-1,4,5,6,7,8-hexahydroquinoline-3-carboxylate (14e): Yellow solid. Yield: 78%. M.p.: 91-93 °C. IR (film, ν_{max} cm^{-1}): 698, 785, 873, 1072, 1219, 1384, 1487, 1609, 1707, 1734, 2852, 2924, 3082, 3217, 3299. ^{1}H RMN ($CDCl_3$, 300 MHz): δ (ppm) 7.08 (d, ^3J = 8.6 Hz, 2H, Ph), 6.61 (s, 1H, NH), 6.59 (d, ^3J = 8.6 Hz, 2H, Ph), 5.59 – 5.52 (m, 1H, CH), 5.42 – 5.35 (m, 1H, CH), 4.98 (s, 1H, CH), 3.679 – 3.63 (m, 1H, CH), 3.60 (s, 3H, O-CH_3), 2.87 – 2.83 (m, 1H, CH_2), 2.65 – 2.61 (m, 1H, CH_2), 2.30 – 2.21 (m, 6H, 3CH_2), 2.17 – 2.02 (m, 4H, 2CH_2), 1.65 – 1.61 (m, 2H, CH_2), 1.55 – 1.48 (m, 2H, CH_2), 1.40 – 1.27 (m, 14H, 7CH_2), 1.03 (s, 3H, CH_3), 0.89 (s, 3H, CH_3), 0.88 (t, ^3J = 6 Hz, 3H, CH_3). ^{13}C NMR ($CDCl_3$, 75 MHz): δ (ppm) 196.3, 167.8, 167.3, 154.6, 149.1, 148.2, 141.2, 138.7, 133.6, 130.0, 129.8, 128.8, 125.2, 115.1, 112.2, 105.7, 71.7, 65.6, 51.1, 50.6, 50.2, 49.0, 43.1, 41.0, 36.8, 35.4, 35.3, 35.3, 32.7, 32.4, 32.0, 31.8, 30.2, 29.8, 29.5, 29.4, 29.3, 29.2, 28.6, 28.5, 27.4, 27.2, 27.1, 25.8, 25.7, 22.7, 22.6, 14.1. Anal. Calcd. (%) for $C_{36}H_{53}NO_5$: C, 74.57; H, 9.21; N, 2.42; Found: C, 73.55; H, 8.90; N, 2.16.

Methyl 7,7-dimethyl-4-(3-nitrophenyl)-5-oxo-2-pentadecyl-1,4,5,6,7,8-hexahydroquinoline-3-carboxylate (15a): Yellow solid. Yield: 73%. M.p.: 96-98°C. IR (film, ν_{max} cm^{-1}): 686, 898, 1070, 1213, 1348, 1490, 1531, 1606, 1710, 1743, 1907, 2355, 2657, 2852, 2924, 3084, 3215, 3290; ^{1}H NMR ($CDCl_3$, 300 MHz): δ (ppm) 8.10 (s, 1H, Ph), 7.99 (d, ^3J = 8.2 Hz, 1H, Ph), 7.73 (d, ^3J = 7.9 Hz, 1H, Ph), 7,41 – 7,35 (m, 1H, Ph), 6.53 (s, 1H, NH), 5.18 (s, 1H, CH), 3.62 (s, 3H, O-CH_3), 2.92 – 2.64 (m, 2H, 2CH_2), 2.45 – 2.11 (m, 4H, 2CH_2), 1.70 – 1.54 (m, 2H, CH_2), 1.45 – 1.26 (m, 24H, 12CH_2), 1.08 (s, 3H, CH_3), 0.91 (s, 3H, CH_3), 0.88 (t, ^3J = 6 Hz, 3H, CH_3). ^{13}C NMR ($CDCl_3$, 75 MHz): δ (ppm) 195.4, 167.0, 149.4, 148.9, 148.4, 134.6, 128.8, 122.6, 121.4, 110.9, 104.6, 51.2, 50.3, 41.0, 36.7, 32.8, 32.6, 31.9, 29.7, 29.7, 29.5, 29.4, 28.8, 27.0, 22.7, 14.2. Anal. Calcd. (%) for $C_{34}H_{50}N_2O_5$: C, 72.05; H, 8.89 N, 4.94; Found: C, 71.44; H, 8.99; N, 4.47.

Methyl-2-heptadecyl-7,7-dimethyl-4-(3-nitrophenyl)-5-oxo-1,4,5,6,7,8-hexahydroquinoline-3-carboxylate (15b): Yellow solid. Yield: 75%. M.p.: 83-85 °C. IR (film, ν_{max} cm^{-1}): 684, 894, 1070, 1215, 1346, 1386, 1490, 1529, 1604, 1710, 2657, 2852, 2924, 3078, 3211, 3284; ^{1}H NMR ($CDCl_3$, 300 MHz): δ (ppm) 8.10 (s, 1H, Ph); 7.98 (d, ^3J = 8.0 Hz, 1H, Ph), 7.73 (d, ^3J = 7.9 Hz, 1H, Ph), 7.38 (t, ^3J = 7.9 Hz, 1H, Ph), 6.42 (s, 1H, NH), 5.18 (s, 1H, CH), 3.62 (s, 3H, O-CH_3), 2.92 – 2.64 (m, 2H, CH_2), 2.43 – 2.10 (m, 4H, 2CH_2), 1.69 – 1.56 (m, 2H, CH_2), 1.25 (m, 28H, 14CH_2), 1.08 (s, 3H, CH_3), 0.91 (s, 3H, CH_3), 0.88 (t, ^3J = 6 Hz, 3H, CH_3). ^{13}C NMR ($CDCl_3$, 75 MHz): δ (ppm) 196.0, 167.6, 150.1, 149.7, 149.0, 135.2, 129.3, 123.2, 121.9, 111.7, 104.9, 51.8, 51.2, 41.6, 37.3, 33.4, 32.6, 31.6, 30.4, 30.3, 30.1, 29.4, 27.6, 23.3, 14.8. Anal. Calcd. (%) for $C_{36}H_{54}N_2O_5$: C, 72.69; H, 9.15; N, 4.71; Found: C, 70.24; H, 9.09; N, 4.16.

Methyl-2-[(*Z*)-(heptadec-8-en-1-yl]-7,7-dimethyl-4-(3-nitrophenyl)-5-oxo-1,4,5,6,7,8-hexahydroquinoline-3-carboxylate (15c): Yellow solid. Yield: 73%. M.p.: 62-64 °C. IR (film, ν_{max} cm^{-1}): 698, 827, 896, 1068, 1213, 1346, 1492, 1529, 1604, 1710, 1907, 2358, 2852, 2924, 3082, 3213, 3290; ^{1}H NMR ($CDCl_3$, 300 MHz): δ (ppm) 8.09 (s, 1H, Ph), 7.98 (d, ^3J = 8.0 Hz, 1H, Ph), 7.73 (d, ^3J = 7.9 Hz, 1H, Ph), 7.38 (t, ^3J = 7.9 Hz, 1H, Ph), 6.36 (s, 1H, NH), 5.42 – 5.27 (m, 2H, 2CH), 5.18 (s, 1H, CH), 3.61 (s, 3H, O-CH_3), 2.93 – 2.63 (m, 2H, CH_2), 2.44 – 2.10 (m, 4H, 2CH_2), 2.08 – 1.94 (m, 4H, 2CH_2), 1.71 – 1.56 (m, 2H, CH_2), 1.50 – 1.27 (m, 20H, 10CH_2), 1.08 (s, 3H, CH_3), 0.91 (s, 3H, CH_3), 0.88 (t, ^3J = 6 Hz, 3H, CH_3). ^{13}C NMR ($CDCl_3$, 75 MHz): δ (ppm) 196.0, 167.6, 150.0, 149.7, 149.5, 149.0, 135.2, 130.7, 130.3, 129.3, 123.2, 121.9, 111.8, 104.9, 51.8, 51.2, 41.6, 37.3, 33.4, 33.3, 32.5, 31.6, 30.4, 30.4, 30.3, 30.3, 30.2, 30.1, 30.0, 29.9, 29.8, 29.4, 27.9, 27.8, 27.6, 23.3, 14.8. Anal. Calcd. (%) for $C_{36}H_{52}N_2O_5$: C, 72.94; H, 8.84; N, 4.73; Found: C, 72.25; H, 8.88; N, 4.49.

Methyl-2-[(8*Z*,11*Z*)-heptadeca-8,11-dien-1-yl]-7,7-dimethyl-4-(3-nitrophenyl)-5-oxo-1,4,5,6,7,8-hexahydroquinoline-3-carboxylate (15d): Yellow solid. Yield: 77%. M.p.: 85-87 °C IR (film, ν_{max} cm^{-1}): 686, 802, 827, 896, 1068, 1215, 1346, 1386, 1492, 1529, 1604, 1710, 1907, 2439, 2854, 2926, 3008, 3080, 3211, 3286. ^{1}H NMR ($CDCl_3$, 300 MHz): δ (ppm) 8.00 (s, 1H, Ph), 7.97 (d, ^3J = 8.3 Hz, 1H, Ph), 7.72 (d, ^3J = 7.9 Hz, 1H, Ph), 7.37 (t, ^3J = 7.9 Hz, 1H, Ph), 6.21 (s, 1H, NH), 5.45 – 5.25 (m, 4H, 4CH), 5.17 (s, 1H, CH), 3.61 (s, 3H, O-CH_3), 2.92 – 2.63 (m, 4H, 2CH_2), 2.45 – 2.10 (m, 4H, 2CH_2), 2.04 – 1.90 (m, 4H, 2CH_2), 1.70 – 1.55 (m, 2H, CH_2), 1.45 – 1.32 (m, 14H, 7CH_2), 1.08 (s, 3H, CH_3), 0.90 (s, 3H, CH_3), 0.88 (t, ^3J = 6 Hz, 3H, CH_3). ^{13}C NMR ($CDCl_3$, 75 MHz): δ (ppm) 195.3, 166.9, 164.9, 149.3, 149.0, 148.3, 134.5, 130.2, 129.9, 128.6, 128.0, 127.8, 122.4, 121.2,

111.1, 104.2, 51.1, 50.5, 40.9, 36.6, 32.7, 32.6, 31.5, 29.6, 29.4, 29.3, 29.2, 28.7, 27.1, 26.9, 25.6, 22.5, 14.0. Anal. Calcd. (%) for $C_{36}H_{50}N_2O_5$: C, 73.19; H, 8.53; N, 4.74; Found: C, 72,70; H, 8.77; N, 4.71.

Methyl-2-[(*S*)-(*Z*)-11-hydroxyheptadec-8-en-1-yl]-7,7-dimethyl-4-(3-nitrophenyl)-5-oxo-1,4,5,6,7,8-hexahydroquinoline-3-carboxylate (15e): Yellow solid. Yield: 74%. M.p.: 62-64 °C. IR (film, ν_{max} cm^{-1}): 696, 837, 1099, 1112, 1145, 1167, 1216, 1347, 1383, 1433, 1493, 1530, 1606, 1710, 2895, 2929, 2964, 3008, 3211, 3284. ^{1}H RMN ($CDCl_3$, 300 MHz): δ (ppm) 8.10 (s, 1H, Ph), 7.99 (d, ^3J = 10.3 Hz, 1H, Ph), 7.74 (d, ^3J = 7.9 Hz, 1H, Ph), 7.39 (t, ^3J = 7.9 Hz, 1H, Ph), 6.46 (s, 1H, NH), 5.61 – 5.54 (m, 1H, CH), 5.45 – 5.39 (m, 1H, CH), 5.19 (s, 1H, CH), 3.67 – 3.59 (m, 1H, CH), 3.62 (s, 3H, O-CH_3), 2.92 – 2.88 (m, 1H, CH_2), 2.75 – 2.70 (m, 1H, CH_2), 2.42 – 2.22 (m, 6H, 3CH_2), 2.18 – 2.06 (m, 2H, CH_2), 1.55 – 1.50 (m, 2H, CH_2), 1.49 (m, 2H, CH_2), 1.33 – 1.30 (m, 16H, 8CH_2), 1.10 (s, 3H, CH_3), 0.92 (s, 3H, CH_3), 0.89 (t, ^3J = 6 Hz, 3H, CH_3). ^{13}C RMN ($CDCl_3$, 75 MHz): δ (ppm) 195.3, 167.0, 149.5, 149.0, 148.9, 148.4, 134.6, 133.5, 128.7, 125.2, 122.5, 121.3, 111.1, 104.2, 71.5, 51.2, 50.5, 41.0, 36.8, 36.6, 35.3, 32.7, 32.6, 31.8, 29.5, 29.4, 29.3, 29.1, 29.0, 28.6, 27.3, 27.0, 25.7, 22.6, 14.1. Anal. Calcd. (%) for $C_{36}H_{52}N_2O_6$: C, 71.02; H, 8.61; N, 4.74; Found: C, 70.59; H, 8.79; N, 4.42.

Methyl-7,7-dimethyl-4-(4-nitrophenyl)-5-oxo-2-pentadecyl-1,4,5,6,7,8-hexahydroquinoline-3-carboxylate (16a): Yellow solid. Yield: 70%. M.p.: 98-100 °C; IR (film, ν_{max} cm^{-1}): 731, 831, 866, 1070, 1111, 1219, 1344, 1384, 1489, 1517, 1606, 1708, 1919, 2358, 2447, 2852, 2924, 3080, 3207, 3286. ^{1}H NMR ($CDCl_3$, 300 MHz): δ (ppm) 8.07 (d, ^3J = 8.5 Hz, 2H, Ph), 7.46 (d, ^3J = 8.8 Hz, 2H, Ph), 6.23 (s, 1H, NH), 5.17 (s, 1H, CH), 3.60 (s, 3H, O-CH_3), 2.89 – 2.66 (m, 2H, 2CH_2), 2.45 – 2.10 (m, 4H, 2CH_2), 1.68 – 1.54 (m, 2H, CH_2), 1.48 – 1.25 (m, 24H, 12CH_2), 1.08 (s, 3H, CH_3), 0.89 (s, 3H, CH_3), 0.87 (t, ^3J = 6 Hz, 3H, CH_3). ^{13}C NMR ($CDCl_3$, 75 MHz): δ (ppm) 195.3, 166.9, 154.2, 149.3, 148.8, 146.3, 128.7, 123.5, 111.0, 104.2, 51.2, 50.6, 41.1, 37.0, 32.7, 31.9, 29.7, 29.4, 27.0, 22.7, 14.1. Anal. Calcd. (%) for $C_{34}H_{50}N_2O_5$: C, 72.05; H, 8.89; N, 4.94; Found: C, 71.86; H, 9.16; N, 4.87.

Methyl-2-heptadecyl-7,7-dimethyl-4-(4-nitrophenyl)-5-oxo-1,4,5,6,7,8-hexahydroquinoline-3-carboxylate (16b): Yellow solid. Yield: 74%. M.p.: 89-91 °C. IR (film, ν_{max} cm^{-1}): 721, 835, 1068, 1107, 1217, 1340, 1481, 1510, 1595, 1639, 1708, 1965, 2443, 2850, 2922, 3072, 3392. ^{1}H NMR ($CDCl_3$, 300 MHz): δ (ppm) 8.07 (d, ^3J = 8.8 Hz, 2H, Ph), 7.46 (d, ^3J = 8.8 Hz, 2H, Ph), 6.23 (s, 1H, NH), 5.17 (s, 1H, CH), 3.59 (s, 3H, O-CH_3), 2.89 – 2.66 (m, 2H, CH_2), 2.43 – 2.10 (m, 4H, 2CH_2), 1.68 – 1.55 (m, 2H, CH_2), 1.25 (m, 28H, 14CH_2), 1.08 (s, 3H, CH_3), 0.89 (s, 3H, CH_3), 0.87 (t, ^3J = 6 Hz, 3H, CH_3). ^{13}C NMR ($CDCl_3$, 75 MHz): δ (ppm) 195.2, 166.9, 154.2, 149.2, 148.6, 146.2, 128.7, 123.4, 111.0, 51.2, 50.5, 41.1, 36.9, 32.7, 31.9, 29.7, 29.4, 28.7, 27.0, 22.7, 14.1. Anal. Calcd. (%) for $C_{36}H_{54}N_2O_5$: C, 72.69; H, 9.15; N, 4.71; Found: C, 72.65; H, 9.16; N, 4.66.

Methyl-2-[(*Z*)-heptadec-8-en-1-yl]-7,7-dimethyl-4-(4-nitrophenyl)-5-oxo-1,4,5,6,7,8-hexahydroquinoline-3-carboxylate (16c): Yellow solid. Yield: 70%. M.p.: 68-70 °C. IR (film, ν_{max} cm^{-1}): 731, 831, 866, 1068, 1226, 1348, 1521, 1610, 1708, 1919, 2447, 2852, 3078, 3203, 3338, 3574. ^{1}H NMR ($CDCl_3$, 300 MHz): δ (ppm) 8.07 (d, ^3J = 8.8 Hz, 2H, Ph), 7.45 (d, ^3J = 8.8 Hz, 2H, Ph), 6.43 (s, 1H, NH), 5.42 – 5.26 (m, 2H, 2CH). 5.16 (s, 1H, CH), 3.59 (s, 3H, O-CH_3), 2.88 – 2.66 (m, 2H, CH_2), 2.44 – 2.09 (m, 4H, 2CH_2), 2.06 – 1.94 (m, 4H, 2CH_2), 1.69 – 1.54 (m, 2H, CH_2), 1.50 – 1.29 (m, 20H, 10CH_2), 1.07 (s, 3H, CH_3), 0.88 (s, 3H, CH_3), 0.86 (t, ^3J = 6 Hz, 3H, CH_3). ^{13}C NMR ($CDCl_3$, 75 MHz): δ (ppm) 195.2, 166.9, 154.2, 149.2, 148.6, 147.3, 146.3, 130.1, 129.7, 128.7, 123.5, 123.1, 111.1, 104.2, 53.4, 52.4, 51.2, 50.5, 41.1, 36.9, 32.7, 31.9, 31.5, 29.6, 29.1, 27.0, 22.7, 14.1. Anal. Calcd. (%) for $C_{36}H_{52}N_2O_5$: C, 72.94; H, 8.84; N, 4.73; Found: C, 72.81; H, 8.78; N, 4.67.

Methyl-2-[(8*Z*,11*Z*)-heptadeca-8,11-dien-1-yl]-7,7-dimethyl-4-(4-nitrophenyl)-5-oxo-1,4,5,6,7,8-hexahydroquinoline-3-carboxylate (16d): Yellow solid. Yield: 71%. M.p.: 86-88 °C; IR (film, ν_{max} cm^{-1}): 698, 729, 831, 866, 1068, 1111, 1219, 1344, 1382, 1489, 1517, 1606, 1707, 1919, 2439, 2854, 2926, 3076, 3203, 3290, 3558. ^{1}H NMR ($CDCl_3$, 300 MHz): δ (ppm) 8.09 (d, ^3J = 9.0 Hz, 2H, Ph), 7.48 (d, ^3J = 8.8 Hz, 2H, Ph), 6.30 (s, 1H, NH), 5.45 – 5.28 (m, 4H, 4CH), 5.18 (s, 1H, CH), 3.61 (s, 3H, O-CH_3), 2.89 – 2.68 (m, 4H, 2CH_2), 2.44 – 2.11 (m, 4H, 2CH_2), 2.06 – 1.87 (m, 4H, 2CH_2), 1.70 – 1.56 (m, 2H, CH_2), 1.49 – 1.25 (m, 14H, 7CH_2), 1.09 (s, 3H, CH_3), 0.90 (s, 3H, CH_3), 0.89 (t, ^3J = 6 Hz, 3H, CH_3). ^{13}C NMR ($CDCl_3$, 75 MHz): δ (ppm) 195.3, 166.9, 154.2, 149.3, 148.8, 146.2, 130.2, 129.9, 128.7, 128.1, 127.8, 123.4, 110.9, 104.1, 51.2, 50.5, 41.0, 36.9, 32.6, 31.5, 29.6, 29.4, 29.2, 28.7, 27.2, 26.9, 25.6, 22.5, 14.1. Anal. Calcd. (%) for $C_{36}H_{50}N_2O_5$: C, 73.19; H, 8.53; N, 4.74; Found: C, 72.09; H, 8.83; N, 4.44.

Methyl-2-[(*S*)-(*Z*)-11-hydroxyheptadec-8-en-1-yl]-7,7-dimethyl-4-(4-nitrophenyl)-5-oxo-1,4,5,6,7,8-hexahydroquinoline-3-carboxylate (16e): Yellow solid. Yield: 75%. M.p.: 69-71 °C. IR (film, ν_{max} cm^{-1}): 696, 837, 1086, 1110, 1145, 1187, 1219, 1222, 1309, 1383, 1387, 1435, 1498, 1510, 1607, 1709, 1743, 2854, 2927, 3008, 3206, 3276, 3422. ^{1}H RMN ($CDCl_3$, 300 MHz): δ (ppm) 8.09 (d, ^3J = 9.1 Hz, 2H, Ph), 7.48 (d, ^3J = 8.9 Hz, 2H, Ph), 6.24 (s, 1H, NH), 5.62 – 5.55 (m, 1H, CH), 5.46 – 5.40 (m, 1H, CH), 5.19 (s, 1H, CH), 3.68 – 3.61 (m, 1H, CH), 3.59 (s, 3H, O-CH_3), 2.88 – 2.75 (m, 2H, CH_2), 2.42 – 2.26 (m, 6H, 3CH_2), 2.24 – 2.07 (m, 2H, CH_2), 1.75 – 1.60 (m, 2H, CH_2), 1.63 – 1.51 (m, 2H, CH_2), 1.25 – 1.50 (m, 16H, 8CH_2), 1.10 (s, 3H, CH_3), 0.90 (s, 3H, CH_3), 0.89 (t, ^3J = 6 Hz, 3H, CH_3). ^{13}C RMN ($CDCl_3$, 75 MHz): δ (ppm) 195.2, 166.9, 164.9, 154.2, 154.2, 149.3, 149.3, 148.7, 148.6, 146.1, 128.1, 128.0, 123.5, 123.3, 111.0, 110.9, 104.0, 71.2, 50.8, 49.9, 37.6, 36.8, 36.5,

36.0, 32.6, 31.8, 29.4, 29.3, 29.0, 29.0, 28.6, 27.2, 27.2, 25.7, 22.6, 14.0. Anal. Calcd. (%) for $C_{36}H_{52}N_2O_6$: C, 71.02; H, 8.61; N, 4.60; Found: C, 70.19; H, 8.68; N, 4.45.

Methyl-4-(2-chlorophenyl)-7,7-dimethyl-5-oxo-2-pentadecyl-1,4,5,6,7,8-hexahydroquinoline-3-carboxylate (17a): Yellow solid. Yield: 75%. M.p.: 107-109 °C. IR (film, ν_{max} cm^{-1}): 597, 645, 731, 745, 1037, 1049, 1084, 1109, 1125, 1189, 1212, 1275, 1287, 1309, 1408, 1383, 1430, 1488, 1607, 1645, 1709, 2851, 2923, 2998, 3084, 3204, 3248, 3284 ^{1}H NMR ($CDCl_3$, 300 MHz): δ (ppm) 7.38 (d, ^3J = 9.3 Hz, 1H, Ph), 7.24 (d, ^3J = 9.0 Hz, 1H, Ph), 7.13 (m, 1H, Ph), 7.07 (m, 1H, Ph), 6.56 (s, 1H, NH), 5.42 (s, 1H, CH), 3.60 (s, 3H, O-CH_3), 2.83 – 2.78 (m, 1H, CH_2), 2.57 – 2.54 (m, 1H, CH_2), 2.36 – 2.08 (m, 4H, $2CH_2$), 1.63 – 1.55 (m, 2H, CH_2), 1.27 – 1.30 (m, 24H, $12CH_2$), 1.07 (s, 3H, CH_3), 0.96 (s, 3H, CH_3), 0.90 (t, J = 6.8 Hz, 3H, CH_3). ^{13}C NMR ($CDCl_3$, 75 MHz): δ (ppm) 195.2, 167.6, 149.1, 148.4, 144.5, 133.1, 131.6, 129.6, 127.2, 126.4, 111.0, 104.7, 50.8, 50.7, 40.9, 35.7, 32.4, 31.9, 29.7, 29.6, 29.5, 29.4, 28.6, 27.1, 22.7, 14.1. Anal. Calcd. (%) for $C_{34}H_{50}ClNO_3$: C, 73.42; H, 9.06; N, 2.52; Found: C, 73.48; H, 9.39; N, 2.55.

Methyl-4-(2-chlorophenyl)-2-heptadecyl-7,7-dimethyl-5-oxo-1,4,5,6,7,8-hexahydroquinoline-3-carboxylate (17b): Yellow solid. Yield: 85%. M.p.: 109-111 °C. IR (film, ν_{max} cm^{-1}): 745, 1037, 1071, 1109, 1198, 1213, 1309, 1383, 1438, 1497, 1608, 1645, 1709, 2851, 2923, 2957, 3084, 3204, 3248, 3283. ^{1}H NMR ($CDCl_3$, 300 MHz): δ (ppm) 7.38 (d, ^3J = 7.8 Hz, 1H, Ph), 7.26 (d, ^3J = 7.8 Hz, 1H, Ph), 7.11 (m, 1H, Ph), 7.01 (m, 1H, Ph), 6.52 (s, 1H, NH), 5.42 (s, 1H, CH), 3.60 (s, 3H, O-CH_3), 2.83 – 2.80 (m, 1H, C$\underline{H}_2$), 2.58 – 2.54 (m, 1H, C$\underline{H}_2$), 2.35 – 2.10 (m, 4H, $2CH_2$), 1.63 – 1.55 (m, 2H, CH_2), 1.35 – 1.24 (m, 28H, $14CH_2$), 1.07 (s, 3H, CH_3), 0.96 (s, 3H, CH_3), 0.90 (t, ^3J = 6 Hz, 3H, CH_3). ^{13}C NMR ($CDCl_3$, 75 MHz): δ (ppm) 195.2, 167.6, 148.9, 148.3, 144.4, 133.2, 131.7, 129.7, 127.2, 126.4, 111.1, 104.7, 50.8, 50.7, 41.0, 35.8, 32.5, 31.9, 29.7, 29.5, 29.4, 28.6, 27.2, 22.7, 14.1. Anal. Calcd. (%) for $C_{36}H_{54}ClNO_3$: C, 74.00; H, 9.32; N, 2.40; Found: C, 74.05; H, 9.40; N, 2.46.

Methyl-4-(2-chlorophenyl)-2-[(*Z*)-heptadec-8-en-1-yl]-7,7-dimethyl-5-oxo-1,4,5,6,7,8-hexahydroquinoline-3-carboxylate (17c): Yellow solid. Yield: 82%. M.p.: 89-91 °C. IR (film, ν_{max} cm^{-1}): 1148, 1168, 1215, 1284, 1385, 1480, 1488, 1494, 1608, 1645, 1709, 2854, 2928, 2998, 3009, 3082, 3211, 3247, 3289. ^{1}H NMR ($CDCl_3$, 300 MHz): δ (ppm) 7.38 (d, ^3J = 7.8 Hz, 1H, Ph), 7.26 (d, ^3J = 8.1 Hz, 1H, Ph), 7.13 (m, 1H, Ph), 7.04 (m, 1H, Ph), 6.38 (s, 1H, NH), 5.42 (s, 1H, CH), 5.40 – 5.33 (m, 2H, CH), 3.60 (s, 3H, O-CH_3), 2.84 – 2.81 (m, 1H, C$\underline{H}_2$), 2.57 – 2.55 (m, 1H, C$\underline{H}_2$), 2.36 – 2.14 (m, 4H, $2CH_2$), 2.05 – 2.00 (m, 4H, $2CH_2$), 1.64 – 1.58 (m, 2H, CH_2), 1.40 – 1.25 (m, 20H, $10CH_2$), 1.08 (s, 3H, CH_3), 0.96 (s, 3H, CH_3), 0.90 (t, ^3J = 6 Hz, 3H, CH_3). ^{13}C NMR ($CDCl_3$, 75 MHz): δ (ppm) 195.2, 167.5, 164.9, 148.8, 148.2, 144.3, 144.2, 133.1, 133.0, 130.8, 130.5, 129.2, 129.1, 128.8, 127.8, 126.5, 111.1, 104.6, 52.0, 51.1, 50.6, 50.5, 49.6, 41.4, 41.0, 36.4, 35.9, 32.5, 31.9, 29.7, 29.5, 29.3, 28.6, 27.2, 22.6, 14.1. Anal. Calcd. (%) for $C_{36}H_{52}ClNO_3$: C, 74.26; H, 9.00; N, 2.41; Found: C, 73.95; H, 9.01; N, 2.35.

Methyl-4-(2-chlorophenyl)-2-[(8*Z*,11*Z*)-heptadeca-8,11-dien-1-yl]-7,7-dimethyl-5-oxo-1,4,5,6,7,8-hexahydroquinoline-3-carboxylate (17d): Yellow solid. M.p.: 72-74 °C. Yield: 86%. IR (film, ν_{max} cm^{-1}): 696, 837, 1168, 1217, 1309, 1431, 1494, 1608, 1705, 2885, 2928, 2954, 3009, 3081, 3207, 3285. ^{1}H NMR ($CDCl_3$, 300 MHz): δ (ppm) 7.38 (d, ^3J = 8.0 Hz, 1H, Ph), 7.25 (d, ^3J = 8.1 Hz, 1H, Ph), 7.13 (m, 1H, Ph), 7.06 (m, 1H, Ph), 6.57 (s, 1H, NH), 5.41 (s, 1H, CH), 5.39 – 5.30 (m, 4H, 4CH), 3.60 (s, 3H, O-CH_3), 2.86 – 2.75 (m, 3H, CH_2, C$\underline{H}_2$), 2.60 – 2.50 (m, H, C$\underline{H}_2$), 2.35 – 2.24 (m, 4H, $2CH_2$), 2.09 – 2.04 (m, 4H, $2CH_2$), 1.64 – 1.55 (m, 2H, CH_2), 1.31 – 1.25 (m, 14H, $7CH_2$), 1.07 (s, 3H, CH_3), 0.95 (s, 3H, CH_3), 0.90 (t, ^3J = 6.9 Hz, 3H, CH_3). ^{13}C NMR ($CDCl_3$, 75 MHz): δ (ppm) 195.4, 167.6, 149.1, 148.3, 144.4, 133.1, 131.6, 130.3, 130.1, 129.7, 128.1, 127.9, 127.3, 126.4, 111.1, 104.7, 50.8, 50.6, 41.0, 35.8, 32.5(2C), 31.5(2), 29.7(2C), 29.4(2C), 29.3, 28.6, 27.2, 25.7, 22.6, 14.1. Anal. Calcd. (%) for $C_{36}H_{50}ClNO_3$: C, 74.52; H, 8.69; N, 2.41; Found: C, 73.87; H, 8.64; N, 2.39.

Methyl-4-(2-chlorophenyl)-2-[(*S*)-(Z)-11-hydroxyheptadec-8-en-1-yl]-7,7-dimethyl-5-oxo-1,4,5,6,7,8-hexahydroquinoline-3-carboxylate (17e): Yellow solid. Yield: 71%. M.p.: 70-72 °C. IR (film, ν_{max} cm^{-1}): 698, 842, 1168, 1217, 1309, 1383, 1431, 1491, 1610, 1707, 2854, 2928, 3010, 3083, 3208, 3292; ^{1}H NMR ($CDCl_3$, 300 MHz): δ (ppm) 7.37 (d, ^3J = 8.0 Hz, 1H, Ph), 7.25 (d, ^3J = 7.8 Hz, 1H, Ph), 7.13 (m, 1H, Ph), 7.03 (m, 1H, Ph), 6.46 (s, 1H, NH), 5.61 – 5.56 (m, 1H, CH), 5.45 (s, 1H, CH), 5.44 – 5.39 (m, 1H, CH), 3.67 – 3.61 (m, 1H, CH), 3.60 (s, 3H, O-CH_3), 2.85 – 2.82 (m, 1H, C$\underline{H}_2$), 2.58 – 2.50 (m, 1H, C$\underline{H}_2$), 2.36 – 2.13 (m, 8H, $4CH_2$), 1.64 – 1.55 (m, 2H, CH_2), 1.52 – 1.46 (m, 2H, CH_2), 1.25 – 1.31 (m, 16H, $8CH_2$), 1.08 (s, 3H, CH_3), 0.96 (s, 3H, CH_3), 0.90 (t, ^3J = 6 Hz, 3H, CH_3). ^{13}C NMR ($CDCl_3$, 75 MHz): δ (ppm) 195.2, 167.5, 164.9, 148.9, 148.3, 144.3, 133.1, 130.9, 127.7, 125.9, 124.4, 111,0, 104.5, 71.7, 71.2, 70.3, 51.0, 50.5, 40.9, 36.8, 36.4, 34.9, 32.4(2C), 31.8 (2C), 29.5, 29.4, 29.3, 29.1, 28.5, 27.3, 27.1, 25.7, 22.6, 14.1. Anal. Calcd. (%) for $C_{36}H_{52}ClNO_4$: C, 72.27; H, 8.76; N, 2.34; Found: C, 71.87; H, 8.03; N, 2.33.

Lipophilicity calculations

The physicochemical parameter, Clog P (the logarithm of n-octanol/water partition coefficient P based on established chemical interactions) was calculated using ChemDraw, Level: Ultra, Version: 12.0.2 (CambridgeSoft, Cambridge, MA, USA).

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Supplementary data

Multicomponent synthesis of new hybrid PHQ-fatty acids

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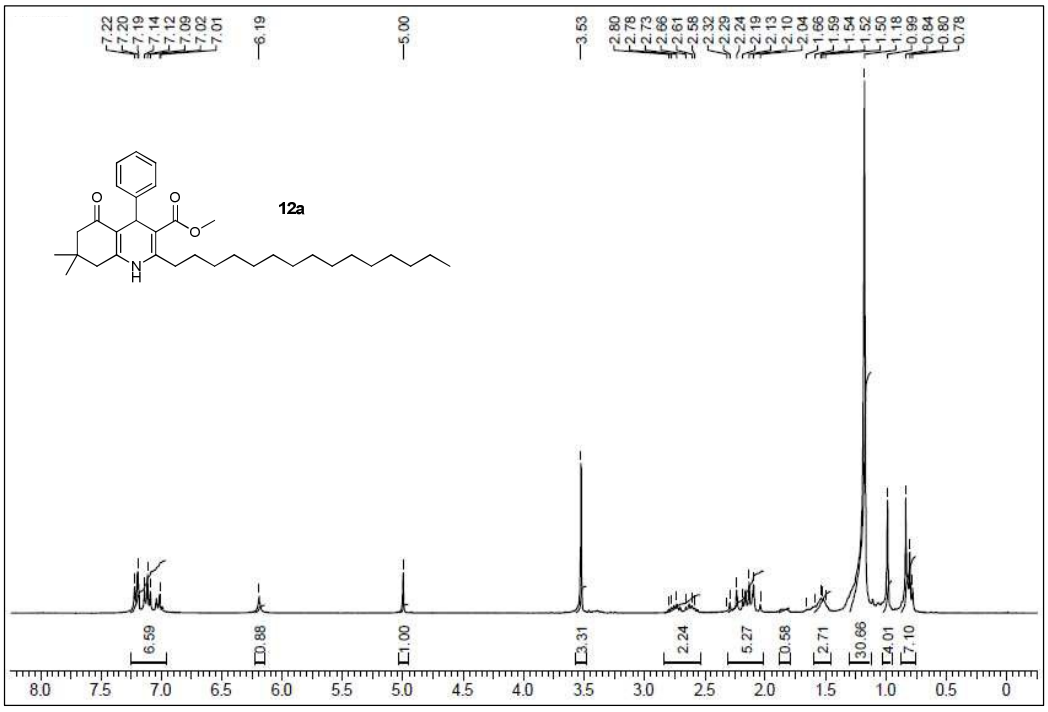

Figure S1. ^{1}H NMR spectrum ($CDCl_3$, 300 MHz) of **12a**.

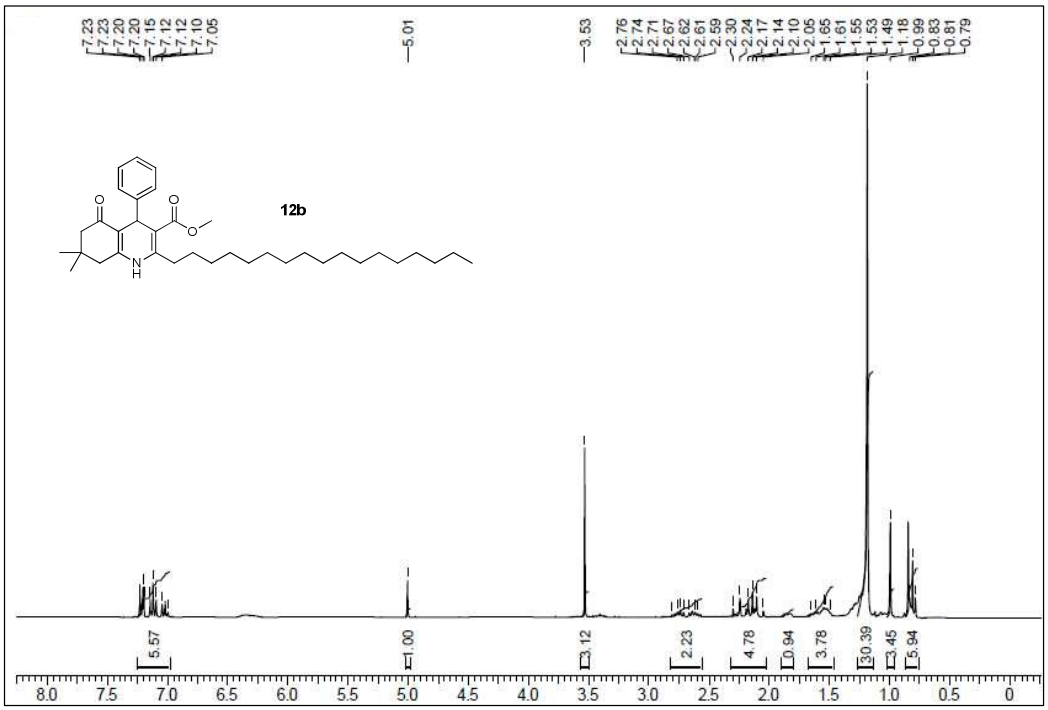

Figure S2. ^{1}H NMR spectrum ($CDCl_3$, 300 MHz) of **12b**.

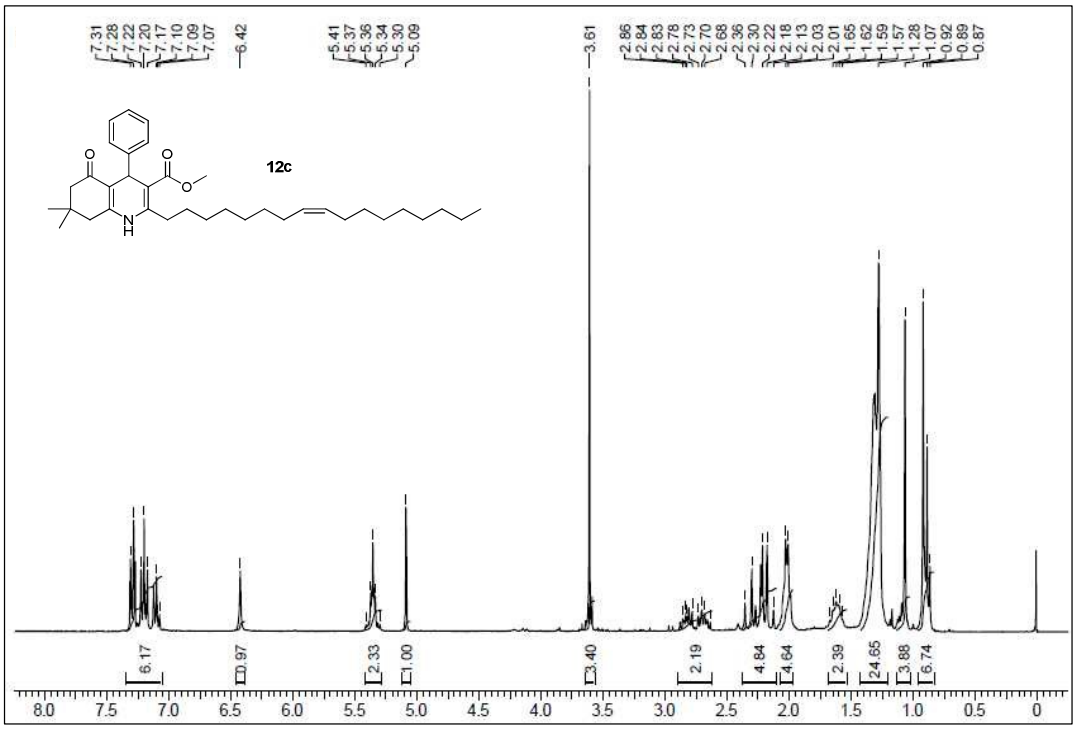

Figure S3.[1]H NMR spectrum ($CDCl_3$, 300 MHz) of **12c**.

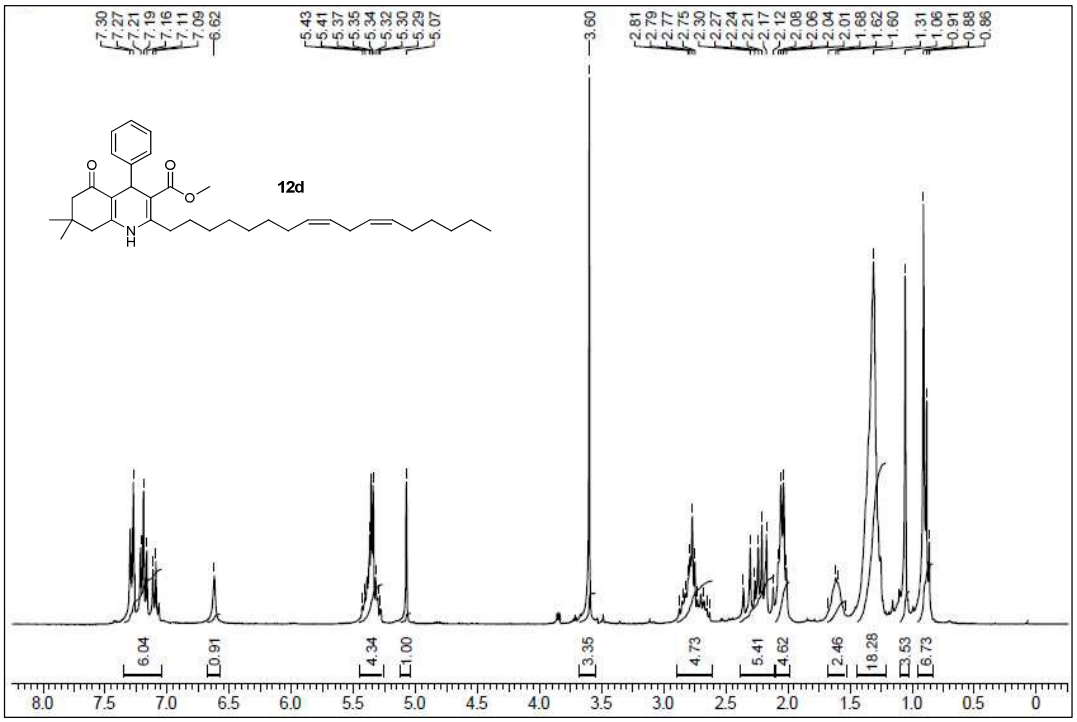

Figure S4.[1]H NMR spectrum ($CDCl_3$, 300 MHz) of **12d**.

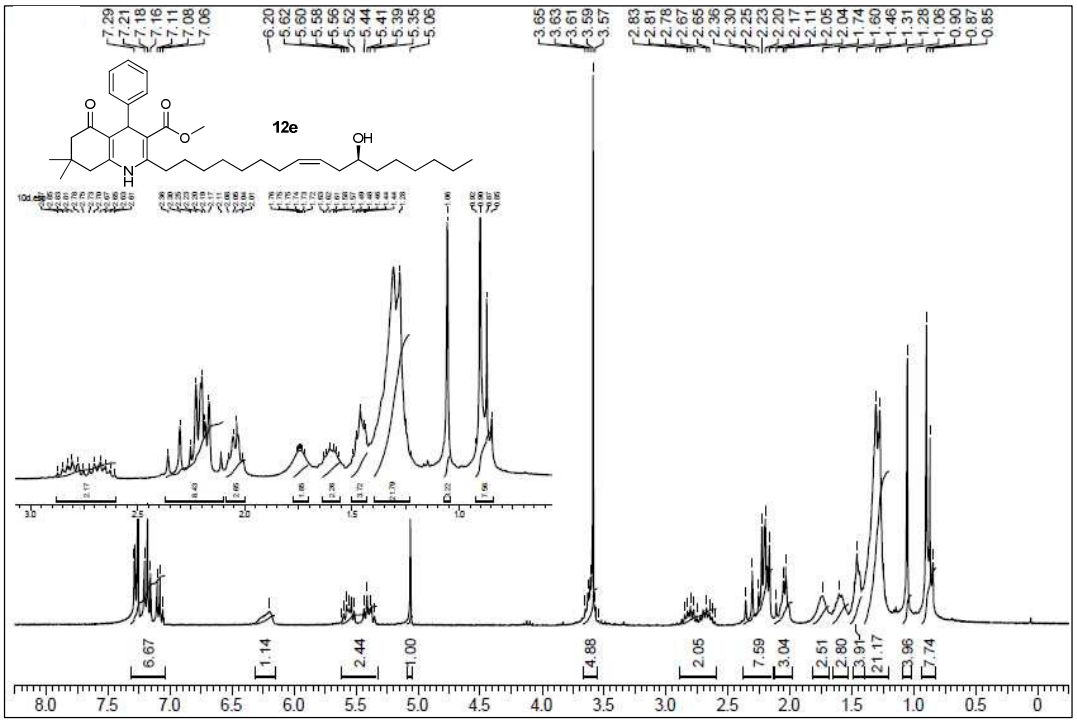

Figure S5. ^{1}H NMR spectrum ($CDCl_3$, 300 MHz) of **12e**.

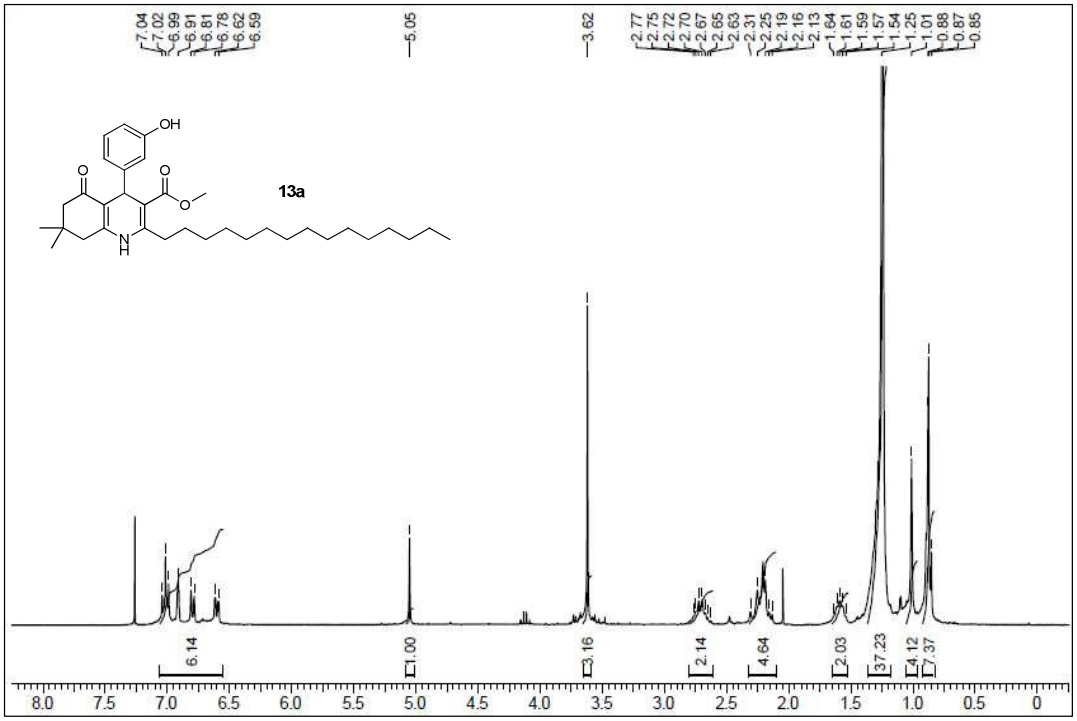

Figure S6. ^{1}H NMR spectrum ($CDCl_3$, 300 MHz) of **13a**.

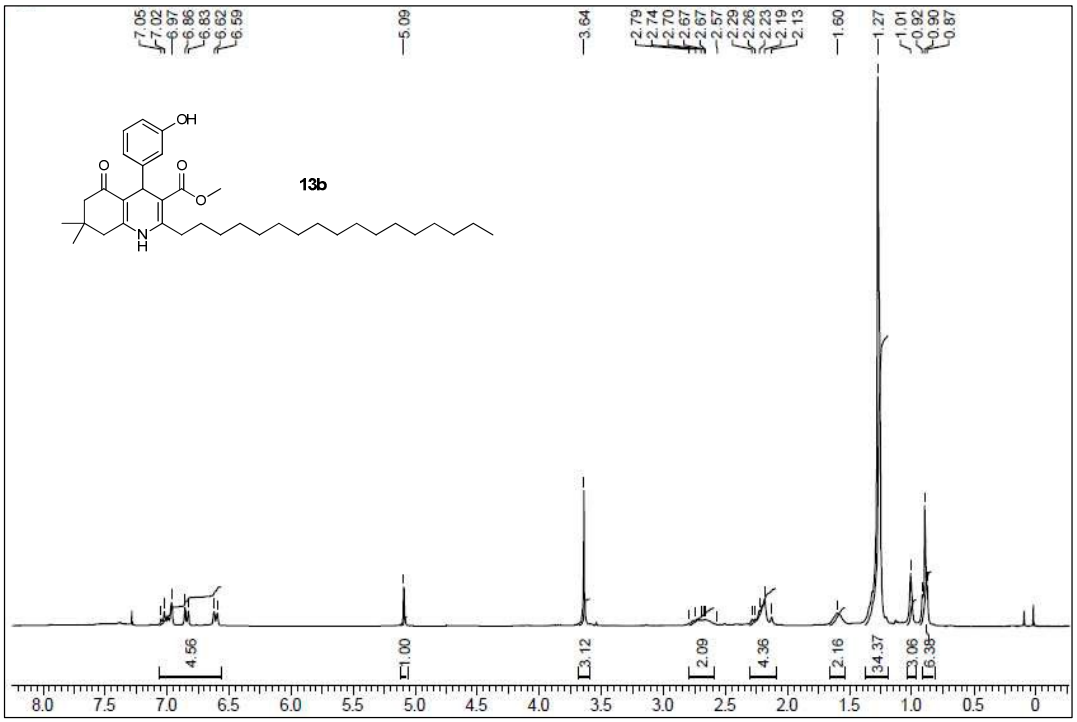

Figure S7.[1]H NMR spectrum ($CDCl_3$, 300 MHz) of **13b**.

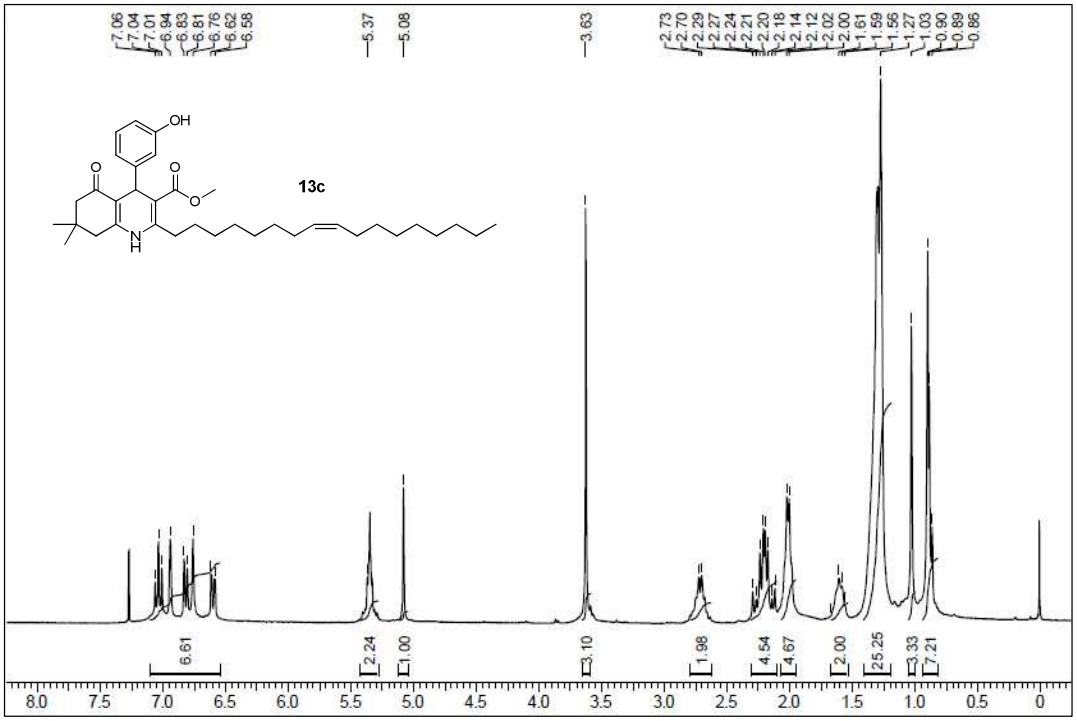

Figure S8.[1]H NMR spectrum ($CDCl_3$, 300 MHz) of **13c**.

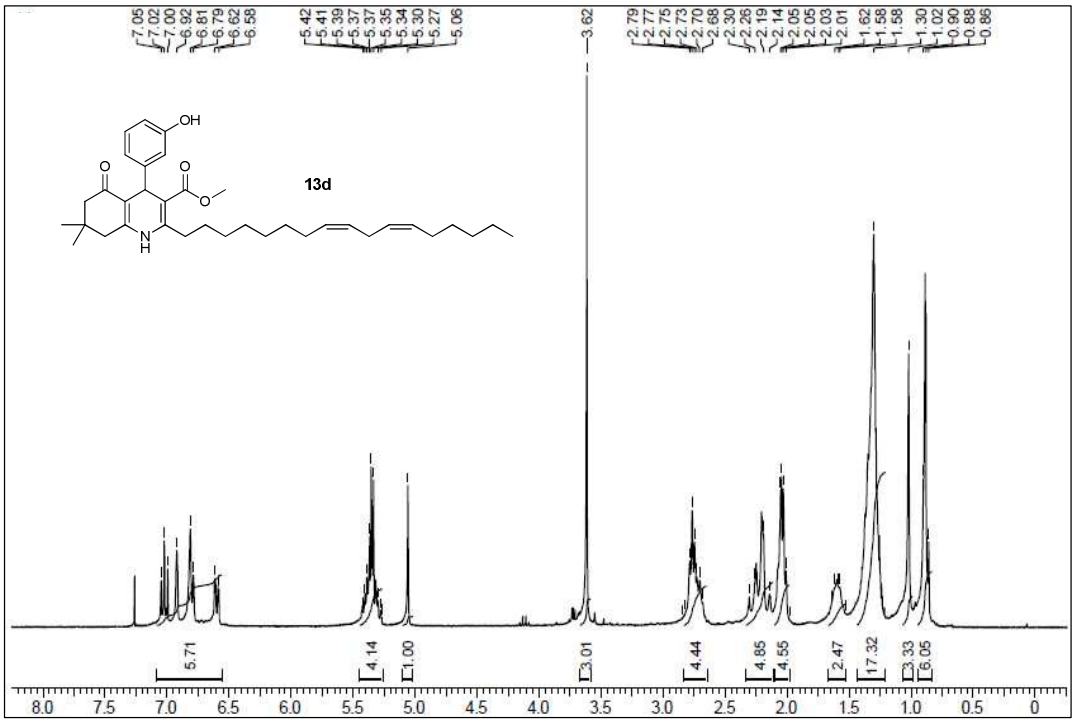

Figure S9.[1]H NMR spectrum ($CDCl_3$, 300 MHz) of **13d**.

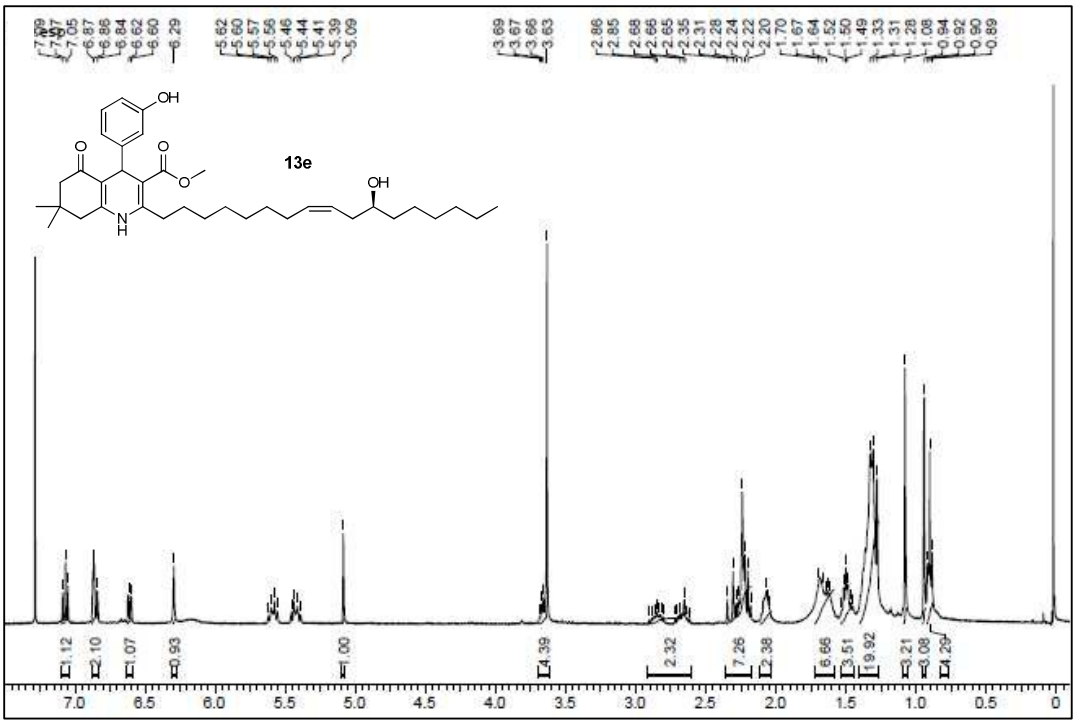

Figure S10.[1]H NMR spectrum ($CDCl_3$, 300 MHz) of **13e**.

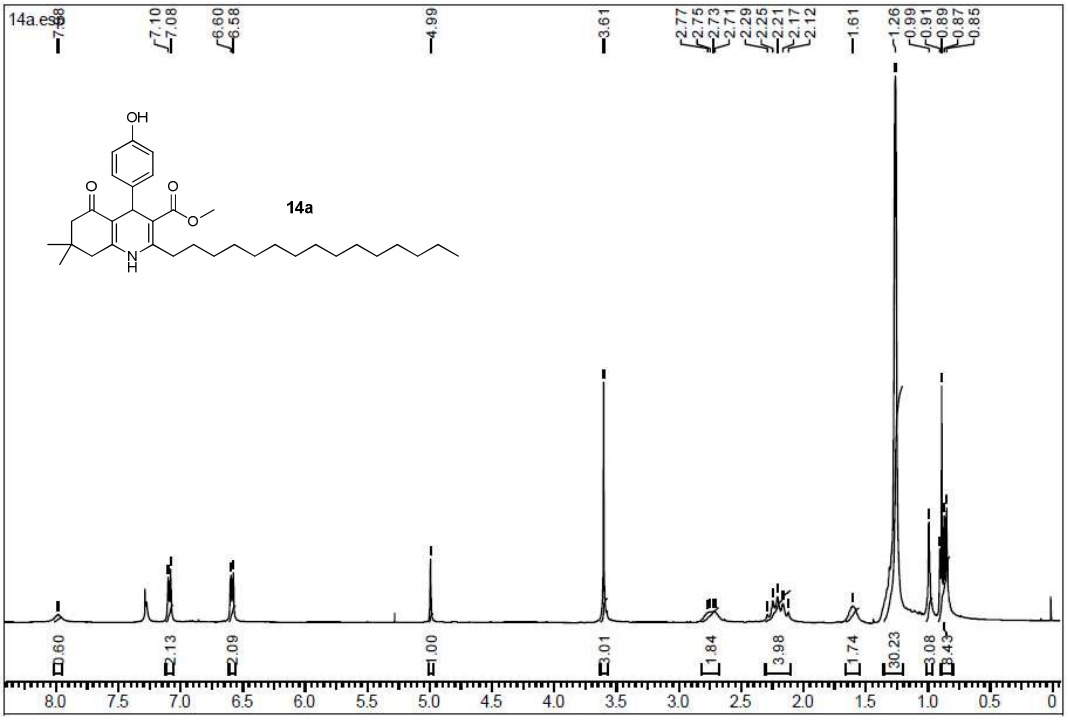

Figure S11.[1]H NMR spectrum ($CDCl_3$, 300 MHz) of **14a**.

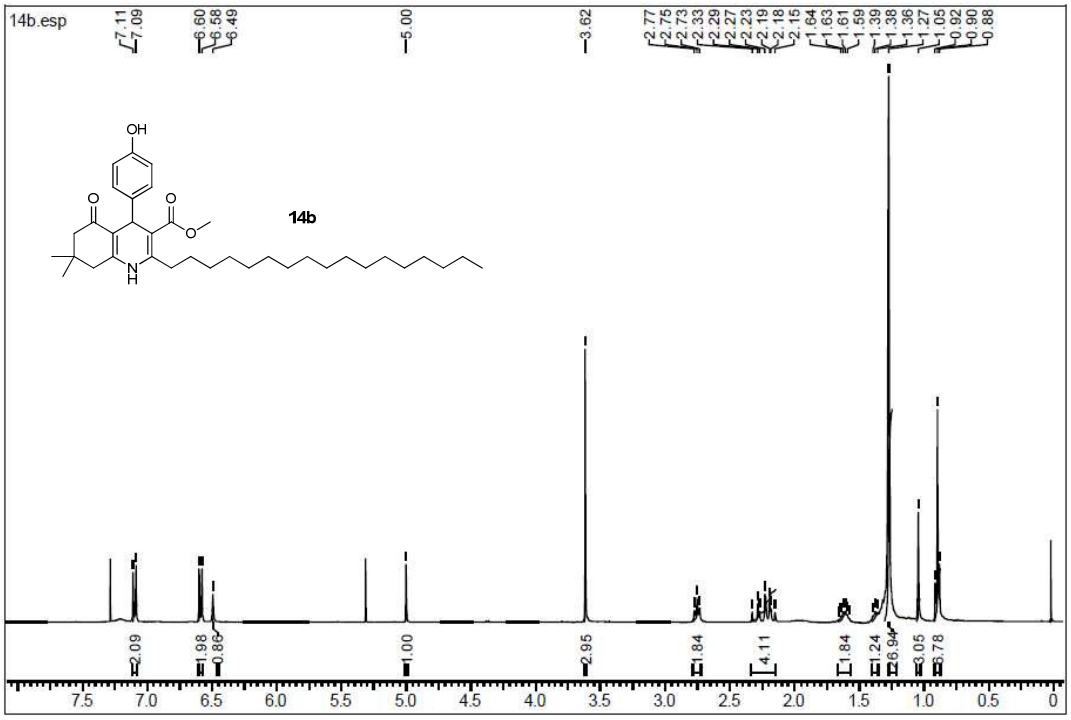

Figure S12.[1]H NMR spectrum ($CDCl_3$, 300 MHz) of **14b**.

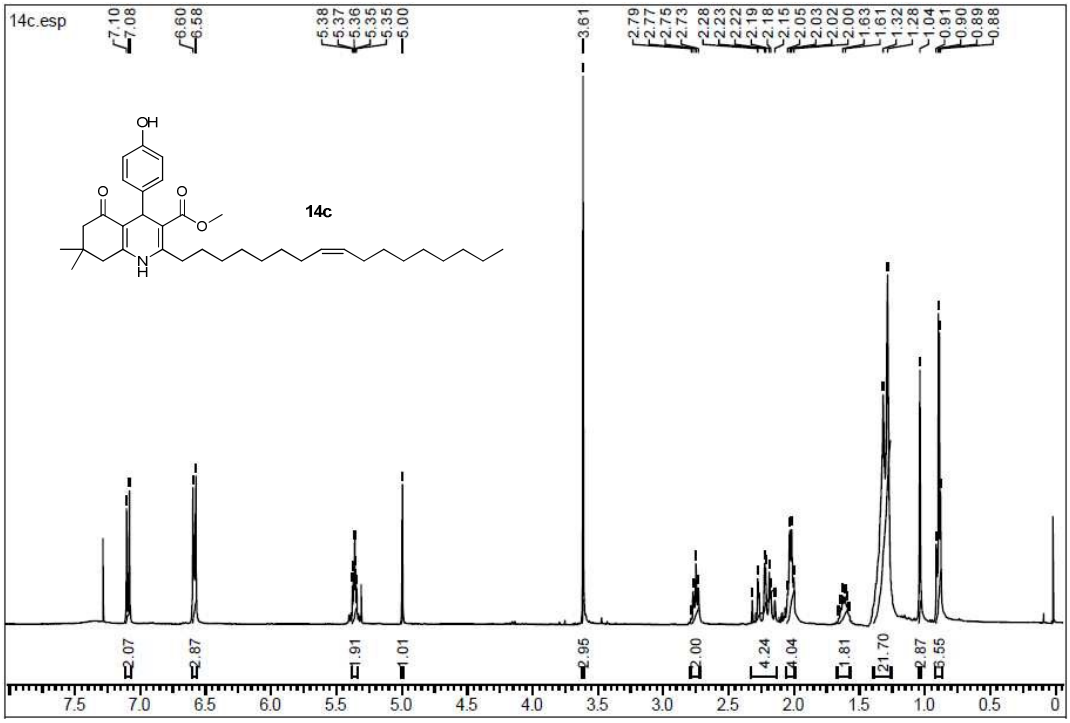

Figure S13.[1]H NMR spectrum ($CDCl_3$, 300 MHz) of **14c**.

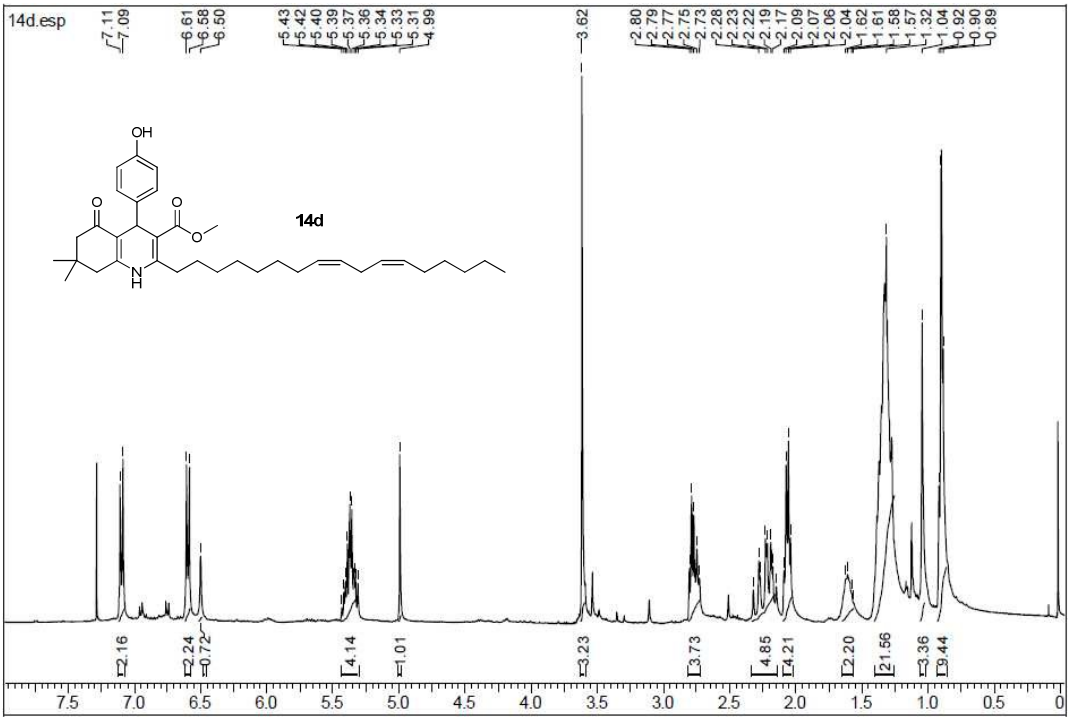

Figure S14.[1]H NMR spectrum ($CDCl_3$, 300 MHz) of **14d**.

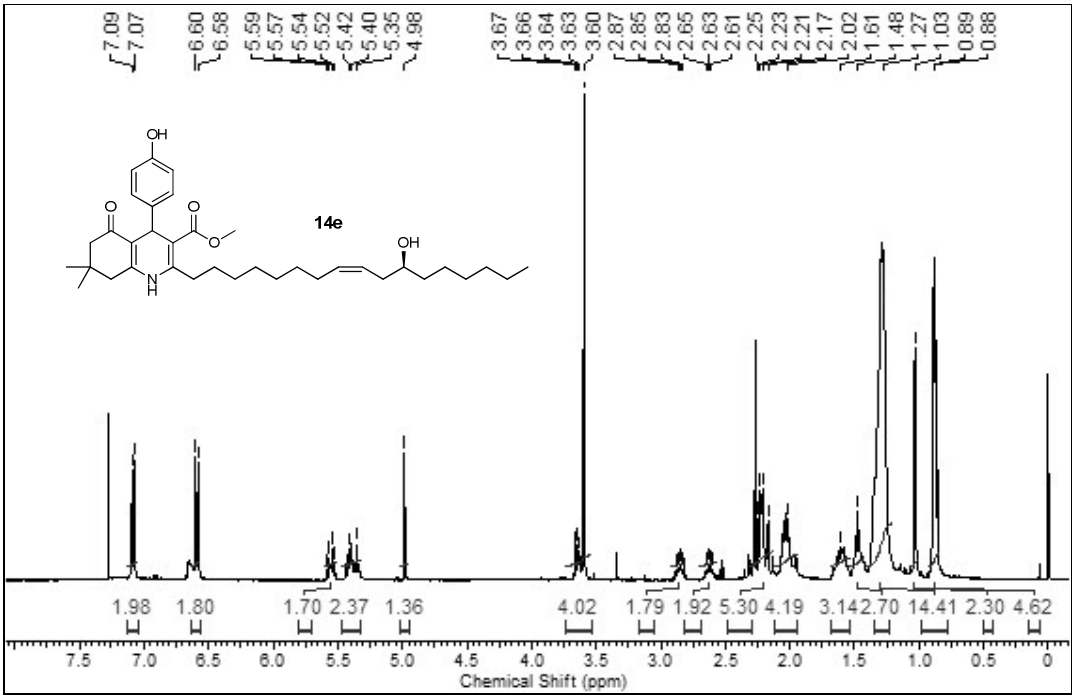

Figure S15. H NMR spectrum ($CDCl_3$, 300 MHz) of **14e**.

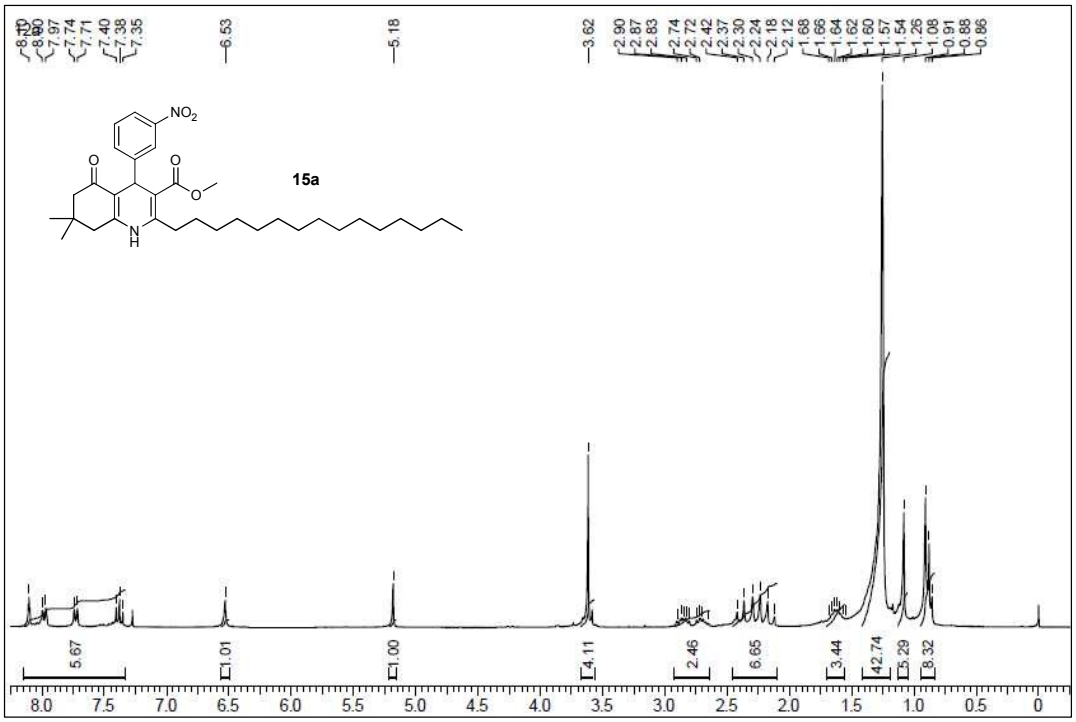

Figure S16.[1]H NMR spectrum ($CDCl_3$, 300 MHz) of **15a**.

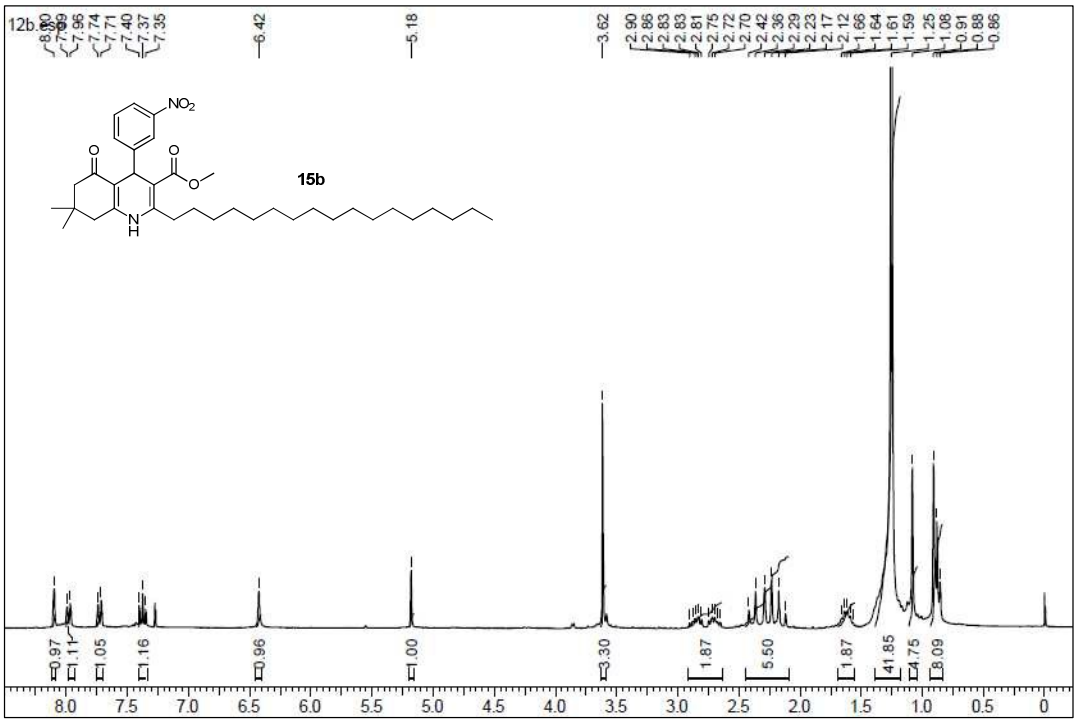

Figure S17.[1]H NMR spectrum ($CDCl_3$, 300 MHz) of **15b**.

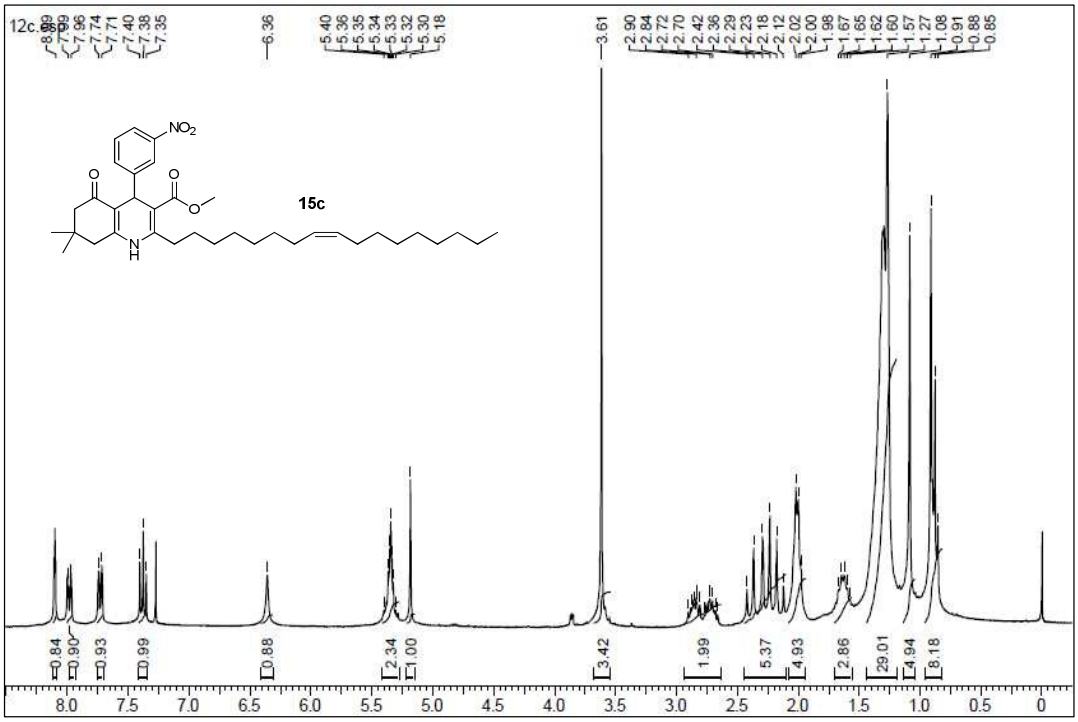

Figure S18.[1]H NMR spectrum ($CDCl_3$, 300 MHz) of **15c**.

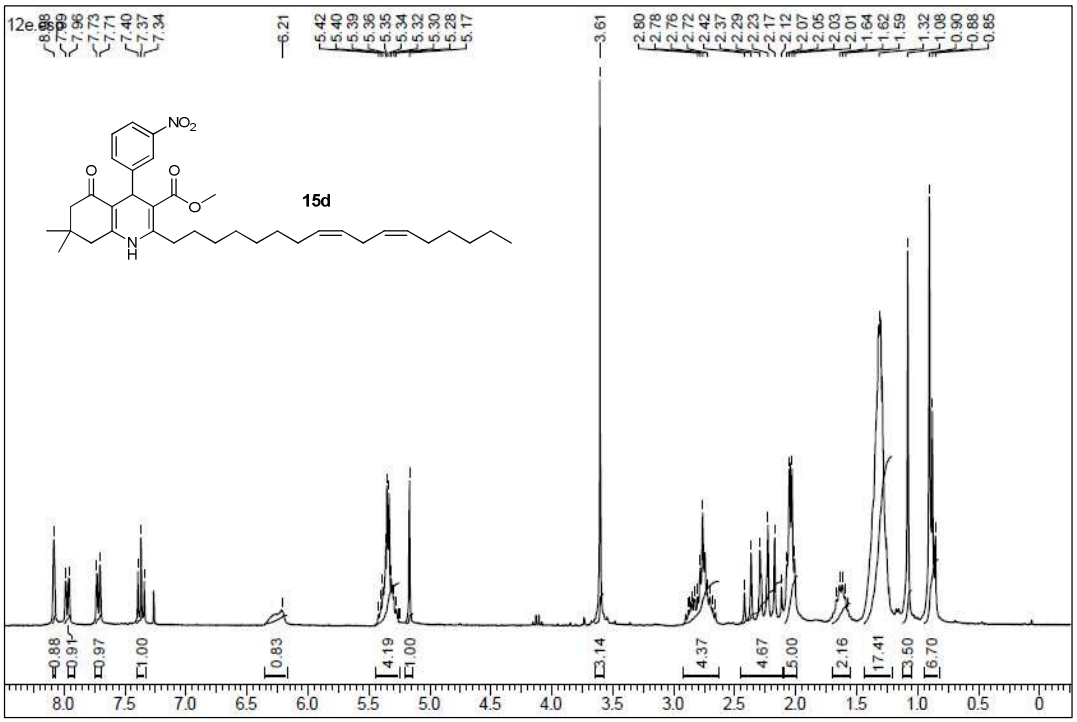

Figure S19.[1]H NMR spectrum ($CDCl_3$, 300 MHz) of **15d**.

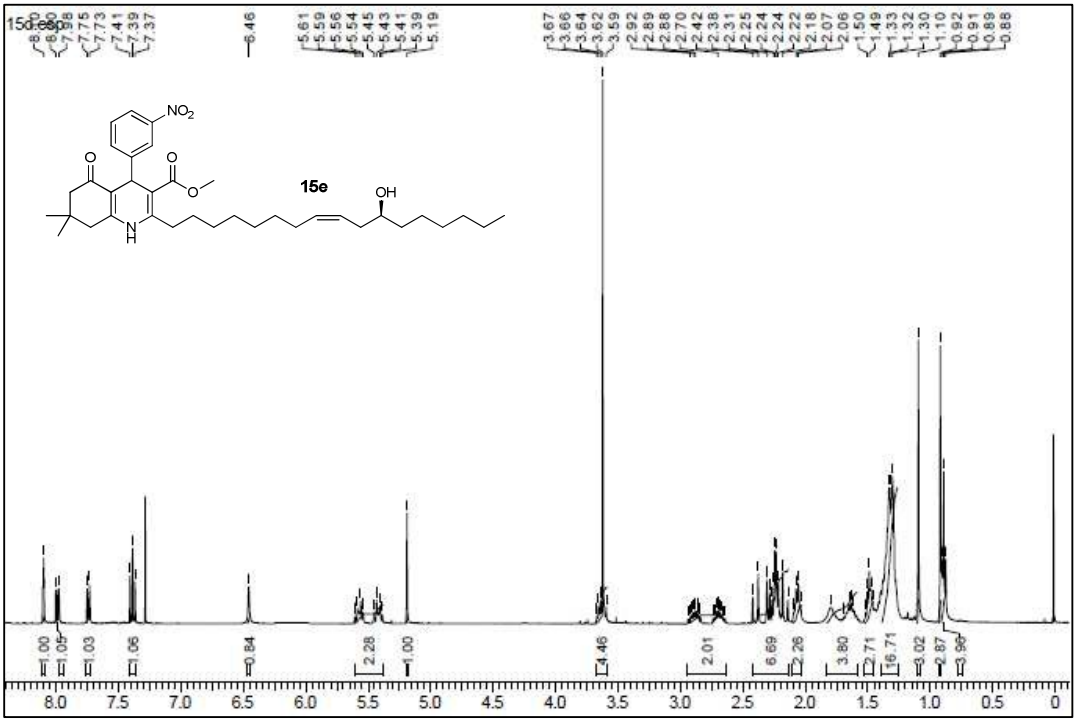

Figure S20.[1]H NMR spectrum ($CDCl_3$, 300 MHz) of **15e**.

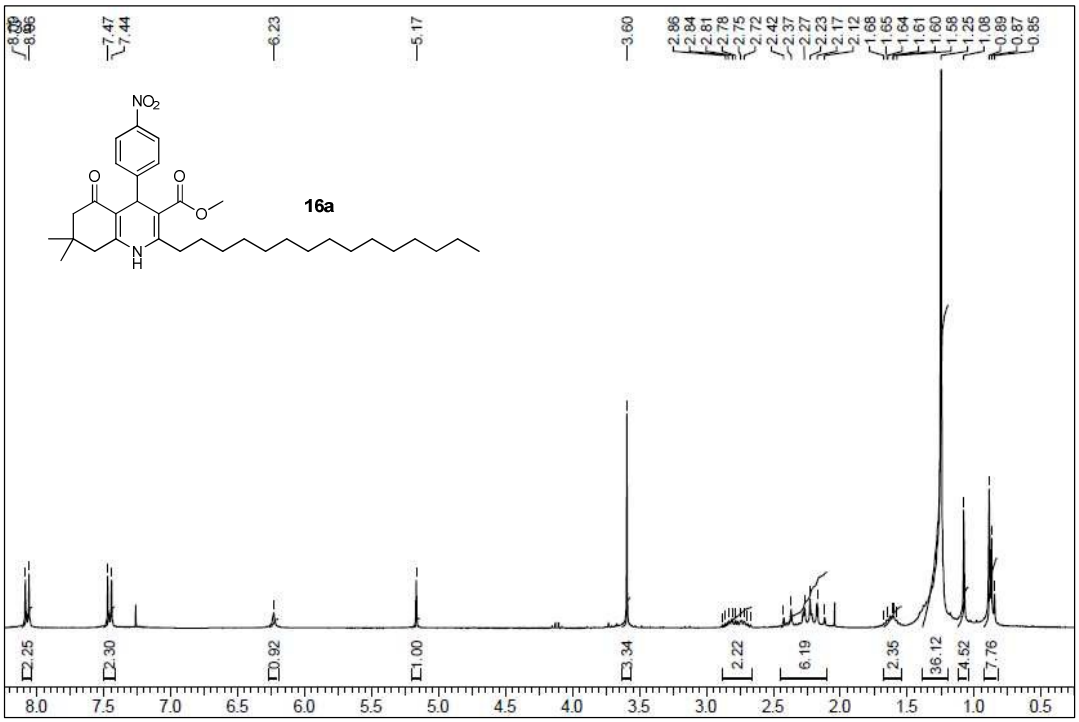

Figure S21.[1]H NMR spectrum ($CDCl_3$, 300 MHz) of **16a**.

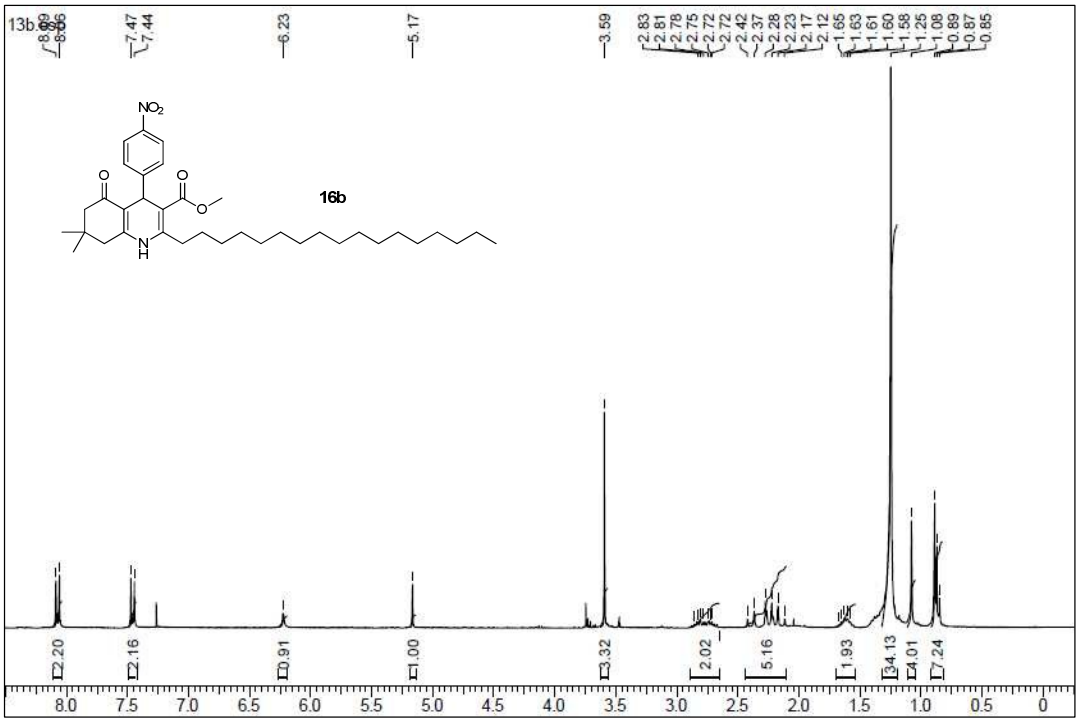

Figure S22.[1]H NMR spectrum ($CDCl_3$, 300 MHz) of **16b**.

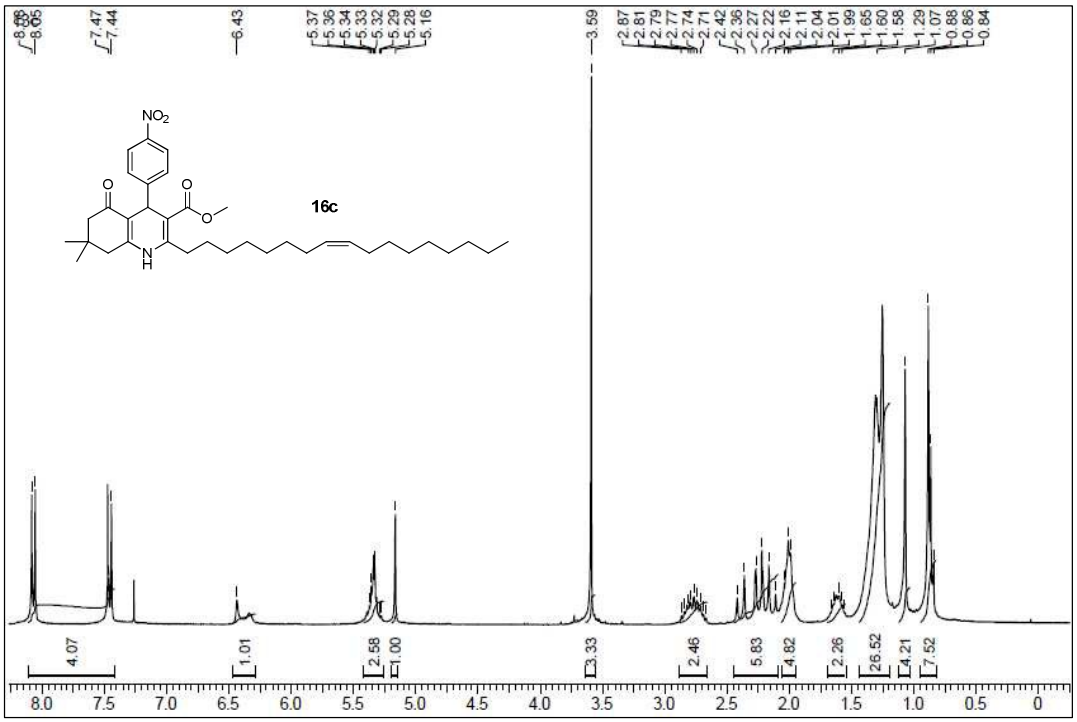

Figure S23.[1]H NMR spectrum ($CDCl_3$, 300 MHz) of **16c**.

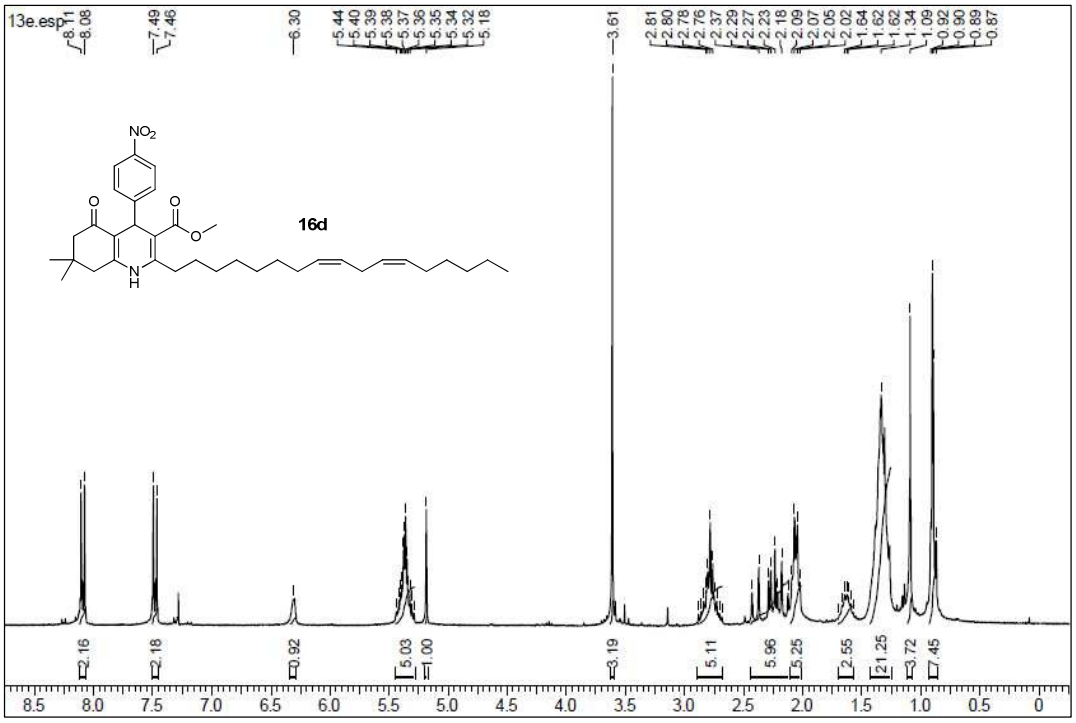

Figure S24.[1]H NMR spectrum ($CDCl_3$, 300 MHz) of **16d**.

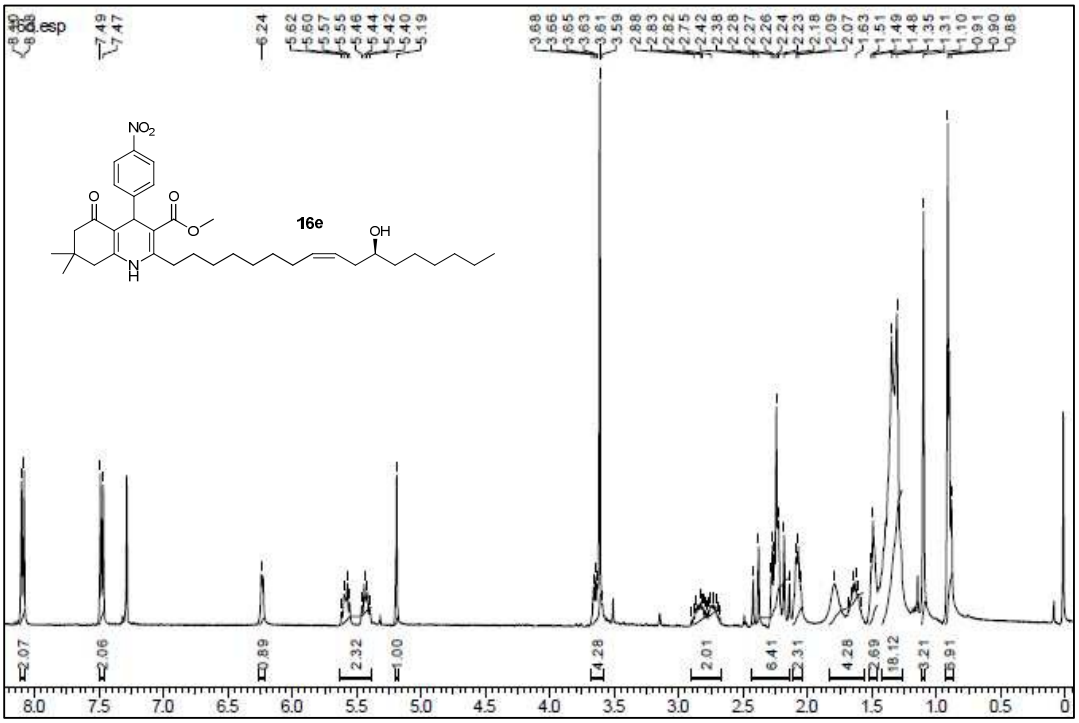

Figure S25.[1]H NMR spectrum ($CDCl_3$, 300 MHz) of **16e**.

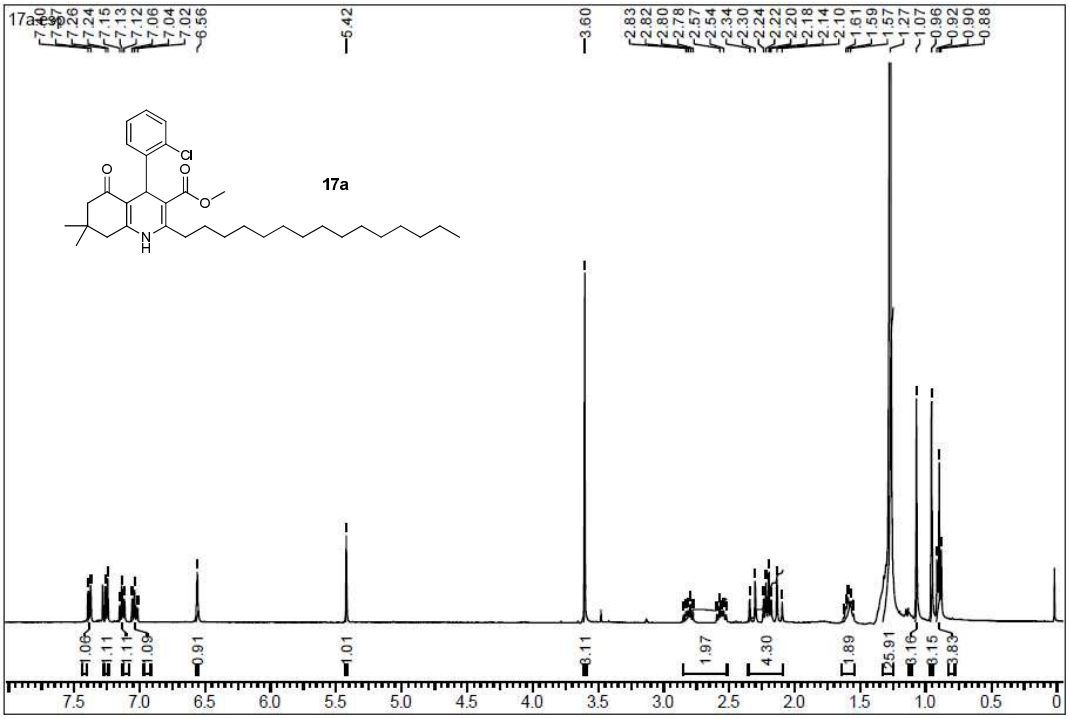

Figure S26.[1]H NMR spectrum ($CDCl_3$, 300 MHz) of **17a**.

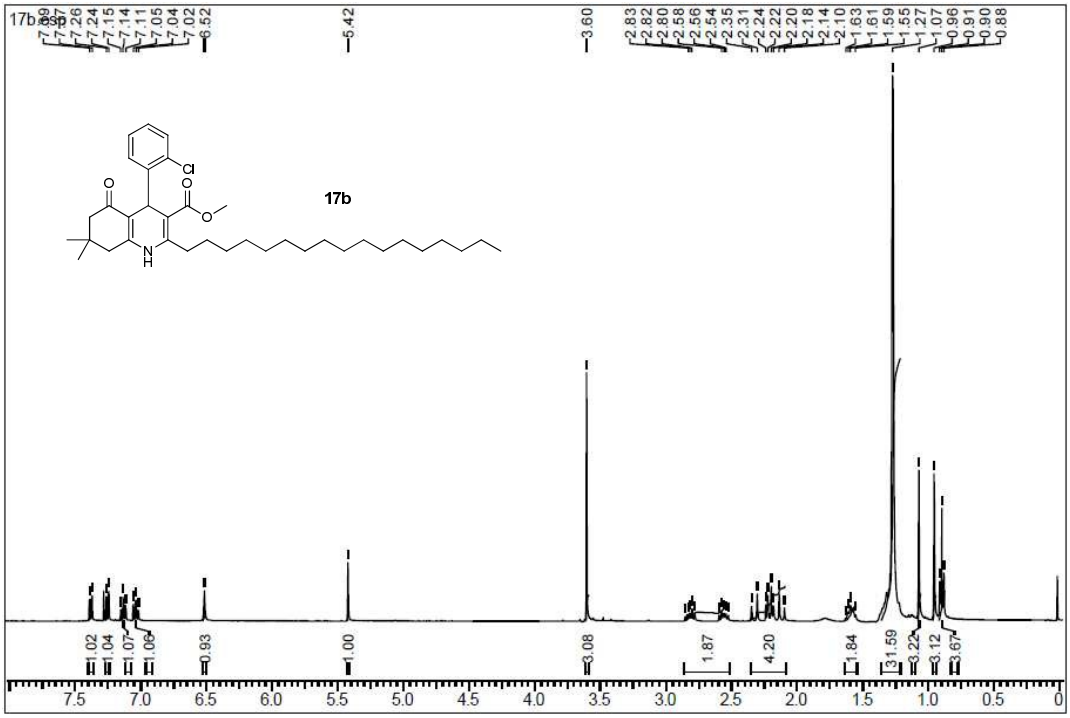

Figure S27.[1]H NMR spectrum ($CDCl_3$, 300 MHz) of **17b**.

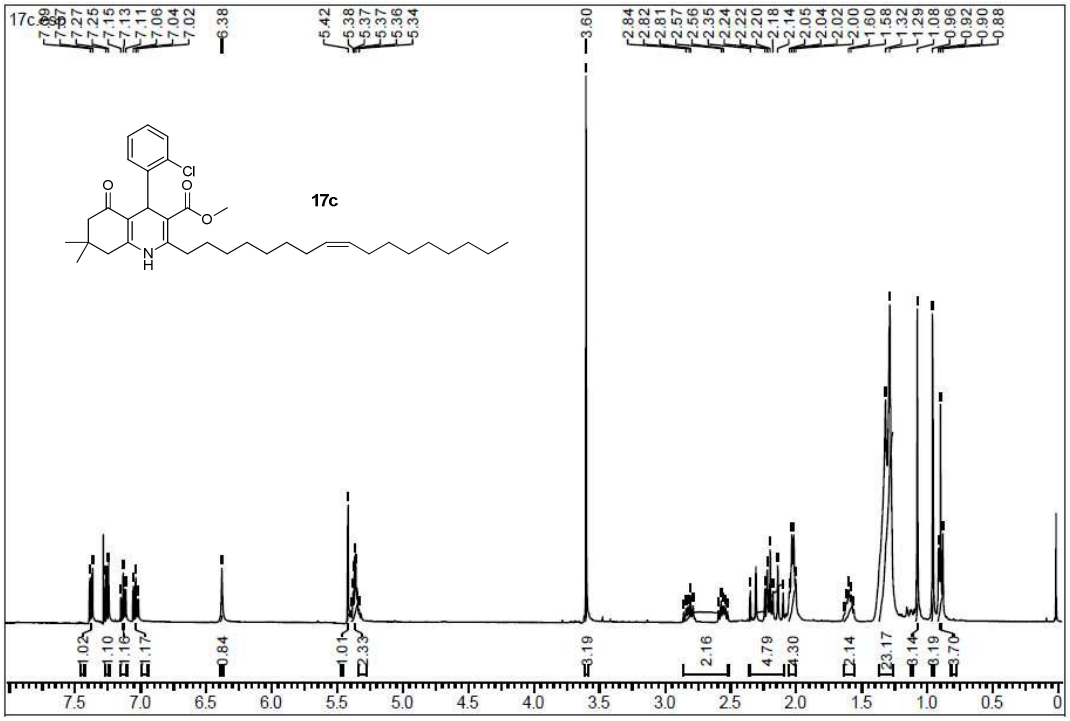

Figure S28.[1]H NMR spectrum ($CDCl_3$, 300 MHz) of **17c**.

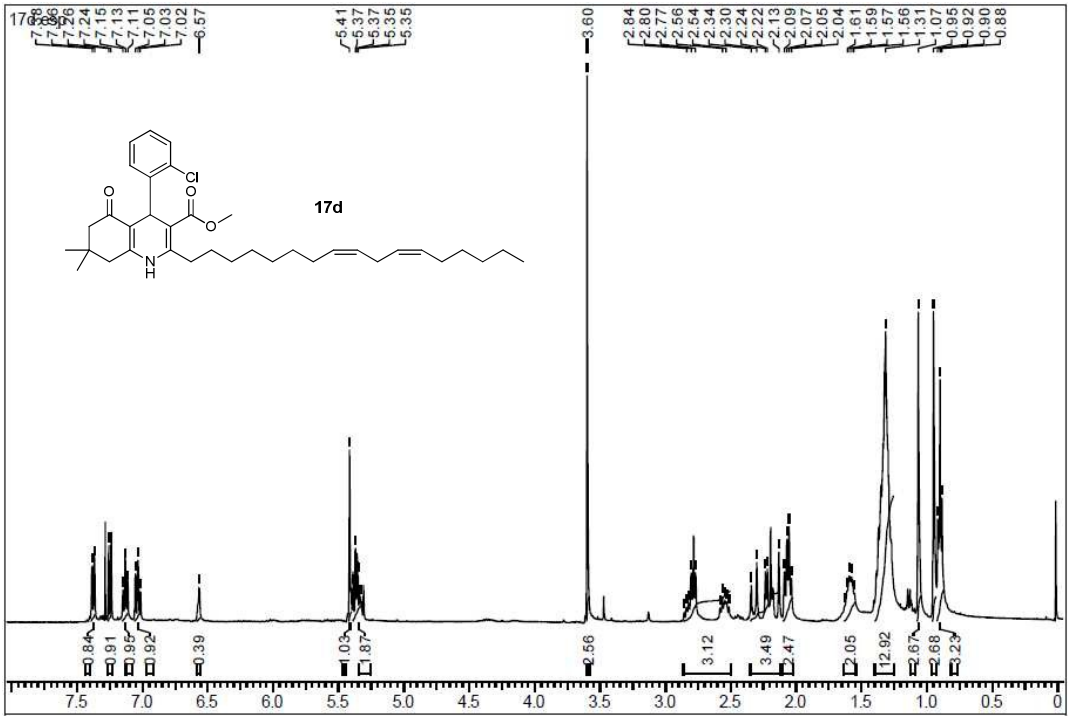

Figure S29.[1]H NMR spectrum ($CDCl_3$, 300 MHz) of **17d**.

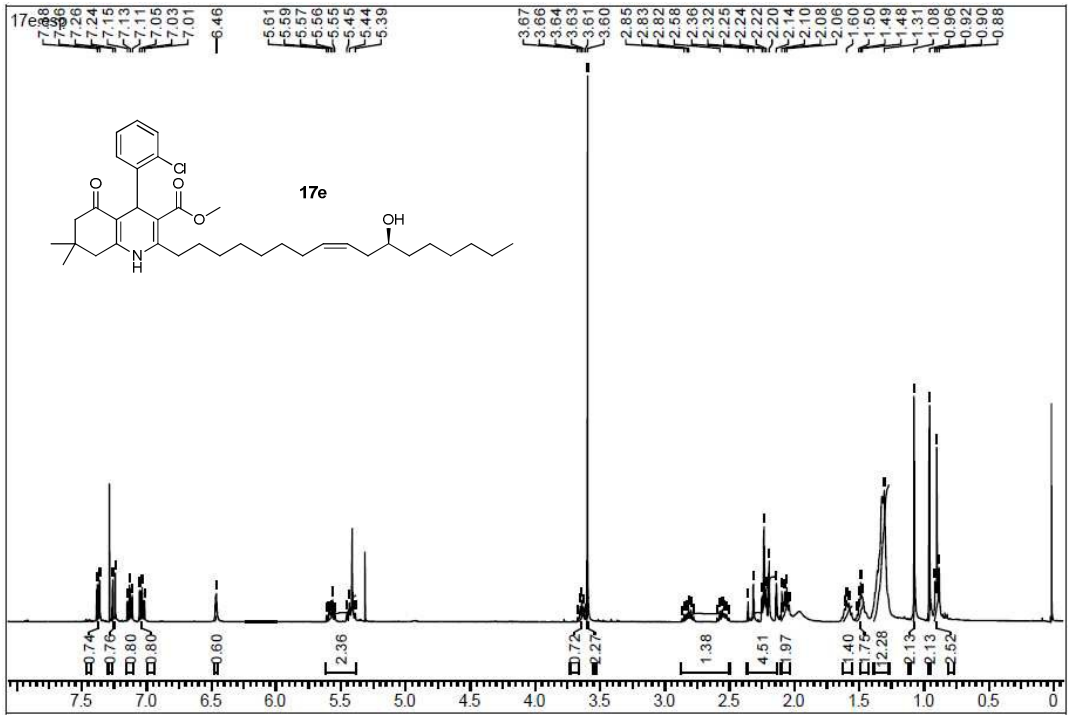

Figure S30.[1]H NMR spectrum ($CDCl_3$, 300 MHz) of **17e**.

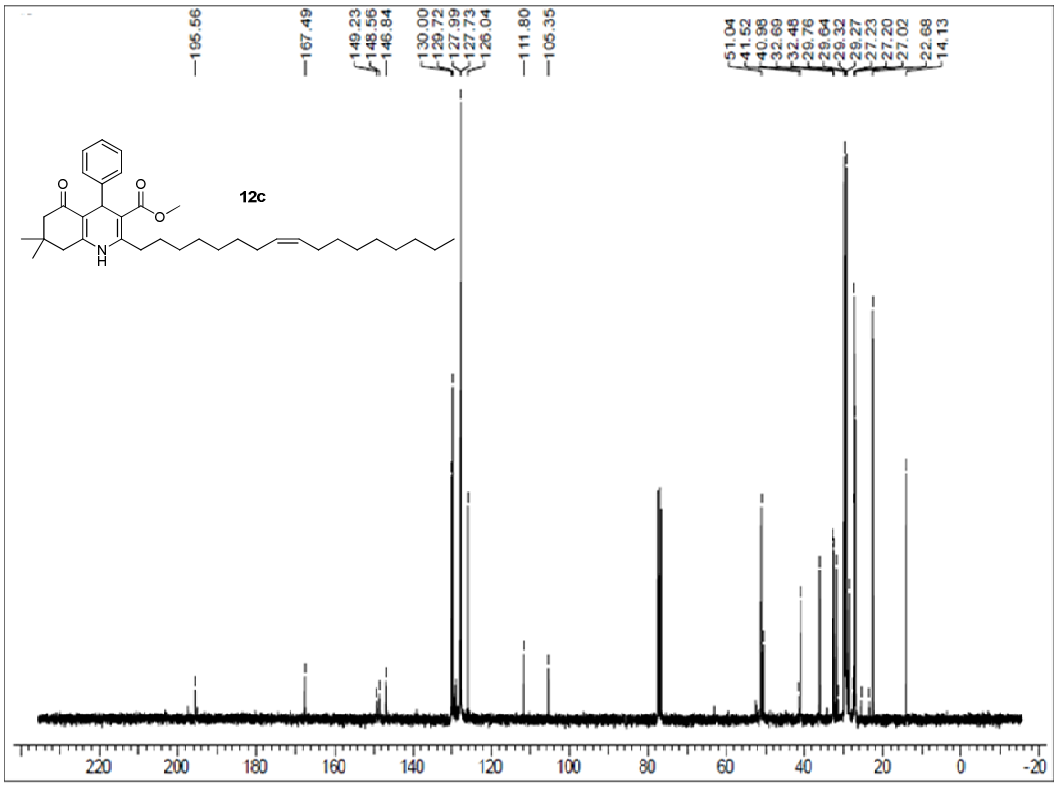

Figure S31.[13]C NMR spectrum ($CDCl_3$, 300 MHz) of **12c**.

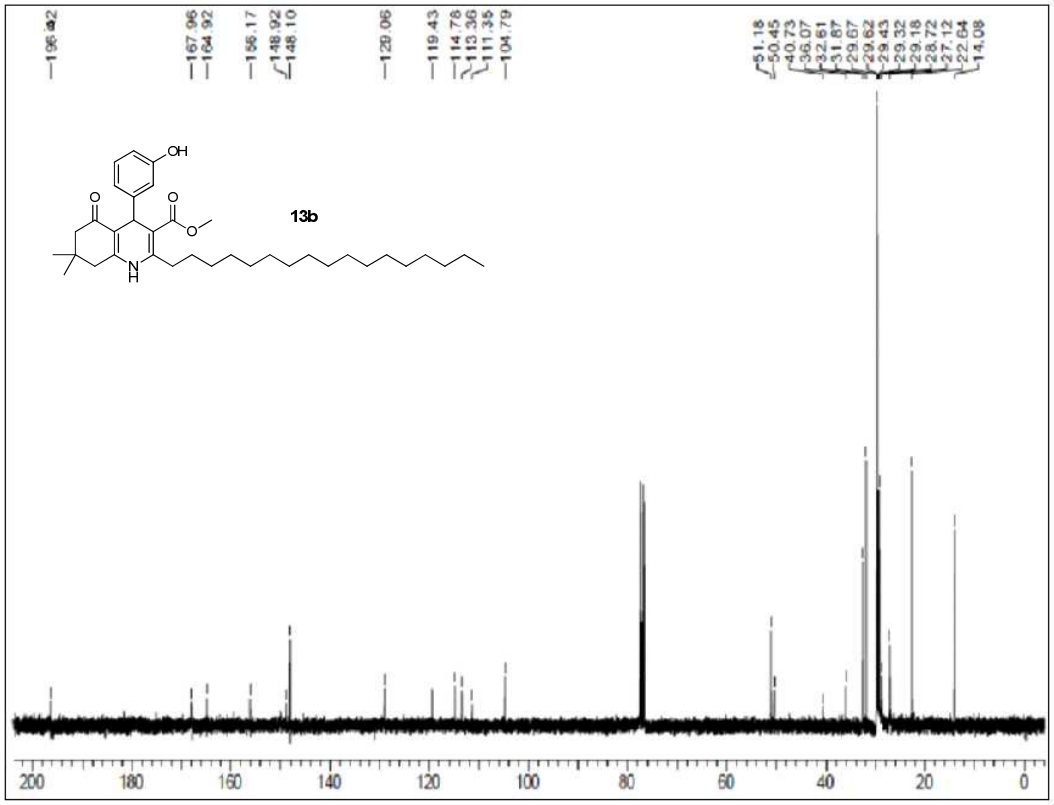

Figure S32.[13]C NMR spectrum ($CDCl_3$, 300 MHz) of **13b**.

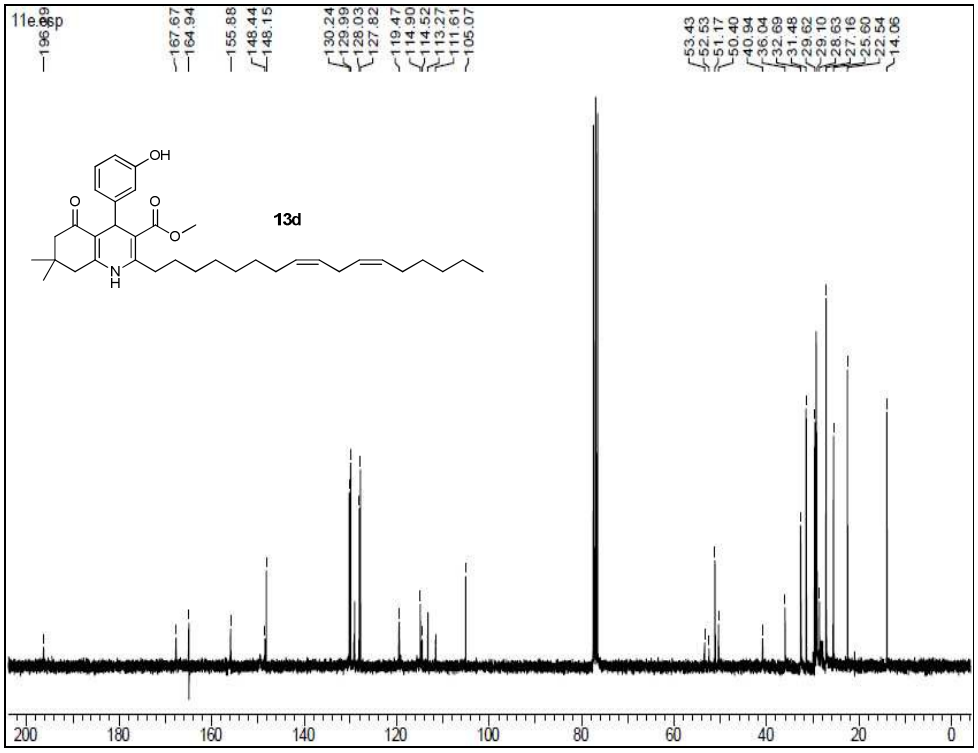

Figure S33. ^{13}C NMR spectrum ($CDCl_3$, 300 MHz) of **13d**.

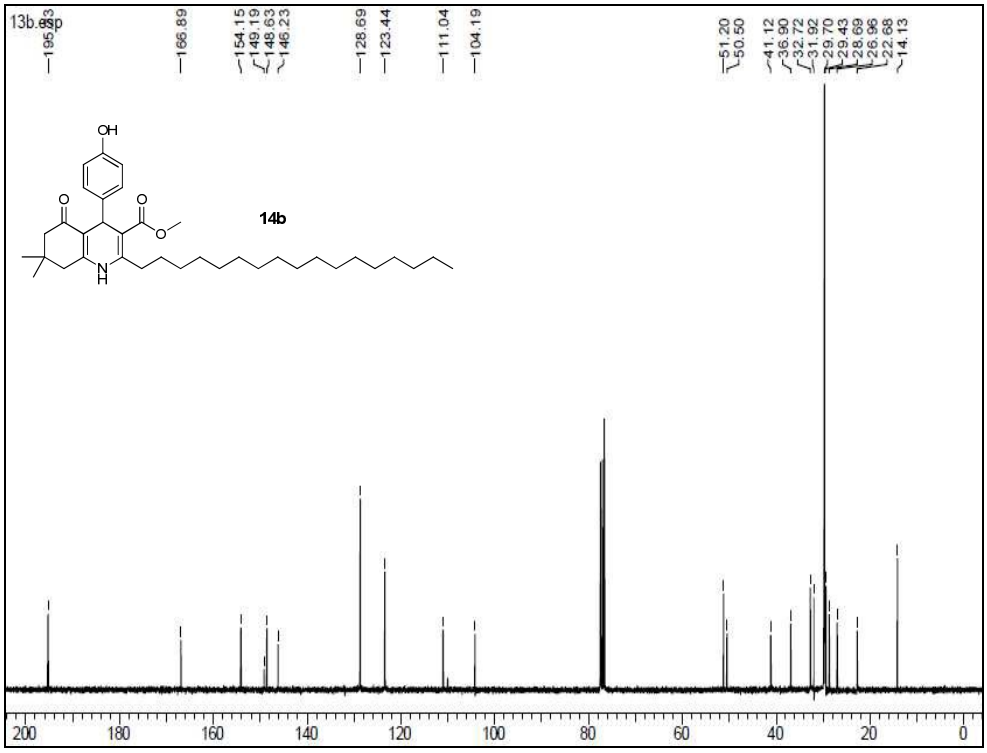

Figure S34. ^{13}C NMR spectrum ($CDCl_3$, 300 MHz) of **14b**.

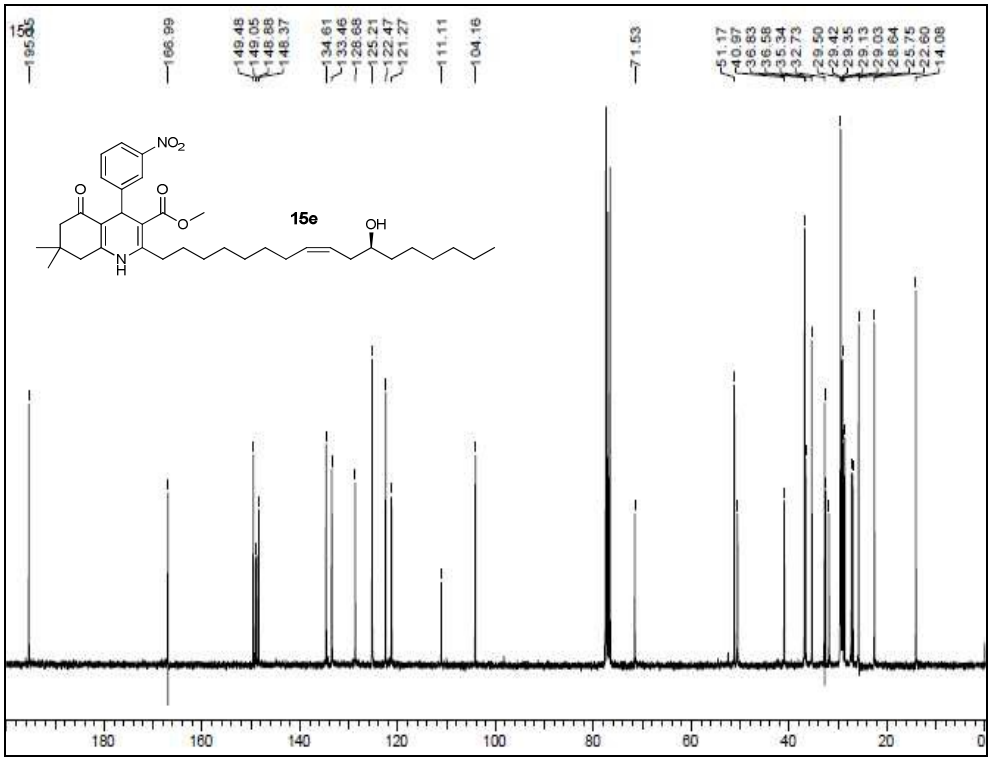

Figure S35.[13]C NMR spectrum ($CDCl_3$, 300 MHz) of **15e**.

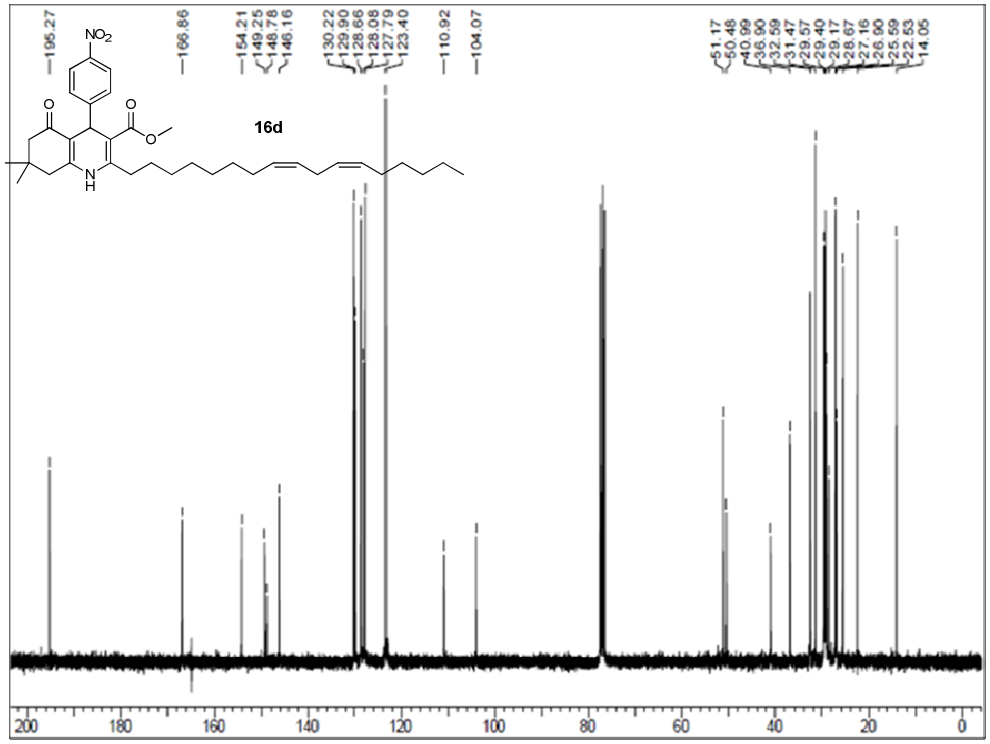

Figure S36.[13]C NMR spectrum ($CDCl_3$, 300 MHz) of **16d**.