Synthesis, Photophysical Properties, Tumor Uptake, and Preliminary in Vivo Photosensitizing Efficacy of a Homologous Series of 3-(1′-Alkyloxy)ethyl-3-devinylpurpurin-18-*N*-alkylimides with Variable Lipophilicity†

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Received December 27, 2000

Starting from methylpheophorbide-a, a homologous series of purpurinimides containing alkyl substituents at two different positions [as 3-(1^1-O-alkyl) and 13^2-*N*-alkyl] were synthesized. These compounds with variable lipophilicity (log *P* 5.32−16.44) exhibit long wavelength absorption near λ_{max}700 nm (ϵ: 45 000 in dichloromethane) with singlet oxygen ($^1O_2$) production in the range of 57−60%. The shifts in in vivo absorptions and tumor/skin uptake of these compounds were determined in C_3H mice bearing RIF tumors by in vivo reflectance spectroscopy. The results obtained from a set of photosensitizers with similar lipophilicity (log *P* 10.68−10.88) indicate that besides the overall lipophilicity, the presence and position of the alkyl groups (*O*-alkyl vs *N*-alkyl) in a molecule play an important role in tumor uptake, tumor selectivity, and in vivo PDT efficacy. At present, all purpurinimide analogues are being evaluated at various doses, and experiments are underway to establish a quantitative structure−activity relationship on a limited set of compounds. The 1D and 2D NMR and mass spectrometry analyses confirmed the structures of the desired purpurinimides and the byproducts formed during various reaction conditions. The mechanisms of the formation of the unexpected 12-formyl- and 12-(hydroxymethyl)purpurinimides under certain reaction conditions are also discussed.

Introduction

Photodynamic therapy (PDT) is a promising cancer treatment that involves the combination of visible light and a photosensitizer.[1] Each factor is harmless by itself, but when combined with oxygen they can produce lethal cytotoxic agents that inactivate the tumor cells.[2] This enables greater selectivity toward diseased tissue, as only those cells that are simultaneously exposed to the photosensitizer, light, and oxygen are exposed to the cytotoxic effect. The dual selectivity of PDT is produced by both a preferential uptake of the photosensitizer by the diseased tissue and the ability to confine activation of the photosensitizer to this diseased tissue by restricting the illumination to that specific region.

Photofrin, a hematoporphyrin derivative, is the only photosensitizer that has been approved worldwide for the treatment of various types of cancers by PDT.[3] It fits some of the criteria for ideal photosensitizers, but it suffers from several drawbacks. First, it is a complex mixture of various monomeric, dimeric, and oligomeric forms. Second, its long wavelength absorption falls at 630 nm, which lies well below the wavelength necessary for the maximum tissue penetration. Finally, it induces prolonged cutaneous phototoxicity, a major adverse effect associated with most of the porphyrin-based photosensitizers. Therefore, in recent years a variety of photosensitizers related to chlorins, bacteriochlorins, porphycenes, phthalocyanines, naphthalocyanines, and expanded porphyrins have been synthesized and evaluated for PDT efficacy.[4] However, only a few studies address the structure−activity relationships in a particular series of photosensitizer.[4]

From our earlier work with various chlorin- and bacteriochlorin-based compounds it has been shown that the presence and position of the substituents in the parent molecule make a remarkable difference in biological activity.[5] Recently, in a congeneric series of the alkyl ether derivatives of pyropheophorbide-a[6] it was observed that the in vivo photodynamic efficacy increased by increasing the length of the carbon chain, being maximum in compounds with *n*-hexyl and *n*-heptyl chains at position-3 (ring A). The structural elements evaluated in this in vivo quantitative structure−activity relationship (QSAR) study included the length and shape (alkyl, alkenyl, cyclic, and secondary analogues) of the ether side chain.[7] Thus, three end points, including tumor growth delay, tumor cell lethality, and vascular perfusion, revealed highly similar QSAR patterns that constituted a function of the alkyl ether chain length and drug lipophilicity, which is defined as the log of the *n*-octanol:water partition coefficient (log *P*). When compensated for differences in tumor photosensitizer concentration, the *n*-hexyl derivative (HPPH) (optimal lipophilicity) was 5-fold more potent than the *n*-dodecyl derivative (more lipophilic) and 3-fold more potent than the *n*-pentyl analogues (less lipophilic). Therefore, drug lipophilicity was highly predictive for photodynamic activity. To determine the effect of the alkyl ether side chains in other series of

† A part of this work was presented at the first International Conference on Porphyrins and Phthalocyanines (ICPP-1), Dijon, France, June 2000.

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10.1021/jm0005510 CCC: $20.00 © 2001 American Chemical Society
Published on Web 05/03/2001

photosensitizers, Pandey et al.[8] introduced a series of O-alkyl side chains at position-8 (ring B) of the most effective isomer of benzoporphyrin derivative (ring A reduced BPD). Among these analogues, the related 8-(1′-hexyloxyethyl)-8-devinyl analogue was found to be more effective than BPD.[8]

In the present study we wanted to explore the effect of the presence of such substituents on photosensitizers different from pyropheophorbide and BPD in their photophysical, physicochemical, and steric factors and to examine the generality of the structure−activity relationship we had previously established for the alkyl ether analogues of pyropheophorbide-a. We believe that information obtained from these studies coupled with those previously obtained from other series of compounds will be of immense value in developing an improved photosensitizer with required photophysical properties.

Importance of the Lipophilicity. In medicinal chemistry, lipophilicity has proven to be an important molecular descriptor that often is well-correlated with the bioactivity of drugs. Lipophilicity is indicated by lipophilic indices, such as the logarithm of a partition coefficient, log *P*, which reflects the equilibrium partitioning of a molecule between a nonpolar and a polar phase, such as an *n*-octanol/water system.[9] Partition coefficients can be measured experimentally by several techniques, ranging from the simple "shake flask" technique to quite popular chromatographic methods such as HPLC. For designing new compounds in a particular series, it is necessary to develop efficient methods for altering the lipophilicity by introducing a variety of substituents or by modifying the basic skeleton. Hence, numerous theoretical methods have been developed to predict lipophilicity based on the log *P* value. The most frequently applied methods are based on the fragmental approach,[10] making use of the additive−constitutive nature of log *P*. The basic idea of these methods lies in the definition of π, the substituent constant, $\pi = \log P_X - \log P_Y$, where P_X is the partition coefficient of a derivative and P_Y is that of the parent compound. It is found that, although π values vary for a given functional group depending on its electronic environment, such variation is small.[11] For example, the π value for a methyl (CH_3) group is 0.5, which is mostly true for both aromatic and aliphatic systems. Adding one saturated carbon group will increase the log *P* value by 0.5. Thus, the easiest way to alter the lipophilicity of a parent molecule is to introduce alkyl chains with variable carbon units.

In the pyropheophorbide series it has been observed that the log of the HPLC retention time is linearly related to the carbon chain length for the corresponding alkyl ether derivative. Similarly, calculated log *P* values (pH 7.4), predicted by a computer program module of the PALLAS system, were linear with chain length, ranging from 3.1 for C1 to 8.6 for C12.[7] Measured log *P* values were also in agreement with the calculated values. Thus, for a congeneric series of compounds, it is possible to determine their log *P* values with the PALLAS computer program and by HPLC experiments and to confirm these results by the classical "shake flask" method.

Structure Modification of Chlorophyll a—the Strategic Consideration. Having developed a QSAR for the alkyl ether analogues of the pyropheophorbide series, we decided to extend this approach to photosensitizers with longer wavelength absorption. For our study, purpurin-18 **1a**[12] was selected as a starting material due to (a) its ready availability from chlorophyll *a*; (b) its strong absorption at ~700 nm, which has an advantage over other porphyrin-based photosensitizers in treating deeply seated tumors; and (c) its high singlet oxygen yield, as well as inherent photosensitizing ability demonstrated by in vitro studies. Purpurin-18 also provides an opportunity for modifying the functional groups substituted at the peripheral positions such as the vinyl, fused anhydride ring, and propionic acid side chain. These modifications generate a series of photosensitizers with variable lipophilicity, thus avoiding many different multistep total syntheses.

Chemical Transformation of the Exocyclic Anhydride Ring. Smith et al.[13] have shown that purpurin-18 in the presence of an alkylamine forms the related imide derivatives in a low yield if the reaction mixture is left at room temperature for several weeks. We were interested in evaluating this class of compounds as it presents a unique opportunity to alter the lipophilicity of the molecule by substituting various *N*-alkyl groups at the fused imide ring and also by replacing the 3-vinyl group with a series of *O*-alkyl derivatives. Therefore, our first objective was to develop an efficient general method for the preparation of purpurin-18-*N*-alkylimides, which could then be modified into a series of desired analogues.

For our study, methylpheophorbide-a **1**, isolated from *Spirulina pacifica*,[14] was converted into purpurin-18 methyl ester **2**[12] and was used as a substrate. As shown in Scheme 1, reaction of **2** (λ_{max} 699 nm) with various alkylamines (e.g. *n*-hexylamine) at room temperature gave the corresponding amides in high yield (95%), as a mixture of **3e** and **4e** in the ratio of 6:1. The amide **4e** was obtained as a minor product, because of the steric hindrance caused by the adjacent reduced pyrrole ring during the ring-opening reaction, and was assigned as 15^2-amide, whereas the major product **3e** was assigned as the 3^2-amide by NMR spectroscopy. Attempts to convert amides **3e** and **4e** into the corresponding imides **9e** by following the methods used in other aromatic systems mainly produced the decomposition products. Leaving the amide solution in CH_2Cl_2 or THF at room temperature for 1 week gave a mixture of purpurins with cyclic anhydride **2** (699 nm) and cyclic imide **9e** (705 nm) in minor amounts and the starting material as a major product. Refluxing the reaction mixture at elevated temperatures slightly improved the yield of purpurin anhydride without formation of any desired imide analogue. Various attempts were then made to optimize the reaction conditions, and these are summarized in Table 1. Interestingly, reaction of the mixture of amides **3e** and **4e** in the presence of Montmorillonite K-10 clay and CH_2Cl_2 as a solvent gave a mixture of cyclic imide **9e** as a minor product (12%) and anhydride analogue **1** as the major component (85%), which could be separated by column chromatography.

To avoid the formation of the undesirable cyclic anhydride **1**, it was thought to be necessary to activate the carboxylic function of intermediate amides, which could generate the desired imide analogue via intramo-

Scheme 1

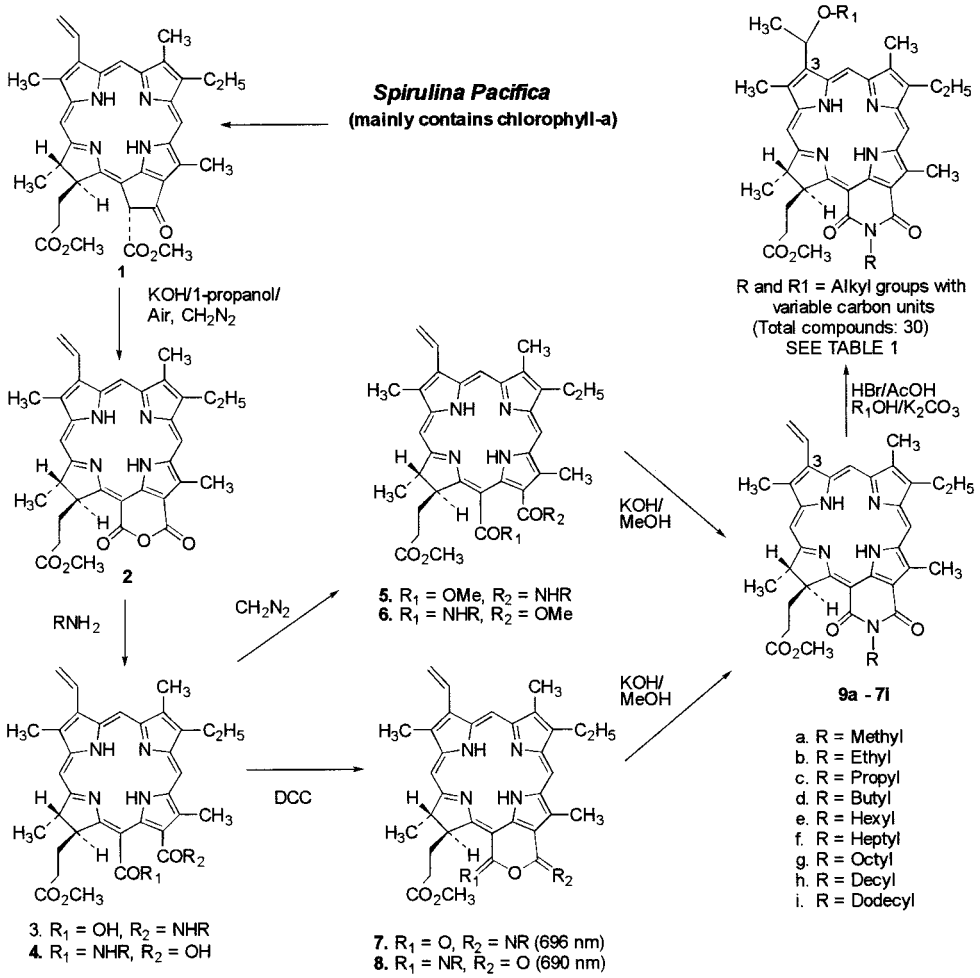


Table 1. Percentage Yields of Purpurinimide and Isoimide under Various Reaction Conditions[a]

method no.	conditions	starting amide (%)	anhydride (%)	imide (%)	isoimide (%)
1	THF, Δ, 4 h	25	70	5	0
2	imidazole, 140 °C, 1 h	decomposition			
3	K-10 clay, CH_2Cl_2, 24 h	0	80−85	10−12	0
4	CH_2Cl_2, 10 days	50	20−25	15−20	0
5	DCC	0	0	0	95
6	DCC; K-10 clay, RT	100	0	0	0
7	DCC; DBU, RT	100	0	0	0
8	DCC; DBU, Δ, 2 h	40	0	60	0
9	DCC; KOH/MeOH RT, 5 min	0	0	85	0
10	DCC; pTS, CH_2Cl_2	95	0	0	0
11	TCD	nd	0	0	0
12	TCD; DBU, RT	100	0	0	0
13	TCD; DBU, toluene, Δ, 2 h	0	50	10	0
14	TCD; DBU, THF, Δ	60	0	30	0
15	TCD; KOH/MeOH, RT, 10 min	90	0	10	0
16	CH_2N_2; KOH/MeOH, RT, 5 min	0	0	85	0

[a] DCC, dicyclohexylcarbodiimide; TCD, 1,1[1]-thiocarbonyldiimidazole; DBU, 1,8-diazabicyclo[5.4.0]undec-7-ene; nd, not determined.

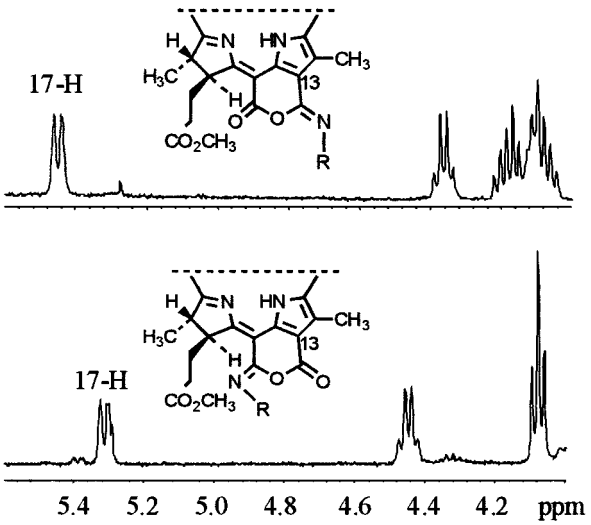
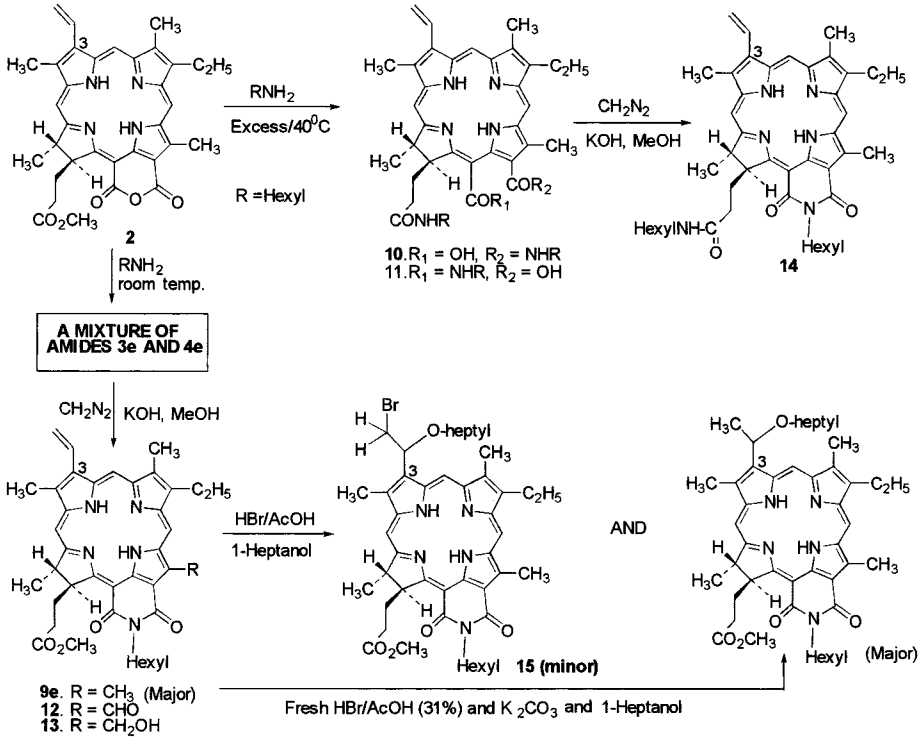


Figure 1. Partial NMR spectra of purpurin-18-13[1]-*N*-hexylisoimide (**7e**) and purpurin-18-15[1]-hexylisoimide (**8e**). The reduced ring D caused a significant upfield shift in the resonances of the 17H proton in **8e** (R = hexyl).

lecular cyclization. Thus, two pathways were investigated. In the first approach, reaction of purpurin amides **3e** and **4e** with dicyclohexylcarbodiimide (DCC) afforded a mixture of two isomers in a ratio of 6:1, in 96% overall yield. This isomeric mixture was found to be a mixture of purpurin isoimide **7e** and **8e** by NMR (proton and C-13) and high-resolution mass spectroscopic studies. Separation of this mixture gave isomerically pure purpurinimides **7e** and **8e** with long wavelength absorptions at λ_{max} 696 and 690 nm, respectively. The structure of the minor product **7e** was further confirmed as 15[1]-

Scheme 2



2

10. R_1 = OH, R_2 = NHR
11. R_1 = NHR, R_2 = OH

14

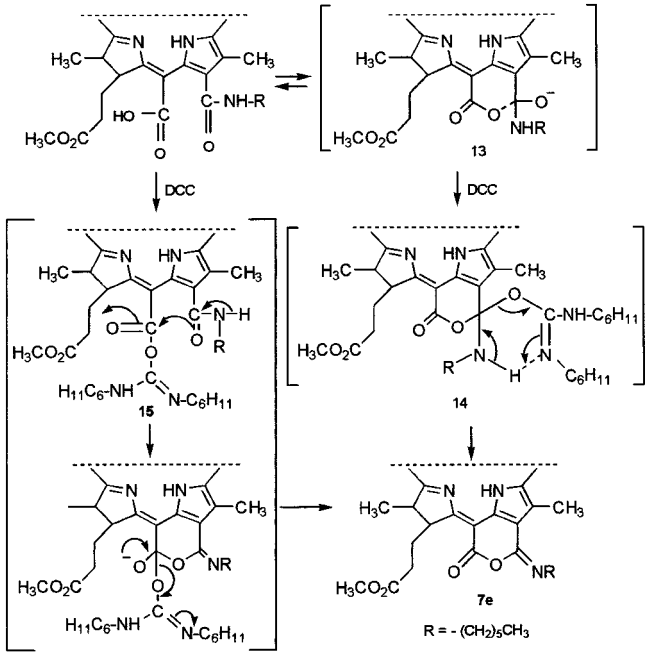
9e. R = CH_3 (Major)
12. R = CHO
13. R = CH_2OH

isoimide on the basis of the observation of NOE interactions between the 15^2-*N*-alkyl group and the 17^3-methyl (CO_2Me) group. Surprisingly, in their ^{1}H NMR spectra (Figure 1), 17H resonance of the 15^1-isoimide **8e** appeared downfield compared to that of 13^1-isoimide **7e**, presumably due to an electronic resonance effect induced by the *N*-alkyl group. Such unique ^{1}H NMR characteristics can thus be employed for distinguishing the 13^2 and 15^2-isoimides. Treatment of isoimides **7e** and **8e** individually or together as an isomeric mixture with DBU/toluene at 60 °C produced imide **9e** in 60% yield. Interestingly, replacing DBU with stronger bases, such as methanolic KOH at room temperature, gave the desired purpurin-18-*N*-hexylimide **9e** in 85% yield.

In the second approach, the intermediate amide mixture containing **3e** and **4e** was converted into corresponding methyl esters **5a** and **6a** by reacting with diazomethane, followed by brief methanolic KOH treatment to produce the desired imide analogue **9e** in excellent yield (>80%, Scheme 2). Because of the difficulty of removing dicyclohexylurea as an impurity in our first approach, this methodology was found to be more suitable for preparing various purpurin-18-*N*-alkylated imides.

Scheme 3 outlines two possible mechanisms for the formation of *N*-alkyl isoimide (e.g. **7e**) by the dehydration of the intermediate amide (e.g. **3e**) with DCC, as well as its final conversion into the corresponding imide **9e**. Thus, donation of a proton from the amide **3e** to DCC could lead to intermediate **13**, which could decompose via the indicated quasi-six-member-ring transition state **14** into N-substituted cyclic isoimides **7e**. It can also be postulated that reaction of DCC with amide **5** first generates the unstable DCC derivative **15**, which upon intramolecular cyclization would produce another unstable isoimide and eventually afford the desired isoimide **7e** and dicyclohexylurea as a byproduct. Such

Scheme 3. A Possible Mechanism for the Formation of a Fused Isoimide Ring System



six-member-ring formation has also been proposed in other aromatic systems.[15] Further base treatment cleaves the isoimide ring of **7e**, and the resulting intermediate amide under intramolecular cyclization could afford the desired imide **9e**. In both approaches, during the formation of imide analogue, several byproducts, **12**, **13**, **14**, and **16**, were also isolated (Schemes 3−5). Among these analogues, chlorin **14**, a slightly slower moving compound than **8e** in TLC exhibited similar visible absorption spectrum as the parent imide **7**. In their NMR spectrum, compound **14** has an extra broad signal (compared to **8e**) at 6.9 ppm integrated for one proton

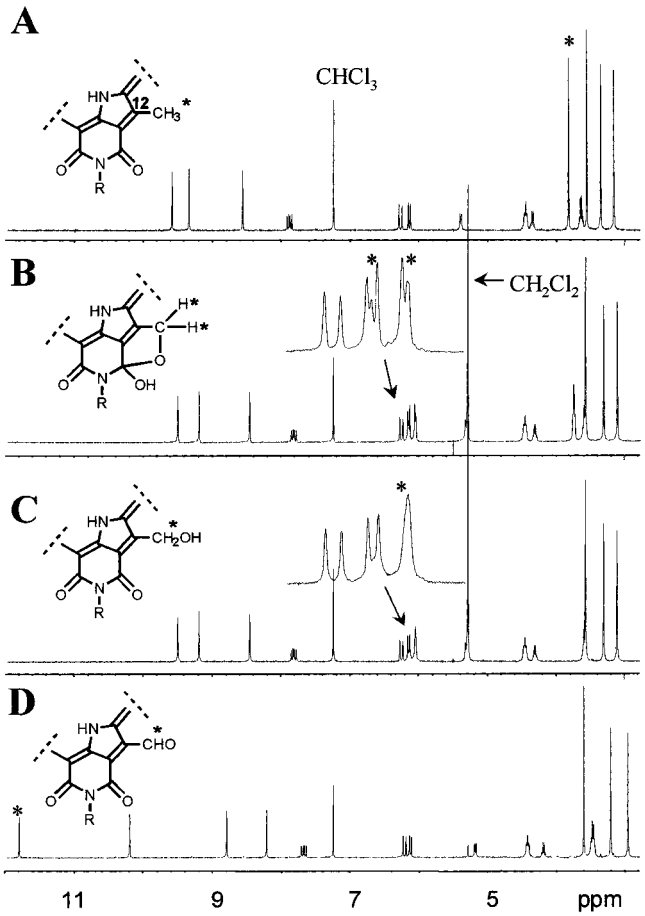


Figure 2. Partial NMR spectra: (A) 12-methylpurpurin-18-*n*-hexylimide **9e**; (B) the unstable intermediate **16**; (C) the 12-hydroxymethyl derivative **13**; and (D) the related 12-formyl analogue **12**.

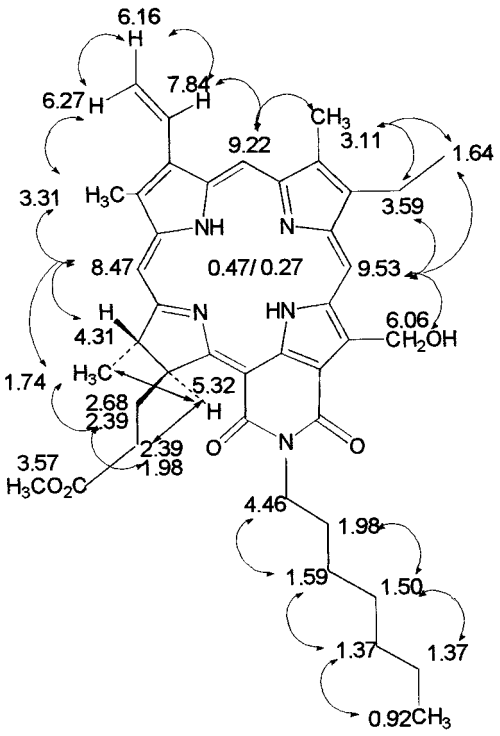


Figure 3. The interactions shown by various protons in purpurinimide **9e**. The assignments are based on the results obtained from the 2D ROESY NMR studies.

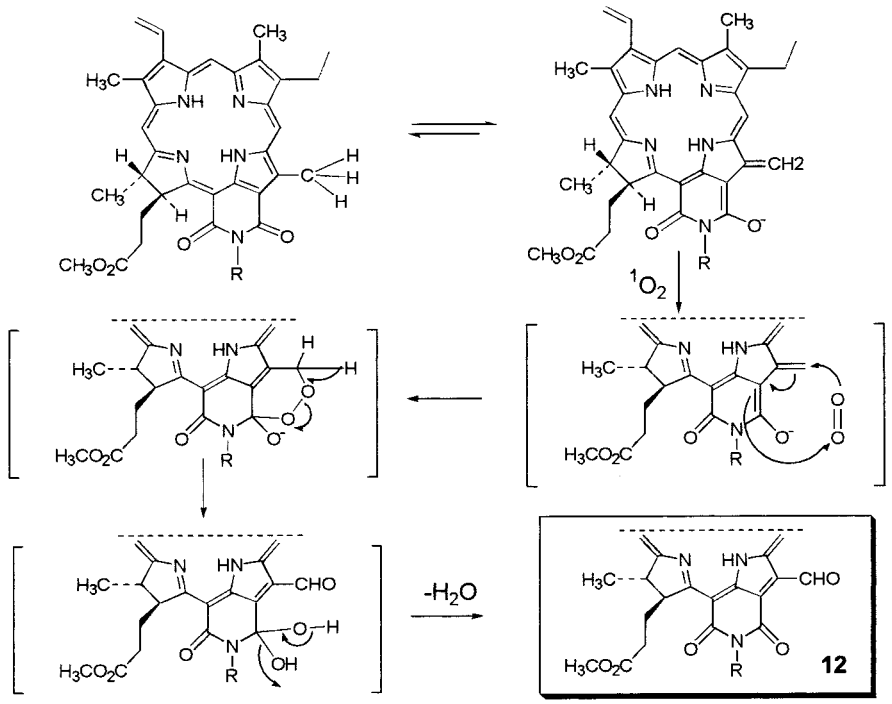
(Figure 1). The 17^3-methyl (CO_2Me) observed at 3.6 ppm for parent imide **9e** was found to be absent. Furthermore, mass spectrometry analysis also confirmed the proposed structure (m/z = 731.4 for R = hexyl). On the basis of these observations, the structure of **14** was assigned as 17^3-hexylamide purpurin-18-*N*-hexylimide, apparently formed by the condensation of the methyl ester functionality with unreacted 1-hexylamine.

The other byproduct (a minor component) observed just behind purpurinimide **9e** as a green band in preparative thin-layer chromatography was isolated in 10% yield. The electronic absorption spectrum of the byproduct exhibited a long wavelength absorption at 717 nm, and compared with the parent imide **9e** it had a bathchromic shift of 12 nm. The ^{1}H NMR spectrum of the product (Figure 2) showed an extra singlet (one proton) at 11.9 ppm along with the meso-protons' resonances; which appeared at 10.3, 8.9, and 8.2 ppm for 10H, 5H and 20H, respectively. The 12-methyl signal observed at 3.8 ppm for the parent imide **9e** was missing, and the mass spectrometry analysis gave a molecular ion peak at m/z of 690.2 (R = heptyl), which was 18 amu more than the corresponding imide (m/z = 672.4, R = heptyl). On the basis of these results, the structure of the byproduct was assigned as 12-formylpurpurin-18-*N*-heptylimide **12**.

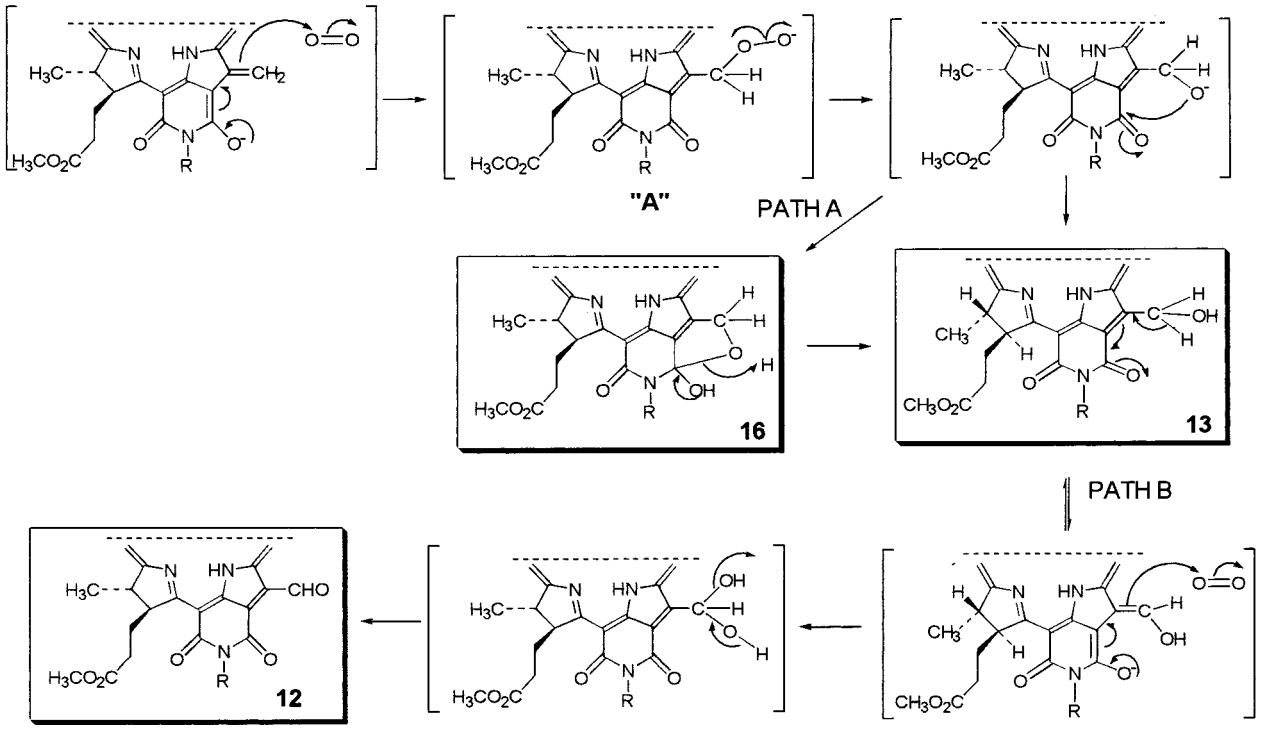
The third byproduct obtained as the most polar band was characterized as 12-(hydroxymethyl)purpurin-18-*N*-hexylimide **13**. As shown in Figure 2, the presence of a sharp singlet at 6.1 ppm, integrating for two protons, and the absence of the 12-methyl resonances confirmed the proposed structure. The structure of compound **13** was further confirmed by mass spectrometry analysis (m/z = 692.2) and 2D-ROESY NMR studies.

There are two possible mechanisms for the formation of the 12-formyl analogue **12**. First, in the presence of light, the compound possibly undergoes a [4 + 2] cycloaddition reaction with singlet oxygen. As shown in Scheme 4, the photooxidation of purpurin-18-imide **9e** under aqueous basic conditions on exposure to light will produce the corresponding 12-formyl derivative **12**. To confirm the involvement of $^1O_2$, the reaction was performed in the dark (under a nitrogen atmosphere) and, as expected, no formyl analogue was isolated. The second mechanism (in the absence of light) is postulated on the basis of the isolation of the 12-hydroxymethyl derivative **13** obtained as a minor compound. As shown in Scheme 5, deprotonation of amide **9e** will lead to its enolization form, which on reacting with the molecular oxygen will form an intermediate, which on cleavage of the O−O bond will afford the intermediate anion. This could follow two pathways: If the reaction sequences follow pathway A, the intermediate, under intramolecular base-catalyzed cyclization, would yield the lactone **16** (for NMR see Figure 2) and that will eventually produce 12-(hydroxymethyl)purpurin-18-*N*-alkylimide **13.** If it follows pathway B, the intermediate could undergo further enolization, which on reacting with molecular oxygen will generate the 12-dihydroxymethyl derivative. The dehydration of the unstable dihydroxymethyl derivative will produce 12-formylpurpurin-18-*N*-alkylimide **12**. A more straightforward path from intermediate "**A**" to aldehyde **12** could also involve heterolytic cleavage of the protonated peroxide with loss of H_2O.

Scheme 4. A Possible Mechanism for the Formation of 12-Formyl Analog in Presence of Singlet Oxygen



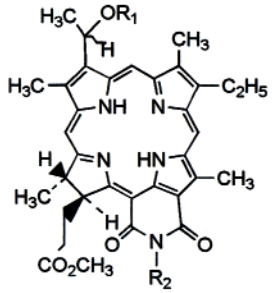
Scheme 5. A Possible Mechanism for the Formation of 12-Formylpurpurinimide via the Corresponding 12-Hydroxymethyl Analog in Presence of Molecular Oxygen



Vinyl Modification. Another functional group in purpurin-18 methyl ester **2** available for chemical modification is the vinyl group present at positon-3 of the macrocycle. On the basis of the previous QSAR studies with the pyropheophorbide ethers,[7] we have shown that the overall lipophilicity of the molecule can be influenced by introducing various alkyl ether substituents in ring A of the macrocycle. Therefore, we decided to investigate the effect of a series of such 3-alkoxyalkyl substituents of various purpurin-18-*N*-alkylimide in PDT efficacy.

For the preparation of 3-alkyl ether analogues of purpurin-18-based photosensitizers, a series of purpurin-18-*N*-alkylimides **9a**−**9i** containing *N*-methyl to *N*-decyl carbon units, respectively, were used as substrates. Theoretically, if these compounds are individually reacted with various alkyl alacohols of 1−12 carbon units, there is a possibility of producing 144 compounds, having partition coefficient values ranging from 5.32 to 16.44. In Table 2, on the basis of their lipophilicity, these compounds were divided into five groups: group I (shown in red), log P = 5.3−7.8; group II (shown in

Table 2. Possible Combinations of the Alkyl Substituents (1−12 Carbon Units) at Two Different Positions of Purpurin-18-*N*-alkylimides (1−12 Carbon Units) and Their Calculated log *P* Values***



$R_2\backslash R_1$ *	1	2	3	4	5	6	7	8	9	10	*11***	12
1	5.32	5.82	6.25	6.75	7.25	7.67	8.20	8.72	9.25	9.75		10.73
2	5.82	6.24	6.74	7.24	7.78	8.28	8.78	9.28	9.78	10.25		11.23
3	6.29	6.79	7.26	7.76	8.26	8.79	9.29	9.79	10.29	10.68		11.73
4	6.80	7.30	7.80	8.28	8.78	9.30	9.80	10.30	10.78	11.26		12.23
*5***												
6	7.82	8.32	8.79	9.30	9.81	10.32	10.83	11.34	11.85	12.36		13.38
7	8.32	8.82	9.32	9.82	10.32	10.83	11.34	11.84	12.34	12.86		13.88
8	8.82	9.32	9.82	10.32	10.82	11.34	11.84	12.36	12.84	13.34		14.40
*9***												
10	9.83	10.33	10.83	11.33	11.83	12.36	12.86	13.36	13.86	14.40		15.44
*11***												
12	10.88	11.38	11.88	12.38	12.88	13.38	13.88	14.38	14.89	15.39		16.44

*R_1 = alkyl ether; e.g., 1 represents methyl, 2 represents ethyl, ... 12 represents dodecyl; R_2 = alkylimide; e.g. 1 represents methyl, 2 represents ethyl, ... 12 represents dodecyl. **The desired reagents are commercially not available. ***On the basis of their lipophilicity, compounds were divided into five groups: I (red), log *P* = 5.3−7.8; II (green), log *P* = 8.2−9.3; III (blue), log *P* = 9.8−10.8; IV (magenta), log *P* = 11.3−12.3; V (black), log *P* = 12.8−16.4.

green), log *P* = 8.2−9.3; group III (shown in blue), log P = 9.8−10.8; group IV (shown in magenta), log *P* = 11.3−12.3; group V (shown in black), log *P* = 12.8−16.4. Instead of synthesizing the whole series, we decided to select the least numbers which could cover the entire range of log *P* values and the greatest variety in structure. Table 4 summarizes the list of purpurinimides synthesized with substituents at two different positions with their calculated log *P* values. Compounds shaded with red color have $R_1 = R_2 = 1-12$ (methyl to dodecyl); compounds shaded with blue color have the same lipophilicity ($R_1 + R_2 = 13 = 11$ methylene units + 2 methyl terminal groups); compounds shaded with green color have fixed length of 13^2-alkylimide side chain (R_2 = hexyl); and compounds shaded with yellow color have fixed length of 3-(1-alkyl ether) side chain (R_1 = hexyl). Table 4 represents a classic example in which compounds **37**, **42**, and **45** have the alkyl ether and *N*-alkyl substituents at various positions with similar log *P* values (10.73−10.88) and similar photophysical characteristics. The singlet oxygen yields, measured in benzene, were similar for all the purpurinimides and were 0.70 ± 0.05. Therefore, our aim was to investigate the PDT efficacy of these and the related photosensitizers listed in Table 4 and to try to investigate a correlation of photosensitizing ability with their lipophilicity and in vivo tumor uptake.

A general method for the preparation of the desired alkyl ether analogues of purpurinimides **9a**−**9i** and the formation of byproducts under certain reaction conditions is depicted in Schemes 1 and 2. In a typical procedure, purpurin-18-*N*-hexylimide **9e** was reacted with 30% HBr/acetic acid and the residue obtained after removing the acid, and then reaction with 1-heptanol produced the desired 3-(1-heptyloxy)ethylpurpurin-18-*N*-hexylimide **37** (60% yield) as a major component and 3-(1-heptyloxy-2-bromo)ethyl derivative **15** as a minor product (Scheme 2). The bromo derivative **15** moves extremely close to its parent compound in TLC and was separated only after repeated preparative thin-layer chromatography. The structures of the starting materials (e.g., see Figure 3) and the final products were confirmed by ^{1}H NMR and mass spectroscopy. Compared to compound **37**, in which 3^1-proton resonance appears as a quartet at ∼5.7 ppm due to the adjacent methyl coupling, the 3^1-proton of the bromo derivative **15** shows a triplet at ∼5.8 ppm caused by the adjacent 3^2-bromomethyl. In compound **37**, 3^2-methyl appears as

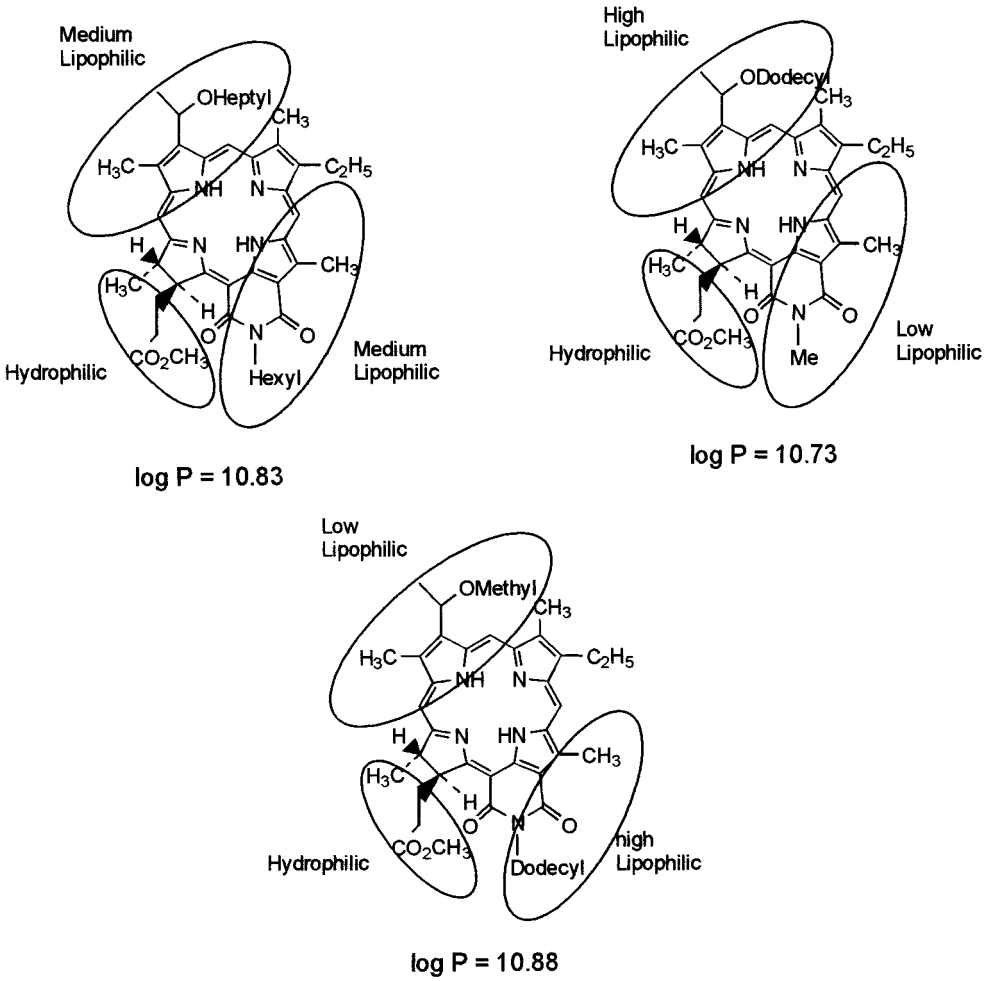


Figure 4. An example of maintaining the similar lipophilicity of various imide analogues by introducing various alkyl substituents at different positions of the molecule.

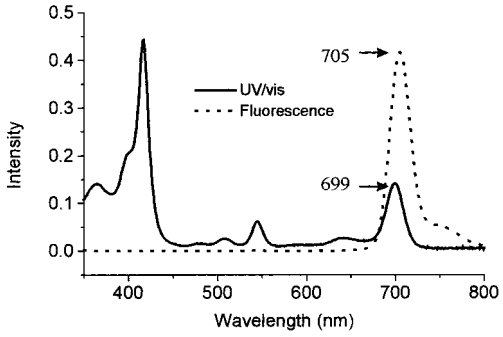


Figure 5. Absorption and fluorescence spectra of purpurinimide **37** (in dichloromethane) excitation of the absorption peak at 699 nm produced emission at 705 nm.

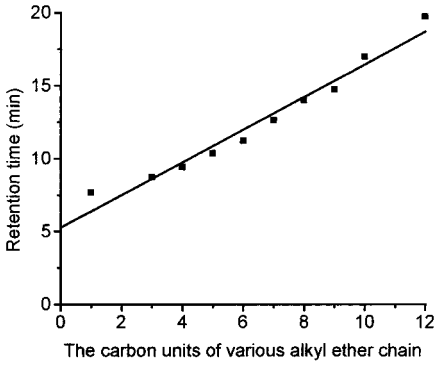


Figure 6. HPLC retention times of a series of 3-(1′-alkoxy) ethyl analogues with variable carbon units of purpurin-18-*N*-hexylimide showing a linear correlation with the lipophilicity of the molecule.

a doublet at upfield region ~2 ppm, whereas in compound **15**, this signal is replaced with a doublet of doublets at ~4.2 ppm. The formation of this product could be eliminated by maintaining anhydrous conditions, using fresh HBr/AcOH (avoiding Br_2), and adding anhydrous K_2CO_3 as an acid quencher before reacting with the desired alcohol. The alkyl ether analogues exhibited strong absorption ($\epsilon = 45\,000$) at near 700 nm. The absorption and fluorescence spectra of a representative compound are shown in Figure 5.

Relationship between Molecular Structure and Lipophilicity. As shown in Figure 6, the alkyl ether analogues of purpurin-18-*N*-hexylimides exhibited a linear relationship with log *P* and HPLC retention time. The log *P* values at pH 7.4 (calculated by the Prolog D module of PALLAS software, Compudrug Chemistry, Ltd. Budapest) showed a linear relationship with the chain length, ranging from 7.82 (**33**) to 13.38 (**41**) with C-1 to C-12 carbon units. Similar correlation was also observed between the retention times and the log *P* values. Therefore, the calculated log *P* values presented for various analogues in Table 4 represent the actual lipophilicity of this series of compounds.

Table 3

compd no.	singlet oxygen quantum yield	compd no.	singlet oxygen quantum yield
20	0.59	**41**	0.57
33	0.57	**42**	0.60

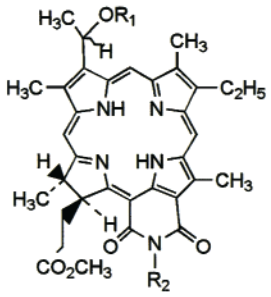
Singlet Oxygen Quantum Yields. Purpurinimides **20**, **33**, **41**, and **42** with variable lipophilicity were subjected to the assay for quantum yield of singlet oxygen. Benzene was used as solvent throughout. The solutions were continuously stirred with a stream of oxygen. All experiments were carried out at room temperature. As can be seen from Table 3, the difference in overall lipophilicity of the molecules did not produce any significant difference in singlet oxygen yields and were observed in the range of 57−60%.

Determination of Tumor Uptake by in Vivo Reflectance Spectroscopy. Most of the purpurinimides were insoluble in water and for the biological studies were dissolved in a 1% Tween 80/5% dextrose solution. The concentration of the photosensitizers in the solutions was calculated on the basis of their extinction coefficient values, using the Beer−Lambert law.[16]

We have previously shown that the absorption spectrum of a compound in living tissue can be obtained by in vivo reflectance spectroscopy.[17] In brief, the experiment measures the light scattered by the tissue. For these experiments, the mice were first anesthetized using ketamine xylazine intraperitoneally. The optical power as a function of wavelength was recorded before the iv injection of the photosensitizer. The drug was then injected and the spectrum again recorded. The in vivo drug absorption spectrum is best displayed by taking the ratio of the postinjection spectrum to the preinjection spectrum. This ratio offers the same advantages as a double-beam absorption spectrophotometer. The preinjection mouse data can be thought of as the reference beam sample (typically a cuvette and solvents), and the postinjection data as the sample beam containing everything in the reference beam plus the experimental drug.

For measuring the tumor uptake, the purpurinimides were injected into mice at a dose of 5.0 μmol/kg. Most of the purpurinimides produced high tumor uptake, and some of them showed considerable difference in tumor to skin uptake at 24 h postinjection, indicating enhanced tissue selectivity, an advantage for all photosensitizers in achieving high therapeutic ratio. These data indicate that, in the purpurinimide series, altering the length of the *N*-alkyl- or *O*-alkyl ether carbon chains resulted in a significant change in tumor uptake. In a series of

Table 4. A List of Alkyl Ether Analogs of Purpurin-18-*N*-alkylimide Synthesized and Their Calculated log *P* Values



R2\R1 *	1	2	3	4	5	6	7	8	9	10	*11***	12
1	5.32 **(16)**					7.67 **(25)**						10.73 **(42)**
2		6.24 **(17)**				8.28 **(26)**						
3			7.26 **(18)**			8.79 **(27)**				10.68 **(43)**		
4				8.28 **(19)**		9.30 **(28)**						
*5***												
6	7.82 **(33)**		8.79 **(34)**	9.30 **(35)**	9.81 **(36)**	10.32 **(20)**	10.83 **(37)**	11.34 **(38)**	11.85 **(39)**	12.36 **(40)**		13.38 **(41)**
7						10.83 **(29)**	11.34 **(21)**					
8						11.34 **(30)**		12.36 **(22)**				
*9***												
10			10.83 **(44)**			12.36 **(31)**				14.40 **(23)**		
*11***												
12	10.88 **(45)**					13.38 **(32)**						16.44 **(24)**

*R_1 = alkyl ether; e.g. 1 represents methyl, 2 represents ethyl, ... 12 represents dodecyl. R_2 = alkylimide; e.g., 1 represents methyl, 2 represents ethyl, ... 12 represents dodecyl. **The desired reagents were not available.

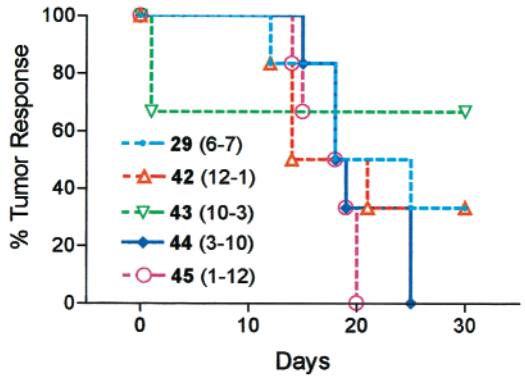


Figure 7. In vivo photosensitizing efficacy of certain purpurinimides with the same number of total carbon units (*O*-alkyl + *N*-alkyl = 13) and similar log *P* values. The mice (six mice/group) were treated with light at 702 nm (in vivo absorption) at 24 h postinjection. Drug dose: 0.4 μM/kg. Compound **29** (*O*-hexyl + *N*-heptyl = 13 carbon units), **42** (*O*-dodecyl + *N*-methyl = 13 carbon units), **43** (*O*-decyl + *N*-propyl = 13 carbon units), **44** (*O*-propyl + *N*-decyl = 13 carbon units), **45** (*O*-methyl + *N*-dodecyl = 13 carbon units). Note: In case of photosensitizer **29**, two of six mice died immediately after the light treatment. Thus, on the basis of the surviving mice, 100% tumor response was observed on day 30.

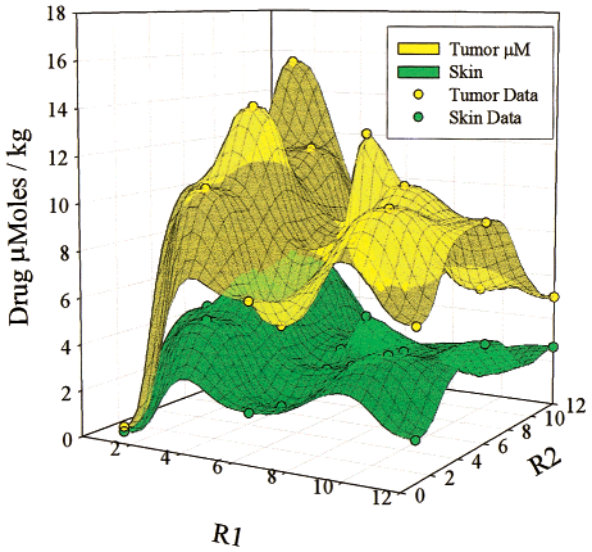


Figure 8. In vivo tumor vs skin uptake of various alkyl ether analogues of *N*-alkyl purpurinimides in C_3H mice implanted with RIF tumors determined by in vivo reflectance spectroscopy at a dose of 5.0 μmol/kg. R_1 and R_2 are *O*-alkyl and *N*-alkyl substituents with variable carbon units respectively (numbers 1, 2, 4−12 indicate the number of carbon units present in *O*-alkyl and *N*-alkyl side chains).

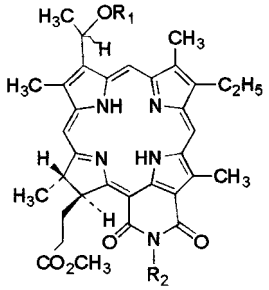
compounds with variable lipophilicity, the skin vs tumor uptake are summarized in Figure 8.

Preliminary in Vivo Studies. To relate the molecular structure of the photosensitizers to their in vivo therapeutic response, the photosensitizing efficacy of photosensitizers was evaluated in C_3H mice implanted with RIF tumors.[7] In initial experiment, groups of six mice were treated at a dose of 1.0 μmol/kg and a light dose of 135 J/cm^2 at 702 nm (in vivo absorption). However, this drug dose was proved to be toxic to many of the animals following the light treatment. To determine the effect(s) of the presence and position of the *O*-alkyl and *N*-alkyl carbon chains, a group of compounds, e.g. **29**, **42**, **43**, **44**, and **45**, with same number of total carbon units (*O*-alkyl + *N*-alkyl; $R_1 + R_2 = 13$)] and log *P* values ranging from 10.68 to 10.88 were evaluated at a lower drug dose (0.4 μmol/kg). As can be seen from Figure 7, among these analogues, purpurinimide **43** (R_1 = decyl, R_2 = propyl) was most effective and produced 67% tumor response on day 30. However, two out of six mice died immediately after the light treatment. The surviving four mice were without tumor regrowth on day 30. It was interesting to observe that the related isomer **44** (R_1 = propyl, R_2 = decyl) showed only 30% tumor response on day 20, with complete tumor regrowth on day 25. Photosensitizer **45** (R_1 = methyl, R_2 = dodecyl) showed 100% tumor regrowth on day 20. However, its related isomer **42** (R_1 = dodecyl, R_2 = methyl) was found to be more effective and produced 35% tumor response on day 30. Under similar treatment conditions, purpurinimide **29** (R_1 = hexyl, R_2 = heptyl) produced 30% tumor response on day 30.

Attempts were also made to determine a correlation between in vivo photosensitizing efficacy of these analogues with tumor uptake obtained by in vivo reflectance spectroscopy at an injected dose of 5.0 μmol/kg, a nontoxic dose in the absence of light treatment. As shown in Table 5, tumor uptake ranged from 4.77 to 11.5 μmol/kg, except for **16**, which was extremely low at 0.3 μmol/kg. For compounds with a similar lipophilicity, an interesting observation was noted. For example, compound **45** (R_1 = methyl, R_2 = dodecyl, log *P* = 10.88) produced higher drug uptake in tumor (15.48 μmol/kg) than **42** (R_1 = dodecyl, R_2 = methyl, log *P* = 10.73, uptake 6.21μmol/kg), but exhibited better tumor selectivity (tumor-to-skin ratio= 3.57). Similar patterns were observed in other photosensitizers with similar log *P* values, even with significant difference in tumor uptake. For example photosensitizers **25** (log *P* = 7.67) and **33** (log *P* = 7.82) showed 6.42 and 10.10 μmol/kg tumor uptake, respectively. Interestingly, **32** and **41** with the same lipophilicity (log P = 13.38) produced 2.00 and 4.30 μmol/kg tumor uptake, respectively. Thus, among the purpurinimides studied so far, in a group of compounds with similar lipophilicity a significant differences in their in vivo tumor uptake and tumor-to-skin ratios were observed. This could be due to a significant difference in their pharmacokinetic and pharmacodynamic characteristics, the subject of ongoing studies.

In summary, in this paper we have described the synthesis and tumor and skin uptake of a series of long-wavelength photosensitiizers related to purpurinimides with variable lipophilicity. The photophysical data indicate that this class of compounds has high singlet oxygen producing ability, a key cytotoxic agent for PDT which is not significantly affected by varying the lipophilicity. The preliminary in vivo results are quite encouraging and suggest their great potential as effective photosensitizers for photodynamic therapy. However, for QSAR studies, it is of utmost importance to evaluate the photosensitizing efficacy of these compounds at various nontoxic doses. Detailed pharmacokinetic and pharmacodynamic studies are required to establish QSAR, and these experiments are currently in progress.

Table 5. Tumor and Skin Uptake in C_3H Mice Implanted with RIF Tumors of Various Purpurinimide[a]



compd no.	R_1 and R_2	log *P*	tumor uptake (μmol)	skin uptake (μmol)	tumor/skin ratio	compd no.	R_1 and R_2	log *P*	tumor uptake (μmol)	skin uptake (μmol)	tumor/skin ratio
16	R_1 = methyl R_2 = methyl	5.32	0.30	0.10	2.87	**37**	R_1 = heptyl R_2 = hexyl	10.83	8.20	2.60	3.15
18	R_1 = propyl R_2 = propyl	7.26	10.5	4.8	2.19	**44**	R_1 = propyl R_2 = decyl	10.83	11.50	6.09	1.89
25	R_1 = hexyl R_2 = methyl	7.67	6.42	1.78	3.61	**45**	R_1 = methyl R_2 = dodecyl	10.88	15.48	5.80	2.67
33	R_1 = methyl R_2 = hexyl	7.82	10.10	4.5	2.24	**39**	R_1 = nonanyl R_2 = hexyl	11.85	10.70	3.54	3.02
27	R_1 = hexyl R_2 = propyl	8.79	4.95	1.48	3.34	**31**	R_1 = hexyl R_2 = decyl	12.36	5.18	1.80	2.88
34	R_1 = propyl R_2 = hexyl	8.79	13.8	6.29	2.19	**32**	R_1 = hexyl R_2 = dodecyl	13.38	4.77	2.00	2.39
20	R_1 = hexyl R_2 = hexyl	10.32	7.30	2.30	3.17	**41**	R_1 = dodecyl R_2 = hexyl	13.38	9.40	4.30	2.19
43	R_1 = decyl R_2 = propyl	10.68	10.26	4.28	2.40	**23**	R_1 = decyl R_2 = decyl	14.40	5.56	1.73	3.21
42	R_1 = dodecyl R_2 = methyl	10.73	6.21	1.74	3.57	**24**	R_1 = dodecyl R_2 = dodecyl	16.44	5.04	2.70	1.87
29	R_1 = hexyl R_2 = heptyl	10.83	8.04	2.95	2.73						

[a] The in vivo uptake was determined by in vivo reflectance spectroscopy at a dose of 5.0 μmol/kg.

Experimental Section

General Methods. Melting points (uncorrected) were measured on a hot-stage apparatus. UV−vis spectra were recorded on a Varian (Cary-50 Bio) spectrophotometer. ^{1}H NMR spectra were recorded in $CDCl_3$ using a Brucker 400 MHz instrument. Mass spectrometry analyses were performed at the Department of Molecular and Cellular Biophysics, RPCI, Buffalo, NY, and at the University of Michigan, East Lansing, MI. Elemental analysis was obtained from Midwest Microlab, LLC, Indianapolis, IN. Where necessary, solvents were dried before use.

Purpurin-18 Methyl Ester (2). Methyl pheophorbide *a* **1** (2 g) was dissolved in 800 mL of diethyl ether. A KOH solution in 1-propanol (24 g dissolved in 80 mL) and 30 mL of pyridine were then added. Air was then bubbled into the solution for 1 h. The reaction mixture was extracted with water (500 mL). The aqueous layer was collected and its pH was adjusted to 2−4 with cold H_2SO_4 solution (25%). It was then extracted with CH_2Cl_2/THF (3:1 ratio, 400 mL). Evaporation of the solvent gave a purple residue. This residue was crystallized from CH_2Cl_2/*n*-hexanes and washed with water until neutral. It was then air-dried overnight to a purple powder, and the crude purpurin-18 carboxylic acid was obtained in 50% (900 mg) yield. Then, 500 mg of this product was reacted with diazomethane, generated by an Aldrich mini-Diazald apparatus, to produce purpurin-18 methyl ester. The residue was chromatographed on a silica column with acetone/CH_2Cl_2 (2% v/v), and the title compound was obtained in 80% yield (410 mg) after crystallizing from CH_2Cl_2/*n*-hexane as purple red crystals. Mp: 267 °C. UV−vis λ_{max} (in CH_2Cl_2): 410 nm (ϵ 1.23 × 10^5), 478 (5.1 × 10^3), 508 (7.5 × 10^3), 546 (2.46 × 10^4), 642 (9.8 × 10^3), 699 (4.95 × 10^4). ^{1}H NMR (400 MHz, 3 mg/1 mL $CDCl_3$, δ ppm): 9.60, 9.39, 8.58 (each s, 1H, for 5H, 10H and 20H); 7.90 (dd, *J* = 18.1, 11.7 Hz, 1H, 3^1CH=CH_2); 6.30 (d, *J* = 18.1,1H, *trans*-3^2CH=CH_2); 6.20 (d, *J* = 11.7,1H, *cis*-3^2CH=CH_2); 5.20 (m, *J* = 9.4, 2.5 Hz, 1H for 17H); 4.46 (q, *J* = 7.1 Hz, 1H for 18H); 3.77 (s, 3H, $12CH_3$); 3.63 (q, *J* = 7.9 Hz, 2H, 8^1CH_2); 3.59 (s, 3H, $17^2CO_2CH_3$); 3.32 and 3.15 (each s, 3H, $2CH_3$ and $7CH_3$); 2.66, 2.45, 2.34, and 1.99 (each m, 1H, 2 × 17^1H and 2 × 17^2H); 1.73 (d, *J* = 7.6 Hz, 3H, $18CH_3$); 1.65 (t, *J* = 7.6 Hz, 3H, 8^2CH_3); 0.25 and −0.12 (each br s, 1H, 2NH). HRMS calcd $C_{34}H_{34}N_4O_5$: 578.2524. Found: 579.2634 (M + 1).

General Procedure for the Preparation of Purpurin-18-*N*-alkylimides. In a typical experiment, purpurin-18 methyl ester (500 mg) dissolved in CH_2Cl_2 was treated with large excess of various alkylamines (0.5 mL) at room temperature for 24 h. The disappearance of the 699 nm band and the appearance of a new 666 nm band in the UV−vis spectrum indicated the completion of the reaction. The reaction solvent and the excess of amine were then evaporated under high vacuum (at or below 30 °C) to give a residue. After crystallization from CH_2Cl_2/hexanes, an isomeric mixture of chlorin-p_6-*N*-alkylamides **3** and **4** (520 mg) so obtained was used for the next step without further purification.

Method 1. The amide intermediates **3** and **4** (500 mg) dissolved in 50 mL of CH_2Cl_2 was treated with DCC (700 mg) at room temperature for 24 h. The reaction was monitored spectrophotometrically. In the UV−vis spectrum, appearance of a new peak at 696 nm marked the completion of the reaction. After the workup (diluted with CH_2Cl_2, washed with water and brine solution, dried over anhydrous sodium sulfate, and filtered and the solvent evaporated), the residue was redissolved in the minimum amount of CH_2Cl_2 and kept in a freezer for 1 h to precipitate out the dicyclohexyl urea as a white solid. The solution obtained after filtration was evaporated. The crude product was chromatographed on a silica column, eluted with 3% acetone in CH_2Cl_2. Purpurin-18-13^1-(*N*-alkyl)isoimide methyl ester **7** (λ_{max} = 696 nm, moving slow in column) and purpurin-18-15^1-(*N*-alkyl)isoimide methyl ester

8 (λ_{max} = 690 nm, moving fast in column) were isolated as individual isomers in 60% and 20% yield, respectively. For the preparation of imide analogue, the mixture of **7** and **8** was then treated with methanolic KOH at room temperature for 3−5 min. The reaction mixture was diluted with 200 mL of CH_2Cl_2, and washed immediately with 2 × 400 mL aqueous solution of acetic acid (2% v/v), 2 × 400 mL water. The organic layer was then dried over anhydrous sodium sulfate, filtered, and evaporated to afford a residue. This residue was chromatographed on a silica column eluting with 2% acetone/CH_2Cl_2 to gave the desired purpurinimides **7** in ∼80% yield.

Method 2. Amide intermediates **3** and **4** were dissolved in CH_2Cl_2 and treated with diazomethane; the methyl ester derivatives **5** and **6** so obtained were then reacted with methanolic KOH for 5 min. The reaction was monitored by UV−vis spectrophotometry.

Following the standard workup, the desired purpurinimide **9** was obtained in ∼80% yield.

Isomeric Mixture of Chlorin-p_6-15-carboxylic Acid 13-Heptylamide 17-Propionic Ester (3f) and Chlorin-p_6-13-carboxylic Acid 15-Heptylamide 17-Propionic Ester (4f): Purpurin-18-methyl ester **2** (500 mg) was reacted with *n*-heptylamine (1 mL) and converted into the related amide derivative, which after crystallization from CH_2Cl_2/*n*-hexanes produced the title compound in 95% yield (565 mg). UV−vis in a solution of THF/CH_2Cl_2 (1:4): 666 (1.78 × 10^4), 612 (1.85 × 10^3), 528 (1.73 × 10^3), 498 (4.92 × 10^3), 402 (5.11 × 10^4) ^{1}H NMR of the mixture of **3f** and **4f** in a ratio of 3:1 (400 MHz, 3 mg/1 mL $CDCl_3$, δ ppm): 9.70, 9.62 and 8.82 (each s, 1H, for 5H, 10H, and 20H of **4f**); 9.69, 9.61, and 8.76 (each s, 1H, for 5H, 10H, and 20H of **3f**); 8.08 (dd, J = 17.4, 11.4 Hz, 1H, 3CH=CH_2); 7.12 (br s, 1H, 15^1*NH*$CH_2CH_2CH_2CH_2CH_2CH_2CH_3$ of **4f**); 7.07 (br s, 1H, 13^1*NH*$CH_2CH_2CH_2CH_2CH_2CH_2CH_3$ of **3f**); 6.34 (d, J = 17.4,1H, 3CH=CH_2); 6.14 (d, J = 11.9, 1H, 3CH=CH_2); 5.05 (m, 1H for 17H); 4.37 (m, 1H for 18H); 3.85, 3.78 and 3.70 (m, 4H, NH$CH_2CH_2CH_2CH_2CH_2CH_2CH_3$ and 8$^1CH_2$ of **3f** and **4f**); 3.59 (s, 3H, 12CH_3 of **3f** and **4f**); 3.49 (s, 3H, 17$^2CO_2CH_3$ of **4f**); 3.47 (s, 3H, 17$^2CO_2CH_3$ of **3f**); ∼3.31 (s, 6H, 2CH_3 and 7CH_3 of **3f** and **4f**); 2.50 (m, 2H, NHCH$_2CH_2$CH$_2$CH$_2$CH$_2$-CH_2CH_3); 2.37, 2.14 and 1.99 (each m, 1H + 2H + 1H, 2 × 17^{1}H and 2 × 17^{2}H); 1.73 (m, 6H, 18CH_3 and 8$^2CH_3$); 1.50−0.42 (m, N−$CH_2CH_2CH_2CH_2CH_2CH_2CH_3$); −1.62 and −1.90 (each br s, 1H, 2N−H). Mass calcd for $C_{41}H_{51}N_5O_5$: 693.4. Found: 693.4 (M + 1).

Purpurin-18-*N*-methylimide (9a). Reaction of purpurin-18-methyl ester **2** (200 mg) with methylamine (1.5 mL, 2.0 M solution in THF) generated the related amide derivative. After treatment with diazomethane, the intermediate on reacting with methanolic KOH produced the title compound in 70% yield (142 mg) after purification (Alumina grade III column with dichloromethane). Mp: 209−211 °C. UV−vis (in CH_2Cl_2): 705 (4.5 × 10^4), 647 (1.2 × 10^4), 549 (2.3 × 10^4), 510 (1.0 × 10^4), 483 (8 × 10^3), 417 (1.2 × 10^5). ^{1}H NMR (400 MHz, 3 mg/1 mL $CDCl_3$, δ ppm): 9.54 (s, 1H, for 10H); 9.31 (s, 1H, for 5H); 8.57 (s, 1H, for 20H); 7.87 (dd, J = 18.0, 11.4 Hz, 1H, 3CH=CH_2); 6.28 (d, J = 18.0,1H, 3CH=CH_2); 6.13 (d, J = 11.4,1H, 3CH=CH_2); 5.35 (m, 1H for 17H); 4.36 (q, J = 7.3 Hz, 1H for 18H); 3.85 (s, 3H, 12CH_3); 3.78 (s, 3H, N−CH_3); 3.59 (q, J = 7.8 Hz, 2H, 8$^1CH_2$); 3.59 (s, 3H, 17$^2CO_2CH_3$); 3.34 (s, 3H, 2CH_3); 3.12 (s, 3H, 7CH_3); 2.72, 2.43, and 2.00 (each m, 1H + 2H + 1H, 2 × 17^{1}H and 2 × 17^{2}H); 1.75 (d, J = 7.0 Hz, 3H, 18CH_3); 1.64 (t, J = 7.0 Hz, 3H, 8$^2CH_3$); −0.08 and −0.16 (each br s, 1H, 2NH).

Mass calcd for $C_{35}H_{37}N_5O_4$: 591.3. Found: 592.9 (M + 1).

Purpurin-18-*N*-ethylimide 9b. Reaction of purpurin-18 methyl ester **2** (200 mg) with ethylamine (1.5 mL, 2.0 M solution in THF) produced the related amide derivative. The intermediate after treatment with diazomethane was reacted with methanolic KOH, which afforded the title compound in 70% yield (146 mg) after purification (Alumina grade III column with dichloromethane). Mp: 213−215 °C. UV−vis (in CH_2Cl_2): 705 (4.5 × 10^4), 647 (1.2 × 10^4), 549 (2.3 × 10^4), 510 (1.0 × 10^4), 483 (8 × 10^3), 417 (1.2 × 10^5). ^{1}H NMR (400 MHz, 3 mg/1 mL $CDCl_3$, δ ppm): 9.57 (s, 1H, for 10H); 9.33 (s, 1H, for 5H); 8.58 (s, 1H, for 20H); 7.88 (dd, J = 18.0, 11.4 Hz, 1H, 3CH=CH_2); 6.28 (d, J = 18.0,1H, 3CH=CH_2); 6.13 (d, J = 11.4,1H, 3CH=CH_2); 5.39 (m, 1H for 17H); 4.56 (m, 2H, N-CH_2-CH_3); 4.39 (q, J = 7.3 Hz, 1H for 18H); 3.81 (s, 3H, 12CH_3); 3.61 (q, J = 7.8 Hz, 2H, 8$^1CH_2$); 3.57 (s, 3H, 17$^2CO_2CH_3$); 3.35 (s, 3H, 2CH_3); 3.13 (s, 3H, 7CH_3); 2.72, 2.41 and 2.00 (each m, 1H + 2H + 1H, 2 × 17^{1}H and 2 × 17^{2}H); 1.76 (d, J = 7.0 Hz, 3H, 18CH_3); 1.65 (t, J = 7.0 Hz, 3H, 8$^2CH_3$); 1.59 (t, J = 6.3 Hz, 3H, N−CH_2CH_3); −0.11 and −0.20 (each br s, 1H, 2NH). Mass calcd for $C_{36}H_{39}N_5O_4$: 605.3. Found: 606.8 (M + 1).

Purpurin-18-*N*-propylimide (9c). Purpurin-18 methyl ester **2** (410 mg) was reacted with 1-propylamine (1.0 mL) by following method 2, and the corresponding imide was isolated in 88% yield (385 mg). Mp: 212−214 °C.UV−vis (in CH_2Cl_2): 705 (4.5 × 10^4), 647 (1.2 × 10^4), 549 (2.3 × 10^4), 510 (1.0 × 10^4), 483 (8 × 10^3), 417 (1.2 × 10^5). ^{1}H NMR (400 MHz, 3 mg/1 mL $CDCl_3$, δ ppm): 9.63 (s, 1H, for 10H); 9.38 (s, 1H, for 5H); 8.58 (s, 1H, for 20H); 7.91 (dd, J = 18.0, 11.7 Hz, 1H, 3CH=CH_2); 6.29 (d, J = 18.0,1H, 3CH=CH_2); 6.16 (d, J = 11.7,1H, 3CH=CH_2); 5.40 (m, 1H for 17H); 4.43 (m, 2H, N-CH_2CH_2-CH_3); 4.34 (q, J = 7.3 Hz, 1H for 18H); 3.84 (s, 3H, 12CH_3); 3.66 (q, J = 7.8 Hz, 2H, 8$^1CH_2$); 3.56 (s, 3H, 17$^2CO_2CH_3$); 3.36 (s, 3H, 2CH_3); 3.18 (s, 3H, 7CH_3); 2.68 and 2.40 (each m, 1H + 2H for 2 × 17^{1}H and 1 × 17^{2}H); 2.02 (m, 3H, 1 × 17^{2}H and N−$CH_2CH_2CH_3$); 1.76 (d, J = 7.0 Hz, 3H, 18CH_3); 1.67 (t, J = 7.0 Hz, 3H, 8$^2CH_3$); 1.19 (t, J = 6.3 Hz, 3H, N−$CH_2CH_2CH_3$); −0.08 and −0.17 (each br s, 1H, 2NH). HRMS calcd for $C_{37}H_{41}N_5O_4$: 620.3237 (M + 1). Found: 620.3221. Anal. Calcd for $C_{37}H_{41}N_5O_4 \cdot {}^1/_2H_2O$: C, 70.66; H, 6.73; N, 11.14. Found: C, 70.90; H, 6.67; N, 11.03.

Purpurin-18-*N*-butylimide (9d). Purpurin-18 methyl ester **2** (200 mg) was reacted with 1-butylamine (1.0 mL) by following method **2,** and the corresponding imide was isolated in 75% yield (164 mg). UV−vis (in CH_2Cl_2): 705 (4.5 × 10^4), 647 (1.2 × 10^4), 549 (2.3 × 10^4), 510 (1.0 × 10^4), 483 (8 × 10^3), 417 (1.2 × 10^5). ^{1}H NMR (400 MHz, 3 mg/1 mL $CDCl_3$, δ ppm): 9.59 (s, 1H, for 10H); 9.35 (s, 1H, for 5H); 8.58 (s, 1H, for 20H); 7.89 (dd, J = 18.0, 11.7 Hz, 1H, 3CH=CH_2); 6.28 (d, J = 18.0,1H, 3CH=CH_2); 6.14 (d, J = 11.7,1H, 3CH=CH_2); 5.41 (m, 1H for 17H); 4.47 (m, 2H, N-$CH_2CH_2CH_2CH_3$); 4.36 (q, J = 7.3 Hz, 1H for 18H); 3.82 (s, 3H, 12CH_3); 3.63 (q, J = 7.8 Hz, 2H, 8$^1CH_2$); 3.56 (s, 3H, 17$^2CO_2CH_3$); 3.35 (s, 3H, 2CH_3); 3.15 (s, 3H, 7CH_3); 2.69 and 2.40 (each m, 1H + 2H for 2 × 17^{1}H and 1 × 17^{2}H); 1.99 (m, 3H, 1 × 17^{2}H and N−$CH_2CH_2CH_2CH_3$); 1.76 (d, J = 7.0 Hz, 3H, 18CH_3); 1.66 (t, J = 7.0 Hz, 3H, 8$^2CH_3$); 1.27 (m, 2H, N−$CH_2CH_2CH_2CH_3$); 1.10 (t, J = 6.3 Hz, 3H, N−$CH_2CH_2CH_2CH_3$); −0.10 and −0.19 (each br s, 1H, 2NH). Mass calcd for $C_{38}H_{43}N_5O_4$: 633.3. Found: 634.5 (M + 1). Anal. Calcd for $C_{38}H_{43}N_5O_4 \cdot {}^1/_2H_2O$: C, 72.00; H, 6.84; N, 11.05. Found: C, 72.10; H, 6.90; N, 10.70.

Purpurin-18-*N*-hexylimide (9e). Purpurin-18 methyl ester **2** (500 mg) was reacted with 1-hexylamine (1.0 mL) by following method 2, and the corresponding imide was isolated in 80% yield (455 mg). Mp: 221−223 °C. UV−vis (in CH_2Cl_2): 705 (4.5 × 10^4), 647 (1.2 × 10^4), 549 (2.3 × 10^4), 510 (1.0 × 10^4), 483 (8 × 10^3), 417 (1.2 × 10^5). ^{1}H NMR (400 MHz, 3 mg/1 mL $CDCl_3$, δ ppm): 9.64 (s, 1H, for 10H); 9.39 (s, 1H, for 5H); 8.58 (s, 1H, for 20H); 7.84 (dd, J = 17.4, 11.2 Hz, 1H, 3CH=CH_2); 6.27 (d, J = 17.4,1H, 3CH=CH_2); 6.16 (d, J = 11.2,1H, 3CH=CH_2); 5.40 (m, 17H); 4.46 (m, 2H, N-$CH_2CH_2CH_2CH_2$-CH_2CH_3); 4.31 (q, J = 7.3 Hz, 1H for 18H); 3.84 (s, 3H, 12CH_3); 3.67 (q, 2H, 8$^1CH_2$); 3.57 (s, 3H, 17$^2CO_2CH_3$); 3.31 (s, 3H, 2CH_3); 3.11 (s, 3H, 7CH_3); 2.68 and 2.39 (each m, 1H + 2H, 2 × 17^{1}H and 1 × 17^{2}H); 1.99 (m, 3H, 1 × 17^{2}H and N−CH_2CH_2-$CH_2CH_2CH_2CH_3$); 1.74 (d, J = 7.2 Hz, 3H, 18CH_3); 1.64 (t, J = 7.2 Hz, 3H, 8$^2CH_3$); 1.61−1.31 (m, total for 6H, N−$CH_2CH_2CH_2CH_2CH_3$); 0.95 (t, 3H, N−$CH_2CH_2CH_2CH_2CH_2CH_3$); −0.07 and −0.16 (each br s, 1H, 2NH). Mass calcd for $C_{40}H_{47}N_5O_4$: 661.4. Found: 661.3. Anal. Calcd for $C_{40}H_{47}N_5O_4 \cdot {}^1/_2H_2O$: C, 71.60; H, 7.21; N, 10.44. Found: C, 71.64; H, 7.10; N, 10.29.

Purpurin-18-*N*-heptylimide (9f). Purpurin-18 methyl ester **2** (500 mg) was reacted with 1-heptylamine (1.0 mL) by following method 2, and the corresponding imide was isolated in 75% yield (437 mg). Purpurin-18 methyl ester **2** (410 mg)

was reacted with 1-heptylamine (1.0 mL) by following method 2, and the corresponding imide was isolated in 75% yield (437 mg). UV−vis (in CH_2Cl_2): 705 (4.5×10^4), 647 (1.2×10^4), 549 (2.3×10^4), 510 (1.0×10^4), 483 (8×10^3), 417 (1.2×10^5). ^{1}H NMR (400 MHz, 3 mg/1 mL $CDCl_3$, δ ppm): 9.62 (s, 1H, for 10H); 9.39 (s, 1H, for 5H); 8.59 (s, 1H, for 20H); 7.84 (dd, J = 17.4, 11.2 Hz, 1H, 3CH=CH_2); 6.27 (d, J = 17.4,1H, 3CH=CH_2); 6.16 (d, J = 11.2, 1H, 3CH=CH_2); 5.40 (m, 17H); 4.46 (m, 2H, N−CH_2CH$_2$CH$_2$CH$_2$CH$_2$CH$_2$CH$_3$); 4.31 (q, J = 7.3 Hz, 1H for 18H); 3.84 (s, 3H, 12CH$_3$); 3.67 (q, 2H, 8^{1}CH$_2$); 3.57 (s, 3H, 17^{2}CO$_2$CH$_3$); 3.31 (s, 3H, 2CH$_3$); 3.11 (s, 3H, 7CH$_3$); 2.68 and 2.39 (each m, 1H + 2H, 2 × 17^{1}H and 1 × 17^{2}H); 1.99 (m, 3H, 1 × 17^{2}H and N−CH$_2$CH$_2$CH$_2$CH$_2$–CH$_2$CH$_2$–CH$_3$); 1.74 (d, J = 7.2 Hz, 3H, 18CH$_3$); 1.64 (t, J = 7.2 Hz, 3H, 8^{2}CH$_3$); 1.62−1.38 (m, total for 8H, N−CH$_2$CH$_2$CH$_2$CH$_2$CH$_2$CH$_2$CH$_3$); 0.95 (t, 3H, N−CH$_2$CH$_2$CH$_2$CH$_2$CH$_2$CH$_2$CH$_3$); −0.17 and −0.46 (each br s, 1H, 2NH). Mass calcd for $C_{41}H_{49}N_5O_4$: 675.4 (M^+). Found: 676.4 (M + 1). Anal. Calcd for $C_{41}H_{49}N_5O_4 \cdot {}^1/_2H_2O$: C, 71.88; H, 7.36; N, 10.23. Found: C, 72.10; H, 7.32; N, 10.15.

Purpurin-18-*N*-octylimide (9g). Purpurin-18 methyl ester **2** (200 mg) was reacted with 1-octylamine (1.0 mL) by following method 2, and the corresponding imide was isolated in 75% yield (178 mg). UV−vis (in CH_2Cl_2): 705 (4.5×10^4), 647 (1.2×10^4), 549 (2.3×10^4), 510 (1.0×10^4), 483 (8×10^3), 417 (1.2×10^5). ^{1}H NMR (400 MHz, 3 mg/1 mL $CDCl_3$, δ ppm): 9.58 (s, 1H, for 10H); 9.33 (s, 1H, for 5H); 8.58 (s, 1H, for 20H); 7.89 (dd, J = 17.4, 11.2 Hz, 1H, 3CH=CH_2); 6.26 (d, J = 17.4, 1H, 3CH=CH_2); 6.13 (d, J = 11.2,1H, 3CH=CH_2); 5.42 (m, 17H); 4.46 (m, 2H, N−CH_2CH$_2$CH$_2$CH$_2$CH$_2$CH$_2$CH$_2$CH$_3$); 4.37 (q, J = 7.3 Hz, 1H for 18H); 3.81 (s, 3H, 12CH$_3$); 3.60 (q, 2H, 8^{1}CH$_2$); 3.57 (s, 3H, 17^{2}CO$_2$CH$_3$); 3.35 (s, 3H, 2CH$_3$); 3.11 (s, 3H, 7CH$_3$); 2.72 and 2.39 (each m, 1H, 2 × 17^{1}H and 1 × 17^{2}H); 2.01 (m, 3H, 1 × 17^{2}H and N−CH$_2$CH$_2$CH$_2$CH$_2$CH$_2$CH$_2$CH$_2$-CH$_3$); 1.74 (d, J = 7.2 Hz, 3H, 18CH$_3$); 1.64 (t, J = 7.2 Hz, 3H, 8^{2}CH$_3$); 1.62−1.25 (m, total for 10H, N−CH$_2$CH$_2$CH$_2$CH$_2$CH$_2$-CH$_2$CH$_2$CH$_3$); 0.90 (t, 3H, N−CH$_2$CH$_2$CH$_2$CH$_2$CH$_2$CH$_2$CH$_2$CH$_3$); −0.14 and −0.23 (each br s, 1H, 2NH). Mass calcd for $C_{42}H_{51}N_5O_4$: 690.6. Found: 690.6 (M + 1). Anal. Calcd for $C_{42}H_{51}N_5O_4 \cdot {}^1/_2H_2O$: C, 73.10; H, 7.45; N, 10.15. Found: C, 72.91; H, 7.47; N, 9.90.

Purpurin-18-*N*-decylimide (9h). Purpurin-18 methyl ester **2** (200 mg) was reacted with 1-heptylamine (1.0 mL) by following method 2, and the corresponding imide was isolated in 75% yield (185 mg). UV−vis (in CH_2Cl_2): 705 (4.5×10^4), 647 (1.2×10^4), 549 (2.3×10^4), 510 (1.0×10^4), 483 (8×10^3), 417 (1.2×10^5). ^{1}H NMR (400 MHz, 3 mg/1 mL $CDCl_3$, δ ppm): 9.62 (s, 1H, for 10H); 9.37 (s, 1H, for 5H); 8.58 (s, 1H, for 20H); 7.91 (dd, J = 17.4, 11.2 Hz, 1H, 3CH=CH_2); 6.28 (d, J = 17.4,1H, 3CH=CH_2); 6.15 (d, J = 11.2,1H, 3CH=CH_2); 5.40 (m, 17H); 4.46 (m, 2H, N−CH_2CH$_2$CH$_2$CH$_2$CH$_2$CH$_2$CH$_2$-CH$_2$CH$_2$CH$_3$); 4.35 (q, J = 7.4 Hz, 1H for 18H); 3.83 (s, 3H, 12CH$_3$); 3.62 (q, 2H, 8^{1}CH$_2$); 3.56 (s, 3H, 17^{2}CO$_2$CH$_3$); 3.35 (s, 3H, 2CH$_3$); 3.12 (s, 3H, 7CH$_3$); 2.68 and 2.40 (each m, 1H, 2 × 17^{1}H and 1 × 17^{2}H); 1.99 (m, 3H, 1 × 17^{2}H and N−CH$_2$CH$_2$-CH$_2$CH$_2$CH$_2$CH$_2$CH$_2$CH$_3$); 1.76 (d, J = 7.2 Hz, 3H, 18CH$_3$); 1.67 (t, J = 7.2 Hz, 3H, 8^{2}CH$_3$); 1.61−1.30 (m, total for 14H, N−CH$_2$CH$_2$CH$_2$CH$_2$CH$_2$CH$_2$CH$_2$CH$_2$CH$_3$); 0.88 (t, 3H, N−CH$_2$CH$_2$CH$_2$CH$_2$CH$_2$CH$_2$CH$_2$CH$_2$CH$_3$); −0.14 and −0.17 (each br s, 1H, 2NH). Mass calcd for $C_{44}H_{55}N_5O_4$: 717.4. Found: 717.8.

Purpurin-18-*N*-dodecylimide (7i). Purpurin-18 methyl ester **2** (500 mg) was reacted with 1-dodecylamine (1.0 mL) by following method 2, and the corresponding imide was isolated in 60% yield (385 mg). UV−vis (in CH_2Cl_2): 705 (4.5×10^4), 647 (1.2×10^4), 549 (2.3×10^4), 510 (1.0×10^4), 483 (8×10^3), 417 (1.2×10^5). ^{1}H NMR (400 MHz, 3 mg/1 mL $CDCl_3$, δ ppm): 9.62 (s, 1H, for 10H); 9.37 (s, 1H, for 5H); 8.59 (s, 1H, for 20H); 7.91 (dd, J = 17.4, 11.2 Hz, 1H, 3CH=CH_2); 6.29 (d, J = 17.4,1H, 3CH=CH_2); 6.17 (d, J = 11.2,1H, 3CH=CH_2); 5.40 (m, 17H); 4.46 (m, 2H, N−CH_2CH$_2$CH$_2$CH$_2$CH$_2$CH$_2$CH$_2$-CH$_2$CH$_2$CH$_2$CH$_2$CH$_3$); 4.35 (q, J = 7.4 Hz, 1H for 18H); 3.83 (s, 3H, 12CH$_3$); 3.62 (q, 2H, 8^{1}CH$_2$); 3.56 (s, 3H, 17^{2}CO$_2$CH$_3$); 3.35 (s, 3H, 2CH$_3$); 3.12 (s, 3H, 7CH$_3$); 2.68 and 2.40 (each m, 1H, 2 × 17^{1}H and 1 × 17^{2}H); 1.99 (m, 3H, 1 × 17^{2}H and N−CH$_2$CH$_2$CH$_2$CH$_2$CH$_2$CH$_2$CH$_2$CH$_2$CH$_2$CH$_2$CH$_2$CH$_3$); 1.76 (d, J = 7.2 Hz, 3H, 18CH$_3$); 1.67 (t, J = 7.2 Hz, 3H, 8^{2}CH$_3$); 1.62−1.29 (m, total for 18H, N−CH$_2$CH$_2$CH$_2$CH$_2$CH$_2$CH$_2$CH$_2$-CH$_2$CH$_2$CH$_2$CH$_3$); 0.88 (t, 3H, N−CH$_2$CH$_2$CH$_2$CH$_2$CH$_2$CH$_2$-CH$_2$CH$_2$CH$_2$CH$_2$CH$_2$CH$_3$); −0.14 and −0.17 (each br s, 1H, 2NH). Mass calcd for $C_{46}H_{59}N_5O_4$: 747.5. Found: 747.0. Anal. Calcd for $C_{46}H_{59}N_5O_4 \cdot {}^1/_2H_2O$: C, 73.16; H, 8.01; N, 9.28. Found: C, 73.06; H, 7.99; N, 8.87.

Purpurin-18-13^1-(*N*-hexyl)isoimide Methyl Ester (7e). Purpurin-18 methyl ester **2** (500 mg) was reacted with 1-hexylamine. The intermediate amide analogue on reacting with dicyclohexylcarbodiimide (DCC) produced a mixture of the title compound and its isomer, 15^1-isoimide **8e**. Chromatographic separation on silica column with 2−5% MeOH in dichloromethane afforded **8e** in 20% yield (115 mg) and **7e** in 60% yield (345 mg).UV−vis (in CH_2Cl_2, rel ϵ): 696 (0.396), 639 (0.057), 537 (0.175), 501 (0.109), 411 (1.000). ^{1}H NMR (400 MHz, 3 mg/1 mL $CDCl_3$, δ ppm): 9.74 (s, 1H, for 10H); 9.57 (s, 1H, for 5H); 8.75 (s, 1H, for 20H); 7.94 (dd, J = 19.2, 12.5 Hz, 1H, 3CH=CH_2); 6.33 (d, J = 19.2,1H, 3CH=CH_2); 6.15 (d, J = 12.5,1H, 3CH=CH_2); 5.24 (m, 17H); 4.52 (q, J = 7.3 Hz, 1H for 18H); 4.06 (m, 2H, N−CH_2CH$_2$CH$_2$CH$_2$CH$_2$CH$_3$); 3.81 (s, 3H, 12CH$_3$); 3.74 (q, J = 7.5 Hz, 2H, 8^{1}CH$_2$); 3.56 (s, 3H, 17^{2}CO$_2$CH$_3$); 3.42 (s, 3H, 2CH$_3$); 3.24 (s, 3H, 7CH$_3$); 2.65 (m, 1H, 1 × 17^{1}H); 2.51−2.00 (m, total for 7H, 1 × 17^{1}H, 2 × 17^{2}H and N−CH$_2$CH$_2$CH$_2$CH$_2$CH$_2$CH$_3$); 1.76 (d, J = 8.0 Hz, 3H, 18CH$_3$); 1.68 (t, J = 7.2 Hz, 3H, 8^{2}CH$_3$); ∼1.58 (m, total for 4H, N−CH$_2$CH$_2$CH$_2$CH$_2$CH$_2$CH$_3$); 0.98 (t, J = 7.8 Hz, 3H, N−CH$_2$-CH$_2$CH$_2$CH$_2$CH$_2$CH$_3$); −0.66 and −0.84 (each br s, 1H, 2N−H). HRMS calcd for $C_{40}H_{47}N_5O_4$: 661.3621. Found: 661.3620.

Purpurin-18-15^1-(*N*-hexyl)isoimide Methyl Ester (8e). UV−vis (in CH_2Cl_2, rel ϵ): 690 (0.565), 639 (0.082), 543 (0.193), 507 (0.101), 411 (1.000). ^{1}H NMR (400 MHz, 3 mg/1 mL $CDCl_3$, δ ppm): 9.73 (s, 1H, for 10H); 9.49 (s, 1H, for 5H); 8.65 (s, 1H, for 20H); 7.92 (dd, J = 17.4, 11.2 Hz, 1H, 3CH=CH_2); 6.31 (d, J = 17.4, 1H, 3CH=CH_2); 6.18 (d, J = 11.2, 1H, 3CH=CH_2); 5.26 (m, 17H); 4.57 (q, J = 8.0 Hz, 1H for 18H); 4.01 (m, 2H, N−CH_2CH$_2$CH$_2$CH$_2$CH$_2$CH$_3$); 3.83 (s, 3H, 12CH$_3$); 3.76 (q, J = 7.5 Hz, 2H, 8^{1}CH$_2$); 3.58 (s, 3H, 17^{2}CO$_2$CH$_3$); 3.46 (s, 3H, 2CH$_3$); 3.28 (s, 3H, 7CH$_3$); 2.65 (m, 1 × 17^{1}H); 2.58−2.00 (m, total for 7H, 1 × 17^{1}H, 2 × 17^{2}H, and N−CH$_2$CH$_2$CH$_2$CH$_2$-CH$_2$CH$_3$); 1.78 (d, J = 7.2 Hz, 3H, 18CH$_3$); 1.72 (t, J = 7.2 Hz, 3H, 8^{2}CH$_3$); ∼1.61 (m, total for 4H, N−CH$_2$CH$_2$CH$_2$CH$_2$CH$_2$-CH$_3$); 0.96 (t, J = 7.8 Hz, 3H, N−CH$_2$CH$_2$CH$_2$CH$_2$CH$_2$CH$_3$); −0.61 and −0.88 (each br s, 1H, 2N−H). Mass calcd for $C_{40}H_{47}N_5O_4$: 661.3621. Found: 661. 3624.

Chlorin-*p*^{6}-13-hexylamide-15-methoxycarbonyl-17-propionic Ester (5e) and 15-Hexylamide Isomer (6e). A mixture of amide **3** and **4** (500 mg) was reacted with a large excess of diazomethane and converted into a mixture of the title compound and its isomer in quantitative yield. After purification (silica column with 3% acetone in dichloromethane), both isomers were isolated pure in 95% total yield (485 mg). UV−vis (in CH_2Cl_2, rel ϵ): 666 (0.333), 615 (0.054), 543 (0.062), 507 (0.107), 411 (1.000). ^{1}H NMR (400 MHz, 3 mg/1 mL $CDCl_3$, δ ppm): 9.70, 9.59, and 8.77 (each s, 1H, for 5H, 10H and 20H); 8.03 (dd, J = 17.4, 11.4 Hz, 1H, 3CH=CH_2); 6.34 (d, J = 17.4, 1H, 3CH=CH_2); 6.25 (m, 1H, 13^{1}NHCH$_2$CH$_2$CH$_2$CH$_2$CH$_2$CH$_3$); 6.14 (d, J = 11.9, 1H, 3CH=CH_2); 5.05 (m, 1H for 17H); 4.44 (m, 1H for 18H); 3.84 and 3.73 (each m, NHCH$_2$CH$_2$CH$_2$CH$_2$-CH$_2$CH$_3$ and 8^{1}CH$_2$); 3.61 (s, 3H, 12CH$_3$); 3.46 and 3.45 (each s, 3H, 17^{2}CO$_2$CH$_3$ and 2CH$_3$); 3.27 (s, 3H, 7CH$_3$); 2.50−1.80 (m, 6H, NHCH$_2$CH$_2$CH$_2$CH$_2$CH$_2$CH$_3$, 2 × 17^{1}H and 2 × 17^{2}H); 1.72 (m, 6H, 18CH$_3$ and 8^{2}CH$_3$); 1.50−1.10 (m, N−CH$_2$-CH$_2$CH$_2$CH$_2$CH$_2$CH$_3$); 0.93 (m, N−CH$_2$CH$_2$CH$_2$CH$_2$CH$_2$CH$_3$); −1.34 and −1.56 (each br s, 1H, 2N−H). Mass calcd for $C_{41}H_{51}N_5O_5$: 693.4. Found: 694.8.

17^3-(Hexylamide)purpurin-18-*N*-hexylimide (14). The title compound **14** was isolated as a byproduct from the above reaction mixture, mainly containing purpurin-18-*N*-hexylimide **9e.** Yield: 10% (63 mg). UV−vis (in CH_2Cl_2): 705 (4.5×10^4), 647 (1.2×10^4), 549 (2.3×10^4), 510 (1.0×10^4), 483 (8×10^3), 417 (1.2×10^5).^{1}H NMR (400 MHz, 3 mg/1 mL $CDCl_3$, δ ppm): 9.58 (s, 1H, for 10H); 9.33 (s, 1H, for 5H); 8.57 (s, 1H, for 20H);

7.88 (dd, J = 17.4, 11.2 Hz, 1H, 3CH=CH_2); 6.97 (br s, 1H, $NH$$CH_2CH_2CH_2CH_2CH_2CH_3$); 6.28 (d, J = 17.4,1H, 3CH=CH_2); 6.14 (d, J = 11.2, 1H, 3CH=CH_2); 5.27 (m, 17H); 4.46 (m, 2H, N−$CH_2CH_2CH_2CH_2CH_2CH_3$); 4.41 (q, J = 7.3 Hz, 1H for 18H); 3.80 (s, 3H, $12CH_3$); 3.63 (q, J = 7.8 Hz, 2H, 8^1CH_2); 3.35 (s, 3H, $2CH_3$); 3.14 (s, 3H, $7CH_3$); 2.72 and 2.44 (each m, 1H +2H, 2 × 17^1H and 1 × 17^2H); 2.00 (m, 3H, 1 × 17^2H and N−$CH_2CH_2CH_2CH_2CH_2CH_3$); 1.72 (d, J = 7.2 Hz, 3H, $18CH_3$); 1.66 (t, J = 7.2 Hz, 3H, 8^2CH_3); 1.63−1.26 (m, total for 16H, N−$CH_2CH_2CH_2CH_2CH_2CH_3$ and $NHCH_2CH_2CH_2CH_2CH_2CH_3$); 0.96 (t, J = 7.1 Hz, 3H, N−$CH_2CH_2CH_2CH_2CH_2CH_3$); 0.87 (t, J = 6.9 Hz, 3H, $NHCH_2CH_2CH_2CH_2CH_2CH_3$); 0.15 and −0.14 (each br s, 1H, 2N−H). Mass calcd for $C_{45}H_{58}N_6O_3$: 730.5. Found: 731.3 (M + 1).

12-Formylpurpurin-18-*N*-hexylimide-17-propionic Ester (12). The title compound was isolated from the reaction mixture mainly containing purpurin-18-*N*-hexylimide **9e** as a byproduct in 5% yield (30 mg). UV−vis (in CH_2Cl_2): 717 (1.15 × 10^4), 660 (4.39 × 10^3), 582 (4.50 × 10^3), 420 (2.72 × 10^4). ^{1}H NMR (400 MHz, 5 mg/1 mL $CDCl_3$, δ ppm): 11.84 (s, 1H, 12-CHO), 10.19 (s, 1H, 5-H), 8.79 (s, 1H, 10-H), 8.24 (s, 1 H, 20-H), 7.69 (dd, 1H, J = 18.8, 12.5 Hz, 3CH=CH_2), 6.24 (d, 1H, J = 18.8, 3CH=CH_2), 6.18 (d, 1H, J = 12.5, 3CH=CH_2), 5.19 (d, 1H, J = 8.6, 17-H), 5.44 (t, 2H, J = 7.8, N−$CH_2CH_2CH_2CH_2CH_2CH_3$), 4.18 (q, H, J = 8.0, 18H), 3.60 (s, 3H, $17^2CO_2CH_3$), 3.43 (q, 2H, J = 7.6, 8^1CH_2), 3.21 (s, 3H, $7CH_3$), 2.92 (s, 3H, $3CH_3$), 2.70 and 2.41 (m, 1H + 2H, 2 × 17^1H, and 1 × 17^2H), 1.95 (m, 5H, 1 × 17^2H and N−$CH_2CH_2CH_2CH_2CH_3$), 1.71 (d, 3H, J = 8.0, 18Me), 1.58 (t, 3H, J = 7.6, 8^2CH_3), 1.65−1.17 (m, 6H, N−$CH_2CH_2CH_2CH_2CH_2CH_3$), 0.95 (t, 3H, N−$CH_2CH_2CH_2CH_2CH_2CH_3$), −0.15 and −0.46 (each br s, 2H, 21- and 23NH). Mass calcd for $C_{40}H_{45}N_5O_5$: 675.3. Found: 676.1 (M + 1).

12-(Hydroxymethyl)purpurin-18-*N*-heptylimide-17-propionic Ester (13). The title compound was isolated from the reaction mixture consisting of mainly purpurin-18-*N*-heptylimide **7f** as a byproduct in 5% yield (30 mg).UV−vis (in CH_2Cl_2): 705 (4.5 × 10^4), 648 (1.2 × 10^4), 555 (2.3 × 10^4), 483 (8 × 10^3), 420 (1.2 × 10^5). ^{1}H NMR (400 MHz, 5 mg/1 mL $CDCl_3$, δ ppm): 9.53, (s, 1H, for 10H); 9.22 (s, 1H, for 5H); 8.47 (s, 1H, for 20H); 7.84 (dd, J = 17.4, 11.2 Hz, 1H, 3CH=CH_2); 6.27 (d, J = 17.4,1H, 3CH=CH_2); 6.16 (d, J = 11.2,1H, 3CH=CH_2); 6.06 (s, 2H, $12CH_2OH$); 5.32 (m, 17H); 4.46 (m, 2H, N−$CH_2CH_2CH_2CH_2CH_2CH_2CH_3$); 4.31 (q, J = 7.3 Hz, 1H for 18H); 3.59 (q, 2H, 8^1CH_2); 3.57 (s, 3H, $17^2CO_2CH_3$); 3.31 (s, 3H, $2CH_3$); 3.11 (s, 3H, $7CH_3$); 2.68 and 2.39 (each m, 1H, 2 × 17^1H and 1 × 17^2H); 1.98 (m, 3H, 1 × 17^2H and N−$CH_2CH_2CH_2CH_2CH_2CH_2CH_3$); 1.74 (d, J = 7.2 Hz, 3H, $18CH_3$); 1.64 (t, J = 7.2 Hz, 3H, 8^2CH_3); 1.55 and 1.37 (each m, total for 8H, N−$CH_2CH_2CH_2CH_2CH_2CH_2CH_3$); 0.92 (t, 3H, N−$CH_2CH_2CH_2CH_2CH_2CH_2CH_3$); 0.47 and 0.27 (each br s, 1H, 2NH). Mass calcd for $C_{41}H_{49}N_5O_5$: 691.4. Found: 692.2 (M + 1).

General Method for the Synthesis of Alkyl Ether Derivatives of Purpurin-18-*N*-alkylimides-17-propionic Ester. For the preparation of alkyl ether derivatives, purpurin-18-*N*-alkylimide **9** (100 mg) was reacted with 30% hydrobromic acid/acetic acid (1.5 mL) using a rubber septum and the reaction stirred at room temperature for 3 h. After evaporating the acids to dryness under high vacuum (0.1 mmHg), the residue was reacted with the desired alcohol (excess). Dry dichloromethane (10 mL) and anhydrous potassium carbonate (40 mg) were then added. The reaction mixture was stirred under a nitrogen atmosphere for 45 min. It was then diluted with dichloromethane (200 mL) and reacted with diazomethane. Evaporation of the solvent gave a residue that was chromatographed over alumina column (Gr III) and eluted with dichloromethane/hexane (ratio varies). The major fraction was collected. Evaporation of the solvent gave the desired alkyl ether derivative. By following the methodology as discussed above, a series of alkyl ether derivatives were synthesized. Most alkyl ether analogues, especially those with long carbon chains, were obtained as sticky solids and could not be crystallized. The yield, UV−vis spectrum, mass spectroscopic data, and ^{1}H NMR of various alkyl ethers were as follows:

3-(1-(Heptyloxy)ethyl)purpurin-18-*N*-hexylimide-17-propionic Ester (37). Purpurin-18-*N*-hexylimide **9e** (400 mg) was converted into the related bromo derivative, which when reacted with 1-heptanol produced the title compound in 70% yield (330 mg) as a sticky solid after purification (alumina grade II column, eluted with 25% *n*-hexanes in CH_2Cl_2). UV−vis (in CH_2Cl_2): 699 (4.53 × 10^4), 642 (7.35 × 10^3), 543 (1.81 × 10^4), 507 (7.54 × 10^3), 414 (1.28 × 10^5). ^{1}H NMR (400 MHz, 3 mg/1 mL $CDCl_3$, δ ppm): 9.77 (s, 1H, for 10H); 9.65 (s, 1H, for 5H); 8.55 (s, 1H, for 20H); 5.79 (q, J = 6.8 Hz, 1H, 3^1H); 5.40 (m, 17H); 4.46 (m, 2H, N−$CH_2CH_2CH_2CH_2CH_2CH_3$); 4.35 (q, J = 7.2 Hz, 1H for 18H); 3.84 (s, 3H, $12CH_3$); 3.67 (q, 2H, 8^1CH_2); 3.60 (m, 2H, O−$CH_2CH_2CH_2CH_2CH_2CH_2CH_3$); 3.56 (s, 3H, $17^2CO_2CH_3$); 3.31 (s, 3H, $2CH_3$); 3.20 (s, 3H, $7CH_3$); 2.67, 2.43, and 2.32 (each m, 1H, 2 × 17^1H and 1 × 17^2H); 2.06 (m, J = 6.7, 2.7 Hz, 3H, 3^1CH_3); 1.99 (m, 2H + 1H, 1 × 17^2H and N−$CH_2CH_2CH_2CH_2CH_2CH_3$); 1.74 (d, J = 7.2 Hz, 3H, $18CH_3$); 1.64 (t, J = 7.2 Hz, 3H, 8^2CH_3); 1.61−1.19 (m, total for 16H, O−$CH_2CH_2CH_2CH_2CH_2CH_2CH_3$ and N−$CH_2CH_2CH_2CH_2CH_2CH_3$); 0.95 (t, 3H, N−$CH_2CH_2CH_2CH_2CH_2CH_3$); 0.78 (m, 3H, O−$CH_2CH_2CH_2CH_2CH_2CH_2CH_3$); −0.08 and −0.17 (each br s, 1H, 2NH). Mass calcd for $C_{47}H_{63}N_5O_5$: 777.5. Found: 778 (M + 1).

3-(1-(Heptyloxy)-2-bromoethyl)purpurin-18-*N*-hexylimide-17-propionic Acid (15). The title compound was isolated as a byproduct in 10% yield (55 mg) from the reaction mixture containing mainly purpurinimide **37** as the major product. UV−vis (in CH_2Cl_2): 699 (4.25 × 10^4), 642 (7.60 × 10^3), 543 (1.91 × 10^4), 507 (6.92 × 10^3), 414 (1.28 × 10^5) ^{1}H NMR (400 MHz, 3 mg/1 mL $CDCl_3$, δ ppm): 9.72 (s, 1H, for 10H); 9.67 (s, 1H, for 5H); 8.58 (s, 1H, for 20H); 5.82 (q, J = 6.8 Hz, 1H, 3^1H); 5.40 (m, 17H); 4.46 (m, 2H, N−$CH_2CH_2CH_2CH_2CH_2CH_3$); 4.35 (m, 1H for 18H); 4.34 and 4.07 (each m, 1H, 3^1CH_2Br); 3.84 (s, 3H, $12CH_3$); 3.67 (q, 2H, 8^1CH_2); 3.60 (m, 2H, O−$CH_2CH_2CH_2CH_2CH_2CH_2CH_3$); 3.56 (s, 3H, $17^2CO_2CH_3$); 3.31 (s, 3H, $2CH_3$); 3.20 (s, 3H, $7CH_3$); 2.67, 2.43 and 2.32 (each m, 1H, 2 × 17^1H and 1 × 17^2H); 1.99 (m, 2H + 1H, 1 × 17^2H and N−$CH_2CH_2CH_2CH_2CH_2CH_3$); 1.74 (d, J = 7.2 Hz, 3H, $18CH_3$); 1.64 (t, J = 7.2 Hz, 3H, 8^2CH_3); 1.61−1.19 (m, total for 16H, O−$CH_2CH_2CH_2CH_2CH_2CH_2CH_3$ and N−$CH_2CH_2CH_2CH_2CH_2CH_3$); 0.95 (t, 3H, N−$CH_2CH_2CH_2CH_2CH_2CH_3$); 0.78 (m, 3H, O−$CH_2CH_2CH_2CH_2CH_2CH_2CH_3$); −0.25 (br s, 2H, 2N−H). Mass calcd for: $C_{47}H_{62}N_5O_5Br$: 855.4. Found: 857.5 (M+2).

3-(1-(Methyloxy)ethyl)purpurin-18-*N*-methylimide-17-propionic Ester (16). Purpurin-18-*N*-methylimide **9a** (50 mg) was converted into the related bromo derivative, which when reacted with anhydrous methanol produced the title compound in 60% yield (32 mg) after purification (silica plate with 2% MeOH in CH_2Cl_2). UV−vis (in CH_2Cl_2): 699 (4.53 × 10^4), 642 (7.35 × 10^3), 543 (1.81 × 10^4), 507 (7.54 × 10^3), 414 (1.28 × 10^5). ^{1}H NMR (400 MHz, 3 mg/1 mL $CDCl_3$, δ ppm): 9.67 and 9.65 (each s, 1H, for 10H and 5H); 8.55 (s, 1H, for 20H); 5.74 (q, J = 6.8 Hz, 1H, 3^1H); 5.35 (m, 1H for 17H); 4.36 (q, J = 7.3 Hz, 1H for 18H); 3.84 (s, 3H, $12CH_3$); 3.78 (s, 3H, N−CH_3); 3.68 (q, J = 7.8 Hz, 2H, 8^1CH_2); 3.58 (s, 3H, $17^2CO_2CH_3$); 3.55 (splitting s, 3H, 3^1OCH_3); 3.33 (s, 3H, $2CH_3$); 3.20 (s, 3H, $7CH_3$); 2.72, 2.41 and 1.99 (each m, 1H + 2H + 1H, 2 × 17^1H and 2 × 17^2H); 2.08 (m, J = 6.7, 2.7 Hz, 3H, 3^1CH_3); 1.73 (d, J = 7.0 Hz, 3H, $18CH_3$); 1.68 (t, J = 7.0 Hz, 3H, 8^2CH_3); −0.12 (br s, 2H, 2NH). Anal. Calcd for $C_{36}H_{41}N_5O_5 \cdot {}^1/_2H_2O$: C, 68.32; H, 6.69; N, 10.07. Found: C, 68.34; H, 6.62; N, 10.69.

3-(1-(Hexyloxy)ethyl)purpurin-18-*N*-methylimide-17-propionic Ester (33). Purpurin-18-*N*-methylimide **9a** (100 mg) was converted into the related bromo derivative, which when reacted with 1-hexanol produced the title compound in 70% yield (82 mg) as a sticky solid (alumina grade II column, eluted with 25% *n*-hexanes in CH_2Cl_2). UV−vis (in CH_2Cl_2): 699 (4.53 × 10^4), 642 (7.35 × 10^3), 543 (1.81 × 10^4), 507 (7.54 × 10^3), 414 (1.28 × 10^5). ^{1}H NMR (400 MHz, 3 mg/1 mL $CDCl_3$, δ ppm): 9.77 (s, 1H, for 10H); 9.65 (s, 1H, for 5H); 8.54 (s, 1H, for 20H); 5.79 (q, J = 6.8 Hz, 1H, 3^1H); 5.35 (m, 1H for 17H); 4.36 (q, J = 7.3 Hz, 1H for 18H); 3.842 and 3.838 (each s, 3H, $12CH_3$ and N−CH_3); 3.67 (m, 4H, 8^1CH_2 and O−$CH_2CH_2CH_2$-

$CH_2CH_2CH_3$); 3.59 (s, 3H, $17^2CO_2CH_3$); 3.31 (s, 3H, $2CH_3$); 3.20 (s, 3H, $7CH_3$); 2.71, 2.41 and 1.99 (each m, 1H + 2H + 1H, 2 × 17^1H and 2 × 17^2H); 2.07 (m, J = 6.7, 2.7 Hz, 3H, 3^1CH_3); 1.75 (d, J = 7.0 Hz, 3H, $18CH_3$); 1.64 (t, J = 7.0 Hz, 3H, 8^2CH_3); 1.55−1.25 (m, total for 8H, O−$CH_2CH_2CH_2CH_2CH_2CH_3$); 0.75 (m, 3H, O−$CH_2CH_2CH_2CH_2CH_2CH_3$); −0.11 (br s, 2H, 2N−H). Mass calcd for $C_{41}H_{51}N_5O_5$: 693.4. Found: 694.5 (M + 1). Anal. Calcd for $C_{41}H_{51}N_5O_5 \cdot {}^1/_2H_2O$: C, 70.04; H, 7.46; N, 9.96. Found: C, 70.10; H, 7.37; N, 9.52.

3-(1-(Dodecyloxy)ethyl)purpurin-18-*N*-methylimide-17-propionic Ester (42). Purpurin-18-*N*-methylimide **9a** (50 mg) was converted into the related bromo derivative, which when reacted with 1-dodecanol produced the title compound in 60% yield (40 g) as a sticky solid after purification (silica plate, with 2% MeOH in CH_2Cl_2). UV−vis spectrum (in CH_2Cl_2): 699 (4.53 × 10^4), 642 (7.35 × 10^3), 543 (1.81 × 10^4), 507 (7.54 × 10^3), 414 (1.28 × 10^5).^{1}H NMR (400 MHz, 3 mg/1 mL $CDCl_3$, δ ppm): 9.76 (s, 1H, for 10H); 9.65 (s, 1H, for 5H); 8.53 (s, 1H, for 20H); 5.78 (q, J = 6.8 Hz, 1H, 3^1H); 5.35 (m, 1H for 17H); 4.36 (q, J = 7.3 Hz, 1H for 18H); 3.84 (s, 3H, $12CH_3$); 3.68 (m, 4H, 8^1CH_2 and O−$CH_2CH_2CH_2CH_2CH_2CH_2CH_2CH_2CH_2CH_2CH_2CH_2CH_3$); 3.59 (s, 3H, $17^2CO_2CH_3$); 3.31 (s, 3H, $2CH_3$); 3.20 (s, 3H, $7CH_3$); 2.71, 2.41 and 1.99 (each m, 1H + 2H + 1H, 2 × 17^1H and 2 × 17^2H); 2.06 (m, J = 6.7, 2.7 Hz, 3H, 3^1CH_3); 1.73 (d, J = 7.0 Hz, 3H, $18CH_3$); 1.68 (t, J = 7.0 Hz, 3H, 8^2CH_3); 1.55−1.10 (m, total for 20H, O−$CH_2CH_2CH_2CH_2CH_2CH_2CH_2CH_2CH_2CH_2CH_2CH_2CH_2CH_2CH_3$); 0.83 (m, 3H, O−$CH_2CH_2CH_2CH_2CH_2CH_2CH_2CH_2CH_2CH_2CH_2CH_2CH_2CH_2CH_3$); −0.11 (br s, 2H, 2N−H). Mass calcd for $C_{47}H_{63}N_5O_5$: 777.5. Found: 779.0 (M^++1).

3-(1-(Ethyloxy)ethyl)purpurin-18-*N*-ethylimide-17-propionic Ester (17). Purpurin-18-*N*-ethylimide **9b** (100 mg) was converted into the related bromo derivative, which when reacted with ethanol produced the title compound in 60% yield (65 mg) after purification over alumina grade II column eluting with CH_2Cl_2.UV−vis (in CH_2Cl_2): 699 (4.53 × 10^4), 642 (7.35 × 10^3), 543 (1.81 × 10^4), 507 (7.54 × 10^3), 414 (1.28 × 10^5). ^{1}H NMR (400 MHz, 3 mg/1 mL $CDCl_3$, δ ppm): 9.79 (s, 1H, for 10H); 9.66 (s, 1H, for 5H); 8.56 (s, 1H, for 20H); 5.83 (q, J = 6.8 Hz, 1H, 3^1H); 5.39 (m, 1H for 17H); 4.56 (m, 2H, N−CH_2CH_3); 4.37 (q, J = 7.3 Hz, 1H for 18H); 3.84 (s, 3H, $12CH_3$); 3.7 (m, 4H, 8^1CH_2 and O−CH_2CH_3); 3.58 (s, 3H, $17^2CO_2CH_3$); 3.34 (s, 3H, $2CH_3$); 3.21 (s, 3H, $7CH_3$); 2.72, 2.41 and 2.00 (each m, 1H + 2H + 1H, 2 × 17^1H, and 2 × 17^2H); 2.07 (m, J = 6.7, 2.7 Hz, 3H, 3^1CH_3); 1.76 (d, J = 7.0 Hz, 3H, $18CH_3$); 1.69 (t, J = 7.0 Hz, 3H, 8^2CH_3); 1.58 (t, J = 6.3 Hz, 3H, N−CH_2CH_3); 1.36 (m, J = 7.1, 5.2 Hz, 3H, O−CH_2CH_3); −0.07 and −0.15 (each br s, 1H, 2NH). Mass calcd for $C_{38}H_{45}N_5O_5$: 651.3. Found: 652.2 (M + 1). Anal. Calcd for $C_{38}H_{45}N_5O_5 \cdot {}^1/_2H_2O$: C, 69.05; H, 7.02; N, 10.60. Found: C, 69.13; H, 6.93; N, 10.33.

3-(1-(Hexyloxy)ethyl)purpurin-18-*N*-ethylimide-17-propionic Ester (26). Purpurin-18-*N*-ethylimide **9b** (100 mg) was converted into the related bromo derivative, which when reacted with 1-hexanol and purified by following the procedure as described for the foregoing compound produced the title product in 65% yield (75 mg) as a sticky solid. UV−vis (in CH_2Cl_2): 699 (4.53 × 10^4), 642 (7.35 × 10^3), 543 (1.81 × 10^4), 507 (7.54 × 10^3), 414 (1.28 × 10^5). ^{1}H NMR (400 MHz, 3 mg/1 mL $CDCl_3$, δ ppm): 9.78 (s, 1H, for 10H); 9.66 (s, 1H, for 5H); 8.54 (s, 1H, for 20H); 5.80 (q, J = 6.8 Hz, 1H, 3^1H); 5.38 (m, 1H for 17H); 4.55 (m, 2H, N−CH_2CH_3); 4.36 (q, J = 7.3 Hz, 1H for 18H); 3.86 (s, 3H, $12CH_3$); 3.67 (m, 4H, 8^1CH_2 and O−$CH_2CH_2CH_2CH_2CH_2CH_3$); 3.57 (s, 3H, $17^2CO_2CH_3$); 3.32 (s, 3H, $2CH_3$); 3.20 (s, 3H, $7CH_3$); 2.70, 2.39, and 2.00 (each m, 1H + 2H + 1H, 2 × 17^1H and 2 × 17^2H); 2.06 (m, J = 6.7, 2.7 Hz, 3H, 3^1CH_3); 1.76 (d, J = 7.0 Hz, 3H, $18CH_3$); 1.69 (t, J = 7.0 Hz, 3H, 8^2CH_3); 1.58 (t, J = 6.3 Hz, 3H, N−CH_2CH_3); 1.48−1.18 (m, total for 8H, O−$CH_2CH_2CH_2CH_2CH_2CH_3$); 0.79 (m, 3H, O−$CH_2CH_2CH_2CH_2CH_2CH_3$); −0.06 and −0.16 (each br s, 1H, 2NH). Mass calcd for $C_{42}H_{53}N_5O_5$: 707.4. Found: 707.4. Anal. Calcd for $C_{42}H_{53}N_5O_5 \cdot {}^1/_2H_2O$: C, 71.24; H, 7.55; N, 9.89. Found: C, 70.81; H, 7.54; N, 9.75.

3-(1-(Methyloxy)ethyl)purpurin-18-*N*-propylimide Methyl Ester (25). Purpurin-18-*N*-propylimide **9c** (70 mg) was converted into the related bromo derivative, which when reacted with anhydrous methanol produced the title compound in 80% yield (58 mg) after purification over silica column, eluting with 2% acetone in CH_2Cl_2. UV−vis (in CH_2Cl_2): 699 (4.53 × 10^4), 642 (7.35 × 10^3), 543 (1.81 × 10^4), 507 (7.54 × 10^3), 414 (1.28 × 10^5).^{1}H NMR (400 MHz, 3 mg/1 mL $CDCl_3$, δ ppm): 9.67 and 9.61 (each s, 1H, for 10H and 5H); 8.54 (s, 1H, for 20H); 5.74 (q, J = 6.8 Hz, 1H, 3^1H); 5.36 (m, 1H for 17H); 4.56 (m, 2H, N−$CH_2CH_2CH_3$); 4.36 (q, J = 7.3 Hz, 1H for 18H); 3.84 (s, 3H, $12CH_3$); 3.66 (q, J = 7.8 Hz, 2H, 8^1CH_2); 3.56 (s, 3H, $17^2CO_2CH_3$); 3.53 (splitting s, 3H, 3^1OCH_3); 3.36 (s, 3H, $2CH_3$); 3.20 (s, 3H, $7CH_3$); 2.72, 2.41, and 1.99 (each m, 1H + 2H + 1H, 2 × 17^1H and 2 × 17^2H); 2.08 (m, J = 6.7, 2.7 Hz, 3H, 3^1CH_3); 2.02 (m, 2H, N−$CH_2CH_2CH_3$); 1.76 (d, J = 7.0 Hz, 3H, $18CH_3$); 1.67 (t, J = 7.0 Hz, 3H, 8^2CH_3); 1.19 (t, J = 6.3 Hz, 3H, N−$CH_2CH_2CH_3$); −0.12 (br s, 2H, 2N−H). HRMS calcd for $C_{38}H_{45}N_5O_5$: 651.3421. Found 651.3445.

3-(1-(Propyloxy)ethyl)purpurin-18-*N*-propylimide-17-propionic Ester (18). Purpurin-18-*N*-propylimide **9c** (70 mg) was converted into the related bromo derivative, which when reacted with 1-propanol produced the title compound in 75% yield (57 mg) after purification on a silica column, eluting with 2% acetone in CH_2Cl_2. UV−vis (in CH_2Cl_2): 699 (4.53 × 10^4), 642 (7.35 × 10^3), 543 (1.81 × 10^4), 507 (7.54 × 10^3), 414 (1.28 × 10^5). ^{1}H NMR (400 MHz, 3 mg/1 mL $CDCl_3$, δ ppm): 9.77 (s, 1H, for 10H); 9.66 (s, 1H, for 5H); 8.54 (s, 1H, for 20H); 5.80 (q, J = 6.8 Hz, 1H, 3^1H); 5.40 (m, 1H for 17H); 4.43 (m, 2H, N−$CH_2CH_2CH_3$); 4.34 (q, J = 7.3 Hz, 1H for 18H); 3.84 (s, 3H, $12CH_3$); 3.66 (m, 4H, 8^1CH_2 and O−$CH_2CH_2CH_3$); 3.56 (s, 3H, $17^2CO_2CH_3$); 3.31 (s, 3H, $2CH_3$); 3.20 (s, 3H, $7CH_3$); 2.66, 2.43, 2.32 (each m, 1H, 2 × 17^1H and 1 × 17^2H); 2.06 (m, J = 6.7, 2.7 Hz, 3H, 3^1CH_3); 2.02 (m, 3H, 1 × 17^2H and N−$CH_2CH_2CH_3$); 1.76 (d, J = 7.0 Hz, 3H, $18CH_3$); 1.67 (t, J = 7.0 Hz, 3H, 8^2CH_3); 1.26 (m, 2H, O−$CH_2CH_2CH_3$); 1.19 (t, J = 6.3 Hz, 3H, N−$CH_2CH_2CH_3$); 0.96 (m, 3H, O−$CH_2CH_2CH_3$); −0.08 and −0.17 (each br s, 1H, 2NH). HRMS calcd for $C_{40}H_{49}N_5O_5$: 679.3734. Found: 679.3755.

3-(1-(Hexyloxy)ethyl)purpurin-18-*N*-propylimide-17-propionic Ester (27). Purpurin-18-*N*-propylimide **9c** (70 mg) was converted into the related bromo derivative, which when reacted with 1-hexanol produced the title compound in 60% yield (49 mg) after purification on a silica column, eluting with 1% acetone in CH_2Cl_2. UV−vis (in CH_2Cl_2): 699 (4.53 × 10^4), 642 (7.35 × 10^3), 543 (1.81 × 10^4), 507 (7.54 × 10^3), 414 (1.28 × 10^5). ^{1}H NMR (400 MHz, 3 mg/1 mL $CDCl_3$, δ ppm): 9.77 (s, 1H, for 10H); 9.66 (s, 1H, for 5H); 8.54 (s, 1H, for 20H); 5.79 (q, J = 6.8 Hz, 1H, 3^1H); 5.40 (m, 1H for 17H); 4.43 (m, 2H, N−$CH_2CH_2CH_3$); 4.34 (q, J = 7.3 Hz, 1H for 18H); 3.84 (s, 3H, $12CH_3$); 3.67 (m, 4H, 8^1CH_2 and O−$CH_2CH_2CH_2CH_2CH_2CH_3$); 3.56 (s, 3H, $17^2CO_2CH_3$); 3.36 (s, 3H, $2CH_3$); 3.20 (s, 3H, $7CH_3$); 2.67, 2.42, and 2.33 (each m, 1H, 2 × 17^1H and 1 × 17^2H); 2.06 (m, J = 6.7, 2.7 Hz, 3H, 3^1CH_3); 2.02 (m, 3H, 1 × 17^2H and N−$CH_2CH_2CH_3$); 1.75 (d, J = 7.0 Hz, 3H, $18CH_3$); 1.69 (t, J = 7.0 Hz, 3H, 8^2CH_3); 1.46−1.16 (m, 2H, O−$CH_2CH_2CH_2CH_2CH_2CH_3$); 1.19 (t, J = 6.3 Hz, 3H, N−$CH_2CH_2CH_2CH_3$); 0.78 (m, 3H, O−$CH_2CH_2CH_2CH_2CH_2CH_3$); −0.08 and −0.17 (each br s, 1H, 2NH). HRMS calcd for $C_{43}H_{55}N_5O_5$: 721.4203. Found: 721.4222.

3-(1-(Decyloxy)ethyl)purpurin-18-*N*-propylimide-17-propionic Ester (43). Purpurin-18-*N*-propylimide **9c** (100 mg) was converted into the related bromo derivative, which when reacted with 1-decanol produced the title compound in 60% yield (75 mg) as a sticky solid after purification on a alumina grade II column, eluting with 25% *n*-hexanes in CH_2Cl_2.UV−vis (in CH_2Cl_2): 699 (4.53 × 10^4), 642 (7.35 × 10^3), 543 (1.81 × 10^4), 507 (7.54 × 10^3), 414 (1.28 × 10^5). ^{1}H NMR (400 MHz, 3 mg/1 mL $CDCl_3$, δ ppm): 9.77 (s, 1H, for 10H); 9.66 (s, 1H, for 5H); 8.55 (s, 1H, for 20H); 5.79 (q, J = 6.8 Hz, 1H, 3^1H); 5.40 (m, 1H for 17H); 4.43 (m, 2H, N−$CH_2CH_2CH_3$); 4.34 (q, J = 7.3 Hz, 1H for 18H); 3.84 (s, 3H, $12CH_3$); 3.66 (m, 4H, 8^1CH_2 and O−$CH_2CH_2CH_2CH_2CH_2CH_2CH_2CH_2CH_2CH_3$); 3.56 (s, 3H, $17^2CO_2CH_3$); 3.31 (s, 3H, $2CH_3$); 3.21 (s, 3H, $7CH_3$); 2.67, 2.44 and 2.31 (each m, 1H, 2 × 17^1H and 1 × 17^2H); 2.07 (m, J = 6.7, 2.7 Hz, 3H, 3^1CH_3); 2.02 (m, 3H, 1 × 17^2H and

N−CH_2*CH_2*CH_3); 1.76 (d, J = 7.0 Hz, 3H, 18CH_3); 1.69 (t, J = 7.0 Hz, 3H, 8^2CH_3); 1.46−1.09 (m, total for 16H, O−CH_2*CH_2*CH_2*CH_2*CH_2*CH_2*CH_2*CH_2*CH_2*CH_3); 1.19 (t, J = 6.3 Hz, 3H, N−CH_2CH_2*CH_3); 0.79 (m, 3H, O−$CH_2CH_2CH_2CH_2CH_2$*$CH_2CH_2CH_2$*CH_3); −0.08 and −0.17 (each br s, 1H, 2N−H). Mass calcd for $C_{47}H_{63}N_5O_5$: 777.5. Found: 779.0 (M + 1).

3-(1-(Butyloxy)ethyl)purpurin-18-*N*-butylimide-17-propionic Ester (19). Purpurin-18-*N*-butylimide **9d** (100 mg) was converted into the related bromo derivative, which when reacted with 1-butanol produced the title compound in 70% yield (78 mg) as a sticky solid obtained after purification on a alumina grade II column, eluting with 25% *n*-hexanes in CH_2Cl_2. UV−vis (in CH_2Cl_2): 699 (4.53 × 10^4), 642 (7.35 × 10^3), 543 (1.81 × 10^4), 507 (7.54 × 10^3), 414 (1.28 × 10^5). ^{1}H NMR (400 MHz, 3 mg/1 mL $CDCl_3$, δ ppm): 9.78 (s, 1H, for 10H); 9.66 (s, 1H, for 5H); 8.55 (s, 1H, for 20H); 5.80 (q, J = 6.8 Hz, 1H, 3^1H); 5.41 (m, 1H for 17H); 4.48 (m, 2H, N−*CH_2*CH_2CH_2*CH_3); 4.36 (q, J = 7.3 Hz, 1H for 18H); 3.84 (s, 3H, 12CH_3); 3.66 (m, 4H, 8^1CH_2 and O−*CH_2*$CH_2CH_2CH_3$); 3.57 (s, 3H, 17^2-CO_2CH_3); 3.31 (s, 3H, 2CH_3); 3.19 (s, 3H, 7CH_3); 2.68, 2.45, 2.32 (each m, 1H, 2 × 17^1H and 1 × 17^2H); 2.06 (m, J = 6.7, 2.7 Hz, 3H, 3^1CH_3); 1.99 (m, 3H, 1 × 17^2H and N−CH_2*CH_2*CH_2CH_3); 1.77 (d, J = 7.0 Hz, 3H, 18CH_3); 1.70 (t, J = 7.0 Hz, 3H, 8^2CH_3); 1.66−1.45 (m, 6H, N−CH_2CH_2*CH_2CH_3 and O−CH_2*$CH_2CH_2CH_3$); 1.10 (t, J = 6.3 Hz, 3H, N−CH_2CH_2-CH_2*CH_3); 0.88 (m, 3H, O−$CH_2CH_2CH_2$*CH_3); −0.07 and −0.16 (each br s, 1H, 2NH). Mass calcd for $C_{42}H_{53}N_5O_5$: 707.7. Found: 707.7 (M + 1). Anal. Calcd for $C_{42}H_{53}N_5O_5 \cdot {}^1/_2H_2O$: C, 71.24; H, 7.55; N, 9.89. Found: C, 70.80; H, 7.56; N, 9.52.

3-(1-(Hexyloxy)ethyl)purpurin-18-*N*-butylimide-17-propionic Ester (28). Purpurin-18-*N*-butylimide **9d** (100 mg) was converted into the related bromo derivative, which when reacted with 1-hexanol produced the title compound in 65% yield (75 mg) as a sticky solid. UV−vis (in CH_2Cl_2): 699 (4.53 × 10^4), 642 (7.35 × 10^3), 543 (1.81 × 10^4), 507 (7.54 × 10^3), 414 (1.28 × 10^5). ^{1}H NMR (400 MHz, 3 mg/1 mL $CDCl_3$, δ ppm): 9.77 (s, 1H, for 10H); 9.66 (s, 1H, for 5H); 8.55 (s, 1H, for 20H); 5.79 (q, J = 6.8 Hz, 1H, 3^1H); 5.41 (m, 1H for 17H); 4.47 (m, 2H, N−*CH_2*$CH_2CH_2CH_3$); 4.36 (q, J = 7.3 Hz, 1H for 18H); 3.85 (s, 3H, 12CH_3); 3.68 (m, 4H, 8^1CH_2 and O−*CH_2*$CH_2CH_2CH_2CH_2CH_3$); 3.56 (s, 3H, $17^2CO_2CH_3$); 3.31 (s, 3H, 2CH_3); 3.21 (s, 3H, 7CH_3); 2.67, 2.44, 2.31 (each m, 1H, 2 × 17^1H and 1 × 17^2H); 2.07 (m, J = 6.7, 2.7 Hz, 3H, 3^1CH_3); 1.99 (m, 3H, 1 × 17^2H and N−CH_2*CH_2*CH_2CH_3); 1.76 (d, J = 7.0 Hz, 3H, 18CH_3); 1.69 (t, J = 7.0 Hz, 3H, 8^2CH_3); 1.66−1.19 (m, total for 10H, N−CH_2CH_2*CH_2CH_3 and O−CH_2*CH_2*CH_2CH_2*CH_2CH_3); 1.10 (t, J = 6.3 Hz, 3H, N−CH_2CH_2-CH_2*CH_3); 0.79 (m, 3H, O−CH_2CH_2-$CH_2CH_2CH_2$*CH_3); −0.07 and −0.16 (each br s, 1H, 2NH). Mass calcd for $C_{44}H_{57}N_5O_5$: 735.4. Found: 735.8.

3-(1-(Methyloxy)ethyl)purpurin-18-*N*-hexylimide-17-propionic Ester (33). Purpurin-18-*N*-hexylimide **9e** (100 mg) was converted into the related bromo derivative, which when reacted with anhydrous methanol produced the title compound in 80% yield (84 mg) as a sticky solid. UV−vis (in CH_2Cl_2): 699 (4.53 × 10^4), 642 (7.35 × 10^3), 543 (1.81 × 10^4), 507 (7.54 × 10^3), 414 (1.28 × 10^5). ^{1}H NMR (400 MHz, 3 mg/1 mL $CDCl_3$, δ ppm): 9.68 and 9.66 (each s, 1H, for 10H and 5H); 8.56 (s, 1H, for 20H); 5.75 (q, J = 6.8 Hz, 1H, 3^1H); 5.41 (m, 1H for 17-H); 4.46 (m, 2H, N−*CH_2*$CH_2CH_2CH_2CH_2CH_3$); 4.31 (q, J = 7.3 Hz, 1H for 18H); 3.84 (s, 3H, 12CH_3); 3.67 (q, J = 7.7 Hz, 2H, 8^1CH_2); 3.57 (s, 3H, $17^2CO_2CH_3$); 3.55 (splitting s, 3H, 3^1-OCH_3); 3.31 (s, 3H, 2CH_3); 3.21 (s, 3H, 7CH_3); 2.68, 2.43 and 2.32 (each m, 1H, 2 × 17^1H and 1 × 17^2H); 2.07 (m, J = 6.7, 2.7 Hz, 3H, 3^1CH_3); 1.99 (m, 3H, 1 × 17^2H and N−CH_2*CH_2*$CH_2CH_2CH_2CH_3$); 1.74 (d, J = 7.2 Hz, 3H, 18CH_3); 1.64 (t, J = 7.2 Hz, 3H, 8^2CH_3); 1.61−1.31 (m, total for 6H, N−CH_2-CH_2*CH_2*CH_2*CH_2CH_3); 0.95 (t, 3H, N−$CH_2CH_2CH_2CH_2CH_2$*CH_3); −0.07 and −0.16 (each br s, 1H, 2NH). Mass calcd for $C_{41}H_{51}N_5O_5$: 693.5. Found: 694.5. Anal. Calcd for $C_{41}H_{51}N_5O_5 \cdot H_2O$: C, 69.16; H, 7.50; N, 9.84. Found: C, 69.25; H, 7.30; N, 9.45.

3-(1-(Propyloxy)ethyl)purpurin-18-*N*-hexylimidepropionic Ester (34). Purpurin-18-*N*-hexylimide **9e** (100 mg) was converted into the related bromo derivative, which when reacted with 1-propanol produced the title compound in 70% yield (76 mg) as a sticky solid. UV−vis (in CH_2Cl_2): 699 (4.53 × 10^4), 642 (7.35 × 10^3), 543 (1.81 × 10^4), 507 (7.54 × 10^3), 414 (1.28 × 10^5). ^{1}H NMR (400 MHz, 3 mg/1 mL $CDCl_3$, δ ppm): 9.77 (s, 1H, for 10H); 9.65 (s, 1H, for 5H); 8.55 (s, 1H, for 20H); 5.80 (q, J = 6.8 Hz, 1H, 3^1H); 5.41 (m, 17H); 4.46 (m, 2H, N−*CH_2*$CH_2CH_2CH_2CH_2CH_3$); 4.35 (q, J = 7.3 Hz, 1H for 18H); 3.84 (s, 3H, 12CH_3); 3.67 (m, 4H, 8^1CH_2 and O−*CH_2*-CH_2CH_3); 3.56 (s, 3H, $17^2CO_2CH_3$); 3.31 (s, 3H, 2CH_3); 3.20 (s, 3H, 7CH_3); 2.67, 2.44 and 2.32 (each m, 1H, 2 × 17^1H and 1 × 17^2H); 2.07 (m, J = 6.7, 2.7 Hz, 3H, 3^1CH_3); 2.00 (m, 3H, 1 × 17^2H and N−CH_2*CH_2CH_2-$CH_2CH_2CH_3$); 1.76 (d, J = 7.2 Hz, 3H, 18CH_3); 1.68 (t, J = 7.2 Hz, 3H, 8^2CH_3); 1.60 and 1.46 (m, total for 8H, N−CH_2CH_2*CH_2*CH_2*CH_2CH_3 and O−CH_2*CH_2-CH_3); 0.96 (m, 6H, O−CH_2CH_2*CH_3 and N−$CH_2CH_2CH_2CH_2$-CH_2*CH_3); −0.07 and −0.16 (each br s, 1H, 2NH). Mass calcd for $C_{43}H_{55}N_5O_5$: 721.4. Found: 722.8 (M + 1).

3-(1-(Butyloxy)ethyl)purpurin-18-*N*-hexylimide-17-propionic Ester (35). Purpurin-18-*N*-hexylimide **7e** (80 mg) was converted into the related bromo derivative, which when reacted with 1-butanol produced the title compound in 60% yield (53 mg) as a sticky solid. UV−vis (in CH_2Cl_2): 699 (4.53 × 10^4), 642 (7.35 × 10^3), 543 (1.81 × 10^4), 507 (7.54 × 10^3), 414 (1.28 × 10^5).^{1}H NMR (400 MHz, 3 mg/1 mL $CDCl_3$, δ ppm): 9.77 (s, 1H, for 10H); 9.65 (s, 1H, for 5H); 8.55 (s, 1H, for 20H); 5.80 (q, J = 6.8 Hz, 1H, 3^1H); 5.41 (m, 17H); 4.45 (m, 2H, N−*CH_2*$CH_2CH_2CH_2CH_2CH_3$); 4.35 (q, J = 7.3 Hz, 1H for 18H); 3.84 (s, 3H, 12CH_3); 3.67 (m, 4H, 8^1CH_2 and O−*CH_2*-$CH_2CH_2CH_2CH_3$); 3.56 (s, 3H, $17^2CO_2CH_3$); 3.33 (s, 3H, 2CH_3); 3.20 (s, 3H, 7CH_3); 2.67, 2.44 and 2.32 (each m, 1H, 2 × 17^1H and 1 × 17^2H); 2.07 (m, J = 6.7, 2.7 Hz, 3H, 3^1CH_3); 2.00 (m, 3H, 1 × 17^2H and N−CH_2*$CH_2CH_2CH_2CH_2CH_3$); 1.76 (d, J = 7.2 Hz, 3H, 18CH_3); 1.69 (t, J = 7.2 Hz, 3H, 8^2CH_3); 1.65−1.37 (m, total for 10H, N−CH_2CH_2*CH_2*CH_2*CH_2CH_3 and O−CH_2*CH_2-CH_2CH_3); 0.96 (t, 3H, N−$CH_2CH_2CH_2CH_2CH_2$*CH_3); 0.88 (m, 3H, O−$CH_2CH_2CH_2$*CH_3); 0.24 and 0.15 (each br s, 1H, 2N−H). Mass calculated for $C_{44}H_{57}N_5O_5$: 735.4. Found: 736.9.

3-(1-(Pentyloxy)ethyl)purpurin-18-*N*-hexylimide-17-propionic Ester (36). Purpurin-18-*N*-hexylimide **9e** (80 mg) was converted into the related bromo derivative, which when reacted with 1-pentanol produced the title compound in 55% yield (50 mg) as a sticky solid. UV−vis (in CH_2Cl_2): 699 (4.53 × 10^4), 642 (7.35 × 10^3), 543 (1.81 × 10^4), 507 (7.54 × 10^3), 414 (1.28 × 10^5). ^{1}H NMR (400 MHz, 3 mg/1 mL $CDCl_3$, δ ppm): 9.77 (s, 1H, for 10H); 9.65 (s, 1H, for 5H); 8.55 (s, 1H, for 20H); 5.80 (q, J = 6.8 Hz, 1H, 3^1H); 5.40 (m, 17H); 4.46 (m, 2H, N−*CH_2*$CH_2CH_2CH_2CH_2CH_3$); 4.35 (q, J = 7.3 Hz, 1H for 18H); 3.84 (s, 3H, 12CH_3); 3.65 (m, 4H, 8^1CH_2 and O−*CH_2*-$CH_2CH_2CH_2CH_3$); 3.56 (s, 3H, $17^2CO_2CH_3$); 3.32 (s, 3H, 2CH_3); 3.20 (s, 3H, 7CH_3); 2.68, 2.44 and 2.32 (each m, 1H, 2 × 17^1H and 1 × 17^2H); 2.06 (m, J = 6.7, 2.7 Hz, 3H, 3^1CH_3); 2.00 (m, 3H, 1 × 17^2H and N−CH_2*$CH_2CH_2CH_2CH_2CH_3$); 1.76 (d, J = 7.2 Hz, 3H, 18CH_3); 1.69 (t, J = 7.2 Hz, 3H, 8^2CH_3); 1.65−1.23 (m, total for 12H, N−CH_2CH_2*CH_2*CH_2*CH_2CH_3 and O−CH_2*CH_2*CH_2*CH_2CH_3); 0.95 (t, 3H, N−$CH_2CH_2CH_2CH_2$-CH_2*CH_3); 0.84 (m, 3H, O−$CH_2CH_2CH_2CH_2$*CH_3); 0.24 and 0.14 (each br s, 1H, 2N−H). Mass calcd for $C_{45}H_{59}N_5O_5$: 749.5. Found: 751 (M + 1).

3-(1-(Hexyloxy)ethyl)purpurin-18-*N*-hexylimidepropionic Ester (20): Purpurin-18-*N*-hexylimide **9e** (80 mg) was converted into the related bromo derivative, which when reacted with 1-hexanol produced the title compound in 40% yield (37 mg) as a sticky solid after purification by preparative plates eluting with 1% acetone in CH_2Cl_2. UV−vis (in CH_2Cl_2): 699 (4.53 × 10^4), 642 (7.35 × 10^3), 543 (1.81 × 10^4), 507 (7.54 × 10^3), 414 (1.28 × 10^5). ^{1}H NMR (400 MHz, 3 mg/1 mL $CDCl_3$, δ ppm): 9.78 (s, 1H, for 10H); 9.65 (s, 1H, for 5H); 8.55 (s, 1H, for 20H); 5.80 (q, J = 6.8 Hz, 1H, 3^1H); 5.40 (m, 17H); 4.46 (m, 2H, N−*CH_2*$CH_2CH_2CH_2CH_2CH_3$); 4.36 (q, J = 7.3 Hz, 1H for 18H); 3.85 (s, 3H, 12CH_3); 3.67 (m, 4H, 8^1CH_2 and O−*CH_2*$CH_2CH_2CH_2CH_2CH_3$); 3.57 (s, 3H, $17^2CO_2CH_3$); 3.32 (s, 3H, 2CH_3); 3.21 (s, 3H, 7CH_3); 2.68, 2.44 and 2.32 (each m, 1H, 2 × 17^1H and 1 × 17^2H); 2.06 (m, J = 6.7, 2.7 Hz, 3H, 3^1CH_3); 2.00 (m, 3H, 1 × 17^2H and N−CH_2*$CH_2CH_2CH_2$-CH_2-

CH_3); 1.74 (d, $J = 7.2$ Hz, 3H, $18CH_3$); 1.69 (t, $J = 7.2$ Hz, 3H, 8^2CH_3); 1.61−1.16 (m, total for 14H, N−$CH_2CH_2CH_2$–CH_2CH_2-CH_3 and O−$CH_2CH_2CH_2CH_2CH_2CH_3$); 0.95 (t, 3H, N−CH_2-$CH_2CH_2CH_2CH_2CH_3$); 0.80 (m, 3H, O−$CH_2CH_2CH_2CH_2CH_2$-CH_3); −0.07 and −0.16 (each br s, 1H, 2NH). Mass calcd for $C_{46}H_{61}N_5O_5$: 763.5. Found: 765.0 (M + 1).

3-(1-(Octyloxy)ethyl)purpurin-18-*N*-hexylimide-17-propionic Ester (38). Purpurin-18-*N*-hexylimide **9e** (80 mg) was converted into the related bromo derivative, which when reacted with 1-octanol produced the title compound in 70% yield (67 mg) as a sticky solid.UV−vis (in CH_2Cl_2): 699 (4.53 × 10^4), 642 (7.35 × 10^3), 543 (1.81 × 10^4), 507 (7.54 × 10^3), 414 (1.28 × 10^5). ^{1}H NMR (400 MHz, 3 mg/1 mL $CDCl_3$, δ ppm): 9.78 (s, 1H, for 10H); 9.63 (s, 1H, for 5H); 8.56 (s, 1H, for 20H); 5.80 (q, $J = 6.8$ Hz, 1H, 3^1H); 5.42 (m, 17H); 4.46 (m, 2H, N−$CH_2CH_2CH_2CH_2CH_2CH_3$); 4.37 (q, $J = 7.3$ Hz, 1H for 18H); 3.83 (s, 3H, $12CH_3$); 3.67 (m, 4H, 8^1CH_2 and O−CH_2-$CH_2CH_2CH_2CH_2CH_2CH_2CH_3$); 3.57 (s, 3H, $17^2CO_2CH_3$); 3.33 (s, 3H, $2CH_3$); 3.20 (s, 3H, $7CH_3$); 2.68, 2.44 and 2.32 (each m, 1H, 2 × 17^1H and 1 × 17^2H); 2.06 (m, $J = 6.7$, 2.7 Hz, 3H, 3^1CH_3); 2.00 (m, 3H, 1 × 17^2H and N−$CH_2CH_2CH_2CH_2$–CH_2-CH_3); 1.77 (d, $J = 7.2$ Hz, 3H, $18CH_3$); 1.69 (t, $J = 7.2$ Hz, 3H, 8^2CH_3); 1.65−1.10 (m, total for 18H, N−$CH_2CH_2CH_2CH_2CH_2$-CH_3 and O−$CH_2CH_2CH_2CH_2CH_2CH_2CH_2CH_3$); 0.96 (t, 3H, N−$CH_2CH_2CH_2CH_2CH_2CH_3$); 0.79 (m, 3H, O−$CH_2CH_2CH_2$-$CH_2CH_2CH_2CH_2CH_3$); −0.08 and −0.16 (each br s, 1H, 2NH). Mass calcd for $C_{48}H_{65}N_5O_5$: 791.5. Found: 792.5 (M + 1).

3-(1-(Nonanyloxy)ethyl)purpurin-18-*N*-hexylimide-17-propionic Ester (39): Purpurin-18-*N*-hexylimide **9e** (90 mg) was converted into the related bromo derivative, which when reacted with 1-nonanol and purified by column chromatography produced the title compound in 50% yield (55 mg) as a sticky solid. UV−vis (in CH_2Cl_2): 699 (4.53 × 10^4), 642 (7.35 × 10^3), 543 (1.81 × 10^4), 507 (7.54 × 10^3), 414 (1.28 × 10^5). ^{1}H NMR (400 MHz, 3 mg/1 mL $CDCl_3$, δ ppm): 9.77 (s, 1H, for 10H); 9.66 (s, 1H, for 5H); 8.54 (s, 1H, for 20H); 5.78 (q, $J = 6.8$ Hz, 1H, 3^1H); 5.40 (m, 17H); 4.45 (m, 2H, N−$CH_2CH_2CH_2$-$CH_2CH_2CH_3$); 4.34 (q, $J = 7.3$ Hz, 1H for 18H); 3.83 (s, 3H, $12CH_3$); 3.67 (m, 4H, 8^1CH_2 and O−$CH_2CH_2CH_2CH_2CH_2CH_2$-$CH_2CH_2CH_3$); 3.57 (s, 3H, $17^2CO_2CH_3$); 3.33 (s, 3H, $2CH_3$); 3.20 (s, 3H, $7CH_3$); 2.68, 2.44 and 2.32 (each m, 1H, 2 × 17^1H and 1 × 17^2H); 2.06 (m, $J = 6.7$, 2.7 Hz, 3H, 3^1-CH_3); 2.00 (m, 3H, 1 × 17^2H and N−$CH_2CH_2CH_2CH_2CH_2CH_3$); 1.77 (d, $J = 7.2$ Hz, 3H, $18CH_3$); 1.69 (t, $J = 7.2$ Hz, 3H, 8^2CH_3); 1.65−1.10 (m, total for 20H, N−$CH_2CH_2CH_2CH_2CH_2CH_3$ and O−CH_2CH_2-$CH_2CH_2CH_2CH_2CH_2CH_2CH_2CH_3$); 0.95 (t, 3H, N−$CH_2CH_2CH_2$-$CH_2CH_2CH_3$); 0.78 (m, 3H, O−$CH_2CH_2CH_2CH_2CH_2CH_2CH_2$-$CH_2CH_3$); −0.08 and −0.17 (each br s, 1H, 2NH). Mass calcd for $C_{49}H_{67}N_5O_5$: 805.5. Found: 806.3.

3-(1-(Decyloxy)ethyl)purpurin-18-*N*-hexylimide-17-propionc Ester (40). Purpurin-18-*N*-hexylimide **9e** (90 mg) was converted into the related bromo derivative, which when reacted with 1-decanol produced the title compound in 55% yield (60 mg) as a sticky solid after purification on an alumina grade II column, eluting with 50% *n*-hexanes in CH_2Cl_2. UV−vis (in CH_2Cl_2): 699 (4.53 × 10^4), 642 (7.35 × 10^3), 543 (1.81 × 10^4), 507 (7.54 × 10^3), 414 (1.28 × 10^5). ^{1}H NMR (400 MHz, 3 mg/1 mL $CDCl_3$, δ ppm): 9.78 (s, 1H, for 10H); 9.65 (s, 1H, for 5H); 8.54 (s, 1H, for 20H); 5.79 (q, $J = 6.8$ Hz, 1H, 3^1H); 5.42 (m, 17H); 4.45 (m, 2H, N−$CH_2CH_2CH_2CH_2CH_2CH_3$); 4.37 (q, $J = 7.3$ Hz, 1H for 18H); 3.83 (s, 3H, $12CH_3$); 3.67 (m, 4H, 8^1CH_2 and O−$CH_2CH_2CH_2CH_2CH_2CH_2CH_2CH_2CH_2CH_3$); 3.57 (s, 3H, $17^2CO_2CH_3$); 3.33 (s, 3H, $2CH_3$); 3.20 (s, 3H, $7CH_3$); 2.68, 2.44 and 2.32 (each m, 1H, 2 × 17^1H and 1 × 17^2H); 2.06 (m, $J = 6.7$, 2.7 Hz, 3H, 3^1CH_3); 2.00 (m, 3H, 1 × 17^2H and N−$CH_2CH_2CH_2CH_2CH_2CH_3$); 1.77 (d, $J = 7.2$ Hz, 3H, $18CH_3$); 1.69 (t, $J = 7.2$ Hz, 3H, 8^2CH_3); 1.65−1.10 (m, total for 22H, N−$CH_2CH_2CH_2CH_2CH_2CH_3$ and O−$CH_2CH_2CH_2CH_2CH_2CH_2$-$CH_2CH_2CH_2CH_3$); 0.95 (t, 3H, N−$CH_2CH_2CH_2CH_2CH_2CH_3$); 0.78 (m, 3H, O−$CH_2CH_2CH_2CH_2CH_2CH_2CH_2CH_2CH_2CH_3$); −0.07 and −0.16 (each br s, 1H, 2NH). Mass calcd for $C_{50}H_{69}N_5O_5$: 819. 5. Found: 821.2 (M + 1).

3-(1-(Dodecyloxy)ethyl)purpurin-18-*N*-hexylimide-17-propionic Ester (41). Purpurin-18-*N*-hexylimide **9e** (70 mg) was converted into the related bromo derivative, which when reacted with 1-dodecanol produced the title compound in 70% yield (63 mg) as a sticky solid after purification on an alumina grade II column, eluting with 50% *n*-hexanes in CH_2Cl_2.UV−vis (in CH_2Cl_2): 699 (4.53 × 10^4), 642 (7.35 × 10^3), 543 (1.81 × 10^4), 507 (7.54 × 10^3), 414 (1.28 × 10^5).^{1}H NMR (400 MHz, 3 mg/1 mL $CDCl_3$, δ ppm): 9.77 (s, 1H, for 10H); 9.65 (s, 1H, for 5H); 8.54 (s, 1H, for 20H); 5.79 (q, $J = 6.8$ Hz, 1H, 3^1H); 5.42 (m, 17H); 4.45 (m, 2H, N−$CH_2CH_2CH_2CH_2CH_2CH_3$); 4.37 (q, $J = 7.3$ Hz, 1H for 18H); 3.83 (s, 3H, $12CH_3$); 3.67 (m, 4H, 8^1CH_2 and O−$CH_2CH_2CH_2CH_2CH_2CH_2CH_2CH_2CH_2CH_2CH_3$); 3.57 (s, 3H, $17^2CO_2CH_3$); 3.33 (s, 3H, $2CH_3$); 3.20 (s, 3H, $7CH_3$); 2.68, 2.44 and 2.32 (each m, 1H, 2 × 17^1H and 1 × 17^2H); 2.06 (m, $J = 6.7$, 2.7 Hz, 3H, 3^1CH_3); 2.00 (m, 3H, 1 × 17^2H and N−$CH_2CH_2CH_2CH_2CH_2CH_3$); 1.74 (d, $J = 7.2$ Hz, 3H, $18CH_3$); 1.69 (t, $J = 7.2$ Hz, 3H, 8^2CH_3); 1.59, 1.49, 1.38 and 1.23 (each m, total for 16H, N−$CH_2CH_2CH_2CH_2CH_2CH_3$ and O−CH_2CH_2-$CH_2CH_2CH_2$–CH_3); 0.92 (m, 3H, N−$CH_2CH_2CH_2CH_2CH_2$-CH_2CH_3); 0.78 (m, 3H, O−$CH_2CH_2CH_2CH_2CH_2CH_3$); −0.08 and −0.17 (each br s, 1H, 2NH). Mass calcd for $C_{47}H_{63}N_5O_5$: 777.5. Found:778.5 (M + 1).

3-(1-(Heptyloxy)ethyl)purpurin-18-*N*-heptylimide-17-propionic Ester (21). Purpurin-18-*N*-heptylimide **9f** (80 mg) was converted into the related bromo derivative, which when reacted with 1-heptanol produced the title compound in 70% yield (65 mg) as a sticky solid after purification on an alumina grade II column, eluting with 25% *n*-hexanes in CH_2Cl_2. UV−vis (in CH_2Cl_2): 699 (4.53 × 10^4), 642 (7.35 × 10^3), 543 (1.81 × 10^4), 507 (7.54 × 10^3), 414 (1.28 × 10^5). ^{1}H NMR (400 MHz, 3 mg/1 mL $CDCl_3$, δ ppm): 9.77 (s, 1H, for 10H); 9.66 (s, 1H, for 5H); 8.54 (s, 1H, for 20H); 5.79 (q, $J = 6.8$ Hz, 1H, 3^1H); 5.40 (m, 17H); 4.45 (m, 2H, N−$CH_2CH_2CH_2CH_2CH_2CH_3$); 4.34 (q, $J = 7.3$ Hz, 1H for 18H); 3.85 (s, 3H, $12CH_3$); 3.67 (m, 4H, 8^1CH_2 and O−$CH_2CH_2CH_2CH_2CH_2CH_3$); 3.57 (s, 3H, $17^2CO_2CH_3$); 3.32 (s, 3H, $2CH_3$); 3.21 (s, 3H, $7CH_3$); 2.68, 2.44 and 2.32 (each m, 1H, 2 × 17^1H and 1 × 17^2H); 2.08 (m, $J = 6.7$, 2.7 Hz, 3H, 3^1CH_3); 2.00 (m, 3H, 1 × 17^2H and N−CH_2CH_2-$CH_2CH_2CH_2CH_2CH_3$); 1.74 (d, $J = 7.2$ Hz, 3H, $18CH_3$); 1.69 (t, $J = 7.2$ Hz, 3H, 8^2CH_3); 1.59, 1.49, 1.38 and 1.23 (each m, total for 18H, N−$CH_2CH_2CH_2CH_2CH_2CH_2$–CH_3 and O−CH_2CH_2-$CH_2CH_2CH_2CH_2CH_2CH_3$); 0.92 (m, 3H, N−$CH_2CH_2CH_2CH_2$-$CH_2CH_2CH_3$); 0.78 (m, 3H, O−$CH_2CH_2CH_2CH_2CH_2CH_2CH_3$); −0.07 and −0.17 (each br s, 1H, 2NH). Mass calcd for $C_{48}H_{65}N_5O_5$: 791.5. Found: 793.1 (M + 1).

3-(1-(Hexyloxy)ethyl)purpurin-18-*N*-octylimide-17-propionic Ester (30). Purpurin-18-*N*-octylimide **9g** (100 mg) was converted into the related bromo derivative, which when reacted with 1-hexanol produced the title compound in 75% yield (85 mg) as a sticky solid after purification on an alumina grade II column, eluted with 33% *n*-hexanes in CH_2Cl_2. UV−

vis (in CH_2Cl_2): 699 (4.53×10^4), 642 (7.35×10^3), 543 (1.81×10^4), 507 (7.54×10^3), 414 (1.28×10^5). ^{1}H NMR (400 MHz, 3 mg/1 mL $CDCl_3$, δ ppm): 9.77 (s, 1H, for 10H); 9.66 (s, 1H, for 5H); 8.54 (s, 1H, for 20H); 5.79 (q, J = 6.8 Hz, 1H, 3^1H); 5.40 (m, 17H); 4.45 (m, 2H, N−*CH_2*$CH_2H_2CH_2CH_2CH_2CH_2$-CH_3); 4.34 (q, J = 7.3 Hz, 1H for 18H); 3.85 (s, 3H, $12CH_3$); 3.67 (m, 4H, 8^1CH_2 and O−*CH_2*$CH_2CH_2CH_2CH_2CH_3$); 3.57 (s, 3H, $17^2CO_2CH_3$); 3.32 (s, 3H, $2CH_3$); 3.21 (s, 3H, $7CH_3$); 2.67, 2.42 and 2.31 (each m, 1H, 2×17^1H and 1×17^2H); 2.07 (m, J = 6.7, 2.7 Hz, 3H, 3^1CH_3); 1.99 (m, 3H, 1×17^2H and N−CH_2*CH_2*$CH_2CH_2CH_2CH_2CH_3$); 1.74 (d, J = 7.2 Hz, 3H, $18CH_3$); 1.69 (t, J = 7.2 Hz, 3H, 8^2CH_3); 1.65−1.19 (m, total for 18H, N−CH_2CH_2*CH_2*CH_2*CH_2*CH_2*CH_2CH_3 and O−CH_2*CH_2*-*CH_2**$CH_2CH_2CH_3$); 0.91 (m, 3H, N−$CH_2CH_2CH_2CH_2CH_2CH_2$-CH_2*CH_3*); 0.79 (m, 3H, O−$CH_2CH_2CH_2CH_2CH_2$*CH_3*); −0.07 and −0.17 (each br s, 1H, 2NH). Mass cald for $C_{48}H_{65}N_5O_5$: 791.5. Found: 793.0 (M + 1).

3-(1-(Octyloxy)ethyl)purpurin-18-*N*-octylimide-17-propionic Ester (22): Purpurin-18-*N*-octylimide **9g** (100 mg) was converted into the related bromo derivative, which when reacted with 1-octanol produced the title compound in 70% yield (83 mg) as a sticky solid after purification on an alumina grade II column, eluting with 33% *n*-hexanes in CH_2Cl_2). UV−vis (in CH_2Cl_2): 699 (4.53×10^4), 642 (7.35×10^3), 543 (1.81×10^4), 507 (7.54×10^3), 414 (1.28×10^5). ^{1}H NMR (400 MHz, 3 mg/1 mL $CDCl_3$, δ ppm): 9.77 (s, 1H, for 10H); 9.66 (s, 1H, for 5H); 8.55 (s, 1H, for 20H); 5.80 (q, J = 6.8 Hz, 1H, 3^1H); 5.41 (m, 17H); 4.45 (m, 2H, N−*CH_2*$CH_2CH_2CH_2CH_2CH_2CH_2$-CH_3); 4.34 (q, J = 7.3 Hz, 1H for 18H); 3.85 (s, 3H, $12CH_3$); 3.67 (m, 4H, 8^1CH_2 and O−*CH_2*$CH_2CH_2CH_2CH_2CH_2CH_2CH_3$); 3.57 (s, 3H, $17^2CO_2CH_3$); 3.32 (s, 3H, $2CH_3$); 3.21 (s, 3H, $7CH_3$); 2.67, 2.42 and 2.31 (each m, 1H, 2×17^1H and 1×17^2H); 2.07 (m, J = 6.7, 2.7 Hz, 3H, 3^1CH_3); 1.99 (m, 3H, 1×17^2H and N−CH_2*CH_2*$CH_2CH_2CH_2CH_2CH_3$); 1.74 (d, J = 7.2 Hz, 3H, $18CH_3$); 1.69 (t, J = 7.2 Hz, 3H, 8^2CH_3); 1.66−1.10 (m, total for 22H, N−CH_2CH_2*CH_2*CH_2*CH_2*CH_2*CH_2CH_3 and O−CH_2*CH_2*-*CH_2**CH_2**CH_2**CH_2CH_3*); 0.91 (m, 3H, N−$CH_2CH_2CH_2CH_2$-CH_2CH_2–CH_2*CH_3*); 0.78 (m, 3H, O−$CH_2CH_2CH_2CH_2CH_2CH_2$-CH_2*CH_3*); −0.07 and −0.17 (each br s, 1H, 2NH). Mass calcd for $C_{50}H_{69}N_5O_5$: 819.5. Found: 821.0.

3-(1-(Propyloxy)ethyl)purpurin-18-*N*-decylimide-17-propionc Ester (44): Purpurin-18-*N*-decylimide **9h** (70 mg) was converted into the related bromo derivative, which when reacted with 1-propanol produced the title compound in 80% yield (60 mg) as a sticky solid after purification over a alumina grade II column and eluting with 33% *n*-hexanes in CH_2Cl_2. UV−vis (in CH_2Cl_2): 699 (4.53×10^4), 642 (7.35×10^3), 543 (1.81×10^4), 507 (7.54×10^3), 414 (1.28×10^5). ^{1}H NMR (400 MHz, 3 mg/1 mL $CDCl_3$, δ ppm): 9.78 (s, 1H, for 10H); 9.66 (s, 1H, for 5H); 8.55 (s, 1H, for 20H); 5.80 (q, J = 6.8 Hz, 1H, 3^1H); 5.40 (m, 17H); 4.46 (m, 2H, N−*CH_2*$CH_2CH_2CH_2CH_2CH_2CH_2$-$CH_2CH_2CH_2CH_3$); 4.35 (q, J = 7.4 Hz, 1H for 18H); 3.85 (s, 3H, $12CH_3$); 3.67 (m, 4H, 8^1CH_2 and O−*CH_2*CH_2CH_3); 3.56 (s, 3H, $17^2CO_2CH_3$); 3.31 (s, 3H, $2CH_3$); 3.20 (s, 3H, $7CH_3$); 2.67, 2.42 and 2.32 (each m, 1H, 2×17^1H and 1×17^2H); 2.07 (m, J = 6.7, 2.7 Hz, 3H, 3^1CH_3); 1.99 (m, 3H, 1×17^2H and N−CH_2*CH_2*$CH_2CH_2CH_2CH_2CH_2CH_2CH_3$); 1.75 (d, J = 7.2 Hz, 3H, $18CH_3$); 1.69 (t, J = 7.2 Hz, 3H, 8^2CH_3); 1.64−1.23 (m, total for 16H, N−CH_2CH_2*CH_2*CH_2*CH_2*CH_2*CH_2*CH_2*CH_2CH_3 and O−CH_2*CH_2CH_3*); 0.96 (m, 3H, O−CH_2CH_2*CH_3*); 0.88 (t, 3H, N−$CH_2CH_2CH_2CH_2CH_2CH_2CH_2CH_2CH_2$*$CH_3$*); −0.07 and −0.17 (each br s, 1H, 2NH). Mass calcd for $C_{47}H_{63}N_5O_5$: 777.5. Found: 779.0 (M + 1).

3-(1-(Hexyloxy)ethyl)purpurin-18-*N*-decylimide-17-propionic Ester (31): Purpurin-18-*N*-decylimide **9h** (70 mg) was converted into the related bromo derivative, which when reacted with 1-hexanol produced the title compound in 70% yield (56 mg) as a sticky solid after purification on an alumina grade II column and eluting with 50% *n*-hexanes in CH_2Cl_2).UV−vis (in CH_2Cl_2): 699 (4.53×10^4), 642 (7.35×10^3), 543 (1.81×10^4), 507 (7.54×10^3), 414 (1.28×10^5).^{1}HNMR (400 MHz, 3 mg/1 mL $CDCl_3$, δ ppm): 9.77 (s, 1H, for 10H); 9.66 (s, 1H, for 5H); 8.55 (s, 1H, for 20H); 5.80 (q, J = 6.8 Hz, 1H, 3^1H); 5.40 (m, 17H); 4.46 (m, 2H, N−*CH_2*$CH_2CH_2CH_2CH_2$-$CH_2CH_2CH_2CH_2CH_3$); 4.36 (q, J = 7.4 Hz, 1H for 18H); 3.85 (s, 3H, $12CH_3$); 3.67 (m, 4H, 8^1CH_2 and O−*CH_2*$CH_2CH_2CH_2$-CH_2CH_3); 3.56 (s, 3H, $17^2CO_2CH_3$); 3.31 (s, 3H, $2CH_3$); 3.21 (s, 3H, $7CH_3$); 2.67, 2.42 and 2.32 (each m, 1H, 2×17^1H and 1×17^2H); 2.06 (m, J = 6.7, 2.7 Hz, 3H, 3^1CH_3); 1.99 (m, 3H, 1×17^2H and N−CH_2*CH_2*$CH_2CH_2CH_2CH_2CH_2CH_2CH_2CH_3$); 1.76 (d, J = 7.2 Hz, 3H, $18CH_3$); 1.69 (t, J = 7.2 Hz, 3H, 8^2CH_3); 1.64−1.19 (m, total for 22H, N−CH_2CH_2*CH_2*CH_2*CH_2*CH_2CH_2-*$CH_2CH_2CH_3$* and O−CH_2*CH_2**CH_2**$CH_2CH_2CH_3$*); 0.89 (t, 3H, N−$CH_2CH_2CH_2CH_2CH_2CH_2CH_2CH_2CH_2$*$CH_3$*); 0.78 (m, 3H, O−$CH_2$-$CH_2CH_2CH_2CH_2$*$CH_3$*); −0.07 and −0.17 (each br s, 1H, 2N−H). Mass calcd for $C_{50}H_{69}N_5O_5$: 819.5. Found: 821.1 (M + 1).

3-(1-(Decyloxy)ethyl)purpurin-18-*N*-decylimide-17-propionic Ester (23). Purpurin-18-*N*-decylimide **7h** (100 mg) was converted into the related bromo derivative, which when reacted with 1-decanol produced the title compound in 70% yield (85 mg) as a sticky solid after purification over a alumina grade II column, eluting with 75% *n*-hexanes in CH_2Cl_2). UV−vis (in CH_2Cl_2): 699 (4.53×10^4), 642 (7.35×10^3), 543 (1.81×10^4), 507 (7.54×10^3), 414 (1.28×10^5).^{1}H NMR (400 MHz, 3 mg/1 mL $CDCl_3$, δ ppm): 9.78 (s, 1H, for 10H); 9.66 (s, 1H, for 5H); 8.55 (s, 1H, for 20H); 5.79 (q, J = 6.8 Hz, 1H, 3^1H); 5.41 (m, 17H); 4.45 (m, 2H, N−*CH_2*$CH_2CH_2CH_2CH_2CH_2CH_2$-$CH_2CH_2CH_3$); 4.35 (q, J = 7.4 Hz, 1H for 18H); 3.85 (s, 3H, $12CH_3$); 3.67 (m, 4H, 8^1CH_2 and O-*CH_2*$CH_2CH_2CH_2CH_2CH_2$-$CH_2CH_2CH_2CH_3$); 3.56 (s, 3H, $17^2CO_2CH_3$); 3.31 (s, 3H, $2CH_3$); 3.21 (s, 3H, $7CH_3$); 2.67, 2.42 and 2.32 (each m, 1H, 2×17^1H and 1×17^2H); 2.06 (m, J = 6.7, 2.7 Hz, 3H, 3^1CH_3); 1.99 (m, 3H, 1×17^2H and N−CH_2*CH_2*$CH_2CH_2CH_2CH_2CH_2CH_2CH_2CH_3$); 1.76 (d, J = 7.2 Hz, 3H, $18CH_3$); 1.69 (t, J = 7.2 Hz, 3H, 8^2CH_3); 1.65−1.09 (m, total for 30H, N−CH_2CH_2*CH_2*CH_2*CH_2*CH_2*CH_2*CH_2CH_3 and O−CH_2*CH_2**CH_2**CH_2**CH_2**CH_2**CH_2CH_3*); 0.88 (t, 3H, N−$CH_2CH_2CH_2CH_2CH_2CH_2CH_2CH_2$-$CH_2$*$CH_3$*); 0.80 (m, 3H, O−$CH_2CH_2CH_2CH_2CH_2CH_2CH_2$-$CH_2$*$CH_3$*); −0.07 and −0.17 (each br s, 1H, 2N−H). Mass calcd for $C_{54}H_{77}N_5O_5$: 875.6. Found: 876.7 (M + 1).

3-(1-(Methyloxy)ethyl)purpurin-18-*N*-dodecylimide-17-propionic Ester (42). Purpurin-18-*N*-dodecylimide **7i** (100 mg) was converted into the related bromo derivative, which when reacted with anhydrous methanol produced the title compound in 75% yield (78 mg) as a sticky solid after purification on an alumina grade II column, eluting with 25% *n*-hexanes in CH_2Cl_2. UV−vis (in CH_2Cl_2): 699 (4.53×10^4), 642 (7.35×10^3), 543 (1.81×10^4), 507 (7.54×10^3), 414 (1.28×10^5). ^{1}H NMR (400 MHz, 3 mg/1 mL $CDCl_3$, δ ppm): 9.68 and 9.66 (each s, 1H, for 10H and 5H); 8.56 (s, 1H, for 20H); 5.75 (q, J = 6.8 Hz, 1H, 3^1H); 5.41 (m, 1H for 17-H); 4.46 (m, 2H, N−*CH_2*$CH_2CH_2CH_2CH_2CH_2CH_2CH_2CH_2CH_2CH_3$); 4.35 (q, J = 7.4 Hz, 1H for 18H); 3.85 (s, 3H, $12CH_3$); 3.69 (q, J = 7.7 Hz, 2H, 8^1CH_2); 3.56 (s, 3H, $17^2CO_2CH_3$); 3.55 (splitting s, 3H, 3^1OCH_3); 3.34 (s, 3H, $2CH_3$); 3.21 (s, 3H, $7CH_3$); 2.68, 2.43 and 2.32 (each m, 1H, 2×17^1H and 1×17^2H); 2.07 (m, J = 6.7, 2.7 Hz, 3H, 3^1CH_3); 1.99 (m, 3H, 1×17^2H and N−CH_2*CH_2*-$CH_2CH_2CH_2CH_2CH_2CH_2CH_2CH_2CH_2CH_3$); 1.76 (d, J = 7.2 Hz, 3H, $18CH_3$); 1.69 (t, J = 7.2 Hz, 3H, 8^2CH_3); 1.64−1.24 (m, total for 18H, N−CH_2CH_2*CH_2*–CH_2**CH_2**CH_2**CH_2**CH_2**CH_2**CH_2-*CH_2CH_3*); 0.88 (t, 3H, N−$CH_2CH_2CH_2CH_2CH_2CH_2CH_2CH_2$-$CH_2CH_2CH_2$*$CH_3$*); −0.10 and −0.17 (each br s, 1H, 2N−H). Mass calcd for $C_{47}H_{63}N_5O_5$: 777.5. Found: 779.2 (M + 1).

3-(1-(Hexyloxy)ethyl)purpurin-18-*N*-dodecylimide-17-propionic Ester (32). Purpurin-18-*N*-dodecylimide **9i** (100 mg) was converted into the related bromo derivative, which when reacted with 1-hexanol produced the title compound in 70% yield (80 mg) as a sticky solid after purification over a alumina grade II column, eluting with 50% *n*-hexanes in CH_2Cl_2. UV−vis (in CH_2Cl_2): 699 (4.53×10^4), 642 (7.35×10^3), 543 (1.81×10^4), 507 (7.54×10^3), 414 (1.28×10^5). ^{1}H NMR (400 MHz, 3 mg/1 mL $CDCl_3$, δ ppm): 9.77 (s, 1H, for 10H); 9.67 (s, 1H, for 5H); 8.55 (s, 1H, for 20H); 5.79 (q, J = 6.8 Hz, 1H, 3^1H); 5.40 (m, 17H); 4.45 (m, 2H, N−*CH_2*$CH_2CH_2CH_2CH_2$-$CH_2CH_2CH_2CH_2CH_2CH_2CH_3$); 4.35 (q, J = 7.4 Hz, 1H for 18H); 3.85 (s, 3H, $12CH_3$); 3.67 (m, 4H, 8^1CH_2 and O−*CH_2*CH_2CH_2-$CH_2CH_2CH_3$); 3.56 (s, 3H, $17^2CO_2CH_3$); 3.31 (s, 3H, $2CH_3$); 3.20 (s, 3H, $7CH_3$); 2.67, 2.42 and 2.30 (each m, 1H, 2×17^1H and

1 × 17²H); 2.07 (m, J = 6.7, 2.7 Hz, 3H, 3¹CH₃); 1.98 (m, 3H, 1 × 17²H and N−$CH_2CH_2$$CH_2CH_2CH_2CH_2CH_2CH_2CH_2CH_2$-$CH_2CH_3$); 1.76 (d, J = 7.2 Hz, 3H, 18CH₃); 1.69 (t, J = 7.2 Hz, 3H, 8²CH₃); 1.65−1.21 (m, total for 26H, N−$CH_2CH_2CH_2CH_2$-$CH_2CH_2CH_2CH_2CH_2CH_2CH_2CH_3$ and O−$CH_2CH_2CH_2CH_2$-CH_2CH_3); 0.88 (t, 3H, N−$CH_2CH_2CH_2CH_2CH_2CH_2CH_2CH_2$-$CH_2CH_2CH_2CH_3$); 0.79 (m, 3H, O−$CH_2CH_2CH_2CH_2CH_2CH_3$); −0.08 and −0.18 (each br s, 1H, 2N−H). Mass calcd for $C_{52}H_{73}N_5O_5$: 847.6. Found: 848.0.

3-(1-(Dodecyloxy)ethyl)purpurin-18-*N*-dodecylimide-17-propionic Ester (24). Purpurin-18-*N*-dodecylimide **9i** (100 mg) was converted into the related bromo derivative, which when reacted with 1-dodecanol produced the title compound in 60% yield (75 mg) as a sticky solid after purification over on an alumina grade II column, eluting with 75% *n*-hexanes in CH_2Cl_2. UV−vis (in CH_2Cl_2): 699 (4.53 × 10⁴), 642 (7.35 × 10³), 543 (1.81 × 10⁴), 507 (7.54 × 10³), 414 (1.28 × 10⁵). ¹H NMR (400 MHz, 3 mg/1 mL $CDCl_3$, δ ppm): 9.78 (s, 1H, for 10H); 9.66 (s, 1H, for 5H); 8.55 (s, 1H, for 20H); 5.79 (q, J = 6.8 Hz, 1H, 3¹H); 5.41 (m, 17H); 4.45 (m, 2H, N−$CH_2CH_2CH_2$-$CH_2CH_2CH_2CH_2CH_2CH_2CH_2CH_2CH_3$); 4.35 (q, J = 7.4 Hz, 1H for 18H); 3.85 (s, 3H, 12CH₃); 3.67 (m, 4H, 8¹CH_2 and O−CH_2-$CH_2CH_2CH_2CH_2CH_2CH_2CH_2CH_2CH_2CH_2CH_3$); 3.56 (s, 3H, 17²$CO_2CH_3$); 3.31 (s, 3H, 2CH₃); 3.21 (s, 3H, 7CH₃); 2.67, 2.42, and 2.32 (each m, 1H, 2 × 17¹H and 1 × 17²H); 2.06 (m, J = 6.7, 2.7 Hz, 3H, 3¹CH₃); 1.99 (m, 3H, 1 × 17²H and N−CH_2CH_2-$CH_2CH_2CH_2CH_2CH_2CH_2CH_2CH_2CH_2CH_2CH_3$); 1.76 (d, J = 7.2 Hz, 3H, 18CH₃); 1.69 (t, J = 7.2 Hz, 3H, 8²CH₃); 1.65−1.09 (m, total for 38H, N−$H_2CH_2CH_2CH_2CH_2CH_2CH_2CH_2CH_2CH_2$-$CH_3$ and O−$CH_2CH_2CH_2CH_2CH_2CH_2CH_2CH_2CH_2CH_2$-$CH_3$); 0.88 (t, 3H, N−$CH_2CH_2CH_2CH_2CH_2CH_2CH_2CH_2CH_2CH_2$-$CH_2CH_2CH_3$); 0.80 (m, 3H, O−$CH_2CH_2CH_2CH_2CH_2CH_2CH_2CH_2$-$CH_2CH_2CH_2CH_3$); −0.07 and −0.17 (each br s, 1H, 2N−H). Mass calcd for $C_{58}H_{85}N_5O_5$: 931.7. Found: 932.4 (M + 1).

Measurement of Singlet Oxygen Quantum Yields. Nanosecond laser flash photolysis experiments were performed using the third harmonic (355 nm) of a Continuum Surelite I Q-switched Nd:YAG laser that generates pulses of ca. 6 ns duration. The solutions of the compounds under examination were contained in 1 × 1 cm cuvette. Singlet oxygen luminescence at 1270 nm was detected at right angles to the laser beam direction by a germanium photodiode (Applied Detector Corp. 403HS) cooled to 77 K. Filters were employed to minimize pick up of scattered laser light and fluorescence. The output from the detector−amplifier combination was applied to the 1 MΩ input connector of a LeCroy 9450 digital CRO. Typically 100 laser shots were averaged together at each of a series of different laser intensities selected by a rotary polarizing attenuator calibrated with a power meter. The time profiles of the singlet oxygen luminescence observed from such experiments were a composite of a fast component resulting from residual scattered laser light and near-infrared fluorescence processed through the time constant of the detector system (ca. 600 ns) and a slower component that arises from the singlet oxygen luminescence decay. Fitting the slow component with an exponential and extrapolating back to zero time provided a measure of the O_2 ($^1\Delta_g$) concentration (L_0) prior to the onset of the decay and its subsequent decay lifetime.

Measurements of L_0 were made at a series of laser intensities for both the test solutions and for a solution of *meso*-tetraphenylporphine (H_2TPP) in benzene (Φ_Δ = 0.62) having the same absorbance at 355 nm. These provided values of L_0(x) and L_0(r) for the series of laser intensities, where x and r refer to the test solution and the reference solution, respectively. At low laser intensities, the plots of L_0(x) versus L_0(r) were linear. From these plots, the slopes k_{x-r} were extracted and used to calculate the quantum yield of singlet oxygen of the unknown solution under the prevailing conditions, according to the expression

$$k_{x-r} = (\Phi^x{}_\Delta \eta^x A^x)/(\Phi^r{}_\Delta \eta^r A^r) \quad (1)$$

where A is the absorbance at the excitation wavelength, $\Phi^x{}_\Delta$ is the singlet oxygen quantum yield ($\Phi^r{}_\Delta$ = 0.62), and η is the quenching efficiency given by

$$\eta = k_{T\Sigma}[O_2]/(k_o + k_{T\Sigma}[O_2]) \quad (2)$$

where k_o is the decay rate constant of the triplet in argon-saturated solutions and $k_{T\Sigma}$ is the bimolecular rate constant for quenching of the triplet state by oxygen. In our experiments, all measurements showed that $k_{T\Sigma} \gg k_o$, making the ratio η^x/η^r close to unity. Thus, relation 1 becomes

$$k_{x-r} = \Phi^x{}_\Delta A^x/\Phi^r{}_\Delta A^r \quad (3)$$

Measurements of singlet oxygen O_2 ($^1\Delta_g$) generated from the standard were made before and after the measurements done with the samples under investigation, which confirmed that the instrument response remained constant.

Acknowledgment. The authors are grateful to the National Institutes of Health (CA 55791) for the financial support. Partial support by shared resources of the Roswell Park Cancer Support Grant (P30CA16056) is also acknowledged.

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JM0005510