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On the structure of fistulosin

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Dedication: In celebration of the heterocyclic chemistry brilliance of Alan R. Katritzky and Charles W. Rees

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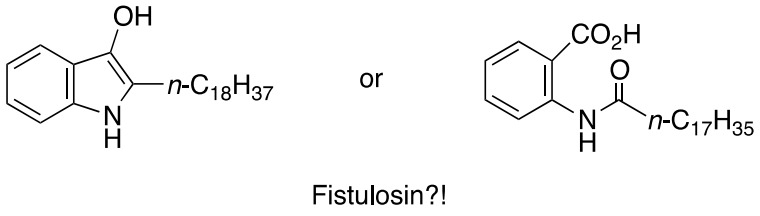
Abstract

We describe our investigation into the purported structure of the Welsh onion metabolite "fistulosin". This compound was assigned as 2-octadecyl-3-hydroxyindole, which might also exist as 2-octadecylindoxyl. Our results show that the corresponding 2-octadecyl-1-(phenylsulfonyl)indoxyl, which we synthesized from 1-(phenylsulfonyl)indole, undergoes facile conversion to alkyl 2-(1-oxononadecyl)aminobenzoate, which supports the work of Söderberg in that fistulosin is actually 2-(1-oxooctadecyl)aminobenzoic acid.



Fistulosin?!

Keywords: Fistulosin, indole, indoxyl, Welsh onion, 2-(1-oxooctadecyl)aminobenzoic acid

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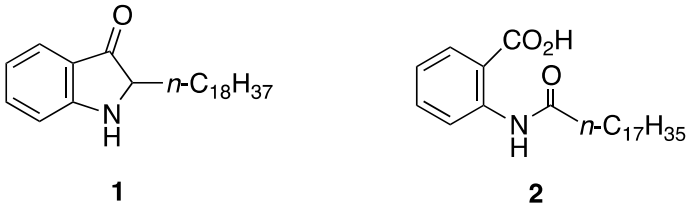
Introduction

In 1999, a compound named fistulosin was isolated from the Welsh onion and assigned the 2-octadecylindoxyl structure **1** and found to possess high antifungal activity.[1] Subsequent reports by Nishida[2] and Söderberg[3] shed serious doubt on the purported structure **1** for fistulosin. Nishida's synthesis of **1** failed to match the data reported for fistulosin,[2] and Söderberg provided compelling evidence that the structure of fistulosin is actually 2-(1-oxooctadecyl)aminobenzoic acid (**2**).[3] We now describe our investigation on the fistulosin conundrum which began in 2003[4] and corroborates the work of Nishida and Söderberg.

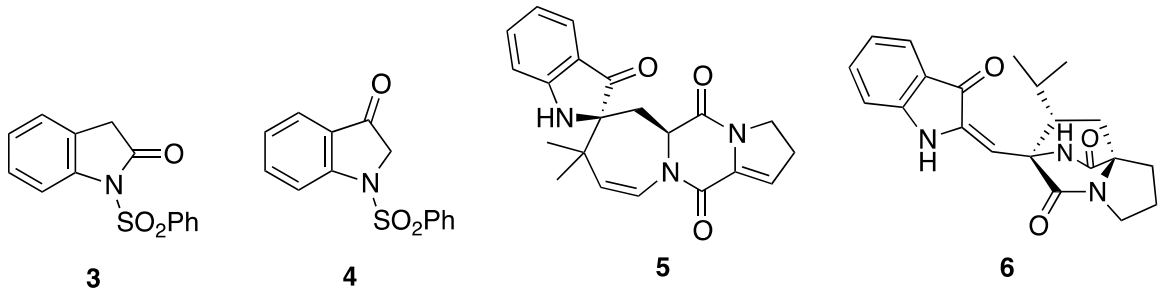


1 **2**

Figure 1. Structures of alleged fistulosin **1** and the likely structure 2-(1-oxooctadecyl)aminobenzoic acid (**2**).

Results and Discussion

The well-known 2-hydroxyindoles (oxindoles) and 3-hydroxyindoles (indoxyls), illustrated for example by the 1-phenylsulfonyl compounds **3** and **4** respectively, exist usually as ketone tautomers unless their enol forms are stabilized by conjugation with electron withdrawing groups.[5] Indoxyls are useful synthetic intermediates for the synthesis of biologically active compounds such as indomethacin,[6] tryptamine,[7] and ellipticine,[8] and this framework is also found in natural compounds like austamide (**5**)[9] and brevianamide D (**6**).[10] Generally, these compounds are synthesized by oxidation of indoles. For example, 1-(phenylsulfonyl)oxindole (**3**) can be prepared by a Baeyer-Villiger oxidation of 2-formylindole with *m*-chloroperbenzoic acid in 71% yield[11] and 1-(phenylsulfonyl)indoxyl (**4**) is available via a direct oxidation of 1-(phenylsulfonyl)indole in 60% yield with magnesium monoperphthalate (MMPP).[12] Given the versatility of 2- and 3-lithioindoles, a direct hydroxylation is promising to give 2- and 3-hydroxyindoles. The hydroxylation of enolates and some aromatic Grignard reagents is already well known using oxaziridine derivatives,[13,14] oxodiperoxymolybdenum complex (MoO_5·Py·HMPA (MoOPH),[15] and even oxygen.[16]



3 **4** **5** **6**

Figure 2. Structures of oxindole **2** and indoxyls **4**–**6**.

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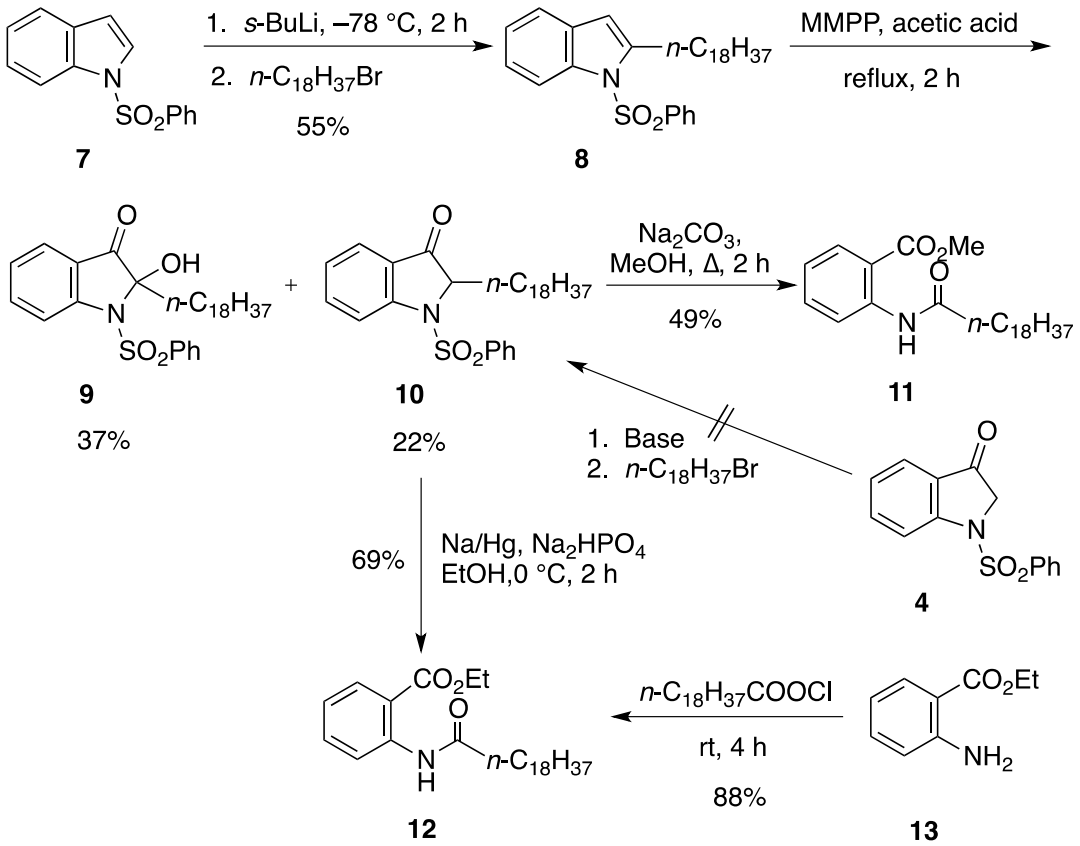
Our approach to fistulosin (**1**) is shown in Scheme 1. Starting from 1-(phenylsulfonyl)indole (**7**), lithiation of the 2-position followed by alkylation with 1-bromooctadecane gave 2-alkylindole **8**, which was oxidized by MMPP in refluxing acetic acid to give two products. The desired 1-(phenylsulfonyl)indoxyl (**10**) was isolated in 22% yield as a minor product. The major product, however, was 2-hydroxyindoxyl **9** in 34% yield. This poor selectivity in oxidation of 2-substituted indoles was also reported by other groups,[17,18] and the use of different peroxides (*m*-CPBA, dimethyldioxirane[19] and oxone) does not improve the yield of the desired product **10**. An effort to alkylate C-2 of indoxyl **4** by base and octadecyl bromide failed, either using lithium diisopropylamide (LDA), sodium methoxide, or KOH in dimethyl sulfoxide (DMSO). Starting material **4** was recovered in each case. Removal of the phenylsulfonyl protection of **10** to give **1** was not achieved. Indeed, treating **10** with sodium carbonate in methanol gave the ring-fragmented amidoester **11**, which appears to be identical to Söderberg's methyl ester obtained from 3-methoxy-2-octadecylindole.[3] Moreover, compound **12** was obtained in a reductive desulfonylation attempt by treating **10** with sodium amalgam in buffered ethanol, in 69% yield. The structure of **12** was confirmed by independent synthesis from acylation of aniline **13** (Scheme 1).



Scheme 1. Our attempted synthesis of **1** via the de-phenylsulfonylation cleavage of **10**.

Although these results are disappointing, some interesting mechanism problems arose. Comparing the oxidative states of starting material **10** to product **12** in the sodium amalgam reactions, we were surprised to find that the protected fistulosin (**10**) is, in fact, oxidized under reducing conditions. Obviously, air oxidation is a likely pathway. However, when we carried out the same reaction in degassed ethanol, we again isolated **12**. We speculate that **1** is generated in the reaction mixture but is quickly oxidized during a rapid work-up. A possible mechanism is proposed in Scheme 2. Simple indoxyl is known to be oxidized to 2-radical **14** by single-

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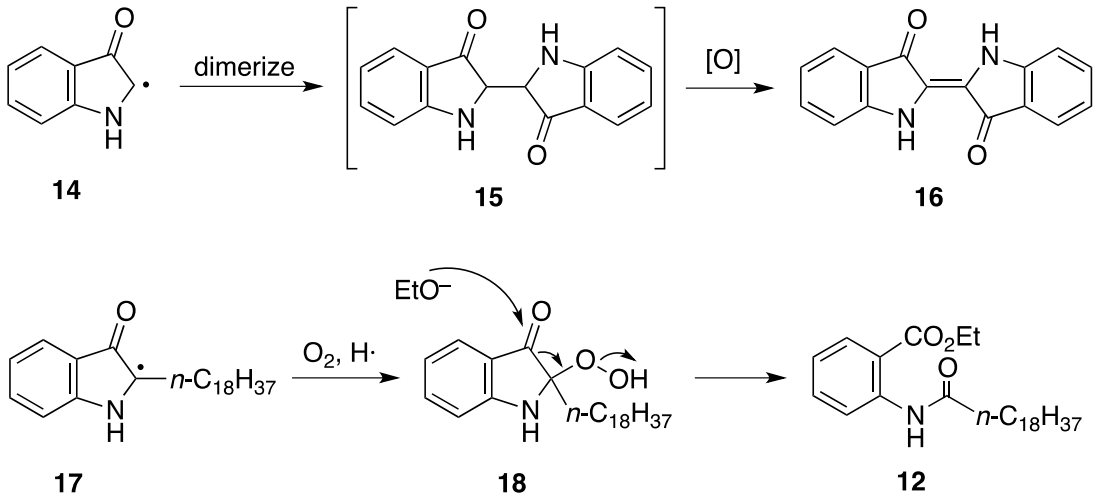
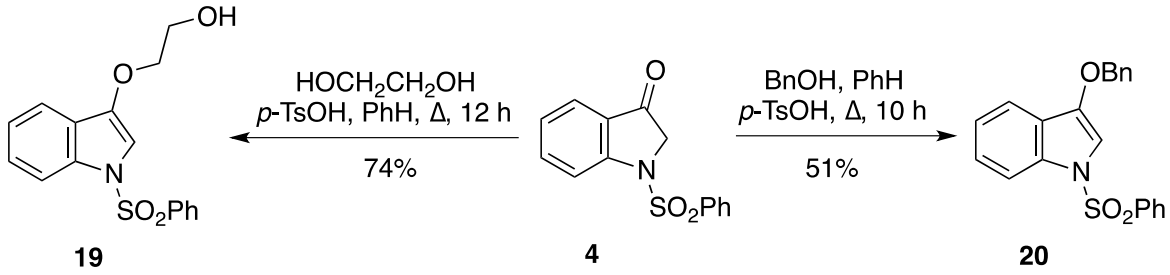
electron transfer (SET) with molecular oxygen and **14** readily dimerizes and is subsequently oxidized to indigo (**16**). Some 2,2-substituted indigos such as peronatin A and B[20] are natural alkaloids and are synthesized by radical dimerization.[21] In our case, a similar oxidation of **1** apparently gives 2-radical **17**, but a 2-substitution may slow down its dimerization. Instead, radical **17** is oxidized to peroxide **18** which leads to ring fragmentation initiated by nucleophilic attack of the 3-carbonyl group by ethoxide. A related C2-C3 ring fragmentation is observed with benzo[*b*]furans upon treatment with chloroperoxidase.[22]



Scheme 2. A proposed mechanism for the formation of ethyl 2-(1-oxononadecyl)aminobenzoate (**12**).

In an attempted ketalization of indoxyl **4** with ethylene glycol, we isolated 3-hydroxyethoxylindole **19** in 74% yield (Scheme 3). This reaction opens a synthetic route to 3-substituted indoles if 3-indoxyls such as **4** are easily accessible. Thus, **4** is treated with benzyl alcohol with acid catalyst in benzene to give 3-benzyloxyindole **20** in 51% yield (Scheme 3). A recent synthesis of 3-alkoxylindoles involved diazoindoles and rhodium(II) catalyst.[23]



Scheme 3. A new synthesis of 3-alkoxylindoles **19** and **20** from indoxyl **4**.

A McMurry reaction[24] could cyclize the ring fragmented amidoester **12** back to an indole ring. Thus, treating **12** with titanium trichloride and zinc in refluxing THF could give 3-ethoxyindole **21** which should be hydrolyzed to **1** under inert atmosphere (Scheme 4).

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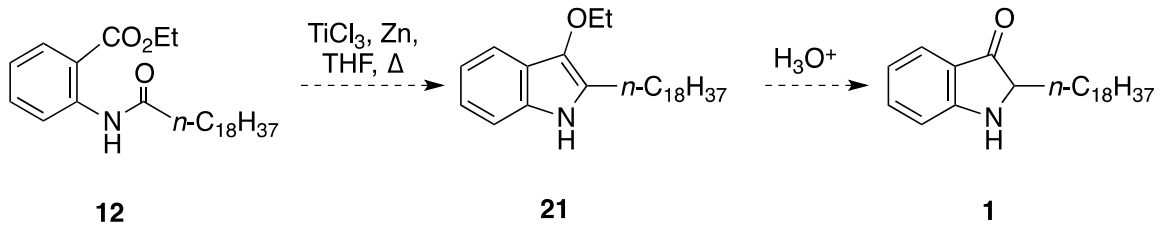

12 **21** **1**

Scheme 4. A proposed route to **1** from **12**, which remains to be seen.

Conclusion

In the absence of a sample of fistulosin or copies of the original spectra of the isolated metabolite named "fistulosin," a direct comparison is impossible. However, our results are consistent with Söderberg's conclusion that the natural product is actually 2-(1-oxooctadecanyl)aminobenzoic acid, and not that originally proposed as shown by Nishida's synthesis of the purported structure.

Experimental Section

General. Melting points were determined using open capillary tubes with a Mel-Temp Laboratory Device apparatus. Thin-layer chromatography (TLC) was performed on Whatman® regular TLC plates. TLC monitoring of reactions performed in DMSO or DMF involved partitioning an aliquot between ether and water and analyzing the ether layer. Visualization of developed plates was achieved with a 254 nm UV lamp and/or with iodine. Flash chromatography refers to the procedure using 230–400 mesh Silycycle® silica gel 60. ^{13}C, ^{19}F and ^{1}H NMR spectra were recorded on a Varian XL-300 and XL-500 Fourier-transform NMR spectrometer. Chemical shifts are reported in parts per million (δ) using the solvent's residue signal ($CDCl_3$: δ_H 7.27, δ_C 77.23, DMSO-d_6: δ_H 2.51, δ_C 39.50) as an internal reference. The apparent multiplicity (s = singlet, d = doublet, t = triplet, q = quartet, m = multiplet, br = broad), number of protons, and coupling constants (in Hz) are reported in that order in parenthesis after the chemical shift. Infrared spectra (IR) were recorded on a BioRad FT-IR Infrared Spectrophotometer. IR spectra were obtained using either neat compounds (neat) or solid KBr pellets (KBr). Ultraviolet spectra (UV) were recorded with a HP 5890 Diode-Array Spectrophotometer and are reported in nanometers. Low- and high-resolution mass spectra (MS and HRMS) were carried out at the Mass Spectrometry Laboratory, School of Chemical Sciences, University of Illinois at Urbana Champaign. Elemental analyses were done by Atlantic Microlab Inc. (Norcross, GA). Tetrahydrofuran (THF) and diethyl ether were distilled from sodium-benzophenone mixture. Dichloromethane, diisopropylamine, xylene, and triethylamine were distilled from calcium hydride. Acid chlorides and carboxylic anhydrides were purchased from either Aldrich® or Acros®, their purity was confirmed by ^{1}H NMR otherwise a distillation from quinoline was done prior to use. All alkyllithium reagents were purchased from either Aldrich® or Acros® and old alkyllithiums were titrated with diphenylacetic acid in dilute THF prior to use. Anhydrous DMF and 1,4-dioxane were purchased from Acros® and used without further purification. Unless otherwise indicated, all other reagents and solvents were purchased from commercial sources and were used without further purification. Water (or "H_2O") refers to reverse osmosis deionized (RODI) water. Brine refers to a saturated aqueous solution of sodium chloride. Reaction temperatures ranging between –78 °C and –40 °C were achieved using a dry

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ice/acetone bath. Reaction temperatures ranging between –10 °C and 0 °C were achieved using ice/NaCl bath. All reported temperatures were measured by an internal thermometer. Nitrogen gas was dried by passing through calcium sulfate. All reactions were performed under a positive nitrogen atmosphere with magnetic stirring unless otherwise noted. Reaction flasks were oven-dried at >130 °C and allowed to cool in a desiccator before assembly under positive nitrogen.

1-(Phenylsulfonyl)indoxyl (4). To a mixture of 1-(phenylsulfonyl)indole[12] (**7**) (2.57 g, 10.0 mmol) and magnesium monoperphthalate (MMPP) (80%, 6.18 g, 10.0 mmol) was added HOAc (60 mL) and the mixture was heated to reflux for 2 h. The mixture was then dissolved in CH_2Cl_2 (200 mL) and was neutralized by saturated $NaHCO_3$ solution (500 mL). The aqueous layer was extracted with Et_2O (3 × 100 mL). The combined organic layer was washed with brine (200 mL) and dried over Na_2SO_4. Removal of solvent gave a brown oil which was purified by flash chromatography (20% EtOAc/hexanes) to give **4** as pinkish crystals (1.57 g, 58%): mp 121–123 °C (Lit.[12] mp 128–130 °C, dec.); ^{1}H NMR ($CDCl_3$) δ 8.06 (m, 1H), 7.85 (m, 2H), 7.58–7.72 (m, 3H), 7.45–7.54 (m, 2H), 7.20 (m, 1H), 4.16 (s, 2H).

2-Octadecyl-1-(phenylsulfonyl)indole (8). To a –78 °C stirred solution of 1-(phenylsulfonyl)indole (**7**) (4.00 g, 15.5 mmol) in dry THF (80 mL) under nitrogen was added a solution of *sec*-BuLi (19 mmol, 14.6 mL, 1.3 M in cyclohexane) dropwise via syringe and the solution was allowed to warm to rt over 0.5 h and stirred for 2 h. The mixture was cooled to –70 °C and a solution of *n*-$C_{18}H_{37}Br$ (6.30 g, 18.7 mmol) in dry THF (30 mL) was added via syringe. The mixture was stirred at –70 °C for 2 h and was allowed to warm to rt for 16 h. The mixture was quenched by saturated aqueous NH_4Cl solution (100 mL) and extracted with Et_2O (3 × 100 mL). The combined organic layer was washed with brine (100 mL) and dried over Na_2SO_4. Removal of solvents gave a brown oil which was purified by flash chromatography (10% EtOAc in hexanes) to give **8** as a yellow solid contaminated with $C_{18}H_{37}Br$. Refluxing this mixed solid with $AgNO_3$ in EtOH followed by purification by flash chromatography gave **8** as a colorless solid (4.38 g, 55%): mp 74–75 °C; ^{1}H NMR ($CDCl_3$) δ 8.21 (m, 1H), 7.76 (m, 2H), 7.55 (m, 1H), 7.40–7.48 (m, 3H), 7.21–7.32 (m, 2H), 6.43 (d, 1H, *J* = 1.2 Hz), 3.01 (t, 2H, *J* = 7.9 Hz), 1.70–1.82 (m, 2H), 1.20–1.45 (m, 30H), 0.92 (t, 3H, *J* = 6.6 Hz); ^{13}C NMR ($CDCl_3$) δ 142.8, 139.5, 133.8, 130.1, 129.4, 126.5, 124.1, 123.8, 120.3, 115.1, 109.0, 32.2, 30.0, 29.9, 29.8, 29.7, 29.6, 29.3, 29.1, 23.0, 14.4; IR (KBr) 2921, 2846, 1467, 1448, 1368, 1171, 1140, 1090, 754, 729, 685, 587, 570 cm^{-1}; UV (EtOH) λ_{max} 214, 254 nm; MS *m/z* 509 (M^+), 446, 368, 304, 271, 207, 130 (100%), 78; *Anal.* Calcd for $C_{32}H_{47}NSO_2$: C, 75.39; H, 9.29; N, 2.74; S, 6.29. Found: C, 75.71; H, 9.26; N, 2.84; S, 6.15.

2-Hydroxy-2-octadecyl-1-(phenylsulfonyl)indoxyl (9) and 2-Octadecyl-1-(phenylsulfonyl)indoxyl (10). To a solution of 2-octadecyl-1-(phenylsulfonyl)indole (**8**) (490 mg, 0.96 mmol) and MMPP (80%, 620 mg, 1.0 mmol) was added HOAc (10 mL) and the mixture was heated to reflux for 2 h. The mixture was dissolved in CH_2Cl_2 (40 mL) and neutralized with saturated aqueous $NaHCO_3$ solution (50 mL). The mixture was extracted with Et_2O (2 × 40 mL) and the combined organic layer was washed with brine (50 mL) and dried over Na_2SO_4. Removal of solvent gave a brown oil which was purified by flash chromatography (10% EtOAc in hexanes) to give two components: **9** as a yellow solid (190 mg, 37%) and **10** as a yellow solid (110 mg, 22%). Compound **9**: mp 78–80 °C (EtOAc/hexanes); ^{1}H NMR ($CDCl_3$) δ 8.08 (m, 2H), 7.73 (m, 1H), 7.56–7.64 (m, 3H), 7.47–7.55 (m, 2H), 7.11–7.18 (m, 1H), 4.05 (br, 1H), 2.45–2.58 (m, 1H), 2.25–2.42 (m, 1H), 1.15–1.40 (m, 32H), 0.92 (t, 3H, *J* = 7.2 Hz); ^{13}C NMR ($CDCl_3$) δ 196.2, 151.4, 139.3, 138.3, 133.8, 129.4, 128.0, 125.4, 123.9, 121.6, 114.3, 94.2, 39.6, 32.1, 29.9, 29.8, 29.7, 29.6, 29.5, 29.4, 23.6, 22.9, 14.3; IR (KBr) 3455, 2921, 2848, 1736 (C=O), 1602, 1460, 1342, 1148, 1117, 990, 950, 759, 724, 687, 594, 556 cm^{-1}; UV(EtOH) λ_{max} 220, 226, 342 nm; MS *m/z* 542 (M^+), 525, 400 (100%), 260, 195, 146, 120; *Anal.* Calcd for $C_{32}H_{47}NO_4S$: C, 70.94; H, 8.74; N, 2.59; S, 5.92. Found: C, 71.04; H, 8.77; N, 2.55; S, 5.86. Compound **10**: mp 64–66 °C (EtOAc/hexanes); ^{1}H NMR ($CDCl_3$) δ 8.09 (m, 1H),

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7.53–7.78 (m, 5H), 7.40–7.47 (m, 2H), 7.21 (m, 1H), 4.00 (dd, 1H, J_1 = 6.0 Hz, J_2 = 3.6 Hz), 2.06–2.32 (m, 2H), 1.12–1.35 (m, 32H), 0.89 (t, 3H, J = 6.6 Hz); ^{13}C NMR ($CDCl_3$) δ 199.0, 153.7, 146.9, 137.4, 136.8, 134.1, 129.6, 127.4, 125.5, 124.9, 124.6, 117.3, 113.0, 67.7, 32.3, 32.2, 30.0, 29.9, 29.8, 29.7, 29.6, 23.3, 23.0, 14.4; IR (KBr) 2920, 2849, 1735 (C=O), 1604, 1463, 1356, 1169, 952, 757, 599 cm^{-1}; UV (EtOH) λ_{max} 218, 324 nm; MS *m/z* 525 (M^+), 446, 384 (100%), 312, 273, 199, 146, 74; *Anal.* Calcd for $C_{32}H_{47}NO_3S$: C, 73.10; H, 9.01; N, 2.66; S, 6.10. Found: C, 73.41; H, 9.15; N, 2.73; S, 5.87.

Methyl 2-(1-oxononadecyl)aminobenzoate (11). A stirred suspension of 2-octadecyl-1-(phenylsulfonyl)indoxyl (**10**) (51 mg, 0.10 mmol) and Na_2CO_3 (0.10 g, 0.94 mmol) in MeOH (4 mL) and THF (2 mL as cosolvent) was heated to reflux under nitrogen for 2 h. The solvent was removed and mixture was diluted with H_2O (10 mL) and extracted with EtOAc (3 × 20 mL). The combined organic layer was washed with brine (50 mL) and dried over Na_2SO_4. Removal of solvent gave an orange oil which was purified by flash chromatography (10% EtOAc in hexanes) to give **11** as a colorless solid (21 mg, 49%): mp 42–44 °C; ^{1}H NMR ($CDCl_3$) δ 11.07 (br, 1H), 8.75 (dd, 1H, J_1 = 8.7 Hz, J_2 = 0.9 Hz), 8.03 (dd, 1H, J_1 = 8.1 Hz, J_2 = 1.5 Hz), 7.55 (m, 1H), 7.08 (m, 1H), 3.94 (s, 3H), 2.44 (t, 2H, J = 7.5 Hz), 1.70–1.80 (m, 2H), 1.20–1.50 (m, 32H), 0.91 (t, 3H, J = 6.6 Hz); ^{13}C NMR ($CDCl_3$) δ 172.6, 169.1, 142.0, 135.0, 131.1, 122.5, 120.6, 110.0, 52.6, 39.0, 32.2, 30.0, 29.9, 29.8, 29.7, 29.6, 29.5, 25.8, 25.1, 23.0, 14.4; IR (KBr) 2917, 2850, 1695 (C=O), 1593, 1533, 1452, 1265, 1167, 1088, 795, 754 cm^{-1}; UV (EtOH) λ_{max} 224, 254, 302 nm; MS *m/z* 431 (M^+), 193, 151 (100%), 119, 83; HRMS *m/z* Calcd for $C_{27}H_{45}NO_3$ (M^+): 431.3399. Found: 431.3403. These spectral data agree with those reported by Söderberg.[3]

Ethyl 2-(1-oxononadecyl)aminobenzoate (12). To a rt stirred solution of 2-octadecyl-1-(phenylsulfonyl)indoxyl (**10**) (102 mg, 0.20 mmol) in EtOH (4 mL) and THF (2 mL as cosolvent) under nitrogen was added dibasic Na_2PO_4 (74 mg, 0.52 mmol) and 6% Na(Hg) (400 mg, 1.0 mmol) and the mixture was stirred at rt for 2 h. The solvent was removed and mixture was diluted with H_2O (10 mL) and extracted with EtOAc (3 × 20 mL). The combined organic layer was washed with brine (50 mL) and dried over Na_2SO_4. Removal of Hg and solvent gave an orange oil which was purified by flash chromatography (10% EtOAc in hexanes) to give **12** as a colorless solid (61 mg, 69%): mp 45–47 °C; ^{1}H NMR ($CDCl_3$) δ 11.11 (br, 1H), 8.75 (dd, 1H, J_1 = 8.4 Hz, J_2 = 0.9 Hz), 8.05 (dd, 1H, J_1 = 8.1 Hz, J_2 = 1.5 Hz), 7.54 (m, 1H), 7.07 (m, 1H), 4.40 (q, 2H, J = 7.2 Hz), 2.44 (t, 2H, J = 7.5 Hz), 1.68–1.72 (m, 2H), 1.20–1.50 (m, 33H), 0.91 (t, 3H, J = 6.9 Hz); ^{13}C NMR ($CDCl_3$) δ 172.6, 168.6, 142.0, 134.8, 131.0, 122.5, 120.6, 115.3, 61.6, 39.0, 32.2, 29.9, 29.8, 29.7, 29.6, 29.5, 25.8, 23.0, 17.6, 14.5, 14.4; IR (KBr) 2915, 2849, 1692 (C=O), 1592, 1534, 1471, 1256, 1165, 1087, 752 cm^{-1}; UV (EtOH) λ_{max} 198, 226, 254, 310 nm; MS *m/z* 445 (M^+) 400, 356, 326, 281, 230, 207, 165 (100%), 146, 119, 101, 69; *Anal.* Calcd for $C_{28}H_{47}NO_3$: C, 75.46; H, 10.63; N, 3.14. Found: C, 75.46; H, 10.77; N, 3.13.

From Acylation of 13. To a rt stirred suspension of nonadecanoic acid (1.00 g, 3.36 mmol) in CH_2Cl_2 was added $(COCl)_2$ (2.1 mL, 24.0 mmol) and the reaction mixture was stirred at rt for 4 h. Solvent and excess ($COCl_2$) was removed in vacuo and further vacuum pump dried for 20 min. The residue was dissolved in CH_2Cl_2 and a solution of pyridine (0.49 mL, 6.0 mmol) and ethyl *o*-aminobenzoate (**13**) (0.50 mL, 3.36 mmol) in CH_2Cl_2 (5 mL) was added dropwise and stirred for 16 h. The organic layer was washed with saturated aqueous NH_4Cl (50 mL) and brine (50 mL) and dried over Na_2SO_4. Removal of solvent gave a brown solid which was recrystallized from methanol to give **12** as a colorless solid (1.32 g, 88%) which is identical (mp, TLC, ^{1}H NMR) to samples prepared from fragmentation of **10**.

3-(2'-Hydroxyethoxy)-1-(phenylsulfonyl)indole (19). To a solution of 1-(phenylsulfonyl)indoxyl (**4**) (300 mg, 1.09 mmol) and *p*-TsOH (6 mg, 0.03 mmol) in benzene was added $(CH_2OH)_2$ (400 mg, 6.44 mmol) and the mixture was refluxed for 12 h with a Dean-Stark trap. Removal of solvent gave a brown oil which was purified by flash chromatography (40% EtOAc in hexanes) to give **19** as a light yellow oil (257 mg, 74%): ^{1}H NMR ($CDCl_3$) δ 8.04 (m, 1H), 7.84 (m, 2H), 7.55 (m, 1H), 7.48 (m, 1H), 7.32–7.42 (m, 3H), 7.22 (m, 1H), 6.98 (s, 1H), 4.13 (m,

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2H), 4.00 (m, 2H), 2.48 (br, 1H); ^{13}C NMR ($CDCl_3$) δ 145.8, 137.7, 134.3, 133.9, 129.4, 126.9, 126.2, 124.8, 123.6, 118.9, 114.4, 104.8, 72.2, 61.4; UV (EtOH) λ_{max} 220, 230, 238, 308 nm; MS *m/z* 317 (M^+), 273, 260, 195, 148, 132 (100%), 119, 77; HRMS *m/z* Calcd for $C_{16}H_{15}NO_4S$ (M^+): 317.0723. Found: 317.0722.

3-Benzyloxy-1-(phenylsulfonyl)indole (20). To a solution of 1-(phenylsulfonyl)indoxyl (**4**) (274 mg, 1.00 mmol) and *p*-TsOH (6 mg, 0.03 mmol) in benzene was added $PhCH_2OH$ (0.21 mg, 2.0 mmol) and the mixture was refluxed for 10 h with a Dean-Stark trap. Removal of solvent gave a brown oil which was purified by flash chromatography (15% EtOAc in hexanes) to give **20** as a colorless oil (185 mg, 51%) which slowly solidified upon storage under vacuum for 24 h: mp 87–90 °C; ^{1}H NMR ($CDCl_3$) δ 8.04 (m, 1H), 7.73 (m, 2H), 7.60 (m, 1H), 7.21–7.51 (m, 10H), 6.96 (s, 1H), 5.13 (s, 2H); ^{13}C NMR ($CDCl_3$) δ 145.6, 137.7, 136.4, 134.4, 133.8, 129.3, 128.9, 128.5, 127.8, 126.9, 126.1, 125.2, 123.6, 119.0, 114.5, 105.4, 72.7; IR (KBr) 1602, 1572, 1449, 1359, 1274, 1211, 1175, 1122, 1102, 1002, 964, 745, 723, 686, 648 cm^{-1}; UV (EtOH) λ_{max} 220, 230, 238, 260 nm; MS *m/z* 363 (M^+, 100%), 272, 223; HRMS *m/z* Calcd for $C_{21}H_{17}NO_3S$ (M^+): 363.0929. Found: 363.0926.

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