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# Attempted synthesis of 3-hydroxy-2-octadecylindole. Proposed structural revision of previously prepared 3-hydroxy-2-octadecylindole and a proposed structure of fistulosin

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ABSTRACT

A synthetic route to 3-hydroxy-2-octadecylindole, the putative structure of the novel indole alkaloid fistulosin, starting from 2-nitro-1-iodobenzene was examined. Key steps include formation of a 1-stannyl-substituted 1-methoxy-1-alkene from a Fischer chromium carbene, intermolecular Kosugi–Migita–Stille coupling, and a palladium-catalyzed reductive N-heteroannulation. Demethylation of 3-methoxy-2-octadecylindole, a possible immediate precursor to 3-hydroxy-2-octadecylindole, was unsuccessful and gave instead methyl 2-(1-oxononadecanyl)aminobenzoate. The structure of the isolated alkaloid was suggested to be 2-(1-oxooctadecanyl)aminobenzoate by comparison of analytical data with a synthetic sample. In addition, oxidation of 2-octadecylindole gave a 2,2′-dimer, a compound identical to previously prepared 3-hydroxy-2-octadecylindole.



## 1. Introduction

A novel alkaloid named fistulosin has been isolated both from the leek root (*Allium porrum*)[1] and from the roots of the Welsh onion (*Allium fistulosum*)[2] by Tomita et al. For example, 51 mg of fistulosin was obtained from 50 kg of roots of the Welsh onion. The structure of fistulosin was proposed to be 3-hydroxy-2-octadecylindole (**1**) based on EI-HRMS, IR, DEPT, $^{1}$H–$^{1}$H COSY, $^{1}$H–$^{13}$C COSY, and selective INEPT experiments. Fistulosin was represented in the keto form in this paper (Fig. 1). 3-Hydroxyindoles are to date almost unknown in nature and to our knowledge fistulosin represents the only example of a fully characterized 2-alkyl-3-hydroxyindole isolated to date.[3] The unique nature of this compound and its reported antifungal activity against a variety of fungi including *Fusarium oxysporum*, *Fusarium solani*, and *Penicillium roqueforti* peaked our interest.

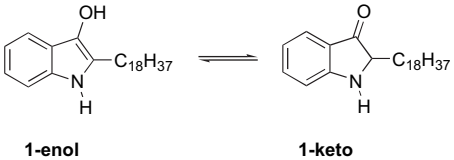


**Figure 1.**

A more careful examination of the $^{1}$H and $^{13}$C NMR data given revealed some discrepancies including an incorrect number of hydrogens, the absence of one quarternary carbon if the compound exists in the enol form, or alternatively the absence of the C2-methine-proton if it is in the keto form. In addition, the experimental exact mass (HRMS) was reported as *m*/*z* 385.6337 for $M^{+}$ and the calculated *m*/*z* (for $C_{26}H_{43}NO$) was reported as *m*/*z* 385.6387. The calculated value appears to be in error since the exact mass for this molecular formula is 385.3345. Considering the large difference between the experimentally determined mass and the calculated value (760 ppm), it seemed unlikely that this is the correct molecular formula.

After we initiated our study, a synthesis of 3-hydroxy-2-octadecylindole was reported by Nishida et al.[4] The final step in their synthesis was an acid-mediated deprotection of the corresponding *N*-tosylated compound **2**. In the event, compound **2** was treated with a large excess of concentrated sulfuric acid at 0 °C for 1.5 h to give **1-keto** (Scheme 1). According to the authors **1-keto** was readily tautomerized to **1-enol** by treatment with, again, a large excess of sulfuric acid at 0 °C for 1.5 h. Based on the significant difference in spectral data for the synthetic compounds (**1-enol**/**keto**) compared to the isolated material, the authors concluded that the structure of fistulosin was not 3-hydroxy-2-octadecylindole. The stability of the

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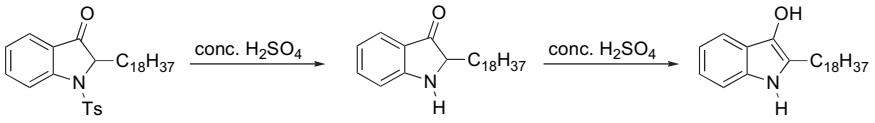
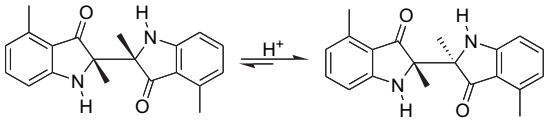



**2** **1-keto** **1-enol**

**Scheme 1.**

synthesized **1-enol** is surprising since a previous study of the parent 3-hydroxylindole indicated a very rapid enol→keto tautomerization in $CDCl_3$.[5] In fact, the enol form was not observed in this solvent but it is observed in DMSO-$d_6$. 3-Hydroxyindole is also highly unstable and rapidly undergoes oxidative dimerization to form indigo.[6]

A small group of 2,2′-dimeric indoles consisting of peronatins A–B (Fig. 2), 7-hydroxy-7′-methoxyperonatin B, and 7,7′-dimethoxyperonatin B has been isolated from damaged fruit bodies of *Collybia peronata* and *Tricholoma scalpturatum*.[7] All four peronatins exhibit very small $M^+$ ions (2–4%) in the mass spectra but have much more pronounced $M/2+1^+$ (100%, EIMS) or $M/2+2^+$ ions (CIMS). The structure of peronatins A–B was confirmed by synthesis via oxidative dimerization of 2,4-dimethylindole (**3**) affording peronatin A under basic conditions and peronatin B under acidic conditions (Scheme 2).[8] Peronatin A can be isomerized to peronatin B under acidic conditions. Although not observed, the authors postulated the formation of 2,4-dimethyl-3-hydroxyindole (**4**) as an intermediate. The sensitivity of 2-alkyl-3-hydroxyindoles was also observed upon base-mediated deacetylation of *N*,*O*-diacetyl 3-hydroxy-2-methylindole (**5**), also producing a 2,2′-dimer (Scheme 2).[9]




**Peronatin A** **Peronatin B**

**Figure 2.**

Considering the NMR similarities between **1-keto/1-enol** and the peronatins, the ease of dimerization of 3-hydroxyindole to indigo, and the formation of the dimeric peronantins from indoles under oxidative conditions, perhaps one or both of the compounds obtained from N-detosylation of **2** are the corresponding 2,2′-dimers (Fig. 3). The HRMS data and fragmentation patterns of **1-keto/1-enol** also support this proposal. The reported molecular ions ($M^+$) for **1-enol** (*m*/*z* 385, 100%) and for **1-keto** (*m*/*z* 385, 18%) may actually be the $(M/2)+1^+$ peak seen from the symmetrical cleavage of the corresponding dimer. A caveat is the possibility that the presence of a long aliphatic chain presents sufficient obstruction for dimerization to occur, however a related oxidative dimerization of 2-*tert*-butylindole has been reported.[10]

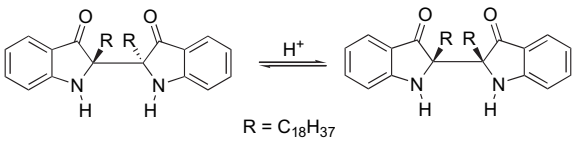
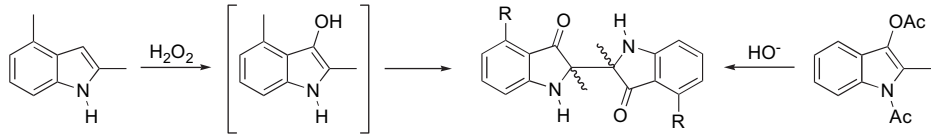



**Figure 3.**

Our studies into the synthesis of 3-hydroxy-2-octadecylindole and related compounds are described herein. A revised structure of the naturally occurring material named fistulosin is also proposed.




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

**Scheme 2.**

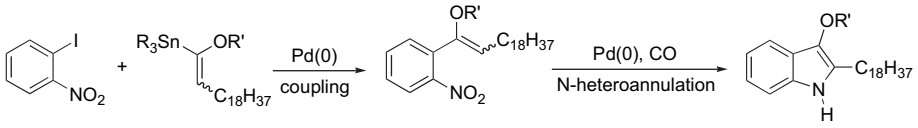
The IR, $^1H$, and $^{13}C$ NMR data reported by Nishida et al.[4] for the synthetic **1-keto** and **1-enol** are remarkably similar. The IR-absorptions for the C=O and C=C–OH are assigned at 1675 $cm^{-1}$ and 1674 $cm^{-1}$, respectively. In the $^1H$ NMR spectrum, the only major differences are the broad singlets reported at $\delta$ 4.70 ppm (**1-keto**) and 6.08 ppm (**1-enol**) integrating to one proton and a significant chemical shift difference between the first methylene of the side-chains. In addition, the carbon resonances for the C-3 indole carbons were assigned for **1-keto** to $\delta$ 202.6 ppm and for **1-enol** to $\delta$ 204.6 ppm. The latter C-3 resonance is significantly shifted downfield compared to the related compounds 3-ethoxyindole (140.8 ppm) and 6-bromo-3-acyloxyindole (130.2 ppm).

The chemical shifts and general trends for synthetic **1-keto/1-enol** are similar to what is observed for the peronatins. The N–H resonances for peronatin A and B were found at $\delta$ 4.38 ppm and $\delta$ 6.12 ppm in the $^1H$ NMR spectra. A significant shift difference was also seen for the methyl groups in the 2-position of peronatin A and B observed at $\delta$ 1.66 ppm and $\delta$ 1.14 ppm, respectively. Finally, the carbonyl resonances for all four peronatins were observed at $\delta$ 204.3–204.9 ppm.

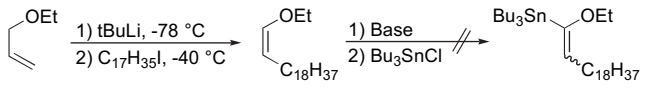
## 2. Results and discussion

We have recently developed a novel route to 3-alkoxysubstituted indoles via a palladium-catalyzed reductive N-heteroannulation of 1-alkoxy-1-(2-nitrophenyl)-1-alkenes.[11] This methodology was successfully applied to the first synthesis of the unusual alkaloid koniamborine.[12] A short synthesis of a potential precursor to 3-hydroxy-2-octadecylindole employing this annulation methodology and a Kosugi–Migita–Stille coupling as the key steps was envisioned (Scheme 3). Cleavage of the O–R′ bond using the appropriate Lewis acid would then afford 3-hydroxy-2-octadecylindole (fistulosin).

The required tin reagent was initially thought to be derived from deprotonation of *Z*-1-ethoxy-1-eicosene (**6**). This compound was readily prepared by lithiation of ethyl allyl ether with *tert*-butyl lithium followed by alkylation with 1-iodoheptadecane (Scheme 4).[13] Unfortunately, we were unable to transform **6** to **7** by α-lithiation and reaction with tributyltin chloride under a variety of reaction conditions.[14]



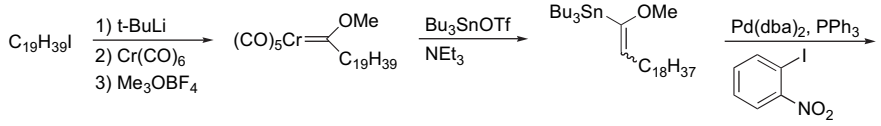

**Scheme 3.**



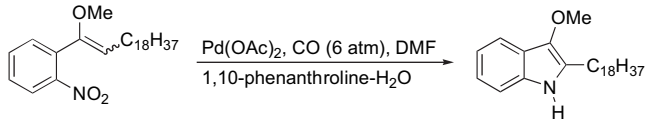

**6** (88%) **7**

**Scheme 4.**

An alternative to α-deprotonation for the formation of 1-alkoxy-1-stannylalkenes is the reaction of alkoxysubstituted Fischer carbene complexes with a trialkyltin triflate developed by McDonald et al.[15] The Fischer carbene complex **8** was prepared in a standard fashion via metal–halogen exchange of 1-iodononadecane using *t*-BuLi followed by reaction with chromium hexacarbonyl and trimethyloxonium tetrafluoroborate (Scheme 5). Carbene **8** was sensitive to air and noticeably decomposed upon standing in air for a few minutes. This complex was treated, immediately after isolation, with tributyltin triflate in the presence of triethylamine to give **9** in 82% yield as a ~3:1 *E*/*Z* mixture. Kosugi–Migita–Stille coupling of **9** with 2-nitro-1-iodobenzene gave the expected product **10** in excellent yield. With the indole precursor **10** in hand, it was subjected to the annulation conditions previously used to prepare a number of 3-alkoxyindoles. Surprisingly, reaction of **10** with carbon monoxide in the presence of a catalytic amount of bis(dibenzylideneacetone)palladium, bis(1,3-diphenylphosphino)-propane, and 1,10-phenanthroline monohydrate did not effect cyclization. However, changing to the simpler catalyst system consisting of palladium diacetate-1,10-phenanthroline monohydrate smoothly gave indole **11** in 95% yield.



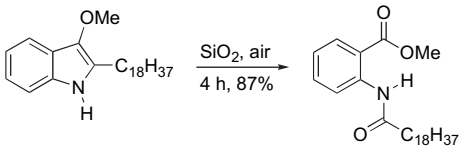

**8** (52%) **9** (81%)




**10** (86%) **11** (95%)

**Scheme 5.**

Demethylation of related 3-methoxyindole-2-carboxylic acid esters to 3-hydroxyindole-2-carboxylic acid esters has been reported using $BBr_3$–$CH_2Cl_2$.[16] However, attempted cleavage of the methyl ether in **11** to afford 3-hydroxy-2-octadecylindole (**1-enol**) under the same reaction conditions did not produce any identifiable product. The same result was obtained using a variety of other commonly used demethylation reagents including HBr, $AlCl_3$, and TMSI. Upon treatment of **11** with silica gel we were surprised to isolate methyl 2-(1-oxononadecyl)aminobenzoate (**12**) in 88% yield (Scheme 6). Similar oxidations of indoles have been reported, for example, auto-oxidation of 2,3-cyclopentenindole affording L-aza-7,8-benzocyclooctene-2,6-dione.[17,18] Tryptophan is also metabolized in the liver in a similar fashion to give *N*-formyl kynurenine and kynurenine.




**11** **12**

**Scheme 6.**

It is interesting to note that a number of long-chained 2-(1-oxoalkyl)aminobenzoic acids related to **12** have been isolated from a variety of plant sources. For example, 2-(1-oxoeicosyl)aminobenzoic acid and 2-(3-hydroxy-1-oxoeicosyl)aminobenzoic acid were isolated from the aerial parts of *Ononis natrix*,[19,20] 2-(1-oxo-13-docosenyl)aminobenzoic acid from *Ononis viscosa* subsp. *breviflora*[21] and from *Ononis natrix*,[22] ethyl 2-(1-oxodocosyl)aminobenzoate from the roots of *Gentiana tibetica*,[23] 2-(1-oxodocosyl)aminobenzoic acid from areal parts of *Inula oculus-christi*,[24] and 2-(1-oxo-C20 to C24)aminobenzoic acids from *Inula japonica*.[25]

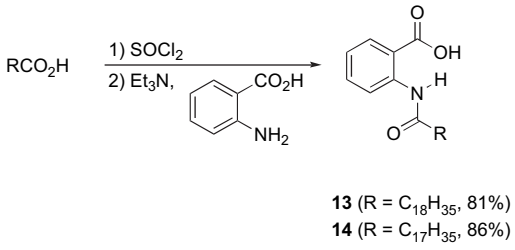
The analytical data from isolated fistulosin and **12** are compared in Table 1. Note again, that the reported data for the isolated material has one proton too many. Apart from the methoxy-resonance, compound **12** exhibits very similar proton and carbon chemical shifts and multiplicities compared to the isolated compound. Based on this, we postulated that the natural product may be structurally closely related to **12**.

Using **12** as a possible starting point to determine the true structure of isolated fistulosin, the corresponding acid, 2-(1-oxononadecyl)aminobenzoic acid (**13**), was prepared (Scheme 7). In the event, nonadecanoyl chloride was prepared from nonadecanoic acid and thionyl chloride. The acid chloride was treated with 2-aminobenzoic acid in the presence of triethylamine to give **13**. Analytical data for this compound are seen in Table 1. The acid proton ($CO_2H$) in **13** was not observed in deuterated chloroform. The NMR data for the compound isolated from the Welsh onion and the leek root and the synthetic compound **13** were compared. Two

**Table 1**
Analytical data for isolated fistulosin, **12**, **13**, and **14**

| | Fistulosin | **12** | **13** | **14** |
|---|---|---|---|---|
| Mp | 80–83 °C | — | 94–95 °C | 81–82 °C |
| IR | 1684 | 1709, 1694 | 1673 | 1673 |
| 1H | 10.8 (br s) | 11.1 (br s) | 11.0 (br s) | 10.9 (br s) |
| 1H | 8.8 (d) | 8.74 (d) | 8.77 (d) | 8.77 (d) |
| 1H | 8.1 (d) | 8.02 (d) | 8.13 (dd) | 8.13 (dd) |
| 1H | 7.6 (t-like) | 7.54 (t) | 7.60 (dt) | 7.60 (dt) |
| 1H | 7.1 (t-like) | 7.07 (t) | 7.11 (dt) | 7.11 (dt) |
| 3H | | 3.93 (s) | | |
| 2H | 2.44 (t-like) | 2.44 (t) | 2.47 (t) | 2.47 (t) |
| 2H | 1.74 (m) | 1.75 (m) | 1.77 (pent) | 1.77 (m) |
| 2H | 1.63 (m) | | | |
| 2H | 1.4 (m) | | 1.40 (pent) | 1.40 (m) |
| | 1.25 (br s, 28H) | 1.37–1.15 (m, 30H) | 1.34–1.24 (m, 28H) | 1.34–1.24 (m, 26H) |
| 3H | 0.88 (t-like) | 0.88 (t) | 0.88 (t) | 0.88 (t) |
| $^{13}$C | | 172.3 | 172.7 | 172.7 |
| | 171.5 | 168.7 | 172.1 | 172.2 |
| | 142.5 | 141.7 | 142.1 | 142.2 |
| | 135.8 | 134.7 | 135.6 | 135.7 |
| | 131.9 | 130.8 | 131.7 | 131.8 |
| | 122.7 | 122.2 | 122.2 | 122.6 |
| | 120.7 | 120.3 | 120.6 | 120.6 |
| | 113.7 | 114.7 | 113.9 | 113.8 |
| | | 52.3 | | |
| | 38.9 | 38.7 | 38.7 | 38.7 |
| | 32.1 | 31.9 | 31.9 | 31.9 |
| | 29.0–29.9 | 29.2–29.7 | 29.2–29.9 | 29.2–29.7 |
| | 25.9 | 25.5 | 25.5 | 25.5 |
| | 23.4 | 22.7 | 22.7 | 22.7 |
| | 14.3 | 14.1 | 14.1 | 14.1 |

All NMR data were obtained in $CDCl_3$ at 500/125 MHz for fistulosin and at 600/150 MHz for **12**, **13**, and **14**.



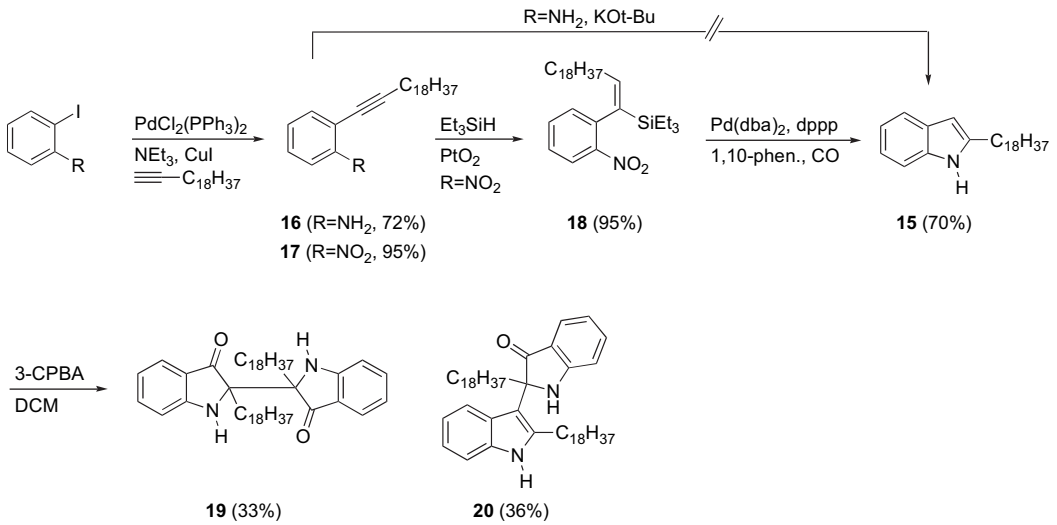

**13** (R = $C_{18}H_{35}$, 81%)
**14** (R = $C_{17}H_{35}$, 86%)

**Scheme 7.**

main differences were observed, a quaternary carbon signal at $\delta$ 172.7 ppm in the $^{13}$C NMR spectrum for **13** absent in the isolated material and a two proton multiplet ($\delta$ 1.64 ppm) in the $^{1}$H NMR spectrum of the naturally occurring compound missing in the spectrum of **13**. We suggest that the signal at $\delta$ 1.64 ppm in the $^{1}$H NMR spectrum is either water or some other impurity in the sample. It is also possible that the authors did not observe the carbonyl carbon at $\delta$ 172.7 ppm due to its low intensity. In any case, the similarity between the remainder of the NMR data is too profound not to suggest at least a close structural relationship. However, the two compounds were not identical since the melting points of the synthetic **13** (94–95 °C) and fistulosin (80–83 °C) were clearly different.

Tomita et al. based their proposed molecular formula of $C_{26}H_{43}NO$ on a *m*/*z* of 385 obtained in FD-MS. Possibly based on this low-resolution data, a smaller area around this mass was examined for HRMS and the $M^+$ was reported to be *m*/*z* 385.6337. As was previously pointed out, the calculated *m*/*z* for $C_{26}H_{43}NO$ is 385.3345 and this value is significantly different from the one determined experimentally.

Long-chain 2-(1-oxoalkyl)aminobenzoic acids have been shown to readily lose water when subjected to MS analysis. For example, in the mass spectrum of 2-(1-oxodocosyl)aminobenzoic acid[24] the molecular ion ($C_{29}H_{49}NO_3$) found at *m*/*z* 459.371 had a 1% relative intensity but the fragment at *m*/*z* 441.359 ($-H_2O$) had a relative intensity of 12%. The same trend was observed for 2-(1-oxoeicosyl)aminobenzoic acid[19] with a molecular ion *m*/*z* 431 (2%) and the peak from the loss of $H_2O$ at *m*/*z* 413 (7%). Based on these observations, perhaps the *m*/*z* 385 reported by Tomita et al. was the result of loss of water from a compound with the molecular weight of 403. Interestingly but perhaps a serendipity, 2-(1-oxooctadecanyl)aminobenzoic acid (**14**) has a molecular weight of 403. In order to compare analytical data, 2-(1-oxooctadecanyl)-aminobenzoic acid (**14**) was prepared from octadecanoyl chloride and 2-aminobenzoic acid as described for **13** (Scheme 7).The NMR data for **14** are, not surprising, almost identical to **13** and very similar to the natural product. In addition, the melting point ranges were the same. Based on the close similarity between the data presented in Table 1, we propose that the compound named fistulosin is actually 2-(1-oxooctadecanyl)aminobenzoic acid (**14**). However, we have unfortunately not been able to obtain a sample of fistulosin or copies of the original spectra of the natural product for final comparison.




**16** (R=$NH_2$, 72%)
**17** (R=$NO_2$, 95%)

**18** (95%)

**15** (70%)

**19** (33%)

**20** (36%)

**Scheme 8.**

We next decided to examine if the structure of synthetic **1-enol** was in fact the dimer shown in Figure 3. It was expected that oxidative dimerization of 2-octadecylindole (**15**) would furnish the 2,2′-dimer. Direct preparation of 2-octadecylindole (**15**) from 2-methylindole using Katritsky's alkylation methodology[26] failed to give more than minor amounts of the expected product. Base-mediated cyclizations of 2-(1-alkyn-1-yl)benzenamines has been used in several cases to prepare 2-substituted indoles.[27] However, cyclization of **16** prepared via a Sonogashira coupling of 2-iodobenzeamine with 1-eicosyne did not give **15** upon reaction with *t*-BuOK (Scheme 8). Indole **15** was instead prepared in a three-step sequence. In the event, Sonogashira cross-coupling of 2-iodo-1-nitrobenzene with 1-eicosyne gave the expected product **17**. This compound was hydrosilylated using triethylsilane in the presence of platinum dioxide as the catalyst.[28] The hydrosilylated product **18** was then submitted to the N-heteroannulation conditions and we were pleased to notice that not only did the cyclization occur, the silyl group was also lost to give **15**. It should be noted that this type of substrate has not previously been examined as a substrate for the reductive N-heteroannulation. Oxidative dimerization of **15** with hydrogen peroxide, according to Van Vranken et al.,[8] under basic or acidic conditions gave complex reaction mixtures that proved to be problematic to purify. However, simply changing the oxidant to 3-CPBA afforded a readily separated mixture of the 2,2′-dimer **19** and the corresponding 2,3′-coupling product **20**.[10] Analytical data for the 2,2′-dimer **19** were in all respects (NMR, IR, mp) identical to the data for **1-enol** prepared by Tomita et al. As was expected from HRMS (APCI) analysis of **19**, a very small $M+H^+$ peak (relative intensity 1%) was observed. Two much more pronounced peaks were observed for $M/2+2H^+$ (relative intensity 45%) and $M/2^+$ (relative intensity 100%). This is in concert with the data reported for the peronatins.[7] We were only able to prepare one of the diastereomeric 2,2′-dimers thus, the question whether or not the structure of synthetic **1-keto** is correct or if it is the missing 2,2′-dimer remains unclear.

## 3. Conclusion

Evidence suggesting the true structure of fistulosin, isolated from the leek root and the Welsh onion, to be 2-(1-oxooctadecylamino)benzoic acid was presented. In addition, the structure of synthetic 3-hydroxy-2-octadecylindole was shown to be the corresponding 2,2′-dimer.

## 4. Experimental section

### 4.1. General procedures

The chemical shifts are expressed in $\delta$ values relative to $SiMe_4$ (0.0 ppm, $^1H$ and $^{13}C$) or $CDCl_3$ (77.0 ppm, $^{13}C$) internal standards. Results of APT (Attached Proton Test) $^{13}C$ NMR experiments are shown in parentheses, where relative to $CDCl_3$, (−) denotes $CH_3$ or CH and (+) denotes $CH_2$ or C.

Anhydrous benzene, *N*-methylpyrrolidinone, and *N*,*N*-dimethylformamide were used as received. Tetrahydrofuran (THF) and diethyl ether were distilled from sodium benzophenone ketyl prior to use. Hexanes, ethyl acetate, triethylamine, and dichloromethane were distilled from calcium hydride. Chemicals prepared according to literature procedures have been footnoted the first time used; all other reagents were obtained from commercial sources and used as received. All reactions were performed under a nitrogen atmosphere in oven-dried glassware unless otherwise stated. Solvents were removed from reaction mixtures and products on a rotary evaporator at water aspirator pressure. Chromatography was performed on silica gel (35–75 μm).

Melting points were determined on a MelTemp and are uncorrected. Elemental analyses were performed in the Department of Chemical Engineering, College of Engineering and Mineral Resources, West Virginia University.

*4.1.1. (Z)-1-Ethoxy-1-eicosene (**6**).* Allyl ethyl ether (620 μL, 5.46 mmol) was stirred in THF (20 mL) at −78 °C under a positive flow of nitrogen. *t*-BuLi (14.4 mL, 1.7 M in pentane, 24.4 mmol) was slowly added to the solution over 15 min. The resulting yellow solution was stirred for an additional 30 min at −78 °C before warming to −40 °C over 4 h. 1-Iodoheptadecane[29] (2.00 g, 5.46 mmol) in THF (40 mL) was quickly added via a cannula to the reaction mixture. The resulting pale yellow solution was allowed to stir for an additional 30 min at −40 °C before warming to ambient temperature over 3 h. Water (2 mL) was carefully added to quench the reaction before extracting with EtOAc (3×100 mL). The combined organic phases were washed with brine (3×20 mL), dried ($MgSO_4$), and filtered. The solvents were removed under reduced pressure to give a white oily reside that was purified by chromatography (hexanes) affording **6** (1.51 g, 4.65 mmol, 88%) as a colorless oil. $^1H$ NMR (270 MHz) $\delta$ 5.91 (dt, *J*=6.3, 1.4 Hz, 1H), 4.32 (q, *J*=7.3 Hz, 1H), 3.76 (q, *J*=7.1 Hz, 2H), 2.05 (m, 2H), 1.26 (br s, 32H), 0.88 (m, 6H); $^{13}C$ NMR (67.5 MHz) $\delta$ 144.4 (−), 107.2 (−), 67.4 (+), 32.0 (+), 29.9 (+), 29.7 (multiple carbons, +), 29.5 (+), 29.4 (+), 29.3 (+), 23.9 (+), 22.7 (+), 15.3 (−), 14.1 (−); IR 1665, 1111 $cm^{-1}$. Anal. Calcd for $C_{22}H_{44}O$: C, 81.41; H, 13.66. Found: C, 81.39; H, 13.42.

*4.1.2. 1-Iodononadecane[30].* A heterogeneous mixture of 1-nonadecanol (10.00 g, 35.15 mmol) and triphenyl phosphite (37.0 mL, 140.6 mmol) was stirred in hexanes (80 mL) at 0 °C for 20 min. Iodine (35.68 g, 140.6 mmol) was added in approximately three equal portions over 30 min. The resulting black slurry was stirred for an additional 1 h at 0 °C. The reaction mixture was returned to ambient temperature and stirred for 12 h. Water (300 mL) was carefully added before extracting with hexanes (3×200 mL). The combined organic phases were washed with a saturated solution of $NaHSO_3$ (aqueous, 3×100 mL), dried ($MgSO_4$), and filtered. Removal of the solvent afforded a brown oil that was immediately purified by chromatography (hexanes) to afford 1-iodononadecane as a white solid (11.53 g, 29.24 mmol, 83%). Physical data (mp) and spectral data ($^1H$ NMR) were in complete accordance with literature values.[31]

*4.1.3. [(Methoxy)(nonadecyl)carbene]pentacarbonylchromium (**5**).* 1-Iodononadecane (11.53 g, 29.24 mmol) was dissolved in $Et_2O$ (150 mL) under $N_2$ in a 500-mL flask. The flask was cooled to −20 °C whereupon the iodide precipitated. *t*-BuLi (37.8 mL, 1.7 M in pentane, 64.3 mmol) was quickly added via a cannula. The resulting cloudy yellow solution was stirred for an additional 30 min at −20 °C before slowly warming to room temperature over 1 h. The solution was stirred for an additional hour before rapid transfer via a cannula to a 500-mL flask containing $Cr(CO)_6$ (6.43 g, 29.2 mmol) in $Et_2O$ (50 mL). The resulting dark brown solution was stirred (18 h) where after the solvent was removed under reduced pressure. Water (80 mL) was added to the brown residue and $Me_3OBF_4$ was added in portions until the solution was acidic (pH=2). The resulting yellow slurry was extracted with hexanes (3×200 mL) and the combined organic phases were dried ($MgSO_4$) and filtered. Removal of the solvent afforded a yellow oily-solid that was immediately purified by chromatography (hexanes) to afford **5** as a bright yellow solid (7.57 g, 15.1 mmol, 52%).[32] $^1H$ NMR (270 MHz) $\delta$ 4.76 (s, 3H), 3.29 (t, *J*=7.7 Hz, 2H), 1.50 (m, 2H), 1.25 (br s, 32H), 0.88 (t, *J*=6.9 Hz, 3H); $^{13}C$ NMR (67.5 MHz) $\delta$ 363.7 (+), 223.1 (+), 216.4 (+), 67.6 (−), 63.2 (+), 32.0 (+), 29.7 (multiple carbons, +), 29.4 (+), 29.3 (+), 26.4 (+), 22.7 (+), 14.1 (−); IR 2062, 1925 $cm^{-1}$.

*4.1.4. Tributyl (1-methoxyicos-1-enyl)stannane (**6**).* Following purification, the carbene (5.31 g, 10.6 mmol) was immediately dissolved in a solution of $NEt_3$ (10 mL) in $Et_2O$ (30 mL). $Bu_3SnOTf$ (6.96 g,

15.9 mmol) was added and the resulting brown solution was stirred for 4 days under a nitrogen atmosphere. The solvent and excess $NEt_3$ were removed under reduced pressure and the brown oily residue was purified by chromatography (hexanes/$NEt_3$, 99:1) to afford **9** (5.17 g, 8.63 mmol, 81%) as a colorless oil. Spectral data from a 3:1 *E*/*Z* mixture: *E*-isomer: $^1$H NMR (270 MHz) $\delta$ 5.23 (t, $J$=7.5 Hz, 1H), 3.45 (s, 3H), 2.18 (m, 2H), 1.90 (m, 2H), 1.25–1.60 (m, 44H), 0.99–0.83 (m, 18H); $^{13}$C NMR $\delta$ 165.6 (+), 112.1 (−), 54.8 (−), 32.0 (+), 29.9 (multiple carbons, +), 29.7 (+), 29.4 (+), 29.1 (+), 27.7 (+), 22.7 (+), 14.1 (−), 13.7 (−), 10.3 (+); partial data for the *Z*-isomer: $^1$H NMR $\delta$ 4.54 (t, $J$=6.9 Hz, 1H), 3.53 (s, 3H); $^{13}$C NMR (67.5 MHz) $\delta$ 163.2 (+), 123.8 (−), 59.4 (−), 27.8 (+), 27.1 (+), 25.1 (+), 18.5 (+), 10.9 (+); IR 2921, 1463 cm$^{-1}$. Anal. Calcd for $C_{33}H_{68}OSn$: C, 66.10; H, 11.43. Found: C, 66.39; H, 11.79.

*4.1.5. 1-(1-Methoxyicos-1-enyl)-2-nitrobenzene (**10**).* A solution of 2-iodo-nitrobenzene (131 mg, 0.525 mmol), bis(dibenzylideneacetone)palladium (15 mg, 0.026 mmol), and triphenylphosphine (28 mg, 0.105 mmol) was stirred in toluene (20 mL) for 5 min under a positive flow of nitrogen. To the yellow solution was added stannane **9** (346 mg, 0.577 mmol) dissolved in toluene (5 mL). The yellow solution was heated at reflux (68 h) whereupon a dark brown solution was formed. The reaction was monitored using TLC (hexanes). The solvent was removed under reduced pressure and the resulting black viscous oil was purified by chromatography (hexanes/EtOAc, 95:5), affording **10** (195 mg, 0.451 mmol, 86%) as a faint yellow oil. Spectral data from a 4:1 *E*/*Z* mixture: *E*-isomer: $^1$H NMR (270 MHz) $\delta$ 7.91 (dd, $J$=8.1, 1.4 Hz, 1H), 7.58 (dt, $J$=7.3, 1.4 Hz, 1H), 7.49 (dd, $J$=7.9, 1.6 Hz, 1H), 7.42 (dt, $J$=7.5, 1.6 Hz, 1H), 4.82 (t, $J$=7.6 Hz, 1H), 3.62 (s, 3H), 1.90 (q, $J$=7.3, 2H), 1.40–1.15 (br m, 32H), 0.88 (t, $J$=6.9 Hz, 3H); $^{13}$C NMR (67.5 MHz) $\delta$ 151.5 (+), 148.9 (+), 132.3 (−), 131.9 (−), 131.6 (+), 129.0 (−), 124.2 (−), 101.9 (−), 55.9 (−), 31.9 (+), 29.7 (multiple carbons, +), 29.6 (+), 29.4 (+), 29.3 (+), 29.0 (+), 25.3 (+), 22.7 (+), 14.1 (−); partial data for the *Z*-isomer: $^1$H NMR (270 MHz) $\delta$ 7.70 (dd, $J$=8.1, 1.1 Hz, 1H), 4.97 (t, $J$=7.5 Hz, 1H), 3.43 (s, 3H); $^{13}$C NMR (67.5 MHz) $\delta$ 150.2 (+), 148.9 (+), 131.7 (−), 130.9 (−), 128.7 (−), 123.5 (−), 116.6 (−), 58.4 (−); IR 2916, 1533 cm$^{-1}$. Anal. Calcd for $C_{27}H_{45}NO_3$: C, 75.13; H, 10.51; N, 3.24. Found: C, 75.51; H, 10.71; N, 3.56.

*4.1.6. 3-Methoxy-2-octadecylindole (**11**).* Compound **10** (445 mg, 1.03 mmol), palladium diacetate (14 mg, 0.062 mmol), and 1,10-phenanthroline monohydrate (25.0 mg, 0.124 mmol) were dissolved in DMF (2 mL) in a threaded ACE glass pressure tube. The tube was fitted with a pressure head, and the solution was saturated with carbon monoxide (four cycles to 6 atm of CO). The reaction mixture was heated (120 °C, 6 atm CO, 82 h). A majority of the solvent was removed under vacuum and the brown residue was purified by chromatography (hexanes/EtOAc/$Et_3N$, 95:4:1) affording **11** (391 mg, 0.978 mmol, 95%) as an oily yellow solid. $^1$H NMR (270 MHz) $\delta$ 7.58 (d, $J$=6.9 Hz, 1H), 7.44 (br s, 1H), 7.24 (dd, $J$=6.9, 2.2 Hz, 1H), 7.11 (t, $J$=7.1, 1.4 HZ, 1H), 7.06 (dt, $J$=7.1, 1.4 Hz, 1H), 3.92 (s, 3H), 2.74 (t, $J$=7.5 Hz, 2H), 1.66 (p, $J$=6.9 Hz, 2H), 1.4–1.2 (br s, 30H), 0.88 (t, $J$=6.9 Hz, 3H); $^{13}$C NMR (67.5 MHz) $\delta$ 135.9 (+), 132.8 (+), 127.0 (+), 121.6 (+), 121.1 (−), 119.0 (−), 117.0 (−), 110.8 (−), 62.1 (−), 31.9 (+), 29.7 (multiple carbons, +), 29.6 (+), 29.4 (+), 29.4 (+), 29.4 (+), 24.7 (+), 22.6 (+), 14.1 (−); IR 3477, 2920, 909, 731 cm$^{-1}$. Anal. Calcd for $C_{27}H_{45}NO$: C, 81.14; H, 11.35; N, 3.50. Found: C, 81.24; H, 11.50; N, 3.56. HRMS (ESI) calcd for $C_{27}H_{46}NO$ ($M+H^+$): 400.3574. Found: 400.3572.

*4.1.7. Methyl 2-(1-oxononadecyl)aminobenzoate (**12**).* 3-Methoxy-2-octadecylindole (**11**) (104 mg, 0.260 mmol) and silica gel (approximately 500 mg) were stirred in reagent grade methanol (10 mL) in a round-bottom flask on a rotary evaporator for 5 min. The solvent was then removed at elevated temperature (boiling water bath) and reduced pressure. The mixture was allowed to stand open to the atmosphere at ambient temperature overnight before purifying the product by chromatography (hexanes/EtOAc, 95:5) affording **12** (98 mg, 0.23 mmol, 87%) as an oily yellow solid. $^1$H NMR (270 MHz) $\delta$ 11.1 (br s, 1H), 8.74 (d, $J$=8.7 Hz, 1H), 8.02 (d, $J$=8.2 Hz, 1H), 7.54 (t, $J$=7.2 Hz, 1H), 7.07 (t, $J$=7.2 Hz, 1H), 3.93 (s, 3H), 2.44 (t, $J$=7.4 Hz, 2H), 1.75 (m, 2H), 1.37–1.15 (m, 30H), 0.88 (t, $J$=6.9 Hz, 3H); $^{13}$C NMR (67.5 MHz) $\delta$ 172.3 (+), 168.7 (+), 141.7 (+), 134.7 (−), 130.8 (−), 122.2 (−), 120.3 (−), 114.7 (+), 52.3 (−), 38.7 (+), 31.9 (+), 29.7 (multiple carbons, +), 29.5 (+), 29.4 (+), 29.2 (+), 25.5 (+), 22.7 (+), 14.1 (−); IR 3266, 1709, 1694 cm$^{-1}$. Anal. Calcd for $C_{27}H_{45}NO_3$: C, 75.13; H, 10.51; N, 3.24. Found: C, 75.34; H, 10.74; N, 2.89. HRMS (ESI) calcd for $C_{27}H_{46}NO_3$ ($M^+$+H) 432.3472, found 432.3471.

*4.1.8. 2-(1-Oxononadecyl)aminobenzoic acid (**13**).* A mixture of nonadecanoic acid (1.00 g, 3.35 mmol) and thionyl chloride (340 μL, 4.69 mmol) was heated at reflux for 8 h. Excess thionyl chloride was removed under reduced pressure to give nonadecanoyl chloride as an orange oil that was used without further purification. 2-Aminobenzoic acid (450 mg, 3.28 mmol) and $NEt_3$ (500 μL, 3.61 mmol) were stirred in $CH_2Cl_2$ (20 mL) for 5 min. A solution of freshly prepared nonadecanoyl chloride (1.04 g, 3.28 mmol) in $CH_2Cl_2$ (30 mL) was added slowly in approximately five equal portions. The resulting solution was stirred for 5 h, water (100 mL) was added and the stirring was continued 5 min. The phases were separated and the aqueous portion was extracted with $CH_2Cl_2$ (3×15 mL). The combined organic phases were dried ($MgSO_4$), filtered, and the solvent was removed. The crude solid was recrystallized from hexanes to afford **13** (1.11 g, 2.67 mmol, 81%) as a white powdery solid. Mp: 94–95 °C. $^1$H NMR (600 MHz) $\delta$ 11.0 (br s, 1H), 8.77 (d, $J$=8.4 Hz, 1H), 8.13 (dd, $J$=7.8, 1.8 Hz, 1H), 7.60 (dt, $J$=7.2, 1.8 Hz, 1H), 7.11 (dt, $J$=7.8, 0.6 Hz, 1H), 2.47 (t, $J$=7.8 Hz, 2H), 1.77 (p, $J$=7.8 Hz, 2H), 1.40 (p, $J$=7.8 Hz, 2H), 1.34–1.24 (m, 28H), 0.88 (t, $J$=7.2 Hz, 3H); $^{13}$C NMR (150 MHz) $\delta$ 172.7, 172.1, 142.1, 135.6, 131.7, 122.6, 120.6, 113.9, 38.7, 31.9, 29.7, 29.6, 29.5, 29.3, 29.2, 25.5, 22.7, 14.1; IR 3336, 2918, 2850, 1673, 1270, 1165, 754 cm$^{-1}$. HRMS (ESI) calcd for $C_{26}H_{44}NO_3$ ($M^+$+H) 418.3321, found 418.3321.

*4.1.9. 2-(1-Oxooctadecyl)aminobenzoic acid (**14**).* Octadecanoic acid (1.00 g, 3.52 mmol) and thionyl chloride (360 μL, 4.92 mmol) were heated at reflux for 8 h. Excess thionyl chloride was removed under reduced pressure to give octadecanoyl chloride as an orange oil that was used without further purification. 2-Aminobenzoic acid (461 mg, 3.36 mmol) and $NEt_3$ (520 μL, 3.70 mmol) were stirred in $CH_2Cl_2$ (30 mL) for 5 min. A solution of freshly prepared octadecanoyl chloride (1.07 g, 3.70 mmol) in $CH_2Cl_2$ (20 mL) was added slowly in approximately five equal portions. The resulting solution was stirred for 5 h, water (100 mL) was added and the stirring was continued for 5 min. The phases were separated and the aqueous portion was extracted with $CH_2Cl_2$ (3×15 mL). The combined organic phases were dried ($MgSO_4$), filtered, and the solvent was removed. The crude solid was recrystallized from hexanes to afford **14** (1.17 g, 2.89 mmol, 86%) as a white solid. Mp: 81–82 °C. $^1$H NMR (600 MHz) $\delta$ 10.9 (br s, 1H), 8.77 (d, $J$=8.4 Hz, 1H), 8.13 (dd, $J$=7.8, 1.8 Hz, 1H), 7.60 (dt, $J$=7.2, 1.8 Hz, 1H), 7.11 (dt, $J$=7.8, 0.6 Hz, 1H), 2.47 (t, $J$=7.8 Hz, 2H), 1.77 (m, 2H), 1.40 (m, 2H), 1.34–1.24 (m, 24H), 0.88 (t, $J$=7.2 Hz, 3H); $^{13}$C NMR (150 MHz) $\delta$ 172.7, 172.2, 142.2, 135.7, 131.8, 122.6, 120.6, 113.8, 38.7, 31.9, 29.7, 29.6, 29.5, 29.3, 29.2, 25.5, 22.7, 14.1; IR 3336, 2918, 2850, 1673, 1270, 1165, 754 cm$^{-1}$. HRMS (ESI) calcd for $C_{25}H_{42}NO_3$ ($M+H^+$) 404.3165, found 404.3161. MS/MS (ESI) found 404.4 and 386.2.

*4.1.10. 2-(1-Icosy-1-nyl)benzenamine (**16**).* To a solution of 2-iodobenzenamine (1.00 g, 4.57 mmol) in $NEt_3$ (10 mL) at ambient temperature was added $PdCl_2$ (41 mg, 0.228 mmol) and $PPh_3$ (120 mg, 0.457 mmol). The resultant suspension was stirred for 10 min followed by addition of 1-eicosyne (2.12 g, 7.62 mmol) and then CuI (44 mg, 0.228 mmol). This mixture was stirred for 24 h

under an $N_2$ atmosphere at ambient temperature, followed by removal of the solvent under reduced pressure. The resulting crude product was purified by chromatography (hexanes/EtOAc, 95:5) to afford **16** (1.21 g, 3.27 mmol, 72%) as a brown solid. Mp 39–41 °C; $^1$H NMR $\delta$ 7.23 (dd, $J$=7.2, 1.2 Hz, 1H), 7.06 (dt, $J$=7.8, 1.2 Hz, 1H), 6.67 (d, $J$=8.4 Hz, 1H), 6.65 (dt, $J$=7.2, 1.2 Hz, 1H), 4.15 (br s, 2H), 2.46 (t, $J$=7.2 Hz, 2H), 1.62 (pent, $J$=7.2 Hz, 2H), 1.45 (pent, $J$=7.2 Hz, 2H), 1.31–1.26 (br m, 28H), 0.88 (t, $J$=7.2 Hz, 3H); $^{13}$C NMR $\delta$ 147.6, 132.0, 128.8, 117.8, 114.1, 109.0, 95.8, 31.9, 29.69, 29.66, 29.65, 29.63, 29.5, 29.4, 29.2, 29.0, 22.7, 19.6, 14.1 (resonances overlap, one resonance missing); IR (ATR) 3490, 3467, 3390, 3371, 2915, 2847, 1607, 1467, 753, 719 cm$^{-1}$; HRMS (ESI) calcd for $C_{26}H_{44}N$ (M+H$^+$) 370.3474, found 370.3475.

*4.1.11. 1-(1-Icosyn-1-yl)-2-nitrobenzene (**17**).* To a solution of 2-iodo-nitrobenzene (2.68 g, 10.8 mmol) in $NEt_3$ (30 mL) at ambient temperature was added $Pd(PPh_3)_2Cl_2$ (377 mg, 0.537 mmol). The resultant suspension was stirred for 10 min followed by addition of 1-eicosyne (5.00 g, 18.0 mmol) followed by CuI (102 mg, 0.537 mmol). This mixture was then stirred for 3 h under an $N_2$ atmosphere at ambient temperature, followed by removal of all volatiles under reduced pressure. The resulting crude product was purified by column chromatography (hexanes/EtOAc, 97:3) to afford **17** (4.12 g, 10.3 mmol, 95%) as a brown solid. Mp 39–42 °C; $^1$H NMR (600 MHz) $\delta$ 7.96 (dd, $J$=8.4, 0.6 Hz, 1H), 7.57 (dd, $J$=7.8, 1.2 Hz, 1H), 7.51 (dt, $J$=7.2, 1.2 Hz, 1H), 7.38 (dt, $J$=7.2, 1.2 Hz, 1H), 2.47 (t, $J$=7.2 Hz, 2H), 1.63 (pent, $J$=7.2 Hz, 2H), 1.46 (pent, $J$=7.2 Hz, 2H), 1.22–1.36 (br m, 28H), 0.88 (t, $J$=7.2 Hz, 3H); $^{13}$C NMR (150 MHz) $\delta$ 150.1, 134.7, 132.4, 127.7, 124.3, 119.4, 99.5, 75.9, 31.9, 29.7 (multiple carbons), 29.6, 29.1, 28.3, 22.7, 19.8, 14.1; IR (ATR) 2917, 2848, 1514, 1339 cm$^{-1}$; HRMS (ESI) calcd for $C_{26}H_{41}NNaO_2$ (M+Na$^+$) 422.3035, found 422.3030.

*4.1.12. Triethyl((E)-1-(2-nitrophenyl)icos-1-enyl)silane (**18**).* $PtO_2$ (278 mg, 1.23 mmol) and **17** (4.90 g, 12.26 mmol) were placed under a $N_2$ atmosphere. Triethylsilane (2.85 g, 24.5 mmol) was introduced via syringe and the mixture was stirred at 60 °C in an oil bath (3 h). The resulting crude product was purified by chromatography (hexanes/EtOAc, 98:2) to afford **18** (5.37 g, 10.4 mmol, 85%) as a yellow oil. $^1$H NMR $\delta$ 7.90 (dd, $J$=8.4, 1.2 Hz, 1H), 7.48 (dt, $J$=7.8, 1.2 Hz, 1H), 7.30 (dt, $J$=7.8, 1.8 Hz, 1H), 7.01(dd, $J$=7.8, 1.2 Hz, 1H), 5.95 (t, $J$=7.2 Hz, 1H), 1.85–1.74 (m, 2H), 1.32–1.12 (m, 32H), 0.90–0.84 (m, 12H), 0.61–0.50 (m, 6H); $^{13}$C NMR $\delta$ 148.1, 143.5, 138.9, 137.3, 132.3, 130.5, 126.3, 124.2, 31.9, 30.8, 29.7, 29.6, 29.5, 29.4, 29.1, 29.0, 22.7, 14.1, 7.2, 3.4 (resonances overlap); IR (ATR) 2921, 2852, 1525, 1347, 718, 705 cm$^{-1}$; HRMS (ESI) calcd for $C_{32}H_{57}NNaO_2Si$ (M+Na$^+$) 538.4056, found 538.4050.

*4.1.13. 2-Octadecyl-1H-indole (**15**).* To a solution of **18** (2.03 g, 3.93 mmol), $Pd(dba)_2$ (135 mg, 0.236 mmol), 1,3-bis-(diphenylphosphino)propane (dppp) (97 mg, 0.236 mmol), and 1,10-phenanthroline monohydrate (94 mg, 0.472 mmol) were dissolved in anhydrous DMF (8 mL) in a threaded ACE glass pressure tube. The tube was fitted with a pressure head, and the solution was saturated with carbon monoxide (four cycles of 6 atm of CO). The reaction mixture was heated at 120 °C (oil bath temperature) under CO (6 atm) for 16 h. Water (30 mL) was added and the orange solution was extracted with ethyl acetate (3×30 mL). The combined organic phases were dried ($MgSO_4$), filtered, and the solvent was removed under reduced pressure. The resulting crude product was purified by chromatography (hexanes/EtOAc, 98:2) to afford **15** (1.01 g, 2.73 mmol, 70%) as a tan solid. Mp 73–74 °C; $^1$H NMR $\delta$ 7.82 (br s, 1H), 7.51 (d, $J$=7.2 Hz, 1H), 7.28 (d, $J$=7.2 Hz, 1H), 7.10 (dt, $J$=7.2, 1.2 Hz, 1H), 7.06 (dt, $J$=7.2, 1.2 Hz, 1H), 6.23 (d, $J$=2.4 Hz, 1H), 2.74 (t, $J$=7.8 Hz, 2H), 1.71 (pent, $J$=7.2 Hz, 2H), 1.39 (m, 2H), 1.35–1.18 (br m, 28H), 0.88 (t, $J$=7.2 Hz, 3H); $^{13}$C NMR $\delta$ 140.0, 135.8, 128.9, 120.9, 119.7, 119.6, 110.2, 99.5, 31.9, 29.7, 29.6, 29.5, 29.4, 29.3, 29.2, 28.3, 22.7, 14.1 (resonances overlap); IR (ATR) 3375, 2915, 2849, 1471, 746, 1456, cm$^{-1}$; HRMS (ESI) calcd for $C_{26}H_{44}N$ (M+H$^+$) 370.3474, found 370.3470.

*4.1.14. 2-Octadecyl-2-(2-octadecyl-3-oxo-2,3-dihydro-1H-indol-2-yl)-1,2-dihydro-3H-indol-3-one (**19**) and 2-octadecyl-2-(2-octadecyl-1H-indol-3-yl)indolin-3-one (**20**).* A solution of 3-chloroperoxybenzoic acid (248 mg, 1.01 mmol) in dichloromethane (5 mL) was added dropwise at ambient temperature to a stirred solution of 2-octadecyl-1*H*-indole (**15**) (310 mg, 0.838 mmol) in the same solvent (2 mL). The mixture was stirred for 1 h, then poured into 5% $NH_4Cl$ (15 mL) and extracted with $CH_2Cl_2$ (3×25 mL). The combined organic phases were dried ($MgSO_4$), filtered, and the solvent was removed under reduced pressure. The resulting crude product was purified by chromatography (hexanes, then hexanes/EtOAc 98:2) to afford **19** (107 mg, 0.139 mmol, 33 %) as a bright yellow solid and **20** (113 mg, 0.150 mmol, 36%) as a dark yellow solid. Spectral data for **19**: mp 105–107 °C; $^1$H NMR (600 MHz) $\delta$ 7.56 (d, $J$=7.8 Hz, 2H), 7.48 (t, $J$=8.4 Hz, 2H), 6.95 (d, $J$=8.4 Hz, 2H), 6.78 (t, $J$=6.6 Hz, 2H), 6.02 (s, 2H), 1.88 (m, 2H), 1.30–0.94 (br m, 66H), 0.88 (t, $J$=6.6 Hz, 6H); $^{13}$C NMR (150 MHz) $\delta$ 204.5, 162.0, 138.0, 124.1, 121.6, 118.3, 111.9, 72.5, 29.8, 29.7, 29.7, 29.7, 29.6, 29.6, 29.5, 29.4, 29.4, 29.4, 29.3, 22.9, 22.7, 14.1 (several resonances overlap); IR (ATR) 3358, 2916, 2849, 1674, 1613, 741, cm$^{-1}$; HRMS (APCI) calcd for $C_{52}H_{85}N_2O_2$ (M+H$^+$, 1%) 769.6611, found 769.6613; $C_{26}H_{44}NO$ (M/2+2H$^+$, 45%) 386.3423, found 386.3422; $C_{26}H_{42}NO$ (M/2$^+$, 100%) 384.3266, found 384.3265;

*4.1.15. Spectral data for **20**.* Mp 49–52 °C; $^1$H NMR (600 MHz) $\delta$ 7.81 (br s, 1H), 7.77 (d, $J$=8.4 Hz, 1H), 7.63 (d, $J$=7.8 Hz, 1H), 7.46 (t, $J$=8.4 Hz, 1H), 7.24 (d, $J$=8.4 Hz, 1H), 7.09 (t, $J$=7.2 Hz, 1H), 7.03 (t, $J$=7.8 Hz, 1H), 6.87 (d, $J$=8.4 Hz, 1H), 6.82 (t, $J$=7.2, 1H), 5.03 (br s, 1H), 2.81 (m, 2H), 2.48 (dt, $J$=12.6, 3.6 Hz, 1H), 2.23 (dt, $J$=12.0, 4.2 Hz, 1H), 1.54 (m, 4H), 1.31–1.21 (br m, 60H), 0.88 (t, $J$=6.6 Hz, 6H); $^{13}$C NMR (150 MHz) $\delta$ 203.3, 160.1, 137.1, 136.8, 135.2, 133.5, 128.4, 127.3, 125.0, 121.2, 120.6, 119.6, 118.8, 112.1, 110.4, 108.9, 70.9, 38.1, 31.9, 30.8, 29.9, 29.72, 29.71, 29.70, 29.68, 29.66, 29.65, 29.64, 29.61, 29.56, 29.47, 29.41, 29.36, 28.4, 23.9, 22.7, 14.1 (several resonances overlap); IR (ATR) 2917, 2850, 1611, 1486, 741, 718, cm$^{-1}$; HRMS (ESI) calcd for $C_{52}H_{85}N_2O$ (M+H$^+$) 753.6656, found 753.6652.

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