Highly Regioselective Synthesis of 2,3,4-Trisubstituted 1*H*-Pyrroles: A Formal Total Synthesis of Lukianol A[†,1]

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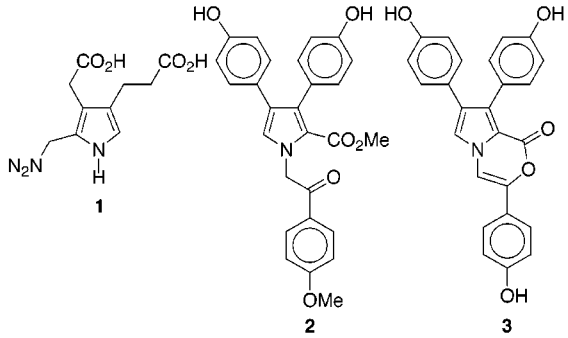
A combined use of α-lithiation and nucleophilic substitutions of *N*,*N*-dimethyl 3,4-bis(trimethylsilyl)-1*H*-pyrrole-1-sulfonamide **8c** led to several 2-substituted 3,4-bis(trimethylsilyl)-1*H*-pyrrole-1-sulfonamides. Utilizing the *β*-effect of a trimethylsilyl group, a highly regioselective synthesis of 2,3,4-trisubstituted 1*H*-pyrroles **23** and **34** was accomplished. The marine natural product lukianol A (**3**) was prepared utilizing this strategy.

Introduction

Regiospecific syntheses of polysubstituted pyrroles belong to an extremely attractive domain in heterocyclic chemistry as a result of their unusual bioactivities.[3] In particular, pyrrole skeletons with 2,3,4-substituents constitute the molecular framework of many biologically active compounds, e.g., porphobilinogen (**1**),[4] as well as the marine natural products lamellarin *O* (**2**)[5] and lukianol A (**3**).[6] Most of the literature methods for the preparation of 2,3,4-trisubstituted pyrroles require the use of acyclic starting materials or pyrroles that contain bromo groups.[7,8] In the former methodology, the C-3 and C-4 substituents are set at a very early stage so that they cannot be varied through "late" intermediates. Consequently, a tedious multistep synthetic procedure is required for the manipulation of each substituent. In the latter methodology, it remains synthetically quite challenging to differentiate the bromo groups.[9]

Herein we present our results on the synthesis of 2,3,4-trisubstituted-1*H*-pyrroles employing 1-protected 3,4-bis-(trimethylsilyl)-1*H*-pyrroles **4**[10] as pivotal precursors. The synthetic design leading to 2,3,4-trisubstituted-1*H*-pyrroles is depicted in Scheme 1. The preparation begins with α-lithiation and subsequent quenching with an electrophile.[11] The second step is a regiospecific *ipso*-iodination[12] making use of the *β*-effect[13] manifested by a trimethylsilyl group. Carbon substituents can be introduced by way of palladium-catalyzed Sonogashira,[14] Heck,[15] and Suzuki[16] cross-coupling reactions. The remaining trimethylsilyl group can likewise be converted to carbon substituents via an iodide intermediate. Finally, deprotection of the 1-substituent will deliver the parent 2,3,4-trisubstituted-1*H*-pyrroles.



Results and Discussion

(a) Synthesis of 2,3,4-Trisubstituted 1*H*-Pyrroles and Alkyl 3,4-Disubstituted 1*H*-Pyrrole-2-carboxylates. 3,4-Bis(trimethysilyl)-1*H*-pyrrole-2-carbaldehyde appeared to be a suitable starting material for the realization of 2,3,4-trisubstituted-1*H*-pyrroles. However,

† Dedicated to Professor Shô Itô on the occasion of his 77th birthday.

(1) Taken in part from the Ph.D. Thesis of J.-H. L., The Chinese University of Hong Kong, 1999.

(2) To whom correspondence concerning X-ray crystallography should be addressed.

(3) Patterson, J. M. *Synthesis* **1976**, 281−304. Jones, R. A.; Chapman, B. J. In *Comprehensive Heterocyclic Chemistry*; Bird, C. W., Ed.; Pergamon Press: Oxford, 1996; Vol. 2, pp 1−38. Black, D. St. C. In *Comprehensive Heterocyclic Chemistry*; Bird, C. W., Ed.; Pergamon Press: Oxford, 1996; Vol. 2, pp 39−118. Sundberg, R. J. In *Comprehensive Heterocyclic Chemistry*; Bird, C. W., Ed.; Pergamon Press: Oxford, 1996; Vol. 2, pp 119−206. Gribble, G. W. In *Comprehensive Heterocyclic Chemistry*; Bird, C. W., Ed.; Pergamon Press: Oxford, 1996; Vol. 2, pp 207−257.

(4) Battersby, A. R.; McDonald, E. In *Porphyrins and Metalloporphyrins*; Smith, K. M., Ed.; Elsevier: Amsterdam, 1975; pp 61−122.

(5) Urban, S.; Butler, M. S.; Capon, R. J. *Aust. J. Chem.* **1994**, *47*, 1919−1924.

(6) Yoshida, W. Y.; Lee, K. K.; Carroll, A. R.; Scheuer, P. J. *Helv. Chim. Acta* **1992**, *75*, 1721−1725.

(7) For some representative syntheses of 2,3,4-trisubstituted-1*H*-pyrroles, see: (a) van Leusen, A. M.; Siderius, H.; Hoogenboom, B. E.; van Leusen, D. *Tetrahedron Lett.* **1972**, 5337−5340. (b) Cohnen, E.; Dewald, R. *Synthesis* **1987**, 566−568. (c) Buchwald, S. L.; Wannamaker, M. W.; Watson, B. T. *J. Am. Chem. Soc.* **1989**, *111*, 776−777. (d) Roskamp, E. J.; Dragovich, P. S.; Hartung, J. B., Jr.; Pedersen, S. F. *J. Org. Chem.* **1989**, *54*, 4736−4737. (e) van Leusen, D.; Flentge, E.; van Leusen, A. M. *Tetrahedron* **1991**, *47*, 4639−4644. (f) Carré, F. H.; Corriu, R. J. P.; Bolin, G.; Moreau, J. J. E.; Vernhet, C. *Organometallics* **1993**, *12*, 2478−2486. (g) Dell'Erba, C.; Giglio, A.; Mugnoli, A.; Novi, M.; Petrillo, G.; Stagnaro, P. *Tetrahedron* **1995**, *51*, 5181−5192. (h) Tietze, L. F.; Kettschau, G.; Heitmann, K. *Synthesis* **1996**, 851−857. (i) ten Have, R.; Leusink, F. R.; van Leusen, A. M. *Synthesis* **1996**, 871−876. (j) Rolfs, A.; Jones, P. G.; Liebscher, J. *J. Chem. Soc., Perkin Trans. 1* **1996**, 2339−2343. (k) Gao, Y.; Shirai, M.; Sato, F. *Tetrahedron Lett.* **1996**, *37*, 7787−7790. (l) Dekura, F.; Honda, T.; Mori, M. *Chem. Lett.* **1997**, 825−826. (m) Yagi, T.; Aoyama, T.; Shioiri, T. *Synlett* **1997**, 1063−1064. (n) Yasuda, M.; Morimoto, J.; Shibata, I.; Baba, A. *Tetrahedron Lett.* **1997**, *38*, 3265−3266. (o) Trautwein, A. W.; Jung, G. *Tetrahedron Lett.* **1998**, *39*, 8263−8266. (p) Shiraishi, H.; Nishitani, T.; Sakaguchi, S.; Ishii, Y. *J. Org. Chem.* **1998**, *63*, 6234−6238. (q) Caldarelli, M.; Habermann, J.; Ley, S. V. *J. Chem. Soc., Perkin Trans. 1* **1999**, 107−110. (r) Marchand, E.; Morel, G.; Sinbandhit, S. *Eur. J. Org. Chem.* **1999**, 1729−1738. (s) Tehrani, K. A.; Borremans, D.; De Kimpe, N. *Tetrahedron* **1999**, *55*, 4133−4152. (t) Alberola, A.; Ortega, A. G.; Sádaba, M. L.; Sañudo, C. *Tetrahedron* **1999**, *55*, 6555−6566. (u) Lim, S.; Jabin, I.; Revial, G. *Tetrahedron Lett.* **1999**, *40*, 4177−4180.

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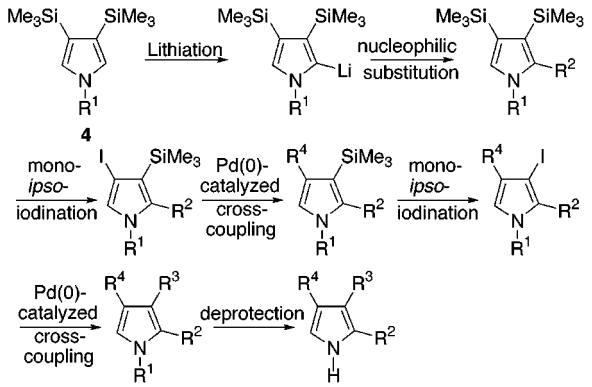
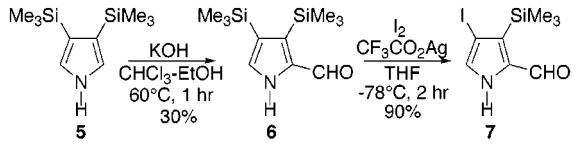
Scheme 1

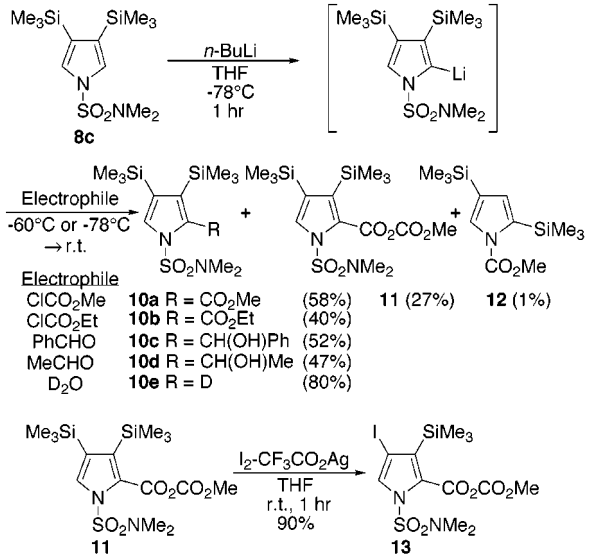


the Vilsmeier−Haack[17] and Gattermann[18] reactions are not suitable because these reactions require acid conditions and therefore are likely to induce protodesilylation. Reimer−Tiemann reaction[19] of the parent 3,4-bis(trimethylsilyl)-1*H*-pyrrole (**5**),[20] on the other hand, afforded the desired pyrrole-2-carbaldehyde **6**, albeit in a low 30% yield (Scheme 2). The structure of **6** was also substantiated by an X-ray study.[21] The subsequent iodination proceeded in both regiospecific and high yield manner.

Scheme 2



Scheme 3



Unfortunately, Sonogashira,[14] Heck,[15] and Suzuki[16] cross-coupling reactions of the iodide **7** failed to take place under a variety of conditions. The formylation approach was abandoned because of these drawbacks.

Direct lithiation of 1-protected pyrroles and subsequent quenching of the resulting lithium salts with electrophiles has provided a general pathway to α-substituted pyrroles.[22,23] However, when 1-(*tert*-butoxycarbonyl)-3,4-bis(trimethylsilyl)-1*H*-pyrrole (**8a**)[20] was allowed to react with *n*-BuLi, followed by addition of $ClCO_2Me$, methyl 3,4-bis(trimethysilyl)-1*H*-pyrrole-1-carboxylate (**9a**) was obtained in 35% yield. The reactivity of the protecting group in *n*-BuLi is the main reason for the failure. A similar reaction was also performed on 1-(*p*-toluenesulfonyl)-3,4-bis(trimethylsilyl)-1*H*-pyrrole (**8b**).[20] However, again no pyrrole α-substitution materialized, and only 1-(2-methoxycarbonyl-*p*-toluenesulfonyl)-3,4-bis(trimethylsilyl)-1*H*-pyrrole (**9b**) was isolated after the reaction was quenched with $ClCO_2Me$.

In view of the unsuccessful attempts on α-lithiation, we reasoned that a 1-(*N*,*N*-dimethylaminosulfonyl) protecting group might help to enhance the acidity of the proton *ortho* to the pyrrole nitrogen and might also stabilize an *ortho*-lithium through coordination with its nitrogen or oxygen atoms. These factors therefore combine to facilitate anion formation at the pyrrole α-carbon.[11] Experimentally, it was uncovered that the addition of 1.1 equiv of *n*-BuLi to **8c**[10] in THF at −78 °C readily generated the desired lithium salt, whose reaction with electrophiles led to 40−80% isolated yields of *N*,*N*-dimethyl 2-substituted-3,4-bis(trimethylsilyl)-1*H*-pyrrole-1-sulfonamides **10a**−**e** (Scheme 3).

The reaction of **8c** with *n*-BuLi and $ClCO_2Me$ in fact furnished the two byproducts **11** and **12** in addition to

(8) For some representative syntheses of alkyl 3,4-disubstituted-1*H*-pyrrole-1-carboxylates, see: (a) Hombrecher, H. K.; Horter, G. *Synthesis* **1990**, 389−391. (b) Barton, D. H. R.; Kervagoret, J.; Zard, S. Z. *Tetrahedron* **1990**, *46*, 7587−7598. (c) La Porta, P.; Capuzzi, L.; Bettarini, F. *Synthesis* **1994**, 287−290. (d) Leroy, J.; Wakselman, C. *Tetrahedron Lett.* **1994**, *35*, 8605−8608. (e) Boëlle, J.; Schneider, R.; Gérardin, P.; Loubinoux, B. *Synthesis* **1997**, 1451−1456. (f) Selic, L.; Stanovnik, B. *Helv. Chim. Acta* **1998**, *81*, 1634−1639. (g) Abel, Y.; Haake, E.; Haake, G.; Schmidt, W.; Struve, D.; Walter, A.; Montforts, F.-P. *Helv. Chim. Acta* **1998**, *81*, 1978−1996. (h) Gupton, J. T.; Krumpe, K. E.; Burnham, B. S.; Dwornik, K. A.; Petrich, S. A.; Du, K. X.; Bruce, M. A.; Vu, P.; Vargas, M.; Keertikar, K. M.; Hosein, K. N.; Jones, C. R.; Sikorski, J. A. *Tetrahedron* **1998**, *54*, 5075−5088. (i) Uno, H.; Tanaka, M.; Inoue, T.; Ono, N. *Synthesis* **1999**, 471−474. (j) Selic, L.; Stanovnik, B. *Synthesis* **1999**, 479−482. (k) Fumoto, Y.; Eguchi, T.; Uno, H.; Ono, N. *J. Org. Chem.* **1999**, *64*, 6518−6521. (l) Leung, S. H.; Edington, D. G.; Griffith, T. E.; James, J. J. *Tetrahedron Lett.* **1999**, *40*, 7189−7191.

(9) Banwell, M. G.; Flynn, B. L. Hamel, E.; Hockless, D. C. R. *J. Chem. Soc., Chem. Commun.* **1997**, 207−208.

(10) Chan, H.-W.; Chan, P.-C.; Liu, J.-H.; Wong, H. N. C. *J. Chem. Soc., Chem. Commun.* **1997**, 1515−1516. Liu, J.-H.; Chan, H.-W.; Wong, H. N. C. *J. Org. Chem.* **2000**, in press.

(11) Iwao, M.; Iihama, T.; Mahalanabis, K. K.; Perrier, H.; Snieckus, V. *J. Org. Chem.* **1989**, *54*, 24−26.

(12) Inter alia, see: Ye, X.-S.; Wong, H. N. C. *J. Org. Chem.* **1997**, *62*, 1940−1954 and references therein.

(13) Ushakov, S. N.; Itenberg, A. M. *Zh. Obshch. Khim.* **1937**, *7*, 2495−2498; *Chem. Abstr.* **1938**, *32*, 2083[3]. Bassindale, A. R.; Taylor, P. G. In *The Chemistry of Organosilicon Compounds. The Activating and Directing Effects of Silicon*; Patai, S.; Rappoport, Z., Eds.; Wiley: Chichester, 1938; Part 2, pp 893−964. Lambert, J. B. *Tetrahedron* **1990**, *46*, 2677−2689. White, J. M. *Aust. J. Chem.* **1995**, *48*, 1227−1251. Lambert, J. B.; Zhao, Y.; Emblidge, R. W.; Salvador, L. A.; Liu, X.-Y.; So, J.-H.; Chelius, E. C. *Acc. Chem. Res.* **1999**, *32*, 183−190.

(14) Sonogashira, K.; Tohda, Y.; Hagihara, N. *Tetrahedron Lett.* **1975**, 4467−4470. Sonogashira, K. In *Comprehensive Organic Synthesis*; Pattenden, G., Ed.; Pergamon Press: Oxford, 1991; Vol. 3, pp 521−549. Rossi, R.; Carpita, A.; Bellina, F. *Org. Prep. Proced. Int.* **1995**, *27*, 129−160.

(15) Heck, R. F. *J. Am. Chem. Soc.* **1968**, *90*, 5518−5526. Heck, R. F. *Org. React.* **1981**, *27*, 345−390. Heck, R. F. *Palladium Reagents in Organic Syntheses*; Academic Press: London, 1985. Crisp, G. T. *Chem. Soc. Rev.* **1998**, *27*, 427−436.

(16) Suzuki, A. *Acc. Chem. Res.* **1982**, *26*, 178−184. Suzuki, A. *Pure Appl. Chem.* **1991**, *63*, 419−422. Suzuki, A. *Pure Appl. Chem.* **1994**, *66*, 213−222.

(17) Jutz, C. *Adv. Org. Chem.* **1976**, *9*, 225−342.

(18) Truce, W. E. *Org. React.* **1957**, *9*, 37−72.

(19) Wynberg, H.; Meijer, E. W. *Org. React.* **1982**, *28*, 1−36.

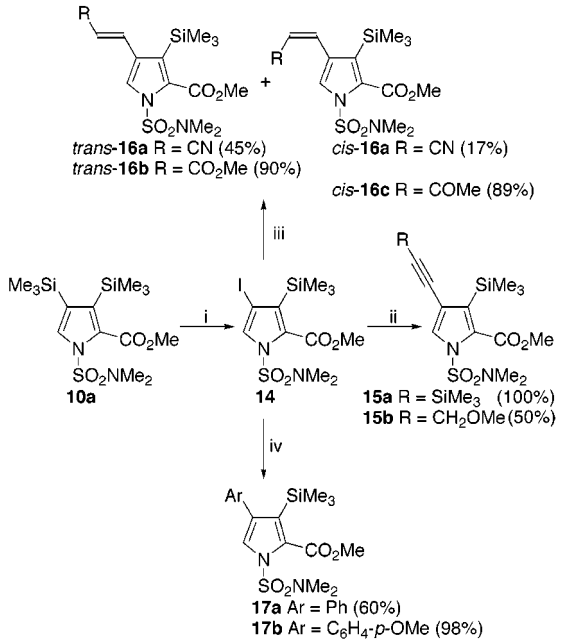
(20) Liu, J.-H.; Chan, H.-W.; Feng, X.; Wang, Q.-G.; Mak, T. C. W.; Wong, H. N. C. *J. Org. Chem.* **1999**, *64*, 1630−1634.

(21) All results of X-ray crystallographic studies are included in the Supporting Information.

(22) Gschwend, H. W.; Rodriguez, H. R. *Org. React.* **1976**, *26*, 1−360.

(23) Chadwick, D. J.; Hodgson, S. T. *J. Chem. Soc., Perkin Trans. 1* **1982**, 1833−1836.

Scheme 4[a]



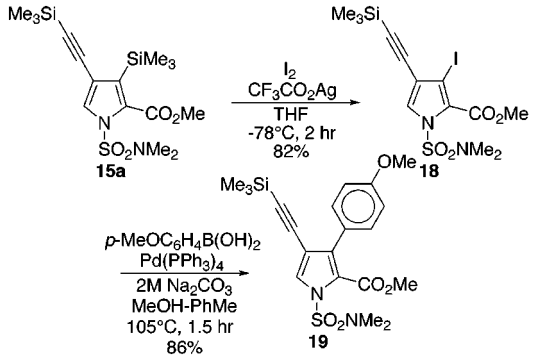
[a] Reagents and conditions: (i) I_2, CF_3CO_2Ag, THF, rt, 2 h, 100%; (ii) R-C≡CH, $PdCl_2(PPh_3)_2$, CuI, Et_2NH, rt, 10 h; (iii) R−CH=CH_2, $PdCl_2(PPh_3)_2$, Et_3N, DMF, 110 °C, 5 h; (iv) $ArB(OH)_2$, $Pd(PPh_3)_4$, 2M Na_2CO_3, MeOH/PhMe, 90−100 °C, 2 h.

the desired **10a** (Scheme 3). The formation of **11** was presumably due to the side reaction of the lithium alkoxide generated after the first quenching in an excess of $ClCO_2Me$. Upon reaction of **11** with iodine in silver trifluoroacetate, iodide **13** was obtained in a good crystalline form whose X-ray diffraction study confirmed its CO_2-CO_2Me moiety.[21]

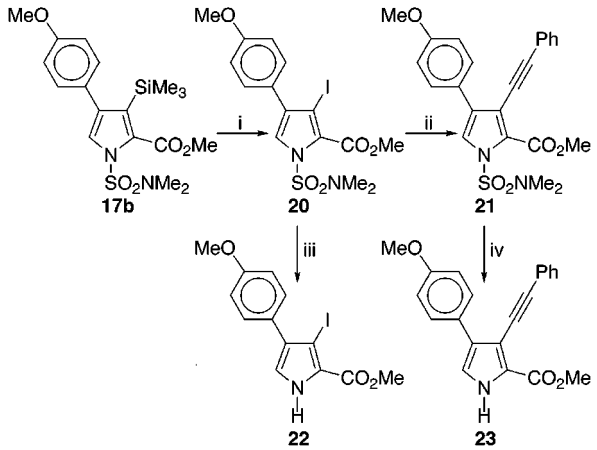
The mono-*ipso*-iodination of **10a** was achieved in a similar way as for **11**. It is not surprising that both steric and electronic factors can play important roles in controlling the iodination in a regioselective manner. In considering these possibilities, it is apparent that the preferential site of iodination was C-4 since this site is more nucleophilic as well as less sterically hindered. Indeed, standard iodination procedure converted **10a** to **14** (Scheme 4). Because of the additional electron-withdrawing 2-carbomethoxy group in **10a**, the temperature used for its iodination was higher than those used for other silylpyrroles without a 2-methoxycarbonyl group.

Sonogashira reaction[14] of **14** with terminal alkynes in the presence of $PdCl_2(PPh_3)_2$, CuI, and diethylamine afforded the alkynyl pyrroles **15a** and **15b** (Scheme 4). On the other hand, Heck reaction[15] of **14** with acrylonitrile gave two chromatographically separable isomeric alkenyl pyrroles *trans*-**16a** and *cis*-**16a** (Scheme 4). Their geometry was ascertained by ^{1}H NMR spectral studies. Alkene *trans*-**16a** with absorptions at δ 5.61 and 7.33 (J = 16.5 Hz) was assigned as the *trans*-isomer, while that with signals at δ 5.32 and 7.12 (J = 11.7 Hz) was the *cis*-**16a**. A similar ^{1}H NMR spectral analysis of the products *trans*-**16b** and *cis*-**16c** obtained through Heck reaction of **14** with methyl acrylate and methyl vinyl ketone revealed their *trans* and *cis* stereochemistry, respectively. The *trans*-geometry of *trans*-**16b** was also unambiguously confirmed by an X-ray crystallographic study,[21] which also indirectly validated the structure of

Scheme 5



Scheme 6[a]



[a] Reagents and conditions: (i) I_2, CF_3CO_2Ag, THF, rt, 1 h, 78%; (ii) Ph−C≡CH, $PdCl_2(PPh_3)_2$, CuI, Et_2NH, rt, 30 h, 60%; (iii) *n*-Bu_4NF, THF, 60 °C, 4 h, 65%; (iv) *n*-Bu_4NF, THF, 70 °C, 1.5 h, 90%.

iodide **14**. Suzuki reaction[16] between **14** and benzeneboronic acid yielded the expected phenylpyrrole **17a**, and a similar reaction of **14** with *p*-methoxybenzeneboronic acid gave **17b** (Scheme 4).

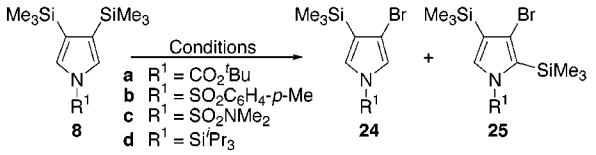
Having achieved several palladium-catalyzed cross-couplings for **14**, we then turned our attention to prepare the desired 2,3,4-trisubstituted 1*H*-pyrroles. Employing **15a** as the starting material, its remaining trimethylsilyl group was again replaced regiospecifically by an iodo group, providing **18** in 82% yield. Finally, Suzuki reaction of **18** with *p*-methoxybenzeneboronic acid gave the 1-protected 2,3,4-trisubstituted pyrrole **19** (Scheme 5).

Compound **17b** was also allowed to undergo an *ipso*-iodination to give iodide **20**, which was converted further through Sonogashira reaction to furnish **21** (Scheme 6). Encouraged by the work of Yasuhara and Sakamoto,[24] *n*-Bu_4NF was chosen as a possible deprotection reagent of *N*,*N*-dimethylaminosulfonyl group from the pyrrole nitrogen. As expected, both of the *N*,*N*-dimethylaminosulfonyl groups of **20** and **21** were cleaved by *n*-Bu_4NF to form the parent pyrroles **22** and **23**, respectively (Scheme 6). In this way, our ultimate goal of preparing 2,3,4-trisubstituted 1*H*-pyrroles without 1-protection was achieved.

ipso-Bromination of **8a**[20] and **8d**[10] to yield bromides **24a** and **24d** was the major reaction when the NBS brominations were performed at −78 to 0 °C for 2 h.

(24) Yasuhara, A.; Sakamoto, T. *Tetrahedron Lett.* **1998**, *39*, 595−596.

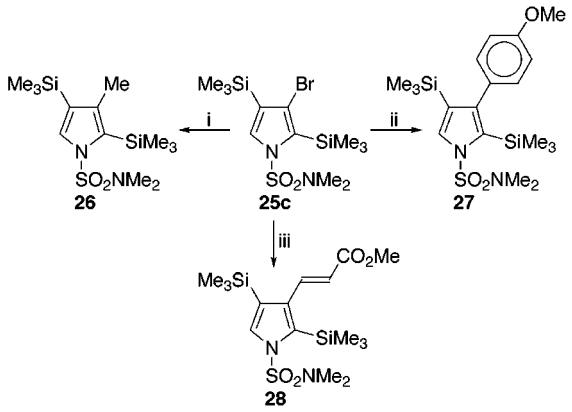
Table 1. Bromination of 8a−d



entry	starting material	condition[a]	product (yield %)
1	**8a**	A	**24a** (87)
2	**8a**	B	**24a** (37) + **25a** (24)
3	**8b**	B	**24b** (28) + **25b** (40)
4	**8c**	B	**24c** (22) + **25c** (55)
5	**8d**	A	**24d** (92)

[a] A: NBS, THF, −78 → 0 °C, 2 hr; B: NBS, THF, rt, 2 h.

Scheme 7[a]

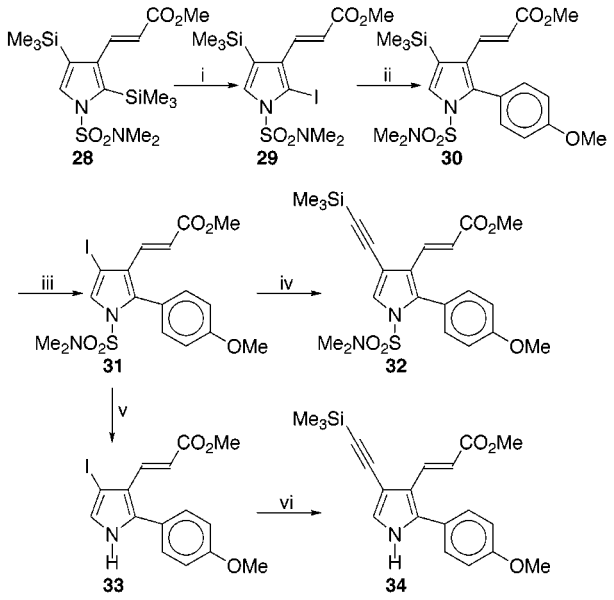


[a] Reagents and conditions: (i) *n*-BuLi, THF−HMPA, −78 °C, 1 h, then Me_2SO_4, −78 to 0 °C, 1 h, 90%; (ii) *p*-$MeOC_6H_4B(OH)_2$, $Pd(PPh_3)_4$, 2 M Na_2CO_3, MeOH/PhMe, 110−120 °C, 14 h; (iii) CH_2═$CHCO_2Me$, $PdCl_2(PPh_3)_2$, Et_3N, DMF, 120 °C, 3 h, 80%.

However, in the case of **8a**,[20] **8b**,[20] and **8c**,[10] when the reactions were carried out at room temperature for the same length of time, mixtures of products were obtained (Table 1). Treatment of **8a** with NBS at room temperature in THF led to the formation of two components, namely, the *ipso*-bromination product **24a** and the substitution−rearrangement product **25a**. The structure of **25a** was confirmed by its conversion to 1-(*tert*-butoxycarbonyl)-2,4-bis(trimethylsilyl)-1*H*-pyrrole, whose ^{1}H NMR spectrum showed two characteristic doublets for the two pyrrolic protons at δ 6.47 (J = 1.5 Hz) and 7.36 (J = 1.5 Hz). Likewise, the *p*-toluenesulfonyl-protected **8b** gave a mixture of **24b** and **25b**. The 3-bromo substitution pattern of **25b** was certified through desilylation with TBAF in THF at 66 °C with concomitant deprotection of the *p*-toluenesulfonyl group, providing the known 3-bromo-1*H*-pyrrole in 78% yield.[25] *N*,*N*-Dimethylaminosulfonyl-protected **8c** gave a mixture of **24c** and **25c**. The structure of **25c** was substantiated by an X-ray crystallographic study.[21]

Compound **25c** was also used as a key intermediate in the realization of several 2,3,4-trisubstituted-1*H*-pyrroles. Thus, lithium-bromo exchange of **25c** followed by addition of dimethyl sulfate generated the methylpyrrole **26** in excellent yield as a colorless oil (Scheme 7). Standard Suzuki and Heck reactions converted **25c** to the arylpyrrole **27** and alkenylpyrrole **28**, respectively (Scheme 7).

Scheme 8[a]



[a] Reagents and conditions: (i) I_2, CF_3CO_2Ag, THF, −78 °C, 6 h, 90%; (ii) *p*-$MeOC_6H_4B(OH)_2$, $Pd(PPh_3)_4$, 2 M Na_2CO_3, MeOH/PhMe, 110−120 °C, 5 h, 100%; (iii) I_2, CF_3CO_2Ag, THF, −78 °C, 6 h, 83%; (iv) Me_3Si-C≡CH, $PdCl_2(PPh_3)_2$, CuI, Et_2NH, rt, 10 h, 90%; (v) *n*-Bu_4NF, THF, 65 °C, 4 h, 84%; (vi) Me_3Si-C≡CH, $PdCl_2(PPh_3)_2$, CuI, Et_2NH, rt,10 h, 100%.

To test our strategy for the preparation of polysubstituted pyrroles, the synthesis of a 2,3,4-trisubstituted-1*H*-pyrrole **34** containing alkenyl, alkynyl, and aryl substituents was executed. Starting from **28**, a regiospecific iodination gave **29** as the only isolable product in 90% yield. Suzuki cross-coupling with *p*-methoxybenzeneboronic acid then gave **30** in excellent yield. The displacement of the second trimethylsilyl group was performed as usual and afforded the iodide **31** whose structure was established also by an X-ray crystallographic study.[21] The alkynyl group was incorporated by utilizing Sonogashira reaction, leading to the 2,3,4-trisubstituted-1*H*-pyrrole **32**. Alternatively, deprotection of **31** by using the aforementioned reagent produced **33**, which on Sonogashira reaction with trimethylsilylethyne in the presence of Pd(0), CuI, and diethylamine gave **34**, a deprotected derivative of **32** (Scheme 8).

In summary, the six-step preparation of **23** (Schemes 3, 4, and 6) and the seven-step preparaton of **34** (Table 1, Schemes 7 and 8) from a common precursor **8c** represent a rather unique and successful entry to polysubstituted pyrrole derivatives.

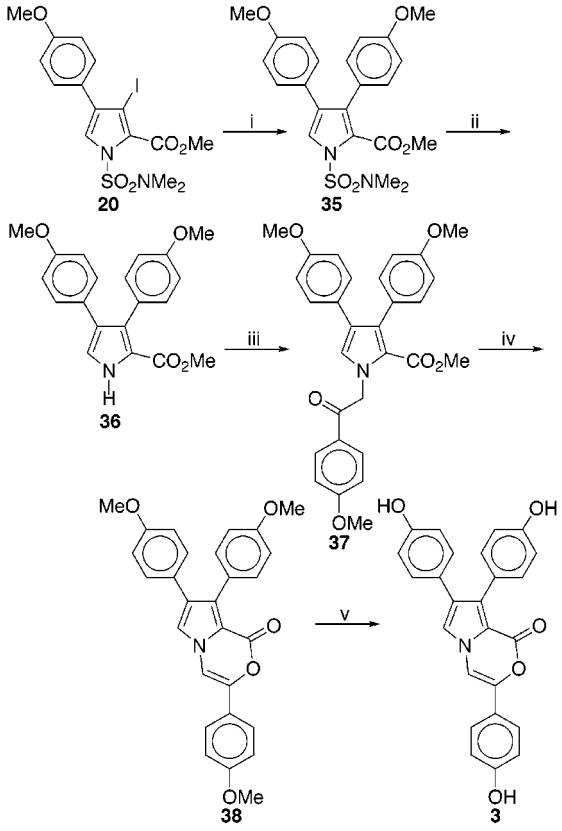
(b) Total Synthesis of Lukianol A. Our approach was also employed in the total synthesis of lukianol A (**3**), which was first isolated from an unidentified Pacific tunicate and which has interesting biological activities.[6] Structurally, **3** possesses a very unique methyl 3,4-diarylpyrrole-2-carboxylate skeleton. Three independent total syntheses of **3** have been recorded since 1995.[9,26]

The total synthesis of **3** was commenced using **20** as a precursor (Scheme 9). The usual condition for the Suzuki reaction involving 2 M Na_2CO_3 in MeOH/toluene gave

(25) Bray, B. L.; Mathies, P. H.; Naef, R.; Solas, D. R.; Tidwell, T. T.; Artis, D. R.; Muchowski, J. M. *J. Org. Chem.* **1990**, *55*, 6317−6328.

(26) (a) Fürstner, A.; Weintritt, H.; Hupperts, A. *J. Org. Chem.* **1995**, *60*, 6637−6641. (b) Boger, D. L.; Boyce, C. W.; Labroli, M. A.; Sehon, C. A.; Jin, Q. *J. Am. Chem. Soc.* **1999**, *121*, 54−62.

Scheme 9[a]



[a] Reagents and conditions: (i) *p*-$MeOC_6H_4B(OH)_2$, $Pd(PPh_3)_4$, 2 M Na_2CO_3, DMF, 150 °C, 1 h, 95%; (ii) Mg, MeOH, rt, 4 h, 85%; (iii) *p*-$MeOC_6H_4COCH_2Br$, K_2CO_3, Me_2CO, 70 °C, 3 h, 90%; (iv) *t*-BuOK, H_2O-Et_2O, 0 °C to rt, then Ac_2O, NaOAc, 100 °C, 2.5 h, 60%; (v) BBr_3, CH_2Cl_2, −78 °C to rt, 12 h, 93%.

very low yield of **35**. Therefore a slightly modified Suzuki cross-coupling of **20** with *p*-methoxybenzeneboronic acid at 150 °C in DMF was instead used, leading to a satisfactory yield of **35**. Noteworthy is that the latter procedure was also amenable for a large scale preparation of **35**. Deprotection of **35** employing *n*-Bu_4NF led to **36** in 50% yield.[9,26a] An alternative deprotection method by using Mg in MeOH at room temperature fortunately gave a much higher yield of **36** (85%). *N*-Alkylation of **36** with *p*-methoxyphenacyl bromide was accomplished to furnish lamellarin *O*-dimethyl ether (**37**)[9,26] in 90% yield. With **37** in hand, the conversion to **3** was identical to that reported by Fürstner.[26a] Hydrolysis of the methyl ester **37** with *t*-BuOK afforded the crude oxo-acid, which without isolation was allowed to react with Ac_2O−NaOAc to form the 1*H*-pyrrolo[2,1-*c*][1,4]oxazin-1-one **38**.[9,26] The three methoxy groups of **38** were easily converted to hydroxyls by treating **38** with BBr_3 in CH_2Cl_2 at −78 °C, affording lukianol A (**3**)[9,26] in 93% yield.

Experimental Section

3,4-Bis(trimethylsilyl)-1*H*-pyrrole-2-carbaldehyde (6). An aqueous NaOH solution prepared by dissolving NaOH (0.5 g) in H_2O (1 mL) was added to a solution of **5**[10,20] (211 mg, 1 mmol) in EtOH (1.5 mL) and $CHCl_3$ (3.7 mL) at 70 °C. The mixture was stirred at 70 °C for 1 h. After extraction with $CHCl_3$, washing with H_2O, drying (Na_2SO_4), filtration,and evaporation, the residue was chromatographed on silica gel (70 g, hexanes/Et_2O 5:2) to give **6** (71 mg, 30%) as needles: mp 93.5−94 °C; ^{1}H NMR ($CDCl_3$) δ 0.31 (s, 9H), 0.42 (s, 9H), 7.25 (d, J = 1.5 Hz, 1H), 9.48 (s, 1H), 10.51 (br. s, 1H); ^{13}C NMR ($CDCl_3$) δ 1.3, 2.8, 127.2, 133.6, 137.4, 140.5, 181.2; MS *m*/*z* 239 (M^+, 26). Anal. Calcd for $C_{11}H_{21}NOSi_2$: C, 55.17; H, 8.84; N, 5.85. Found: C, 54.95; H, 9.04; N, 5.76.

3-Trimethylsilyl-4-iodo-1*H*-pyrrole-2-carbaldehyde (7). (Procedure 1) To a solution of **6** (240 mg, 1 mmol) and CF_3CO_2Ag (221 mg, 1 mmol) in THF (15 mL) at −78 °C under N_2 was added dropwise a solution of I_2 (254 mg, 1 mmol) in THF (10 mL). The reaction mixture was stirred for 2 h at −78 °C. The resulting mixture was diluted with Et_2O and then filtered through Celite. The filtrate was washed succeccively with 50% $Na_2S_2O_3$, H_2O, and brine. After drying ($MgSO_4$), filtration, and evaporation, the residue was chromatographed on silica (15 g, hexanes/Et_2O 3:1) to afford **7** (263 mg, 90%) as a brown oil: ^{1}H NMR ($CDCl_3$) δ 0.46 (s, 9H), 7.26 (t, J = 1.5 Hz, 1H), 9.66 (s, 1H), 10.84 (br. s, 1H); ^{13}C NMR ($CDCl_3$) δ 1.1, 71.6, 132.7, 134.0, 138.4, 180.3; MS *m*/*z* 293 (M^+, 2). Anal. Calcd for $C_8H_{12}INOSi$: C, 32.77; H, 4.13; N, 4.78. Found: C, 32.92; H, 4.08; N, 4.68.

Methyl 3,4-Bis(trimethylsilyl)-1*H*-pyrrole-1-carboxylate (9a). (Procedure 2) To a solution of **8a**[20] (93 mg, 0.3 mmol) in THF (2 mL) was added *n*-BuLi (0.2 mL, 0.32 mmol) in hexane at −78 °C, and the mixture was stirred for 1 h. $ClCO_2Me$ (30 μL, 0.39 mmol) was then added, and the temperature was allowed to rise from −78 to 0 °C in 2 h. The mixture was then poured into H_2O and extracted with Et_2O. The ethereal extract was washed with H_2O and brine and dried over Na_2SO_4. After evaporation, the residue was chromatographed on silica gel (15 g, hexanes/Et_2O 60:1) to afford **9a** (28 mg, 35%) as a colorless oil: ^{1}H NMR ($CDCl_3$) δ 0.27 (s, 18H), 3.96 (s, 3H), 7.40 (s, 2H); ^{13}C NMR ($CDCl_3$) δ 0.4, 53.9, 126.9, 128.7, 150.5; MS *m*/*z* 269 (M^+, 17). Anal. Calcd for $C_{12}H_{23}NO_2Si_2$: C, 53.48; H, 8.60; N, 5.20. Found: C, 53.46; H, 8.69; N, 5.31.

1-(2-Methoxycarbonyl-4-toluenesulfonyl)-3,4-bis(trimethylsilyl)-1*H*-pyrrole (9b). According to Procedure 2, this compound was prepared by reaction of **8b**[20] (73 mg, 0.2 mmol) in THF (2 mL) with *n*-BuLi (130 μL, 0.21 mmol) in hexane at −78 °C for 1 h. $ClCO_2Me$ (17 μL, 0.22 mmol) was then added, and the temperature was allowed to rise from −78 to 0 °C in 2 h. Usual workup and purification by chromatography on silica gel (20 g, hexanes/CH_2Cl_2 5:2) gave **9b** (33.8 mg, 40%) as a colorless oil: ^{1}H NMR ($CDCl_3$) δ 0.25 (s, 18H), 2.42 (s, 3H), 4.00 (s, 3H), 7.29 (s, 2H), 7.34−7.39 (m, 2H), 7.58 (d, J = 8.1 Hz, 1H); ^{13}C NMR ($CDCl_3$) δ 0.8, 21.3, 53.2, 127.3, 128.6, 129.0, 129.7, 131.6, 132.7, 134.1, 144.9, 167.4; MS *m*/*z* 423 (M^+, 100); HRMS calcd for $C_{19}H_{29}NO_4SSi_2$ 423.1350, found 423.1344.

***N*,*N*-Dimethyl 2-Methoxycarbonyl-3,4-bis(trimethylsilyl)-1*H*-pyrrole-1-sulfonamide (10a), *N*,*N*-Dimethyl 2-Methoxycarbonyloxycarbonyl-3,4-bis(trimethylsilyl)-1*H*-pyrrole-1-sulfonamide (11), and Methyl 2,4-Bis(trimethylsilyl)-1*H*-pyrrole-1-carboxylate (12).** According to Procedure 2, these compounds were prepared by reaction of **8c**[10] (2.87 g, 9 mmol) in dry THF (60 mL) at −78 °C for 1 h until the mixture was warmed to −60 °C. A solution of $ClCO_2Me$ (1.16 mL, 15 mmol) in THF (6 mL) was added, and the mixture was stirred until warming to room temperature. Usual workup and purification by chromatography on silica gel (210 g, hexanes/Et_2O 5:2) afforded three components. Compound **10a** (1.97 g, 58%) as white crystals: mp 123 °C; ^{1}H NMR ($CDCl_3$) δ 0.24 (s, 9H), 0.27 (s, 9H), 2.89 (s, 6H), 3.84 (s, 3H), 7.11 (s, 1H); ^{13}C NMR ($CDCl_3$) δ 0.7, 0.9, 38.3, 52.5, 125.1, 126.6, 130.8, 133.3, 164.6; MS *m*/*z* 376 (M^+, 8). Anal. Calcd for $C_{14}H_{28}N_2O_4SSi_2$: C, 44.65; H, 7.49; N, 7.44. Found: C, 44.53; H, 7.69; N, 7.40. Compound **11** (1.02 g, 27%) as white solids: mp 109 °C; ^{1}H NMR ($CDCl_3$) δ 0.28 (s, 9H), 0.31 (s, 9H), 2.91 (s, 6H), 3.94 (s, 3H), 7.21 (s, 1H); ^{13}C NMR ($CDCl_3$) δ 0.9, 0.9, 38.2, 56.0, 125.9, 130.3, 131.9, 132.7, 148.9, 157.3; MS *m*/*z* 420 (M^+, 19). Anal. Calcd for $C_{15}H_{28}N_2O_6SSi_2$: C, 42.84; H, 6.72; N, 6.67. Found: C, 42.79; H, 6.76; N, 6.59. Compound **12** (24 mg, 1%) as colorless residue: ^{1}H NMR ($CDCl_3$) δ 0.21 (s, 9H), 0.27 (s, 9H), 3.96 (s, 3H), 6.49 (d, J = 0.9 Hz, 1H), 7.47 (d, J = 0.9 Hz, 1H); ^{13}C NMR ($CDCl_3$) δ −0.6, −0.4, 53.7, 122.6, 128.5, 130.0, 135.9, 151.5; MS *m*/*z* 269 (M^+, 5); HRMS calcd for $C_{12}H_{23}NO_2Si_2$ 269.1262, found 269.1288.

***N,N*-Dimethyl 2-Methoxycarbonyloxycarbonyl-3-trimethylsilyl-4-iodo-1*H*-pyrrole-1-sulfonamide (13).** This compound was prepared from **11** (210 mg, 0.5 mmol), I_2 (140 mg, 0.6 mmol) and CF_3CO_2Ag (121 mg, 0.6 mmol) according to Procedure 1. Purification by chromatography on silica gel (25 g, hexanes/Et_2O 7:3) afforded **13** (10 mg, 90%) as colorless crystals suitable for X-ray crystallographic study: mp 117 °C; ^{1}H NMR ($CDCl_3$) δ 0.37 (s, 9H), 2.93 (s, 6H), 3.95 (s, 3H), 7.30 (s, 1H); ^{13}C NMR ($CDCl_3$) δ −0.1, 38.4, 56.2, 70.7, 77.2, 128.0, 128.9, 129.9, 148.7, 156.3. Anal. Calcd for $C_{12}H_{19}IN_2O_6SSi$: C, 30.39; H, 4.04; N, 5.91. Found: C, 30.58; H, 3.99; N, 5.86.

***N,N*-Dimethyl 2-Ethoxycarbonyl-3,4-bis(trimethylsilyl)-1*H*-pyrrole-1-sulfonamide (10b).** According to Procedure 2, this compound was prepared by reaction of **8c**[10] (956 mg, 3 mmol) in THF (20 mL) and *n*-BuLi (2.25 mL, 3.6 mmol) in hexane at −78 °C for 1 h. $ClCO_2Et$ (287 μL, 3 mmol) was added, and the mixture was stirred until warming to room temperature. Usual workup and purification by chromatography on silica gel (80 g, hexanes/Et_2O 4:1) afforded **10b** (469 mg, 40%) as white crystals: mp 109 °C; ^{1}H NMR ($CDCl_3$) δ 0.25 (s, 9H), 0.27 (s, 9H), 1.36 (t, J = 1.2 Hz, 3H), 2.91 (s, 6H), 4.30 (q, J = 1.2 Hz, 2H), 7.11 (s, 1H); ^{13}C NMR ($CDCl_3$) δ 0.9, 0.9, 13.8, 38.3, 62.0, 125.1, 126.2, 130.6, 133.8, 164.4; MS *m/z* 390 (M^+, 27). Anal. Calcd for $C_{15}H_{30}N_2O_4SSi_2$: C, 46.12; H, 7.74; N, 7.17. Found: C, 45.99; H, 7.96; N, 7.38.

***N,N*-Dimethyl 2-(1-Hydroxybenzyl)-3,4-bis(trimethylsilyl)-1*H*-pyrrole-1-sulfonamide (10c).** According to Procedure 2, this compound was prepared by reaction of **8c**[10] (319 mg, 1 mmol) in THF (5 mL) and *n*-BuLi (0.75 mL, 1.2 mmol) in hexane at −78 °C for 1 h. Benzaldehyde (0.2 mL, 2 mmol) was added, and the mixture was stirred until warming to room temperature. Usual workup and purification by chromatography on silica gel (40 g, hexanes/Et_2O 5:1) afforded **10c** (220 mg, 52%) as white crystals: mp 101.5 °C; ^{1}H NMR ($CDCl_3$) δ 0.32 (s, 9H), 0.34 (s, 9H), 2.42 (s, 6H), 4.32 (d, J = 11.4 Hz, 1H), 6.26 (d, J = 11.4 Hz, 1H), 7.15 (s, 1H), 7.21−7.34 (m, 5H); ^{13}C NMR ($CDCl_3$) δ 1.3, 2.2, 37.4, 69.0, 124.5, 125.7, 126.8, 127.9, 128.1, 132.4, 142.2, 142.7; MS *m/z* 424 (M^+, 0.5). Anal. Calcd for $C_{19}H_{32}N_2O_3SSi_2$: C, 53.73; H, 7.59; N, 6.60. Found: C, 53.86; H, 7.86; N, 6.63.

***N,N*-Dimethyl 2-(1-Hydroxyethyl)-3,4-bis(trimethylsilyl)-1*H*-pyrrole-1-sulfonamide (10d).** According to Procedure 2, this compound was prepared by reaction of **8c**[10] (319 mg, 1 mmol) in THF (5 mL) and *n*-BuLi (0.75 mL, 1.2 mmol) in hexane at −78 °C for 1 h. Acetaldehyde (0.2 mL, 3.6 mmol) was added, and the mixture was stirred until warming to room temperature. Usual workup and purification by chromatography on silica gel (40 g, hexanes/Et_2O 3:1) afforded **10d** (170 mg, 47%) as white crystals: mp 83 °C; ^{1}H NMR ($CDCl_3$) δ 0.26 (s, 9H), 0.33 (s, 9H), 1.62 (d, J = 6.9 Hz, 3H), 2.88 (s, 6H), 3.56 (d, J = 10.5 Hz, 1H), 5.24 (dd, J = 10.5, 6.9 Hz, 1H), 7.04 (s, 1H); ^{13}C NMR (d_6-acetone) δ 1.5, 3.2, 24.4, 38.1, 64.3, 64.4, 123.2, 124.3, 131.7, 148.0; MS *m/z* 362 (M^+, 1); HRMS calcd for $C_{14}H_{30}N_2O_3SSi_2$ 362.1510; found 362.1501.

***N,N*-Dimethyl 2-Deuterio-3,4-bis(trimethylsilyl)-1*H*-pyrrole-1-sulfonamide (10e).** According to Procedure 2, this compound was prepared by reaction of **8c**[10] (319 mg, 1 mmol) in THF (5 mL) and *n*-BuLi (0.75 mL, 1.2 mmol) in hexane at −78 °C for 1 h. D_2O (36 μL, 2 mmol) was added, and the mixture was stirred until warming to room temperature. Usual workup and purification by chromatography on silica gel (40 g, hexanes/Et_2O 10:1) afforded **10e** (255 mg, 80%) as white crystals: mp 109 °C; ^{1}H NMR ($CDCl_3$) δ 0.27 (s, 18H), 2.81 (s, 6H), 7.13 (s, 1H); ^{13}C NMR ($CDCl_3$) δ 0.3, 38.3, 125.9, 128.9; MS *m/z* 319 (M^+, 16). Anal. Calcd for $C_{12}H_{25}DN_2O_2SSi_2$: C, 45.16; H, 7.90; N, 8.78. Found: C, 44.79; H, 8.07; N, 8.62.

***N,N*-Dimethyl 2-Methoxycarbonyl-3-trimethylsilyl-4-iodo-1*H*-pyrrole-1-sulfonamide (14).** This compound was prepared from **10a** (1.88 g, 5 mmol), I_2 (1.4 g, 5.5 mmol) and CF_3CO_2Ag (1.21 g, 5.5 mmol) according to Procedure 1. Purification by chromatography on silica gel (120 g, hexanes/Et_2O 7:3) afforded **14** (2.14 g, 100%) as a brown residue: ^{1}H NMR ($CDCl_3$) δ 0.29 (s, 9H), 2.89 (s, 6H), 3.83 (s, 3H), 7.20 (s, 1H); ^{13}C NMR ($CDCl_3$) δ −0.5, 38.3, 52.8, 70.4, 124.0, 127.9, 131.8, 163.4; MS *m/z* 430 (M^+, 12). Anal. Calcd for $C_{11}H_{19}IN_2O_4SSi$: C, 30.70; H, 4.45; N, 6.51. Found: C, 30.69; H, 4.43; N, 6.49.

***N,N*-Dimethyl 2-Methoxycarbonyl-3-trimethylsilyl-4-trimethylsilylethynyl-1*H*-pyrrole-1-sulfonamide (15a). (Procedure 3)** $PdCl_2(PPh_3)_2$ (25 mg, 0.03 mmol) and CuI (38 mg, 0.2 mmol) were added to a solution of **14** (129 mg, 0.3 mmol), trimethylsilylethyne (67 μL, 0.47 mmol), and Et_2NH (1 mL). This mixture was stirred for 10 h at room temperature under N_2. After evaporation, the residue was chromatographed on silica gel (40 g, hexanes/Et_2O 3:1) to afford **15a** (120 mg, 100%) as needles: mp 86 °C; ^{1}H NMR ($CDCl_3$) δ 0.21 (s, 9H), 0.27 (s, 9H), 2.91 (s, 6H), 3.83 (s, 3H), 7.32 (s, 1H); ^{13}C NMR ($CDCl_3$) δ −0.7, −0.3, 38.4, 52.7, 96.7, 99.2, 111.9, 125.2, 128.0, 130.4, 163.5; MS *m/z* 400 (M^+, 0.4). Anal. Calcd for $C_{16}H_{28}N_2O_4SSi$: C, 47.97; H, 7.04; N, 6.99. Found: C, 47.92; H, 7.03; N, 6.99.

***N,N*-Dimethyl 2-Methoxycarbonyl-3-trimethylsilyl-4-(3-methoxypropynyl)-1*H*-pyrrole-1-sulfonamide (15b).** This compound was prepared from $PdCl_2(PPh_3)_2$ (25 mg, 0.03 mmol), CuI (40 mg, 0.2 mmol), **14** (129 mg, 0.3 mmol), 3-methoxypropyne (36 μL, 0.4 mmol), and Et_2NH (1 mL) according to Procedure 3. Purification by chromatography on silica gel (30 g, hexanes/Et_2O 4:3) afforded **15b** (56 mg, 50%) as needles: mp 76 °C; ^{1}H NMR ($CDCl_3$) δ 0.27 (s, 9H), 2.91 (s, 6H), 3.41 (s, 3H), 3.84 (s, 3H), 4.26 (s, 2H), 7.31 (s, 1H); ^{13}C NMR ($CDCl_3$) δ −0.6, 38.3, 52.6, 57.6, 60.4, 80.5, 87.0, 111.1, 125.1, 128.1, 130.5, 163.3; MS *m/z* 372 (M^+, 28). Anal. Calcd for $C_{15}H_{24}N_2O_5SSi$: C, 48.37; H, 6.49; N, 7.52. Found: C, 48.12; H, 6.44; N, 7.42.

***N,N*-Dimethyl 2-Methoxycarbonyl-3-trimethylsilyl-4-(*trans*-2-cyanoethenyl)-1*H*-pyrrole-1-sulfonamide (*trans*-16a) and *N,N*-Dimethyl 2-Methoxycarbonyl-3-trimethylsilyl-4-(*cis*-2-cyanoethenyl)-1*H*-pyrrole-1-sulfonamide (*cis*-16a). (Procedure 4)** To a solution of **14** (430 mg, 1 mmol) in DMF (10 mL) was added acrylonitrile (0.9 mL, 13.7 mmol), Et_3N (4 mL), and $PdCl_2(PPh_3)_2$ (100 mg, 0.14 mmol) at room temperature. The reaction mixture was refluxed with stirring at 110 °C for 5 h under N_2. After that the mixture was extracted with Et_2O, washed with H_2O, dried (Na_2SO_4), filtered, and evaporated. The residue was chromatographed on silica gel (50 g, hexanes/EtOAc 4:1) to afford two components. Compound *trans*-**16a** (149 mg, 42%) as yellow solids: mp 110 °C; ^{1}H NMR ($CDCl_3$) δ 0.26 (s, 9H), 2.95 (s, 6H), 3.86 (s, 3H), 5.61 (d, J = 16.5 Hz, 1H), 7.33 (d, J = 16.5 Hz, 1H), 7.42 (s, 1H); ^{13}C NMR ($CDCl_3$) δ 0.1, 38.3, 52.7, 95.9, 118.0, 122.5, 122.9, 125.5, 132.1, 144.0, 163.2; MS *m/z* 355 (M^+, 22). Anal. Calcd for $C_{14}H_{21}N_3O_4SSi$: C, 47.30; H, 5.95; N, 11.82. Found: C, 46.95; H, 6.02; N, 11.87. Compound *cis*-**16a** (60 mg, 17%) as yellow solids: mp 95 °C; ^{1}H NMR ($CDCl_3$) δ 0.24 (s, 9H), 2.98 (s, 6H), 3.86 (s, 3H), 5.32 (d, J = 11.7 Hz, 1H), 7.12 (d, J = 11.7 Hz, 1H), 7.94 (s, 1H); ^{13}C NMR ($CDCl_3$) δ 0.1, 38.5, 52.8, 94.3, 117.8, 122.6, 124.0, 124.4, 131.7, 142.5, 163.5; MS *m/z* 355 (M^+, 25). Anal. Calcd for $C_{14}H_{21}N_3O_4SSi$: C, 47.30; H, 5.95; N, 11.82. Found: C, 47.17; H, 6.01; N, 11.82.

***N,N*-Dimethyl 2-Methoxycarbonyl-3-trimethylsilyl-4-(*trans*-2-methoxycarbonylethenyl)-1*H*-pyrrole-1-sulfonamide (*trans*-16b).** This compound was prepared from **14** (645 mg, 1.5 mmol), methyl acrylate (1.86 mL, 20.7 mmol), $PdCl_2(PPh_3)_2$ (150 mg, 0.2 mmol), and Et_3N (6 mL) in DMF (15 mL) according to Procedure 4. Purification by chromatography on silica gel (40 g, hexanes/EtOAc 3:1) afforded *trans*-**16b** (524 mg, 90%) as colorless needles: mp 96 °C; ^{1}H NMR ($CDCl_3$) δ 0.26 (s, 9H), 2.93 (s, 6H), 3.77 (s, 3H), 3.85 (s, 3H), 6.15 (d, J = 15.9 Hz, 1H), 7.41 (s, 1H), 7.63 (d, J = 15.6 Hz, 1H); ^{13}C NMR ($CDCl_3$) δ 0.1, 38.3, 51.6, 52.6, 117.7, 122.4, 123.4, 126.2, 131.9, 138.1, 163.5, 167.1; MS *m/z* 389 (MH^+, 57). Anal. Calcd for $C_{15}H_{24}N_2O_6SSi$: C, 46.37; H, 6.23; N, 7.21. Found: C, 46.19; H, 6.23; N, 7.17.

***N,N*-Dimethyl 2-Methoxycarbonyl-3-trimethylsilyl-4-(*cis*-2-acetylethenyl)-1*H*-pyrrole-1-sulfonamide (*cis*-16c).** This compound was prepared from **14** (430 mg, 1 mmol), methyl vinyl ketone (1.17 mL, 14 mmol), $PdCl_2(PPh_3)_2$ (100 mg, 0.14 mmol), and Et_3N (4 mL) in DMF (10 mL) according to Procedure 4. Purification by chromatography on silica gel

(30 g, hexanes/EtOAc 3:1) afforded *cis*-**16c** (332 mg, 89%) as a dark brown residue: ^{1}H NMR ($CDCl_3$) δ 0.02 (s, 9H), 2.97 (s, 6H), 3.83 (s, 3H), 3.88 (s, 3H), 6.88 (d, J = 8.7 Hz, 1H), 7.06 (s, 1H), 7.19 (d, J = 8.7 Hz, 1H); ^{13}C NMR ($CDCl_3$) δ 0.3, 27.2, 38.4, 52.7, 122.6, 123.7, 126.2, 127.3, 132.1, 136.8, 163.4, 197.9; MS m/z 373 (MH^+, 4). Anal. Calcd for $C_{15}H_{24}N_2O_5SSi$: C, 48.37; H, 6.49; N, 7.52. Found: C, 48.75; H, 6.43; N, 7.71.

***N,N*-Dimethyl 2-Methoxycarbonyl-3-trimethylsilyl-4-phenyl-1*H*-pyrrole-1-sulfonamide (17a). (Procedure 5)** To a solution of **14** (258 mg, 0.6 mmol), benzeneboronic acid (73 mg, 0.6 mmol), and $Pd(PPh_3)_4$ (30 mg, 0.03 mmol) in MeOH/toluene (1:1, 2 mL) was added a 2 M Na_2CO_3 solution (0.3 mL). The resulting mixture was heated at 90−100 °C for 2 h and was then poured into ice water. After extraction with Et_2O, washing with H_2O, drying (Na_2SO_4), filtration, and evaporation, the residue was chromatographed on silica gel (35 g, hexanes/EtOAc 30:13) to give **17a** (140 mg, 60%) as white crystals: mp 160 °C; ^{1}H NMR ($CDCl_3$) δ 0.01 (s, 9H), 2.97 (s, 6H), 3.88 (s, 3H), 7.10 (s, 1H), 7.27−7.35 (m, 5H); ^{13}C NMR ($CDCl_3$) δ 0.2, 38.4, 52.5, 122.4, 123.8, 127.3, 127.9, 129.5, 131.3, 132.9, 135.8, 163.8; MS m/z 380 (M^+, 29). Anal. Calcd for $C_{17}H_{24}N_2O_4SSi$: C, 53.66; H, 6.36; N, 7.36. Found: C, 53.26; H, 6.19; N, 7.27.

***N,N*-Dimethyl 2-Methoxycarbonyl-3-trimethylsilyl-4-(*p*-methoxyphenyl)-1*H*-pyrrole-1-sulfonamide (17b).** This compound was prepared from **14** (860 mg, 2 mmol), *p*-methoxybenzeneboronic acid (365 mg, 2.4 mmol), $Pd(PPh_3)_4$ (116 mg, 0.1 mmol), and 2 M Na_2SO_4 (0.8 mL) in MeOH/toluene (1:1, 6 mL) according to Procedure 5. Purification by chromatography on silica gel (35 g, hexanes/Et_2O 7:3) afforded **17b** (804 mg, 98%) as needles: mp 117 °C; ^{1}H NMR ($CDCl_3$) δ 0.02 (s, 9H), 2.97 (s, 6H), 3.83 (s, 3H), 3.88 (s, 3H), 6.88 (d, J = 8.7 Hz, 2H), 7.06 (s, 1H), 7.19 (d, J = 8.7 Hz, 2H); ^{13}C NMR ($CDCl_3$) δ 0.2, 38.4, 52.5, 55.2, 113.3, 122.4, 123.9, 128.1, 130.6, 131.2, 132.5, 159.0, 163.8; MS m/z 410 (M^+, 9). Anal. Calcd for $C_{18}H_{26}N_2O_5SSi$: C, 52.66; H, 6.38; N, 6.82. Found: C, 52.46; H, 6.49; N, 6.80.

***N,N*-Dimethyl 2-Methoxycarbonyl-3-iodo-4-trimethylsilylethynyl-1*H*-pyrrole-1-sulfonamide (18).** This compound was prepared from **15a** (601 mg, 1.5 mmol), I_2 (419 mg, 1.5 mmol,) and CF_3CO_2Ag (663 mg, 3 mmol) according to Procedure 1. Purification by chromatography on silica gel (40 g, hexanes/EtOAc 4:1) afforded **18** (559 mg, 82%) as yellow crystals: mp 142 °C; ^{1}H NMR ($CDCl_3$) δ 0.26 (s, 9H), 2.92 (s, 6H), 3.84 (s, 3H), 7.33 (s, 1H); ^{13}C NMR ($CDCl_3$) δ −0.6, 7.7, 38.4, 52.7, 87.9, 112.1, 125.8, 129.0, 130.3, 163.2; MS m/z 454 (M^+, 35). Anal. Calcd for $C_{13}H_{19}IN_2O_4SSi$: C, 34.37; H, 4.21; N, 6.17. Found: C, 34.34; H, 4.25; N, 6.03.

***N,N*-Dimethyl 2-Methoxycarbonyl-3-(*p*-methoxyphenyl)-4-trimethylsilylethynyl-1*H*-pyrrole-1-sulfonamide (19).** This compound was prepared from **18** (318 mg, 0.7 mmol), *p*-methoxybenzeneboronic acid (128 mg, 0.84 mmol), $Pd(PPh_3)_4$ (50 mg, 0.04 mmol), and 2 M Na_2SO_4 (0.5 mL) in MeOH/toluene (1:1, 3 mL) according to Procedure 5. Purification by chromatography on silica gel (40 g, hexanes/Et_2O 7:3) afforded **19** (260 mg, 86%) as white crystals: mp 129 °C; ^{1}H NMR ($CDCl_3$) δ 0.33 (s, 9H), 2.94 (s, 6H), 3.81 (s, 3H), 3.86 (s, 3H), 6.87 (d, J = 8.7 Hz, 2H), 7.36 (s, 1H), 7.41 (d, J = 9.0 Hz, 2H); ^{13}C NMR ($CDCl_3$) δ −0.6, 38.4, 52.6, 55.3, 82.2, 91.1, 112.2, 114.0, 115.4, 125.0, 127.0, 130.6, 132.5, 159.5, 163.5; MS m/z 434 (M^+, 100). Anal. Calcd for $C_{20}H_{26}N_2O_5SSi$: C, 55.28; H, 6.03; N, 6.45. Found: C, 55.25; H, 6.11; N, 6.41.

***N,N*-Dimethyl 2-Methoxycarbonyl-3-iodo-4-(*p*-methoxyphenyl)-1*H*-pyrrole-1-sulfonamide (20).** This compound was prepared from **17b** (164 mg, 0.4 mmol), I_2 (112 mg, 0.4 mmol), and CF_3CO_2Ag (88 mg, 0.4 mmol) according to Procedure 1. Purification by chromatography on silica gel (40 g, hexanes/EtOAc 4:1) afforded **20** (145 mg, 78%) as yellow crystals: mp 129 °C; ^{1}H NMR ($CDCl_3$) δ 3.01 (s, 6H), 3.84 (s, 3H), 3.94 (s, 3H), 6.95 (d, J = 9.0 Hz, 2H), 7.22 (s, 1H), 7.37 (d, J = 9.0 Hz, 2H); ^{13}C NMR ($CDCl_3$) δ 38.5, 52.7, 55.3, 75.8, 113.7, 122.4, 125.4, 128.2, 129.6, 130.2, 159.4, 161.4; MS m/z 464 (M^+, 40). Anal. Calcd for $C_{15}H_{17}IN_2O_5S$: C, 38.81; H, 3.69; N, 6.03. Found: C, 38.71; H, 3.63; N, 6.00.

***N,N*-Dimethyl 2-Methoxycarbonyl-3-phenylethynyl-4-(*p*-methoxyphenyl)-1*H*-pyrrole-1-sulfonamide (21).** This compound was prepared from $PdCl_2(PPh_3)_2$ (75 mg, 0.09 mmol), CuI (120 mg, 0.6 mmol), **20** (464 mg, 1 mmol), phenylethyne (329 μL, 3 mmol), and Et_2NH (3 mL) according to Procedure 3. Purification by chromatography on silica gel (40 g, hexanes/EtOAc 6:1) afforded **21** (263 mg, 60%) as yellow crystals: mp 154 °C; ^{1}H NMR ($CDCl_3$) δ 3.03 (s, 6H), 3.85 (s, 3H), 3.99 (s, 3H), 6.98 (d, J = 8.7 Hz, 2H), 7.34−7.36 (m, 3H), 7.44−7.49 (m, 3H), 7.69 (d, J = 8.7 Hz, 2H); ^{13}C NMR ($CDCl_3$) δ 38.5, 52.2, 55.2, 82.1, 96.1, 113.4, 113.9, 123.1, 124.1, 124.6, 126.9, 127.1, 128.3, 128.5, 128.7, 131.4, 159.2, 160.1; MS m/z 438 (M^+, 100). Anal. Calcd for $C_{23}H_{22}N_2O_5S$: C, 63.00; H, 5.06; N, 6.39. Found: C, 62.99; H, 5.26; N, 6.10.

Methyl 3-Iodo-4-(*p*-methoxyphenyl)-1*H*-pyrrole-2-carboxylate (22). A solution of **20** (93 mg, 0.2 mmol) and *n*-Bu_4NF (0.4 mL, 0.4 mmol) in THF (6 mL) was stirred at 60 °C for 4 h. After extraction with EtOAc, washing with H_2O, drying (Na_2SO_4), filtration, and evaporation, the residue was chromatographed on silica gel (30 g, hexanes/EtOAc 4:1) to give **22** (47 mg, 65%) as yellow crystals: mp 131 °C; ^{1}H NMR ($CDCl_3$) δ 3.85 (s, 3H), 3.92 (s, 3H), 6.95 (d, J = 8.7 Hz, 2H), 7.00 (d, J = 3.3 Hz, 1H), 7.40 (d, J = 8.7 Hz, 2H), 9.53 (br. s, 1H); ^{13}C NMR ($CDCl_3$) δ 51.6, 55.3, 71.9, 113.6, 120.9, 123.6, 127.0, 130.3, 131.4, 158.9, 160.5; MS m/z 357 (M^+, 26). Anal. Calcd for $C_{13}H_{12}INO_3$: C, 43.72; H, 3.39; N, 3.92. Found: C, 43.65; H, 3.26; N, 3.79.

Methyl 3-Phenylethynyl-4-(*p*-methoxyphenyl)-1*H*-pyrrole-2-carboxylate (23). A solution of **21** (170 mg, 0.4 mmol) and *n*-Bu_4NF (0.8 mL, 0.8 mmol) in THF (12 mL) was stirred at 70 °C for 1.5 h. After extraction with EtOAc, washing with H_2O, drying (Na_2SO_4), filtration, and evaporation, the residue was chromatographed on silica gel (20 g, hexanes/EtOAc 4:1) to give **23** (116 mg, 90%) as yellow crystals: mp 162 °C; ^{1}H NMR ($CDCl_3$) δ 3.85 (s, 3H), 3.98 (s, 3H), 6.97 (dd, J = 6.9, 1.8 Hz, 2H), 7.07 (d, J = 3.0 Hz, 1H), 7.33−7.35 (m, 3H), 7.50−7.53 (m, 2H), 7.73 (dd, J = 6.9, 1.8 Hz, 2H), 9.49 (br. s, 1H); ^{13}C NMR ($CDCl_3$) δ 51.8, 55.3, 83.7, 94.9, 113.8, 119.6, 123.8, 124.6, 126.4, 128.0, 128.3, 128.4, 128.7, 131.4, 158.6, 161.2; MS m/z 331 (M^+, 100). Anal. Calcd for $C_{21}H_{17}NO_3$: C, 76.11; H, 5.17; N, 4.23. Found: C, 76.19; H, 5.08; N, 4.10.

1-(*tert*-Butoxycarbonyl)-3-bromo-4-trimethylsilyl-1*H*-pyrrole (24a). (Procedure 6) To a solution of **8a**[20] (311 mg, 1 mmol) in THF (20 mL) cooled at −10 °C was added solid NBS (178 mg, 1 mmol,) and the mixture was stirred for 2 h. 50% $Na_2S_2O_3$ (30 mL) and Et_2O (150 mL) were then added. The ethereal layer was separated, washed with H_2O, dried over Na_2SO_4, and evaporated. The residue was purified by chromatography on silica gel (40 g, hexanes/Et_2O 100:1) to afford **24a** (277 mg, 87%) as colorless crystals: mp 40−41 °C; ^{1}H NMR ($CDCl_3$) δ 0.28 (s, 9H), 1.61 (s, 9H), 7.13 (d, J = 1.9 Hz, 1H), 7.28 (d, J = 2.4 Hz, 1H); ^{13}C NMR ($CDCl_3$) δ −1.1, 27.9, 84.3, 106.2, 120.8, 123.1, 125.9, 147.7; MS m/z 317 (M^+, 60). Anal. Calcd for $C_{12}H_{20}BrNO_2Si$: C, 45.28; H, 6.33; N, 4.40. Found: C, 45.30; H, 6.56; N, 4.30.

1-(*tert*-Butoxycarbonyl)-2,4-bis(trimethylsilyl)-3-bromo-1*H*-pyrrole (25a). This compound was prepared from **8a**[20] (31 mg, 0.1 mmol) and NBS (18 mg, 0.1 mmol) at room temperature according to Procedure 6. Purification by chromatography on silica gel (15 g, hexanes/Et_2O 100:1) afforded two compounds, compound **24a** (12 mg, 37%), whose spectral data were identical to those of an authentic sample prepared previously, and compound **25a** (9.4 mg, 24%) as colorless crystals: mp 40−41 °C; ^{1}H NMR ($CDCl_3$) δ 0.29 (s, 9H), 0.38 (s, 9H), 1.59 (s, 9H), 7.22 (s, 1H); ^{13}C NMR ($CDCl_3$) δ −0.9, 1.9, 27.9, 83.9, 118.7, 124.2, 130.5, 132.2, 148.6; MS m/z 389 (M^+, 20). Anal. Calcd for $C_{15}H_{28}BrNO_2Si_2$: C, 46.14; H, 7.23; N, 3.59. Found: C, 45.86; H, 7.41; N, 3.39.

1-(*tert*-Butoxycarbonyl)-2,4-bis(trimethylsilyl)-1*H*-pyrrole. According to Procedure 2, to a solution of **25a** (59 mg, 0.15 mmol) in THF (3 mL) cooled at −70 °C under N_2 was added a solution of *n*-BuLi (0.11 mL, 0.18 mmol) in hexane. The mixture was stirred for 1 h, and H_2O (2 mL) in THF (1 mL) was added. The resulting mixture was again stirred for 1 h during which time the reaction was allowed to rise to −60

°C. The mixture was then poured into H_2O (10 mL) and was extracted with Et_2O. The ethereal extract was washed with H_2O and brine and was dried over Na_2SO_4. After evaporation, the residue was chromatographed on silica gel (15 g, hexanes) to give 1-(*tert*-butoxycarbonyl)-2,4-bis(trimethylsilyl)-1*H*-pyrrole (39 mg, 85%) as colorless crystals: mp 44 °C; ^{1}H NMR ($CDCl_3$) δ 0.21 (s, 9H), 0.27 (s, 9H), 1.60 (s, 9H), 6.47 (d, J = 1.5 Hz, 1H), 7.36 (d, J = 1.5 Hz, 1H); ^{13}C NMR ($CDCl_3$) δ −0.5, −0.3, 28.0, 83.3, 121.7, 127.8, 129.7, 135.8, 149.5; MS *m*/*z* 311 (M^+, 34). Anal. Calcd for $C_{15}H_{29}NO_2Si_2$: C, 57.82; H, 9.38; N, 4.49. Found: C, 57.55; H, 9.67; N, 4.43.

1-(*p*-Toluenesulfonyl)-3-bromo-4-trimethylsilyl-1*H*-pyrrole (24b) and 1-(*p*-Toluenesulfonyl)-2,4-bis(trimethylsilyl)-3-bromo-1*H*-pyrrole (25b). These compounds were prepared from **8b**[20] (731 mg, 2 mmol) and NBS (356 mg, 2 mmol) at room temperature according to Procedure 6. Purification by chromatography on silica gel (40 g, hexanes/Et_2O 8:1) afforded two components. Compound **24b** (208 mg, 28%) as colorless crystals: mp 86 °C; ^{1}H NMR ($CDCl_3$) δ 0.25 (s, 9H), 2.42 (s, 3H), 7.01 (d, J = 2.1 Hz, 1H), 7.20 (d, J = 2.4 Hz, 1H), 7.32 (d, J = 8.1 Hz, 2H), 7.77 (d, J = 8.1 Hz, 2H); ^{13}C NMR ($CDCl_3$) δ −1.2, 21.7, 107.5, 120.7, 124.6, 126.0, 127.1, 130.2, 135.5, 145.4; MS *m*/*z* 373 (M^+, 50). Anal. Calcd for $C_{14}H_{18}BrNO_2SSi$: C, 45.16; H, 4.87; N, 3.76. Found: C, 45.33; H, 4.95; N, 3.58. Compound **25b** (355 mg, 40%) as colorless crystals: mp 89 °C; ^{1}H NMR ($CDCl_3$) δ 0.28 (s, 9H), 0.35 (s, 9H), 2.42 (s, 3H), 7.28 (d, J = 9.3 Hz, 2H), 7.33 (s, 1H), 7.43 (d, J = 8.4 Hz, 2H); ^{13}C NMR ($CDCl_3$) δ −1.0, 2.2, 21.5, 120.8, 125.8, 129.8, 132.8, 133.6, 137.1, 144.6; MS *m*/*z* 445 (M^+, 5). Anal. Calcd for $C_{17}H_{26}BrNO_2SSi_2$: C, 45.93; H, 5.89; N, 3.15. Found: C, 45.93; H, 6.11; N, 2.99.

3-Bromo-1*H*-pyrrole.[25] A solution of **25b** (44 mg, 0.1 mmol) and *n*-Bu_4NF (0.3 mL, 0.3 mmol) in THF (4 mL) was stirred at 66 °C for 2 h. After extraction with Et_2O, washing with H_2O, drying (Na_2SO_4), filtration, and evaporation, the residue was chromatographed on silica gel (10 g, hexanes/EtOAc 10:1) to give 3-bromo-1*H*-pyrrole (11 mg, 78%) as an unstable oil, whose spectroscopic data were identical to those reported.[25]

***N*,*N*-Dimethyl 3-Bromo-4-trimethylsilyl-1*H*-pyrrole-1-sulfonamide (24c) and *N*,*N*-Dimethyl 2,4-Bis(trimethylsilyl)-3-bromo-1*H*-pyrrole-1-sulfonamide (25c).** These compounds were prepared from **8c**[10] (9.54 g, 30 mmol) and NBS (5.87 g, 33 mmol) at room temperature according to Procedure 6. Purification by chromatography on silica gel (150 g, hexanes/Et_2O 15:1) afforded two components. Compound **24c** (2.15 g, 22%) as white crystals: mp 96 °C; ^{1}H NMR ($CDCl_3$) δ 0.28 (s, 9H), 2.82 (s, 6H), 6.93 (d, J = 2.4 Hz, 1H), 7.13 (d, J = 2.4 Hz, 1H); ^{13}C NMR ($CDCl_3$) δ −1.1, 38.3, 106.0, 121.0, 122.7, 126.6; MS *m*/*z* 325 (M^+, 2). Anal. Calcd for $C_9H_{17}BrN_2O_2SSi$: C, 33.23; H, 5.27; N, 8.61. Found: C, 32.88; H, 5.16; N, 8.62. Compound **25c** (6.55 g, 55%) as colorless crystals: mp 81−82 °C; ^{1}H NMR ($CDCl_3$) δ 0.29 (s, 9H), 0.44 (s, 9H), 2.80 (s, 6H), 7.09 (s, 1H); ^{13}C NMR ($CDCl_3$) δ −1.0, 2.2, 38.3, 119.3, 124.7, 131.6, 133.0; MS *m*/*z* 398 (M^+, 2). Anal. Calcd for $C_{12}H_{25}BrN_2O_2SSi$: C, 36.26; H, 6.34; N, 7.05. Found: C, 36.04; H, 6.42; N, 7.02.

1-Triisopropylsilyl-3-bromo-4-trimethylsilyl-1*H*-pyrrole (24d).[27] This compound was prepared from **8d**[10] (36.7 mg, 0.1 mmol) in THF (2 mL) and NBS (17.8 mg, 0.1 mmol) according to Procedure 6. Purification by chromatography on silica gel (20 g, hexanes) gave **24d** (34.4 mg, 92%) as a colorless liquid: ^{1}H NMR ($CDCl_3$) δ 0.27 (s, 9H), 1.09 (d, J = 7.4 Hz, 18H), 1.40 (sept, J = 7.4 Hz, 3H), 6.61 (d, J = 2.2 Hz, 1H), 6.79 (d, J = 2.2 Hz, 1H); ^{13}C NMR ($CDCl_3$) δ 0.6, 11.6, 17.7, 104.0, 120.2, 124.8, 130.7; MS *m*/*z* 375 (M^+, 70).

***N*,*N*-Dimethyl 2,4-Bis(trimethylsilyl)-3-methyl-1*H*-pyrrole-1-sulfonamide (26).** According to Procedure 2, this compound was prepared by reaction of **25c** (40 mg, 0.1 mmol) in a solution of HMPA (19 μL, 0.11 mmol) and THF (1 mL). A solution of *n*-BuLi (75 μL, 0.12 mmol) in hexane was added, and the mixture was stirred at −78 °C for 1 h. Me_2SO_4 (10 μL, 0.11 mmol) was added, and the mixture was stirred for 1 h until warming to room temperature. Usual workup and purification by chromatography on silica gel (15 g, hexanes/Et_2O 40:3) afforded **26** (30 mg, 90%) as a colorless oil: ^{1}H NMR ($CDCl_3$) δ 0.14 (s, 9H), 0.15 (s, 9H), 2.83 (s, 6H), 3.54 (s, 3H), 6.62 (s, 1H); ^{13}C NMR ($CDCl_3$) δ −1.9, −0.1, 34.9, 38.1, 97.4, 101.2, 103.6, 139.0; MS *m*/*z* 332 (M^+, 89). Anal. Calcd for $C_{13}H_{28}N_2O_2SSi_2$: C, 46.95; H, 8.49; N, 8.42. Found: C, 46.55; H, 8.45; N, 8.48.

***N*,*N*-Dimethyl 2,4-Bis(trimethylsilyl)-3-(*p*-methoxyphenyl)-1*H*-pyrrole-1-sulfonamide (27).** This compound was prepared from **25c** (397 mg, 1 mmol), *p*-methoxybenzeneboronic acid (152 mg, 1 mmol), $Pd(PPh_3)_4$ (63 mg, 0.04 mmol), and 2 M Na_2SO_4 (0.6 mL) in MeOH/toluene (1:1, 4 mL) according to Procedure 5. Purification by chromatography on silica gel (100 g, hexanes/Et_2O 16:1) afforded **27** (302 mg, 71%) as white solids: mp 97 °C; ^{1}H NMR ($CDCl_3$) δ −0.05 (s, 9H), 0.01 (s, 9H), 2.83 (s, 6H), 3.83 (s, 3H), 6.84 (d, J = 8.4 Hz, 2H), 7.09 (d, J = 8.7 Hz, 2H), 7.18 (s, 1H); ^{13}C NMR ($CDCl_3$) δ −0.3, 1.6, 38.3, 55.1, 112.7, 124.3, 130.8, 131.0, 131.7, 133.1, 145.1, 158.9; MS *m*/*z* 424 (M^+, 1). Anal. Calcd for $C_{19}H_{32}N_2O_3SSi_2$: C, 53.73; H, 7.59; N, 6.60. Found: C, 53.69; H, 7.49; N, 6.53.

***N*,*N*-Dimethyl 2,4-Bis(trimethylsilyl)-3-(*trans*-2-methoxycarbonylethenyl)-1*H*-pyrrole-1-sulfonamide (28).** This compound was prepared from **25c** (1.19 g, 3 mmol), methyl acrylate (3.7 mL, 41.5 mmol), $PdCl_2(PPh_3)_2$ (300 mg, 0.4 mmol), and Et_3N (12 mL) in DMF (30 mL) according to Procedure 4. Purification by chromatography on silica gel (36 g, hexanes/Et_2O 7:1) afforded **28** (965 mg, 80%) as colorless needles: mp 100 °C; ^{1}H NMR ($CDCl_3$) δ 0.26 (s, 9H), 0.38 (s, 9H), 2.81 (s, 6H), 3.80 (s, 3H), 6.01 (d, J = 15.9 Hz, 1H), 7.15 (s, 1H), 7.90 (d, J = 15.9 Hz, 1H); ^{13}C NMR ($CDCl_3$) δ −0.1, 2.3, 38.2, 51.5, 121.2, 122.0, 132.3, 137.4, 138.3, 142.1, 166.9; MS *m*/*z* 402 (M^+, 1). Anal. Calcd for $C_{16}H_{30}N_2O_4SSi_2$: C, 47.73; H, 7.51; N, 6.96. Found: C, 47.93; H, 7.51; N, 7.15.

***N*,*N*-Dimethylsilyl 2-Iodo-3-(*trans*-2-methoxycarbonylethenyl)-4-trimethylsilyl-1*H*-pyrrole-1-sulfonamide (29).** This compound was prepared from **28** (805 mg, 2 mmol), I_2 (558 mg, 2.2 mmol), and CF_3CO_2Ag (968 mg, 4.4 mmol) according to Procedure 1. Purification by chromatography on silica gel (50 g, hexanes/EtOAc 7:1) afforded **29** (821 mg, 90%) as a yellow residue: ^{1}H NMR ($CDCl_3$) δ 0.28 (s, 9H), 2.96 (s, 6H), 3.80 (s, 3H), 6.39 (d, J = 16.2 Hz, 1H), 7.46 (s, 1H), 7.61 (d, J = 16.2 Hz, 1H); ^{13}C NMR ($CDCl_3$) δ −0.4, 38.5, 51.7, 74.1, 119.8, 121.3, 133.6, 134.7, 139.8, 167.2; MS *m*/*z* 456 (M^+, 59). Anal. Calcd for $C_{13}H_{21}IN_2O_4SSi$: C, 34.21; H, 4.64; N, 6.14. Found: C, 34.64; H, 4.73; N, 6.05.

***N*,*N*-Dimethyl 2-(*p*-methoxyphenyl)-3-(*trans*-2-methoxycarbonylethenyl)-4-trimethylsilyl-1*H*-pyrrole-1-sulfonamide (30).** This compound was prepared from **29** (1.36 g, 3 mmol), *p*-methoxybenzeneboronic acid (456 mg, 3 mmol), $Pd(PPh_3)_4$ (230 mg, 0.2 mmol), and 2 M Na_2SO_4 (1 mL) in MeOH/toluene (1:1, 9 mL) according to Procedure 5. Purification by chromatography on silica gel (90 g, hexanes/EtOAc 11:2) afforded **30** (1.31 g, 100%) as brown solids: mp 117 °C; ^{1}H NMR ($CDCl_3$) δ 0.32 (s, 9H), 2.42 (s, 6H), 3.67 (s, 3H), 3.85 (s, 3H), 5.83 (d, J = 16.2 Hz, 1H), 6.96 (d, J = 8.7 Hz, 2H), 7.22 (s, 1H), 7.31 (d, J = 8.7 Hz, 2H), 7.37 (d, J = 16.2 Hz, 1H); ^{13}C NMR ($CDCl_3$) δ −0.2, 37.0, 51.4, 55.3, 113.6, 117.2, 118.4, 122.0, 126.4, 130.9, 133.0, 139.0, 160.2, 167.8; MS *m*/*z* 436 (M^+, 100). Anal. Calcd for $C_{20}H_{28}N_2O_5SSi$: C, 55.02; H, 6.46; N, 6.42. Found: C, 54.98; H, 6.65; N, 6.30.

***N*,*N*-Dimethyl 2-(*p*-Methoxyphenyl)-3-(*trans*-2-methoxycarbonylethenyl)-4-iodo-1*H*-pyrrole-1-sulfonamide (31).** This compound was prepared from **30** (436 mg, 1 mmol), I_2 (267 mg, 1 mmol) and CF_3CO_2Ag (243 mg, 1 mmol) according to Procedure 1. Purification by chromatography on silica gel (30 g, hexanes/EtOAc 200:85) afforded **31** (407 mg, 83%) as a yellow crystals: mp 137 °C; ^{1}H NMR ($CDCl_3$) δ 2.43 (s, 6H), 3.68 (s, 3H), 3.84 (s, 3H), 6.44 (d, J = 16.5 Hz, 1H), 6.96 (d, J = 8.7 Hz, 2H), 7.23 (d, J = 16.5 Hz, 1H), 7.28 (d, J = 8.7 Hz, 2H), 7.42 (s, 1H); ^{13}C NMR ($CDCl_3$) δ 37.1, 51.5, 55.3, 64.8, 113.7, 117.4, 120.6, 122.0, 129.4, 133.0, 135.1, 136.9, 160.6, 167.4; MS *m*/*z* 490 (M^+, 100). Anal. Calcd for $C_{17}H_{19}IN_2O_5S$: C, 41.64; H, 3.91; N, 5.71. Found: C, 41.65; H, 3.90; N, 5.63.

(27) Shum, P. W.; Kozikowski, A. P. *Tetrahedron Lett.* **1990**, *31*, 6785−6788.

***N,N*-Dimethyl 2-(*p*-Methoxyphenyl)-3-(*trans*-2-methoxycarbonylethenyl)-4-trimethylsilylethynyl-1*H*-pyrrole-1-sulfonamide (32).** This compound was prepared from $PdCl_2(PPh_3)_2$ (33 mg, 0.04 mmol), CuI (60 mg, 0.3 mmol), **31** (196 mg, 0.4 mmol), trimethylsilylethyne (90 μL, 0.64 mmol), and Et_2NH (1.5 mL) according to Procedure 3. Purification by chromatography on silica gel (40 g, hexanes/EtOAc 10:3) afforded **32** (166 mg, 90%) as yellow crystals: mp 160 °C; ^{1}H NMR ($CDCl_3$) δ 0.27 (s, 9H), 2.42 (s, 6H), 3.69 (s, 3H), 3.85 (s, 3H), 6.95 (d, J = 8.7 Hz, 2H), 7.02 (d, J = 15.9 Hz, 1H), 7.20 (d, J = 15.9 Hz, 1H), 7.29 (d, J = 8.7 Hz, 2H), 7.48 (s, 1H); ^{13}C NMR ($CDCl_3$) δ −0.3, 37.2, 51.4, 55.3, 98.0, 99.2, 104.4, 113.6, 117.8, 120.4, 122.1, 129.0, 133.3, 135.1, 135.9, 160.5, 168.1; MS m/z 460 (M^+, 100). Anal. Calcd for $C_{22}H_{28}N_2O_5SSi$: C, 57.37; H, 6.13; N, 6.08. Found: C, 57.38; H, 6.14; N, 6.01.

2-(*p*-Methoxyphenyl)-3-(*trans*-2-methoxycarbonylethenyl)-4-iodo-1*H*-pyrrole (33). A solution of **31** (245 mg, 0.5 mmol) and *n*-Bu_4NF (1 mL, 1 mmol) in THF (9 mL) was stirred at 65 °C for 4 h. After extraction with EtOAc, washing with H_2O, drying (Na_2SO_4), filtration, and evaporation, the residue was chromatographed on silica gel (30 g, hexanes/EtOAc 5:2) to give **33** (161 mg, 84%) as a yellow residue: ^{1}H NMR ($CDCl_3$) δ 3.73 (s, 3H), 3.84 (s, 3H), 6.74 (d, J = 16.2 Hz, 1H), 6.94 (s, 1H), 6.95 (d, J = 9.0 Hz, 2H), 7.29 (d, J = 9.0 Hz, 2H), 7.66 (d, J = 16.2 Hz, 1H), 8.65 (br. s, 1H); ^{13}C NMR ($CDCl_3$) δ 51.4, 55.4, 63.4, 114.3, 114.5, 116.1, 123.5, 124.9, 129.8, 136.1, 138.3, 159.9, 168.4; MS m/z 383 (M^+, 13). Anal. Calcd for $C_{15}H_{14}INO_3$: C, 47.02; H, 3.68; N, 3.66. Found: C, 46.96; H, 3.52; N, 3.51.

2-(*p*-Methoxyphenyl)-3-(*trans*-2-methoxycarbonylethenyl)-4-trimethylsilylethynyl-1*H*-pyrrole (34). This compound was prepared from $PdCl_2(PPh_3)_2$ (41 mg, 0.04 mmol), CuI (80 mg, 0.4 mmol), **33** (192 mg, 0.5 mmol), trimethylsilylethyne (112 μL, 0.8 mmol), and Et_2NH (2 mL) according to Procedure 3. Purification by chromatography on silica gel (16 g, hexanes/EtOAc 5:2) afforded **34** (177 mg, 100%) as sticky solids: mp 150 °C (dec); ^{1}H NMR ($CDCl_3$) δ 0.27 (s, 9H), 3.70 (s, 3H), 3.79 (s, 3H), 6.88 (d, J = 8.4 Hz, 2H), 6.99 (d, J = 2.7 Hz, 1H), 7.06 (d, J = 15.9 Hz, 1H), 7.23 (d, J = 8.7 Hz, 2H), 7.68 (d, J = 15.9 Hz, 1H), 8.92 (br. s, 1H); ^{13}C NMR ($CDCl_3$) δ −0.2, 51.3, 55.3, 97.4, 100.3, 104.4, 114.4, 114.6, 116.3, 123.2, 124.4, 129.6, 135.4, 137.6, 159.7, 169.3; MS m/z 353 (M^+, 100). Anal. Calcd for $C_{20}H_{23}NO_3Si$: C, 67.96; H, 6.56; N, 3.96. Found: C, 67.99; H, 6.59; N, 3.88.

***N,N*-Dimethyl 2-Methoxycarbonyl-3,4-bis(*p*-methoxyphenyl)-1*H*-pyrrole-1-sulfonamide (35).** This compound was prepared from **20** (232 mg, 0.5 mmol), *p*-methoxybenzeneboronic acid (91 mg, 0.6 mmol), $Pd(PPh_3)_4$ (38 mg, 0.03 mmol), and 2 M Na_2SO_4 (0.2 mL) in MeOH/toluene (1:1, 1.5 mL) according to Procedure 5. Purification by chromatography on silica gel (25 g, hexanes/EtOAc 25:9) afforded **35** (211 mg, 95%) as a yellow foam: ^{1}H NMR ($CDCl_3$) δ 3.01 (s, 6H), 3.68 (s, 3H), 3.76 (s, 3H), 3.80 (s, 3H), 6.76 (d, J = 8.7 Hz, 2H), 6.82 (d, J = 8.7 Hz, 2H), 7.02 (d, J = 8.7 Hz, 2H), 7.10 (d, J = 8.7 Hz, 2H), 7.26 (s, 1H); ^{13}C NMR ($CDCl_3$) δ 38.5, 52.3, 55.1, 55.1, 113.4, 113.7, 122.1, 123.2, 124.8, 125.2, 125.9, 129.5, 129.9, 131.0, 158.6, 158.8, 162.4; MS m/z 444 (M^+, 100). Anal. Calcd for $C_{22}H_{24}N_2O_6S$: C, 59.45; H, 5.44; N, 6.30. Found: C, 59.41; H, 5.59; N, 5.99.

Methyl 3,4-Bis(*p*-methoxyphenyl)-1*H*-pyrrole-2-carboxylate (36).[9,16a] To a solution of **35** (444 mg, 1 mmol) in anhydrous MeOH (12 mL) was added Mg turnings (360 mg, 15 mmol). The mixture was stirred for 4 h at room temperature until all Mg was dissolved. Quenching at 0 °C with 3 N HCl was followed by extraction with EtOAc. The organic extract was washed with H_2O, dried over Na_2SO_4, and evaporated. The residue was chromatographed on silica gel (70 g, hexanes/EtOAc 25:9) to give **36** (290 mg, 85%) as yellow solids: mp 169−171 °C (lit.[26a] mp 169−171 °C); ^{1}H NMR ($CDCl_3$) δ 3.73 (s, 3H), 3.77 (s, 3H), 3.82 (s, 3H), 6.76 (d, J = 8.7 Hz, 2H), 6.85 (d, J = 8.4 Hz, 2H), 7.01−7.04 (m, 3H), 7.20 (d, J = 8.4 Hz, 2H), 9.29 (br. s, 1H); ^{13}C NMR($CDCl_3$) δ 51.2, 55.1, 55.1, 113.0, 113.6, 119.3, 120.1, 126.4, 127.0, 129.0, 129.4, 131.8, 157.9, 158.4, 161.5; MS m/z 337 (M^+, 10).

Lamellarin *O* Dimethyl Ether (37).[9,26] A mixture of **36** (34 mg, 0.1 mmol), 4-methoxyphenacyl bromide (43 mg, 0.2 mmol), K_2CO_3 (115 mg, 0.8 mmol) and acetone (7 mL) was heated at 70 °C for 3 h under N_2. After evaporation, the residue was purified by chromatography on silica gel (15 g, hexanes/EtOAc 25:9) to give **37** (44 mg, 90%) as yellow solids: mp 55−58 °C (lit.[26a] mp 55−58 °C); ^{1}H NMR ($CDCl_3$) δ 3.46 (s, 3H), 3.74 (s, 3H), 3.82 (s, 3H), 3.88 (s, 3H), 5.71 (s, 2H), 6.72 (d, J = 8.7 Hz, 2H), 6.83 (d, J = 8.4 Hz, 2H), 6.92 (s, 1H), 6.99 (d, J = 8.7 Hz, 2H), 7.00 (d, J = 8.7 Hz, 2H), 7.17 (d, J = 8.7 Hz, 2H), 8.02 (d, J = 8.7 Hz, 2H); ^{13}C NMR ($CDCl_3$) δ 50.7, 55.0, 55.5, 112.8, 113.4, 114.0, 119.7, 124.5, 126.9, 127.1, 127.8, 129.3, 130.2, 131.0, 131.8, 157.7, 158.2, 162.2, 163.9, 191.8; MS m/z 485 (M^+, 100).

1*H*-3,7,8-Tris(4-methoxyphenyl)pyrrolo[2,1-*c*][1,4]-oxazin-1-one (38).[9,26] To a *t*-BuOK suspension (79 mg, 0.7 mmol) in Et_2O (4 mL) was injected H_2O (4 μL) carefully at 0 °C under N_2, and the mixture was stirred for 5 min. The reaction was then added to a solution of **37** (36 mg, 0.07 mmol) in Et_2O (4 mL) at 0 °C. After the addition, the mixture was allowed to warm to room temperature and was stirred at ambient temperature. The mixture was then quenched with H_2O. The organic layer was separated. After extraction with Et_2O, the aqueous layer was acidified with 1 N HCl. The precipitated oxo-acid was extracted with Et_2O and CH_2Cl_2. The combined organic extract was dried over Na_2SO_4. After filtration and evaporation, the residue was dissolved in Ac_2O (6 mL), and NaOAc (120 mg, 1.5 mmol) was added. The mixture was heated at 100 °C for 2.5 h. The excess of Ac_2O was coevaporated with toluene in vacuo. The crude residue was again dissolved in Et_2O, washed with aqueous $NaHCO_3$, dried (Na_2SO_4), and evaporated. The residue was chromatographed on silica gel (20 g, hexanes/EtOAc 25:9) to give the lukianol A trimethyl ether **38** (20 mg, 60%) as white solids: mp 207 °C (lit.[26a] mp 206−207 °C); ^{1}H NMR (d_6-DMSO) δ 3.71 (s, 3H), 3.77 (s, 3H), 3.80 (s, 3H), 6.84 (d, J = 8.7 Hz, 2H), 6.89 (d, J = 9.0 Hz, 2H), 7.06 (m, 4H), 7.18 (d, J = 8.7 Hz, 2H), 7.65 (s, 1H), 7.67 (d, J = 9.0 Hz, 2H), 8.18 (s, 1H); ^{13}C NMR (d_6-DMSO) δ 55.2, 55.5, 103.9, 112.4, 113.4, 114.1, 114.7, 120.5, 123.0, 124.9, 125.6, 127.3, 128.6, 129.6, 132.0, 140.7, 153.7, 158.4, 158.7, 160.2; MS m/z 453 (M^+, 100).

Lukianol A (3).[9,26] To a stirred solution of **38** (19 mg, 0.04 mmol) in anhydrous CH_2Cl_2 (5 mL) under N_2 cooled at −78 °C was added BBr_3 (0.38 mL, 0.38 mmol) dropwise. The stirring was continued for 1 h at −78 °C, and the mixture was allowed to warm to room temperature during 12 h. After usual workup, the residue was purified by chromatography on silica gel (15 g, hexanes/EtOAc 1:1) to give **3** (16 mg, 93%) as white solids: mp 264−266 °C (lit.[26a] mp 264−266 °C); ^{1}H NMR (d_6-DMSO) δ 6.65 (d, J = 8.4 Hz, 2H), 6.69 (d, J = 8.4 Hz, 2H), 6.86 (d, J = 8.7 Hz, 2H), 6.94 (d, J = 8.4 Hz, 2H), 7.04 (d, J = 8.4 Hz, 2H), 7.55 (d, J = 8.7 Hz, 2H), 7.58 (s, 1H), 8.07 (s, 1H), 9.45 (br. s, 2H), 9.87 (br. s, 1H); ^{13}C NMR (d_6-DMSO) δ 103.3, 112.1, 114.8, 115.4, 116.0, 120.2, 121.5, 123.3, 124.1, 125.7, 127.6, 129.0, 129.6, 131.9, 141.0, 153.8, 156.5, 156.8, 158.6; MS m/z 411 (M^+, 100).

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Supporting Information Available: ^{1}H and ^{13}C NMR spectra for the compounds prepared, and X-ray structural results of **6**, **13**, *trans*-**16b**, **25c**, and **31**. This material is available free of charge via the Internet at http://pubs.acs.org.

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