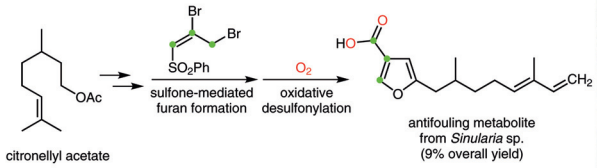
Synthesis C. N. Ungarean et al. Paper

Total Synthesis of an Antifouling Marine Furanosesquiterpene

Chad N. Ungarean[1]
Jeremy D. Mason[2]
Benjamin R. Eyer
Nicholas S. Duca
Jaimie M. Mong
S. Shaun Murphree*

Department of Chemistry, Allegheny College,
520 North Main Street, Meadville, PA 16335,
USA
smurphre@allegheny.edu



Received: 03.11.2016
Accepted after revision: 19.01.2017
Published online: 10.02.2017
DOI: 10.1055/s-0036-1588711; Art ID: ss-2016-z0777-op

Abstract An antifouling sesquiterpene isolated from *Sinularia* sp. was synthesized from citronellyl acetate in eight steps and 9% overall yield. The furan moiety was constructed using a multifunctional sulfone reagent.

Key words furans, sulfones, natural products, total synthesis, heterocycles

Biofouling constitutes a significant economic challenge. Fouling organisms are ubiquitous in marine habitats, and they negatively impact shipping operations, water purification, and aquatic recreation.[3] Inorganic antifoulants have been the first line of defense for many years,[4] but increasing environmental concerns prompted the International Maritime Organization to adopt a ban on the use of organotins and other harmful antifouling systems in marine coatings in 2001.[5] Consequently, research into non-bioaccumulating, environmentally benign fouling inhibitors has taken on a renewed sense of urgency, and particular attention has been devoted to natural products of marine origin.[6]

In this context, the furanosesquiterpene **1** has been isolated from several subspecies of the soft coral *Sinularia species*,[7–11] and preliminary studies have estimated its efficacy against the blue mussel (*Mytilus edulis*) at a loading of 0.2 mg/mL to be 74% that of copper(II) sulfate, a highly effective (but environmentally persistent) inorganic antifoulant;[12,13] moreover, at concentrations of 30 μM it exhibited moderate (26%) inhibition of inducible NO synthase (iNOS) activity in J774 macrophages.[14] However, extraction of **1** from natural sources yields low quantities, and to our knowledge a total synthesis has not been reported previously. We were therefore intrigued with this compound as a target for our recently reported sulfone-mediated preparative method for converting 1,3-diketones into 2,4-disubstituted furans.[15] Using this approach (Figure 1), we envisioned that furoic acid **1** could be accessed via diketone **2**, which in turn could be efficiently constructed from the readily available citronellyl acetate (**3**).

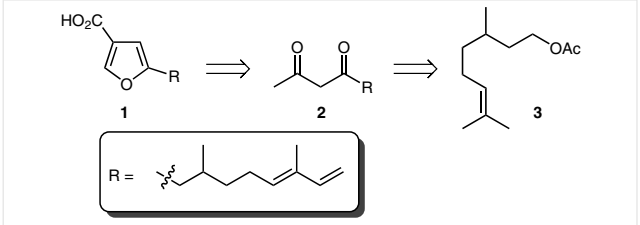
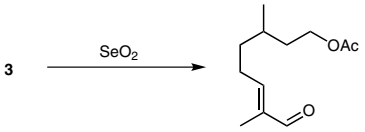


Figure 1 Retrosynthetic strategy for furanosesquiterpene **1**

For the construction of diketone **2**, we took inspiration from a synthesis of the insect pheromone methyl 2,6,10-trimethyldodecanoate reported by Zarbin et al.,[16] which launched by subjecting citronellyl acetate (**3**) to selenium dioxide mediated allylic oxidation to provide aldehyde **4** (Table 1). Using superstoichiometric quantities of SeO_2, the *E*-aldehyde **4** was isolated in 41% yield upon reflux in ethanol for 15 min (entry 1). Higher yields and shorter reaction times could be achieved using a microwave protocol (entry 2), albeit with a somewhat more limited scalability. In both of these approaches, a small amount of *Z*-isomer was observed, which was difficult to remove by chromatography without yield loss. In contrast, the use of substoichiometric amounts of SeO_2 adsorbed onto silica in dichloromethane at room temperature in the presence of aqueous *tert*-butyl hydroperoxide as a terminal oxidant[17] (entry 3) provided practically exclusively the *E*-isomer in yields comparable to those found in entry 1. However, with an eye toward scale-up, we explored the possibility of isolating gram quantities of aldehyde **4** without the high solvent demand associated

with chromatography. The most effective alternative was found to be Kugelrohr distillation (130 °C/2 Torr), which has a higher throughput than a flash column and delivers the product in significantly higher yield (entry 4). One drawback, however, is that a small amount of *E*/*Z* isomerization occurs, which could not be circumvented. To take advantage of its convenience and scalability, we nonetheless carried the material forward with an eye toward removal of the *Z*-isomer after the next step.

Table 1 Allylic Oxidation of Citronellyl Acetate (**3**)



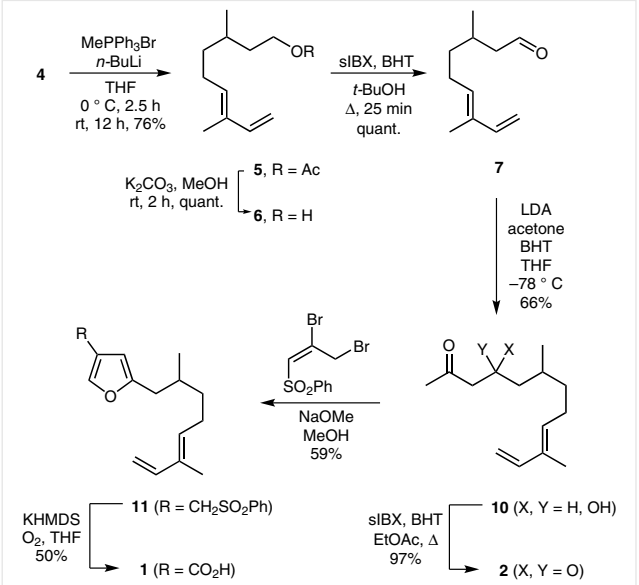
4

Entry	SeO_2 (equiv)	*t*-BuOOH (equiv)	Solvent	Time	T (°C)	Yield[a] (%)
1	2.0	0	EtOH	15 min	78	41[b]
2	2.0	0	EtOH	10 min	100[c]	50[b]
3	0.5[d]	2.5	CH_2Cl_2/H_2O	24 h	r.t.	39
4	0.5[d]	2.5	CH_2Cl_2/H_2O	24 h	r.t.	60[e]
5[f]	0.5	3.0	CH_2Cl_2/H_2O	3 h	r.t.	40

[a] Isolated by column chromatography unless otherwise stated.
[b] Approximately 2–4% *Z*-isomer present (by NMR).
[c] Microwave protocol.
[d] Adsorbed onto silica.
[e] Isolated by bulb-to-bulb distillation. *Z* isomer also present.
[f] Results reported in ref. 16.

Methylenation of the aldehyde functionality was effected using standard Wittig chemistry. Thus, treatment of methyltriphenylphosphonium bromide with *n*-butyllithium, followed by addition of aldehyde **4** resulted in smooth conversion into the corresponding *E*-diene acetate **5** in 76% yield (Scheme 1). Subsequent deprotection of the alcohol could be accomplished conveniently through potassium carbonate promoted transesterification in methanol, which afforded alcohol **6** in excellent yield on a variety of scales.

Among several protocols screened for the conversion of the primary alcohol into aldehyde **7**, oxidation with stabilized IBX (sIBX)[18] in *tert*-butyl alcohol proceeded with the highest yield.[19] Vexingly, a small amount (ca. 5%) of isomerization was observed about the internal double bond under these reaction conditions. It is unclear whether the *E*/*Z* isomerization is induced by sIBX itself or results from traces of iodine in the reagent. To our knowledge, the IBX-mediated isomerization of double bonds has not been reported, although the iodine-promoted variant is well known, and previous studies have shown the efficacy of radical scavengers in retarding the iodine-catalyzed isomerization of dienes.[20] Thus, we were pleased to observe no *Z*-isomer



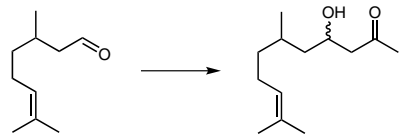
Scheme 1 Synthesis of furan **1**

when the oxidation was carried out in the presence of 10 mol% 2,6-di-*tert*-butyl-4-methylphenol (BHT). Since the conversion is practically quantitative, the BHT was carried forward to avoid yield loss in purification.

The next step was to install the 1,3-diketone moiety necessary for the sulfone-mediated furan formation, which we envisioned to occur via an aldol-oxidation sequence on aldehyde **7**. We chose to optimize this reaction using commercially available citronellal (**8**) (Table 2). As one of the strategies surveyed, we examined the titanocene-catalyzed Reformatsky addition of chloroacetone onto citronellal, which has been previously reported to give a 91% yield of hydroxy ketone **9** as a mixture of diastereomers,[21] although in our hands, the isolated yield was somewhat lower (entry 1). We also thought it prudent to explore some operationally simpler alternatives. Toward this end, treating citronellal with catalytic quantities of proline in a medium of acetone/DMSO[22] did provide a modest yield of the aldol **9**, although the chief product was the corresponding enone (entry 2). Results could be improved by using superstoichiometric amounts of proline and acetone as a solvent (entry 3).[23] Similar yields (53%) could be obtained using catalytic sodium methoxide in methanol at 5 °C[24] (entry 4). Still better results were achieved by changing the base to LDA and using one equivalent of acetone in THF (entry 5).[25]

Gratifyingly, these conditions worked equally well on substrate **7**, providing aldol **10** in 66% yield. Subsequent oxidation to diketone **2** proceeded smoothly using stabilized IBX,[26] although the product degraded upon storage and was used immediately for the next step. Again, the addition of BHT was necessary to prevent *E*/*Z* isomerization during the oxidation.

Table 2 Optimization of Aldol Condensation Using Citronellal (**8**)



8 **9**

Entry	Conditions	Yield (%)
1	Cp_2TiCl_2 (2 equiv), Mn (8 equiv), chloroacetone (2 equiv), 2,4,6-collidine (8 equiv), TMSCl (4 equiv), THF	58
2	proline (0.3 equiv), 20% acetone/DMSO	21[a]
3	proline (2 equiv), acetone	49
4	NaOMe (0.33 equiv), acetone (3.6 equiv), MeOH	53
5	LDA (1.2 equiv), acetone (1.0 equiv), THF	63

[a] The corresponding enone was produced in 65% yield.

With diketone **2** in hand, the phenylsulfonylmethylfuran **11** could be accessed by treatment with 2,3-dibromo-1-(phenylsulfonyl)prop-1-ene in the presence of methanolic sodium methoxide.[15] The carboxylic acid functionality could then be installed using an oxidative desulfonylation strategy,[27] in which the sulfonyl dianion formed using potassium hexamethyldisilazanide is allowed to undergo oxidation in dry air, providing the target furanosesquiterpene **1** in fair yield.

In summary, we have reported a convenient and scalable synthesis of the potential antifouling compound **1**, which is suitable for preparing gram quantities of the synthetic target in 8 steps and 9% overall yield from the readily available citronellyl acetate. Antifouling evaluation of compound **1** is currently underway.

THF was distilled first over CaH_2 and then over Na/benzophenone ketyl. Hexanes for chromatography were distilled over CaH_2. MeOH, EtOAc, acetone, and CH_2Cl_2 were purchased as HPLC grade and used without further purification. *n*-BuLi was titrated against diphenylacetic acid before use. All other reagents were purchased from Aldrich Chemical Company and used as received.

Only diagnostic absorptions in the infrared spectrum are reported. NMR spectra were recorded in $CDCl_3$ (unless otherwise noted) using a JEOL Eclipse 400+ FT-NMR spectrometer. Elemental analyses were performed at Atlantic Microlabs in Norcross, GA. All air-sensitive reactions were performed under N_2 atmosphere. Column chromatography was carried out using SilicaFlash P60 silica gel (40–63 µm) purchased from Silicycle.

(*E*)-3,7-Dimethyl-8-oxooct-6-enyl Acetate (4)

To a stirred suspension of 5 wt% SeO_2 on silica (15.0 g, 6.75 mmol) in CH_2Cl_2 (135 mL) was added aq 70 wt% *t*BuOOH (4.9 mL, 34.1 mmol) as a bolus followed by a solution of citronellyl acetate (3.0 mL, 2.7 g, 13.5 mmol) in CH_2Cl_2 (12.5 mL) added over a period of 15 min. The resulting suspension was stirred vigorously open to the atmosphere for 24 h, and then filtered through a frit. The filtrate was concentrated in vacuo to yield a yellow oil (3.58 g), which was purified by Kugelrohr distillation (130 °C oven temperature/2 Torr) to afford aldehyde **4** (2.86 g, 60%) as a pale yellow oil comprised of a 96:4 mixture of *E*- and *Z*-isomers. The *E*-isomer can be isolated using column chromatography (30% Et_2O/hexane) to give analytically pure material with spectroscopic data identical to those reported in the literature.[16]

(*E*)-3,7-Dimethylnona-6,8-dienyl Acetate (5)

To a stirred suspension of $MePPh_3Br$ (3.74 g, 10.5 mmol) in anhyd THF (85 mL) at 0 °C was added dropwise 1.5 M *n*-BuLi in hexanes (6.8 mL, 10.2 mmol), whereupon the contents immediately turned yellow. The mixture was warmed to 0 °C and allowed to stir for 2.5 h, after which it was transferred dropwise via syringe to a solution of (*E*)-3,7-dimethyl-8-oxooct-6-enyl acetate (**4**, 1.76 g, 8.29 mmol) in anhyd THF (75 mL) at –78 °C. The cooling bath was removed and the yellow solution was stirred at r.t. overnight. The solvent was removed in vacuo, and the resulting oil was passed through a small silica plug (ca. 3 in), eluting with Et_2O (250 mL). The eluent was concentrated in vacuo to give an oil (1.62 g), which was purified by column chromatography (10% EtOAc/hexane) to afford diene **5** (1.15 g, 76%) as a colorless oil with spectroscopic data identical to those reported in the literature.[16]

(*E*)-3,7-Dimethylnona-6,8-dien-1-ol (6)

To a solution of dienyl acetate **5** (1.26 g, 5.98 mmol) in HPLC grade MeOH (19 mL) was added K_2CO_3 (826.5 mg, 5.98 mmol). The resulting suspension was stirred for 2 h at r.t., after which the solid was removed by filtration. The filtrate was concentrated in vacuo and the residue was partitioned between water (100 mL) and Et_2O (3 × 60 mL). The combined organic phases were washed with water (2 × 50 mL) and brine, dried (Na_2SO_4), and concentrated in vacuo to provide alcohol **6** (1.00 g, quant.) as a pale straw-colored oil, which was immediately used in the next step without further purification. Spectroscopic data were identical to those reported in the literature.[16]

(*E*)-3,7-Dimethylnona-6,8-dienal (7)

To a solution of dienol **6** (257 mg, 1.53 mmol) and BHT (33.8 mg, 0.15 mmol) in *t*-BuOH (23 mL) was added stabilized 2-iodoxybenzoic acid (45 wt%, 1.9059 g, 3.06 mmol). The suspension was heated at reflux for 25 min with stirring, after which the mixture was cooled, hexanes (120 mL) were added, and the organics were washed with sat. $NaHCO_3$/brine (5 × 120 mL). The organic layer was dried (Na_2SO_4), and concentrated in vacuo to provide an oil (289 mg) containing product **7** (254 mg, 99.6%), as well as residual BHT, which was used immediately in the next step. A sample purified by chromatography (5% EtOAc/hexanes) yielded analytically pure material with spectroscopic data identical to those reported in the literature.[16]

4-Hydroxy-6,10-dimethylundec-9-en-2-one (9)

A solution of *i*-Pr_2NH (0.87 mL, 6.2 mmol) in THF (6.0 mL) at –78 °C was treated with 2.2 M *n*-BuLi (2.8 mL, 6.2 mmol) and allowed to stir at –78 °C for 10 min. A solution of HPLC grade acetone (0.39 mL, 5.2 mmol) in THF (0.8 mL) was added to the LDA thus formed, and the solution was stirred at –78 °C for 1 h. Citronellal (**8**, 0.864 mL, 4.8 mmol) in THF (1.0 mL) was then added over a period of 15 min. The mixture was stirred for an additional 12 min at –78 °C, quenched by the addition of sat. aq NH_4Cl (3 mL), and partitioned between sat. aq NH_4Cl (40 mL) and Et_2O (2 × 30 mL). The combined organic extracts were washed with brine (2 ×), dried (Na_2SO_4), and concentrated in vacuo to give an oil, which was purified by column chromatography

(30% EtOAc/hexane) to afford product **9** (678 mg, 63%) as a straw-colored oil with spectroscopic properties identical to those reported in the literature.[21]

(*E*)-4-Hydroxy-6,10-dimethyldodeca-9,11-dien-2-one (10)

A solution of *i*-Pr_2NH (0.87 mL, 6.2 mmol) in THF (6.0 mL) at –78 °C was treated with 2.2 M *n*-BuLi (2.8 mL, 6.2 mmol) and allowed to stir at –78 °C for 10 min. A solution of HPLC grade acetone (0.39 mL, 5.2 mmol) in THF (0.8 mL) was added to the LDA thus formed, and the solution was stirred at –78 °C for 1 h. Unpurified dienal **7** (922 mg, 792 mg aldehyde, 4.8 mmol) in THF (1.0 mL) was then added over a period of 15 min. The mixture was stirred for an additional 12 min at –78 °C, quenched by the addition of sat. aq NH_4Cl (3 mL), and partitioned between sat. aq NH_4Cl (40 mL) and Et_2O (2 × 30 mL). The combined organic extracts were washed with brine (2 ×), dried (Na_2SO_4), and concentrated in vacuo to give an oil, which was purified by column chromatography (30% EtOAc/hexane) to afford product **10** (708 mg, 66%) as a clear oil (mixture of diastereomers).

IR (neat, NaCl): 3436, 3088, 2925, 1713, 1081 cm^{-1}.

^1H NMR ($CDCl_3$, 400 MHz): δ = 6.35 (dd, *J* = 17.4, 10.7 Hz, 1 H), 5.46 (t, *J* = 7.3 Hz, 1 H), 5.06 (dd, *J* = 17.4, 2.9 Hz, 1 H), 4.91 (dd, *J* = 10.7, 2.9 Hz, 1 H), 4.22–4.06 (m, 1 H), 2.66–2.55 (m, 1 H), 2.55–2.44 (m, 1 H), 2.17 (s, 3 H), 2.23–2.01 (m, 2 H), 1.73 (m, 3 H), 1.65–1.00 (m, 5 H), 0.92 (d, *J* = 6.6 Hz, 3 H).

^{13}C NMR ($CDCl_3$, 100 MHz): δ = 210.1, 141.7, 134.0, 133.9, 133.3, 110.6, 110.5, 65.7, 65.3, 50.8, 50.2, 43.7, 37.4, 36.3, 30.9, 29.1, 28.8, 25.8, 25.6, 20.1, 19.1, 11.8, 11.7.

Anal. Calcd for $C_{14}H_{24}O_2$: C, 74.95; H, 10.78. Found: C, 74.87; H, 10.57.

(*E*)-6,10-Dimethyldodeca-9,11-dien-2,4-dione (2)

Dienone (**10**, 645 mg, 2.87 mmol) and BHT (61.4 mg, 0.29 mmol) were dissolved in HPLC grade EtOAc (25 mL). To the solution was added stabilized 2-iodoxybenzoic acid (45 wt%, 5.356 g, 8.61 mmol). The suspension was heated at reflux for 50 min with stirring, after which the mixture was cooled to r.t. and hexanes (323 mL) was added. The organics were washed with sat. $NaHCO_3$/brine (5 × 323 mL), dried (Na_2SO_4), and concentrated in vacuo to provide an oil (680 mg) containing product **2** (619 mg, 97%), as well as residual BHT. This unstable material was used immediately in the next step. An analytically pure sample was obtained by column chromatography (5% EtOAc/hexanes).

IR (neat, NaCl): 2957, 2925, 1607, 1458, 1382, 1285, 1240, 990, 843, 777 cm^{-1}.

^1H NMR ($CDCl_3$, 400 MHz): δ = 15.54 (s, 1 H, enol tautomer), 6.35 (dd, J_1 = 17.5 Hz, J_2 = 10.7 Hz, 1 H), 5.46 (s, 1 H, enol tautomer), 5.45 (t, *J* = 6.8 Hz, 1 H), 5.07 (d, *J* = 17.0 Hz, 1 H), 4.92 (d, *J* = 10.7 Hz, 1 H), 3.54 (s, 2 H, keto tautomer), 1.87–2.36 (m, 7 H), 1.72 (s, 3 H), 1.15–1.61 (m, 3 H), 0.93 (d, *J* = 6.4 Hz, 3 H).

^{13}C NMR ($CDCl_3$, 100 MHz): δ = 192.9, 192.2, 141.6, 134.2, 132.8, 132.7, 110.7, 100.8, 58.4, 51.1, 45.6, 36.6, 36.4, 30.7, 28.7, 25.8, 25.3, 19.6, 11.7.

Anal. Calcd for $C_{14}H_{22}O_2$: C, 75.63; H, 9.97. Found: C, 75.45; H, 9.82.

(*E*)-2-(2,6-Dimethylocta-5,7-dienyl)-4-(phenylsulfonylmethyl)furan (11)

A mixture of diendione **2** (362.4 mg, 1.63 mmol) and BHT (41.9 mg, 0.19 mmol) was dissolved in anhyd MeOH (8.5 mL). The solution was cooled to 0 °C and treated dropwise with 0.5 M NaOMe solution (3.6 mL, 1.8 mmol). The solution was stirred for an additional 20 min at r.t., cooled again to 0 °C, after which 2,3-dibromo-1-(phenylsulfonyl)prop-1-ene (555.9 mg, 1.64 mmol) was added in one portion. The mixture was stirred at r.t. for 2.5 h, cooled to 0 °C, and treated with a second portion of 0.5 M NaOMe solution (3.9 mL, 1.95 mmol). After stirring for 16 h at r.t., the reaction was quenched with sat. NH_4Cl (6 mL). MeOH was removed in vacuo and the mixture was poured into sat. NH_4Cl (35 mL), extracted with CH_2Cl_2 (3 × 15 mL), washed with water (60 mL), and dried (Na_2SO_4). The organic layers were concentrated in vacuo to provide an oil (713 mg), which was purified by column chromatography (15% EtOAc/hexane) to afford phenylsulfonylmethylfuran **11** (376 mg, 59% from **10**) as a light yellow oil.

IR (neat, NaCl): 2956, 2924, 1447, 1320, 1156, 1086, 883, 688 cm^{-1}.

^1H NMR ($CDCl_3$, 400 MHz): δ = 7.77–7.69 (m, 2 H), 7.65–7.56 (m, 1 H), 7.47 (t, *J* = 7.8 Hz, 2 H), 7.05 (d, *J* = 1.0 Hz, 1 H), 6.36 (dd, *J* = 17.4, 10.7 Hz, 1 H), 5.88 (s, 1 H), 5.44 (t, *J* = 7.3 Hz, 1 H), 5.08 (d, *J* = 17.5 Hz, 1 H), 4.93 (d, *J* = 10.7 Hz, 1 H), 4.13 (s, 2 H), 2.54 (dd, *J* = 14.9, 6.0 Hz, 1 H), 2.38 (dd, *J* = 14.8, 7.7 Hz, 1 H), 2.24–2.04 (m, 2 H), 1.83–1.72 (m, 1 H), 1.73 (d, *J* = 1.2 Hz, 3 H), 1.45–1.30 (m, 1 H), 1.28–1.13 (m, 1 H), 0.86 (d, *J* = 6.7 Hz, 3 H).

^{13}C NMR ($CDCl_3$, 100 MHz): δ = 156.4, 141.6, 141.2, 137.9, 134.1, 133.8, 133.0, 129.0, 128.7, 113.1, 110.7, 108.0, 53.7, 36.1, 35.3, 32.3, 25.8, 19.5, 11.8.

Anal. Calcd for $C_{21}H_{26}O_3S$: C, 70.36; H, 7.31. Found: C, 70.15; H, 7.17.

(*E*)-2-(2,6-Dimethylocta-5,7-dienyl)-4-furoic Acid (1)

To a solution of furan **9** (173.2 mg, 0.48 mmol) in anhyd THF (5.7 mL) cooled to –78 °C was added dropwise 0.5 M KHMDS in toluene (2.4 mL). The solution was stirred for 45 min at –78 °C and thereafter sparged with dry air through a 22-gauge needle for 2.5 h. The solution was warmed to r.t. and quenched with sat. NH_4Cl (5 mL), diluted with Et_2O (40 mL), and washed with 0.1 M HCl (2 × 40 mL). The organic phase was dried (Na_2SO_4) and concentrated in vacuo to afford an oil, which was purified using column chromatography (10% MeOH/CH_2Cl_2) to afford natural product **1** (59.1 mg, 50%) as a light straw-colored oil with spectroscopic properties identical to those reported in the literature.

Acknowledgment

The authors gratefully acknowledge financial support from the Petroleum Research Fund (PRF 42382-B1), the Arnold and Mabel Beckman Foundation, and the Shanbrom Fund of Allegheny College. We also thank Doug Taber for stimulating discussion about this project.

Supporting Information

Supporting information for this article is available online at http://dx.doi.org/10.1055/s-0036-1588711.

References

(1) New address: Department of Chemistry, University of Illinois at Urbana-Champaign, 505 South Mathews Avenue Urbana, IL 61801.
(2) New address: Department of Chemistry, Pennsylvania State University, 201 Old Main, University Park, Pennsylvania 16802.
(3) Petrone, L. *Adv. Colloid Interface Sci.* **2013**, *195–196*, 1.
(4) Townsin, R. L. *Biofouling* **2003**, *19*, Suppl. 9.
(5) Champ, M. A. *Sci. Total Environ.* **2000**, *258*, 21.

(6) Li, Y.-X.; Wu, H.-X.; Xu, Y.; Shao, C.-L.; Wang, C.-Y.; Qian, P.-Y. *Mar. Biotechnol.* **2013**, *15*, 552.
(7) Su, J.-H.; Huang, C.-Y.; Li, P.-J.; Lu, Y.; Wen, Z.-H.; Kao, Y.-H.; Sheu, J.-H. *Arch. Pharm. Res.* **2012**, *35*, 779.
(8) Cheng, S.-Y.; Huang, K.-J.; Wang, S.-K.; Wen, Z.-H.; Chen, P.-W.; Duh, C.-Y. *J. Nat. Prod.* **2010**, *73*, 771.
(9) Park, S. K.; Scheuer, P. J. *J. Korean Chem. Soc.* **1994**, *38*, 749.
(10) Bowden, B. F.; Coll, J. C.; de Silva, E. D.; de Costa, M. S. L.; Djura, P. J.; Mahendran, M.; Tapiolas, D. M. *Aust. J. Chem.* **1983**, *36*, 371.
(11) Lakshmi, V.; Schmitz, F. J. *J. Nat. Prod.* **1986**, *49*, 728.
(12) Mizobuchi, S.; Konya, K.; Miki, W. JP 07089811, **1995**; *Chem. Abstr.* **1995**, *123*, 231479
(13) Mizubuchi, S.; Kon-ya, K.; Adachi, K.; Sakai, M.; Miki, W. *Fish. Sci.* **1994**, *60*, 345.
(14) Putra, M. Y.; Ianaro, A.; Panza, E.; Bavestrello, G.; Cerrano, C.; Fattorusso, E.; Taglialatela-Scafati, O. *Tetrahedron Lett.* **2012**, *53*, 3937.
(15) Haines, N. R.; VanZanten, A. N.; Cuneo, A. A.; Miller, J. R.; Andrews, W. J.; Carlson, D. A.; Harrington, R. M.; Kiefer, A. M.; Mason, J. D.; Pigza, J. A.; Murphree, S. S. *J. Org. Chem.* **2011**, *76*, 8131.
(16) Zarbin, P. H. G.; Reckziegel, A.; Plass, E.; De Oliveira, A. R. M.; Simonelli, F.; Marques, F. D. A. *J. Braz. Chem. Soc.* **2000**, *11*, 572.
(17) Singh, J.; Sabharwal, A.; Sayal, P. K. *Chem. Ind.* **1989**, 533.
(18) Ozanne, A.; Pouységu, L.; Depernet, D.; François, B.; Quideau, S. *Org. Lett.* **2003**, *5*, 2903.
(19) Van Arman, S. A. *Tetrahedron Lett.* **2009**, *50*, 4693.
(20) Ideses, R.; Shani, A. *J. Am. Oil Chem. Soc.* **1989**, *66*, 948.
(21) Estévez, R. E.; Paradas, M.; Millán, A.; Jiménez, T.; Robles, R.; Cuerva, J. M.; Oltra, J. E. *J. Org. Chem.* **2008**, *73*, 1616.
(22) List, B.; Lerner, R. A.; Barbas, C. F. III *J. Am. Chem. Soc.* **2000**, *122*, 2395.
(23) List, B.; Pojarliev, P.; Castello, C. *Org. Lett.* **2001**, *3*, 573.
(24) Vani, P. V. S. N.; Chida, A. S.; Srinivasan, R.; Chandrasekharam, M.; Singh, A. K. *Synth. Commun.* **2001**, *31*, 219.
(25) Yuasa, Y.; Kato, Y. *Org. Process Res. Dev.* **2002**, *6*, 628.
(26) Bartlett, S. L.; Beaudry, C. M. *J. Org. Chem.* **2011**, *76*, 9852.
(27) Bonaparte, A. C.; Betush, M. P.; Panseri, B. M.; Mastarone, D. J.; Murphy, R. K.; Murphree, S. S. *Org. Lett.* **2011**, *13*, 1447.