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Total Synthesis of Calothrixins A and B by Palladium-Catalyzed Tandem Cyclization/Cross-Coupling Reaction of Indolylborate

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The palladium-catalyzed tandem cyclization/cross-coupling reaction of triethyl(indol-2-yl)borate with vinyl bromide was successfully used in the concise total synthesis of the indolophenanthridine alkaloids, calothrixins A and B.

Introduction

Calothrixins A (**1**) and B (**2**) were originally isolated in 1999 from lyophilized extracts of *Calothrix* cyanobacteria, which were collected in the Australian Capital Territory (Figure 1).[1] The structures have an unusual pentacyclic indolo[3,2-*j*]phenanthridine system, incorporating indole, quinone, and quinoline moieties, that was identified by spectroscopic and single-crystal X-ray analyses. Both **1** and **2** were found to inhibit the growth of human HeLa cancer cells and of a chloroquine-resistant strain of the human malaria parasite *Plasmodium falciparum*.[2] Recently, **1** and **2** were shown to act as human topoisomerase I poisons; both compounds reversibly stabilize the topoisomerase–DNA binary complex, leading to cell death.[3] The total synthesis of calothrixins A (**1**) and B (**2**) was first completed in 2000 by Kelly and co-workers, who twice used *o*-lithiation to construct the indolophenanthridine core of **2**, and then performed *N*-oxidation of **2** with *m*-CPBA (*meta*-chloroperbenzoic acid) to obtain **1**.[4] Since then, several methods for synthesizing **1** and **2** have been developed:[5] the core structure has been assembled by cyclization of 2-indolylacyl radical onto the quinoline ring, by Friedel–Crafts acylation and metalation strategies, by hetero-Diels–Alder reaction between 2-azadiene and 3-bromo-9*H*-carbazole, and by allene-mediated electrocyclization.[5] Moreover, the biomimetic total synthesis of **2** via a common indolo[2,3-*a*]carbazole intermediate was accomplished by Hibino[6] and Moody,[7] independently.

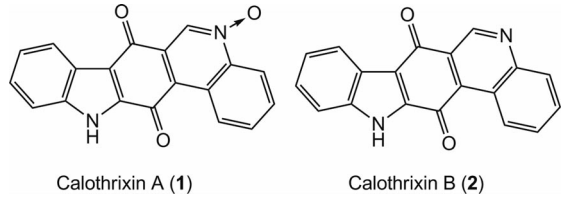

Figure 1. Calothrixins A (**1**) and B (**2**).

Recent studies have highlighted the palladium-catalyzed cross-coupling reaction using organoboron compounds (Suzuki–Miyaura coupling) as a promising synthetic method.[8] However, tetracoordinate organoboron compounds (ate complexes) have proved impractical for palladium-catalyzed cross-coupling,[9] although a method using heteroaryltrifluoroborates has recently been developed.[10] In connection with our continuing interest in the chemical reactivity and synthetic applications of trialkyl(indol-2-yl)borates (indolylborates),[11] we found that indolylborate **4**, a tetracoordinate complex, showed high reactivity in palladium-catalyzed cross-coupling. Accordingly, we set out to develop the cross-coupling reaction of indolylborates as a synthetic tool for the synthesis of indole derivatives. In this paper, we report the full details of our approach to calothrixins A (**1**) and B (**2**) using palladium-catalyzed tandem cyclization/cross-coupling reactions of indolylborates.[12]

Our synthetic approach is outlined in Scheme 1. Triene **6** was envisioned to be accessible by a one-pot cross-coupling reaction of indolylborate **4** (generated in situ from indole **3**) with bromide **5**. Subsequent 6π-electrocyclization of triene **6** would then produce indolophenanthridine **7**, which in turn could be converted into the target calothrixins.

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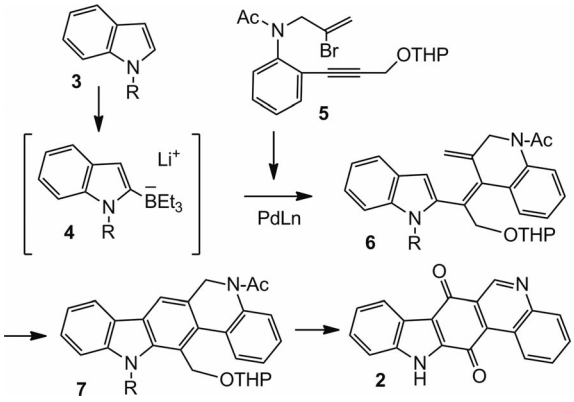
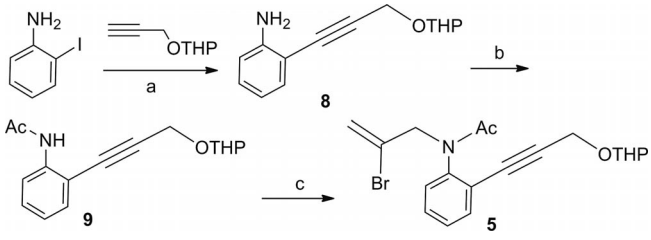


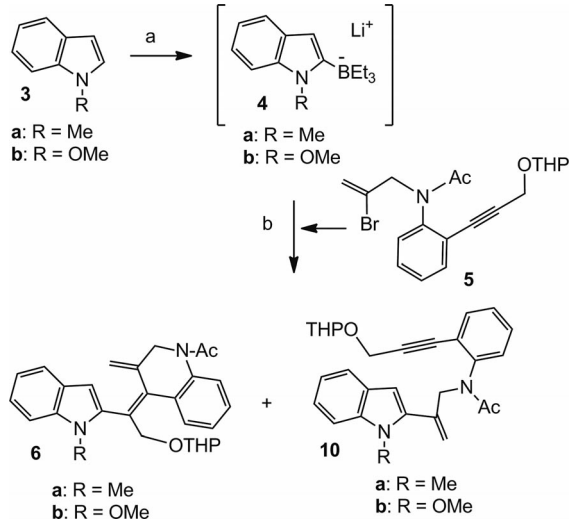
Scheme 1. Synthetic strategy.

Results and Discussion

Bromide **5** was readily prepared by the reaction sequence outlined in Scheme 2. Sonogashira coupling of 2-iodoaniline with 2-(prop-2-yn-1-yloxy)tetrahydro-2*H*-pyran in the presence of $PdCl_2(PPh_3)_2$ (3 mol-%) and CuI (10 mol-%) in Et_2NH at room temperature for 1 h smoothly produced phenylacetylene **8** in 80% yield.[13] Treatment of **8** with acetyl chloride in the presence of Et_3N in CH_2Cl_2 gave acetoamide **9** in 85% yield. Finally, bromide **5** was obtained in 80% yield by treating **9** with NaH and 2,3-dibromopropene in THF.



Scheme 2. Reagents and conditions: (a) $PdCl_2(PPh_3)_2$, Et_2NH, CuI, r.t., 80%; (b) AcCl, Et_3N, CH_2Cl_2, 85%; (c) 2,3-dibromopropene, NaH, THF, 80%.



Scheme 3. Reagents and conditions: (a) *n*BuLi or *t*BuLi, THF, then BEt_3; (b) see Table 1.

Table 1. Cross-coupling reactions of **4** with **5**.[a]

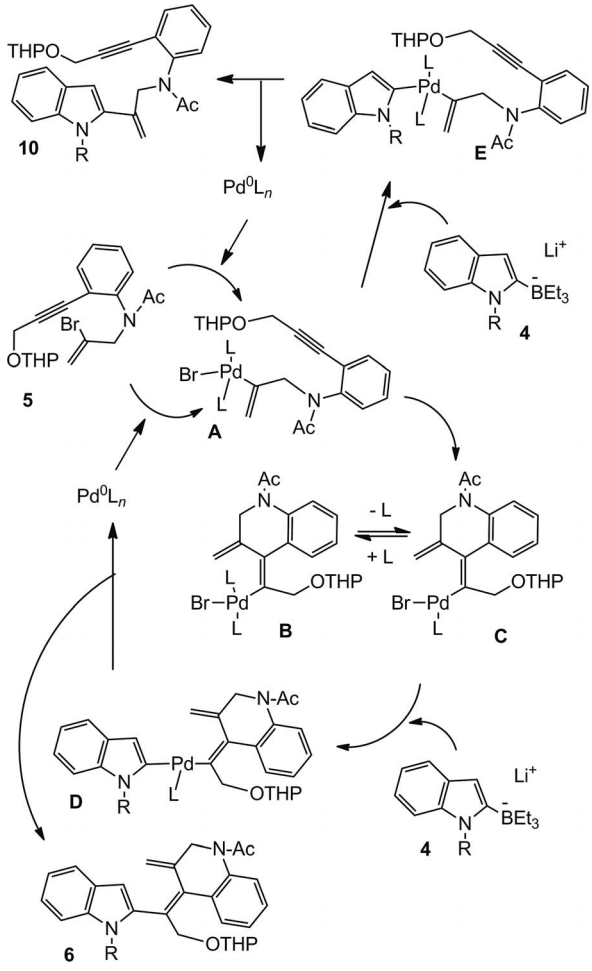
Entry	4	Conditions	Yield [%] (product)[b]	
1	**4a**	$PdCl_2(MeCN)_2$,[c] 0.5 h	48 (**6a**)	5 (**10a**)
2	**4a**	$Pd(OAc)_2$,[c] 0.5 h	45 (**6a**)	8 (**10a**)
3	**4a**	$Pd_2(dba)_3{\cdot}CHCl_3$,[d] 0.5 h	52 (**6a**)	7 (**10a**)
4	**4a**	$Pd(OAc)_2$,[c] PPh_3,[e] 2 h	23 (**6a**)	7 (**10a**)
5	**4a**	$PdCl_2(PPh_3)_2$,[c] 2 h	25 (**6a**)	8 (**10a**)
6	**4a**	$Pd_2(dba)_3{\cdot}CHCl_3$,[d] PPh_3,[e] 2 h	25 (**6a**)	8 (**10a**)
7	**4a**	$PdCl_2[P(o\text{Tol})_3]_2$,[c] 0.5 h	55 (**6a**)	5 (**10a**)
8	**4a**	$Pd(OAc)_2$,[c] $P(o\text{Tol})_3$,[e] 0.5 h	53 (**6a**)	6 (**10a**)
9	**4a**	$Pd_2(dba)_3{\cdot}CHCl_3$,[d] $P(o\text{Tol})_3$,[e] 0.5 h	72 (**6a**)	4 (**10a**)
10	**4b**	$Pd(OAc)_2$,[c] 0.5 h	42 (**6b**)	5 (**10b**)
11	**4b**	$Pd_2(dba)_3{\cdot}CHCl_3$,[d] 0.5 h	50 (**6b**)	6 (**10b**)
12	**4b**	$PdCl_2(PPh_3)_2$,[c] 2 h	20 (**6b**)	7 (**10b**)
13	**4b**	$Pd_2(dba)_3{\cdot}CHCl_3$,[d] PPh_3,[e] 2 h	18 (**6b**)	7 (**10b**)
14	**4b**	$Pd(OAc)_2$,[c] $P(o\text{Tol})_3$,[e] 0.5 h	55 (**6b**)	8 (**10b**)
15	**4b**	$PdCl_2[P(o\text{Tol})_3]_2$,[c] 0.5 h	60 (**6b**)	8 (**10b**)
16	**4b**	$Pd_2(dba)_3{\cdot}CHCl_3$,[c] $P(o\text{Tol})_3$,[d] 0.5 h	68 (**6b**)	5 (**10b**)

[a] The reaction of **4** (2 equiv.) with **5** was performed in the presence of a catalytic amount of a palladium complex in THF at 60 °C under an argon atmosphere. [b] Yield [%] based on **5**. [c] 5 mol-%. [d] 2.5 mol-%. [e] 10 mol-%.

The cross-coupling reaction was first attempted by heating **4** (generated in situ from indole **3** and *t*BuLi or *n*BuLi, followed by treatment with BEt_3) together with bromide **5** in the presence of a catalytic amount of a palladium complex in THF under an argon atmosphere at 60 °C. The reaction produced triene **6** together with a small amount of 2-vinylindole **10** (Scheme 3). The results are summarized in Table 1.

In the reaction using a Pd complex without PPh_3 as a ligand, bromide **5** was consumed within 0.5 h, and **6** was obtained in moderate yield (Table 1, entries 1–3, 10 and 11). The presence of PPh_3 reduced the yield of **6** and necessitated a longer heating time (Table 1, entries 4–6 and 12–13). The combination of a $P(o\text{Tol})_3$ ligand with the Pd complex, on the other hand, increased the yield of **6** (Table 1, entries 7–9 and 14–16). The reaction using $Pd_2(dba)_3{\cdot}CHCl_3$ (2.5 mol-%) in conjunction with $P(o\text{Tol})_3$ (10 mol-%) resulted in the highest yield of **6**. The yield of **10** was invariably low, regardless of the palladium complex used. The outcome of the cross-coupling reaction can be understood in terms of a common mechanism (Scheme 4).[14] The catalytically active Pd^0 species underwent oxidative addition with bromide **5** to produce vinylpalladium complex **A**. Although transmetallation between **4** and complex **A** followed by reductive elimination of Pd^0L_n from complex **E** produced **10**, intramolecular cyclization of complex **A** (carbopalladation), leading to formation of complex **B** or **C**, occurred more rapidly than the transmetallation step. PPh_3 might stabilize tetracoordinate complex **B** and suppress the transfer of the indole ring from **4** in the transmetallation step, thus providing the opportunity for side-reactions to occur. In contrast, coordination of bulky $P(o\text{Tol})_3$ shifted the equi-

librium between **B** and **C** towards the less crowded tricoordinate complex **C**, thus promoting the transfer of the indole ring from **4**, and leading to formation of complex **D**. Reductive elimination of Pd^0L_n from complex **D** gave triene **6**.



Scheme 4. A possible reaction pathway.

Next, we turned our attention to assembling the indolophenanthridine ring-system of **7** by 6π-electrocyclization of triene **6**. There are a number of studies on the 6π-electrocyclization process, which has become a powerful and important synthetic tool often used in natural product synthesis.[15] We have previously reported that photochemical and $TiCl_4$-promoted 6π-electrocyclization processes were effective for constructing pyridocarbazoles.[16] First, photochemical cyclization of **6a** was attempted: using a high-pressure mercury lamp to irradiate of **6a** in benzene cooled in an ice-water bath resulted only in a complex mixture, without any isolable products. In contrast, treatment of **6a** with $TiCl_4$ in CH_2Cl_2 at –78 °C under an argon atmosphere gave alcohol **6c** without any cyclization products. Because Lewis acids are known to lower the activation energy of some pericyclic reactions by complexation with unsaturated systems,[15] various Lewis acids were screened for the 6π-electrocyclization of **6a** (Table 2).

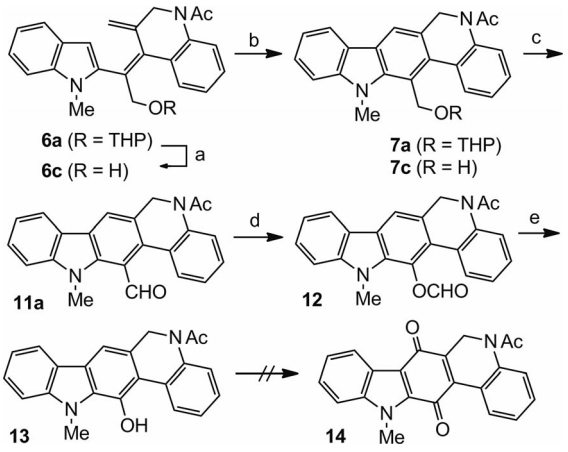
Table 2. Lewis acid promoted cyclization of **6a**.[a]

Entry	Conditions	Yield [%] (product)
1	$InCl_3$,[b] DMF, 120 °C, 1 h	no reaction
2	$In(OTf)_3$,[b] DMF, 120 °C, 2 h	20 (**7a**)
3	$In(OTf)_3$,[b] MeCN, r.t., 4 h	no reaction
4	Cp_2ZrCl_2,[c] MeCN, r.t., 4 h	51 (**7a**)
5	Cp_2ZrCl_2,[c] MeCN, r.t., 4 h	No reaction
6	$[Cp^*IrCl_2]_2$,[c][e] MeCN, r.t., 4 h	70 (**7a**)
7	$[Cp^*IrCl_2]_2$,[d][e] MeCN, r.t., 4 h	no reaction
8	$Cu(OTf)_2$,[c] MeCN, r.t., 1 h	no reaction
9	CuOTf,[c] MeCN, r.t., 1 h	no reaction
10	$(CuOTf)_2$·toluene,[c] MeCN, r.t., 1 h	74 (**7c**) + 13 (**6c**)
11	$(CuOTf)_2$·toluene,[d] MeCN, reflux, 16 h[f]	complex mixture
12	$(CuOTf)_2$·toluene,[d] MeCN, reflux, 16 h[g]	47 (**7c**)
13	$(CuOTf)_2$·toluene,[d] MeCN, reflux, 16 h[h]	65 (**7c**) + 10 (**6c**)

[a] All reactions were performed in air. [b] 2 equiv. [c] 1 equiv. [d] 0.1 equiv. [e] Cp* = 1,2,3,4,5-pentamethylcyclopedienyl. [f] A mixture of $(CuOTf)_2$·toluene and **6a** in MeCN was heated under reflux. [g] A solution of $(CuOTf)_2$·toluene in MeCN was added dropwise to a refluxing solution of **6a** in MeCN. [h] A solution of **6a** in MeCN was added dropwise to a refluxing solution of $(CuOTf)_2$·toluene in MeCN.

Heating **6a** with $In(OTf)_3$ in DMF at 120 °C produced **7a** in 20% yield, whereas $InCl_3$ was completely ineffective (Table 2, entries 1 and 2). Treatment of **6a** with Zr and Ir complexes in MeCN at room temperature gave **7a** in 51 and 70% yields, respectively (Table 2, entries 4 and 6). Moreover, performing the reaction using $(CuOTf)_2$·toluene complex (1 equiv.) at room temperature led to the formation of **7c** (74%) and **6c** (13%), in which the *O*-THP group had been removed (Table 2, entry 10). However, other Cu complexes [CuOTf and $Cu(OTf)_2$] were completely ineffective. Further evaluation revealed that the reaction could be catalyzed by $(CuOTf)_2$·toluene (10 mol-%); dropwise addition of a MeCN solution of **6a** to a refluxing MeCN solution of $(CuOTf)_2$·toluene (10 mol-%) provided **7c** (65%) and **6c** (10%) (Table 2, entry 13). In contrast, simply heating a mixture of **6a** and $(CuOTf)_2$·toluene (10 mol-%) in MeCN resulted in the formation of a complex mixture of products, and dropwise addition of a MeCN solution of $(CuOTf)_2$·toluene (10 mol-%) to a refluxing MeCN solution of **6a** provided **7c** in 47% yield (Table 2, entries 11 and 12). When $(CuOTf)_2$·toluene was used in the cyclization reaction of **6a**, uncyclized alcohol **6c** was formed along with cyclized compound **7c**, presumably with faster cleavage of the *O*-THP group preceding the cyclization step. The cyclization reaction was therefore carried out using **6c** (Scheme 4). The *O*-THP group of **6a** was removed with a catalytic amount of camphorsulfonic acid (CSA) in $MeOH/CH_2Cl_2$ (5:1) at room temperature to give **6c** in 90% yield. Then, treating **6c** with 1 equiv. of $(CuOTf)_2$·toluene in MeCN at room temperature for 1 h provided **7c** in 82% yield. Compound **7c** was also obtained in 71% yield from the catalyzed reaction of **6c** with 0.1 equiv. of $(CuOTf)_2$·toluene in MeCN under reflux for 16 h (Scheme 5). Only a few examples of Lewis-acid-mediated 6π-electrocyclization are known,[15] and the reaction described here is, to the best of our knowledge, the first example of Cu-catalyzed 6π-electrocyclization.[17] The $(CuOTf)_2$·toluene complex, the color of which

gradually changed from an initial pale-green after the bottle was newly opened to gray, was effective in promoting the reaction.

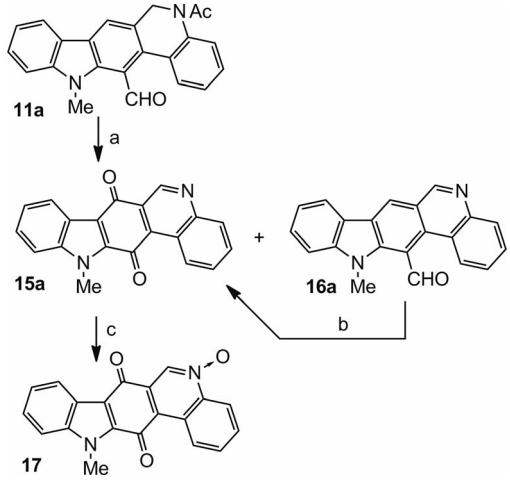


Scheme 5. Reagents and conditions: (a) CSA, MeOH/CH_2Cl_2 (5:1), r.t., 90%; (b) **6c**, $(CuOTf)_2$·toluene (1 equiv.), MeCN, r.t., 82% (**7c**); **6c**, $(CuOTf)_2$·toluene (0.1 equiv.), MeCN, reflux, 71% (**7c**); (c) **7c**, PCC, CH_2Cl_2, r.t., 80%; (d) $(PhSe)_2$ (0.1 equiv.), 30% aq. H_2O_2, CH_2Cl_2, room temp., 70%; (e) MeOH, NaOMe, 90%.

Having found conditions for obtaining indolophenanthridine **7c** in high yield, we next examined the transformation of **7c** to quinone **14**. Oxidation of **7c** with pyridinium chlorochromate (PCC) in CH_2Cl_2 gave aldehyde **11a** in 80% yield. Subjecting **11a** to Dakin oxidation with $(PhSe)_2$ and 30% H_2O_2 in CH_2Cl_2[18] produced formate **12**, and then methanolysis of **12** with NaOMe in MeOH provided phenol **13**. However, all attempts to oxidize **13** into quinone **14** using 10% NaOH with O_2, MnO_2, DDQ (2,3-dichloro-5,6-dicyano-1,4-benzoquinone), CAN [cerium(IV) ammonium nitrate], or $PhI(OAc)_2$ as oxidant were unsuccessful, and resulted either in complex mixtures of products or in the recovery of **13** (Scheme 5).

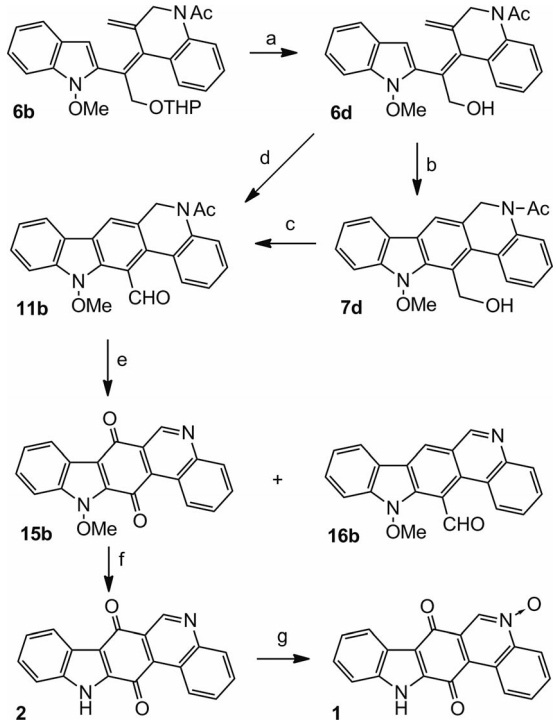
From a search for suitable reaction conditions, oxidation of **11a** with $(PhSe)_2$ and 30% H_2O_2 at room temperature for 24 h, followed by treatment with 10% NaOH under an oxygen atmosphere for 24 h was found to produce *N*-methylcalothrixin B (**15a**) in 50% yield, along with aldehyde **16a** in 15% yield. Aldehyde **16a** was converted to **15a** by Dakin oxidation with $(PhSe)_2$ and 30% aqueous H_2O_2 solution in 60% yield. Moreover, oxidation of **15a** with OXONE® in 50% aqueous acetone in the presence of K_2CO_3 gave *N*-methylcalothrixin A (**17**) in 63% yield (Scheme 6).

Having completed the synthesis of *N*-methylcalothrixins A (**17**) and B (**15a**) from *N*-methylindole (**3a**), we next investigated the total synthesis of calothrixins A (**1**) and B (**2**) using triene **6b** (Scheme 7). First, the *O*-THP group of **6b** was removed by treatment with CSA to give **6d** in 90% yield. The Cu-mediated 6π-electrocyclization of **6d** successfully produced phenanthridine **7d**. Reaction of **6d** with 1 equiv. $(CuOTf)_2$·toluene complex at room temperature for 1 h gave **7d** in 83% yield; heating **6d** at reflux with 10 mol-



Scheme 6. Reagents and conditions: (a) $(PhSe)_2$ (0.1 equiv.), 30% aq. H_2O_2, CH_2Cl_2, r.t., then 10% aq. NaOH, O_2, r.t., 50% (**15a**), 15% (**16a**); (b) $(PhSe)_2$ (0.3 equiv.), 30% aq. H_2O_2, CH_2Cl_2, r.t., then 10% aq. NaOH, O_2, r.t., 60%; (c) OXONE®, K_2CO_3, acetone/H_2O (1:1), 63%.

% $(CuOTf)_2$·toluene complex for 16 h produced **7d** in 72% yield. In addition, **7d** was found to be obtained in good yield (79%) by treating **6d** with 0.2 equiv. $(CuOTf)_2$·toluene



Scheme 7. Reagents and conditions: (a) CSA, MeOH/CH_2Cl_2 (5:1), r.t., 90%; (b) $(CuOTf)_2$·toluene (1 equiv.), MeCN, r.t., 1 h, 83%; $(CuOTf)_2$·toluene (0.1 equiv.), MeCN, reflux, 16 h, 72%; $(CuOTf)_2$·toluene (0.2 equiv.), MeCN/CH_2Cl_2 (1:1), r.t., 24 h, 79%; (c) PCC, CH_2Cl_2, r.t., 80%; (d) $(CuOTf)_2$·toluene (0.2 equiv.), PCC (3 equiv.), MeCN/CH_2Cl_2 (1:1), 50 °C, 3 h, 70%; (e) $(PhSe)_2$ (0.1 equiv.), 30% aq. H_2O_2, CH_2Cl_2, r.t., then 10% aq. NaOH, O_2, 53% (**15b**), 18% (**16b**); $Cu(OAc)_2$ (1 equiv.), PCC (3 equiv.), CH_2Cl_2, reflux, 10 h, 60%; (f) 10% Pd/C, H_2, THF, 85%; (g) OXONE®, K_2CO_3, acetone/H_2O (1:1), 70%.

complex in $MeCN/CH_2Cl_2$ at room temperature for 24 h. PCC oxidation of alcohol **7d** produced aldehyde **11b** in 80% yield. We also attempted the one-pot conversion of **6d** to **11b**; a mixture of **6d**, $(CuOTf)_2$·toluene complex (0.2 equiv.) and PCC (3 equiv.) in CH_2Cl_2/CH_3CN (1:1) was heated at 50 °C for 3 h. This provided **11b** in 70% yield in one pot. Next, Dakin oxidation of aldehyde **11b** with $(PhSe)_2$ (0.1 equiv.) and 30% aqueous H_2O_2 solution in CH_2Cl_2, followed by treatment with 10% aqueous NaOH solution under an O_2 atmosphere gave quinone **15b** in 53% yield, along with aldehyde **16b** in 18% yield, but the oxidation was sometimes poorly reproducible. Therefore, we sought to develop a more efficient oxidation of **11b** to form **15b**. After evaluating the oxidation conditions, pre-mixed $Cu(OAc)_2$ with PCC was found to be suitable as an oxidant;[19] heating a mixture of pre-mixed $Cu(OAc)_2$ (1 equiv.) and PCC (4 equiv.) with **11b** in CH_2Cl_2 under reflux for 10 h produced **15b** in 60% yield. Finally, the *N*-OMe group of **15b** was removed by catalytic hydrogenation using 10% Pd/C in THF to give calothrixin B (**2**) in 85% yield. The *N*-oxidation of **2** with OXONE® in aqueous acetone in the presence of K_2CO_3 provided calothrixin A (**1**) in 70% yield.

Conclusions

In summary, we have developed a concise total synthesis of calothrixins A (**1**) and B (**2**) and their respective *N*-methyl derivatives **17** and **15a**. The key features of the synthesis are one-pot generation of key intermediate **6** through the palladium-catalyzed tandem cyclization/cross-coupling reaction of indolylborate **4** with bromide **5**. We have also developed a new protocol for 6π-electrocyclization using $(CuOTf)_2$·toluene complex, which is unprecedented to the best of our knowledge. We are currently investigating further application of this cross-coupling methodology using indolylborate **4** in the synthesis of other indole alkaloids.

Experimental Section

General Methods: Melting points were recorded with a Yamato MP21 apparatus. HRMS (ESI) spectra were recorded with a JEOL JMS-T100LP mass spectrometer. IR spectra were measured with a Shimadzu IRAffinity-1 FTIR spectrophotometer. ^1H NMR and ^{13}C NMR spectra were recorded with a JEOL JNM-ECA500 (500 MHz) spectrometer, and chemical shifts are expressed in ppm (δ) with TMS as an internal reference. Column chromatography was performed on silica gel (Silica Gel 60N, Kanto Chemical Co., Ltd.).

2-[3-(Tetrahydro-2*H*-pyran-2-yloxy)prop-1-yn-1-yl]aniline (8): A mixture of 2-iodoaniline (2 g, 9.1 mmol), 2-(prop-2-yn-1-yloxy)-tetrahydro-2*H*-pyran (1.96 g, 14 mmol), $PdCl_2(PPh_3)_2$ (191 mg, 0.273 mmol), and CuI (173 mg, 0.91 mmol) in diethylamine (40 mL) was stirred at room temperature for 1 h under an argon atmosphere. This was an exothermic reaction. After this time, the mixture was concentrated in vacuo, and the residue was diluted with EtOAc (200 mL), washed with brine, and dried with $MgSO_4$. The solvent was removed, and the residue was separated by column chromatography on SiO_2 (hexane/EtOAc, 3:1) to give **8** (1.68 g, 80%) as a pale yellow oil. IR (neat): $\tilde{\nu}$ = 3360, 1614 cm^{-1}. ^1H NMR (500 MHz, $CDCl_3$): δ = 1.50–1.69 (m, 4 H), 1.72–1.80 (m, 1 H), 1.80–1.89 (m, 1 H), 3.53–3.60 (m, 1 H), 3.86–3.92 (m, 1 H), 4.22 (br. s, 2 H), 4.52 (d, *J* = 15.9 Hz, 1 H), 4.56 (d, *J* = 15.9 Hz, 1 H), 4.91 (t, *J* = 3.4 Hz, 1 H), 6.64–6.69 (m, 2 H), 7.10 (dt, *J* = 1.7, 7.5 Hz, 1 H), 7.28 (dd, *J* = 3.5, 8.0 Hz, 1 H) ppm. ^{13}C NMR (125 MHz, $CDCl_3$): δ = 19.1, 25.4, 30.4, 55.1, 62.2, 82.6, 90.5, 97.0, 107.4, 114.3, 117.8, 129.9, 132.5, 148.3 ppm. HRMS (ESI): calcd. for $C_{14}H_{17}NO_2Na$ $[M + Na]^+$ 254.1157; found 254.1122.

***N*-{2-[3-(Tetrahydro-2*H*-pyran-2-yloxy)prop-1-yn-1-yl]phenyl}-acetamide (9):** Acetyl chloride (1.35 g, 17.2 mmol) was added slowly to a solution of **8** (2 g, 8.6 mmol) and Et_3N (2.6 mL, 25.8 mmol) in CH_2Cl_2 (100 mL) under ice-cooling. The mixture was then allowed to warm gradually to room temperature and stirred for an additional 2 h. The mixture was concentrated on a rotary evaporator, and the residue was diluted with EtOAc (200 mL). The organic phase was washed with brine, and dried with $MgSO_4$. The solvent was removed, and the residue was separated by column chromatography on SiO_2 (hexane/EtOAc, 1:5) to give **9** (1.99 g, 85%) as a colorless solid. M.p. 56–58 °C (hexane/EtOAc). IR ($CHCl_3$): $\tilde{\nu}$ = 3402, 1695 cm^{-1}. ^1H NMR (500 MHz, $CDCl_3$): δ = 1.50–1.70 (m, 4 H), 1.72–1.89 (m, 2 H), 2.21 (s, 3 H), 3.54–3.60 (m, 1 H), 3.86–3.93 (m, 1 H), 4.53 (d, *J* = 16.6 Hz, 1 H), 4.57 (d, *J* = 16.6 Hz, 1 H), 4.91 (t, *J* = 3.4 Hz, 1 H), 7.00 (t, *J* = 7.5 Hz, 1 H), 7.31 (dt, *J* = 1.7, 7.4 Hz, 1 H), 7.38 (d, *J* = 8.0 Hz, 1 H), 8.02 (br. s, 1 H), 8.37 (d, *J* = 8.0 Hz, 1 H) ppm. ^{13}C NMR (125 MHz, $CDCl_3$): δ = 19.0, 24.9, 25.4, 30.4, 55.3, 62.1, 81.3, 92.7, 97.6, 129.9, 131.8, 139.5, 168.5 ppm. HRMS (ESI): calcd. for $C_{16}H_{19}NO_3Na$ $[M + Na]^+$ 296.1262; found 296.1235.

***N*-(2-Bromoprop-2-en-1-yl)-*N*-{2-[3-(tetrahydro-2*H*-pyran-2-yloxy)-prop-1-yn-1-yl]phenyl}acetamide (5):** Compound **9** (2.73 g, 10 mmol) was added slowly to a suspension of NaH (55% dispersion in mineral oil, 872 mg, 20 mmol) in THF (100 mL) at 0 °C. The mixture was stirred for 30 min, after which time 2,3-dibromopropene (3 g, 15 mmol) was added dropwise. The mixture was allowed to warm gradually to room temperature and stirred for 2 h. The mixture was concentrated on a rotary evaporator, and the residue was diluted with EtOAc (300 mL). The organic phase was washed with brine and dried with $MgSO_4$. The solvent was removed, and the residue was separated by silica gel column chromatography (hexane/EtOAc, 4:1) to give **5** (3.1 g, 80%) as a pale yellow oil. IR (neat): $\tilde{\nu}$ = 1672 cm^{-1}. ^1H NMR (500 MHz, $CDCl_3$): δ = 1.50–1.65 (m, 4 H), 1.72–1.86 (m, 2 H), 1.85 (s, 3 H), 3.51–3.59 (m, 1 H), 3.82–3.89 (m, 1 H), 3.93 (d, *J* = 15.3 Hz, 1 H), 4.45 (d, *J* = 16.4 Hz, 1 H), 4.49 (d, *J* = 16.4 Hz, 1 H), 4.81 (t, *J* = 3.0 Hz, 1 H), 5.26 (d, *J* = 15.3 Hz, 1 H), 5.48 (s, 1 H), 5.65 (s, 1 H), 7.29–7.38 (m, 3 H), 7.53 (d, *J* = 7.5 Hz, 1 H) ppm. ^{13}C NMR (125 MHz, $CDCl_3$): δ = 19.2, 22.5, 25.4, 30.3, 54.6, 55.2, 62.3, 81.5, 91.4, 97.0, 120.0, 122.2, 128.4, 128.7, 129.5, 129.6, 129.7, 129.8, 133.7, 143.3, 170.5 ppm. HRMS (ESI): calcd. for $C_{19}H_{22}BrNO_3Na$ $[M + Na]^+$ 414.0680, 416.0660; found 414.0656, 416.0637.

Palladium-Catalyzed Cross-Coupling Reaction of 4a with 5: *t*BuLi (1.6 M in pentane, 8.25 mL, 13.2 mmol) was added to a solution of *N*-methylindole (**3a**; 1.44 g, 11 mmol) in THF (100 mL) at 0 °C under an argon atmosphere, and the mixture was allowed to warm to room temperature. After the mixture was stirred for 1 h, BEt_3 (1 M in hexane, 13.2 mL, 13.2 mmol) was added, and the mixture was stirred for a further 1 h. Then, **5** (2.15 g, 5.5 mmol) and a catalytic amount of palladium complex (see Table 1 for catalyst structures and quantities) were added. After stirring at room temperature for

10 min, the mixture was heated at 60 °C (see Table 1 for reaction times). The mixture was then cooled to 0 °C, and 10% aqueous NaOH solution (20 mL) and 30% aqueous H_2O_2 solution (10 mL). After stirring for 20 min, the mixture was diluted with EtOAc (500 mL), washed with brine, and dried with $MgSO_4$. The solvent was removed, and the residue was separated by column chromatography on SiO_2 (hexane/EtOAc, 1.5:1) to give **6a** as a pale yellow solid and **10a** as a pale yellow oil (see Table 1 for yields of **6a** and **10a**).

(4*Z*)-4-[1-(1-Methyl-1*H*-indol-2-yl)-2-(tetrahydro-2*H*-pyran-2-yloxy)ethylidene]-3-methylidene-1-(prop-1-en-2-yl)-1,2,3,4-tetrahydroquinoline (6a): M.p. 70–72 °C (hexane/EtOAc). IR ($CHCl_3$): $\tilde{\nu}$ = 1651 cm^{-1}. ^1H NMR (500 MHz, $CDCl_3$): δ = 1.43–1.80 (m, 6 H), 2.21 (s, 3 H), 3.30–3.36 (m, 1 H), 3.56 (s, 3 H), 3.57–3.63 (m, 1 H), 4.21 (d, J = 11.1 Hz, 1 H), 4.54 (s, 2 H), 4.64 (d, J = 11.1 Hz, 1 H), 4.82 (s, 1 H), 6.51 (s, 1 H), 7.10 (t, J = 7.4 Hz, 1 H), 7.19 (t, J = 7.0 Hz, 1 H), 7.23 (d, J = 8.0 Hz, 1 H), 7.30 (d, J = 8.0 Hz, 1 H), 7.33 (t, J = 7.4 Hz, 1 H), 7.39 (t, J = 7.4 Hz, 1 H), 7.59 (d, J = 8.0 Hz, 1 H), 7.66 (d, J = 8.0 Hz, 1 H) ppm, the signals of two protons (N-CH_2) do not appear. ^{13}C NMR (125 MHz, $CDCl_3$): δ = 19.1, 22.3, 25.4, 30.3, 30.5, 47.3, 61.8, 69.5, 98.8, 101.4, 109.5, 113.6, 119.4, 120.4, 121.2, 124.9, 126.4, 126.8, 127.9, 128.8, 129.0, 132.9, 137.0, 139.0, 139.1, 140.0, 142.9, 169.3 ppm. HRMS (ESI): calcd. for $C_{28}H_{30}N_2O_3Na$ [M + Na]$^+$ 465.2154; found 465.2139.

***N*-[2-(1-Methyl-1*H*-indol-2-yl)prop-2-en-1-yl]-*N*-{2-[3-(tetrahydro-2*H*-pyran-2-yloxy)prop-1-yn-1-yl]phenyl}acetamide (10a):** IR ($CHCl_3$): $\tilde{\nu}$ = 1654 cm^{-1}. ^1H NMR (500 MHz, $CDCl_3$): δ = 1.50–1.69 (m, 4 H), 1.72–1.89 (m, 2 H), 1.79 (s, 3 H), 3.52 (s, 3 H), 3.51–3.60 (m, 1 H), 3.83–3.88 (m, 1 H), 4.20–4.33 (m, 2 H), 4.36 (d, J = 14.9 Hz, 1 H), 4.78 (t, J = 3.4 Hz, 1 H), 5.16 (s, 1 H), 5.38 (dd, J = 3.9, 14.9 Hz, 1 H), 5.39 (s, 1 H), 6.59 (s, 1 H), 6.70 (d, J = 8.0 Hz, 1 H), 7.09 (t, J = 7.5 Hz, 1 H), 7.17 (t, J = 7.5 Hz, 1 H), 7.21 (t, J = 7.5 Hz, 1 H), 7.20–7.29 (m, 2 H), 7.50 (d, J = 8.0 Hz, 1 H), 7.58 (d, J = 8.0 Hz, 1 H) ppm. ^{13}C NMR (125 MHz, $CDCl_3$): δ = 19.2, 22.5, 25.4, 30.3, 31.4, 52.2, 54.5, 62.3, 81.6, 91.1, 97.0, 102.1, 109.5, 118.8, 119.8, 120.9, 122.1, 122.5, 127.5, 127.5, 128.0, 129.1, 129.5, 133.5, 135.6, 135.8, 138.6, 138.8, 143.4, 170.8 ppm. HRMS (ESI): calcd. for $C_{28}H_{30}N_2O_3Na$ [M + Na]$^+$ 465.2154; found 465.2151.

Palladium-Catalyzed Cross-Coupling Reaction of 4b with 5: *n*BuLi (1.6 M in hexane, 8.25 mL, 13.2 mmol) was added to a solution of *N*-methoxyindole (**3b**; 1.6 g, 11 mmol) in THF (100 mL) at –20 °C under an argon atmosphere. After the mixture was stirred for 30 min, BEt_3 (1 M in hexane, 13.2 mL, 13.2 mmol) was added. After stirring for 30 min at –20 °C, the mixture was allowed to warm gradually to room temperature and stirred for 1 h. Then, **5** (2.15 g, 5.5 mmol) and a catalytic amount of palladium complex (see Table 1 for catalyst structures and quantities) were added. After stirring at room temperature for 10 min, the mixture was heated at 60 °C (see Table 1 for reaction times). The mixture was then cooled to 0 °C, and 10% aqueous NaOH solution (20 mL) and 30% aqueous H_2O_2 solution (10 mL) were added. After stirring for 20 min, the mixture was diluted with EtOAc (500 mL), washed with brine, and dried with $MgSO_4$. The solvent was removed, and the residue was separated by column chromatography on SiO_2 (hexane/EtOAc, 15:1) to give **6b** as pale yellow crystals and **10b** as a pale yellow oil (see Table 1 for yields of **6b** and **10b**).

(4*Z*)-4-[1-(1-Methoxy-1*H*-indol-2-yl)-2-(tetrahydro-2*H*-pyran-2-yloxy)ethylidene]-3-methylidene-1-(prop-1-en-2-yl)-1,2,3,4-tetrahydroquinoline (6b): M.p. 146–148 °C (hexane/EtOAc). IR ($CHCl_3$): $\tilde{\nu}$ = 1653 cm^{-1}. ^1H NMR (500 MHz, $CDCl_3$): δ = 1.40–1.50 (m, 2 H), 1.50–1.60 (m, 2 H), 1.60–1.68 (m, 1 H), 1.68–1.77 (m, 2 H), 2.19 (s, 3 H), 3.37–3.46 (m, 1 H), 3.65–3.73 (m, 1 H), 3.81 (s, 3 H), 4.32 (d, J = 10.0 Hz, 1 H), 4.59–4.70 (m, 4 H), 4.75–4.82 (m, 2 H), 6.48 (s, 1 H), 7.09 (t, J = 7.4 Hz, 1 H), 7.21 (t, J = 7.4 Hz, 1 H), 7.32 (t, J = 7.4 Hz, 1 H), 7.36–7.43 (m, 2 H), 7.56 (d, J = 8.0 Hz, 1 H), 7.59 (d, J = 7.5 Hz, 1 H) ppm. ^{13}C NMR (125 MHz, $CDCl_3$): δ = 19.2, 22.4, 25.4, 30.5, 37.4, 61.9, 64.9, 68.5, 98.8, 98.9, 108.4, 111.3, 119.9, 120.6, 122.1, 123.0, 123.6, 125.1, 126.4, 128.4, 128.6, 132.0, 133.5, 134.6, 139.8, 139.9, 144.5, 169.2 ppm. HRMS (ESI) calcd. for $C_{28}H_{30}N_2O_4Na$ [M + Na]$^+$ 481.2103; found 481.2082.

***N*-[2-(1-Methoxy-1*H*-indol-2-yl)prop-2-en-1-yl]-*N*-{2-[3-(tetrahydro-2*H*-pyran-2-yloxy)prop-1-yn-1-yl]phenyl}acetamide (10b):** IR (neat): $\tilde{\nu}$ = 1670 cm^{-1}. ^1H NMR (500 MHz, $CDCl_3$): δ = 1.48–1.65 (m, 4 H), 1.67–1.88 (m, 2 H), 1.84 (s, 3 H), 3.52–3.60 (m, 1 H), 3.69 (s, 3 H), 3.80–3.90 (m, 1 H), 4.20–4.37 (m, 2 H), 4.38, 4.42 (2 d, J = 15.0 Hz, 1 H), 4.75, 4.79 (2 s, 1 H), 5.17 (s, 1 H), 5.38, 5.42 (2 d, J = 15.0 Hz, 1 H), 5.91 (s, 1 H), 6.64, 6.65 (2 s, 1 H), 6.88 (dd, J = 3.5, 7.5 Hz, 1 H), 7.08 (t, J = 7.5 Hz, 1 H), 7.17 (t, J = 7.5 Hz, 1 H), 7.20–7.26 (m, 2 H), 7.36 (d, J = 8.0 Hz, 1 H), 7.50 (d, J = 8.0 Hz, 1 H), 7.56 (d, J = 8.0 Hz, 1 H) ppm. ^{13}C NMR (125 MHz, $CDCl_3$): δ = 19.2, 22.8, 25.4, 30.4, 51.3, 54.5, 62.3, 81.6, 91.2, 97.0, 97.1, 99.9, 108.3, 117.8, 120.4, 121.5, 122.5, 123.1, 123.5, 128.1, 129.1, 129.6, 133.0, 133.1, 133.5, 133.6, 134.0, 143.2, 170.4 ppm. HRMS (ESI): calcd. for $C_{28}H_{30}N_2O_4Na$ [M + Na]$^+$ 481.2103; found 481.2103.

6π-Electrocyclization of 6a with Pentamethylcyclopentadienyliridium(III) Dimer (1 equiv.): A solution of **6a** (354 mg, 0.8 mmol) in MeCN (3 mL) was added dropwise to a suspension of pentamethylcyclopentadienyliridium(III) dimer (636 mg, 0.8 mmol) in MeCN (20 mL) at room temperature, and the deep red mixture was stirred for 4 h. Insoluble materials were removed by filtration through a silica gel pad with suction. The filtrate was concentrated, and the residue was separated by column chromatography on SiO_2 (hexane/EtOAc, 5:1) to give **7a** (246 mg, 70%) as a pale yellow oil.

1-{12-Methyl-13-[(tetrahydro-2*H*-pyran-2-yloxy)methyl]-6,12-dihydro-5*H*-indolo[3,2-*j*]phenanthridin-5-yl}ethanone (7a): IR (neat): $\tilde{\nu}$ = 1651 cm^{-1}. ^1H NMR (500 MHz, $CDCl_3$): δ = 1.61–1.97 (m, 5 H), 2.20, 2.36 (2 s, 3 H), 3.61–3.64 (m, 2 H), 4.08–4.11 (m, 1 H), 4.27 (s, 3 H), 4.87 (s, 1 H), 4.54–6.00 (m, 4 H), 7.19–7.46 (m, 6 H), 7.50 (t, J = 7.4 Hz, 1 H), 8.04–8.06 (m, 2 H) ppm. ^{13}C NMR (125 MHz, $CDCl_3$): δ = 21.0, 22.1, 25.5, 31.6, 32.7, 47.1, 64.7, 65.6, 100.7, 109.1, 109.2, 116.3, 118.1, 119.5, 120.2, 122.4, 123.4, 124.7, 125.9, 126.3, 128.8, 129.2, 131.0, 132.9, 140.0, 142.2, 142.9, 168.7 ppm. HRMS (ESI): calcd. for $C_{28}H_{28}N_2O_3Na$ [M + Na]$^+$ 463.1998; found 463.1979.

6π-Electrocyclization of 6a or 6c with $(CuOTf)_2$·toluene (1 equiv.): A solution of **6a** (354 mg, 0.8 mmol) or **6c** (287 mg, 0.8 mmol) in MeCN (3 mL) was added dropwise to a suspension of $(CuOTf)_2$·toluene (410 mg, 0.8 mmol) in MeCN (20 mL) at room temperature, and the deep red mixture was stirred for 1 h. Insoluble materials were removed by filtration through a silica gel pad with suction. The filtrate was concentrated in vacuo, and the residue was separated by column chromatography on SiO_2 (hexane/EtOAc, 2:1). Triene **6a** provided **7c** (210 mg, 74%) as colorless crystals and **6c** (37 mg, 13%) as pale yellow crystals; **7c** (233 mg, 82%) was obtained from **6c**.

6π-Electrocyclization of 6a or 6c with $(CuOTf)_2$·toluene (0.1 equiv.): A solution of **6a** (354 mg, 0.8 mmol) or **6c** (287 mg, 0.8 mmol) in MeCN (3 mL) was added dropwise to a suspension of $(CuOTf)_2$·toluene (41 mg, 0.08 mmol) in MeCN (15 mL) under reflux, and the deep red mixture was heated under reflux for 16 h. After cooling, insoluble materials were removed by filtration through a silica gel pad with suction. The filtrate was concentrated, and the residue

was separated by column chromatography on SiO_2 (hexane/EtOAc, 2:1). Triene **6a** provided **7c** (184 mg, 65%) and **6c** (29 mg, 10%); **7c** (201 mg, 71%) was obtained from **6c**.

1-[13-(Hydroxymethyl)-12-methyl-6,12-dihydro-5*H*-indolo[3,2-*j*]-phenanthridin-5-yl]ethanone (7c): M.p. 198–200 °C (hexane/EtOAc). IR ($CHCl_3$): $\tilde{\nu}$ = 3595, 1647 cm^{-1}. ^1H NMR (500 MHz, $CDCl_3$): δ = 2.22 (s, 3 H), 2.20–2.22 (m, 1 H), 4.30 (s, 3 H), 4.60–5.90 (m, 4 H), 7.25 (t, J = 7.5 Hz, 1 H), 7.32–7.46 (m, 4 H), 7.50 (t, J = 7.5 Hz, 1 H), 8.02–8.07 (m, 2 H), 8.18 (br. s, 1 H) ppm. ^{13}C NMR (125 MHz, $CDCl_3$): δ = 22.1, 32.4, 47.0, 59.7, 109.1, 118.0, 118.2, 119.6, 120.2, 122.3, 123.5, 124.8, 126.0, 126.4, 127.8, 129.2, 130.1, 130.7, 132.1, 140.0, 141.5, 142.9, 168.7 ppm. HRMS (ESI) calcd. for $C_{23}H_{20}N_2O_2Na$ [M + Na]$^+$ 379.1422; found 379.1391.

1-[(4*Z*)-4-[2-Hydroxy-1-(1-methyl-1*H*-indol-2-yl)ethylidene]-3-methylidene-3,4-dihydroquinolin-1(2*H*)-yl]ethanone (6c): M.p. 106–108 °C (hexane/EtOAc). IR ($CHCl_3$): $\tilde{\nu}$ = 3620, 1653 cm^{-1}. ^1H NMR (500 MHz, $CDCl_3$): δ = 2.22 (s, 3 H), 3.55 (s, 3 H), 3.58 (br. s, 1 H), 4.55 (s, 1 H), 4.59 (s, 2 H), 4.84 (s, 1 H), 6.56 (s, 1 H), 7.13 (t, J = 7.5 Hz, 1 H), 7.23 (t, J = 7.4 Hz, 1 H), 7.24 (d, J = 7.5 Hz, 1 H), 7.32 (d, J = 7.6 Hz, 1 H), 7.34 (t, J = 7.4 Hz, 1 H), 7.40 (t, J = 7.4 Hz, 1 H), 7.47 (d, J = 7.0 Hz, 1 H), 7.61 (d, J = 8.0 Hz, 1 H) ppm, the signals of two protons (N-CH_2) do not appear. ^{13}C NMR (125 MHz, $CDCl_3$): δ = 22.3, 30.3, 47.1, 64.0, 101.4, 109.8, 113.6, 119.9, 120.4, 121.8, 124.9, 126.4, 126.5, 127.8, 128.9, 129.0, 132.5, 136.5, 136.8, 137.5, 140.1, 143.1, 169.3 ppm. HRMS (ESI): calcd. for $C_{23}H_{22}N_2O_2Na$ [M + Na]$^+$ 381.1579; found 381.1557.

Conversion of 6a to 6c: CSA (5 mg, 0.02 mmol) was added to a solution of **6a** (1 g, 2.26 mmol) in MeOH (100 mL) and CH_2Cl_2 (20 mL). The mixture was stirred for 24 h at room temperature under an argon atmosphere. The mixture was filtered through a silica gel pad with suction, and the filtrate was concentrated in vacuo. The residue was separated by column chromatography on SiO_2 (CH_2Cl_2/EtOAc, 3:1) to give **6c** (728 mg, 90%).

5-Acetyl-12-methyl-6,12-dihydro-5*H*-indolo[3,2-*j*]phenanthridine-13-carbaldehyde (11a): A mixture of PCC (363 mg, 1.68 mmol) and Celite (1 g) in CH_2Cl_2 (20 mL) was stirred at room temperature for 10 min, and then a solution of **7c** (200 mg, 0.56 mmol) in CH_2Cl_2 (5 mL) was added. The mixture was stirred at room temperature for 3 h under an argon atmosphere. Insoluble materials were removed by filtration with suction, the filtrate was concentrated, and the residue was separated by column chromatography on SiO_2 (EtOAc/CH_2Cl_2, 1:3) to give **11a** (158 mg, 80%) as a pale yellow oil. IR ($CHCl_3$): $\tilde{\nu}$ = 1658 cm^{-1}. ^1H NMR (500 MHz, $CDCl_3$): δ = 2.26 (s, 3 H), 4.04 (s, 3 H), 7.31 (t, J = 7.5 Hz, 1 H), 7.38–7.42 (m, 2 H), 7.45 (d, J = 7.5 Hz, 1 H), 7.48 (d, J = 8.5 Hz, 1 H), 7.52–7.60 (m, 2 H), 8.07 (d, J = 7.5 Hz, 1 H), 8.23 (s, 1 H), 10.37 (s, 1 H) ppm, the signals of two protons (N-CH_2) do not appear. ^{13}C NMR (125 MHz, $CDCl_3$): δ = 22.1, 36.0, 45.8, 110.1, 118.6, 120.2, 120.6, 122.1, 122.3, 125.0, 126.1, 127.2, 128.9, 129.7, 132.4, 135.1, 139.9, 140.2, 143.9, 168.9, 192.1 ppm. HRMS (ESI): calcd. for $C_{23}H_{18}N_2O_2Na$ [M + Na]$^+$ 377.1266; found 377.1217.

5-Acetyl-12-methyl-6,12-dihydro-5*H*-indolo[3,2-*j*]phenanthridin-13-yl Formate (12): Diphenyl diselenide (9 mg, 0.03 mmol) was added to a mixture of **11a** (100 mg, 0.28 mmol) and 30% aqueous H_2O_2 solution (0.2 mL) in CH_2Cl_2 (15 mL). The mixture was stirred at room temperature for 20 h under an argon atmosphere. The mixture was diluted with CH_2Cl_2 (15 mL), washed with brine and dried with $MgSO_4$. The solvent was removed, and the residue was separated by column chromatography on SiO_2 (hexane/EtOAc, 2:1) to give **12** (72 mg, 70%) as a pale orange oil. IR ($CHCl_3$): $\tilde{\nu}$ = 1766, 1651 cm^{-1}. ^1H NMR (500 MHz, $CDCl_3$): δ = 2.18 (s, 3 H), 4.05 (s, 3 H), 7.27 (t, J = 7.5 Hz, 1 H), 7.30–7.38 (m, 3 H), 7.39 (d, J = 8.0 Hz, 1 H), 7.52 (t, J = 7.5 Hz, 1 H), 7.96 (s, 1 H), 8.05 (d, 1 H, J = 7.5 Hz), 8.12–8.15 (m, 1 H), 8.27 (s, 1 H) ppm, the signals of two protons (N-CH_2) do not appear. ^{13}C NMR (125 MHz, $CDCl_3$): δ = 22.2, 31.8, 46.2, 109.0, 116.2, 120.0, 120.6, 122.2, 122.5, 125.3, 125.5, 126.5, 127.0, 127.8, 128.2, 128.4, 129.3, 132.3, 132.9, 139.5, 142.6, 160.0, 169.1 ppm. HRMS (ESI): calcd. for $C_{23}H_{18}N_2O_3Na$ [M + Na]$^+$ 393.1215; found 393.1181.

1-(13-Hydroxy-12-methyl-6,12-dihydro-5*H*-indolo[3,2-*j*]phenanthridin-5-yl)ethanone (13): A mixture of **12** (50 mg, 0.14 mmol) and NaOMe (8 mg, 0.14 mmol) in MeOH (10 mL) was stirred at room temperature for 0.5 h under an argon atmosphere. The mixture was diluted with CH_2Cl_2 (100 mL), washed with brine and dried with $MgSO_4$. The solvent was removed and the residue was separated by column chromatography on SiO_2 (hexane/EtOAc, 1:1) to give **13** (43 mg, 90%) as a colorless solid. M.p. 159–161 °C (EtOAc/hexane). IR ($CHCl_3$): $\tilde{\nu}$ = 3565, 1732 cm^{-1}. ^1H NMR ([D$_6$]acetone, 500 MHz): δ = 2.79 (s, 3 H), 4.25 (s, 3 H), 4.75 (br. s, 2 H), 7.17 (t, J = 7.5 Hz, 1 H), 7.28–7.36 (m, 2 H), 7.40–7.51 (m, 3 H), 7.71 (br. s, 1 H), 8.07 (d, J = 7.5 Hz, 1 H), 8.12 (br. s, 1 H), 8.42 (br. s, 1 H) ppm. ^{13}C NMR (CD_3OD, 125 MHz): δ = 20.6, 22.3, 31.1, 31.4, 46.6, 108.5, 110.0, 118.7, 118.8, 119.7, 122.5, 124.0, 124.7, 125.7, 126.2, 126.6, 128.1, 128.6, 130.2, 132.3, 138.5, 140.7, 142.4, 170.0 ppm. HRMS (ESI): calcd. for $C_{22}H_{18}N_2O_2Na$ [M + Na]$^+$ 365.1266; found 365.1237.

Dakin Oxidation of 11a: Diphenyl diselenide (9 mg, 0.03 mmol) was added to a mixture of **11a** (100 mg, 0.28 mmol) and 30% aqueous H_2O_2 solution (0.5 mL) in CH_2Cl_2 (15 mL). The mixture was stirred at room temperature for 24 h under an argon atmosphere. 10% aqueous NaOH solution (10 mL) was added, and the mixture was stirred for 16 h under an oxygen atmosphere. The mixture was diluted with CH_2Cl_2 (30 mL), washed with brine and dried with $MgSO_4$. The solvent was removed, and the residue was separated by column chromatography on SiO_2 (CH_2Cl_2/EtOAc, 30:1) to give **15a** (44 mg, 50%) as an orange solid, and **16a** (13 mg, 15%) as a pale yellow oil.

***N*-Methylcalothrixin B (15a):** M.p. 268–271 °C (hexane/EtOAc). IR (KBr): $\tilde{\nu}$ = 1656, 1639 cm^{-1}. ^1H NMR (500 MHz, [D$_6$]DMSO): δ = 4.21 (s, 3 H), 7.42 (t, J = 7.5 Hz, 1 H), 7.52 (t, J = 7.5 Hz, 1 H), 7.80 (d, J = 8.6 Hz, 1 H), 7.85 (t, J = 7.5 Hz, 1 H), 7.92 (t, J = 7.5 Hz, 1 H), 8.14 (d, J = 8.0 Hz, 1 H), 8.22 (d, J = 8.0 Hz, 1 H), 9.47 (d, J = 8.6 Hz, 1 H), 9.57 (s, 1 H) ppm. ^{13}C NMR (125 MHz, [D$_6$]DMSO): δ = 32.8, 112.8, 116.2, 122.8, 122.9, 123.1, 124.9, 125.3, 127.8, 127.9, 130.4, 130.7, 132.0, 134.0, 136.8, 140.6, 147.7, 152.0, 180.7, 182.1 ppm. HRMS (ESI): calcd. for $C_{20}H_{13}N_2O_2$ [M + H]$^+$ 313.0977; found 313.09518.

12-Methyl-12*H*-indolo[3,2-*j*]phenanthridine-13-carbaldehyde (16a): IR ($CHCl_3$): $\tilde{\nu}$ = 1732 cm^{-1}. ^1H NMR (500 MHz, $CDCl_3$): δ = 4.23 (s, 3 H), 7.46 (t, J = 6.9 Hz, 1 H), 7.59 (d, J = 8.6 Hz, 1 H), 7.68 (t, J = 8.0 Hz, 1 H), 7.75 (t, J = 8.1 Hz, 1 H), 7.87 (t, J = 8.1 Hz, 1 H), 8.27 (d, J = 8.0 Hz, 1 H), 8.36 (d, J = 8.0 Hz, 2 H), 8.91 (s, 1 H), 9.46 (s, 1 H), 10.66 (s, 1 H) ppm. ^{13}C NMR (125 MHz, $CDCl_3$): δ = 37.3, 110.6, 114.9, 120.8, 121.2, 121.8, 122.4, 123.1, 126.5, 127.1, 128.6, 129.5, 129.7, 129.8, 130.3, 131.1, 135.0, 144.4, 145.0, 153.5, 190.9 ppm. HRMS (ESI): calcd. for $C_{21}H_{15}N_2O$ [M + H]$^+$ 311.1184; found 311.1180.

Conversion of 16a into 15a: Diphenyl diselenide (28 mg, 0.09 mmol) was added to a mixture of **16a** (93 mg, 0.29 mmol) and 30% aqueous H_2O_2 solution (0.09 mL) in CH_2Cl_2 (10 mL). The mixture was stirred for 48 h at room temperature under an argon atmosphere. 10% aqueous NaOH solution (10 mL) was added, and the mixture was stirred for 16 h under atmospheric pressure of oxygen. The mixture was diluted with CH_2Cl_2, washed with brine, and dried

with $MgSO_4$. The solvent was removed and the residue was separated by column chromatography on SiO_2 (CH_2Cl_2/EtOAc, 20:1) to give **15a** (54 mg, 60%).

***N*-Methylcalothrixin A (17):** Oxone® (399 mg, 0.65 mmol) was added portionwise to a mixture of **15a** (40 mg, 0.13 mmol) and K_2CO_3 (90 mg, 0.65 mmol) in acetone (8 mL) and water (8 mL) at 0 °C. The mixture was allowed to warm gradually to room temperature and stirred for an additional 48 h. The mixture was diluted with CH_2Cl_2 (50 mL), washed with brine and dried with $MgSO_4$. The solvent was removed, and 50% aqueous acetone was added to the residue. The red-colored precipitate was collected by filtration with suction and washed with a small portion of acetone to give **17** (26 mg, 63%) as a red solid. M.p. 280–286 °C decomposed (acetone). IR (KBr): $\tilde{\nu}$ = 1660 cm^{-1}. ^1H NMR (500 MHz, [D$_6$]DMSO): δ = 4.23 (S, 3 H), 7.43 (t, J = 8.6 Hz, 1 H), 7.52 (t, J = 8.0 Hz, 1 H), 7.78 (d, J = 8.6 Hz, 1 H), 7.94 (t, J = 4.0 Hz, 2 H), 8.19 (d, J = 8.0 Hz, 1 H), 8.60 (d, J = 9.7 Hz, 1 H), 8.86 (s, 1 H), 9.60 (d, J = 5.8 Hz, 1 H) ppm. ^{13}C NMR (125 MHz, [D$_6$]DMSO): δ = 32.9, 112.8, 116.2, 119.7, 122.8, 123.0, 123.1, 125.5, 127.5, 127.7, 128.9, 129.9, 131.8, 132.2, 132.4, 137.2, 140.3, 144.0, 178.2, 179.7 ppm. HRMS (ESI): calcd. for $C_{20}H_{13}N_2O_3$ [M + H]$^+$ 329.0926; found 329.0922.

1-[(4*Z*)-4-[2-Hydroxy-1-(1-methoxy-1*H*-indol-2-yl)ethylidene]-3-methylidene-3,4-dihydroquinolin-1(2*H*)-yl]ethanone (6d): CSA (51 mg, 0.218 mmol) was added to a mixture of **6b** (1 g, 2.18 mmol) in MeOH (100 mL) and CH_2Cl_2 (20 mL). The mixture was stirred for 24 h at room temperature under an argon atmosphere. The mixture was filtered through a silica gel pad with suction, and the filtrate was concentrated in vacuo. The residue was separated by column chromatography on SiO_2 (hexane/EtOAc, 2:1) to give **6d** (733 mg, 90%) as a colorless solid. M.p. 152–155 °C (hexane/CH_2Cl_2). IR ($CHCl_3$): $\tilde{\nu}$ = 3396, 1658 cm^{-1}. ^1H NMR (500 MHz, $CDCl_3$): δ = 2.20, 2.35 (2 s, 3 H), 3.85 (s, 3 H), 4.67 (m, 5 H), 4.80 (s, 1 H), 6.46 (s, 1 H), 7.11 (t, J = 7.5 Hz, 1 H), 7.21–7.24 (m, 2 H), 7.33 (t, J = 7.5 Hz, 1 H), 7.38 (td, J = 1.2, 7.1 Hz, 1 H), 7.42 (d, J = 8.0 Hz, 1 H), 7.49 (d, J = 7.5 Hz, 1 H), 7.56 (d, J = 8.0 Hz, 1 H) ppm, the signal of OH is not detected. ^{13}C NMR (125 MHz, $CDCl_3$): δ = 22.5, 47.5, 63.1, 65.2, 98.7, 108.6, 111.5, 120.4, 120.8, 122.6, 123.7, 125.2, 125.9, 126.5, 128.5, 128.8, 132.4, 133.1, 133.3, 138.0, 139.8, 144.4, 169.5 ppm. HRMS (ESI): calcd. for $C_{23}H_{22}N_2NaO_3$ [M + Na]$^+$ 397.1528; found 397.1538.

6π-Electrocyclization of 6d with (CuOTf)$_2$·Toluene (1 equiv.): A solution of **6d** (300 mg, 0.8 mmol) in MeCN (3 mL) was added dropwise to a suspension of (CuOTf)$_2$·toluene (410 mg, 0.8 mmol) in MeCN (15 mL) at room temperature, and the deep red mixture was stirred for 1 h. Insoluble materials were removed by filtration through a silica gel pad with suction. The filtrate was concentrated in vacuo, and the residue was separated by column chromatography on SiO_2 (hexane/EtOAc, 2:1) to give **7d** (247 mg, 83%) as a colorless solid.

6π-Electrocyclization of 6d with (CuOTf)$_2$·Toluene (0.1 equiv.): A solution of **6d** (600 mg, 1.6 mmol) in MeCN (5 mL) was added dropwise to a refluxing suspension of (CuOTf)$_2$·toluene (82 mg, 0.16 mmol) in MeCN (25 mL), and the deep red mixture was heated under reflux for 16 h. After cooling, insoluble materials were removed by filtration through a silica gel pad with suction. The filtrate was concentrated in vacuo, and the residue was separated by column chromatography on SiO_2 (hexane/EtOAc, 2:1) to give **7d** (428 mg, 72%) as a colorless solid.

6π-Electrocyclization of 6d with (CuOTf)$_2$·Toluene (0.2 equiv.): A solution of **6d** (600 mg, 1.6 mmol) in MeCN (5 mL) and CH_2Cl_2 (5 mL) was added dropwise to a suspension of (CuOTf)$_2$·toluene (164 mg, 0.32 mmol) in MeCN (20 mL) and CH_2Cl_2 (20 mL), and the deep red mixture was stirred at room temperature for 24 h. Insoluble materials were removed by filtration through a silica gel pad with suction. The filtrate was concentrated in vacuo, and the residue was separated by column chromatography on SiO_2 (hexane/EtOAc, 2:1) to give **7d** (470 mg, 79%) as a colorless solid.

(5-Acetyl-12-methoxy-6,12-dihydro-5*H*-indolo[3,2-*j*]phenanthridin-13-yl)methanol (7d): M.p. 168–169 °C (hexane/CH_2Cl_2). IR ($CHCl_3$): $\tilde{\nu}$ = 3574, 1647 cm^{-1}. ^1H NMR (500 MHz, $CDCl_3$): δ = 2.22, 2.35 (2 s, 3 H), 4.27 (s, 3 H), 4.93–5.39 (m, 4 H), 5.89 (br. s, 1 H), 7.38–7.42 (m, 2 H), 7.31 (t, J = 6.9 Hz, 1 H), 7.34 (d, J = 7.4 Hz, 1 H), 7.50 (t, J = 7.5 Hz, 1 H), 7.56 (d, J = 8.1 Hz, 1 H), 7.92 (s, 1 H), 7.97 (d, J = 8.0 Hz, 1 H), 8.17 (d, J = 7.4 Hz, 1 H) ppm. ^{13}C NMR (125 MHz, $CDCl_3$): δ = 22.1, 46.7, 59.9, 64.6, 110.1, 117.7, 120.8, 121.2, 121.3, 121.6, 122.0, 124.7, 126.4, 127.1, 128.1, 130.2, 130.4, 131.8, 132.0, 139.8, 139.9, 141.2, 168.9 ppm. HRMS (ESI): calcd. for $C_{23}H_{20}N_2NaO_3$ [M + Na]$^+$ 395.1372; found 395.1364.

5-Acetyl-12-methoxy-6,12-dihydro-5*H*-indolo[3,2-*j*]phenanthridine-13-carbaldehyde (11b): PCC (711 mg, 3.3 mmol) and Celite (2 g) in CH_2Cl_2 (30 mL) were stirred for 10 min at room temperature, and then a solution of **7d** (410 mg, 1.1 mmol) in CH_2Cl_2 (10 mL) was added. The mixture was stirred for 3 h at room temperature under an argon atmosphere. Insoluble materials were removed by filtration with suction. The filtrate was concentrated in vacuo, and the residue was separated by column chromatography on SiO_2 (hexane/EtOAc, 2:1) to give **11b** (326 mg, 80%) as a pale yellow oil. IR (neat): $\tilde{\nu}$ = 1694, 1651 cm^{-1}. ^1H NMR (500 MHz, $CDCl_3$): δ = 2.28, 2.44 (2 s, 3 H), 4.08, 4.11, 4.16 (3 s, 3 H), 7.30 (t, J = 7.5 Hz, 1 H), 7.33 (t, J = 7.5 Hz, 1 H), 7.36 (d, J = 8.1 Hz, 1 H), 7.42 (t, J = 7.5 Hz, 1 H), 7.45–7.55 (m, 3 H), 7.99, 8.03 (2 d, J = 8.0 Hz, 1 H), 8.09, 8.20 (2 s, 1 H), 10.46, 10.56, 10.75 (3 s, 1 H) ppm, the signals of two protons (N-CH_2) do not appear. ^{13}C NMR (125 MHz, $CDCl_3$): δ = 21.2, 22.2, 22.8, 29.8, 45.9, 60.5, 63.5, 109.4, 111.6, 115.3, 118.8, 119.4, 120.6, 120.7, 121.4, 121.5, 121.6, 121.8, 123.6, 123.7, 124.0, 125.0, 125.1, 126.1, 126.2, 127.2, 127.6, 128.3, 128.6, 128.8, 128.9, 129.0, 131.1, 131.3, 131.5, 131.9, 132.3, 133.9, 135.3, 139.3, 139.8, 140.1, 140.7, 169.1, 171.3, 192.2, 193.1 ppm. HRMS (ESI): calcd. for $C_{23}H_{18}N_2NaO_3$ [M + Na]$^+$ 393.1215; found 393.1202.

One-Pot Conversion of 6d to 11b: Compound **6d** (500 mg, 1.33 mmol) was added to a mixture of PCC (860 mg, 4 mmol) and (CuOTf)$_2$·toluene (134 mg, 0.26 mmol) in CH_2Cl_2 (30 mL) and MeCN (30 mL) at room temperature After stirring for 1 h, the mixture was heated at 50 °C for 3 h. After cooling, the mixture was concentrated, and the residue was separated by column chromatography on SiO_2 (CH_2Cl_2/EtOAc, 30:1) to give **11b** (344 mg, 70%).

Dakin Oxidation of 11b: Diphenyl diselenide (28 mg, 0.09 mmol) was added to a mixture of **11b** (326 mg, 0.88 mmol), 30% aqueous H_2O_2 solution (0.3 mL) and CH_2Cl_2 (30 mL). After the mixture was stirred at room temperature for 24 h under an argon atmosphere, 10% aqueous NaOH solution (10 mL) was added, and the mixture was stirred for 16 h under atmospheric pressure of oxygen. The mixture was diluted with CH_2Cl_2 (50 mL), washed with brine, and dried with $MgSO_4$. The solvent was removed and the residue was separated by column chromatography on SiO_2 (CH_2Cl_2/EtOAc, 30:1) to give **15b** (153 mg, 53%) as a red powder, and **16b** (52 mg, 18%) as a colorless oil.

Conversion of 11b to 15b with Cu(OAc)$_2$ and PCC: A mixture of $Cu(OAc)_2$ (50 mg, 0.28 mmol) and PCC (240 mg, 1.1 mmol) in CH_2Cl_2 (50 mL) was stirred at room temperature for 10 min, and then **11b** (100 mg, 0.27 mmol) was added. The mixture was heated

under reflux for 10 h. After cooling, the mixture was separated by column chromatography on SiO_2 (CH_2Cl_2/EtOAc, 30:1) to give **15b** (55 mg, 60%).

12-Methoxy-7*H*-indolo[3,2-*j*]phenanthridine-7,13(12*H*)-dione (15b): M.p. 268–271 °C decomposed (hexane/CH_2Cl_2). IR (KBr): $\tilde{\nu}$ = 1663, 1645 cm^{-1}. ^1H NMR (500 MHz, $CDCl_3$): δ = 4.37 (s, 3 H), 7.45 (td, J = 1.2, 8.0 Hz, 1 H), 7.55 (td, J = 1.2, 8.1 Hz, 1 H), 7.62 (d, J = 8.6 Hz, 1 H), 7.87 (td, J = 1.2, 7.7 Hz, 1 H), 7.79 (td, J = 1.2, 7.4 Hz, 1 H), 8.21 (d, J = 8.0 Hz, 1 H), 8.42 (d, J = 8.0 Hz, 1 H), 9.62 (d, J = 8.6 Hz, 1 H), 9.80 (s, 1 H) ppm. ^{13}C NMR (125 MHz, $CDCl_3$): δ = 66.6, 109.9, 113.3, 119.4, 123.1, 123.9, 124.6, 125.6, 127.7, 128.5, 130.3, 130.5, 131.6, 131.8, 133.2, 135.5, 148.1, 152.4, 179.6, 180.7 ppm. HRMS (ESI): calcd. for $C_{20}H_{13}N_2O_3$ $[M + H]^+$ 329.0926; found 329.0900.

12-Methoxy-12*H*-indolo[3,2-*j*]phenanthridine-13-carbaldehyde (16b): IR ($CHCl_3$): $\tilde{\nu}$ = 1724, 1694 cm^{-1}. ^1H NMR (500 MHz, $CDCl_3$): δ = 4.18 (s, 3 H), 7.42 (td, J = 1.2, 6.3 Hz, 1 H), 7.60–7.66 (m, 3 H), 7.78 (t, J = 8.0 Hz, 1 H), 8.21 (d, J = 7.5 Hz, 1 H), 8.23 (d, J = 8.1 Hz, 1 H), 8.28 (d, J = 8.0 Hz, 1 H), 8.75 (s, 1 H), 9.38 (s, 1 H), 11.29 (s, 1 H) ppm. ^{13}C NMR (125 MHz, $CDCl_3$): δ = 63.6, 109.2, 116.5, 119.4, 121.2, 121.9, 122.1, 122.7, 123.4, 124.0, 126.5, 127.9, 128.6, 129.2, 130.3, 130.4, 137.3, 140.1, 145.7, 153.9, 194.4 ppm. HRMS (ESI): calcd. for $C_{21}H_{14}N_2NaO_2$ $[M + Na]^+$ 349.0953; found 349.0950.

Calothrixin B (2): Catalytic hydrogenation of **15b** (200 mg, 0.6 mmol) was carried out in THF (300 mL) in the presence of 10% Pd/C (200 mg) under atmospheric pressure of hydrogen for 20 h. The catalyst was removed by filtration with suction, and the filtrate was concentrated in vacuo. The residue was washed with diethyl ether to give calothrixin B (**2**) (160 mg, 80%) as a red solid. M.p. 273–275 °C (acetone). IR (KBr): $\tilde{\nu}$ = 3393, 1655 cm^{-1}. ^1H NMR (500 MHz, [D_6]DMSO): δ = 7.37 (t, J = 7.7 Hz, 1 H), 7.45 (t, J = 7.6 Hz, 1 H), 7.61 (d, J = 7.6 Hz, 1 H), 7.85 (t, J = 7.7 Hz, 1 H), 7.92 (t, J = 8.4 Hz, 1 H), 8.14 (d, J = 8.4 Hz, 1 H), 8.18 (d, J = 7.7 Hz, 1 H),9.55 (d, J = 8.4 Hz, 1 H), 9.62 (s, 1 H), 12.87 (br. s, 1 H) ppm. ^{13}C NMR (125 MHz, [D_6]DMSO): δ = 114.5, 116.1, 122.8, 123.1, 123.9, 124.8, 125.5, 127.6, 127.7, 130.4, 130.8, 132.1, 133.2, 148.1, 151.8, 180.9, 181.4 ppm. HRMS (ESI): calcd. for $C_{19}H_{11}N_2O_2$ $[M + H]^+$ 299.0821; found 299.0823.

Calothrixin A (1): Oxone® (307 mg, 0.5 mmol) was added in portions to a mixture of **2** (30 mg, 0.1 mmol) and K_2CO_3 (69 mg, 0.5 mmol) in 50% aqueous acetone (10 mL) at 0 °C. Then, the mixture was allowed to warm gradually to room temperature and stirred for 48 h. The mixture was diluted with CH_2Cl_2 (50 mL), washed with brine, and dried with $MgSO_4$. The solvent was removed, and 50% aqueous acetone (5 mL) was added to the residue. The red precipitate was collected by filtration with suction and washed with a small amount of acetone to give calothrixin A (**1**) (22 mg, 70%) as a red solid. M.p. 284–286 °C decomposed (acetone). IR (KBr): $\tilde{\nu}$ = 3320, 1663 cm^{-1}. ^1H NMR (500 MHz, [D_6]-DMSO): δ = 7.37 (t, J = 6.7 Hz, 1 H), 7.42 (t, J = 7.7 Hz, 1 H), 7.59 (d, J = 8.6 Hz, 1 H), 7.90–7.95 (m, 2 H), 8.11 (d, J = 7.7 Hz, 1 H), 8.58 (d, J = 10.1 Hz, 1 H), 8.87 (s, 1 H), 9.65 (d, J = 6.7 Hz, 1 H), 12.90 (br. s, 1 H) ppm. ^{13}C NMR (125 MHz, [D_6]DMSO): δ = 114.6, 115.7, 119.7, 122.5, 122.6, 124.1, 125.0, 127.4, 127.6, 128.7, 130.5, 132.3, 132.5, 138.8, 139.3, 143.7, 178.3, 178.8 ppm. HRMS (ESI): calcd. for $C_{19}H_{11}N_2O_3$ $[M + H]^+$ 315.0770; found 315.0775.

Supporting Information (see footnote on the first page of this article): Copies of the ^1H NMR and ^{13}C NMR spectra.

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[1] R. W. Rickards, J. M. Rothschild, A. C. Willis, N. M. de Chazal, J. Kirk, K. Kirk, K. J. Saliba, G. D. Smith, *Tetrahedron* **1999**, *55*, 13513–13520.
[2] P. H. Bernardo, C. L. L. Chai, G. A. Heath, P. J. Mahon, G. D. Smith, P. Waring, B. A. Wilkes, *J. Med. Chem.* **2004**, *47*, 4958–4963.
[3] Q. A. Khan, J. Lu, S. M. Hecht, *J. Nat. Prod.* **2009**, *72*, 438–442.
[4] T. R. Kelly, Y. Zhao, M. Cavero, M. Torneiro, *Org. Lett.* **2000**, *2*, 3735–3737.
[5] a) For a review, see: T. Choshi, S. Hibino, *Heterocycles* **2009**, *77*, 85–97; b) M.-L. Bennasar, T. Roca, F. Ferrando, *Org. Lett.* **2006**, *8*, 561–564; c) P. H. Bernardo, C. L. L. Chai, *J. Org. Chem.* **2003**, *68*, 8906–8909; d) P. H. Bernardo, C. L. L. Chai, J. A. Elix, *Tetrahedron Lett.* **2002**, *43*, 2939–2940; e) D. Sissouma, L. Maingot, S. Collet, A. Guingant, *J. Org. Chem.* **2006**, *71*, 8434–8389; f) S. Tohyama, T. Choshi, K. Matsumoto, A. Yamabuki, K. Ikegata, J. Nobuhiro, S. Hibino, *Tetrahedron Lett.* **2005**, *46*, 5263–5264.
[6] a) A. Yamabuki, H. Fujinawa, T. Choshi, S. Tohyama, K. Matsumoto, K. Ohnuma, J. Nobuhiro, S. Hibino, *Tetrahedron Lett.* **2006**, *47*, 5859–5861; b) S. Tohyama, T. Choshi, K. Matsumoto, A. Yamabuki, Y. Hieda, J. Nobuhiro, S. Hibino, *Heterocycles* **2010**, *82*, 397–416.
[7] a) C. S. P. McErlean, J. Sperry, A. J. Blake, C. J. Moody, *Tetrahedron* **2007**, *63*, 10963–10970; b) J. Sperry, C. S. P. McErlean, A. M. Z. Slawin, C. J. Moody, *Tetrahedron Lett.* **2007**, *48*, 231–234.
[8] a) N. Miyaura, A. Suzuki, *J. Chem. Soc., Chem. Commun.* **1979**, 866–867; b) N. Miyaura, A. Suzuki, *Chem. Rev.* **1995**, *95*, 2457–2483; c) S. Kotha, K. Lahirik, D. Kashinath, *Tetrahedron* **2002**, *58*, 9633–9695.
[9] a) N. Miyaura, K. Yamada, H. Suginome, A. Suzuki, *J. Am. Chem. Soc.* **1985**, *107*, 972–980; b) E. Negishi, T. Takahashi, S. Baba, D. E. van Horn, N. Okukado, *J. Am. Chem. Soc.* **1987**, *109*, 2393–2401; c) S. Sharma, A. C. Oehlschlager, *Tetrahedron Lett.* **1988**, *29*, 261–264.
[10] a) G. A. Molander, C. S. Yun, M. Ribagorda, B. Biolatto, *J. Org. Chem.* **2003**, *68*, 5534–5539; b) G. A. Molander, B. Canturk, L. E. Kennedy, *J. Org. Chem.* **2009**, *74*, 973–980.
[11] M. Ishikura, *Heterocycles* **2011**, *83*, 247–273.
[12] T. Abe, T. Ikeda, R. Yanada, M. Ishikura, *Org. Lett.* **2011**, *13*, 3356–3359.
[13] a) S. Takahashi, Y. Kuroyama, K. Sonogashira, N. Hagihara, *Synthesis* **1980**, 627–631; b) S. Negishi, L. Anastasia, *Chem. Rev.* **2003**, *103*, 1979–2017.
[14] a) F. Paul, J. Patt, J. F. Hartwig, *Organometallics* **1995**, *14*, 3030–3039; b) C. Amator, A. Jutand, *J. Organomet. Chem.* **1999**, *576*, 254–278; c) E. Galardon, S. Ramdeehul, J. M. Brown, A. Cowley, K. K. Hii, A. Jutand, *Angew. Chem.* **2002**, *114*, 1838–1841; *Angew. Chem. Int. Ed.* **2002**, *41*, 1760–1763; d) F. B. Landeros, J. F. Hartwig, *J. Am. Chem. Soc.* **2005**, *127*, 6944–6945; e) E. Negishi, F. Liu in *Metal-catalyzed Cross-coupling Reactions* (Eds.: F. Diederich, J. F. Stang), Wiley–VCH, Weinheim, Germany, **1997**, pp. 1–47.
[15] a) G. Desimoni, G. Tacconi, A. Barco, G. P. Pollini in *Natural Products Synthesis through Pericyclic Reactions*, American Chemical Society, Washington, D. C., **1983**; b) R. Hayashi, M. C. Walton, R. P. Hsung, J. H. Schwab, X. Yu, *Org. Lett.* **2010**, *12*, 5768–5771; c) V. Sofiyev, G. Navarro, D. Trauner, *Org. Lett.* **2008**, *10*, 149–152; d) S. B. J. Kan, E. A. Anderson,

Org. Lett. **2008**, *10*, 2323–2326; e) C. Hulot, G. Blong, J. Suffert, *J. Am. Chem. Soc.* **2008**, *130*, 5046–5047.

[16] M. Ishikura, A. Hino, T. Yaginuma, I. Agata, N. Katagiri, *Tetrahedron* **2000**, *56*, 193–207.

[17] a) L. M. Bishop, J. E. Barbarow, R. G. Bergman, D. Trauner, *Angew. Chem.* **2008**, *120*, 8220–8223; *Angew. Chem. Int. Ed.* **2008**, *47*, 8100–8103; b) D. J. Tantillo, *Angew. Chem.* **2009**, *121*, 33–34; *Angew. Chem. Int. Ed.* **2009**, *48*, 31–32.

[18] a) J. D. Stewart, *Curr. Org. Chem.* **1998**, *2*, 195–216; b) C. Bolm, O. Beckmann, T. K. K. Luong in *Metal-Catalyzed Baeyer–Villiger Reactions* (Eds.: M. Beller, C. Bolm), Wiley–VCH, Weinheim, **1998**, pp. 213–218; c) L. Syper, J. Mlochowski, *Tetrahedron* **1987**, *43*, 207–213; d) L. Syper, *Synthesis* **1989**, 167–172.

[19] a) V. J. Freer, P. Yates, *Chem. Lett.* **1984**, 2031–2032; b) K. Niknam, *Asian J. Chem.* **2005**, *17*, 2818–2820; c) G. Piancatelli, A. Scettri, M. D'Auria, *Synthesis* **1982**, 245–258; d) E. T. T. Kumpulainen, A. M. P. Koskinen, *Chem. Eur. J.* **2009**, *15*, 10901–10911.

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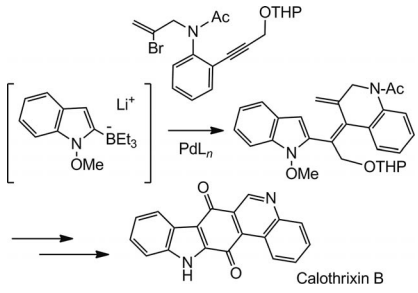
Palladium-catalyzed cross-coupling reaction of indolylborate with vinyl bromide proceeded smoothly, leading to triene. This intermediate was successfully used for the total synthesis of calothrixins A and B.



Keywords: Cross-coupling / Total synthesis / Palladium / Copper / Electrocyclic reactions

