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# Friedel−Crafts Acylation and Metalation Strategies in the Synthesis of Calothrixins A and B

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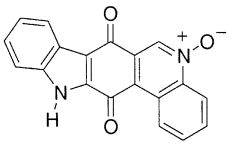
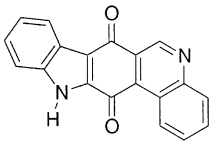
The total syntheses of calothrixins A and B starting from readily available indole and the acid chloride **4** are described.

## Introduction

The novel natural products calothrixins A (**1a**) and B (**1b**) were first isolated and identified in 1999 by Rickards and co-workers.[1] The calothrixins have been shown to inhibit the growth of the chloroquine-resistant strain of the human malaria parasite, *Plasmodium falciparum*, as well as display potent cell-killing abilities against certain cancer cell lines.[1−3] Structurally the calothrixins have the novel indolophenanthridine skeleton, which combines the chemical motifs of a quinoline, an indole group, and a quinone moiety in the same molecule. The latter two motifs feature prominently in bioactive natural products. For example, indoles such as the Vinca alkaloids vinblastine, vincristine, and vindesine display anticancer properties and are used clinically.[4] Similarly, the anticancer properties of quinones are well established with compounds such as mitomycin C, streptonigrin, and adriamycin in clinical use.[5] Thus the combined presence of these biologically important chemical motifs in the calothrixins was exciting and presents a new class of natural products as lead bioactive compounds.



**1a**



**1b**

Kelly et al. reported the first synthesis of the calothrixins in 2000.[6] The key step employed in the construction of the pentacyclic ring system utilized ortholithiation strategies, using the easily accessible starting materials quinoline-4-carboxamide and *N*-MOM-3-formylindole. Despite the short synthetic sequence, the overall yield to calothrixin B was poor due to the difficult lithiation step. This paper describes an alternative synthesis to calothrixins A and B. Our strategy differs from the Kelly synthesis in that the pentacyclic ring system is installed by using Friedel−Crafts acylation and metalation strategies. Though our synthesis is much longer in sequence, excellent yields are obtained in each step of the synthesis. The preliminary report of this synthetic strategy to calothrixin B has been published in a communication.[7]

## Results and Discussion

Our retrosynthetic strategy in Scheme 1 employs an initial disconnection at the C-12a to C-13 bond. A second disconnection can be made between C-7a and C-7, giving reactants corresponding to indole **3** and the acid chloride **4**. The acid chloride **4** can be synthesized from the corresponding quinoline **5**, which in turn is prepared from quinoline-3,4-anhydride **6**.[8,9] In the synthetic sense, coupling of the commercially available indole **3** to the acid chloride is desired to yield the ketone **2a**. The ketone **2a** is then cyclized to the target compound by using lithiation or similar strategies (Scheme 1).

The regioselectivity of the ring opening of the quinoline anhydride **6** to the monomethyl ester **5** was investigated. The ring opening of the analogous pyridine-3,4-anhydride to yield the 4-methyl ester has been reported to occur with high regioselectivity in the presence of sodium methoxide.[10] When quinoline anhydride **6** was treated with sodium methoxide, a disappointing 1:1 mixture of regioisomers was formed. Our studies showed that much better regioselectivity (5:1 of 4-methyl ester vs 3-methyl ester) was observed when dry methanol was used to effect

(1) Rickards, R. W.; Rothschild, J. M.; Willis, A. C.; de Chazal, N. M.; Kirk, J.; Kirk, K.; Saliba, K. J.; Smith, G. D. *Tetrahedron* **1999**, *55*, 13513−20.
(2) Doan, N. T.; Stewart, P. R.; Smith, G. D. *FEMS Microbiol. Lett.* **2001**, *196*, 135−9.
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**SCHEME 1. Retrosynthesis of Calothrixin B**

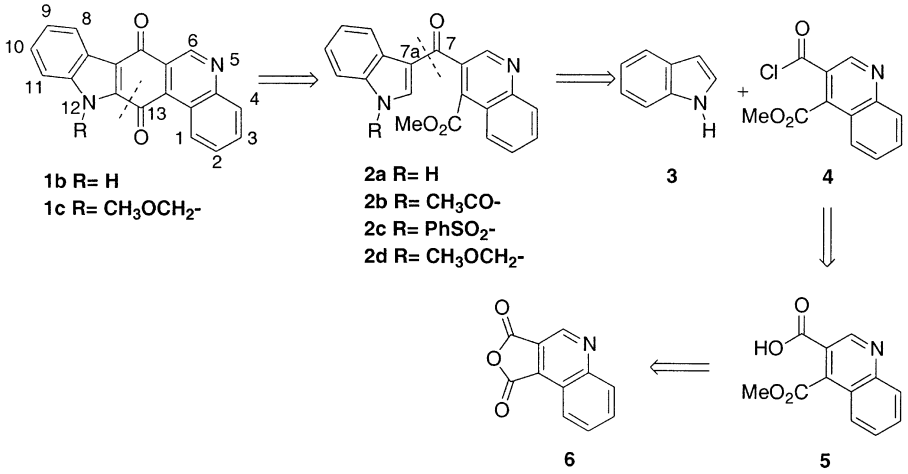



**TABLE 1. Coupling of Indole to 3-Chlorocarbonyl-4-methoxycarbonylquinoline (4)**

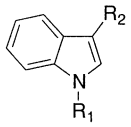
| entry | indole | reaction conditions | product | % yields |
|---|---|---|---|---|
| 1 | **7a** | $AlCl_3$, DCM, rt | – | – |
| 2 | **7b** | $AlCl_3$, DCM, rt | – | – |
| 3 | **3** | $Et_2AlCl$, DCM, 0 °C | **2a** | 27 |
| 4 | **7d** | *n*-BuLi, THF, −100 °C | – | – |
| 5 | **7d** | *n*-BuLi, $ZnCl_2$, THF, −78 °C to rt | **2a** | 47 |
| 6 | **7f** | *t*-BuLi, $ZnCl_2$, THF, −78 °C to rt | **2a** | 42 |
| 7 | **3** | MeMgCl, $ZnCl_2$, DCM, $AlCl_3$, rt | **2a** | 79 |
| 8 | **3** | MeMgCl, $ZnCl_2$, DCM, rt | **2a** | 90 |

the anhydride ring opening, and a typical isolated yield of 70% of the desired quinoline **5** was obtained.

The quinoline **5** was then quantitatively converted to the acid chloride **4** by refluxing in neat thionyl chloride. Due to the instability of the acid chloride **4**, the crude product was used in the next step of the synthesis.

**Coupling of Indole to 3-Chlorocarbonyl-4-methoxycarbonylquinoline (4).** Our initial task was to establish the most efficient method for carrying out the C3-acylation of indole using the acid chloride **4**. The results are summarized in Table 1.

In view of literature precedence reported for the synthesis of related carbazolediones,[10] initial attempts at C3 acylation utilized the Friedel−Crafts acylation of *N*-phenylsulfonylindole (**7a**) and *N*-tosylindole (**7b**) in the presence of $AlCl_3$ with the quinoline acid chloride **4**. Only the unreacted **7a** and **7b** were recovered, respectively. Other Lewis acid catalysts (e.g. $TiCl_4$, $BF_3{\cdot}OEt_2$) were also employed in the reaction with **7b** but none of the desired product was observed to form. In model studies, we were able to effect the Friedel−Crafts acylation of *N*-tosyl indole (**7b**) with acetic anhydride in the presence of $AlCl_3$ in 51% yield. Thus our difficulty in achieving this coupling with the acid chloride **4** was attributed to a combination of factors, i.e., the decreased reactivity of this acid chloride as well as the decreased reactivity of the substrate **7b** presumably due to the presence of the electron-withdrawing *N*-tosyl group. To circumvent this problem, we attempted to use the more reactive indole **3** in Friedel−Crafts acylation reactions. To our delight, treatment of the indole **3** with the acid chloride **4** in the presence of $Et_2AlCl$ gave the desired ketone **2a** as a pale yellow powder in albeit low 27% yield. Low resolution mass spectrometry showed a molecular ion peak at *m*/*z* 330.0 and the correct formula was confirmed by HRMS. As the yields were low, however, other synthetic approaches were considered.



**7a $R_1$= $PhSO_2$-, $R_2$= H**
**7b $R_1$= Ts-, $R_2$= H**
**7c $R_1$= $PhSO_2$-, $R_2$= I**
**7d $R_1$= Ts-, $R_2$= I**
**7e $R_1$= Ts-, $R_2$= ZnCl**
**7f $R_1$= TBDMS-, $R_2$= I**
**7g $R_1$= ZnCl, $R_2$= H**

There are limited reports for the metalation of the C3-position of *N*-sulfonyl indoles.[11] For example, the halogen−metal exchange reaction of *N*-phenylsulfonyl-3-iodoindole (**7c**) can be readily carried out by using *n*-BuLi and treatment of the C3-metalated compound with an acid chloride or alkyl halide is reported to yield the 3-substituted compound. As 3-lithio indole species are not stable above −100 °C due to rearrangement of the anion to the more stable 2-lithio indole, the lithiation reaction of the indole **7d** was carried out at temperatures below −100 °C. The coupling of the acid chloride **4** to the indole **7d** under these conditions, however, was unsuccessful. A $D_2O$ quench of the lithiation reaction showed that 75% deuterium incorporation was observed at the C3-position and only 25% deuterium incorporation was observed in the C2-position. This suggests that the failure to obtain the desired compound was not due to the inability to form the C3 anion but was presumably due to the lower reactivity of the acid chloride **4** at temperatures below −100 °C.

In an alternative procedure, *N*-tosyl-3-iodoindole (**7d**) was lithiated in the presence of $ZnCl_2$ in THF to presumably yield the more stable intermediate **7e.** Addition of the acid chloride **4** to the reaction mixture at room temperature and subsequent workup gave the ketone **2a** in 47% yield. When *N*-TBDMS-3-iodoindole (**7f**) was used instead of *N*-tosyl-3-iodoindole (**7d**), lithiation in the presence of $ZnCl_2$ gave the ketone **2a** in comparable yields. As these yields were still too low for our purposes, an alternative method was investigated.

(11) Saulnier, M. G.; Gribble, G. W. *J. Org. Chem.* **1982**, *47*, 757−61.

Our studies so far have shown that the desired ketone **2a** could be synthesized either by using the unprotected indole and $Et_2AlCl$ in conjunction with the acid chloride **4**, or via transmetalation of C3-lithioindole with $ZnCl_2$, followed by the addition of **4**. The simplicity of the first method was offset by the low yields obtained. The second method offered better yields but was still too low for our purposes. A survey of the literature suggests that a third method for the coupling of indoles to acid chlorides may be relatively simple to effect with high yields in return.

Reports by Bergman and Venemalm, as well as Yang et al., have shown that Friedel−Crafts acylation can be carried out regioselectively by using *N*-chlorozinc indole **7g** to give 3-acylindoles in good yields.[12−14] Following the methodology of Yang, indole **3** was treated with MeMgCl in the presence of $ZnCl_2$ and subsequent addition of the acid chloride **4** followed by the addition of $AlCl_3$ gave the desired ketone **2a** in 79% yield. When the Friedel−Crafts acylation reaction was attempted in the absence of $AlCl_3$, the desired ketone **2a** was reproducibly obtained in excellent yields (90%). Under analogous conditions, treatment of indole **3** with quinoline anhydride **6** in the presence of $AlCl_3$ gave a complex reaction mixture upon workup while in the absence of $AlCl_3$, no reaction was observed.

***N*-Protection and Cyclization to Calothrixin B Derivative.** With the key synthetic precursor **2a** in hand, the success of the final C−C bond formation to form the pentacyclic ring of calothrixin B now relied on the choice of a suitable *N*-protecting group. Thus three *N*-protected derivatives (**2b**−**d**) were prepared following general literature procedures.[15]

The synthesis of the *N*-acetyl compound **2b** from ketone **2a** was achieved by using NaH and acetyl chloride. Attempts to purify the compound on silica, however, resulted in cleavage of the protecting group. Subsequent attempts at the purification of compound **2b** with successive recrystallizations were difficult and time-consuming and led to low recoveries of the product (18%). Thus this strategy was abandoned in favor of other approaches.

In contrast, the *N*-phenylsulfonyl precursor **2c** was stable to purification and was obtained as a bright yellow compound in good yields. However, attempts to cyclize **2c** under various conditions (LDA, LDA and TMEDA, LHMDS and TMEDA, *t*-BuLi) only resulted in the cleavage of the phenylsulfonyl group and the recovery of **2a**.

Synthesis of the *N*-MOM derivative **2d** was readily carried out by treating the ketone **2a** with NaH in THF followed by the addition of MOMCl. Purification yielded the *N*-MOM derivative **2d** in very high yields (90%). Lithiation of **2d** with 2 equiv of LDA (or alternatively LHMDS) in the presence of TMEDA gave the desired compound *N*-MOM calothrixin B (**1c**) in 92% yield. The $^1$H NMR spectrum and the melting point of our synthetic compound were in excellent agreement with those reported in the literature.[6]

**Deprotection and Subsequent Conversions to Calothrixins A and B.** We initially attempted to remove the *N*-MOM group under acidic conditions as reported by Kelly.[6] In our hands, however, only the starting material was recovered after heating for 2 days. When the reaction conditions were modified and a DMSO−HCl mixture was used, hydrolysis of the *N*-MOM group was observed but the yields of the desired calothrixin B were difficult to reproduce and complex mixtures were frequently obtained. The use of $BF_3Et_2O$−LiBr[16] and $AlCl_3$[17] were two other methods attempted for the *N*-MOM cleavage, but only the starting material and complex mixtures were obtained, respectively. Clean and facile cleavage of the *N*-MOM group was finally achieved by using $BBr_3$ (1.2 equiv) in DCM. The reaction mixture was then heated in saturated $NaHCO_3$ at 60 °C and subsequent workup gave the desired product calothrixin B (**1b**) in 85% yield.

The $^1$H NMR spectrum of the synthetic calothrixin B matched the spectra reported by Rickards et al.[1] The $^{13}$C NMR spectrum had small differences of ±(0.1−0.3) ppm when compared to the literature data for both the synthetic and the natural calothrixin B. However, these differences in carbon chemical shifts have been noted in the literature[6] and have been attributed to the presence of water in the $d_6$-DMSO. The MS and HRMS data obtained for our sample were consistent with the literature data for the natural product. Furthermore, analysis by TLC with various solvent systems and co-spotting with synthetic and natural **1b** showed that the synthetic calothrixin B was identical with the authentic calothrixin B.

Thus in the studies above, we have demonstrated that calothrixin B (**1b**) can be synthesized in high yields and excellent purities. Conversion of **1b** to calothrixin A (**1a**) was then readily achieved by using *m*-CPBA as the oxidant.[6] The physical and spectroscopic data for our synthetic **1a** are in excellent agreement with the authentic natural product **1a**.

## Experimental Section

**3-Carboxy-4-methoxycarbonylquinoline (5).** Quinoline-3,4-anhydride[8] **6** (0.40 g, 2 mmol) was dissolved in dry distilled methanol (50 mL) and refluxed for 30 min. The reaction was monitored via TLC (acetone) for the disappearance of the anhydride ($R_f$ 0.80). The solvent was removed under reduced pressure and the residue was redissolved in saturated $NaHCO_3$ solution (5 mL) and $H_2O$ (10 mL). The solution was then acidified to precipitate the desired regioisomer. Recrystallization from hot acetone yielded the quinoline **5** as a colorless compound (0.32 g, 70% yield). $R_f$ (MeOH) 0.24; mp 230−2 °C dec; $^1$H NMR ($d_6$-DMSO) $\delta$ 4.00 (s, 3H), 7.78 (t, $J$ = 7 Hz, 1H), 7.87 (d, $J$ = 7 Hz, 1H), 7.97 (t, $J$ = 7 Hz, 1H), 8.12 (d, $J$ = 8 Hz, 1H), 9.36 (s, 1 H, 1H); $^{13}$C NMR ($d_6$-DMSO) $\delta$ 53.1, 120.2, 122.4, 125.8, 128.9, 129.4, 132.4, 141.4, 148.9, 150.0, 165.4, 166.8; UV−vis (MeOH) $\epsilon_{235nm}$ 32611 $M^{-1}$; IR ($cm^{-1}$) 1256, 1316, 1732, 2427; MS *m*/*z* (%) 231 (100, **M**), 200.0 (100), 187.0 (42), 172.0 (14), 155.0 (87), 127.0 (92), 116.0 (22), 101.0 (30), 89.0 (32), 74.0 (35), 63.0 (26); HRMS calcd for $C_{12}H_9NO_4$ 231.0532, found 231.0534. Anal. Calcd for $C_{12}H_9NO_4$: C, 62.34; H, 3.92; N, 6.06. Found: C, 62.06; H, 3.80; N, 5.92.

**3-Chlorocarbonyl-4-methoxycarbonylquinoline (4).** The quinoline **5** (0.43 g, 1.86 mmol) was refluxed for 30 min in neat

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(13) Yang, C.; Patel, H. H.; Ku, Y.-y.; Shah, R.; Sawick, D. *Synth. Commun.* **1997**, *27*, 2125−32.
(14) Dieter, R. K. *Tetrahedron* **1999**, *55*, 4177−236.
(15) Beccalli, E. M.; Broggini, G.; Marchesini, A.; Rossi, E. *Tetrahedron* **2002**, *58*, 6673−8.
(16) Sundberg, R. J.; Russell, H. F. *J. Org. Chem.* **1973**, *38*, 3324−30.
(17) Sotelo, E.; Coelho, A.; Raviña, E. *Tetrahedron Lett.* **2001**, *42*, 8633−6.

$SOCl_2$ (5 mL) until a clear yellow solution was obtained. The solvent was removed under reduced pressure and the acid chloride was coevaporated with anhydrous ether, then dried over $K_2CO_3$ under vacuum for 7.5 h. The crude product was obtained in quantitative yield. The $CDCl_3$ utilized was passed through a plug of anhydrous $Na_2SO_4$ as the acid chloride is sensitive to traces of $H_2O$. $^1$H NMR ($CDCl_3$) $\delta$ 4.20 (s, 3H), 8.19 (s, 2H), 8.40 (br s, 1H), 9.00 (d, $J$ = 8 Hz, 1 H), 9.87 (s, 1H); $^{13}$C NMR ($CDCl_3$) $\delta$ 54.5, 122.4, 123.2, 124.3, 127.5, 132.5, 138.6, 139.8, 144.9, 148.9, 163.0, 163.1.

**3-(3-Indolyl)carbonyl-4-methoxycarbonylquinoline (2a).** To a mixture of indole **3** (0.50 g, 4.3 mmol) and anhydrous $ZnCl_2$ (1.16 g, 2 equiv) in dry DCM (20 mL) was added dropwise MeMgCl (3 M in THF, 1 equiv). The mixture was stirred for 2 h at room temperature to generate *N*-chlorozinc indole in situ. The suspension was then quickly added to a solution of **4** (2.0 g, 7.9 mmol) in dry DCM (20 mL) and stirred at room temperature for 16 h. The reaction was stopped by the addition of aqueous saturated ammonium chloride solution (5 mL). The aqueous layer was then extracted with three portions of DCM (15 mL each). The combined organic layers were then washed successively with saturated $NaHCO_3$ solution (5 mL) and saturated NaCl solution (50 mL), then dried with $MgSO_4$. Column chromatography on silica (1:1 ethyl acetate:light petroleum) followed by recrystallization in acetone/*n*-hexane afforded **2a** as a fine yellow powder (1.28 g, 90% yield). $R_f$ (1:1 ethyl acetate/ light petroleum) 0.38; mp 196 °C; $^1$H NMR ($CDCl_3$) $\delta$ 3.75 (s, 3 H), 7.29 (m, 2H), 7.39 (d, $J$ = 8 Hz, 1H), 7.48 (s, 1H), 7.68 (t, $J$ = 8 Hz, 1H), 7.84 (t, $J$ = 8 Hz, 1H), 8.12 (d, $J$ = 8 Hz, 1H), 8.19 (d, $J$ = 8 Hz, 1H), 8.39 (d, $J$ = 8 Hz, 1H), 9.19 (s, 1H), 10.23 (s, 1H); $^{13}$C NMR ($CDCl_3$) $\delta$ 53.1, 111.7, 117.5, 122.3, 123.2, 123.6, 124.4, 125.7, 125.8, 128.6, 129.7, 131.2, 131.8, 134.8, 136.5, 138.1, 148.8, 148.9, 167.2, 188.1; UV−vis (DCM) $\epsilon_{244nm}$ 41570 M$^{-1}$; IR (cm$^{-1}$) 1596, 1726, 2951, 3253; MS *m*/*z* (%) 330.0 (85, **M**), 299.0 (25), 270.0 (60), 242.0 (35), 214.0 (25), 144.0 (100), 116.0 (37), 89.0 (26); HRMS calcd for $C_{20}H_{14}N_2O_3$ 330.1004, found 330.1008. Anal. Calcd for $C_{20}H_{14}N_2O_3$: C, 72.72; H, 4.27; N, 8.48. Found: C, 72.44; H, 4.26; N, 8.18.

**3-(1-Methoxymethylindol-3-yl)carbonyl-4-methoxycarbonylquinoline (2d).** To a solution of the ketone **2a** (0.10 g, 0.3 mmol) in dry THF (20 mL) at 0 °C was added NaH (1.2 equiv). The suspension was warmed to room temperature over 30 min and a bright red color was observed. The suspension was then cooled to 0 °C and MOMCl (36 $\mu$L, 0.6 mmol) was added. The reaction mixture was warmed to room temperature and stirred for a further 45 min. The progress of the reaction was monitored via TLC (1:1 ethyl acetate/light petroleum) for the disappearance of the starting material. Upon completion of the reaction, the reaction mixture was poured into saturated $NaHCO_3$ solution (15 mL) and thrice extracted with DCM (10 mL portions). The combined organic layers were dried with $MgSO_4$ and filtered, and the solvent was removed under reduced pressure to yield the desired compound. Purification via column chromatography (1:1 ethyl acetate/light petroleum) followed by recrystallization from acetone/*n*-hexane gave the desired compound as a white powder (0.1 g, 90% yield). The product was dried for 24 h over $K_2CO_3$ under vacuum prior to the next step. $R_f$ (1:1 ethyl acetate/light petroleum) 0.45; mp 163 °C; $^1$H NMR ($CDCl_3$) $\delta$ 3.18 (s, 3H), 3.64 (s, 3H), 5.33 (s, 2H), 7.30 (m, 2H), 7.44 (m, 2H), 7.60 (t, $J$ = 8 Hz, 1H), 7.77 (t, $J$ = 8 Hz, 1H), 8.05 (d, $J$ = 8 Hz, 1H), 8.13 (d, $J$ = 8 Hz, 1H), 8.36 (d, $J$ = 8 Hz, 1H), 9.13 (s, 1H); $^{13}$C NMR ($CDCl_3$) $\delta$ 52.9, 56.3, 78.3, 100.6, 117.1, 122.6, 123.5, 123.6, 124.6, 125.7, 126.7, 128.5, 129.7, 131.1, 131.6, 136.8, 137.3, 137.8, 148.8, 166.9, 187.8; UV−vis (DCM) $\epsilon_{247nm}$ 33008 M$^{-1}$; IR (cm$^{-1}$) 1619, 1728, 2951, 3119; MS *m*/*z* (%) 374.1 (100, **M**), 343.1 (25), 188.1 (50), 143.1 (50), 128.1 (20), 100.1 (49); HRMS calcd for $C_{22}H_{18}N_2O_4$ 374.1266, found 374.1266. Anal. Calcd for $C_{22}H_{18}N_2O_4$: C, 70.58; H, 4.85; N, 7.48. Found: C, 70.52; H, 4.80; N, 7.28.

***N*-Methoxymethyl Calothrixin B (1c).** To a solution of **2d** (0.27 g, 0.72 mmol) in dry THF (60 mL) and TMEDA (0.11 mL, 1 equiv) at −78 °C was added LHMDS (2.2 equiv). The solution was stirred for 2 h at −78 °C, then warmed to room temperature and stirred for a further 16 h during which the reaction mixture turned bright red-orange. The reaction was quenched with saturated $NaHCO_3$ solution (50 mL). The organic components were thrice extracted from the aqueous solution with DCM (50 mL portions), washed with saturated NaCl solution (50 mL), dried with $MgSO_4$, and filtered. Removal of the solvent under reduced pressure yielded the crude product as an orange-red solid. Column chromatography on silica (2:3 ethyl acetate/*n*-hexane) followed by recrystallization from hot ethyl acetate and *n*-hexane gave the desired product as an amorphous orange solid (0.23 g, 92% yield). The spectroscopic data obtained are similar to the values reported in the literature. mp 233−4 °C (lit.[6] mp 234−5 °C); $R_f$ (2:3 ethyl acetate/*n*-hexane) 0.59; $^1$H NMR ($CDCl_3$) $\delta$ 3.44 (s, 3H), 6.17 (s, 2H), 7.46 (t, $J$ = 8 Hz, 1H), 7.53 (t, $J$ = 8 Hz, 1H), 7.60 (d, $J$ = 9 Hz, 1H), 7.77 (t, $J$ = 7 Hz, 1H), 7.86 (t, $J$ = 7 Hz, 1H), 8.21 (d, $J$ = 8 Hz, 1H), 8.45 (d, $J$ = 8 Hz, 1H), 9.60 (d, $J$ = 8 Hz, 1H), 9.79 (s, 1H).

**Synthesis of Calothrixin B (1b).** To a cold solution of **1c** (55 mg, 0.16 mmol) in dry DCM (10 mL) at 0 °C was added a solution of $BBr_3$ (1 M in hexanes, 1.2 equiv). The solution was warmed to room temperature and stirred for a further 30 min. To the solution was added saturated $NaHCO_3$ solution (10 mL) and the mixture as stirred vigorously for 1 h at 60 °C. Ethyl acetate (50 mL) was then added to extract the organic components of the reaction. The combined organic layers were then dried with $MgSO_4$, filtered, and concentrated in vacuo to yield the desired product as a red powder. Recrystallization from hot acetone gave the pure product as a red powder (41 mg, 85% yield). Comparison of the product with authentic calothrixin B by using thin-layer chromatography in various solvent systems showed the compounds were identical. $R_f$ (1:2 ethyl acetate/light petroleum) 0.47; mp ≥300 °C (lit.[1] ≥300 °C); $^1$H NMR ($d_6$-DMSO) $\delta$ 7.39 (t, $J$ = 7 Hz, 1H), 7.47 (t, $J$ = 7 Hz, 1H), 7.62 (d, $J$ = 7 Hz, 1H), 7.89 (t, $J$ = 7 Hz, 1H), 7.96 (t, $J$ = 7 Hz, 1H), 8.17 (br d, $J$ = 9 Hz, 2H), 9.58 (d, $J$ = 9 Hz, 1H), 9.62 (s, 1H), N*H* not detected.

**Synthesis of Calothrixin A (1a).** The title compound was prepared from **1b** (69 mg) by using the literature procedure[6] to obtain calothrixin A as a bright orange compound (74 mg, 73% yield). $R_f$ (1:2 ethyl acetate/light petroleum) 0.47; mp ≥280 °C dec (lit.[1] ≥280 °C); $^1$H NMR ($d_6$-DMSO) $\delta$ 7.38 (t, $J$ = 7 Hz, 1H), 7.45 (t, $J$ = 7 Hz, 1H), 7.60 (d, $J$ = 8 Hz, 1H), 7.98 (t, $J$ = 4 Hz, 2H), 8.12 (d, $J$ = 8 Hz, 1H), 8.60 (br d, $J$ = 9 Hz, 1H), 8.88 (s, 1H), 9.68 (d, $J$ = 9 Hz, 1H), N*H* not detected.

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**Supporting Information Available:** $^1$H and $^{13}$C NMR spectra of the reported compounds as well as supplementary experimental procedures. This material is available free of charge via the Internet at http://pubs.acs.org.

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