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Synthesis of 3-hydroxyindolin-2-one alkaloids, (±)-donaxaridine and (±)-convolutamydines A and E, through enolization–Claisen rearrangement of 2-allyloxyindolin-3-ones

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Abstract—Claisen rearrangement triggered by enolization of 2-allyloxyindolin-3-ones with DBU was performed in order to prepare 3-allyl-3-hydroxyindolin-2-ones. Total synthesis of 3-hydroxyindolin-2-one alkaloids, (±)-donaxaridine, as well as (±)-convolutamydines A and E, was achieved by transformation of the allyl moiety of 3-allyl-3-hydroxyindolin-2-ones.

1. Introduction

3-Substituted 3-hydroxyindolin-2-ones are useful synthetic intermediates for alkaloids and biologically active compounds such as donaxaridine (**1**),[1] convolutamydines (**2**),[2] dioxibrassinine,[3] welwitindolinone C,[4] 3′-hydroxyglucoisatisin,[5] and TMC-95s,[6] in addition to several others (Fig. 1) .[7] In particular, 3-allyl-3-hydroxyindolin-2-ones are attractive intermediates for synthesis of biologically active compounds. Although a number of routes to 3-substituted 3-hydroxyindolin-2-ones are known,[8–17] there are relatively few synthetic methods for 3-allyl-3-hydroxyindolin-2-ones. The known examples are addition of allylmetallic (indium,[18] gallium[19] and boran[20]) reagents to isatin, but there are difficulties in obtaining the desired 3-allyl-3-hydroxyindolin-2-one owing to the low regioselectivity of the allylic reaction site.[18,19] Reaction of allylmagnesium chloride with isatin resulted in diallylation to give only 2,2-diallylindolin-3-one.[21] Recently, Mérour et al.[21] reported alkaline hydrolysis of 2-ethoxycarbonyl-2-allyloxyindolin-3-ones followed by decarboxylation and Claisen rearrangement to give 3-allyl-3-hydroxyindolin-2-one. We have previously shown a synthetic methodology for regioselective introduction of an allyl moiety to an indole nucleus using Claisen rearrangement, converting 3-allyloxyindole to 2-allylindolin-3-one,[22] 3-alkyl-2-allyloxyindole to 3-alkyl-3-allylindolin-2-one[23] and 3-vinyloxyindoline to 4-carbamoylmethylindoles.[24] We herein report a method for synthesis of the 3-hydroxyindolin-2-one alkaloids, (±)-donaxaridine (**1**) as well as (±)-convolutamydines A (**2a**) and E (**2b**), using Claisen rearrangement triggered by enolization of 2-allyloxyindolin-3-ones **3** to 3-allyl-3-hydroxyindolin-2-ones **4** (Scheme 1).

2. Results and discussion

2.1. Preparation of 3-allyl-3-hydroxyindolin-2-ones

The starting 2-allyloxyindolin-3-ones **3** were readily available using our synthetic method.[23] Initially, we examined the enolization of 2-allyloxyindolin-3-one **3a** with DBU and DBN as a base under several reaction conditions and the results are summarized in Table 1. When **3a** was treated with DBU at 40 °C in acetonitrile, the desired enolization readily took place through Claisen rearrangement of an intermediary indole to afford 3-allyl-3-hydroxyindolin-2-one **4a**, its deacetyl derivative **5a**, and carboxylic acid **6** in 9, 12, and 36% yields, respectively (Scheme 2 and Table 1, entry 1). It is known that Claisen rearrangement of the enolate of α-allyloxy carbonyl compounds competes with [2,3]-Wittig rearrangement.[25] However, comparison of the ^{13}C NMR spectrum of **5a** with those of 3-hydroxyindolin-2-one **7** and 2-hydroxyindolin-3-one **8**[26] shows that the product in the reaction of **4a** is not the [2,3]-Wittig rearrangement product **5a′** but the Claisen rearrangement product **5a** (Fig. 2). Formation of **5a** and **6** is effected by hydrolysis of **4a** under basic reaction conditions, and thus **4a** was smoothly hydrolyzed with lithium hydroxide at room temperature to give **5a** in 85% yield. When the reaction was performed in methylene chloride

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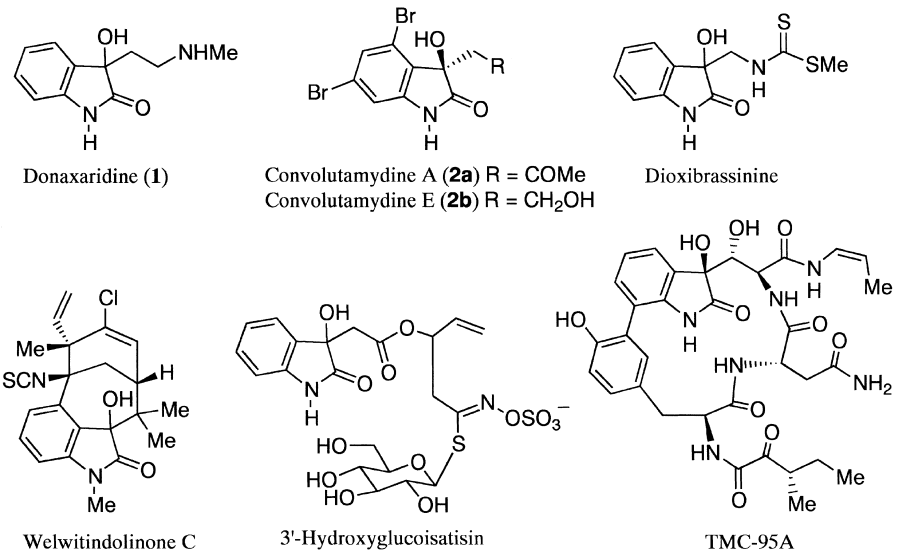
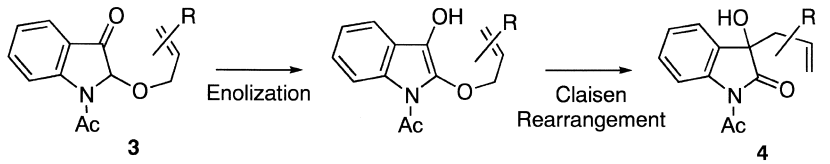
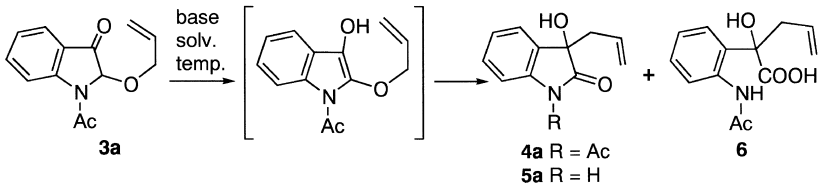


Figure 1. 3-Hydroxy-indolin-2-one alkaloids.



Scheme 1. Enolization–Claisen rearrangement.



Scheme 2. Enolization–Claisen rearrangement of 2-allyloxyindolin-3-one **3a**.

Table 1. Reaction conditions in enolization–Claisen rearrangement of 2-allyloxyin, rdolin-3-one **3a**

Entry	Base	Solvent	Reaction temperature (°C)	Reaction time (min)	Yield (%)		
					4a	**5a**	**6**
1	DBU	MeCN	40	30	9	12	36
2	DBU	CH_2Cl_2	40	10	12	16	30
3	DBU	Toluene	40	20	70	16	—
4	DBU	Toluene	rt	80	56	13	—
5	DBU	Toluene	110	5	—	55	3
6	DBN	Toluene	40	10	2	70	2
7	DBN	Toluene	rt	60	—	63	6

instead of acetonitrile, the reaction was completed in a shorter time, though by-product **6** was still formed (entry 2). Using toluene as the reaction solvent resulted in reduced formation of **6**, thus improving the total yields of **4a** and **5a** (entry 3). Further attempts to carry out the reaction at various temperatures (entries 4 and 5) confirmed that the reaction conditions shown in entry 3 were the most suitable. When DBN was used instead of DBU, the reaction proceeded more smoothly to give the desired **5a** as the chief product in good yield; however, small amounts of by-product **6** were formed (entries 6 and 7).

Next, we investigated the DBU-promoted reaction of various 2-allyloxyindolin-3-ones **3b-f**. The results are summarized in Scheme 3 and Table 2. When **3b** was treated with DBU in toluene at 40 °C for 10 min, 3-(2-methyl-2-buten-2-yl)-3-hydroxyindolin-2-one **4b** and the deacetylated **5b** were obtained in 70 and 9% yields (entry 1). The

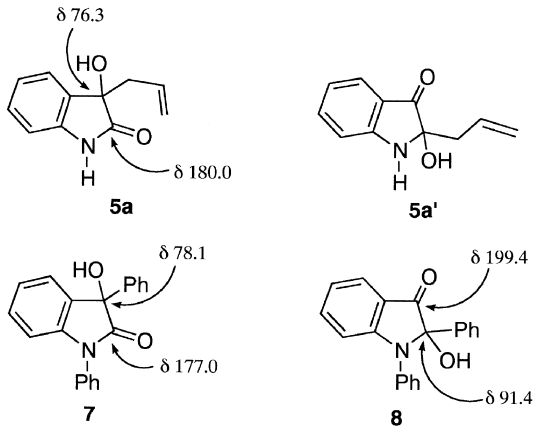
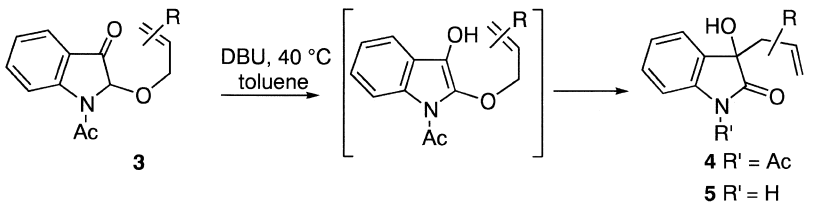


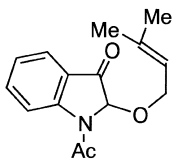
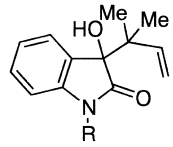
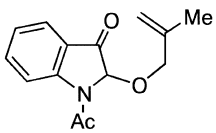
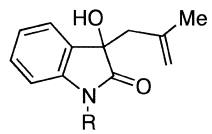
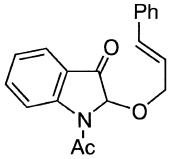
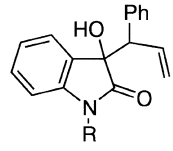
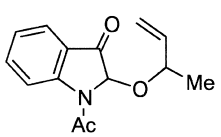
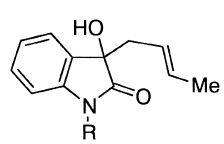
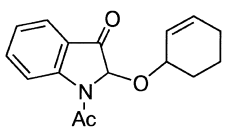
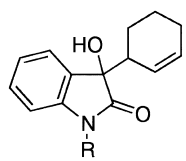
Figure 2. ^{13}C NMR spectra of hydroxyindolin-2-ones and 2-hydroxyindolin-3-one.

reaction of **3c** under the same conditions required prolonged heating (120 min) to give the Claisen products **4c** and **5c** in moderate yields (entry 2). A similar reaction of (*E*)-cinnamyl derivative **3d** for 20 min afforded a mixture of the diastereoisomers of **4d** (50%, 1.5:1) together with **5d** (20%) (entry 3). As examples of secondary rather than primary ethers, reactions of 2-buten-2-yl and cyclo-2-hexenyl derivatives **3e** and **3f** were performed. The reaction of **3e** proceeded through stereoselective Claisen rearrangement to give (*E*)-buten-2-ylindolin-3-ones **4e** (54%) and **5e** (8%) (entry 4). The (*E*)-product **4e** is predominantly produced via chair-like transition state **A** which is more favorable than boat-like transition state **B** (Fig. 3).[25] For the reaction of **3f**, **4f** and **5f** were obtained as respective mixtures of their diastereoisomers (4:1) in 59% and 18% yields (entry 5).



Scheme 3. Enolization–Claisen rearrangement of 2 allyloxyindolin 3-one **3b-f**.

Table 2. Preparation of 3-allyl-3-hydroxyindolin-2-ones **4** and **5**

Entry	Indolin-3-one **3**		Reaction time (min)	Product (yield)	
1		**3b**	10		**4b** (70%) **5b** (9%)
2		**3c**	120		**4c** (45%) **5c** (10%)
3		**3d**	20		**4d** (50%)[a] **5d** (20%)[a]
4		**3e**	10		**4e** (54%) **5e** (8%)
5		**3f**	80		**4f** (59%)[a] **5f** (18%)[a]

[a] The ratio of diastereomers measured by HPLC; **4d** (1:1.4), **5d** (1.1:1), **4f** (2:1), **5f** (4:1).

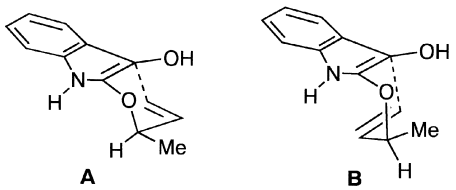


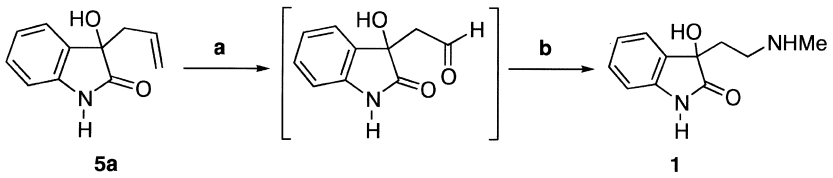
Figure 3. Transition states **A** and **B** in Claisen rearrangement of **3e**.

2.2. Synthesis of (±)-donaxaridine and (±)-convolutamydines A and E

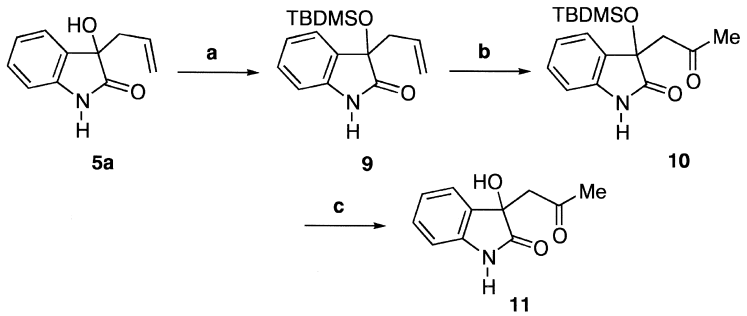
For the synthesis of 3-hydroxyindolin-2-one alkaloids, donaxaridine (**1**) and convolutamydines A (**2a**) and E (**2b**), we attempted transformation of the allyl group of 3-allyl-3-hydroxyindolin-2-one **5a** to aldehyde and acetonyl groups. When **5a** was treated with OsO_4 and *N*-methylmorpholine *N*-oxide (NMO) followed by $NaIO_4$, the unstable aldehyde was obtained and used in the following reaction without purification. Reductive amination of the aldehyde with $NaBH_3CN$ in the presence of methylammonium chloride gave the 3-methylaminoethyl-3-hydroxyindolin-2-one (±)-donaxaridine (**1**) in 41% overall yield from **5a** (Scheme 4). All spectral data are identical to those of the natural and synthetic samples.[1]

For transformation of the allyl group to the acetonyl group, we utilized Wacker oxidation because Wacker oxidation of olefins containing β-oxygenated functional groups with O_2–$PdCl_2$–$CuCl_2$ or –CuCl in DMF–H_2O regioselectively afforded the corresponding ketones.[27] However, Wacker oxidation of **5a** and its *O*-TBDMS derivative **9** under these conditions was very slow (Scheme 5 and Table 3, entries 1–5). When **9** was allowed to react with O_2–$PdCl_2$–CuCl in 1,4-dioxane-H_2O, the desired Wacker oxidation readily took place to afford **10** in high yield (entry 6). In addition, the reaction using other Pd catalysts was attempted to give moderate results (entries 7 and 8). Deprotection of **10** with tetrabutylammonium fluoride (TBAF) and acetic acid gave the 3-acetonyl-3-hydroxyindolin-2-one **11** in moderate yield.[28]

Finally, we applied these preparative methods to the total synthesis of (±)-convolutamydines A (**2a**) and E (**2b**). 4,6-Dibromoindolin-3-one **14** was readily obtained from 4,6-dibromoindole **12**[29] by molybdenum peroxide oxidation followed by demethoxylation[30] in 50% overall



Scheme 4. Reagents: (a) OsO_4, NMO, MeCN, rt, 2 h and then $NaIO_4$, dioxane–H_2O (2:1), rt, 10 min. (b) $MeNH_2$·HCl, MeOH, rt, 3 h and then $NaBH_3CN$, rt, 36 h, 41% (overall yield from **5a**).



Scheme 5. Reagents: (a) TBDMSOTf, 2,6-lutidine, CH_2Cl_2, 0 °C to rt, 3 days, 73%. (b) See Table 3. (c) TBAF, AcOH, 0 °C to rt, 50%.

Table 3. Wacker oxidation of 3-allylindolin-2-ones **5a** and **9** with O_2

Entry	Olefin	Reagents (equiv.)	Solvents	Temperature (°C)	Time	Yield (%)
1	**5a**	$PdCl_2$–$CuCl_2$ (0.1:1)	DMF–H_2O[a]	rt	1 week	—
2	**9**	$PdCl_2$–$CuCl_2$ (0.1:1)	DMF–H_2O[a]	rt	1 week	8
3	**9**	$PdCl_2$–$CuCl_2$ (1:10)	DMF–H_2O[a]	rt	1 week	10
4	**9**	$PdCl_2$–$CuCl_2$ (1:10)	DMF–H_2O[a]	50	1 week	11
5	**9**	$PdCl_2$–CuCl (0.1:1)	DMF–H_2O[a]	50	4 days	5
6	**9**	$PdCl_2$–CuCl (0.1:1)	dioxane–H_2O[a]	50	5 h	88
7	**9**	$PdCl_2(PhCN)_2$–$CuCl_2$ (0.1:1)	DMF–H_2O[a]	50	1 day	25
8	**9**	Na_2PdCl_2–*t*-BuO_2H (0.2:1.5)	AcOH–H_2O[b]	50	5 h	71

[a] The ratio of solvents (7:1).
[b] The ratio of solvents (1:1).

yield. Successive bromination of **14**, substitution with allyl alcohol, DBU-promoted enolization–Claisen rearrangement of **15** and hydrolysis with LiOH gave the desired 4,6-dibromo-3-hydroxyindolin-2-one **16** in 84% yield (Scheme 6). The OsO_4–$NaIO_4$ oxidation of **16** followed by $NaBH_4$ reduction yielded (±)-convolutamydine E (**2b**) in 65% yield (Scheme 7).

Synthesis of (±)-convolutamydine A (**2a**) was achieved by TBDMS protection of **16** followed by Wacker oxidation of **17**[31] and deprotection of **18** with tris(dimethylamino)sulfur (trimethylsilyl)difluoride (TAS-F) (Scheme 7).[32] All spectral data of **2a** and **2b** are identical to those of the natural and synthetic samples.[2]

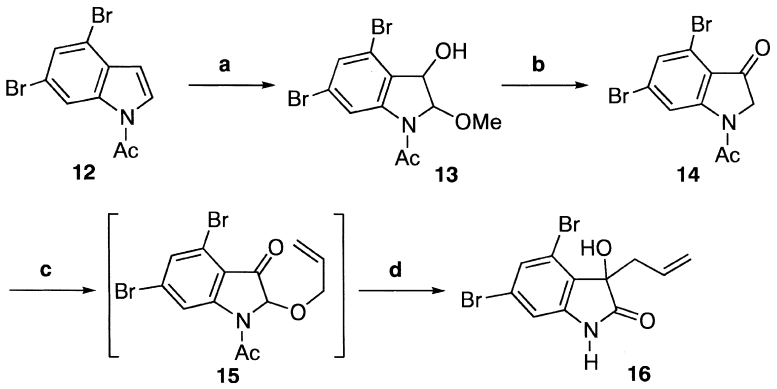
3. Conclusion

In conclusion, we have presented a general and useful method for synthesis of 3-allyl-3-hydroxyindolin-2-ones **5** using Claisen rearrangement triggered by DBU-promoted enolization of 2-allyloxyindolin-3-ones **3**. As examples of the synthetic utility of **5**, we performed transformation of the allyl group in **5a** to aldehyde and acetonyl groups, and respectively applied these methodologies to achieve total synthesis of (±)-donaxaridine (**1**) as well as (±)-convolutamydines A (**2a**) and E (**2b**).

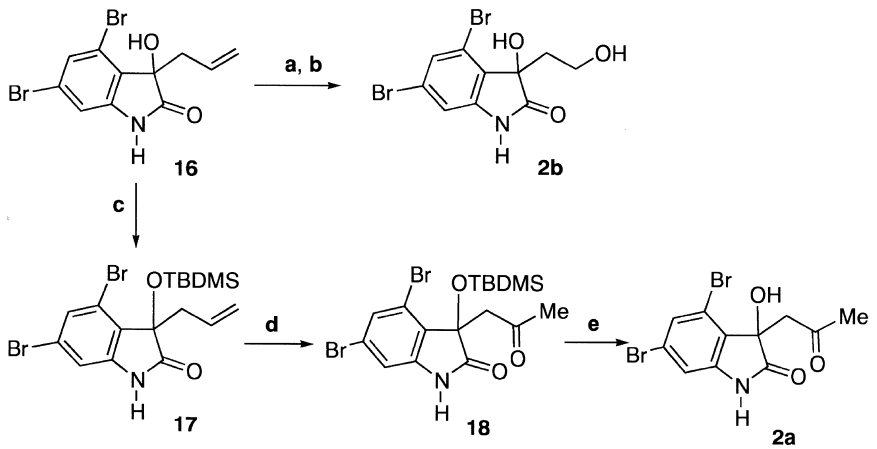
4. Experimental

4.1. General

^{1}H NMR spectra were obtained using a JEOL JNM-EX-300, JNM-EX-400, or JNM-LA-500 spectrometer with tetramethylsilane as an internal standard. *J*-Values are given in Hz. Mass spectra were obtained using a JEOL JMS-DX302 or JMS-700 instrument with a direct inlet system operating at 70 eV. IR spectra were recorded with a Shimadzu FTIR-8100 spectrophotometer. All mp values are uncorrected, and were measured on a Yanagimoto micromelting point apparatus. HPLC was performed on a JASCO PU-1580 with a JASCO Finepak SIL-5 column. Elemental analyses were obtained using a Yanaco CHN Corder MT-6 elemental analyzer. Column chromatography was carried out on silica gel (Kanto Chemical Co. Inc., Silica Gel 60N, 100–200 mesh and Merck, Silica Gel 60, 230–400 mesh). Preparative TLC was undertaken using Merck Silica Gel 60 F_{254}.



Scheme 6. Reagents: (a) MoO_5·HMPA, MeOH, rt, 1 week, 90%. (b) CSA, MeCN, reflux, 56%. (c) Br_2, CH_2Cl_2, 0 °C, for 2h, and then allyl alcohol, MS 4A, DMF, rt, for 2 days. (d) DBU, toluene, 40 °C, 3 h, and then LiOH, MeOH, rt, 3 days, 84% (overall yield from **14**).



Scheme 7. Reagents: (a) OsO_4, NMO, MeCN, rt 1 h, and then $NaIO_4$, dioxane–H_2O, rt, 1 h. (b) $NaBH_4$ MeOH, 0 °C, 30 min., 65% (c) TBDMSOTf, 2,6-lutidine, 0 °C to rt, 3 days, and then AcOH, H_2O, THF, 80 °C, 2 h, 69%. (d) $PdCl_2$, CuCl, dioxane–H_2O (7:1), 50 °C, 24 h, 12%, (e) TAS–F, 0–15 °C, 2.5 h, 75%.

4.2. General procedure for the preparation of 3-allyl-3-hydroxyindolin-2-ones 4-5

A solution of 2-allyloxyindolin-3-ones **3** (1.0 mmol) and DBU or DBN (1.0 mmol) in dry solvent (13 ml) as shown in Table 1 was stirred at a designated temperature (rt ~110 °C) under nitrogen atmosphere for a designated period (10–120 min), as shown in Tables 1 and 2. The reaction mixture was neutralized with AcOH at 0 °C and extracted with EtOAc. The extract was washed with H_2O, dried over $MgSO_4$, and concentrated under reduced pressure to give a residue. The residue was subjected to chromatography on a silica gel column with EtOAc–hexane (1:1–2) as an eluent to give 3-allyl-3-hydroxyindolin-2-ones **4**, deacetyl derivatives **5**, and carboxylic acid **6**.

4.2.1. 1-Acetyl-3-allyl-3-hydroxyindolin-2-one (4a). Mp 98–101 °C (EtOAc–hexane). IR ($CHCl_3$) cm^{-1}: 3559, 1763, 1717. ^1H NMR ($CDCl_3$, 300 MHz) δ: 2.59 (3H, s, –Ac), 2.60 (1H, dd, J=13.1, 8.8 Hz, $-CH_2-$), 2.68 (1H, dd, J=13.1, 6.2 Hz, $-CH_2-$), 2.80 (1H, br, –OH), 5.07 (1H, d, J=11.2 Hz, $-CH{=}CH_2$), 5.08 (1H, d, J=16.0 Hz, $-CH{=}CH_2$), 5.49 (1H, m, $-CH{=}CH_2$), 7.19 (1H, td, J=7.5, 1.0 Hz, Ar-H), 7.32 (1H, td, J=7.5, 1.5 Hz, Ar-H), 7.37 (1H, ddd, J=7.5, 1.5, 0.6 Hz, Ar-H), 8.15 (1H, d, J=7.5 Hz, Ar-H). MS m/z (%): 231 (M^+, 11), 190 (47), 162 (22), 148 (100), 43 (11). HRMS m/z calcd for $C_{13}H_{13}NO_3$: 231.0895. Found: 231.0896. Anal. Calcd for $C_{13}H_{13}NO_3$: C, 67.52; H, 5.67; N, 6.06. Found: C, 67.39; H, 5.72; N, 5.82.

4.2.2. 3-Allyl-3-hydroxyindolin-2-one (5a). Mp 112–115 °C (EtOAc–hexane); [lit.[20] 123–124 °C]. IR ($CHCl_3$) cm^{-1}: 1728, 1624. ^1H NMR ($CDCl_3$, 400 MHz) δ: 2.61 (1H, dd, J=13.2, 8.5 Hz, $-CH_2-$), 2.75 (1H, dd, J=13.2, 6.3 Hz, $-CH_2-$), 3.65 (1H, brs, –OH), 5.10 (1H, d, J=18.1 Hz, $-CH{=}CH_2$), 5.11 (1H, d, J=8.8 Hz, $-CH{=}CH_2$), 5.65 (1H, m, $-CH{=}CH_2$), 6.88 (1H, d, J=7.6 Hz, Ar-H), 7.07 (1H, t, J=7.6 Hz, Ar-H), 7.25 (1H, t, J=7.3 Hz, Ar-H), 7.36 (1H, d, J=7.3 Hz, Ar-H). ^{13}C NMR ($CDCl_3$, 100 MHz) δ: 42.9, 76.3, 110.3, 120.4, 122.9, 124.3, 129.5, 130.06, 130.14, 140.1, 180.0. MS m/z (%): 189 (M^+, 9), 148 (100), 120 (3), 92 (3), 65 (3), 39 (2). HRMS m/z calcd for $C_{11}H_{11}NO_2$: 189.0790. Found: 189.0788.

4.2.3. 1-Acetyl-3-(2-methyl-3-buten-2-yl)-3-hydroxyindolin-2-one (4b). Mp 73–75 °C (EtOAc–hexane). IR ($CHCl_3$) cm^{-1}: 3565, 1765, 1713. ^1H NMR ($CDCl_3$, 300 MHz) δ: 1.06 (3H, s, C–Me), 1.17 (3H, s, C–Me), 2.61 (3H, s, –Ac), 2.84 (1H, brs, –OH), 5.14 (1H, dd, J=17.6, 1.1 Hz, $-CH{=}CH_2$), 5.22 (1H, dd, J=10.8, 1.1 Hz, $-CH{=}CH_2$), 5.94 (1H, dd, J=17.6, 10.8 Hz, $-CH{=}CH_2$), 7.21 (1H, td, J=7.5, 1.1 Hz, Ar-H), 7.36 (1H, td, J=7.7, 1.5 Hz, Ar-H), 7.42 (1H, dd, J=7.5, 1.5 Hz, Ar-H), 8.21 (1H, dt, J=8.4, 0.6 Hz, Ar-H). MS m/z (%): 259 (M^+, 0.2), 217 (0.2), 191 (100), 162 (9), 149 (80), 69 (55), 41 (14). HRMS m/z calcd for $C_{15}H_{17}NO_3$: 259.1208. Found: 259.1208.

4.2.4. 3-(2-Methyl-3-buten-2-yl)-3-hydroxyindolin-2-one (5b). Mp 188–190 °C (EtOAc–hexane). IR ($CHCl_3$) cm^{-1}: 3431, 1732. ^1H NMR ($CDCl_3$, 300 MHz) δ: 1.12 (3H, s, C–Me), 1.18 (3H, s, C–Me), 2.84 (1H, brs, –OH), 5.15 (1H, dd, J=17.4, 1.2 Hz, $-CH{=}CH_2$), 5.24 (1H, dd, J=10.8, 1.2 Hz, $-CH{=}CH_2$), 6.19 (1H, dd, J=17.4, 10.8 Hz, $-CH{=}CH_2$), 6.81 (1H, d, J=7.6 Hz, Ar-H), 7.02 (1H, td, J=7.6, 0.9 Hz, Ar-H), 7.25 (1H, td, J=7.6 1.3 Hz, Ar-H), 7.37 (1H, dd, J=7.6, 0.7 Hz, Ar-H). MS m/z (%): 217 (M^+, 2), 149 (100), 119 (3), 69 (15), 41 (7). HRMS m/z calcd for $C_{13}H_{15}NO_2$: 217.1103. Found: 217.1098. Anal. Calcd for $C_{13}H_{15}NO_2$: C, 71.87; H, 6.96; N, 6.45. Found: C, 72.05; H, 6.99; N, 6.17.

4.2.5. 1-Acetyl-3-(2-methyl-2-propenyl)-3-hydroxyindolin-2-one (4c). Viscous oil. IR ($CHCl_3$) cm^{-1}: 3559, 1765, 1713. ^1H NMR ($CDCl_3$, 300 MHz) δ: 1.40 (3H, s, $-CMe{=}CH_2$), 2.60 (3H, s, –Ac), 2.66 (1H, d, J=12.9 Hz, $-CH_2-$), 2.75 (1H, dd, J=12.9, 0.7 Hz, $-CH_2-$), 2.98 (1H, br, –OH), 4.63 (1H, d, J=0.9 Hz, $-CMe{=}CH_2$), 4.80 (1H, t, J=1.7 Hz, $-CMe{=}CH_2$), 7.24 (1H, td, J=7.4, 1.1 Hz, Ar-H), 7.37 (1H, td, J=7.4, 1.5 Hz, Ar-H), 7.42 (1H, ddd, J=7.4, 1.5, 0.6 Hz, Ar-H), 8.18 (1H, d, J=7.7 Hz, Ar-H). ^{13}C NMR ($CDCl_3$, 100 MHz) δ: 23.8, 26.5, 47.2, 76.4, 116.5, 116.6, 123.9, 125.4, 128.8, 130.1, 138.3, 139.6, 170.3, 178.5. MS m/z (%): 245 (M^+, 22), 190 (42), 162 (31), 148 (100), 130 (3), 102 (3), 90 (4), 43 (10). HRMS m/z calcd for $C_{14}H_{15}NO_3$: 245.1052. Found: 245.1052.

4.2.6. 3-(2-Methyl-2-propenyl)-3-hydroxyindolin-2-one (5c). Mp 163 °C (EtOAc–hexane). IR ($CHCl_3$) cm^{-1}: 3435, 1736. ^1H NMR ($CDCl_3$, 300 MHz) δ: 1.54 (3H, s, $-CMe{=}CH_2$), 1.60 (1H, br, –OH), 2.68 (2H, s, $-CH_2-$), 4.65 (1H, d, J=1.1 Hz, $-CMe{=}CH_2$), 4.78 (1H, t, J=1.7 Hz, $-CMe{=}CH_2$), 6.83 (1H, d, J=7.5 Hz, Ar-H), 7.05 (1H, td, J=7.5, 0.9 Hz, Ar-H), 7.24 (1H, td, J=7.5, 1.3 Hz, Ar-H), 7.35 (1H, d, J=7.5 Hz, Ar-H), 7.76 (1H, br, –NH). MS m/z (%): 203 (M^+, 11), 185 (4), 148 (100), 119 (5), 92 (3), 65 (3). HRMS m/z calcd for $C_{12}H_{13}NO_2$: 203.0946. Found: 203.0945. Anal. Calcd for $C_{12}H_{13}NO_2$: C, 70.92; H, 6.45; N, 6.89. Found: C, 70.74; H, 6.54; N, 6.55.

4.2.7. 1-Acetyl-3-(1-phenyl-2-propenyl)-3-hydroxyindolin-2-one (4d). Viscous oil. IR ($CHCl_3$) cm^{-1}: 3550, 1765, 1715. ^1H NMR ($CDCl_3$, 300 MHz) δ: 2.31 (3H×0.6, s, –Ac), 2.55 (3H×0.4, s, –Ac), 2.97 (1H×0.6, br, –OH), 3.18 (1H×0.4, br, –OH), 3.82 (1H×0.4, d, J=10.5 Hz, –CH-Ph), 3.86 (1H×0.6, d, J=8.3 Hz, –CH-Ph), 5.26 (1H×0.6, dt, J=16.9, 1.3 Hz, $-CH{=}CH_2$), 5.39 (1H, ddd, J=10.5, 2.4, 1.3 Hz, $-CH{=}CH_2$), 5.43 (1H×0.4, dd, J=16.9, 1.3 Hz, $-CH{=}CH_2$), 6.30 (1H×0.4, m, $-CH{=}CH_2$), 6.37 (1H×0.6, m, $-CH{=}CH_2$), 6.70 (1H, m, Ar-H), 6.9–7.5 (7H, m, Ph, Ar-H), 7.97 (1H×0.4, d, J=8.1 Hz, Ar-H), 7.99 (1H×0.6, d, J=7.9 Hz, Ar-H). MS m/z (%): 307 (M^+, 0.3), 289 (0.5), 247 (0.6), 148 (12), 117 (100), 91 (4). HRMS m/z calcd for $C_{19}H_{17}NO_3$: 307.1208. Found: 307.1205.

The ratio (1:1.4) of two diastereoisomers was determined by HPLC.

4.2.8. 3-(1-Phenyl-2-propenyl)-3-hydroxyindolin-2-one (5d). Mp 179–181 °C (EtOAc–hexane) [lit.[18] mp 160–162 °C; 1:1 diastereomer mixture]. IR ($CHCl_3$) cm^{-1}: 3420, 1736. ^1H NMR ($CDCl_3$, 300 MHz) δ: 2.79 (1H, brs, –OH), 3.85 (1H×0.4, d, J=9.7 Hz, –CH-Ph), 3.88 (1H×0.6, d, J=8.1 Hz, –CH-Ph), 5.25 (1H×0.4, dt, J=17.0, 1.4 Hz,

–CH=CH_2), 5.3–5.4 (1H, m, –CH=CH_2), 5.44 (1H×0.6, dd, J=17.0, 1.4 Hz, –CH=CH_2), 6.3–6.55 (1H, m, –CH=CH$_2$), 6.63 (1H, m, Ar-H), 6.8–7.55 (7H, m, Ar-H). MS m/z (%): 265 (M^+, 2), 247 (2), 148 (38), 117 (100), 91 (7). HRMS m/z calcd for $C_{17}H_{15}NO_2$: 265.1103. Found: 265.1095.

The ratio (1.1:1) of two diastereoisomers was determined by HPLC.

4.2.9. (*E*)-1-Acetyl-3-(2-butenyl)-3-hydroxyindolin-2-one (4e). Mp 50–55 °C (EtOAc–hexane). IR ($CHCl_3$) cm^{-1}: 3561, 1765, 1713. ^{1}H NMR ($CDCl_3$, 300 MHz) δ: 1.60 (3H, d, J=6.3 Hz, –CH=CHMe), 2.61 (3H, s, –Ac), 2.5–2.69 (2H, m, –CH_2–CH=CH), 2.97 (1H, br, –OH), 5.19 (1H, dddd, J=15.2, 8.7, 6.3, 1.7 Hz, –CH=CHMe), 5.56 (1H, dq, J=15.2, 6.3 Hz, –CH=CHMe), 7.23 (1H, td, J=7.5, 1.1 Hz, Ar-H), 7.36 (1H, td, J=7.5, 1.8 Hz, Ar-H), 7.42 (1H, ddd, J=7.5, 1.5, 0.6 Hz, Ar-H), 8.18 (1H, d, J=8.2 Hz, Ar-H). MS m/z (%): 245 (M^+, 12), 203 (3), 191 (43), 162 (32), 148 (100), 130 (3), 102 (3), 90 (4), 43(11). HRMS m/z calcd for $C_{14}H_{15}NO_3$: 245.1051. Found: 245.1053.

4.2.10. (*E*)-3-(2-Butenyl)-3-hydroxyindolin-2-one (5e). Mp 115–120 °C (EtOAc–hexane). IR ($CHCl_3$) cm^{-1}: 3435, 1726. ^{1}H NMR ($CDCl_3$, 300 MHz) δ: 1.61 (3H, d, J=6.4 Hz, –CH=CHMe), 2.52 (1H, dd, J=13.5, 8.5 Hz, –CH_2–CH=CH), 2.63 (1H, dd, J=13.5, 6.4 Hz, –CH_2–CH=CH), 5.31 (1H, ddd, J=15.0, 8.4, 6.4 Hz, –CH=CHMe), 5.63 (1H, dq, J=15.0, 6.4 Hz, –CH=CHMe), 6.84 (1H, d, J=7.6 Hz, Ar-H), 7.06 (1H, td, J=7.6, 0.9 Hz, Ar-H), 7.25 (1H, td, J=7.6, 1.3 Hz, Ar-H), 7.34 (1H, d, J=7.6 Hz, Ar-H), 7.67 (1H, br, –NH). MS m/z (%): 203 (M^+, 12), 185 (7), 170 (8), 148 (100), 119 (3), 92 (4), 65 (3). HRMS m/z calcd for $C_{12}H_{13}NO_2$: 203.0946. Found: 203.0943.

4.2.11. 1-Acetyl-3-(2-cyclohexenyl)-3-hydroxyindolin-2-one (4f). Mp 158–160 °C (EtOAc–hexane). IR ($CHCl_3$) cm^{-1}: 3550, 1738. ^{1}H NMR ($CDCl_3$, 300 MHz) δ: 0.7–2.0 (6H, m, –(CH$_2$)$_3$–), 2.58 and 2.59 (3H, s, –COMe), 2.77 (1H, m, –CH–CH$_2$–), 5.6–5.9 (2H, m, –CH=CH–), 7.1–7.2 (1H, m, Ar-H), 7.25–7.4 (2H, m, Ar-H), 8.17 (1H, d, J=8.3 Hz, Ar-H). MS m/z (%): 271 (M^+, 1), 253 (9), 211 (12), 191 (100), 149 (69), 81 (73), 43 (8). HRMS m/z calcd for $C_{16}H_{17}NO_3$: 271.1208. Found: 271.1210.

The ratio (2:1) of two diastereoisomers was determined by HPLC.

4.2.12. 3-(2-Cyclohexenyl)-3-hydroxyindolin-2-one (5f). Mp 158–163 °C (EtOAc–hexane). IR ($CHCl_3$) cm^{-1}: 3440, 1728. ^{1}H NMR ($CDCl_3$, 300 MHz) δ: 0.87 (1H, m, –CH), 1.4–2.0 (5H, m, –(CH$_2$)$_3$–), 2.80 (1H, m, –CH–CH$_2$–), 5.6–5.8 (2H×0.2, m, –CH=CH–), 5.95 (1H×0.8, m, –CH=CH–), 6.07 (1H×0.8, m, –CH=CH–), 6.85 (1H, d, J=7.5 Hz, Ar-H), 7.04 (1H×0.8, td, J=7.5, 0.9 Hz, Ar-H), 7.07 (1H×0.2, td, J=7.5, 0.9 Hz, Ar-H), 7.3–7.45 (2H, m, Ar-H). MS m/z (%): 229 (M^+, 3), 149 (100), 119 (3), 92 (3), 81 (23), 65 (3). HRMS m/z calcd for $C_{14}H_{15}NO_2$: 229.1103. Found: 229.1094. Anal. Calcd for $C_{14}H_{15}NO_2$: C, 73.34; H, 6.59; N, 6.11. Found: C, 73.04; H, 6.34; N, 5.88.

The ratio (4:1) of two diastereoisomers was determined by HPLC.

4.2.13. 2-[2-(Acetylamino)phenyl]-2-hydroxypent-4-enoic acid (6). Viscous oil. IR ($CHCl_3$) cm^{-1}: 3437, 3368, 1740, 1624. ^{1}H NMR ($CDCl_3$, 300MHz) δ: 2.07 (3H, s, –COMe), 2.61 (1H, dd, J=13.6, 7.9 Hz, –CH_2–CH=), 2.81 (1H, ddt, J=13.6, 6.4, 1.2 Hz, –CH_2–CH=), 5.09 (1H, dq, J=17.2, 1.0 Hz, –CH=CH_2), 5.10 (1H, dq, J=9.5, 1.0 Hz, –CH=CH_2), 5.62 (1H, dddd, J=16.3, 11.0, 8.3, 6.6 Hz, –CH=CH$_2$), 6.85 (1H, d, J=7.7 Hz, Ar-H), 7.03 (1H, td, J=7.5, 0.9 Hz, Ar-H), 7.21 (1H, d, J=7.7 Hz, Ar-H), 7.26 (1H, td, J=7.7, 1.3 Hz, Ar-H). ^{13}C NMR ($CDCl_3$, 75 MHz) δ: 22.6, 40.9, 79.4, 110. 0, 120.7, 122.6, 123.3, 127.6, 129.2, 129.7, 140.6, 169.0, 171.2, 175.6. MS m/z (%): 213 (M^+-H_2O, 23), 190 (13), 148 (100). HRMS (M^+-H_2O) m/z calcd for $C_{13}H_{13}NO_3$: 231.0896. Found: 231.0900.

4.3. Synthesis of (±)-donaxaridine (1)

4.3.1. Hydrolysis of 1-acetyl-3-allyl-3-hydroxyindolin-2-one (4a) to 3-allyl-3-hydroxyindolin-2-one (5a). A solution of **4a** (51 mg, 0.2 mmol) and LiOH (10%, 0.1 ml) in MeOH (2 ml) was stirred at room temperature for 75 min. The resulting mixture was evaporated under reduced pressure to give a residue, which was extracted with EtOAc. The extract was washed with water, dried over $MgSO_4$, and concentrated under reduced pressure to give a residue. The residue was purified by column chromatography on silica gel with EtOAc–hexane (2:1) as an eluent to give **5a** (45 mg, 85%).

4.3.2. 3-(2-Methylaminoethyl)-3-hydroxyindolin-2-one [(±)-donaxaridine, 1]. A solution of **5a** (89 mg, 0.47 mmol), OsO_4 (4% in water, 182 μl, d=4.9, 0.14 mmol), and NMO (50% in water, 194 μl, d=1.13, 0.94 mmol) in MeCN (3.5 ml) was stirred at room temperature for 2 h. The reaction mixture was filtered through Celite® 545. The filtrate was concentrated under reduced pressure to give a residue containing 1,2-diol. A solution of the residue and $NaIO_4$ (100 mg, 0.78 mmol) in 1,4-dioxane–H_2O (1.5 ml, 2:1) was stirred at room temperature for 10 min. After diluting the resulting mixture with diethyl ether, the organic layer was washed with H_2O, and the aqueous layer was extracted with EtOAc. The combined organic solution was dried over $MgSO_4$, and concentrated under reduced pressure to give the crude aldehyde **7** [IR ($CHCl_3$) cm^{-1}; 3435, 1738, 1728. ^{1}H NMR ($CDCl_3$, 300 MHz) δ: 2.95 (1H, dd, J=16.6, 1.7 Hz, –CH_2CHO), 3.02 (1H, dd, J=16.6, 1.7 Hz, –CH_2CHO), 4.24 (1H, br, OH), 6.89 (1H, d, J=7.7 Hz, Ar-H), 7.05 (1H, t, J=7.7 Hz, Ar-H), 7.25 (1H, t, J=7.7 Hz, Ar-H), 7.32 (1H, d, J=7.7 Hz, Ar-H), 8.54 (1H, br, NH), 9.80 (1H, t, J=1.7 Hz, –CH$_2$CHO)], which was used without further purification because of its instability.

A solution of **7** and MeNH$_2$·HCl (56 mg, 0.85 mmol) in MeOH (2.7 ml) was stirred at room temperature. After disappearance of **7** was confirmed by TLC (3 h), $NaBH_3CN$ (82 mg, 1.3 mmol) was added to the reaction mixture at room temperature. The mixture was stirred for 36 h and extracted with CH_2Cl_2. The extract was washed with H_2O,

dried over $MgSO_4$, and concentrated under reduced pressure to give a residue. The residue was subjected to chromatography on a silica gel column with EtOAc–hexane (2: 1) as an eluent to give (±)-donaxaridine (**1**, 40 mg, 41%). Mp 175 °C; [lit.[1a] 175–176 °C]. IR (KBr) cm^{-1}; 3404, 3236, 1673, 1613, 1470, 1308. ^1H NMR ($CDCl_3$, 300 MHz) δ: 2.42 (1H, td, J=12.8, 9.0 Hz, –C–CH_2–CH_2–), 2.77 (1H, ddd, J=12.8, 6.2, 1.7 Hz, –C–CH_2–CH_2–), 2.97 (3H, s, –NMe), 3.26 (1H, td, J=9.5, 6.2 Hz, –CH_2–N–), 3.34 (1H, ddd, J=9.5, 9.5, 1.7 Hz, –CH_2–N–), 4.31 (1H, brs, –OH), 4.71 (1H, br, –NH), 6.69 (1H, td, J=7.6, 1.3 Hz, Ar-H), 6.72 (1H, dd, J=7.9, 0.7 Hz, Ar-H), 6.88 (1H, dd, J=7.6, 1.5 Hz, Ar-H), 7.11 (1H, td, J=7.6, 1.5 Hz, Ar-H). MS m/z (%): 206 (M^+, 100), 188 (9), 177 (8), 173 (7), 159 (6), 149 (42), 148 (11), 147 (29), 146 (37), 135 (24), 130 (19), 120 (58), 93 (13), 92 (18), 77 (6), 65 (15), 58 (43). HRMS m/z calcd for $C_{11}H_{14}N_2O_2$:206.1055. Found: 206.1050.

4.4. Synthesis of 3-acetonyl-3-hydroxyindolin-2-one (11)

4.4.1. 3-Allyl-3-*tert*-butyldimethylsilyloxyindolin-2-one (9). A solution of 3-hydroxyindolin-2-one **5a** (57 mg, 0.3 mmol), 2,6-lutidine (128 mg, 1.2 mmol), and *tert*-butyldimethylsilyl triflate (317 mg, 1.2 mmol) in dry CH_2Cl_2 (4 ml) was stirred at 0 °C to room temperature for 1 h. The reaction mixture was diluted with CH_2Cl_2. The organic layer was washed with brine, dried over $MgSO_4$, and evaporated to give a residue, of which a solution in THF–AcOH–H_2O (1:1:1, l ml) was stirred at 80 °C for 5 h. The resulting mixture was diluted with CH_2Cl_2. The organic layer was washed with brine, dried over $MgSO_4$, and concentrated under reduced pressure to give a residue, which was purified by silica gel column chromatography with EtOAc–hexane (1:3) as an eluent to give TBDMS ether **9** (67 mg, 73%). viscous oil. IR ($CHCl_3$) cm^{-1}: 1720. ^1H NMR (300 MHz, $CDCl_3$) δ: −0.26 (3H, s, –SiMe), 0.06 (3H, s, –SiMe), 0.87 (9H, s, –Si^{t}Bu), 2.53 (1H, dd, J=13.4, 8.2 Hz, –CH_2CH=), 2.74 (1H, dd, J=13.4, 6.4 Hz, –CH_2CH=), 5.02 (2H, m, –CH=CH_2), 5.66 (1H, m, –CH=CH_2), 6.86 (1H, d, J=7.7 Hz, Ar-H), 7.03 (1H, dd, J=7.7, 8.3 Hz, Ar-H), 7.25 (2H, m, Ar-H), 8.74 (1H, brs, –NH). ^{13}C NMR ($CDCl_3$, 100 MHz) δ: −3.9, −3.5, 18.2, 25.8, 44.3, 78.0, 110.2, 119.1, 122.2, 124.6, 129.2, 130.9, 131.0, 140.0, 180.0. MS (FAB) m/z (%): 304 (MH^+, 11), 246 (18), 205 (19), 172 (100). HRMS (FAB, MH^+) m/z calcd for $C_{17}H_{26}NO_2Si$: 304.1733. Found: 304.1739.

4.4.2. Typical procedure for Wacker oxidation of 3-allylindolin-2-one 9 to 3-(2-oxopropyl)-3-TBDMS-oxyindolin-2-one (10). A suspension of palladium (II) chloride (8 mg, 0.0043 mmol) and copper (I) chloride (4.3 mg, 0.043 mmol) in dioxane–H_2O (7:1, 1 ml) was vigorously stirred with bubbling oxygen gas at room temperature for 1 h. The indolin-2-one **9** (13 mg, 0.043 mmol) was added to the mixture. After heating at 50 °C for 5 h, the reaction mixture was cooled to room temperature and diluted with CH_2Cl_2. The precipitate was filtered off, and the filtrate was dried over $MgSO_4$, and evaporated off. The obtained residue was purified by flash silica gel column chromatography with EtOAc–hexane (2:3) as an eluent to give 3-(2-oxopropyl)-indolin-2-one **10** (12 mg, 88%). viscous oil. ^1H NMR (300 MHz, $CDCl_3$) δ: −0.19 (3H, s, –SiMe), 0.08 (3H, s, –SiMe), 0.95 (9H, s, –Si^{t}Bu), 2.14 (3H, s, –COMe), 3.07 (1H, d, J=15.9 Hz, –CH_2CO–), 3.25 (1H, d, J=15.9 Hz, –CH_2CO–), 6.83 (1H, d, J=7.8 Hz, Ar-H), 7.02 (1H, t, J=7.8 Hz, Ar-H), 7.21–7.29 (2H, m, Ar-H), 7.46 (1H, brs, –NH). MS (FAB) m/z (%): 320 (MH^+, 54), 262 (37), 188 (38), 146 (100), 73 (44). HRMS (FAB, MH^+) m/z calcd for $C_{17}H_{25}NO_3Si$: 320.1682. Found: 320.1671.

4.4.3. 3-(2-Oxopropyl)-3-hydroxyindolin-2-one (11). A solution of TBDMS derivative **10** (8.4 mg, 0.026 mmol), TBAF (1.0 M, 22 μl, 22 μmol), and AcOH (15 μl) in THF (1 ml) was stirred at room temperature for 3 days. After addition of EtOAc, the organic layer was washed with brine, dried over $MgSO_4$, and concentrated under reduced pressure. The residue was purified by preparative TLC with EtOAc as a developing solvent to give 3-hydroxy-indolin-2-one **11** (2.5 mg, 50%). Mp 165–168 °C [lit.[9a] mp 166–168 °C]. IR ($CHCl_3$) cm^{-1}: 3445, 1740, 1624. ^1H NMR (300 MHz, $CDCl_3$) δ: 2.20 (3H, s, –COMe), 2.97 (1H, d, J=17.0 Hz, –CH_2CO–), 3.19 (1H, d, J=17.0 Hz, –CH_2CO–), 4.37 (1H, br, –OH), 6.87 (1H, d, J=7.5 Hz, Ar-H), 7.05 (1H, td, J=7.5, 0.9 Hz, Ar-H), 7.27 (1H, td, J=7.5, 1.2 Hz, Ar-H), 7.35 (1H, d, J=7.5 Hz, Ar-H), 7.65 (1H, br, –NH). MS m/z (%): 205 (M^+, 88), 187 (24), 172 (27), 162 (98), 148 (100), 120 (72), 92 (41), 43 (36). HRMS m/z calcd for $C_{11}H_{11}NO_3$: 205.0739. Found: 205.0742.

4.5. Syntheses of (±)-convolutamydines A (2a) and E (2b)

4.5.1. 1-Acetyl-4,6-dibromo-3-hydroxy-2-methoxyindoline (13). A solution of 1-acetyl-4,6-dibromoindole[29] (**12**, 7.0 g, 22.0 mmol) and hexamethylphosphoramide-oxodiperoxomolybdenum (VI) (MoO_5·HMPA) (17.2 g 46.3 mmol) in MeOH (450 ml) was stirred at room temperature for a week. The resulting mixture was concentrated under reduced pressure, treated with sat. Na_2SO_3, and extracted with CH_2Cl_2. The extract was washed with H_2O, dried over $MgSO_4$, and concentrated under reduced pressure. The obtained residue was purified by silica gel column chromatography with EtOAc–hexane (1:1) as an eluent to give 3-hydroxy-2-methoxyindoline **13** (7.2 g, 90%). Mp 165–168 °C (CH_2Cl_2). IR ($CHCl_3$) cm^{-1}: 3600, 1686. ^1H NMR ?300 MHz, $CDCl_3$) δ: 2.32 (3H, s, N–COMe), 2.37 (1H, brs, OH), 3.43 (3H, s, –OMe), 4.89 (1H, brs, –CH–OH), 5.28 (1H, brs, –CH–OMe), 7.46 (1H, d, J=1.7 Hz, Ar-H), 8.27 (1H, br, Ar-H). MS m/z (%): 367 (M+4, 25), 365 (M+2, 53), 363 (M^+, 26), 324 (47), 322 (89), 320 (43), 292 (62), 290 (100), 288 (46), 280 (26), 278 (21), 263 (16), 213 (10), 211 (16), 149 (13), 43 (59). HRMS m/z calcd for $C_{11}H_{11}Br_2NO_3$: 362.9106. Found: 362.9106.

4.5.2. 1-Acetyl-4,6-dibromoindolin-3-one (14). A solution of **13** (364 mg, 1.0 mmol) and 10-camphorsulfonic acid (715 mg, 3.08 mmol) in MeCN was heated under reflux for 30 min. The reaction mixture was evaporated under reduced pressure and extracted with EtOAc. The extract was washed with sat. $NaHCO_3$ and brine, dried over $MgSO_4$, and concentrated under reduce pressure. The residue was purified by silica gel column chromatography with EtOAc–hexane (1:1) as an eluent to give indolin-3-one **14** (186 mg, 56%). Mp 160–164 °C (EtOAc–hexane). IR ($CHCl_3$) cm^{-1}: 1727, 1693. ^1H NMR (300 MHz, $CDCl_3$) δ: 2.33 (3H, s, N–COMe), 4.32 (2H, s, $COCH_2N$–), 7.49

(1H, d, J=1.5 Hz, Ar-H), 8.76 (1H, brs, Ar-H). ^{13}C NMR ($CDCl_3$, 100 MHz) δ: 24.5, 56.7, 119.5, 120.4, 121.5, 131.5, 132.1, 155.0, 167.8, 190.7. MS m/z (%): 335 (M+4, 23), 333 (M+2, 47), 331 (M^+, 24), 293 (48), 291 (100), 289 (51), 263 (23), 43 (25). HRMS m/z calcd for $C_{10}H_7Br_2NO_2$: 330.8844. Found: 330.8836.

4.5.3. 3-Allyl-4,6-dibromo-3-hydroxyindolin-2-one (16). A solution of bromine (1.0 M in CH_2Cl_2, 78 μl) was added to a solution of **14** (7.8 mg, 23.5 μmol) in CH_2Cl_2 at 0 °C for 2 h. The reaction mixture was extracted with EtOAc, and the extract was then washed with sat. $NaHCO_3$ and brine, dried over $MgSO_4$, and concentrated under reduce pressure to give a residue. A mixture of the residue (9.7 mg), allyl alcohol (d=0.85, 6.2 μl, 91 μmol) and MS 4A (22 mg) in DMF (1 ml) was stirred at room temperature for 2 days. The reaction mixture was diluted with diethyl ether and filtrated through Celite® 545. The filtrate was evaporated under reduced pressure to give a residue, which was extracted with EtOAc and 5% NH_4OH. The organic layer was washed with brine, dried over $MgSO_4$, and concentrated under reduced pressure. The obtained residue (9.1 mg) and DBU (3.6 mg, 23.5 μmol) in toluene (1 ml) was stirred at 40 °C for 3 h. The mixture was neutralized with AcOH, diluted in H_2O, and extracted with EtOAc. The extract was washed with brine, dried over $MgSO_4$, and concentrated under reduced pressure. A mixture of the residue and 10% LiOH (25 μl) in MeOH was stirred at room temperature for 3 days. After evaporation, an EtOAc solution of the residue was washed with H_2O and brine, dried over $MgSO_4$, and concentrated. The residue was purified by silica gel column chromatography with EtOAc–hexane (1:1) as an eluent to give indolin-2-one **16** (6.9 mg, 84%). Mp 220–222 °C (EtOAc–hexane). IR (KBr) cm^{-1}: 3378, 1733, 1641. ^{1}H NMR (300 MHz, acetone-d_6) δ: 2.59 (1H, dd, J=12.8, 7.4 Hz, $-CH_2-$), 3.08 (1H, dd, J=12.8, 7.4 Hz, $-CH_2-$), 4.77 (1H, ddt, J=10.1, 2.2, 1.3 Hz, $=CH_2$), 4.91 (1H, ddt, J=17.3, 2.2, 1.3 Hz, $=CH_2$), 5.09 (1H, s, –OH), 5.22 (1H, ddt, J=17.3, 10.1, 7.4 Hz, $-CH=CH_2$), 6.94 (1H, d, J=1.7 Hz, Ar-H), 7.22 (1H, d, J=1.7 Hz, Ar-H). MS m/z (%): 349 (M+4, 2), 347 (M+2, 4), 345 (M^+, 2), 308 (49), 306 (100), 304 (51). HRMS m/z calcd for $C_{11}H_9Br_2NO_2$: 344.9000. Found: 344.9003.

4.5.4. (±)-Convolutamydine E (2b). A solution of 3-allylindolin-2-one **16** (10 mg, 29 μmol), OsO_4 (4% aqueous solution, d=1.04, 53 μl, 8.7 μmol), and NMO (50% aqueous solution, d=1.13, 13 μl, 63 μmol) in MeCN (3 ml) was stirred at room temperature for 1 h. The reaction mixture was evaporated under reduced pressure. A solution of the residue and $NaIO_4$ (7.5 mg, 30 μmol) in aqueous 1,4-dioxan (3 ml) was stirred at room temperature for 1 h. The reaction mixture was extracted with EtOAc, and the extract was then washed with H_2O and brine, dried over $MgSO_4$, and concentrated under reduced pressure. To a solution of the residue in MeOH (2 ml), $NaBH_4$ (11 mg, 0.3 mmol) was gradually added at 0 °C, and the mixture was then stirred at 0 °C for 30 min. After adding aqueous NH_4Cl followed by evaporating the MeOH under reduced pressure, the residue was extracted with EtOAc. The organic layer was washed with H_2O and brine, dried over $MgSO_4$, and concentrated under reduced pressure. The residue was purified by silica gel column chromatography with EtOAc–hexane (3:1) as an eluent to give (±)-convolutamydine E (**2b**, 6.6 mg, 65%). Mp 204–206 °C ($CHCl_3$) [lit.[2c] oil]. IR (KBr) cm^{-1}: 3350, 1736, 1605, 1261, 1088, 801. ^{1}H NMR (300 MHz, C_5D_5N) δ: 3.10 (2H, t, J=7.3 Hz, $-C-CH_2CH_2O-$), 3.96 (2H, m, $-C-CH_2CH_2O-$), 7.02 (1H, d, J=1.6 Hz, Ar-H), 7.41 (1H, d, J=1.6 Hz, Ar-H), 8.31 (1H, s, –NH). ^{13}C NMR (C_5D_5N, 125 MHz) δ: 39.3, 58.1, 77.4, 112.6, 112.6, 120.9, 128.2, 130.2, 146.7, 180.6. MS (FAB) m/z (%): 354 (MH^++4, 50), 352 (MH^++2, 99), 350 (MH^+, 53), 336 (20), 334 (32), 332 (16), 306 (57), 304 (100), 302 (50). HRMS (FAB, MH^+) m/z calcd for $C_{10}H_9Br_2NO_3$: 349.9027. Found: 349.9031.

4.5.5. 3-Allyl-4,6-dibromo-3-(*tert*-butyldimethylsilyloxy)indolin-2-one (17). A solution of 3-hydroxyindolin-2-one **16** (59 mg, 0.17 mmol), TBDMSOTf (235 mg, 0.89 mmol), and 2,6-lutidin (95 mg, 0.89 mmol) in CH_2Cl_2 was stirred at 0 °C to room temperature. After 3 days, the reaction mixture was quenched with brine and extracted with CH_2Cl_2. The extract was dried over $MgSO_4$ and concentrated under reduced pressure. A solution of the residue in AcOH–THF–H_2O (1:1:1, 1 ml) was stirred at 80 °C for 2 h. After cooling, the reaction mixture was extracted with EtOAc. The extract was washed with H_2O and brine, dried over $MgSO_4$, and concentrated under reduced pressure. The residue was subjected to chromatography on a silica gel column with EtOAc–hexane (1:4) as an eluent to give 3-silyloxy-indolin-2-one **17** (56 mg, 69%). Viscous oil. IR ($CHCl_3$) cm^{-1}: 3427, 1732, 1641. ^{1}H NMR (300 MHz, $CDCl_3$) δ: −0.13 (3H, s, –SiMe), 0.06 (3H, s, –SiMe), 0.90 (9H, s, –Si^{t}Bu), 2.78 (1H, dd, J=12.8, 7.5 Hz, $=CH-CH-$), 3.24 (1H, dd, J=12.8, 7.0 Hz, $=CH-CH-$), 4.92 (1H, d, J=9.9 Hz, $C=CH_2$), 5.17 (1H, d, J=16.5 Hz, $C=CH_2$), 5.29 (1H, m, $-CH=CH_2$), 6.97 (1H, d, J=1.4 Hz, Ar-H), 7.34 (1H, d, J=1.4 Hz, Ar-H), 8.25 (1H, br, NH). ^{13}C NMR ($CDCl_3$, 100 MHz) δ: −3.5, −3.4, 18.4, 25.8, 40.7, 79.3, 112.3, 120.0, 120.5, 123.2, 127.8, 129.4, 129.7, 142.6, 177.3. MS (FAB) m/z (%): 464 (MH^++4, 4), 462 (MH^++2, 7), 460 (MH^+, 5), 4221 (7), 420 (10), 4187 (6), 4065 (15), 404 (24), 402 (12), 365 (12), 363 23), 361 12), 332 (51), 330 (100), 328 (52). HRMS (FAB, MH^+) m/z calcd for $C_{17}H_{23}Br_2NO_2Si$: 459.9943. Found: 459.9920.

4.5.6. 4,6-Dibromo-3-(*tert*-butyldimethylsilyloxy)-3-(2-oxopropyl)indolin-2-one (18). A suspension of palladium (II) chloride (3.2 mg, 0. 019 mmol) and copper (I) chloride (18.8 mg, 0.19 mmol) in dioxane–H_2O (7:1, 3 ml) was vigorously stirred with bubbling oxygen gas at room temperature for 1 h under oxygen atmosphere. The indolin-2-one **17** (87 mg, 0.19 mmol) was added to the mixture. After heating at 50 °C for 24 h, the reaction mixture was cooled to room temperature and diluted with CH_2Cl_2. The precipitate was filtered off, and the filtrate was dried over $MgSO_4$, and evaporated off. The obtained residue was purified by flash silica gel column chromatography with EtOAc–hexane (1:1) as an eluent to give 3-(*tert*-butyldimethylsilyloxy)-3-(2-oxopropyl)indolin-2-one (**18**, 11 mg, 12%). Viscous oil. IR ($CHCl_3$) cm^{-1}: 3431, 1747, 1718. ^{1}H NMR (300 MHz, $CDCl_3$) δ: −0.21 (3H, s, –SiMe), 0.04 (3H, s, –SiMe), 0.87 (9H, s, –Si^{t}Bu), 2.08 (3H, s, –COMe), 3.31 (1H, d, J=18.2 Hz, –CHCO–), 3.99 (1H, d, J=18.2 Hz, –CHCO–), 6.97 (1H, d, J=1.4 Hz, Ar-H), 7.27 (1H, d, J=1.4 Hz, Ar-H), 7.56 (1H, br, –NH). MS (FAB) m/z (%): 480

(MH^++4, 14), 478 (MH^++2, 26), 476 (MH^+, 13), 422 (12), 420 (23), 418 12), 348 (16), 346 (30), 344 (16), 306 (50), 34 (100), 302 (34). HRMS (FAB, MH^+) *m/z* calcd for $C_{17}H_{23}Br_2NO_3Si$: 475.9892. Found: 475.9879.

4.5.7. (±)-Convolutamydine A (2a). Tris(dimethylamino)-sulfur (trimethylsilyl)difluoride (TAS-F) (6.4 mg, 23 μmol) was gradually added to a stirred solution of indolin-2-one **17** (11 mg, 23 μmol) in dry DMF (1 ml) at 0 °C. The mixture was stirred at 15 °C for 2.5 h, diluted with EtOAc, washed with sat. $KHSO_4$, and extracted with EtOAc. The extract was dried over $MgSO_4$ and evaporated. The obtained residue was purified by silica gel column chromatography with EtOAc–hexane (3:2) as an eluent to give (±)-convolutamydine A (**2a**, 6.3 mg, 75%). Mp 192–195 °C (EtOAc–hexane) [lit.[2b] mp 190–195 °C]. IR ($CHCl_3$) cm^{-1}: 3430, 1747, 1610. ^1H NMR (300 MHz, $CDCl_3$) δ: 2.16 (3H, s, –COMe), 3.34 (1H, d, *J*=17.3 Hz, –CHCO–), 3.73 (1H, d, *J*=17.3 Hz, –CHCO–), 5.12 (1H, br, –OH), 7.00 (1H, d, *J*=1.6 Hz, Ar-H), 7.32 (1H, d, *J*=1.7 Hz, Ar-H), 7.74 (1H, s, –NH). MS *m/z* (%): 365 (M+4, 20), 363 (M+2, 42), 361 (M^+, 21), 322 (8), 320 (16), 318 (10), 308 (47), 306 (100), 304 (59), 279 (44), 277 (91), 275 (48), 252 (14), 250 (31), 248 (18), 170 (18), 168 (18), 88 (12). HRMS *m/z* calcd for $C_{11}H_9Br_2NO_3$: 360.8949. Found: 360.8947.

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