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Synthesis of Diversely Functionalized Hexahydropyrrolo[2,3-*b*]indoles Using Domino Reactions, Olefination, Isomerization and Claisen Rearrangement Followed by Reductive Cyclization

Tomomi Kawasaki,* Atsuyo Ogawa, Romi Terashima, Toshiko Saheki, Naoko Ban, Hiroko Sekiguchi, Ken-ei Sakaguchi, and Masanori Sakamoto

Meiji Pharmaceutical University, 2-522-1 Noshio, Kiyose, Tokyo 204-8588, Japan

kawasaki@my-pharm.ac.jp

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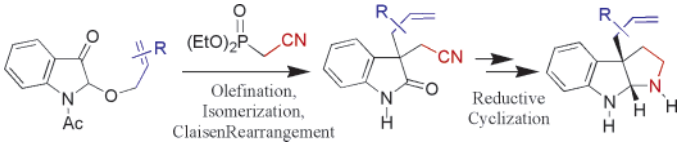

Hexahydropyrrolo[2,3-*b*]indoles **6** were synthesized in five steps from indolin-3-one **8** by a general and efficient method, in which elements of molecular diversity were readily added onto the 3a-position of the pyrrolo[2,3-*b*]indole ring system. Horner−Wadsworth−Emmons reaction of 2-allyloxyindolin-3-ones **7**, derived from indolin-3-one **8** and a variety of allylic alcohols, smoothly proceeded with successive Claisen rearrangement to give the corresponding 3-allyl-3-cyanomethylindolin-2-ones **15**. Indolin-2-ones **15** were converted into pyrrolo[2,3-*b*]indoles **6** using partial hydrolysis followed by reductive cyclization with $LiAlH_4$. Synthesis of *N*-methylated pyrrolo[2,3-*b*]indole derivatives **23** and **26** is also described.

Introduction

The hexahydropyrrolo[2,3-*b*]indole ring system containing a carbon substituent at the 3a-site is a widely distributed structural framework present in a number of biologically active alkaloids[1] such as physostigmine,[2] urchordamines,[3] asperazine,[4] chimonanthines,[5] leptosins,[6] and so on. Among them, ardeemin (**1**),[7] amauromine (**2**),[8] flustramines (**3**),[9] mollenine A (**4**),[10] pseudophrynaminol (**5**),[11] aszonalenine,[12] oscillatorin,[13] and roquefortines[14] represent the 3a-allylic members of this subfamily (Figure 1). The unique structural array and the interesting biological activities displayed by this class of compounds have made them attractive synthetic targets. As a result, several synthetic approaches toward the core 3a-allylic pyrrolo[2,3-*b*]indole **6** have been reported in the past 2

(1) For recent reviews of hexahydropyrrolo[2,3-*b*]indole alkaloids, see: (a) Hino, T.; Nakagawa, M. *Alkaloids* **1988**, *34*, 1−75. (b) Anthoni, U.; Christophersen, C.; Nielsen, P. H. In *Alkaloids*: *Chemical and Biological Perspectives*; Pelletiesr, S. W., Ed.; Pergamon Press: New York, 1999; Vol. 13, pp 163−236.

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(11) (a) Review: Dayl, J. W.; Garraffo, H. M.; Spande, T. F. In *Alkaloids*: *Chemical and Biological Perspectives*; Pelletiesr, S. W., Ed.; Pergamon Press: New York, 1999; Vol. 13, pp 1−161. (b) Spande, T. F.; Edwards, M. W.; Pannell, L. K.; Daly, J. W. *J. Org. Chem.* **1988**, *53*, 1222−1226. (c) Smith, B. P.; Tyler, M. J.; Kaneko, T.; Garraffo, H. M.; Spande, T. F.; Daly, J. W. *J. Nat. Prod.* **2002**, *65*, 439−447.

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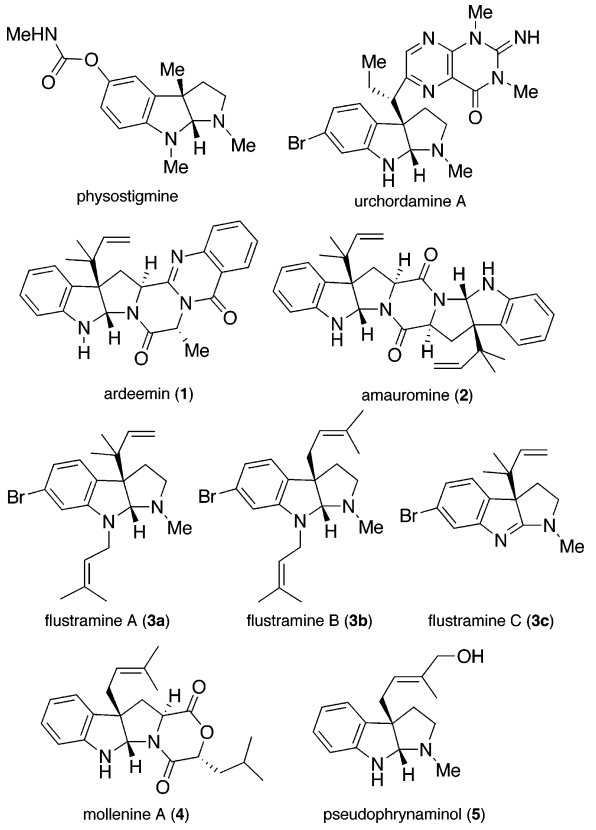


FIGURE 1. 3a-Carbon-substituted pyrrolo[2,3-*b*]indole alkaloids.

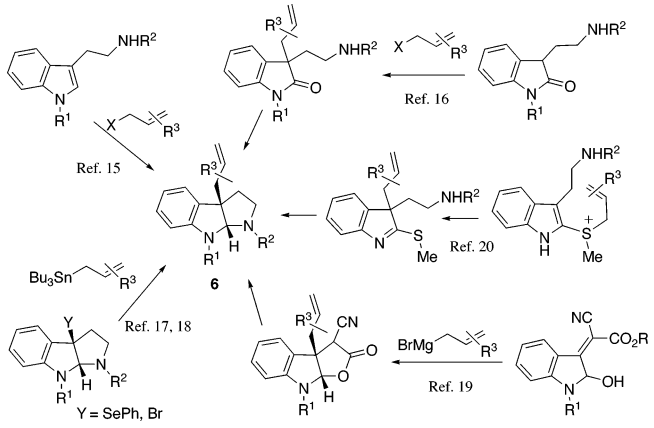
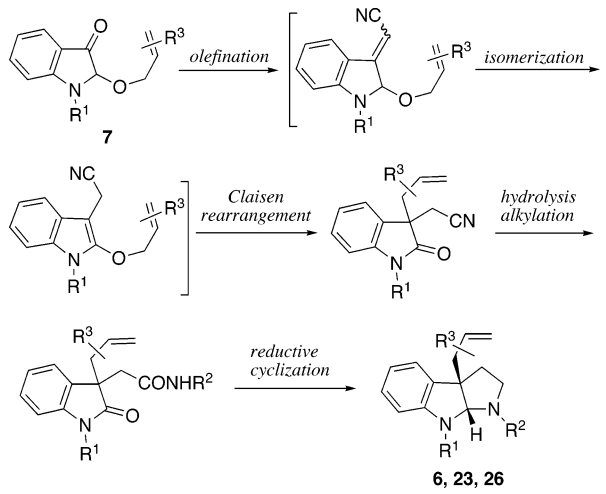


FIGURE 2. Routes to 3a-allylic derivatives of pyrrolo[2,3-*b*]-indoles.

decades (Figure 2), through alkylation of indoles[15] and indolin-2-ones,[16] direct substitution of 3a-phenylselenyl-[17] or 3a-bromo-pyrrolo[2,3-*b*]indoles with allyl tributylstannanes,[18] Grignard reagent addition of 3-alkylideneindolin-2-ols,[19] and thio-Claisen rearrangement.[20] Previously we reported an efficient synthetic method for 3a-allylpyrrolo[2,3-*b*]indoles **6** through domino reaction

SCHEME 1. Key Synthetic Strategy of 3a-Allylpyrrolo[2,3-*b*]indoles 6, 23, and 26



of 2-allyloxyindolin-3-ones **7**, olefination, isomerization, and Claisen rearrangement, followed by reductive cyclization, and the total syntheses of flustramine C (**3c**) and pseudophrynaminol (**5**) (Scheme 1).[21] In view of the potential of these natural products as lead compounds to new and more biologically active agents, formulation of a diverse synthesis of pyrrolo[2,3-*b*]indole alkaloids containing allylic moieties at the 3a-site and analogues is essential.[17b] This study has now led to an effective means for preparing pyrrolo[2,3-*b*]indoles **6**, **23**, and **26** possessing various allylic groups at the 3a-position.

Results and Discussion

Initially, we carried out the preparation of the starting 2-allyloxyindolin-3-ones **7** using bromination of the readily available indolin-3-one **8**[22] followed by reaction of 2-bro-

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(19) (a) Morales-Ríos, M. S.; Suárez-Castillo, O. R.; Joseph-Nathan, P. *J. Org. Chem.* **1999**, *64*, 1086−1087. (b) Morales-Ríos, M. S.; Suárez-Castillo, O. R.; Trujillo-Serrato, J. J.; Joseph-Nathan, P. *J. Org. Chem.* **2001**, *66*, 1186−1192. (c) Morales-Ríos, M. S.; Suárez-Castillo, O. R.; Joseph-Nathan, P. *Tetrahedron* **2002**, *58*, 1479−1484.

(20) (a) Takase, S.; Uchida, I.; Tanaka, H.; Aoki, H. *Heterocycles* **1984**, *22*, 2491−2494. (b) Takase, S.; Itoh, Y.; Uchida, I.; Tanaka, H.; Aoki, H. *Tetrahedron Lett.* **1985**, *26*, 847−850. (c) Takase, S.; Uchida, I.; Tanaka, H.; Aoki, H. *Tetrahedron* **1986**, *42*, 5879−5886. (d) Takase, S.; Itoh, Y.; Uchida, I.; Tanaka, H.; Aoki, H. *Tetrahedron* **1986**, *42*, 5887−5894. (e) Bhat, B.; Harrison, D. M. *Tetrahedron Lett.* **1986**, *27*, 5873−5874. (f) Bhat, B.; Harrison, D. M. *Tetrahedron* **1993**, *49*, 10655−10662.

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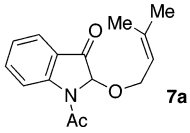
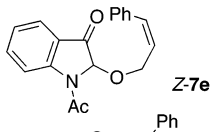
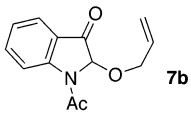
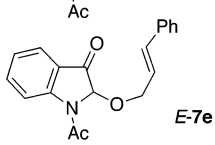
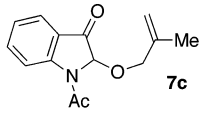
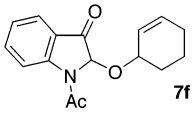
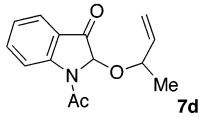
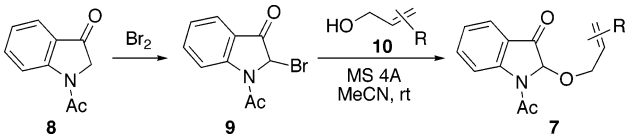
TABLE 1. Preparation of 2-Allyloxyindolin-3-ones 7

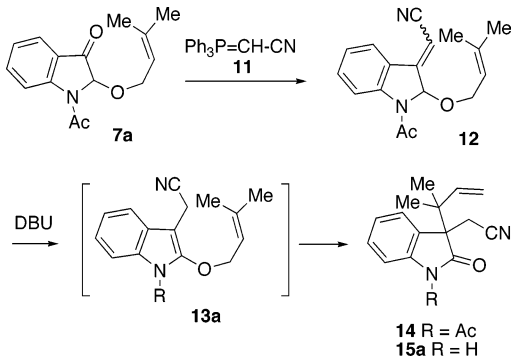
entry	ether 7	yield (%)[a]	entry	ether 7	yield (%)[a]
1	 **7a**	61[b]	7	 *Z*-**7e**	63
2		73[c]			
3		91			
4	 **7b**	97	8	 *E*-**7e**	57
5	 **7c**	83	9	 **7f**	61
6	 **7d**	64			

[a] Isolated yield of **7** from **8**. [b] The reaction was performed without MS 4Å in CH_2Cl_2. [c] The reaction was carried out with MS 4Å in CH_2Cl_2.

SCHEME 2



SCHEME 3



moindolin-3-one **9**[23] with a variety of allyl alcohols **10** (Scheme 2); the results are summarized in Table 1. Thus the reaction of **9** with 3-methyl-2-butenyl alcohol (**10a**) in CH_2Cl_2 at room temperature gave the desired ether **7a** in moderate yield (Table 1, entry 1). When the reaction was performed in the presence of molecular sieves (MS) 4Å as the solid base,[24] the yield of **7a** was improved (entry 2). The reaction using acetonitrile instead of CH_2Cl_2 proceeded smoothly to afford **7a** in high yield (entry 3). Similarly, 2-allyloxyindolin-3-ones **7b**−**f** were readily obtained by the reaction of **9** with a variety of allylic alcohols **10b**−**f** (entries 4−9), respectively.

Next, for introduction of the C_2N unit constructing the pyrrolo-ring system of **6**, we performed the Wittig olefination of 2-allyloxyindolin-3-one **7a** with the cyanomethylidene phosphonium ylide **11**. When **7a** was treated with the ylide **11** in refluxing toluene for 5 h, the Wittig reaction proceeded to give a mixture of *E*- and *Z*-isomers (1:3) of 3-cyanomethylideneindoline **12** in 70% yield (Scheme 3; Table 2, entry 1).[25,26] Reaction of **12** with DBU at room temperature for 2 days took place with isomerization followed by Claisen rearrangement of an intermediary indole **13a** to afford 3-(2-methyl-2-butenyl)-3-cyanomethylindolin-2-one **14** and its deacetylate **15a** in 13% and 47% yields (Table 2, entry 1), respectively. These reactions were carried out in one pot to improve the yields of **14** and **15a** (entry 2).

TABLE 2. Wittig Olefination of 7a and Claisen Rearrangement

		yield (%)		
entry	cinditions	**12**	**14**	**15a**
1	1. toluene, reflux, 5 h	70[a]		
	2. DBU, rt, 2 days[b]		13[c]	47[c]
2	toluene, reflux, 3 h, then DBU, 80 °C, 5 h		14	72

[a] *E*:*Z* = 1:3. [b] Treatment of **12** with DBU. [c] Isolated yields from **12**.

Previously, we reported that Horner−Wadsworth−Emmons olefination of indolin-3-ones proceeded smoothly at lower temperature (0 °C) to afford the corresponding 3-alkylidene indolines in high yields,[27] and we next tried the Horner−Wadsworth−Emmons reaction of 2-allyloxyindolin-3-one **7a** as an alternative olefination method. On

(23) Velezheva, V. S.; Mel'man, A. I.; Smushkevich, Y. I.; Pol'shakov, V. I.; Anisimova, O. S. *Khim.-Fram. Zh. SSSR* **1996**, *24*, 46−51; *Chem. Abstr.* **1991**, *114*, 228786u.

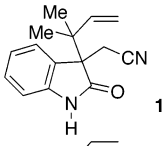
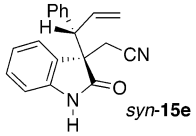
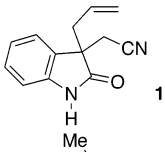
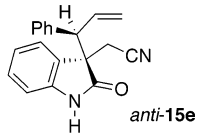
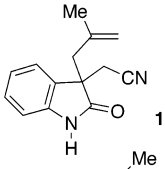
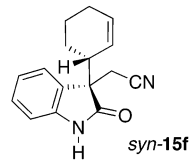
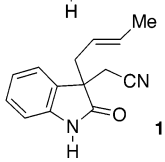
(24) The use of triethylamine as the base resulted in immediate decomposition of **7a** and **9** because of their instability toward the base at room temperature.

(25) The geometrical arrangement of **12a** was confirmed by comparison of chemical shifts of signals due to vinyl protons of the *E*- and *Z*-isomers with those of similar 3-alkylideneindolines reported: (a) Kawasaki, T.; Nonaka, Y.; Ohtsuka, H.; Sato, H.; Sakamoto, M. *J. Chem. Soc., Perkin Trans. 1* **1990**, 1101−1106. (b) Kouko, T. Kobayashi, J.; Ohta, A.; Sakamoto, M.; Kawasaki, T. *Synthesis* **2004**, 2463−2470.

(26) In Wittig olefination of **7a**, no isomerization of **12a** to **13a** was detected.

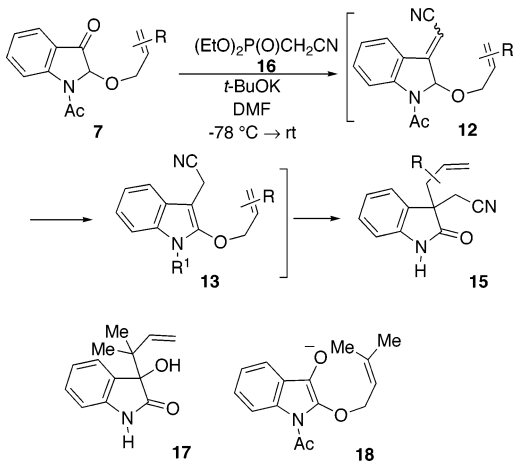
(27) Kawasaki, T.; Nonaka,Y.; Watanabe, K.; Ogawa, A.; Higuchi, K.; Terashima, R.; Masuda, K.; Sakamoto, M. *J. Org. Chem.* **2001**, *66*, 1200−1204.

TABLE 3. Domino Reactions, Horner−Wadsworth−Emmons Olefination of 2-Allyloxyindolin-3-ones 7, Isomerization, Claisen Rearrangement, and Deacetylation to Indolin-2-ones 15

entry	15	react. time (h)	yield (%)	entry	15	react. time (h)	yield (%)
1[a]	 **15a**	2	48[c]	7	 *syn*-**15e**	12	84 (21 : 1)[e]
2[b]		4	65[d]				
3		4	quant.				
4	 **15b**	1.5	81	8	 *anti*-**15e**	12	74 (1 : 2.2)[e]
5	 **15c**	2	88	9	 *syn*-**15f**	13	79
6	 **15d**	19	79				

[a] The reaction using NaH as a base was carried out at 0 °C to rt. [b] The reaction using *t*-BuOK as a base was carried out at 0 °C to rt. [c] Formation of **17** (30%). [d] Formation of **17** (17%). [e] The ratio of diastereomers was determined by HPLE.

SCHEME 4



treating **7a** with cyanomethylphosphonate **16** in the presence of NaH at 0 °C to room temperature, the domino reactions, olefination of **7a**, isomerization of **12a**, Claisen rearrangement of **13a**, and deacetylation, took place smoothly to afford indolin-2-one **15a** in 48% yield together with 3-hydroxyindolin-2-one **17** (30%) (Scheme 4; Table 3, entry 1). The formation of **17** is caused by Claisen rearrangement of the enolate **18** generated from **7a** under the basic reaction conditions.[28] Using potassium *tert*-butoxide instead of NaH under the same reaction conditions improved the yield of **15a** (65%), but still with accompanying formation of the byproduct **17** (17%) (entry 2). When the reaction was carried out at lower temperature (−78 °C to room temperature), the domino reactions occurred selectively to produce indolin-2-one **15a** in a quantitative yield without formation of **17** (entry 3). This reaction constructed readily the two adjacent quaternary carbons in **15a**. Similar domino reactions of 2-allyloxyindolin-3-ones **7b−f** with the phosphonate **16** provided the corresponding 3-allyl-3-cyanomethylindolin-2-ones **15b−f** in high yields (entries 4−9). The reaction of 3-butenyl ether **7d** proceeded stereoselectively via a chairlike transition state **A** over **B** (Figure 3) in Claisen rearrangement of the intermediary indole **13d** to afford (*E*)-3-(2-buten-2-yl)indolin-2-one **15d** in 79% yield (entry 6).[29] The reaction of (*Z*)-cinnamyl ether **7e** proceeded stereoselectively to give a diastereomeric mixture (21:1) of *syn*-**15e** and *anti*-**15e** in 84% yield (entry 7). The relative configuration of *syn*-**15e** was confirmed by the NOE experiment of lactone **19**, which was derived from *syn*-**15e** using OsO_4-hydroxylation, $NaIO_4$-oxidative cleavage, $NaBH_4$-reduction, and intramolecular alcoholysis (Scheme 5). In contrast, the reaction of (*E*)-**7e** afforded a mixture (1:2.2) of *syn*-**15e** and *anti*-**15e** (74%) (entry 8). The Claisen rearrangement of (*Z*)-indole **13e** generated from (*Z*)-**7e** progressed predominantly via the boatlike transition state **C** over the chairlike **D** because of the

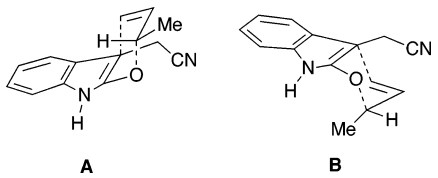


FIGURE 3. Transition states in the Claisen rearrangement of **13d** (R^1 = H).

(28) Recently we have reported a similar enolization−Claisen rearrangement of **7a** with DBU at 40 °C to give **17**: Kawasaki, T.; Nagaoka, M.; Satoh, T.; Okamoto, A.; Ukon, R.; Ogawa, A. *Tetrahedron* **2004**, *60*, 3493−3503.

(29) The molecular orbital calculation of transition states in Claisen rearrangement of **13d** (R^1 = H) was performed by using SPARTAN ver. 5.1.2 (pBP-DN**). The difference ($\Delta\Delta G^{\ddagger}_{A-B}$ = 4.88 kcal/mol) between the free activation energy of two chairlike transition states **A** and **B** suggests that Claisen rearrangement proceeded predominantly via the transition state **A** over **B** to *E*-isomer **15d**.

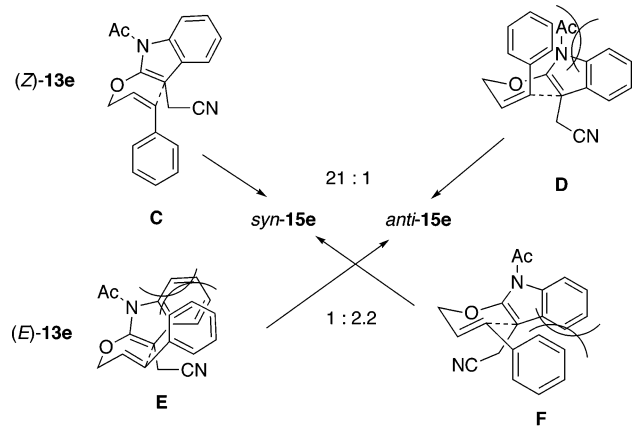


FIGURE 4. Transition states in the Claisen rearrangement of (*Z*)- and (*E*)-**13e**.

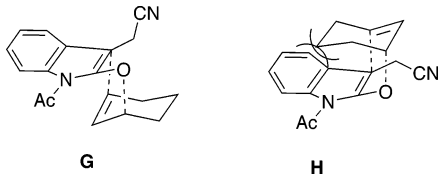
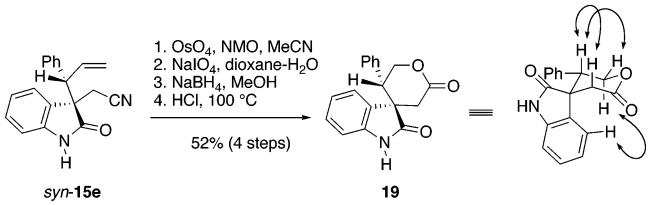


FIGURE 5. Transition states in the Claisen rearrangement of **13f**.

SCHEME 5. Transformation of *syn*-15e to 19 and NOE Experiment of 19



steric repulsion between the phenyl group and the indole ring in the transition state **D** (Figure 4). The lower stereoselectivity in the reaction of (*E*)-**7e** is caused by a slight difference in stability between transition states **E** and **F**. In the case of *cyclo*-hexenyl ether **7f** (entry 9), the reaction took place stereoselectively to yield **15f** (79%) as a single isomer, of which the stereochemistry was presumed to be *syn* on the basis of the following result. The Claisen rearrangement of *cyclo*-penteny-2-*cyclo*-hexenyl ether takes place predominantly via the boatlike transition state.[30] The Claisen rearrangement of indole **13f** derived from **7f** proceeds via the boatlike transition state **G** over the chairlike **H** because of the steric repulsion between the hexenyl and the indole rings in the transition state **H** (Figure 5). Recently several groups have reported a similar Claisen rearrangement of 2-allyloxyindoles generated by reaction of allyl alcohol to 1-methoxyindole[31a] and 3-chloroindolinine[31b] to provide 3-allylindolin-2-ones. This method using the domino

(30) Cave, R. J.; Lythgoe, B.; Metcalfe, D. A.; Waterhouse, I. *J. Chem. Soc., Perkin Trans. 1* **1977**, 1218−1228.

(31) (a) Somei, M.; Yamada, F.; Izumi, T.: Nakajou, M. *Heterocycles* **1997**, *45*, 2327−2330. (b) Booker-Milburn, K. I.; Fedouloff, M.; Paknoham, S. J.; Strachan, J. B.; Melville, J. L.; Voyle, M. *Tetrahedron Lett.* **2000**, *41*, 4657−4661.

SCHEME 6

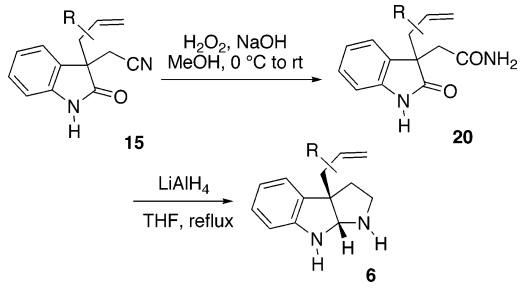


TABLE 4. Synthesis of Pyrrolo[2,3-*b*]indoles 6 through Hydrolysis of Nitriles 15 Followed by Reductive Cyclization of Amides 20

nitrile **15**	amide **20**	yield (%)	pyrroloindole **6**	yield (%)
15a	**20a**	85	**6a**	67
15b	**20b**	75	**6b**	72
15c	**20c**	57	**6c**	46
syn-**15e**	**20e**	70[a]	**6e**	49[a]
15f	**20f**	70	**6f**	63

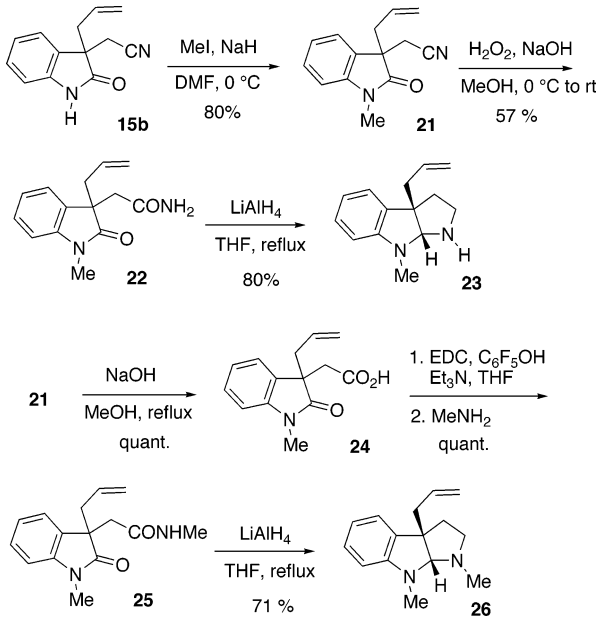
[a] Ratio of diastereomers 21:1.

reactions is efficient to introduce both an allylic moiety and the C_2N unit of pyrrolo[2,3-*b*]indoles **6** simultaneously.

Finally, we attempted transformation of 3-allyl-3-cyanomethylindolin-2-ones **15** to 3a-allylhexahydropyrrolo[2,3-*b*]indoles **6**. Partial hydrolysis of **15** with hydrogen peroxide in the presence of NaOH in methanol afforded amides **20** in good yields. On treatment of **20** with $LiAlH_4$ in boiling THF, reduction of amides **20** followed by cyclization proceeded to give the corresponding pyrrolo[2,3-*b*]indoles **6** containing a variety of allylic moieties at the 3a-site, respectively (Scheme 6; Table 4).

Synthesis of 1-methyl and 1,8-dimethylpyrrolo[2,3-*b*]-indole derivatives **23** and **26** like physostigmine was accomplished in the following manner. Methylation of 3-allyl-3-cyanomethylindolin-2-one **15b** followed by partial hydrolysis of 3-cyanomethyl-1-methylindolin-2-one **21** with hydrogen peroxide and NaOH provided *N*-methylamide **22** in good yield. In a similar manner as described

SCHEME 7. Synthesis of *N*-Methylated Pyrrolo[2,3-*b*]indoles 23 and 26



above, reduction of **22** with $LiAlH_4$ was carried out to afford 8-methylpyrrolo[2,3-*b*]indole **23** in 80% yield (Scheme 7). Hydrolysis of *N*-methylindolin-2-one **21** with NaOH in boiling methanol and condensation of *N*-methylcarboxylic acid **24** with pentafluorophenol using EDC followed by reaction with methylamine yielded N^1,*N*-dimethylamide **25** in high yield. $LiAlH_4$−Reduction of **25** gave 1,8-dimethylpyrrolo[2,3-*b*]indole **26** in 71% yield (Scheme 7).

In summary, we have developed a new and efficient method for synthesizing 3a-allylhexahydropyrrolo[2,3-*b*]-indoles **6**, **23**, and **26** comprising the domino reactions of 2-allyloxyindolin-3-ones **7**, olefination, isomerization, Claisen rearrangement, and deacetylation, to 3-allyl-3-cyanomethylindolin-2-ones **15** followed by reductive cyclization. This approach should also serve as a general method for access to natural products and for preparing libraries of structurally diverse pyrrolo[2,3-*b*]indoles that may exhibit interesting biological activities.

Experimental Section

1-Acetyl-2-bromoindolin-3-one (**9**) was prepared according to the reported procedure.[23] The allylic alcohols **10a**−**d**, (*E*)-**10e**, and **10f** were commercially available. (*Z*)-Cinnamyl alcohol (*Z*)-**10e** was prepared according to the reported method.[32]

General Procedure for Preparation of 1-Acetyl-2-allyloxyindolin-3-ones 7. A suspension of 2-bromoindolin-3-one **9** (1.0 mmol), allylic alcohol **10** (3.3−5.0 mmol) and MS 4Å (0.7 g) in dry acetonitrile (5 mL) or acetonitrile/DMF (10:1, 2 mL) was stirred at room temperature under nitrogen atmosphere. After consuming the bromide **9** (for 3.5 h to 3 days), the reaction mixture was diluted with Et_2O and filtered through Celite. The filtrate was concentrated under reduced pressure to give a residue, which was diluted with Et_2O. The ether solution was washed with 5% NH_4OH and brine, dried over $MgSO_4$, and concentrated under reduced pressure. The obtained residue was chromatographed by silica gel column with AcOEt/hexane (1:3−4) for **7a**, **7b**, (*Z*)- and (*E*)-**7e**, or Et_2O−hexane (1:1−4) for **7c**, **7d**, **7f** as an eluent to give 2-allyloxyindolin-3-ones **7a**−**f**.

1-Acetyl-2-(3-methylbut-2-enyloxy)indolin-3-one (7a): a viscous oil. IR ($CHCl_3$) 1730, 1681, 1607 cm^{-1}; ^1H NMR ($CDCl_3$, 300 MHz) δ 1.59 (s, 3H), 1.70 (s, 3H), 2.40 (s, 3H), 4.10 (dd, 1H, J = 10.8, 7.2 Hz), 4.21 (dd, 1H, J = 10.8, 7.5 Hz), 5.21 (s, 1H), 5.32 (dd, 1H, J = 7.5, 7.2 Hz), 7.19 (t, 1H, J = 7.7 Hz), 7.65 (1H, t, J = 7.7 Hz), 7.68 (d, 1H, J = 7.7 Hz), 8.46 (d, 1H, J = 7.7 Hz); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 17.9, 23.6, 25.7, 62.1, 85.0, 117.9, 119.0, 122.2, 123.7, 124.1, 137.7, 139.5, 152.7, 169.3, 195.0; HRMS (EI) *m/z* calcd for $C_{15}H_{17}NO_3$ 259.1207, found 259.1212.

1-Acetyl-2-allyloxyindolin-3-one (7b): a viscous oil. IR ($CHCl_3$) 1732, 1688, 1609 cm^{-1}; ^1H NMR ($CDCl_3$, 270 MHz) δ 2.41 (s, 3H), 4.08 (ddt, 1H, J = 11.9, 5.9, 1.3 Hz), 4.22 (ddt, 1H, J = 11.9, 5.6, 1.3 Hz), 5.22 (dq, 1H, J = 10.2, 1.3 Hz), 5.25 (s, 1H), 5.30 (dq, 1H, J = 17.2, 1.3 Hz), 5.90 (dddd, 1H, J = 17.2, 10.2, 5.9, 5.6 Hz), 7.22 (ddd, 1H, J = 7.6 Hz), 7.68 (1H, t, J = 7.6 Hz), 7.73 (dd, 1H, J = 7.6 Hz), 8.46 (d, 1H, J = 7.6 Hz); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 23.8, 66.6, 85.3, 118.0, 118.5, 122.3, 124.0, 124.4, 132.5, 138.0, 153.0, 169.4, 194.6; HRMS (EI) *m/z* calcd for $C_{13}H_{13}NO_3$ 231.0895, found 231.0898.

1-Acetyl-2-(2-methylallyloxy)indolin-3-one (7c): a viscous oil. IR ($CHCl_3$) 1732, 1686, 1609 cm^{-1}; ^1H NMR ($CDCl_3$, 300 MHz) δ 1.75 (s, 3H), 2.40 (s, 3H), 3.91 (d, 1H, J = 11.1 Hz), 4.11 (d, 1H, J = 11.1 Hz), 4.90 (s, 1H), 4.97 (s, 1H), 5.26 (s, 1H), 7.21 (t, 1H, J = 7.7 Hz), 7.64−7.75 (m, 2H), 8.49 (d, 1H, J = 7.7 Hz); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 19.8, 23.7, 69.2, 85.6, 113.4, 118.0, 122.3, 123.9, 124.3, 138.0, 140.1, 152.9, 169.4, 194.5; HRMS (EI) *m/z* calcd for $C_{14}H_{15}NO_3$ 245.1052, found 245.1055.

1-Acetyl-2-(but-3-en-2-yloxy)indolin-3-one (7d): a mixture (1:2) of its diastereomers as a viscous oil. IR ($CHCl_3$) 1730, 1686, 1609 cm^{-1}; ^1H NMR ($CDCl_3$, 270 MHz) δ 1.28 (d, 2/3 × 3H, J = 6.3 Hz), 1.30 (d, 1/3 × 3H, J = 6.3 Hz), 2.33 (s, 2/3 × 3H), 2.40 (1/3 × 3H), 4.29 (pent, 1/3 × 1H, J = 7.5 Hz), 4.64 (pent, 2/3 × 1H, J = 7.5 Hz), 4.88 (d, 1/3 × 1H, J = 17.5 Hz), 4.93 (d, 1/3 × 1H, J = 10.9 Hz), 5.17 (s, 2/3 × 1H), 5.23 (d, 2/3 × 1H, J = 10.9 Hz), 5.27 (d, 2/3 × 1H, J = 17.5 Hz), 5.30 (s, 1/3 × 1H), 5.7−5.88 (m, 1H), 7.17 (t, J = 7.6 Hz), 7.58−7.75 (m, 2H), 8.40 (d, 1/2 × 1H, J = 8.2 Hz), 8.45 (d, 2/2 × 1H, J = 8.2 Hz); HRMS (EI) *m/z* calcd for $C_{14}H_{15}NO_3$ 245.1051, found 245.1054.

(*Z*)-1-Acetyl-2-cinnamyloxyindolin-3-one (*Z*-7e): a viscous oil. IR ($CHCl_3$) 1732, 1688, 1608 cm^{-1}; ^1H NMR ($CDCl_3$, 300 MHz) δ 2.39 (s, 3H), 4.36 (ddd, 1H, J = 12.0, 6.8, 1.5 Hz), 4.49 (ddd, 1H, J = 12.0, 6.5, 1.5 Hz), 5.23 (s, 1H), 5.81 (dt, 1H, J = 11.7, 6.5 Hz), 6.62 (d, 1H, J = 11.7 Hz), 7.10−7.35 (m, 6H), 7.65 (d, 1H, J = 8.3, 7.3 Hz), 7.70 (d, 1H, J = 7.3 Hz), 8.44 (brd, 1H, J = 8.3 Hz); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 23.9, 66.5, 85.2, 118.0, 122.3, 123.5, 124.0, 124.4, 126.5, 126.5, 128.0, 128.4, 128.4, 134.2, 135.9, 138.0, 152.9, 169.3, 194.8; HRMS (FAB) *m/z* calcd for $C_{19}H_{18}NO_3$ (M + 1) 308.1287, found 308.1297.

(*E*)-1-Acetyl-2-cinnamyloxyindolin-3-one (*E*-7e): mp 82−84 °C (Et_2O/hexane). IR ($CHCl_3$) 1732, 1688, 1609 cm^{-1}; ^1H NMR ($CDCl_3$, 300 MHz) δ 2.42 (s, 3H), 4.27 (ddd, 1H, J = 11.8, 6.4, 1.1 Hz), 4.40 (ddd, 1H,, J = 11.8, 6.2, 1.1 Hz), 5.28 (s, 1H), 6.23 (dt, 1H, J = 16.0, 6.2 Hz), 6.57 (d, 1H, J = 16.0 Hz), 7.21 (dt, 1H, J = 7.5, 0.9 Hz), 7.25−7.35 (m, 5H), 7.67 (ddd, 1H, J = 8.4, 7.5, 1.5 Hz), 7.72 (d, J = 7.5 Hz), 8.47 (d, 1H, J = 8.4 Hz); HRMS (EI) *m/z* calcd for $C_{19}H_{17}NO_3$ 307.1208, found 307.1204. Anal. Calcd for $C_{19}H_{17}NO_3$: C, 74.25; H, 5.58; N, 4.56. Found: C, 74.18; H, 5.55; N, 4.41.

1-Acetyl-2-(cyclohex-2-enyloxy)indolin-3-one (7f): a mixture (1:1) of its diastereomers as a viscous oil. IR ($CHCl_3$) 1730, 1686, 1609 cm^{-1}; ^1H NMR ($CDCl_3$, 300 MHz) δ 1.45−2.1 (m, 6H), 2.42 (s, 1/2 × 3H), 2.43 (s, 1/2 × 3H), 4.32 (br, 1H), 5.29 (s, 1/2 × 1H), 5.32 (s, 1/2 × 1H), 5.54−6.00 (m, 2H), 7.21 (t, 1H, J = 7.6 Hz), 7.67 (t, 1H, J = 7.6 Hz), 7.73 (d, 1H, J = 7.6 Hz), 8.47 (br, 1H); HRMS (EI) *m/z* calcd for $C_{16}H_{17}NO_3$ 271.1208, found 271.1205.

(32) Fukuda, T.; Irie, R.; Katsuki, T. *Tetrahedron* **1999**, *55*, 649−664.

2-[3-(2-Methylbut-3-en-2-yl)-2-oxoindolin-3-yl]acetonitrile (15a). Procedure A: Using Wittig Reaction, Isomerization, and Claisen Rearrangement. (1) Wittig Reaction of 2-Allyloxyindolin-3-one 7a: 2-[2-(3-Methylbut-2-enyloxy)-1-acetylindolin-3-ylidene]acetonitrile (12a). A solution of indolin-3-one **7a** (301 mg, 1.0 mmol) and triphenylphosphoranylidene acetonitrile (**11**) (60 mg, 0.23 mmol) in dry toluene (5 mL) was heated under reflux for 5 h. The reaction mixture was concentrated under reduced pressure. The residue was chromatographed on a silica gel column with AcOEt/hexane (1:5) as an eluent to give a mixture of (*E*)- and (*Z*)-2-(2-(3-methylbut-2-enyloxy)-1-acetylindolin-3-ylidene)acetonitriles (**12a**) (46 mg, 70%; *E*:*Z* = 1:3) as a viscous oil. IR ($CHCl_3$) cm^{-1} 2217, 1682, 1466, 1391; ^1H NMR ($CDCl_3$, 270 MHz) (*E*-**12a**) δ 1.45 (s, 3H), 1.62 (s, 3H), 2.38 (s, 3H), 3.72 (m, 2H), 5.20 (m, 1H), 5.84 (d, 1H, *J* = 2.3 Hz), 6.26 (d, 1H, *J* = 2.3 Hz), 7.07 (t, 1H, *J* = 7.6 Hz), 7.13 (t, 1H, *J* = 7.6 Hz), 7.39 (d, 1H, *J* = 7.6 Hz), 7.45 (d, 1H, *J* = 7.6 Hz); (*Z*-**12a**) δ 1.45 (s, 3H), 1.64 (s, 3H), 2.34 (s, 3H), 3.72 (m, 2H), 5.20 (m, 1H), 5.55 (d, 1H, *J* = 1.7 Hz), 6.0 (d, 1H, *J* = 1.7 Hz), 7.07 (t, 1H, *J* = 7.6 Hz), 7.13 (t, 1H, *J* = 7.6 Hz), 7.39 (d, 1H, *J* = 7.6 Hz), 7.45 (d, 1H, *J* = 7.6 Hz); HRMS (EI) *m/z* calcd for $C_{17}H_{18}N_2O_2$ 282.1367, found 282.1370.

The stereochemistry of the *Z*-isomer of **12a** was confirmed by comparison of its NMR data with that of 3-alkylideneindolines.[25]

(2) Isomerization and Claisen Rearrangement of 2-(Indolin-3-ylidene)acetonitrile 12a. 1,8-Diazabicyclo[5,4,0]-7-undecene (DBU, *d* = 1.01, 16 μL, 0.11 mmol) was added to a solution of **12a** (32 mg, 0.11 mmol) in dry toluene (5 mL) at room temperature. After standing at the same temperature for 2 days, the reaction mixture was evaporated under reduced pressure. The residue was purified by column chromatography on a silica gel with AcOEt/hexane (3:1) as an eluent to give 2-(2-oxoindolin-3-yl)acetonitrile **14** (4.8 mg, 13%) and its deacetylated derivative **15a** (14 mg, 47%).

2-[1-Acetyl-3-(2-methylbut-3-en-2-yl)-2-oxoindolin-3-yl]-acetonitrile (14): a viscous oil. IR ($CHCl_3$) 2250, 1750, 1717, 1605 cm^{-1}; ^1H NMR ($CDCl_3$, 270 MHz) δ: 1.07 (s, 3 H), 1.13 (s, 3 H), 2.68 (s, 3 H), 2.89 (d, 1 H, *J* = 16.5 Hz), 3.08 (d, 1 H, *J* = 16.5 Hz), 5.10 (d, 1 H, *J* = 17.5 Hz), 5.22 (d, 1 H, *J* = 10.9 Hz), 5.88 (dd, 1 H, *J* = 17.5, 10.9 Hz), 7.22−7.34 (m, 2H), 7.42 (t, 1H, *J* = 8.2 Hz), 8.29 (d, 1H, *J* = 8.2 Hz); HRMS *m/z* calcd for $C_{17}H_{18}N_2O_2$ 282.1367, found 282.1370.

2-[3-(2-Methylbut-3-en-2-yl)-2-oxoindolin-3-yl]acetonitrile (15a): mp 154−155 °C (AcOEt/hexane). IR ($CHCl_3$) 3434, 2255, 1716 cm^{-1}; ^1H NMR ($CDCl_3$, 270 MHz) δ 1.08 (s, 3H), 1.16 (s, 3H), 2.86 (d, 1H, *J* = 14.5 Hz), 3.01 (d, 1H, *J* = 14.5 Hz), 5.09 (d, 1H, *J* = 17.5 Hz), 5.22 (d, 1H, *J* = 10.2 Hz), 6.08 (dd, 1H, *J* = 10.2, 17.5 Hz), 6.92 (d, 1H, *J* = 7.6 Hz), 7.07 (t, 1H, *J* = 7.6 Hz), 7.27 (d, 1H, *J* = 7.6 Hz), 7.29 (t, 1H, *J* = 7.6 Hz), 8.12 (brs,1H); ^{13}C NMR ($CDCl_3$, 67.8 MHz) δ 21.6, 21.9, 22.0, 41.7, 55.4, 110.0, 115.3, 116.8, 122.4, 125.8, 129.3, 128.2, 141.4, 141.9, 178.1; HRMS (EI) *m/z* calcd for $C_{15}H_{16}N_2O$ 240.1263, found 240.1263. Anal. Calcd for $C_{15}H_{16}N_2O$: C, 74.97; H, 6.71; N, 11.66. Found: C, 74.62; H, 6.61; N, 11.31.

Procedure B: One-Pot Reaction of 7a to 14 and 15a. A solution of indolin-3-one **7a** (30 mg, 0.12 mmol) and ylide **11** (175 mg, 0.58 mmol) in dry toluene (3 mL) was heated under reflux for 5 h. The reaction mixture was treated with DBU (17 μL, 0.12 mmol) at room temperature for 2 days. The resulted mixture was worked up in a similar manner as above to give **14** (4.6 mg, 14%) and **15a** (20 mg, 72%).

Procedure C: Domino Reaction using Horner−Wadsworth−Emmons Olefination. A solution of diethyl cyanomethylphosphonate (**16**) (322 μL, 2.0 mmol) in dry DMF (0.5 mL) was added to a suspension of NaH (60% in mineral oil, 1.8 mmol) in dry DMF (0.5 mL) at 0 °C. After stirring at room temperature for 20 min, a solution of indolin-3-one **7a** (218 mg, 0.84 mmol) was gradually added to the mixture at 0 °C, and the mixture was stirred at room temperature for 2 h. The reaction mixture was quenched by adding crushed ice and extracted with Et_2O. The extract was washed with brine, dried over $MgSO_4$, and concentrated under reduced pressure. The obtained residue was subjected to chromatography on silica gel column with AcOEt/hexane (1:2) as an eluent to give **15a** (97 mg, 48%) and 3-hydroxy-3-(2-methylbut-3-en-2-yl)indolin-2-one (**17**) (54 mg, 30%).[28]

When this reaction of **7a** (27 mg, 0.10 mmol) with **16** (55 μL, 0.34 mmol) was similarly carried out using potassium *tert*-butoxide (35 mg, 0.31 mmol) instead of NaH as a base, **15a** (16 mg, 65%) and **17** (4 mg, 17%) were obtained.

Procedure D: General Procedure for Preparation of 3-Allyl-3-cyanomethylindolin-2-ones 15 via Domino Reactions using Horner−Wadsworth−Emmons Reaction. A solution of phosphonate **16** (3.3 mmol) in dry DMF (2 mL) was added to a suspension of potassium *tert*-butoxide (3.1 mmol) in dry DMF (3 mL) at 0 °C. After stirring at the same temperature for 1 h, the mixture was cooled to −78 °C. A solution of indolin-3-ones **7** (1.0 mmol) in dry DMF (3 mL) was gradually added to the mixture at −78 °C, and the mixture was warmed slowly to room temperature. After stirring at the same temperature for a designated period (1.5−22 h) as shown in Table 3, the mixture was cooled to 0 °C, quenched by adding 10% aqueous HCl, and extracted with Et_2O. The extract was washed with brine, dried over $MgSO_4$, and concentrated under reduced pressure. The obtained residue was chromatographed by silica gel column with AcOEt/hexane (1:2−3) for **15a**, **15c**, *syn*- and *anti*-**15e**, **15f**, or Et_2O−hexane (3−4:1) for **15b**, **15d** as an eluent to give the corresponding indolin-2-ones **15**, respectively.

2-(3-Allyl-2-oxoindolin-3-yl)acetonitrile (15b): a viscous oil. IR ($CHCl_3$) 3436, 2255, 1725, 1622 cm^{-1}; ^1H NMR ($CDCl_3$, 300 MHz) δ 2.68 (d, 1H, *J* = 16.5 Hz), 2.61−2.73 (m, 2H), 2.88 (d, 1H, *J* = 16.5 Hz), 5.05 (d, 1H, *J* = 10.1 Hz), 5.12 (d, 1H, *J* = 16.9 Hz), 5.49 (dddd, 1H, *J* = 16.9, 10.1, 7.7, 6.6 Hz), 6.94 (d, 1H, *J* = 7.8 Hz), 7.12 (t, 1H, *J* = 7.8 Hz), 7.30 (t, 1H, *J* = 7.8 Hz), 7.43 (d, 1H, *J* = 7.8 Hz), 8.38 (brs, 1H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 24.9, 40.2, 49.3, 110.4, 116.2, 120.3, 122.9, 123.5, 129.07, 129.15, 130.2, 140.3, 178.7; HRMS (EI) *m/z* calcd for $C_{13}H_{12}N_2O$ 212.0949, found 212.0955.

2-[3-(2-Methylallyl)-2-oxoindolin-3-yl]acetonitrile (15c): mp 109−110 °C (AcOEt/hexane). IR ($CHCl_3$) 3436, 2250, 1720, 1624 cm^{-1}; ^1H NMR ($CDCl_3$, 300 MHz) δ 1.39 (s, 3H), 2.67 (d, 1H, *J* = 16.7 Hz), 2.75 (d, 1H, *J* = 14.7 Hz), 2.76 (d, 1H, *J* = 14.7 Hz), 2.86 (d, 1H, *J* = 16.7 Hz), 4.62 (brs, 1H), 4.67 (m, 1H), 6.96 (d, 1H, *J* = 7.6 Hz), 7.11 (dt, 1H, *J* = 7.6, 1.1 Hz), 7.28 (dt, 1H, *J* = 7.6, 1.1 Hz), 7.43 (dt, 1H, *J* = 7.6 Hz); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 23.7, 26.6, 43.4, 49.7, 110.3, 115.8, 116.2, 122.9, 124.1, 129.1, 129.2, 139.1, 140.3, 178.5; HRMS (EI) *m/z* calcd for $C_{14}H_{14}N_2O$ 226.1106, found 226.1107. Anal. Calcd for $C_{14}H_{14}N_2O$: C, 74.31; H, 6.24; N, 12.38. Found: C, 74.43; H, 6.35; N, 12.36.

2-[3-((*E*)-But-2-enyl)-2-oxoindolin-3-yl]acetonitrile (15d): a viscous oil. IR ($CHCl_3$) 3436, 3023, 1725, 1624 cm^{-1}. ^1H NMR ($CDCl_3$, 270 MHz) δ 1.55 (d, 3H, *J* = 6.6 Hz), 2.57 (dd, 1H, *J* = 13.5, 7.9 Hz), 2.65 (dd, 1H, *J* = 13.5, 7.9 Hz), 2.67 (d, 1H, *J* = 16.5 Hz), 2.86 (d, 1H, *J* = 16.5 Hz), 5.14 (1H, dt, *J* = 15.2, 7.9 Hz), 5.55 (1H, dq, *J* = 15.2, 6.6 Hz), 6.96 (d, 1H, *J* = 7.6 Hz), 7.11 (t, 1H, *J* = 7.6 Hz), 7.29 (t, 1H, *J* = 7.6 Hz), 7.40 (d, 1H, *J* = 7.6 Hz), 8.53 (brs, 1H, −NH); HRMS (EI) *m/z* calcd for $C_{14}H_{14}N_2O$ 226.1105, found 226.1108.

(3*R,1′*S**)-2-[2-Oxo-3-(1-phenylallyl)indolin-3-yl]acetonitrile (*syn*-15e)**: mp 179−181 °C (hexane). IR ($CHCl_3$) 3436, 2255, 1720, 1622, 1601 cm^{-1}; ^1H NMR ($CDCl_3$, 300 MHz) δ 2.74 (d, 1H, *J* = 16.6 Hz), 2.90 (d, 1H, *J* = 16.6 Hz), 3.89 (d, 1H, *J* = 10.3 Hz), 5.26 (dd, 1H, *J* = 10.1, 1.0 Hz), 5.43 (dd, 1H, *J* = 16.9, 1.0 Hz), 6.41 (ddd, 1H, *J* = 16.9, 10.3, 10.1 Hz), 6.72 (d, 1H, *J* = 7.6 Hz), 7.0−7.17 (m, 6H), 7.20 (dt, 1H, *J* = 7.6, 1.3 Hz), 7.38 (d, 1H, *J* = 7.6 Hz), 7.82 (brs, 1H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 24.7, 52.9, 55.9, 109.9, 116.2, 119.3, 122.6, 124.4, 127.3, 128.0, 128.0, 128.3, 128.6, 128.6, 129.1, 133.9, 137.4, 140.1, 177.5; HRMS (EI) *m/z* calcd for $C_{19}H_{16}N_2O$

288.1263, found 288.1261. Anal. Calcd for $C_{19}H_{16}N_2O$: C, 79.14; H, 5.59; N, 9.72. Found: C, 78.99; H, 5.73; N, 9.62.

(3*R*,1′R)-2-[2-Oxo-3-(1-phenylallyl)indolin-3-yl]acetonitrile (*anti*-15e)**: a mixture (2:1) of its diastereomers. ^{1}H NMR ($CDCl_3$, 300 MHz) δ 2.73 (d, 1/3 × 1H, J = 16.6 Hz), 2.89 (d, 1/3 × 1H, J = 16.6 Hz), 2.92 (d, 2/3 × 1H, J = 16.8 Hz), 2.93 (d, 2/3 × 1H, J = 17.1 Hz), 3.79 (d, 2/3 × 1H, J = 10.1 Hz), 3.88 (d, 1/3 × 1H, J = 10.3 Hz), 5.25 (dd, 1/3 × 1H, J = 10.1, 1.4 Hz), 5.36 (dt, 2/3 × 1H, J = 15.2, 1.0 Hz), 5.37 (dd, 2/3 × 1H, J = 10.1, 1.0 Hz), 5.42 (dt, 1/3 × 1H, J = 16.9, 1.0 Hz), 6.28 (dt, 2/3 × 1H, J = 17.1, 10.3 Hz), 6.41 (dt, 1/3 × 1H, J = 16.8, 10.1 Hz), 6.73 (d, 1/3 × 1H, J = 7.6 Hz), 6.81 (dt, 2/3 × 1H, J = 7.0, 1.5 Hz), 7.0−7.2 (m, 6H), 7.21 (d, 1/3 × 1H, J = 7.6, 1.3 Hz), 7.30 (dt, 2/3 × 1H, J = 7.6, 1.3 Hz), 7.38 (d, 1/3 × 1H, J = 7.6 Hz), 7.47 (d, 2/3 × 1H, J = 7.6 Hz), 7.74 (brs, 21/3 × 1H), 8.00 (brs, 1/3 × 1H); HRMS (EI) *m/z* calcd for $C_{19}H_{16}N_2O$ 288.1263, found 288.1265. Anal. Calcd for $C_{19}H_{16}N_2O$: C, 79.14; H, 5.59; N, 9.72. Found: C, 79.31; H, 5.70; N, 9.41.

(3*R*,1′R)-2-[3-(Cyclohex-2-enyl)-2-oxoindolin-3-yl]-acetonitrile (15f)**: a viscous oil as a single isomer. IR ($CHCl_3$) 3434, 2250, 1721, 1622 cm^{-1}; ^{1}H NMR ($CDCl_3$, 300 MHz) δ 1.31−1.60 (m, 2H), 1.68−1.87 (m, 2H), 1.87−2.00 (m, 2H), 2.79 (d, 1H, J = 16.5 Hz), 2.84−2.9 (m, 1H), 2.99 (d, 1H, J = 16.5 Hz), 5.49 (brd, 1H, J = 10.3 Hz), 5.71−5.78 (m, 1H), 6.96 (d, 1H, J = 7.6 Hz), 7.08 (dt, 1H, J = 7.6 Hz), 7.28 (t, 1H, J = 7.6 Hz), 7.36 (d, 1H, J = 7.6 Hz), 8.76 (brs, 1H); ^{13}C NMR ($CDCl_3$, 67.8 MHz) δ 21.9, 23.3, 24.2, 24.8, 41.8, 52.2, 110.2, 116.4, 123.0, 124.0, 124.4, 129.1, 129.3, 130.8, 140.5, 178.2; HRMS (EI) *m/z* calcd for $C_{16}H_{16}N_2O$ 252.1263, found 252.1264.

Transformation of *syn*-15e to Spirolactone 19. A mixture of *syn*-**15e** (100 mg, 0.35 mmol), OsO_4 (4% aqueous, 100 μL) and *N*-methylmolpholine oxide (50% aqueous, 166 μL) in acetonitrile (10 mL) was stirred at room temperature for 3 days. After concentrating the reaction mixture under reduced pressure, the residue was dissolved in 1,4-dioxane/water (2:1, 8 mL). Powdered $NaIO_4$ (110 mg, 0.51 mmol) was gradually added to the mixture at room temperature with stirring. After filtration of the reaction mixture through Celite, the filtrate was extracted with Et_2O. The extract was washed with brine, dried over $MgSO_4$, and concentrated under reduced pressure. The residue was dissolved in MeOH (10 mL). $NaBH_4$ was gradually added with stirring to the solution at 0 °C. After removal of MeOH, the resulted mixture was extracted with AcOEt. The extract was washed with brine, dried over $MgSO_4$, and concentrated under reduced pressure. The residue was chromatographed on silica gel column with AcOEt/hexane (3:2) to give an alcohol (53.3 mg, 52% from **15e**). A mixture of the alcohol (25 mg, 0.086 mmol) and 10% aqueous HCl (0.15 mL) was heated at 100 °C for 6 h. After cooling, the reaction mixture was extracted with AcOEt. The extract was washed with brine, dried over $MgSO_4$, and concentrated under reduced pressure. The residue was purified by column chromatography on silica gel with AcOEt/hexane (1:1) to give lactone **19** (25 mg, quantitative yield) as a viscous oil. IR ($CHCl_3$) 3410, 1780, 1690 cm^{-1}; ^{1}H NMR ($CDCl_3$, 300 MHz) δ 2.71 (dd, 1H, J = 16.5 Hz), 3.31 (d, 1H, J = 16.5 Hz), 3.71 (dd, 1H, J = 10.5, 7.7 Hz), 4.46 (dd, 1H, J = 10.5, 9.5 Hz), 4.60 (dd, 1H, J = 9.5, 7.7 Hz), 6.53 (d, 1H, J = 7.5 Hz), 6.65 (d, 2H, J = 8.0 Hz), 7.02 (t, 2H, J = 7.6 Hz), 7.08 (d, 1H, J = 4.0 Hz), 7.10 (t, 1H, J = 7.9 Hz), 7.16 (t, 1H, J = 7.6 Hz), 7.23 (dd, 1H, J = 7.9, 4.1 Hz), 7.60 (br, 1H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 39.3, 51.3, 54.3, 68.9, 116.2, 119.2, 123.5, 126.5, 127.98, 128.01, 128.16, 129.4, 132.7, 137.0, 167.5, 176.5; HRMS (EI) *m/z* calcd for $C_{18}H_{15}NO_3$ 293.1052, found 293.1061.

General Procedure for Hydrolysis of Nitrile 15 to Amide 20. To a solution of nitrile **15** (1 mmol) and aqueous hydrogen peroxide (10 mmol) in MeOH (10 mL) was added 10% aqueous NaOH (1.1 mL) at 0 °C. The mixture was stirred at room temperature until the starting material was consumed (3.5−29 h). After adding saturated aqueous Na_2SO_3, the resulted mixture was concentrated under reduced pressure to give a residue. A mixture of the residue and water was extracted with AcOEt. The extract was washed with brine, dried over $MgSO_4$, and evaporated under reduced pressure to give a solid, which was washed with hexane to afford amide **20** as white crystals.

2-[3-(2-Methylbut-3-en-2-yl)-2-oxoindolin-3-yl]acetamide (20a): mp 223−225 °C (AcOEt). IR ($CHCl_3$) 3443, 3173, 1705, 1672, 1616 cm^{-1}; ^{1}H NMR (CD_3OD, 300 MHz) δ 0.97 (s, 3H), 1.04 (s, 3H), 2.86 (d, 1H, J = 14.9 Hz), 2.91 (d, 1H, J = 14.9 Hz), 4.96 (d, 1H, J = 17.4 Hz), 5.04 (d, 1H, J = 10.8 Hz), 6.00 (dd, 1H, J = 17.4, 10.8 Hz), 6.78 (d, 1H, J = 7.7 Hz), 6.88 (t, 1H, J = 7.7 Hz), 7.13 (t, 1H, J = 7.7 Hz), 7.14 (d, 1H, J = 7.7 Hz); ^{13}C NMR (CD_3OD, 100 MHz) δ 22.3, 22.6, 38.6, 42.5, 56.9, 110.2, 114.1, 121.6, 126.3, 128.8, 131.5, 144.3, 144.4, 174.6, 182.8; HRMS (EI) *m/z* calcd for $C_{15}H_{18}N_2O_2$ 258.1368, found 258.1371.

2-(3-Allyl-2-oxoindolin-3-yl)acetamide (20b): mp 221−224 °C (AcOEt/hexane). IR (KBr) 3431, 3204, 1698, 1671, 1620 cm^{-1}; ^{1}H NMR (CD_3OD, 300 MHz) δ 2.35 (dd, 1H, J = 13.3, 7.6 Hz), 2.44 (dd, 1H, J = 13.3, 6.9 Hz), 2.72 (d, 1H, J = 16.1 Hz), 2.75(d, 1H, J = 16.1 Hz), 4.64 (ddt, 1H, J = 10.1, 2.0, 1.0 Hz), 4.86 (ddt, 1H, J = 17.1, 2.0, 1.3 Hz), 5.32 (dddt, 1H, J = 17.1, 10.1, 7.6, 6.9 Hz), 6.76 (dd, 1H, J = 7.6, 1.0 Hz), 6.89 (dt, 1H, J = 7.6, 1.0 Hz), 7.07 (dt, 1H, J = 7.6, 1.3 Hz), 7.12 (dd, 1H, J = 7.6, 1.3 Hz); ^{13}C NMR (CD_3OD, 100 MHz) δ 42.3, 43.4, 52.0, 110.7, 119.2, 122.7, 124.2, 128.8, 132.7, 132.8, 143.3, 173.9, 183.2; HRMS (EI) *m/z* calcd for $C_{13}H_{14}N_2O_2$ 230.1055, found 230.1050.

2-[3-(2-Methylallyl)-2-oxoindolin-3-yl]acetamide (20c): mp 225−227 °C (AcOEt/hexane). IR (KBr) 3447, 3275, 3184, 1713, 1691, 1668, 1614 cm^{-1}; ^{1}H NMR (CD_3OD, 300 MHz) δ 1.27 (s, 3H), 2.52 (s, 2H), 2.76 (s, 2H), 4.48 (s, 1H), 4.56 (s, 1H), 6.80 (d, 1H, J = 7.6 Hz), 6.94 (t, 1H, J = 7.6 Hz), 7.12 (t, 1H, J = 7.6 Hz), 7.20 (d, 1H, J = 7.6 Hz); ^{13}C NMR (CD_3OD, 100 MHz) δ 24.2, 43.6, 46.4, 52.6, 110.7, 115.4, 122.6, 124.6, 128.9, 132.8, 141.4, 143.6, 173.8, 183.2; HRMS (EI) *m/z* calcd for $C_{14}H_{16}N_2O_2$ 244.1212, found 244.1215.

(3*R*,1′S)-2-[2-Oxo-3-(1-phenylallyl)indolin-3-yl]acetamide (*Z*-20e)**: mp 205−207 °C (CH_2Cl_2). IR (KBr) 3439, 3277, 3179, 1705, 1672, 1653, 1616 cm^{-1}; ^{1}H NMR (CD_3OD, 300 MHz) δ 2.70 (d, 1H, J = 15.2 Hz), 3.00 (d, 1H, J = 15.2 Hz), 3.67 (d, 1H, J = 10.1 Hz), 5.10 (dd, 1H, J = 10.1, 2.0 Hz), 5.17 (ddd, 1H, J = 16.9, 1.8, 0.6 Hz), 6.24 (dt, 1H, J = 16.9, 10.1 Hz), 6.64(d, 1H, J = 7.4 Hz), 6.90−7.18 (m, 8H); ^{13}C NMR (CD_3OD, 100 MHz) δ 42.2, 55.7, 58.9, 110.4, 117.9, 122.1, 125.1, 127.7, 128.5, 128.5, 128.9, 130.1, 130.1, 131.4, 136.9, 140.1, 143.7, 174.0, 182.6; HRMS (EI) calcd for $C_{19}H_{18}N_2O_2$ (*m/z*) 306.1368 found (*m/z*) 306.1371.

(3*R*,1′R)-2-[3-(Cyclohex-2-enyl)-2-oxoindolin-3-yl]-acetamide (20f)**: mp 290−291 °C (AcOEt/hexane). IR (KBr) 3435, 3316, 3208, 1720, 1670, 1620 cm^{-1}; ^{1}H NMR (DMSO-d_6, 300 MHz) δ 1.24−1.50 (m, 2H), 1.62−1.90 (m, 4H), 2.43 (brs, 1H), 2.59 (d, 1H, J = 15.0 Hz), 2.85 (d, 1H, J = 15.0 Hz), 5.32 (d, 1H, J = 10.1 Hz), 5.50 (brd, 1H, J = 10.1 Hz), 6.49 (brs, 1H), 6.72 (d, 1H, J = 7.5 Hz), 6.84 (t, 1H, J = 7.5 Hz), 7.08 (t, 1H, J = 7.5 Hz), 7.15 (d, 1H, J = 7.5 Hz); ^{13}C NMR (DNSO-d_6, 100 MHz) δ 21.9, 23.8, 24.6, 39.0, 42.7, 52.3, 108.6, 120.1, 123.3, 126.3, 126.9, 128.5, 131.1, 142.7, 170.4, 179.8; HRMS (EI) *m/z* calcd for $C_{16}H_{18}N_2O_2$ 270.1368, found 270.1372.

General Procedure for Reduction of Amide 20 to Pyrrolo[2,3-*b*]indoles 6. A solution of **20** (0.5 mmol) with $LiAlH_4$ (1.0 M THF solution, 5 mmol) in dry THF (30 mL) was heated under reflux for the desired period (1−6.5 h). After cooling to 0 °C, the reaction mixture was treated with THF/water (10:1) and diluted with AcOEt. The mixture was filtered through Celite. The filtrate was concentrated under reduced pressure to give a residue, which was diluted with AcOEt. The organic solution was washed with saturated aqueous Na_2CO_3 and brine, dried over $MgSO_4$, and evaporated off. The obtained residue was chromatographed on a silica gel column with CH_2Cl_2/MeOH (10:1) as an eluent to give 3a-allylpyrrolo[2,3-*b*]-indoles **6**.

(3a*R,8a*R**)-1,2,3,3a,8,8a-Hexahydro-3a-(2-methylbut-3-en-2-yl)pyrrolo[2,3-*b*]indole (6a)**: mp 57−60 °C (pentane). IR ($CHCl_3$) 3425, 1608, 1485, 1472 cm^{-1}; ^1H NMR ($CDCl_3$, 300 MHz) δ 1.00 (s, 3H), 1.12 (s, 3H), 1.89 (ddd, 1H, J = 11.9, 5.3, 1.3 Hz), 2.11 (dt, 1H, J = 11.9, 6.8 Hz), 2.59 (dt, 1H, J = 11.0, 5.3 Hz), 2.98 (ddd 1H, J = 11.0, 6.8, 1.3 Hz), 3.60 (br, 2H), 4.93 (s, 1H), 5.03 (d, 1H, J = 17.3, 1.4 Hz), 5.08 (dd, 1H, J = 10.8, 1.4 Hz), 6.03 (dd, 1H, J = 17.3, 10.8 Hz), 6.54 (d, 1H, J = 7.5 Hz), 6.68 (dt, 1H, J = 7.5, 1.2 Hz), 7.02 (td, 1H, J = 7.5, 1.2 Hz), 7.34 (d, 1H, J = 7.5 Hz); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 23.1, 23.5, 37.0, 41.2, 46.2, 65.3, 80.2, 108.4, 113.2, 118.0, 125.1, 127.9, 131.5, 144.6, 150.9; HRMS (EI) *m/z* calcd for $C_{15}H_{20}N_2$ 228.1626, found 228.1629. Anal. Calcd for C $C_{15}H_{20}N_2$: C, 78.90; H, 8.83; N, 12.27. Found: C, 78.52; H, 9.18; N, 12.15.

(3a*S,8a*R**)-3a-Allyl-1,2,3,3a,8,8a-hexahydropyrrolo-[2,3-*b*]indole (6b)**: a viscous oil. IR ($CHCl_3$) 3425, 1608, 1485, 1466 cm^{-1}; ^1H NMR ($CDCl_3$, 300 MHz) δ 1.85 (dt, 1H, J = 11.9, 6.8 Hz), 1.96 (ddd, 1H, J = 11.9, 5.7, 1.7 Hz), 2.40 (dd, 1H, J = 13.7, 8.2 Hz), 2.55 (dd, 1H, J = 13.7, 6.4 Hz), 2.69 (dt, 1H, J = 10.9, 5.5 Hz), 2.95 (ddd, 1H, J = 10.9, 6.8, 1.7 Hz), 4.82 (s, 1H), 4.97 (dd, 1H, J = 10.1, 1.3 Hz), 5.01 (dd, 1H, J = 16.9, 1.3 Hz), 5.64 (dddd, 1H, J = 16.9, 10.1, 8.2, 6.4 Hz), 6.48 (d, 1H, J = 7.6 Hz), 6.65 (t, 1H, J = 7.6 Hz), 6.96 (d, 1H, J = 7.6 Hz), 6.97 (d, 1H, J = 7.6 Hz); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 41.1, 43.8, 45.8, 57.9, 82.4, 108.4, 117.6, 118.4, 123.5, 127.7, 133.4, 134.6, 150.2; HRMS (EI) *m/z* calcd for $C_{13}H_{16}N_2$ 200.1313, found 200.1316.

(3a*S,8a*R**)-1,2,3,3a,8,8a-Hexahydro-3a-(2-methylallyl)-pyrrolo[2,3-*b*]indole (6c)**: a viscous oil. IR ($CHCl_3$) 3428, 1643, 1609 cm^{-1}; ^1H NMR ($CDCl_3$, 300 MHz) δ 1.52 (s, 3H), 1.93 (dt, 1H, J = 11.8, 6.6 Hz), 2.07 (ddd, 1H, J = 11.8, 5.3, 1.5 Hz), 2.45 (d, 1H, J = 13.9 Hz), 2.67 (d, 1H, J = 13.9 Hz), 2.72 (dt, 1H, J = 10.8, 5.3 Hz), 3.01 (ddd, 1H, J = 10.8, 6.6, 1.5 Hz), 4.66 (s, 1H), 4.76 (s, 1H), 5.00 (s, 1H), 6.53 (d, 1H, J = 7.5 Hz), 6.70 (t, 1H, J = 7.5 Hz), 7.00 (t, 1H, J = 7.5 Hz), 7.02 (d, 1H, J = 7.5 Hz); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 24.1, 42.7, 45.5, 47.3, 58.1, 82.1, 108.5, 114.2, 118.4, 123.9, 127.7, 133.2, 143.2, 150.1; HRMS (EI) *m/z* calcd for $C_{14}H_{18}N_2$ 214.1470, found 214.1469.

(3a*R,8a*R**)-1,2,3,3a,8,8a-Hexahydro-3a-[(1*S**)-1-phenylallyl]pyrrolo[2,3-*b*]indole (*syn*-6e)**: a viscous oil. IR ($CHCl_3$) 3430, 1610, 1518, 1483 cm^{-1}; ^1H NMR ($CDCl_3$, 300 MHz) δ 1.87 (dd, 1H, J = 11.9, 4.8 Hz), 2.20 (dt, 1H, J = 11.9, 6.6 Hz), 2.60 (dt, 1H, J = 11.0, 4.8 Hz), 3.00 (dd, 1H, J = 11.0, 6.6 Hz), 3.63 (d, 1H, J = 9.7 Hz), 4.96 (s, 1H), 5.14 (d, 1H, J = 10.3 Hz), 5.15 (d, 1H, J = 16.7 Hz), 6.08 (dd, 1H, J = 16.7, 10.3, 9.7 Hz), 6.52 (d, 1H, J = 7.7 Hz), 6.65 (t, 1H, J = 7.3 Hz), 6.655 (d, 1H, J = 7.5 Hz), 7.00 (t, 1H, J = 7.3 Hz), 7.12−7.31 (m, 4H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 40.8, 46.6, 58.2, 62.6, 82.4, 109.1, 117.6, 118.6, 126.2, 127.2, 128.4, 128.6, 129.6, 134.6, 138.8, 142.1, 152.1; HRMS (EI) *m/z* calcd for $C_{19}H_{20}N_2$ 276.1626, found 276.1625.

(3a*R,8a*R**)-3a-[(1*R**)-Cyclohex-2-enyl]-1,2,3,3a,8,8a-hexahydropyrrolo[2,3-*b*]indole (6f)**: a viscous oil. IR ($CHCl_3$) 3430, 1607, 1485 cm^{-1}; ^1H NMR ($CDCl_3$, 300 MHz) δ 1.24 (m, 1H), 1.46 (m, 1H), 1.58−1.80 (m, 2H), 1.84−2.00 (m, 2H), 1.98 (ddd, 1H, J = 12.1, 6.8, 1.5 Hz), 2.15 (dt, 1H, J = 12.1, 6.8 Hz), 2.59 (m, 1H), 2.69 (dt, 1H, J = 11.0, 5.5 Hz), 3.04 (ddd, 1H, J = 11.0, 6.8, 1.5 Hz), 4.88 (s, 1H), 5.71−5.84 (m, 2H), 6.54 (d, 1H, J = 7.3, Hz), 6.70 (t, 1H, J = 7.3 Hz), 7.02 (t, 1H, J = 7.3, Hz), 7.04 (d, 1H, J = 7.3, Hz); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 22.6, 25.5, 26.3, 39.6, 43.0, 45.8, 61.9, 80.9, 108.3, 118.3, 123.9, 127.3, 127.7, 130.2, 132.4, 150.7; HRMS (EI) *m/z* calcd for $C_{16}H_{20}N_2$ 240.1626, found 240.1623.

2-(3-Allyl-1-methyl-2-oxoindolin-3-yl)acetonitrile (21). A solution of indolin-2-one **15b** (205 mg, 0.97 mmol) in dry DMF (6 mL) was added to a suspension of NaH (60% in minaral oil, 46 mg, 1.15 mmol) in DMF (3 mL) at 0 °C under nitrogen atmosphere. After stirring at the same temperature for 30 min, methyl iodide (d = 2.28, 72 μL, 1.16 mmol) was added to the mixture under the same conditions, and the reaction was immediately completed. After adding gradually water, the mixture was extracted with Et_2O, and the extract was washed with brine, dried over $MgSO_4$ and concentrated under reduced pressure. The residue was purified by silica gel column chromatography with AcOEt/hexane (1:2) as an eluent to give **21** (175 mg, 80%) as a viscous oil. IR ($CHCl_3$) 1717, 1617 cm^{-1}; ^1H NMR ($CDCl_3$, 300 MHz) δ 2.63 (d, 1H, J = 16.7 Hz), 2.64 (dd, 1H, J = 13.4, 6.7 Hz), 2.69 (dd, 1H, J = 13.4, 6.7 Hz), 2.86 (d, 1H, J = 16.7 Hz), 3.21 (s, 3H), 4.99 (dq, 1H, J = 10.0, 1.3 Hz), 5.08 (dq, 1H, J = 16.9, 1.3 Hz), 5.42 (ddt, 1H, J = 16.9, 10.0, 6.7 Hz), 6.89 (d, 1H, J = 7.9 Hz), 7.13 (t, 1H, J = 7.6 Hz), 7.35 (t, 1H, J = 7.6 Hz), 7.44 (d, 1H, J = 7.6 Hz); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 25.1, 26.5, 40.4, 48.8, 108.5, 116.3, 120.2, 123.0, 123.4, 128.8, 129.1, 130.4, 143.1, 176.1; HRMS (EI) *m/z* calcd for $C_{14}H_{14}N_2O$ 226.1106, found 226.1110.

2-(3-Allyl-1-methyl-2-oxoindolin-3-yl)acetamide (22). To a solution of nitrile **21** (60 mg, 0.27 mmol) and 30% aqueous hydrogen peroxide (500 μL, 13.5 mmol) in MeOH (2 mL) was added 10% aqueous NaOH (500 μL) at 0 °C. The mixture was stirred at room temperature until the starting material was consumed (10 h). After adding saturated aqueous Na_2SO_3, the mixture was evaprated under reduced pressure to give a residue. A mixture of the residue and water was extracted with AcOEt. The extract was washed with brine, dried over $MgSO_4$, and concentrated under reduced pressure. The residue was purified by column chromatography on silica gel with AcOEt/hexane (5:1) to afford amide **22** (37 mg, 57%) as a solid. IR ($CHCl_3$) 3470, 3408, 1694, 1614 cm^{-1}; ^1H NMR ($CDCl_3$, 300 MHz) δ 2.55 (dd, 1H, J = 14.0, 7.7 Hz), 2.61 (dd, 1H, J = 14.0, 7.0 Hz), 2.81 (d, 1H, J = 14.9 Hz), 2.86 (d, 1H, J = 14.9 Hz), 3.22 (s, 3H), 4.95 (d, 1H, J = 9.9, 1.1 Hz), 5.01 (dd, 1H, J = 17.1 1.3 Hz), 5.27 (br, 1H), 5.41 (ddt, 1H, J = 17.1, 9.9, 7.0 Hz), 6.24 (br, 1H), 6.84 (d, 1H, J = 7.5 Hz), 7.08 (t, 1H, J = 7.5 Hz), 7.25 (d, 1H, J = 7.5 Hz), 7.28 (t, 1H, J = 7.5 Hz); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 26.3, 41.4, 42.1, 50.0, 108.0, 119.3, 122.4, 123.0, 128.0, 130.5, 131.1, 143.1, 170.5, 178.9; HRMS (EI) calcd for $C_{14}H_{16}N_2O_2$ (*m/z*) 244.1212 found (*m/z*) 244.1214. Anal. Calcd for C $C_{14}H_{16}N_2O_2$: C, 68.83; H, 6.60; N, 11.47. Found: C, 68.57; H, 6.94; N, 11.18.

(3a*S*,*8a*R)-3a-allyl-1,2,3,3a,8,8a-hexahydro-8-methylpyrrolo[2,3-*b*]indole (23).** A solution of **22** (10 mg, 0.04 mmol) with $LiAlH_4$ (1.0 M THF solution, 410 μL, 0.41 mmol) in dry THF (1 mL) was heated under reflux for 1.5 h. After cooling to 0 °C, the reaction mixture was treated with THF/water (10:1) and diluted with AcOEt. The mixture was filtered through Celite. The filtrate was concentrated under reduced pressure to give a residue, which was diluted with AcOEt. The organic solution was washed with saturated aqueous Na_2CO_3 and brine, dried over $MgSO_4$, and concentrated under reduced pressure. The obtained residue was purified by column chromatography on silica gel with CH_2Cl_2/MeOH (10:1) as an eluent to give pyrrolo[2,3-*b*]indole **23** (7.0 mg, 80%) as a viscous oil. IR ($CHCl_3$) 1606, 1495 cm^{-1}; ^1H NMR ($CDCl_3$, 300 MHz) δ 1.90 (ddd, 1H, J = 12.1, 10.6, 6.8 Hz), 1.99 (ddd, 1H, J = 12.1, 5.9, 2.0 Hz), 2.10 (br, 1H), 2.44 (dd, 1H, 13.9, 7.9), 2.59 (ddt, 1H, J = 13.9, 6.3, 1.5 Hz), 2.68 (ddd, 1H, J = 10.8, 10.6, 5.9 Hz), 2.83 (s, 3H), 3.04 (ddd, 1H, J = 10.8, 6.8, 2.0 Hz), 4.62 (s, 1H), 5.04 (dt, 1H, J = 10.3, 1.0 Hz), 5.07 (dt, 1H, J = 17.1, 1.5 Hz), 5.70 (dddd, 1H, J = 17.1, 10.3, 7.9, 6.3 Hz), 6.32 (d, 1H, J = 7.6 Hz), 6.61 (dt, 1H, J = 7.6, 1.0 Hz), 7.00 (ddd, 1H, J = 7.6, 1.3, 1.0 Hz), 7.07 (dt, 1H, J = 7.6, 1.3 Hz); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 31.9, 41.1, 43.7, 45.9, 56.2, 89.1, 104.8, 116.6, 117.6, 123.0, 127.8, 133.6, 134.7, 151.4; HRMS (EI) calcd for $C_{14}H_{18}N_2$ (*m/z*) 214.1470, found (*m/z*) 214.1468.

2-(3-Allyl-1-methyl-2-oxoindolin-3-yl)acetic Acid (24). A solution of the acetonitrile **21** (109 mg, 0.48 mmol) and 35% aqueous NaOH (0.66 mL) in MeOH (2 mL) was heated under reflux for 7 h. After cooling, the reaction mixture was acidified with 10% aqueous HCl and extracted with AcOEt. The extract was washed with brine, dried over $MgSO_4$, and concentrated under reduced pressure to give **24** (120 mg, quantitative yield) as a viscous oil. IR ($CHCl_3$) 3020 (br), 1710, 1643, 1615 cm^{-1};

^{1}H NMR ($CDCl_3$, 300 MHz) δ 2.43 (dd, 1H, J = 13.6, 7.5 Hz), 2.50 (dd, 1H, J = 13.6, 7.0 Hz), 2.82 (d, 1H, J = 16.5 Hz), 2.97 (d, 1H, J = 16.5 Hz), 3.17 (s, 3H), 4.95 (dq, 1H, J = 10.0, 1.8 Hz), 4.98 (dq, 1H, J = 17.0, 1.8 Hz), 5.38 (dddd, 1H, J = 17.0, 10.0, 7.5, 7.0 Hz), 6.81 (d, 1H, J = 7.6 Hz), 7.04 (t, 1H, J = 7.6 Hz), 7.16 (d, 1H, J = 7.6 Hz), 7.27 (t, 1H, J = 7.6 Hz); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 26.5, 40.2, 41.6, 49.4, 108.2, 119.8, 122.6, 122.8, 128.4, 130.3, 130.8, 143.5, 172.5, 179.1; HRMS (EI) *m/z* calcd for $C_{14}H_{15}NO_3$ 245.1052, found 245.1055.

2-(3-Allyl-1-methyl-2-oxoindolin-3-yl)-*N*-methylacetamide (25). To a solution of the carboxylic acid **24** (115 mg, 0.47 mmol), pentafluorophenol (259 mg, 1.4 mmol), and triethylamine (d = 0.73, 130 μL, 0.94 mmol) in THF (3 mL) was added EDC·HCl (135 mg, 0.70 mmol) at room temperature. After 5 min, anhydrous methylamine (gas) was conducted into the reaction mixture for 5 min The resulted mixture was neutralized with 10% aqueous HCl and extracted with Et_2O. The extract was washed with brine, dried over $MgSO_4$, and concentrated under reduced pressure. The residue was purified by silica gel column chromatography with AcOEt/hexane (20:1) as an eluent to give **25** (121 mg, quantitative yield) as a viscous oil. IR ($CHCl_3$) 3465, 1698, 1615 cm^{-1}; ^{1}H NMR ($CDCl_3$, 300 MHz) δ 2.53 (dd, 1H, J = 13.4, 7.6 Hz), 2.59 (dd, 1H, J = 13.4, 7.1 Hz), 2.67 (d, 3H, J = 4.7 Hz), 2.71 (d, 1H, J = 14.9 Hz), 2.85 (d, 1H, J = 14.9 Hz), 3.21 (s, 3H), 4.94 (dq, 1H, J = 10.9, 1.0 Hz), 4.98 (dd, 1H, J = 17.3, 1.8 Hz), 5.39 (dddd, 1H, J = 17.3, 10.9, 7.6, 7.1 Hz), 6.46 (brs, 1H), 6.83 (d, 1H, J = 7.7 Hz), 7.06 (t, 1H, J = 7.7 Hz), 7.23 (d, 1H, J = 7.7 Hz), 7.26 (t, 1H, J = 7.7 Hz); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 26.38, 26.40, 41.5, 42.4, 50.3, 108.1, 119.4, 122.6, 123.0, 128.1, 130.8, 131.2, 143.1, 169.7, 179.3; HRMS (EI) *m/z* calcd for $C_{15}H_{18}N_2O_2$ 258.1368, found 258.1374.

(3a*S*,*8a*R)-3a-Allyl-1,2,3,3a,8,8a-hexahydro-1,8-dimethylpyrrolo[2,3-*b*]indole (26).** A solution of **25** (20 mg, 0.077 mmol) with $LiAlH_4$ (1.0 M THF solution, 774 μL, 0.77 mmol) in dry THF (2 mL) was heated under reflux for 1 h. After cooling to 0 °C, the reaction mixture was treated with THF/water (10:1) and diluted with AcOEt. The mixture was filtered through Celite. The filtrate was concentrated under reduced pressure to give a residue, which was diluted with AcOEt. The organic solution was washed with saturated aqueous Na_2CO_3 and brine, dried over $MgSO_4$, and concentrated under reduced pressure. The obtained residue was purified by column chromatography on silica gel with $CHCl_3$/MeOH (15:1) as an eluent to give pyrrolo[2,3-*b*]indole **26** (12.4 mg, 71%) as a viscous oil. IR ($CHCl_3$) 1639, 1605 cm^{-1}; ^{1}H NMR ($CDCl_3$, 300 MHz) δ 1.94 (ddd, 1H, J = 12.0, 6.1, 3.5 Hz), 2.06 (ddd, 1H, J = 12.0, 9.2, 6.8 Hz), 2.41 (ddt, 1H, J = 13.9, 8.3, 1.0 Hz), 2.51 (s, 3H), 2.49−2.63 (m, 2H), 2.70 (ddd, 1H, J = 9.2, 6.8, 3.3 Hz), 2.92 (s, 3H), 4.20 (s, 1H), 5.01 (ddt, 1H, J = 10.3, 2.2, 1.0 Hz), 5.05 (ddt, 1H, J = 17.1, 2.2, 1.0 Hz), 5.58 (dddd, 1H, J = 17.1, 10.3, 8.4, 6.1 Hz), 6.40 (d, 1H, J = 7.6 Hz), 6.67 (dt, 1H, J = 7.6, 1.0 Hz), 6.99 (dd, 1H, J = 7.6, 1.0 Hz), 7.08 (dt, 1H, J = 7.6, 1.0 Hz); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 36.6, 38.0, 39.1, 44.5, 52.8, 56.7, 93.9, 106.6, 117.43, 117.44, 122.7, 127.7, 134.6, 135.0, 152.6; HRMS (EI) *m/z* calcd for $C_{15}H_{20}N_2$ 228.1626, found 228.1632.

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Supporting Information Available: The force field parameters for computations of transition states **A** and **B** in the Claisen rearrangement of **13d** (R^1 = H), and ^{1}H NMR and ^{13}C NMR spectra for selected compounds. This material is available free of charge via the Internet at http://pubs.acs.org.

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