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SHORT APPROACH TO BISINDOLE ALKALOID, YUEHCHUKENE, USING 2-INDOLYLCYANOCUPRATE

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Abstract – A short total synthesis of a bisindole alkaloid, yuechukene, was achieved through the dimerization of β-dehydroprenylindole generated *in situ* from 1-(indol-3-yl)-3-methylbut-2-en-1-amine.

INTRODUCTION

A novel bisindole alkaloid, yuehchukene (**1**), was first isolated from the root of *Murraya paniculata* (L.) Jack in racemic form, and the structure was characterized as a dimer of β-dehydroprenylindole (**2**) based on both spectral analysis and X-ray crystallography (Figure 1).[1] Yuehchukene (**1**) exhibits strong anti-implantation activity in rats as well as mice.[2] Additionally, a combination of cyclophosphamide and **1** provides a fairly strong cytotoxic effect on the MCR-7 cell line when compared with cyclophosphamide alone.[3] Owing to the potential biological activities of **1**, it is an attractive target for synthesis.[4] We previously reported the total synthesis of **1** with the key step being a palladium-catalyzed carbonylative cross-coupling reaction of triethyl(indol-2-yl)borate.[5] The hypothesis[6] that **1** is the biogenetic product of the dimerization of **2** has prompted the development of biomimetic approach using 1-(indol-3-yl)-3-methylbut-2-en-1-ol or 4-(indol-3-yl)-2-methylbut-3-en-2-ol as the key precursor of **2** under neutral conitions or acid catalysis.[7] In connection with our continuing interest in synthetic application of 2-indolylcyanocuprate **4**, we previously reported the regioselective construction of 2,3-disubstituted indoles through the reaction of 2-indolylcyanocuprate **4** with electrophiles in a one-pot procedure.[8] It was envisioned that 1-(indol-3-yl)-3-methylbut-2-en-1-amine **7**, regioselectively obtainable by the reaction of **4** with iminium **6**,[8a] could serve as a useful synthetic equivalent of **2**.[9] In this paper, we describe a short total synthesis of yuehchukene (**1**) through the dimerization of **7**.

This paper is dedicated to Prof. Ei-ichi Negishi on the occasion of his 77th birthday.

RESULTS AND DISCUSSION

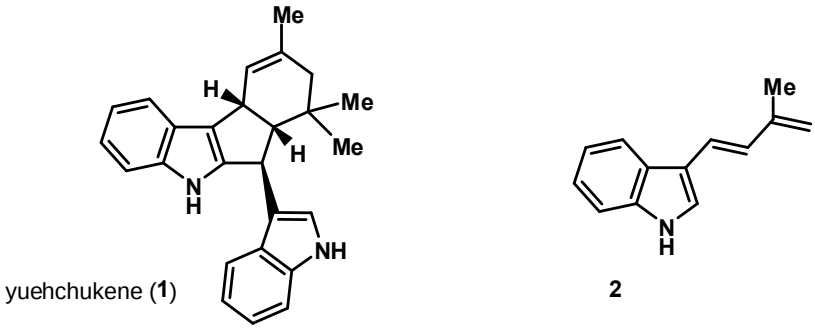
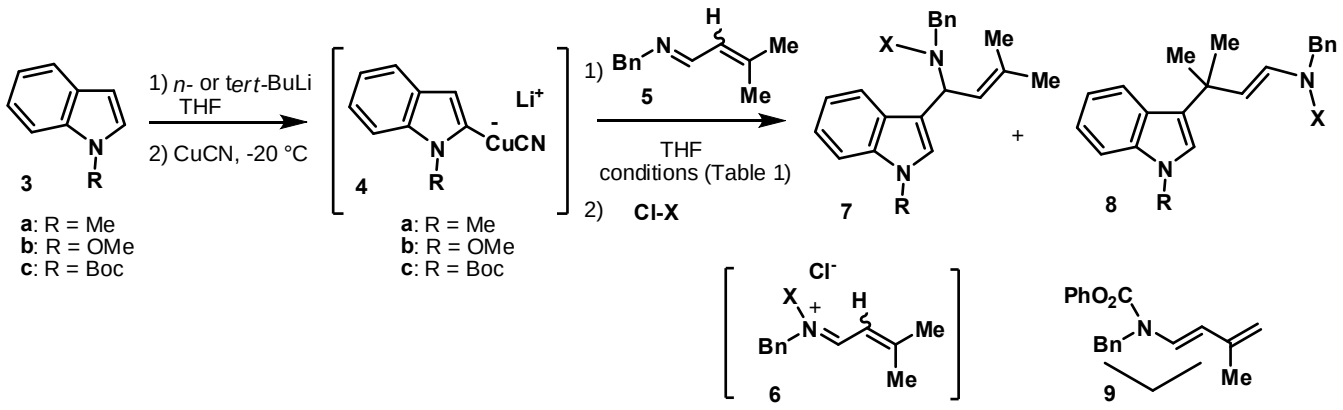


Figure 1. Yuehchukene (**1**) and β-dehydroprenylindole (**2**)

Our initial attempts to obtain the 3-substituted indole **7** through the reaction of **6** (derived from imine **5** and $ClCO_2Ph$) with indole or indolyl anion (generated by treating indole with NaH in THF) were unsuccessful, resulting in only the recovery of indole or the formation of a complex mixture of products. As a result, the reaction of **4** (generated *in situ* from indole **3** and *tert*- or *n*-BuLi in THF, followed by treatment with CuCN at -20 °C) with iminium **6** was undertaken by way of a one-pot procedure.[8a] The reaction was carried out through slow addition of an acyl chloride to a pre-mixed solution of **4** and **5** in THF in the presence of HMPA at -20 °C, resulting in the formation of two types of products 1,2-adduct **7** and 1,4-adduct **8** (Scheme 1 and Table 1).[10] After screening various acyl chlorides (X-Cl), in the reaction of **4a** with **5**, $ClCO_2Ph$ was found to give **7d** in the highest yield (65%) along with **8d** in 14% yield (Entry 4). Furthermore, reacting **4b** with **5** by adding $ClCO_2Ph$ afforded **7e** in 60% and **8e** in 12% yields (Entry 6). However, performing the reaction of **4a** with **5** in the presence of *i*-Pr_2NEt and HMPA using $ClCO_2Ph$ at -20 °C lowered the yield of **7d** to 30% (Entry 5). This was ascribed to the facile generation of dienamine **9** from **6** (X = CO_2Ph) *via* deprotonation/isomerization, which was enhanced by the presence of *i*-Pr_2NEt.[8a] No reaction was observed between **4c** and **5** when using $ClCO_2Ph$ (Entry 7).



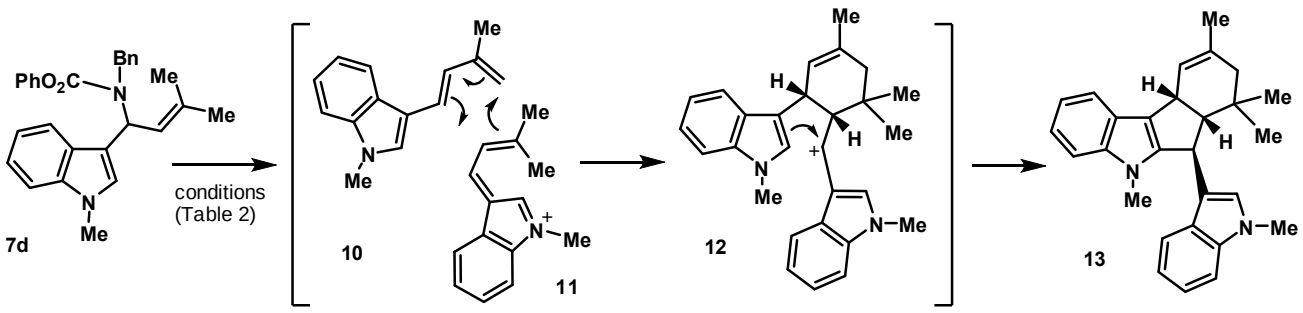
Scheme 1

Table 1. Reaction of **4** with **5** using acyl chloride (X-Cl)

Entry	R	X-Cl	Conditions	Yield (%)[a]	
				7	**8**
1	Me	ClCOMe	HMPA / -20 °C to rt	48 (**7a**)	17 (**8a**)
2	Me	ClCOPh	HMPA / -20 °C to rt	50 (**7b**)	13 (**8b**)
3	Me	$ClCO_2Me$	HMPA / -20 °C to rt	45 (**7c**)	13 (**8c**)
4	Me	$ClCO_2Ph$	HMPA / -20 °C to rt	65 (**7d**)	14 (**8d**)
5	Me	$ClCO_2Ph$	HMPA / *i*-Pr_2NEt / -20 °C to rt[b]	30 (**7d**)	5 (**8d**)
6	OMe	$ClCO_2Ph$	HMPA / -20 °C to rt	60 (**7e**)	12 (**8e**)
7	Boc	$ClCO_2Ph$	HMPA / -20 °C to rt	----	----

[a]Isolated yield based on **3**. [b]*i*-Pr_2NEt (3 equiv).

Next, we turned our attention to the dimerization of **7d** (Table 2). Initially, **7d** was simply heated in ethylene glycol at 150 °C, but no isolable products were obtained (Entry 1). Heating **7d** in the presence of 2 equiv of TFA and AcOH in ethylene glycol at 150 °C resulted in the formation of a complex mixture of products (Entries 2 and 3), whereas treating **7d** with TMSCl (2 equiv) in CH_2Cl_2 at room temperature produced *N,N'*-dimethylyuehchukene **13**, but in only low yield (~10%) (Entry 6). After performing the dimerization reaction under various conditions, using TMSCl (2 equiv) in DME in pre-heated oil bath at 100 °C was found to provide **13** in 20% yield (Entry 7). The highest yield of **13** (35%) was obtained through the slow addition of a DME solution of TMSCl (1 equiv) to a refluxing solution of **7d** in DME (Entry 8).



Scheme 2

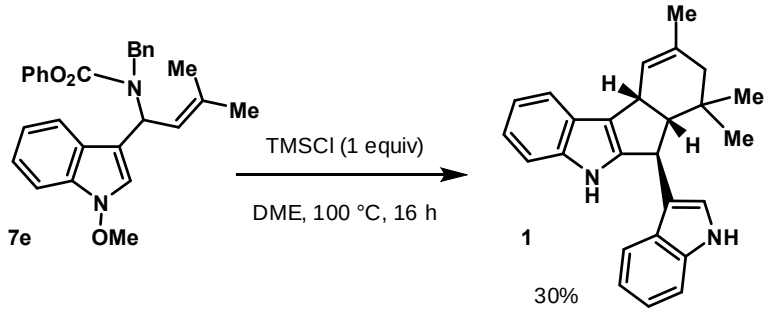
The dimerization reaction is presumed to proceed by the *in situ* generation of diene **10** and its dienophilic tautomer **11** from **7d**, the subsequent Diels-Alder reaction between **10** and **11**, followed by the intramolecular cyclization of **12** to **13** (Scheme 2).[6]

Table 2. Conversion of **7d** to *N,N'*-dimethylyuehchukene (**13**)

Entry	Conditions	Yield (%)[a]
1	$(CH_2OH)_2$ / 150 °C/ 24 h	-----
2	$(CH_2OH)_2$ / TFA (2 equiv) / 150 °C/ 24 h	-----
3	$(CH_2OH)_2$ / AcOH (2 equiv) / 150 °C/ 24 h	-----
4	$(CH_2OH)_2$ / TMSCl (2 equiv) / 150 °C/ 3 h	-----
5	CH_2Cl_2 / TMSCl (2 equiv) / rt / 16 h	10
6	CH_2Cl_2 / TMSCl (0.1 equiv) / rt / 16 h	----
7	DME / TMSCl (2 equiv) / 100 °C / 6 h[b]	20
8	DME / TMSCl (1 equiv) / 100 °C / 16 h[c]	35

[a]Isolated yield based on **3a**. [b]Pre-heated oil bath at 100 °C. [c]The reaction was performed by adding a DME solution of TMSCl to a refluxing solution of **7d** in DME.

After having found suitable conditions for the dimerization of **7d**, **7e** was subjected to the dimerization in a similar manner. After a solution of TMSCl (1 equiv) was added dropwise to a solution of **7e** at 100 °C, the mixture was heated at 100 °C for an additional 16 h, producing yuehchukene (**1**) in 30% yield (Scheme 3).[11]



Scheme 3

In summary, we have developed a short total synthesis of *N,N'*-dimethylyuehchukene (**13**) and yuehchukene (**1**) from the corresponding indoles **3a** and **3b** *via* 2-indolylcyanocuprates **4a** and **4b**. We are currently investigating further application of 2-indolylcyanocuprates **4** in the synthesis of other indole alkaloids.

EXPERIMENTAL

Melting points were recorded on a Yamato MP21 and are uncorrected. HR-ESI-MS spectra were recorded on a JEOL JMS-T100LP mass spectrometer, and HR-EI-MS spectra were recorded on a Micromass

AutoSpec 3100 mass spectrometer. IR spectra were measured on a Shimadzu IRAffinity-1 FT-IR spectrophotometer. The NMR experiments were performed with a JEOL JNM-ECA500 (500 MHz) spectrometer, and chemical shifts are expressed in ppm (δ) with TMS as an internal reference. Column chromatography was performed on silica gel (Silica Gel 60N, Kanto Chemical Co., Ltd.).

General procedure for the reaction of 4a with 5 using acyl chloride (X-Cl): *tert*-BuLi (1.6 M in pentane, 1.5 mL, 2.4 mmol) was added to a solution of 1-methylindole (**3a**) (262 mg, 2 mmol) in THF (30 mL) at 0 °C under an argon atmosphere, and the mixture was stirred at room temperature for 1 h. After the mixture was cooled to -20 °C, CuCN (214 mg, 2.4 mmol) was added to the mixture at -20 °C, and the mixture was stirred for 30 min. After HMPA (1 mL) and imine **5** (519 mg, 3 mmol) were added, acyl chloride (X-Cl) (3 mmol) was added slowly to the mixture. The reaction mixture was gradually warmed to room temperature and stirred overnight. The mixture was diluted with AcOEt (200 mL), washed with brine and dried over $MgSO_4$. The solvent was removed, and the residue was separated by silica gel column chromatography with hexane/AcOEt (15:1) to give **7** and **8** (Table 1).

***N*-Benzyl-*N*-[3-methyl-1-(1-methyl-1*H*-indol-3-yl)but-2-en-1-yl]acetamide** (**7a):** IR ($CHCl_3$): 1622 cm^{-1}. ^{1}H-NMR ($CDCl_3$) δ: 1.70 (s, 3H), 1.85 (s, 3H), 1.99 (s, 3H), 3.74 (s, 3H), 4.33 (d, 1H, *J* = 17.8 Hz), 4.41 (d, 1H, *J* = 18.4 Hz), 5.45 (d, 1H, *J* = 9.8 Hz), 6.90 (s, 1H), 7.04–7.29 (m, 9H), 7.66 (d, 1H, *J* = 8.0 Hz). ^{13}C-NMR ($CDCl_3$) δ: 18.9, 22.6, 25.8, 32.9, 48.1, 48.2, 109.3, 114.6, 119.6, 120.1, 122.0, 122.1, 126.1, 126.8, 127.8, 127.9, 128.2, 128.4, 136.4, 137.5, 139.0, 170.1. HR-EI-MS *m/z*: Calcd for $C_{23}H_{26}N_2O$ (M^+): 346.2045. Found: 346.2045.

***N*-Benzyl-*N*-[(1*E*)-3-methyl-3-(1-methyl-1*H*-indol-3-yl)but-1-en-1-yl]acetamide** (**8a):** IR ($CHCl_3$): 1638 cm^{-1}. ^{1}H-NMR ($CDCl_3$) δ: 1.45 (s, 3H), 1.56 (s, 3H), 2.10 (s, 3H), 3.66 (s, 3H), 4.89 (s, 2H), 5.38 (d, 1H, *J* = 14.4 Hz), 6.44 (d, 1H, *J* = 14.4 Hz), 7.02 (d, 1H, *J* = 8.0 Hz), 7.14–7.31 (m, 8H), 7.51 (d, 1H, *J* = 8.0 Hz). ^{13}C-NMR ($CDCl_3$) δ: 22.2, 29.1, 29.5, 32.6, 36.0, 46.5, 109.4, 118.5, 121.3, 121.4, 122.3, 124.8, 125.4, 125.9, 127.0, 127.3, 128.5, 128.9, 137.5, 137.8, 169.8. HR-EI-MS *m/z*: Calcd for $C_{23}H_{26}N_2O$ (M^+): 346.2045. Found: 346.2041.

***N*-Benzyl-*N*-[3-methyl-1-(1-methyl-1*H*-indol-3-yl)but-2-en-1-yl]benzamide** (**7b**): IR ($CHCl_3$): 1620 cm^{-1}. ^{1}H-NMR ($CDCl_3$) δ: 1.71 (s, 3H), 1.82 (s, 3H), 3.60 (s, 3H), 4.46 (s, 1H), 4.49 (s, 1H), 5.33 (d, 1H, *J* = 14.9 Hz), 5.56 (br s, 1H), 6.40 (br s, 1H), 7.00–7.45 (m, 13H), 7.71 (br s, 1H). ^{13}C-NMR ($CDCl_3$) δ: 19.6, 25.6, 42.4, 47.9, 50.2, 112.4, 117.6, 119.0, 126.5, 127.1, 127.2, 128.0, 128.6, 131.9, 135.2, 136.5, 169.5. HR-EI-MS *m/z*: Calcd for $C_{28}H_{28}N_2O$ (M^+): 408.2202. Found: 408.2199.

***N*-Benzyl-*N*-[(1*E*)-3-methyl-3-(1-methyl-1*H*-indol-3-yl)but-1-en-1-yl]benzamide** (**8b):** IR ($CHCl_3$): 1638 cm^{-1}. ^{1}H-NMR ($CDCl_3$) δ: 1.49 (s, 6H), 3.65 (s, 3H), 4.80 (s, 2H), 5.13 (d, 1H, *J* = 14.4 Hz), 6.35 (d, 1H, *J* = 14.4 Hz), 7.05 (d, 1H, *J* = 8.0 Hz), 7.15-7.37 (m, 13H), 7.54 (d, 1H, *J* = 8.0 Hz). ^{13}C-NMR

($CDCl_3$) δ: 32.1, 32.3, 42.4, 48.4, 49.3, 111.1, 116.2, 119.0, 120.1, 122.2, 122.3, 126.3, 126.5, 126.6, 126.8, 127.0, 127.1, 127.5, 127.8, 128.5, 128.6, 128.9, 132.2, 134.2, 137.6, 141.7, 169.3. HR-EI-MS *m/z*: Calcd for $C_{23}H_{26}N_2O$ (M^+): 346.2045. Found: 346.2041.

Methyl Benzyl[3-methyl-1-(1-methyl-1*H*-indol-3-yl)but-2-en-1-yl]carbamate (**7c**)**:** IR ($CHCl_3$): 1680 cm^{-1}. ^{1}H-NMR ($CDCl_3$) δ: 1.68 (s, 3H), 1.75 (s, 3H), 3.74 (s, 3H), 3.78 (br s, 3H), 4.15 (s, 1H), 4.18 (s, 1H), 4.51 (br s, 1H), 5.46 (d, 1H, *J* = 9.2 Hz), 6.52 (br s, 1H), 6.87 (br s, 1H), 7.06–7.30 (m, 8H), 7.62 (br s, 1H). ^{13}C-NMR ($CDCl_3$) δ: 14.3, 18.5, 25.8, 32.9, 47.0, 51.4, 52.8, 60.5, 109.3, 114.4, 119.5, 119.9, 122.1, 122.9, 126.4, 127.1, 128.0, 135.5, 137.5, 140.0, 157.3. HR-EI-MS *m/z*: Calcd for $C_{23}H_{26}N_2O_2$ (M^+): 362.1994. Found: 362.1989.

Methyl Benzyl[(1*E*)-3-methyl-3-(1-methyl-1*H*-indol-3-yl)but-1-en-1-yl]carbamate (8c): IR ($CHCl_3$): 1686 cm^{-1}. ^{1}H-NMR ($CDCl_3$) δ: 1.41 (s, 6H), 3.65 (s, 3H), 3.71 (br s, 3H), 4.82 (br d, 2H, *J* = 12.1 Hz), 5.27 (d, 1H, *J* = 14.9 Hz), 6.60, 6.65(two br s, 1H), 6.89–7.31(m, 9H), 7.49 (d, 1H, *J* = 8.0 Hz). ^{13}C-NMR ($CDCl_3$) δ: 18.9, 22.6, 25.8, 32.9, 48.1, 48.2, 109.3, 114.6, 119.6, 120.1, 122.0, 122.1, 126.1, 126.8, 127.8, 127.9, 128.2, 128.4, 136.4, 137.5, 139.0, 170.1. HR-EI-MS *m/z*: Calcd for $C_{28}H_{26}N_2O_2$ (M^+): 362.1994. Found: 362.1989.

Phenyl Benzyl[3-methyl-1-(1-methyl-1*H*-indol-3-yl)but-2-en-1-yl]carbamate (**7d**)**:** IR ($CHCl_3$): 1702 cm^{-1}. ^{1}H-NMR ($CDCl_3$) δ: 1.71 (s, 3H), 1.77 (s, 3H), 3.76 (s, 3H), 4.31 (m, 1H), 4.61 (d, 1H, *J* = 16.1 Hz), 5.56 (d, 1H, *J* = 8.6 Hz), 6.58 (br s, 1H), 6.90–7.41 (m, 14H), 7.73 (br s, 1H). ^{13}C-NMR ($CDCl_3$) δ: 18.6, 25.8, 32.9, 47.4, 51.6, 109.4, 114.1, 119.6, 119.9, 121.9, 122.1, 125.2, 126.6, 127.1, 128.1, 129.3, 136.3, 137.5, 139.7, 151.6, 155.1. HR-EI-MS *m/z*: Calcd for $C_{28}H_{28}N_2O_2$ (M^+): 424.2151. Found: 424.2149.

Phenyl Benzyl[(1*E*)-3-methyl-3-(1-methyl-1*H*-indol-3-yl)but-1-en-1-yl]carbamate (8d): IR ($CHCl_3$): 1716 cm^{-1}. ^{1}H-NMR ($CDCl_3$) δ: 1.51 (s, 6H), 3.65 (s, 3H), 4.91, 4.95 (two s, 2H), 5.40 (d, 1H, *J* = 15.0 Hz) 6.42, 6.52 (two s, 1H), 7.00–7.43 (m, 14H), 7.61 (d, 1H, *J* = 8.0 Hz). ^{13}C-NMR ($CDCl_3$) δ: 29.2, 32.6, 35.8, 48.4, 109.4, 118.5, 121.2, 121.3, 121.8, 121.9, 123.0, 123.2, 124.2, 125.0, 125.1, 125.7, 126.6, 127.2, 127.3, 128.7, 129.4, 137.2, 137.8, 151.2, 151.4, 153.3. HR-EI-MS *m/z*: Calcd for $C_{28}H_{28}N_2O_2$ (M^+): 424.2151. Found: 424.2145.

Reaction of 4b with 5 using $ClCO_2Ph$: *n*-BuLi (1.6 M in hexane, 1.5 mL, 2.4 mmol) was added to a solution of 1-methoxyindole (**3b**) (294 mg, 2 mmol) in THF (30 mL) at -20 °C under an argon atmosphere, and the mixture was stirred for 30 min. Then, CuCN (214 mg, 2.4 mmol) was added to the mixture at -20 °C and the whole was stirred for 30 min. After HMPA (1 mL) and imine **5** (519 mg, 3 mmol) were added to the mixture at -20 °C, $ClCO_2Ph$ (468 mg, 3 mmol) was added slowly. The mixture was gradually warmed to room temperature and stirred overnight. The mixture was diluted with AcOEt (200 mL), washed with brine and dried over $MgSO_4$. After the solvent was removed, the residue was

separated by silica gel column chromatography with hexane/AcOEt (15:1) to give **7e** and **8e** (Table 1).

Phenyl Benzyl[1-(1-methoxy-1*H*-indol-3-yl)-3-methylbut-2-en-1-yl]carbamate (7e): a pale yellow oil. IR (neat): 1714, 1699, 1595 cm^{-1}. ^{1}H-NMR ($CDCl_3$) δ: 1.72, 1.77 (two s, 6H), 4.04 (s, 3H), 4.32 (d, 1H, *J* = 15.0 Hz), 4.60 (d, 1H, *J* = 15.0 Hz), 5.53 (d, 1H, *J* = 9 Hz), 6.43-6.62 (m, 0.5 H), 6.90-7.05 (m, 1H), 7.10-7.23 (m, 10H), 7.23-7.39 (m, 3H), 7.41 (d, 1H, *J* = 9 Hz), 7.60-7.76 (m, 0.5H). ^{13}C-NMR ($CDCl_3$) δ: 18.6, 25.8, 47.4, 51.3, 65.9, 108.4, 111.5, 120.1, 120.3, 121.8, 122.4, 122.9, 125.3, 126.6, 126.8, 128.1, 129.3, 132.8, 136.9, 139.4, 151.5, 155.0. HR-ESI-MS *m/z*: Calcd for $C_{28}H_{28}N_2O_3Na$ [$(M+Na)^+$]: 463.1998. Found: 463.2008.

Phenyl Benzyl[(1*E*)-3-(1-methoxy-1*H*-indol-3-yl)-3-methylbut-1-en-1-yl]carbamate (8e): a pale yellow oil. IR (neat): 1714, 1660 cm^{-1}. ^{1}H-NMR ($CDCl_3$) δ: 1.48, 1.54 (two s, 6H), 4.00 (s, 3H), 4.90 (s, 1H), 4.93 (s, 1H), 5.36 (d, 1H, *J* = 14.8 Hz), 6.66, 6.75 (two s, 1H), 6.90-7.09 (m, 2H), 7.10-7.24 (m, 2H), 7.30-7.40 (m, 10H) 7.56 (d, 1H, *J* = 7.3 Hz). ^{13}C-NMR ($CDCl_3$) δ: 29.1, 35.9, 48.4, 65.5, 108.4, 119.2, 119.4, 119.5, 120.6, 120.8, 121.4, 121.7, 122.0, 122.1, 122.2, 122.5, 122.7, 124.4, 125.2, 125.7, 126.5, 127.2, 127.3, 128.7, 129.4, 133.5, 137.1, 151.1, 151.3, 153.2, 153.3. HR-ESI-MS *m/z*: Calcd for $C_{28}H_{28}N_2O_3Na$ [$(M+Na)^+$]: 463.1998. Found: 463.1996.

***N,N'*-Dimethylyuehchukene (13):** To a solution of **7d** (110 mg, 0.26 mmol) in DME (30 mL) at 100 °C under an argon atmosphere, a solution of TMSCl (33 μL, 0.26 mmol) in DME (100 μL) was added dropwise over 10 min, and the mixture was heated at 100 °C for 16 h. After cooling, the mixture was diluted with AcOEt (200 mL), washed with 10% aq. $NaHCO_3$ solution and brine, and dried over $MgSO_4$. The solvent was removed and the residue was separated by silica gel column chromatography with hexane/AcOEt (7:1) to give **13** (35 mg, 35%) as a pale yellow oil. IR ($CHCl_3$): 3007, 2957, 2928 cm^{-1}. ^{1}H-NMR ($CDCl_3$) δ: 0.83 (s, 3H), 1.08 (s, 3H), 1.62 (d, 1H, *J* = 17.2 Hz), 1.64 (s, 3H), 2.19 (d, 1H, *J* = 17.2 Hz), 3.06 (t, 1H, *J* = 6.9 Hz), 3.11 (s, 3H), 3.76 (s, 3H), 4.02 (d, 1H, *J* = 4.6 Hz), 4.56 (d, 1H, *J* = 7.5 Hz), 5.71 (s, 1H), 6.88 (s, 1H), 7.00 (t, 1H, *J* = 7.4 Hz), 7.07-7.10 (m, 2H), 7.13 (m, 1H), 7.20 (t, 1H, *J* = 7.5 Hz), 7.29 (d, 1H, *J* = 8.6 Hz), 7.40 (d, 1H, *J* = 8.1 Hz), 7.58 (dd, 1H, *J* = 3.4, 6.3 Hz). ^{13}C-NMR ($CDCl_3$) δ: 24.2, 28.5, 29.2, 29.9, 32.8, 33.6, 37.2, 38.4, 41.5, 62.5, 109.3, 109.5, 117.7, 118.4, 118.9, 119.0, 119.3, 119.6, 119.9, 121.5, 123.1, 123.5, 127.2, 127.3, 130.3, 137.2, 141.2, 146.3. HR-ESI-MS *m/z*: Calcd for $C_{28}H_{31}N_2$ [$(M+H)^+$]: 395.248. Found: 395.2481.

Yuehchukene (1): To a solution of **7e** (125 mg, 0.28 mmol) in DME (30 mL) at 100 °C under an argon atmosphere, a solution of TMSCl (36 μL, 0.28 mmol) in DME (100 μL) was added dropwise over 10 min, and the mixture was heated at 100 °C for 16 h. After cooling, the mixture was diluted with AcOEt (200 mL), washed with 10% aq. $NaHCO_3$ solution and brine, and dried over $MgSO_4$. The solvent was removed and the residue was separated by silica gel column chromatography with hexane/AcOEt (4:1) to give **1**

(31 mg, 30%) as amorphous powders. IR ($CHCl_3$): 3476, 3422, 3009 cm^{-1}. ^{1}H-NMR ($CDCl_3$) δ: 0.86 (s, 3H), 1.09 (s, 3H), 1.62 (d, 1H, *J* = 17.7 Hz), 1.66 (s, 3H), 2.28 (d, 1H, *J* = 17.7 Hz), 3.16 (t, 1H, *J* = 7.5 Hz), 4.02 (d, 1H, *J* = 5.0 Hz), 4.56 (d, 1H, *J* = 8.5 Hz), 5.70 (s, 1H), 6.99-7.06 (m, 3H), 7.07-7.12 (m, 2H), 7.18 (t, 1H, *J* = 8.5 Hz), 7.34 (d, 1H, *J* = 7.5 Hz), 7.43 (d, 1H, *J* = 8.0 Hz), 7.46 (br s, 1H), 7.58 (d, 1H, *J* = 8.0 Hz), 8.03 (br s, 1H). ^{13}C-NMR ($CDCl_3$) δ: 24.2, 29.0, 29.2, 33.6, 37.7, 38.4, 41.1, 60.9, 111.4, 111.8, 118.4, 118.5, 119.4, 119.6, 120.5, 120.6, 122.1, 122.5, 123.1, 124.3, 126.9, 130.3, 136.5, 140.3, 145.3. HR-ESI-MS: Calcd for $C_{26}H_{27}N_2$ [$(M+H)^+$]: 367.2174. Found: 367.2167.

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11. The reaction mechanism of the cleavage of the OMe group was supposed as follows: