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A CONCISE PREPARATION OF YUEHCHUKENE AND ITS ANALOGUES

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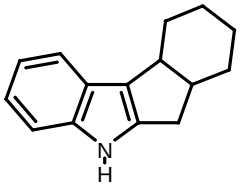
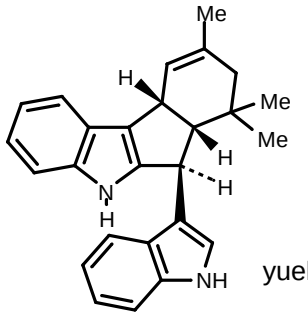
Abstract **-** The palladium catalyzed carbonylative cross-coupling reaction of indolylborates (**2**) with vinyl triflates (**3**) afforded indol-2-yl ketones (**4**), which were subsequently converted to hexahydroindeno[2,1-*b*]indoles (**5**) with the aid of an acid. This protocol was well adapted for the total synthesis of yuehchukene.

Yuehchukene is a novel class of bisindole alkaloids, first isolated as a racemate from *Murraya paniculata* (L.) Jack, with a basic structure consisting of hexahydroindeno[2,1-*b*]indole.[1] This compound has been suggested to exhibit mixed estrogen and anti-estrogen activities as well as potent anti-implantation activity, which may establish it as an important lead compound for the design of drugs to treat antifertility and breast cancer.[2] Due to these biological properties, yuehchukene has recently begun to attract considerable interest in the synthetic community.[3] The most nortworthy of these recently developed synthetic strategies are the use of Diels-Alder reaction of dehydroprenylindoles,[3b,w] and the ring closure of 2-acylindoles to hexahydroindeno[2,1-*b*]indoles.[3n] Also of particular interest are reports by Bergman that suggest that properly substituted indol-2-yl ketones have an obvious application for the preparation of yuechukene and a wide variety of its analogues.[3]



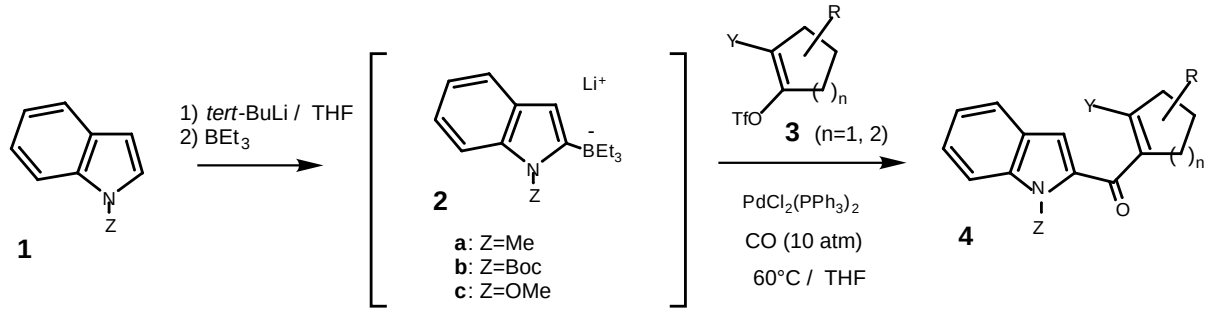
hexahydroindeno[2,1-*b*]indole



yuehchukene

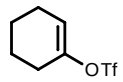
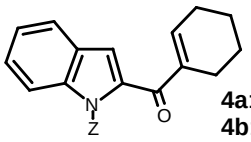
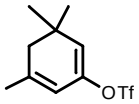
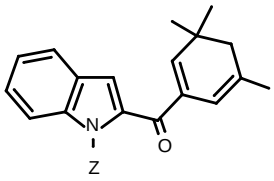
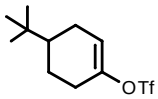
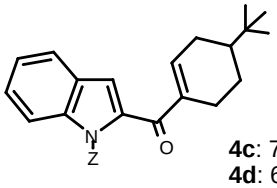
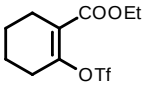
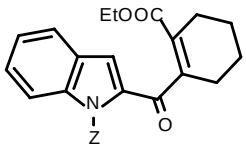
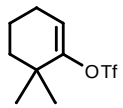
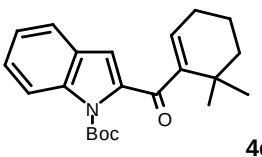
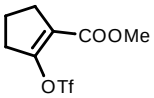
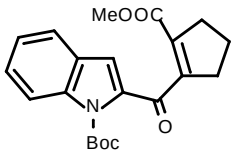
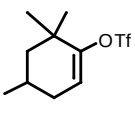
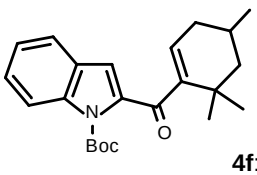
Indolylborates (**2**), readily available from indoles (**1**) *in situ*, are valuable synthetic intermediates, and the development of their synthetic capabilities has been our continuing interest.[4] During these studies, the palladium catalyzed carbonylative cross-coupling reaction with 1-methylindol-2-ylborate (**2a**) has been proven to be an effective protocol for the preparation of 1-methylindol-2-yl ketones.[5] The principal feature of our approach, taking advantage of the cross-coupling protocol with **2**, is the ready availability of indol-2-yl ketones, and the further conversion of them allows access to novel yuehchukene analogues. The present paper describes the details of our concise approach to yuehchukene and its analogues, a part of which has been reported previously.[6]

Vinyl triflates (**3**) were prepared from the corresponding cyclic ketones by standard methods.[7] Initial treatment of indolylborates (**2b**,**c**) [derived from the corresponding indoles (**1**) *in situ*][8] with **3** in the presence of a catalytic amount of palladium complex in THF under a pressurized carbon monoxide atmosphere (10 atm) at 60°C for 20 h produced indol-2-yl ketones (**4**) (Scheme 1). Following our



Scheme 1

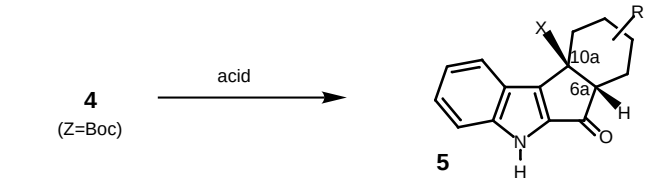
Table 1 Formation of indol-2-yl ketones (**4**)

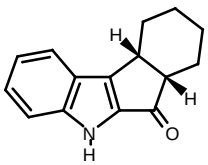
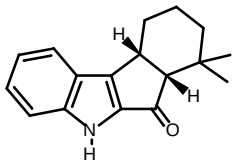
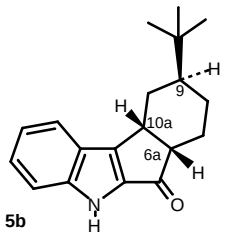
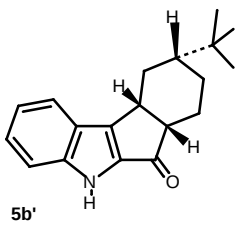
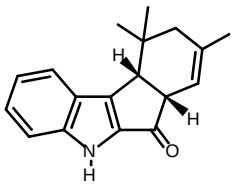
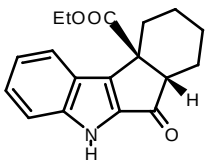
3	**4**[a]	**3**	**4**[a]
 **3a**	 **4a**: 50 % (Z=Boc) **4b**: 60 % (Z=OMe)	 **3e**	 **4g** : 56 % (Z=Boc) **4h**: 60 % (Z=OMe)
 **3b**	 **4c**: 73 % (Z=Boc) **4d**: 60 % (Z=OMe)	 **3f**	 **4i** : 45 % (Z=Boc) **4j** : 58 % (Z=OMe)
 **3c**	 **4e**: 30 %	 **3g**	 **4k** : 38 %
 **3d**	 **4f**: 40 %		

a All yields (%) are based on indole (**1**)

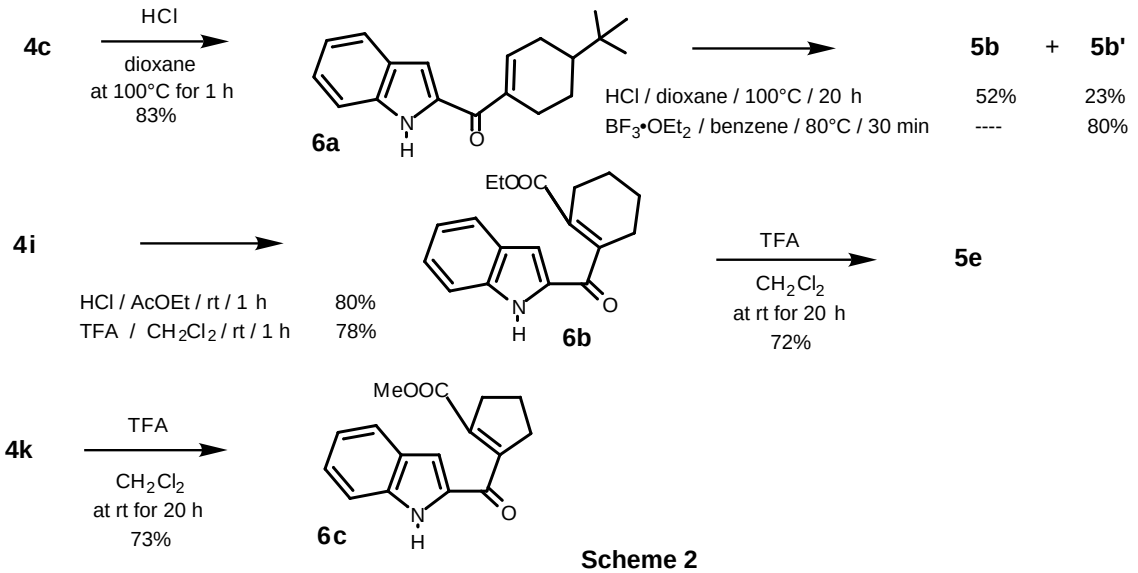
earlier study, $PdCl_2(PPh_3)_2$ was commonly used as a palladium complex, and **2c** as well as **2b** can tolerate these reaction conditions (Table 1). With the ketones (**4**) in hand, we next investigated the ring closure of **4** (Z=Boc) leading to the hexahydroindeno[2,1-*b*]indoles (**5**), for which acidic treatments (HCl in dioxane at 100°C, TFA in CH_2Cl_2 at rt, and BF_3•OEt_2 in benzene at 80°C) of **4** were employed (Table 2). The stereochemistry of C/D ring fusion in **5** was assigned as *cis*, based on NOE experiments. As seen in Table 2, an extended reaction period was required for the completion of the cyclization reaction of **4** with HCl and TFA, while BF_3•OEt_2 promoted the rapid cyclization. The cyclization of **4c** and **4i** with HCl and TFA for 1 h produced **6a** and **6b**, respectively, as the primary products accompanied by the deprotection of the *N*-Boc group. Further treatment of **6a** and **6b** with acids led to **5b** and/or **5b'** and **5e**, respectively. Otherwise, an attempt to cyclize **4k** with TFA in CH_2Cl_2 at rt, even for 20 h, failed to achieve the isolation of **6c** in 73 % yield (Scheme 2). Worthy of note is the formation of diastereoisomers (**5b** and **5b'**)[9] on the cyclization of **4c**, where the nature of the acid used was crucial to the reaction outcome. Protic acids (TFA, HCl) promoted the cyclization of **4c** in the direction of the preferential formation of **5b**, while the use of BF_3•OEt_2 resulted in the exclusive formation of **5b'**.

Table 2 Acid-promoted ring closure of **4**



4	Yield (%) [a] of **5** (condition) [b]	**4**	Yield (%) [a] of **5** (condition) [b]
4a	 **5a** : 82% (B)	**4e**	 **5c** : 78% (B)
4c	 **5b** / **5b'** = 51% / 25 % (A) **5b** / **5b'** = 50% / 23% (B) **5b** / **5b'** = 0 / 80% (C)  **5b'**	**4g**	 **5d** : 77% (B)
		4i	 **5e** : 73% (B)

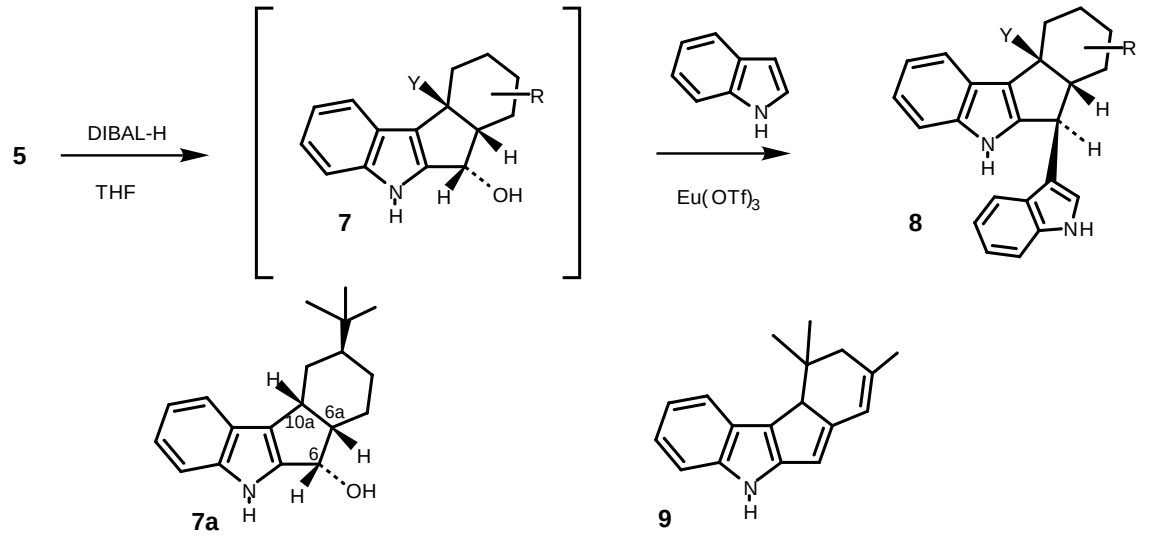
[a] Isolated yields (%) based on **4** [b] Conditions; A: 10% HCl in dioxane at 100°C for 20 h, B: TFA in CH_2Cl_2 at rt for 20 h, C: BF_3•OEt_2 in benzene at 80°C for 30 min.



Scheme 2

Further, the cyclization of **6a** with HCl in dioxane at 100°C for 20 h provided **5b** (52%) and **5b'** (23%), whereas BF_3•OEt_2-aided cyclization at 80°C for 30 min led solely to **5b'** in 80% yield. An intramolecular Michael addition path[10] can account for the protic acid-promoted ring closure of **4c**.[11] However, the exclusive formation of **5b'** observed in the BF_3•OEt_2-promoted cyclization of **4c** and **6a** could not be interpreted through the Michael addition path. Alternatively, an electrocyclic reaction (Nazarov reaction)[12] through dienylcation arising from **4c** and BF_3•OEt_2 could explain the exclusive formation of **5b'**.[13]

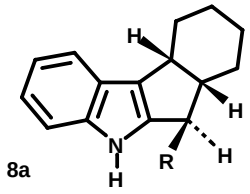
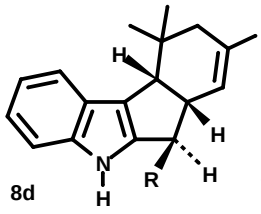
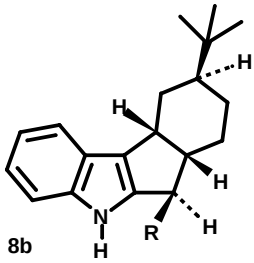
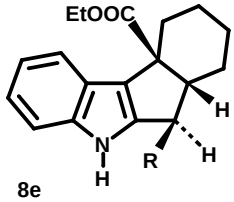
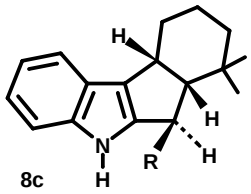
Since the desired hexahydroindeno[2,1-*b*]indoles (**5**) were obtained, efforts were then focused on the further conversion of **5** to yuehchukene derivatives (**8**) (Scheme 3). Ketones (**5**) were reduced with DIBAL-H in THF at -78°C to provide intrinsically unstable alcohols (**7**), which were used for the next step without purification. Surprisingly, alcohols (**7a**) was stable enough to be isolated and characterized. The relative configuration of the 6-OH group in **7a** was determined by NOE experiments, in which a distinctive enhancement of 6a-H (δ 2.79-2.87) and 10a-H (δ 3.42) was observed upon irradiation of 6-H (δ 5.35).



Scheme 3

The next task was the installation of an indol-3-yl group at the 6 position in **7**. In our previous report, BF_3•OEt_2 successfully promoted the reaction of alcohols (**7**) with indole to form *N*-methylated yuehchukene analogues. However, on using BF_3•OEt_2, the reaction of **7** arising from **5d** and indole was complicated, resulting in the isolation of diene (**9**). Eventually, $Eu(OTf)_3$ proved to be advantageous for the conversion **5** to **8** (Table 3).

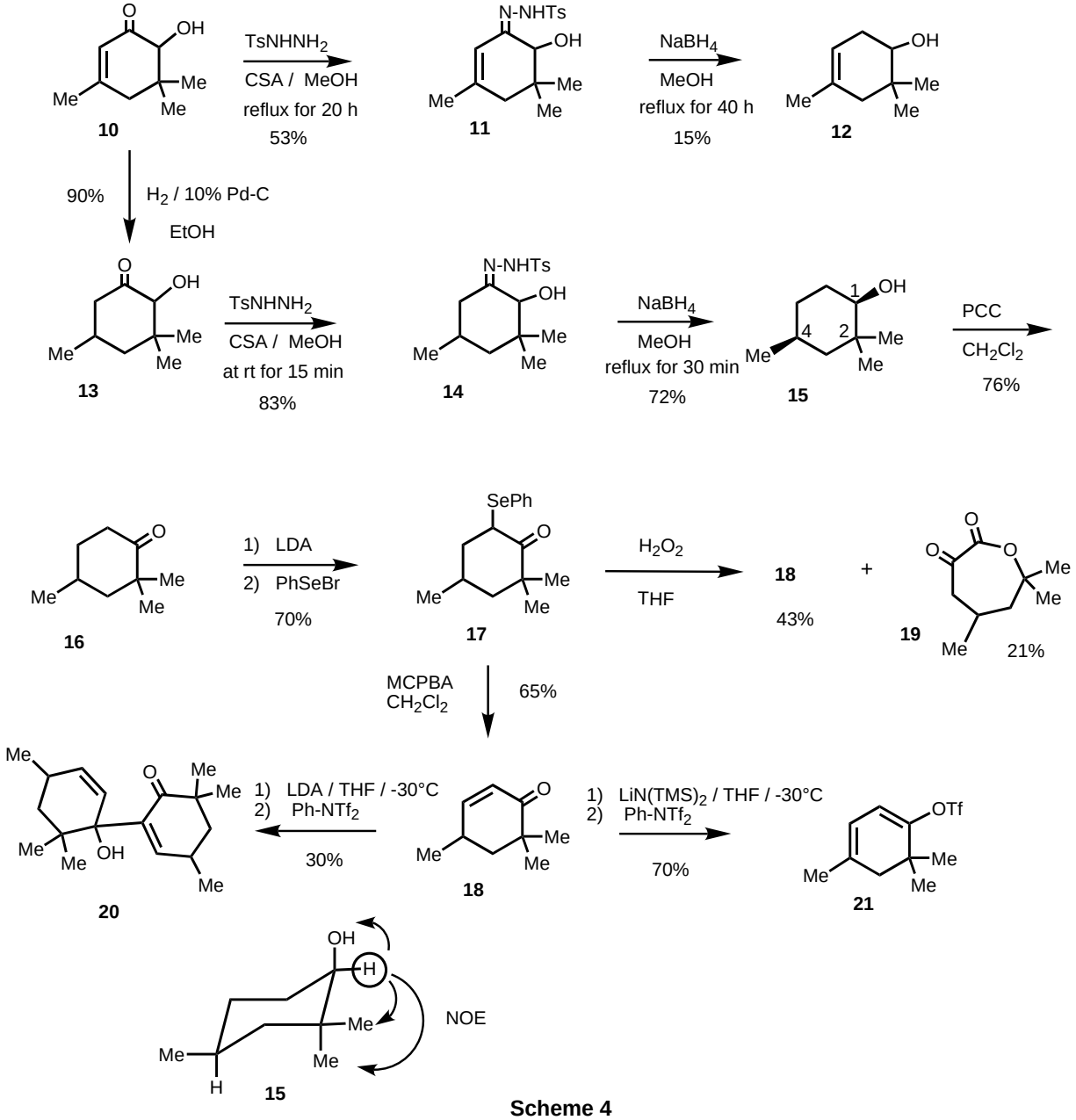
Table 3 Conversion of **5** to yuehchukene derivatives (**8**)[a]

5	Yield (%) of **10**[a]	**5**	Yield (%) of **10**[a]
5a	 **8a** 60 %	**5d**	 **8d** 40 %
5b	 **8b** 60 %	**5e**	 **8e** 56 %
5c	 **8c** 45 %		

[a] R=indol-3-yl [b] Isolated yields (%) based on **5**

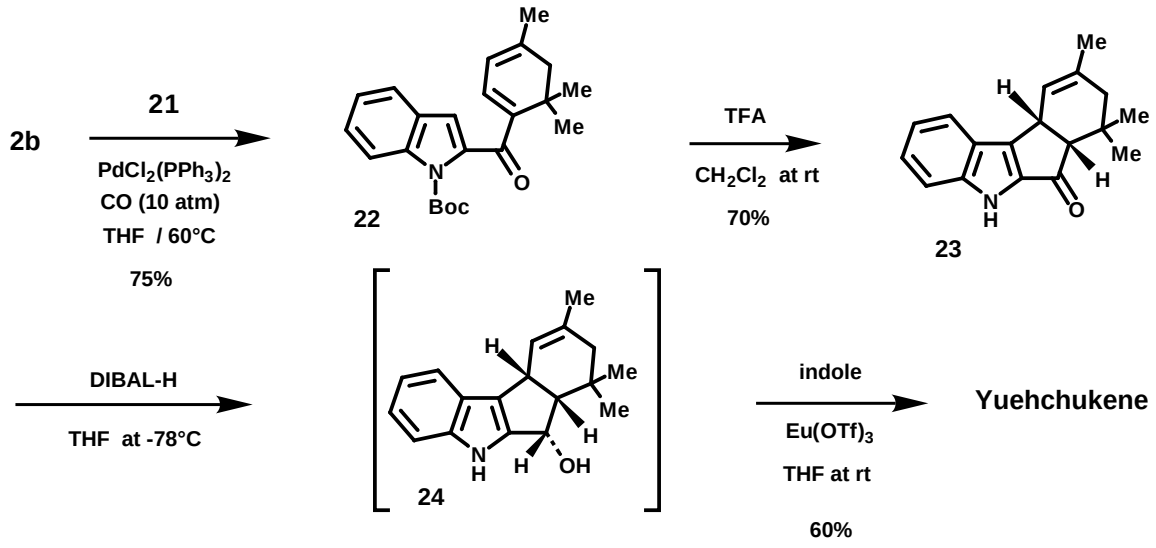
Hereupon, it was assumed that the total synthesis of yuehchukene could be reliably achieved based on the present protocol using **2b**. Considering the synthetic scheme, the preparation of the requisite triflate (**21**) was undertaken first (Scheme 4). Starting with the known hydroxyisophorone (**10**) derived from isophorone according to the literature,[14] we attempted the reaction of **10** with tosylhydrazide to give hydrazone (**11**), followed by the reduction of **11** with $NaBH_4$ to give alcohol (**12**). However, these processes were quite sluggish and resulted in an appreciable reduction in yields. As it was envisioned that the presence of a conjugated double bond would attenuate the lability of the carbonyl group, the double bond was catalytically hydrogenated over 10% Pd-C in EtOH to provide saturated ketone (**13**) as a single isomer. Thus, hydrazone (**14**) was readily available in 83% yield from **13** with tosylhydrazide in MeOH at room temperature, and the subsequent reduction of **14** with $NaBH_4$ in MeOH under reflux was completed within 30 min to give alcohol (**15**) in 72% yield. Stereochemistry of **15** was determined based on NOE, where a distinctive enhancement of both the methyl groups at C-2 (δ 0.92 and δ 0.94) upon irradiation of methine proton at C-1 (δ 3.41). Neither of the methyl groups at C-2 showed NOE correlation with the methyl group at C-4 (δ 0.86). Oxidation of **15** with PCC in CH_2Cl_2

smoothly provided ketone (**16**), which was in turn converted to phenylselenide (**17**) by an ordinal procedure (LDA / PhSeBr). Subsequential oxidation of **17** with H_2O_2 in THF was somewhat complicated, resulting in the formation of enone (**18**) in 43% yield, lactone (**19**) in 21% yield and a mixture of unknown species. Lactone (**19**) seems to arise from the known Pummerer-type reaction of selenoxide,[15] followed by Baeyer-Villiger oxidation. Otherwise, the use of MCPBA in CH_2Cl_2 as an oxidant successfully provided **18** in 65% yield. Next, the transformation of **18** to the desired triflate (**21**) involved the formation of a dienolate anion with a base, and its subsequent treatment with a triflating agent. Our initial attempt to enolize **18** with LDA, followed by the addition of *N*-phenyltrifluoromethanesulfonimide ($PhN(Tf)_2$) proved to be unsuccessful, resulting in the sole isolation of dimer (**20**) as a single isomer, the stereochemistry of which is uncertain. Treatment of **18** with lithium bis(trimethylsilyl)amide, followed by the addition of $PhN(Tf)_2$, produced triflate (**21**) in 70% yield.



Scheme 4

Then, the palladium-catalyzed carbonylative cross-coupling reaction of **2b** with triflate (**21**) in the presence of a catalytic amount of $PdCl_2(PPh_3)_2$ under a carbon monoxide atmosphere (10 atm) in THF at 60°C was performed successfully to give indol-2-yl ketone (**22**) in 75% yield (Scheme 5). A "one-pot" protocol of the cyclization and removal of the *N*-Boc group was concurrently succeeded by the treatment of **22** with TFA in CH_2Cl_2 at room temperature for 20 h, giving rise to hexahydroindeno[2,1-*b*]indole (**23**), the conversion of which to yuehchukene is reported by Kutney[3s] and Bergman.[3v] We used DIBAL-H for the reduction of **23** to alcohol (**24**), which was then subjected, without further purification, to the reaction with indole in the presence of $Eu(OTf)_3$ leading to yuehchukene in 60 % yield.



Scheme 5

In summary, we have described herein a practical approach to yuehchukene and its analogues by the use of the palladium-catalyzed carbonylative cross-coupling reaction of indolylborates (**2**) as a key reaction.

EXPERIMENTAL

Melting points were recorded on Yamato MP21. All melting points and boiling points are uncorrected. MS and high-resolution MS were recorded on a Micromass AutoSpec 3100 mass spectrometer. IR spectra were measured on a Hitachi Model 270-30 spectrometer. The NMR experiments were performed with a JEOL JNM-LA300 or JNM-EX400 spectrometer, and chemical shifts are expressed in ppm (δ) with TMS as an internal reference. The following abbreviations are used: s=singlet, d=doublet, t=triplet, q=quartet, m=multiplet, br=broad. Medium pressure liquid chromatography (MPLC) and flash chromatography were performed on silica gel (Silica gel 60N, Kanto Chemical Co., Inc.). HPLC was performed on Mightysil RP-18 GP 250-10 (5 μm) (Kanto Chemical Co., Inc.). Dehydrated THF and Et_2O were purchased from Kanto Chemical Co., Inc.

General procedure for the palladium-catalyzed carbonylative cross-coupling reaction of indolylborates (2) with vinyl triflates (3)

Indolylborates (**2**) were generated from indoles (**1**) (2 mmol) in THF (10 mL) under argon atmosphere *in situ*,[8] and then, the reaction apparatus was filled with carbon monoxide. Vinyl triflates (**3**) (3 mmol) and $PdCl_2(PPh_3)_2$ (35 mg, 0.05 mmol) were added at once, and carbon monoxide was introduced up to 10 atm. Then, the reaction mixture was heated at 60°C for 20 h. After cooling, the mixture was treated with 10% NaOH (5 mL) and 30% H_2O_2 (2 mL) under ice-cooling for 10 min, and diluted with AcOEt. The organic layer was washed with brine, and dried over anhydrous $MgSO_4$. The solvent was removed, and the residue was separated by MPLC with AcOEt-hexane as an eluent to give indol-2-yl ketones (**4**).

***tert*-Butyl 2-(Cyclohex-1-enylcarbonyl)indole-1-carboxylate (4a) .** viscous liquid. IR (neat): 1738, 1640 cm^{-1}. ^{1}H-NMR ($CDCl_3$) δ: 1.55 (s, 9H), 1.62-1.73 (m, 4H), 2.21-2.26 (m, 2H), 2.41-2.45 (m, 2H), 6.73 (s, 1H), 6.75-6.80 (m, 1H), 7.24 (td, 1H, *J*=1, 8.3 Hz), 7.37 (ddd, 1H, *J*=1.5, 7.3, 8.3 Hz), 7.55 (d, 1H, *J*=7.8 Hz), 8.14 (d, 1H, *J*=8.8 Hz). ^{13}C-NMR ($CDCl_3$) δ: 21.7, 21.9, 23.2, 26.3, 27.8, 84.4, 112.3, 115.1, 121.7, 123.2, 125.9, 128.1, 136.8, 136.9, 140.0, 144.7, 149.2, 189.6. HR-MS *m/z*: Calcd for $C_{20}H_{23}NO_3$: 325.1677. Found: 325.1671.

Cyclohex-1-enyl 1-Methoxyindol-2-yl Ketone (4b) . viscous liquid. IR (neat): 1630 cm^{-1}. ^{1}H-NMR ($CDCl_3$) δ: 1.64-1.77 (m, 4H), 2.22-2.31 (m, 2H), 2.43-2.45 (m, 2H), 4.26 (s, 3H), 6.74 (d, 1H, *J*=1 Hz), 6.89-6.91 (m, 1H), 7.14 (t, 1H, *J*=7.8 Hz), 7.35 (ddd, 1H, *J*=1, 6.8, 7.8 Hz), 7.48 (d, 1H, *J*=8.3 Hz), 7.61 (d, 1H, *J*=7.8 Hz). ^{13}C-NMR ($CDCl_3$) δ: 21.7, 22.0, 23.8, 26.1, 66.3, 107.9, 109.2, 121.2, 121.8, 122.6, 125.6, 133.4, 135.5, 139.8, 143.3, 187.6. HR-MS *m/z*: Calcd for $C_{16}H_{17}NO_2$: 255.1259. Found: 255.1245.

***tert*-Butyl 2-{[4-(*tert*-Butyl)cyclohex-1-enyl]carbonyl}indole -1- carboxylate (4c).** viscous liquid. IR (neat) : 1736, 1642 cm^{-1}. ^{1}H-NMR ($CDCl_3$) δ: 0.90 (s, 9H), 1.11-1.34 (m, 3H), 1.56 (s, 9H), 1.99-2.04 (m, 2H), 2.25-2.33 (m, 1H), 2.71-2.76 (m, 1H), 6.73 (d, 1H, *J*=1 Hz), 6.79-6.81 (m, 1H), 7.25 (ddd, 1H, *J*=1, 7.8, 8.3 Hz), 7.38 (ddd, 1H, *J*=1, 7.8, 8.3 Hz), 7.57 (d, 1H, *J*=7.8 Hz), 8.13 (dd, 1H, *J*=1, 8.3 Hz). ^{13}C-NMR ($CDCl_3$) δ: 23.4, 24.7, 27.1, 27.8, 28.0, 32.2, 43.6, 84.4, 112.3, 115.1, 121.6, 123.2, 125.9, 128.0, 136.9, 137.0, 139.9, 145.1, 149.2, 189.3. HR-MS *m/z*: Calcd for $C_{24}H_{31}NO_3$: 381.2302. Found: 381.2310.

4-(*tert*-Butyl)cyclohex-1-enyl 1-Methoxyindol-2-yl Ketone (4d) : viscous liquid. IR (neat): 1634 cm^{-1}. ^{1}H-NMR ($CDCl_3$) δ: 0.91 (s, 9H), 1.15-1.25 (m, 1H), 1.34-1.41 (m, 1H), 1.95-2.08 (m, 2H), 2.24-2.35 (m, 2H), 2.69-2.75 (m, 1H), 4.25 (s, 3H), 6.74 (s, 1H), 6.89-6.92 (m, 1H), 7.13 (t, 1H, *J*=6.8 Hz), 7.34 (t, 1H, *J*=6.8 Hz), 7.47 (d, 1H, *J*=8.3 Hz), 7.60 (d, 1H, *J*=8.3 Hz). ^{13}C-NMR ($CDCl_3$) δ: 23.5, 25.3, 27.1, 27.9, 32.2, 43.5, 66.3, 107.9, 109.2, 121.2, 121.8, 122.6, 125.6, 133.4, 135.5, 139.6, 143.7, 187.3. HR-MS *m/z*: Calcd for $C_{20}H_{25}NO_2$: 311.1885. Found: 311.1884.

***tert*-Butyl 2-[(6,6-Dimethylcyclohex-1-enyl)carbonyl]indole-1-carboxylate (4e).** mp 109-110°C (from AcOEt-hexane). IR ($CHCl_3$): 1734, 1646 cm^{-1}. ^{1}H-NMR ($CDCl_3$) δ: 1.33 (s, 6H), 1.57 (s, 9H), 1.53-1.60 (m, 2H), 1.67-1.73 (m, 2H), 2.21-2.25 (m, 2H), 6.71-6.73 (m, 1H), 6.72 (d, 1H, *J*=1 Hz), 7.23 (dt, 1H, *J*=1, 7.8 Hz),7.38 (ddd, 1H, *J*=1, 6.8, 8.3 Hz), 7.56 (d, 1H, *J*=7.8 Hz), 8.07 (dd, 1H, *J*=1, 8.3 Hz). ^{13}C-NMR ($CDCl_3$) δ: 18.2, 26.5, 27.8, 27.9, 33.4, 40.1, 84.2, 114.1, 114.9, 121.9, 123.1, 126.3, 127.7, 137.7, 139.5, 143.5, 147.1, 149.4, 189.2. MS *m/z*: 353 (M^+). *Anal.* Calcd for $C_{22}H_{27}NO_3$: C, 74.76; H, 7.70; N, 3.96. Found: C, 74.73; H, 7.79; N, 3.86.

***tert*-Butyl 2-[(4,6,6-Trimethylcyclohex-1-enyl)carbonyl]indole-1-carboxylate (4f).** mp 133-134°C (from AcOEt-hexane). IR ($CHCl_3$): 1734, 1646 cm^{-1}. ^{1}H-NMR ($CDCl_3$) δ: 0.99 (d, 3H, *J*= 6.4 Hz), 1.26 (s, 3H), 1.23-1.30 (m, 1H), 1.42 (s, 3H), 1.48-1.53 (m, 1H), 1.57 (s, 9H), 1.74-1.92 (m, 2H), 2.26-2.32 (m, 1H), 6.69-6.72 (m, 1H), 6.71 (s, 1H), 7.22 (t, 1H, *J*=7.3 Hz), 7.36 (t, 1H, *J*=7.3 Hz), 7.54 (d, 1H, *J*=7.3 Hz), 8.08 (d, 1H, *J*=8.3 Hz). ^{13}C-NMR ($CDCl_3$) δ: 22.0, 24.5, 27.8, 28.0, 28.2, 34.8, 35.2, 49.2, 84.2, 114.1, 114.8, 121.9, 123.1, 126.3, 127.6, 137.6, 139.6, 143.4, 146.8, 149.4, 189.2. MS *m/z*: 367 (M^+). *Anal*. Calcd for $C_{23}H_{29}NO_3$: C, 75.16; H, 7.96; N, 3.81. Found: C, 75.26; H, 8.07; N, 3.86.

***tert*-Butyl 2-[(3,5,5-Trimethylcyclohexa-1(6),2-dienyl)carbonyl]indole-1-carboxylate (4g).** mp 93-94°C (from AcOEt-hexane). IR ($CHCl_3$): 1732, 1646 cm^{-1}. ^{1}H-NMR ($CDCl_3$) δ: 1.04 (s, 6H), 1.52 (s, 9H), 1.88 (s, 3H), 2.07 (s, 2H), 6.21 (s, 1H), 6.35 (s, 1H), 6.77 (s, 1H), 7.27 (t, 1H, *J*=7.8 Hz), 7.40 (t, 1H, *J*=7.8 Hz), 7.59 (d, 1H, *J*=7.8 Hz), 8.17 (d, 1H, *J*=8.3 Hz). ^{13}C-NMR ($CDCl_3$) δ: 23.6, 27.3, 27.7, 33.1, 43.0, 84.6, 112.7, 114.6, 115.1, 121.8, 123.2, 126.0, 128.0, 135.5, 136.7, 136.8, 137.1, 147.8, 149.1, 187.5. MS *m/z*: 365 (M^+). *Anal.* Calcd for $C_{23}H_{27}NO_3$: C, 75.59; H, 7.45; N, 3.83. Found: C, 75.65; H, 7.53; N, 3.79.

1-Methoxyindol-2-yl 3,5,5-Trimethylcyclohexa-1(6),2-dienyl Ketone (4h). viscous liquid. IR (neat): 1636 cm^{-1}. ^{1}H-NMR ($CDCl_3$) δ: 1.09 (s, 6H), 1.87 (s, 3H), 2.09 (br s, 2H), 4.27 (s, 3H), 6.26 (br s, 1H), 6.36 (s, 1H), 6.80 (s, 1H), 7.15 (t, 1H, *J*=7.8 Hz), 7.36 (t, 1H, *J*=7.8 Hz), 7.49 (d, 1H, *J*=8.3 Hz), 7.63 (d, 1H, *J*=7.8 Hz). ^{13}C-NMR ($CDCl_3$) δ: 23.6, 27.5, 33.1, 42.9, 66.3, 108.5, 109.3, 115.4, 121.3, 121.7, 122.8, 125.9, 133.2, 135.4, 135.7, 136.6, 146.8, 185.4. HR-MS *m/z:* Calcd for $C_{19}H_{21}NO_2$: 295.1572. Found: 295.1556.

***tert*-Butyl 2-{[2-(Ethoxycarbonyl)cyclohex-1-enyl]carbonyl}indole-1-carboxylate (4i).** viscous liquid. IR (neat): 1720, 1666 cm^{-1}. ^{1}H-NMR ($CDCl_3$) δ: 1.00 (t, 3H, *J*=7.3 Hz), 1.65 (s, 9H), 1.73-1.75 (m, 4H), 2.45-2.47 (m, 4H), 3.93 (q, 2H, *J*=7.3 Hz), 7.04 (s, 1H), 7.23 (t, 1H, *J*=7.3 Hz), 7.41(ddd, 1H, *J*=1, 6.8, 8.3 Hz), 7.59 (d, 1H, *J*=7.8 Hz), 8.02 (d, 1H, *J*=7.8 Hz). ^{13}C-NMR ($CDCl_3$) δ: 13.6, 21.3, 21.4, 25.7, 27.6, 28.0, 60.6, 84.3, 114.3, 116.9, 122.5, 123.0, 126.9, 127.3, 131.8, 136.5, 138.7, 145.5, 149.4, 167.1, 188.1. HR-MS *m/z*: Calcd for $C_{23}H_{27}NO_5$: 397.1889. Found: 397.1912.

Ethyl 2-[(1-Methoxylindol-2-yl)carbonyl]cyclohex-1-ene-1-carboxylate (4j). viscous liquid. IR (neat): 1710,1654 cm^{-1}. ^{1}H-NMR ($CDCl_3$) δ: 0.98 (t, 3H, *J*=7.3 Hz), 1.76-1.78 (m, 4H), 2.47-2.51 (m, 4H), 3.93 (q, 2H, *J*=7.3 Hz), 4.24 (s, 3H), 6.82 (s, 1H), 7.13 (t, 1H, *J*=8.3 Hz), 7.38 (t, 1H, *J*=7.8 Hz), 7.50 (d, 1H, *J*=8.3 Hz), 7.60 (d, 1H, *J*=7.8 Hz). ^{13}C-NMR ($CDCl_3$) δ: 13.6, 21.4, 21.6, 24.8, 29.0, 60.7, 65.9, 108.2, 109.3, 121.3, 121.6, 122.9, 126.4, 128.8, 131.6, 135.5, 148.7, 166.3, 189.2. HR-MS *m/z*: Calcd for $C_{19}H_{21}NO_4$: 327.1471. Found: 327.1460.

***tert*-Butyl 2-{[2-(Methoxycarbonyl)cyclopent-1-enyl}indole-1-carboxylate (4k).** mp 74-75°C (from AcOEt-hexane). IR ($CHCl_3$): 1726, 1654 cm^{-1}. ^{1}H-NMR ($CDCl_3$) δ: 1.63 (s, 9H), 2.02-2.10 (m, 2H), 2.83-2.95 (m, 4H), 3.36 (s, 3H), 7.01 (s, 1H), 7.25 (dt, 1H, *J*=1, 7.3 Hz), 7.42 (dt, 1H, *J*=1, 7.3 Hz), 7.60 (d, 1H, *J*=7.8 Hz), 8.04 (d, 1H, *J*=8.3 Hz). ^{13}C-NMR ($CDCl_3$) δ: 22.1, 27.7, 34.9, 36.5, 51.6, 84.6, 114.8, 116.3, 122.6, 123.3, 127.3, 127.4, 137.5, 137.7, 138.5, 149.5, 149.6, 165.3, 185.2. MS *m/z*: 369 (M^+). *Anal.* Calcd for $C_{21}H_{23}NO_5$: C, 68.28; H, 6.28; N, 3.79. Found: C, 68.36; H, 6.36; N, 3.91.

General procedure for acid aided cyclization of indol-2-yl ketones (4) to hexahydroindeno[2,1-*b*]indoles (5)

Procedure A: A mixture of indol-2-yl ketones (**4**) (1 mmol) and 10% HCl (0.5 mL) in dioxane (20 mL) was heated at 100°C for 20 h. After cooling, 10% NaOH (10 mL) was added, and the mixture was extracted with AcOEt. The extract was washed with brine and dried over anhydrous $MgSO_4$. The solvent was removed, and the residue was separated by MPLC with AcOEt-hexane as an eluent to give **5**. Diastereoisomeric mixture (**5b** and **5b'**) was separated by HPLC with MeOH:H_2O = 10:1 as an eluent.

Procedure B: A mixture of indol-2-yl ketones (**4**) (1 mmol) and TFA (1 mL) in CH_2Cl_2 (20 mL) was sitirred at rt for 20 h. Then, 10% NaOH (10 mL) was added, and the mixture was extracted with AcOEt. The extract was washed with brine, and dried over anhydrous $MgSO_4$. The solvent was removed, and the residue was separated by MPLC with AcOEt-hexane as an eluent to give **5**. Diastereoisomeric mixture (**5b** and **5b'**) was separated by HPLC with MeOH:H_2O = 10:1 as an eluent.

Procedure C: A mixture of indol-2-yl ketones (**4**) (1 mmol) and BF_3•OEt_2 (2 mmol) in benzene (20 mL) was heated at 80°C for 30 min. After cooling, 10% NaOH (10 mL) was added, and the mixture was extracted with AcOEt. The extract was washed with brine, and dried over anhydrous $MgSO_4$. The solvent was removed, and the residue was separated by MPLC with AcOEt-hexane as an eluent to give **5**. A diastereoisomeric mixture (**5b** and **5b'**) was separated by HPLC with MeOH:H_2O = 10:1 as an eluent.

***rel*-(6a*S*, 10a*R*)-7,8,9,10,10a,6a-Hexahydroindeno[2,1-*b*]indol-6-one (5a).** mp 199-200°C (from AcOEt-hexane). IR ($CHCl_3$): 3476, 1674 cm^{-1}. ^{1}H-NMR ($CDCl_3$) δ: 1.40-1.61 (m, 5H), 1.88-2.01 (m, 2H), 2.21-2.28 (m, 1H), 3.13 (q, 1H, *J*=6.4 Hz), 3.55-3.60 (m, 1H), 7.16 (t, 1H, *J*=7.3 Hz), 7.38 (ddd, 1H, *J*=1, 7.3, 8.3 Hz), 7.56 (d, 1H, *J*=8.3 Hz), 7.71 (d, 1H, *J*=8.3 Hz), 9.98 (br s, 1H). ^{13}C-NMR ($CDCl_3$) δ: 20.5, 20.6, 23.4, 28.1, 33.9, 52.2, 113.7, 120.5, 121.7, 123.1, 127.1, 137.8, 143.8, 150.3, 197.5. MS *m/z*: 225 (M^+). *Anal.* Calcd for $C_{15}H_{15}NO$: C, 79.96; H, 6.72; N, 6.22. Found: C, 79.77; H, 6.76; N, 6.14.

***rel*-(6a*S*, 9*S*, 10a*R*)-9-(*tert*-Butyl)-7,8,9,10,10a,6a-hexahydroindeno[2,1-*b*]indol-6-one (5b).** mp 206-207°C (from AcOEt-hexane). IR ($CHCl_3$): 3472, 1672 cm^{-1}. ^{1}H-NMR ($CDCl_3$) δ: 0.76 (s, 9H), 0.92-1.02 (m, 1H), 1.23-1.33 (m, 1H), 1.37-1.49 (m, 1H), 1.73-1.82 (m, 1H), 1.87-1.96 (m, 2H), 2.19 (dt, 1H, *J*=4, 13 Hz), 3.06-3.11 (m, 1H), 3.79-3.83 (m, 1H), 7.18 (t, 1H, *J*=7.3 Hz), 7.39 (ddd, 1H, *J*=1, 7.3, 8.3 Hz), 7.51 (d, 1H, *J*=8.3 Hz), 7.73 (d, 1H, *J*=7.8 Hz), 9.07 (br s, 1H). ^{13}C-NMR ($CDCl_3$) δ: 21.6, 24.3, 26.0, 26.9, 32.9, 34.0, 39.2, 51.9, 114.0, 120.4, 121.6, 123.3, 127.1, 138.7, 144.5, 149.9, 198.8. MS *m/z*: 281 (M^+). *Anal.* Calcd for $C_{19}H_{23}NO$: C, 81.10; H, 8.24; N, 4.98. Found: C, 80.99; H, 8.36; N, 4.97.

***rel*-(6a*S*, 9*R*, 10a*R*)-9-(*tert*-Butyl)-7,8,9,10,10a,6a-hexahydroindeno[2,1-*b*]indol-6-one (5b').** mp 209-210°C (from AcOEt-hexane). IR ($CHCl_3$): 3472, 1674 cm^{-1}. ^{1}H-NMR ($CDCl_3$) δ: 0.85 (s, 9H), 0.88-1.05 (m, 1H), 1.21-1.34 (m, 1H), 1.37-1.45 (m, 1H), 1.65-1.75 (m, 1H), 1.84-1.98 (m, 2H), 2.32-2.37 (m, 1H), 3.02-3.10 (m, 1H), 3.45-3.50 (m, 1H), 7.18 (t, 1H, *J*=7.8 Hz), 7.38 (ddd, 1H, *J*=1, 6.8, 7.8 Hz), 7.52 (d, 1H, *J*=8.3 Hz), 7.74 (d, 1H, *J*=7.8 Hz), 9.43 (br s, 1H). ^{13}C-NMR ($CDCl_3$) δ: 23.7, 24.1, 27.2, 30.7, 33.0, 35.5, 44.8, 52.2, 113.8, 120.5, 121.8, 122.9, 127.1, 137.2, 143.9, 150.6, 197.2. MS

m/z: 281 (M^+). *Anal.* Calcd for $C_{19}H_{23}NO$: C, 81.10; H, 8.24; N, 4.98. Found: C, 80.96; H, 8.18; N, 4.92.

***rel*-(6a*R*, 10a*R*)-7,7-Dimethyl-6a,7,8,9,10,10a-hexahydroindeno[2,1-*b*]indol-6-one (5c).** mp 165-166°C (from AcOEt-hexane). IR ($CHCl_3$): 3472, 1666 cm^{-1}. ^{1}H-NMR ($CDCl_3$) δ: 1.07 (s, 3H), 1.30 (s,3H), 1.41-1.47 (m, 2H), 1.62-1.74 (m, 3H), 2.24-2.30 (m, 1H), 2.85 (d, 1H, *J*=5.8 Hz), 3.54 -3.60 (m, 1H), 7.16 (ddd, 1H, *J*=1, 7.3, 8.3 Hz), 7.37 (ddd, 1H, *J*=1, 6.8, 8.3 Hz), 7.49 (d, 1H, *J*=8.3 Hz), 7.71 (dd, 1H, *J*=1, 8.3 Hz), 9.32 (br s, 1H). ^{13}C-NMR ($CDCl_3$) δ: 19.0, 25.1, 27.8, 32.4, 33.5, 34.1, 37.1, 61.5, 113.9, 120.3, 121.6, 122.9, 126.9, 138.6, 144.0, 149.7, 197.0. MS *m/z*: 253 (M^+). *Anal.* Calcd for $C_{17}H_{19}NO$: C, 80.59; H, 7.56; N, 5.53. Found: C, 80.42; H, 7.67; N, 5.37.

***rel*-(6a*S*, 10a*R*)-8,10,10-Trimethyl-6a,9,10,10a-tetrahydroindeno[2,1-*b*]indol-6-one (5d).** mp 191-192°C (from AcOEt-hexane). IR ($CHCl_3$): 3468, 1672 cm^{-1}. ^{1}H-NMR ($CDCl_3$) δ: 0.45 (s, 3H), 1.37 (s, 3H), 1.75 (d, 1H, *J*=16.6 Hz), 1.77 (s, 1H), 2.15 (d, 1H, *J*=16.6 Hz), 3.44 (d, 1H, *J*=5.8 Hz), 3.58(br s, 1H), 5.86 (s, 1H), 7.19 (ddd, 1H, *J*=1, 6.8, 7.8 Hz), 7.39 (ddd, 1H, *J*=1, 6.8, 7.8 Hz), 7.54 (d, 1H, *J*=8.3 Hz), 7.81 (d, 1H, *J*=7.8Hz), 9.52 (br s, 1H). ^{13}C-NMR ($CDCl_3$) δ: 23.3, 24.0, 30.2, 34.4, 44.8, 45.1, 55.0, 113.8, 117.2, 120.5, 123.0, 124.0, 126.8, 134.7, 138.3, 143.7, 146.1, 194.7. MS *m/z*: 265 (M^+). *Anal.* Calcd for $C_{18}H_{19}NO$: C, 81.46; H, 7.22; N, 5.28. Found: C, 81.24; H, 7.34; N, 5.21.

Ethyl *rel*-(6a*S*, 10a*S*)-6-Oxo-6a,7,8,9,10,10a-hexahydroindeno[2,1-*b*]indole-10a-carboxylate (5e). mp 163-164°C (from AcOEt-hexane). viscous liquid. IR ($CHCl_3$): 3468, 1722, 1678 cm^{-1}. ^{1}H-NMR ($CDCl_3$) δ: 1.31 (t, 3H, *J*=7.3 Hz), 1.25-1.40 (m, 2H), 1.47-1.54 (m, 1H), 1.57-1.64 (m, 1H), 1.81-1.87 (m, 1H), 1.95-2.02 (m, 1H), 2.13-2.21 (m, 1H), 2.52-2.59 (m, 1H), 3.67 (dd, 1H, *J*=4.8, 6.3 Hz), 4.22-4.30 (m, 2H), 7.19 (t, 1H, *J*=6.8 Hz), 7.39 (ddd, 1H, *J*=1, 6.8, 8.3 Hz), 7.53 (d, 1H, *J*=8.3 Hz), 7.91 (d, 1H, *J*=8.3 Hz), 9.57 (br s, 1H). ^{13}C-NMR ($CDCl_3$) δ: 14.2, 19.0, 19.7, 22.2, 32.4, 49.6, 54.8, 61.4, 113.7, 120.9, 122.6, 122.7, 127.2, 136.9, 143.7, 146.6, 174.1, 195.4. MS *m/z*: 297 (M^+). *Anal.* Calcd for $C_{18}H_{19}NO_3$: C, 72.69; H, 6.44; N, 4.71. Found: C, 72.66; H, 6.56; N, 4.65.

4-(*tert*-Butyl)cyclohex-1-enyl Indol-2-yl Ketone (6a). A mixture of **4c** (381 mg) and 10% HCl (1 mL) in dioxane (10 mL) was heated at 100°C for 1 h. After cooling, 10% NaOH (10 mL) was added, and the mixture was extracted with AcOEt. The extract was washed with brine and dried over anhydrous $MgSO_4$. The solvent was removed and the residue was separated by MPLC with AcOEt-hexane=1:3 as an eluent to give 233 mg (83 %) of **6a**. mp 161-162°C (from AcOEt-hexane). IR ($CHCl_3$): 3460, 1612 cm^{-1}. ^{1}H-NMR ($CDCl_3$) δ: 0.93 (s, 9H), 1.22-1.29 (m, 1H), 1.37-1.44 (m, 1H), 1.98-2.12 (m, 2H), 2.30-2.42 (m, 2H), 2.70-2.75 (m, 1H), 6.99-7.01 (m, 1H), 7.08 (s, 1H), 7.13 (t, 1H, *J*=7.8 Hz), 7.32 (t, 1H, *J*=7.8 Hz), 7.44 (d, 1H, *J*=8.3 Hz), 7.69 (d, 1H, *J*=7.8 Hz), 9.46 (br s, 1H). ^{13}C-NMR ($CDCl_3$) δ: 23.5, 25.8, 27.1, 27.8, 32.2, 43.5, 110.6, 112.2, 120.7, 122.8, 125.8, 127.5, 134.3, 137.4, 138.3, 140.7, 188.4. MS *m/z*: 281 (M^+). *Anal.* Calcd for $C_{19}H_{23}NO$: C, 81.10; H, 8.24; N, 4.98. Found: C, 80.98; H, 8.38; N, 4.86.

Ethyl 2-(Indol-2-ylcarbonyl)cyclohex-1-enecarboxylate (6b). A mixture of **4i** (397 mg) and 10% HCl (1 mL) in AcOEt (10 mL) was stirred at rt for 1 h. Then, the mixture was rendered alkaline with 10% NaOH, and extracted with AcOEt. The extract was washed with brine and dried over anhydrous $MgSO_4$. The solvent was removed, and the residue was separated by MPLC with AcOEt-hexane=1:3

as an eluent to give 238 mg (80 %) of **6b**. mp 112-113°C (from AcOEt-hexane). IR ($CHCl_3$): 3464, 1708, 1632 cm^{-1}. ^{1}H-NMR ($CDCl_3$) δ: 0.93 (t, 3H, *J*=7.3 Hz), 1.75-1.81 (m, 4H), 2.46-2.49 (m, 4H), 3.90 (q, 2H, *J*=7.3 Hz), 6.93 (dd, 1H, *J*=1, 2 Hz), 7.13 (ddd, 1H, *J*=1, 6.8, 8.3 Hz), 7.33 (ddd, 1H, *J*=1, 6.8, 8.3 Hz), 7.42 (dd, 1H, *J*=1, 8.3 Hz), 7.65 (dd, 1H, *J*=1, 8.3 Hz), 9.11 (br s, 1H). ^{13}C-NMR ($CDCl_3$) δ: 13.6, 21.4, 21.6, 24.9, 28.9, 60.8, 110.2, 112.1, 120.9, 123.0, 126.2, 127.5, 129.4, 134.4, 137.6, 147.5, 166.5, 191.0. MS *m/z*: 297 (M^+). *Anal.* Calcd for $C_{18}H_{19}NO_3$: C, 72.69; H, 6.44; N, 4.71. Found: C, 72.70; H, 6.53; N, 4.69.

Methyl 2-(Indol-2-ylcarbonyl)cyclopent-1-enecarboxylate (6c). A mixture of **4k** (369 mg) and trifluoroacetic acid (1mL) in CH_2Cl_2 (10 mL) was stirred at rt for 20 h. Then, the mixture was rendered alkaline with 10% NaOH, and extracted with AcOEt. The extract washed with brine and dried over anhydrous $MgSO_4$. The solvent was removed, and the residue was separated by MPLC with AcOEt-hexane=1:3 as an eluent to give 196 mg (73 %) of **6c**. mp 158-159°C (from AcOEt-hexane). IR ($CHCl_3$): 1624, 1712, 3464 cm^{-1}. ^{1}H-NMR ($CDCl_3$) δ: 2.09-2.17 (m, 2H), 2.84-2.95 (m, 4H), 3.50 (s, 3H), 7.00 (dd, 1H, *J*=1, 2 Hz), 7.14 (ddd, 1H, *J*=1, 6.8, 8.3 Hz), 7.35 (ddd, 1H, *J*=1, 6.8, 8.3 Hz), 7.43 (dd, 1H, *J*=1, 8.3 Hz), 7.67 (dd, 1H, *J*=1, 8.3 Hz), 9.14 (br s, 1H). ^{13}C-NMR ($CDCl_3$) δ: 22.7, 33.5, 37.9, 51.7, 111.3, 112.4, 121.0, 123.2, 126.7, 127.5, 134.4, 135.1, 137.9, 151.8, 164.8, 187.8. MS *m/z*: 269 (M^+). *Anal.* Calcd for $C_{16}H_{15}NO_3$: C, 71.36; H, 5.61; N, 5.20. Found: C, 71.33; H, 5.78; N, 5.19.

General procedure for the conversion of 5 to yuehchukene analogues (8)

Diisobutylaluminium hydride (1 M solution in toluene, 2 mL, 2 mmol) was added to a solution of **5** (1 mmol) in THF (10 mL) at -78°C under an argon atmosphere, and the the mixture was stirred for 1 h. After the mixture was diluted with AcOEt, the organic layer was washed with brine and dried over anhydrous $MgSO_4$. The solvent was removed, and the residue was filtered through silica gel, and the filtrate was concentrated to give crude **7**, that was used for next reaction without further purification.

Procedure A: To a solution of crude **7** in ether, indole (234 mg, 2 mmol) and BF_3•OEt_2 (0.3 mL, 2 mmol) were added, and the whole was stirred at rt for 3 h. Then, 10% NaOH (5 mL) was added to the mixture, and the mixture was extracted with AcOEt. The extract was washed with brine, and dried over anhydrous $MgSO_4$. The solvent was removed, and the residue was separated by MPLC with AcOEt-hexane as an eluent to give **8**.

Procedure B: A mixture of crude **7** and $Eu(OTf)_3$ (60 mg, 0.1 mmol) in THF (10 mL) was stirred at rt overnight. The mixture was diluted with AcOEt, and the organic layer was washed with brine and dried over anhydrous $MgSO_4$. The solvent was removed, and the residue was separated by MPLC with AcOEt-hexane as an eluent to give **8**.

***rel*-(6*S*, 6a*S*, 9*S*, 10a*R*)-9-(*tert*-Butyl)-6,6a,7,8,9,10,10a-heptahydrobenzo[1',2'-5,1]cyclopenta[3,4-*b*]indol-6-ol (7a).** viscous liquid. IR ($CHCl_3$): 3604, 3476 cm^{-1}. ^{1}H-NMR ($CDCl_3$) δ: 0.88 (s, 9H), 0.92-1.14 (m, 1H), 1.34-1.56 (m, 3H), 1.74-1.83 (m, 2H), 2.51-2.56 (m, 1H), 2.79-2.87 (m, 1H), 3.42 (br s, 1H), 5.35 (br s, 1H), 7.07-7.17 (m, 2H), 7.35 (d, 1H, *J*=7.8 Hz), 7.53 (d, 1H, *J*=7.8 Hz), 8.12 (br s, 1H). ^{13}C-NMR ($CDCl_3$) δ: 23.3, 25.5, 27.3, 28.5, 32.4, 37.5, 43.3, 48.6, 74.1, 112.1, 118.9, 119.7, 121.3, 121.5, 124.6, 140.6, 143.3. HR-MS *m/z*: Calcd for $C_{19}H_{25}NO$: 283.1936. Found: 283.1916.

***rel*-(6*S*, 6a*S*, 10a*R*)-6-Indol-3-yl-5,6,6a,7,8,9,10,10a-octahydrobenzo[1',2'-5,1]cyclopenta[3,4-*b*]indole (8a).** viscous liquid. IR (neat): 3480 cm^{-1}. ^{1}H-NMR ($CDCl_3$) δ: 1.20-1.67 (m, 6H), 1.77-1.87 (m, 1H), 2.08-2.14 (m, 1H), 2.95-3.01 (m, 1H), 3.22-3.28 (m, 1H), 4.37 (d, 1H, *J*=8.3 Hz), 6.90 (d, 1H, *J*=2 Hz), 6.97 (t, 1H, J=7.3 Hz), 7.04-7.11 (m, 2H), 7.13-7.17 (m, 2H), 7.30 (d, 1H, *J*=7.8 Hz), 7.34 (d, 1H, *J*=7.8 Hz), 7.54 (d, 1H, *J*=7.8 Hz), 7.63 (br s, 1H), 7.85 (br s, 1H). ^{13}C-NMR ($CDCl_3$) δ: 22.7, 23.9, 26.8, 30.5, 37.4, 39.4, 52.3, 111.2, 111.6, 116.2, 118.5, 119.3, 119.4, 119.5, 120.3, 121.9, 122.1, 124.2, 124.5, 126.8, 136.6, 139.9, 144.5. HR-MS *m/z*: Calcd for $C_{23}H_{22}N_2$: 326.1782. Found: 326.1766.

***rel*-(6*S*, 6a*S*, 9*S*, 10a*R*)-9-(*tert*-Butyl)-6-indol-3-yl-5,6,6a,7,8,9,10,10a-octahydrobenzo[1',2'-5,1]cyclopenta[3,4-*b*]indole (8b).** viscous liquid. IR ($CHCl_3$): 3484 cm^{-1}. ^{1}H-NMR ($CDCl_3$) δ: 0.87 (s, 9H), 1.05 (dt, 1H, *J*=3, 12 Hz), 1.15-1.22 (m, 1H), 1.41-1.48 (m, 1H), 1.59-1.71 (m, 2H), 2.10-2.17 (m, 1H), 2.53 (dd, 1H, *J*=2, 13 Hz), 2.69-2.75 (m, 1H), 3.66-3.69 (m, 1H), 4.16 (s, 1H), 6.55 (d, 1H, *J*=2 Hz), 7.09-7.16 (m, 3H), 7.20 (ddd, 1H, *J*=1, 6.8, 7.8 Hz), 7.30-7.35 (m, 2H), 7.53 (d, 1H, *J*=8.3 Hz), 7.56-7.59 (m, 1H), 7.84 (br s, 1H), 7.89 (br s, 1H). ^{13}C-NMR ($CDCl_3$) δ: 25.9, 27.4, 28.1, 30.6, 32.4, 37.9, 42.7, 43.8, 51.8, 111.2, 111.7, 117.4, 118.4, 118.8, 119.4, 119.5, 120.4, 121.0, 121.6, 122.1, 125.1, 126.8, 136.6, 140.6, 144.9. HR-MS *m/z*: Calcd for $C_{27}H_{30}N_2$: 382.2409. Found: 382.2423.

***rel*-(6*S*, 6a*R*, 10a*R*)-6-Indol-3-yl-7,7-dimethyl-5,6,6a,7,8,9,10,10a-octahydrobenzo[1',2'-1,5]-cyclopenta[3,2-*b*]indole (8c).** viscous liquid. IR ($CHCl_3$): 3480 cm^{-1}. ^{1}H-NMR ($CDCl_3$) δ: 0.77 (s, 3H), 1.04 (s, 3H), 1.04-1.34 (m, 2H), 1.50-1.63 (m, 3H), 2.03-2.19 (m, 1H), 2.99 (dd, 1H, *J*=6.4, 9.8 Hz), 3.37-3.43 (m, 1H), 4.54 (d, 1H, *J*=9.8 Hz), 6.97-7.09 (m, 5H), 7.16 (t, 1H, *J*=8.3 Hz), 7.33 (d, 1H, *J*=8.3 Hz), 7.42 (d, 1H, *J*=7.8 Hz),7.44 (br s, 1H), 7.51 (d, 1H, *J*=8.3 Hz), 7.97 (br s, 1H). ^{13}C-NMR ($CDCl_3$) δ: 20.4, 29.2, 30.9, 31.7, 33.5, 35.9, 36.5. 36.8, 62.1, 111.2, 111.6, 118.0, 118.4, 119.3, 119.4, 119.5, 120.2, 121.9, 122.6, 123.4, 124.2, 126.8, 136.4, 139.7, 145.5. HR-MS *m/z*: Calcd for $C_{25}H_{26}N_2$: 354.2096. Found: 354.2109.

***rel*-(6*S*, 6a*S*, 10a*S*)-6-Indol-3-yl-8,10,10-trimethyl-5,6,6a,9,10,10a-hexahydroindeno[2,1-*b*]indole (8d).** viscous liquid. IR ($CHCl_3$): 3480 cm^{-1}. ^{1}H-NMR ($CDCl_3$) δ: 0.72 (s, 3H), 1.32 (s, 3H), 1.73 (s, 3H), 1.77 (d, 1H, *J*=16 Hz), 2.14 (d, 1H, *J*=16 Hz), 3.20 (d, 1H, *J*=7.8 Hz), 3.52-3.60 (m, 1H), 4.46 (d, 1H, *J*=9.3 Hz), 5.56 (s, 1H), 6.96 (t, 1H, *J*=7.3 Hz), 7.07-7.26 (m, 6H), 7.37 (d, 1H, *J*=8.3 Hz), 7.62 (d, 1H, *J*=7.3 Hz), 7.74 (br s, 1H), 8.03 (br s, 1H). ^{13}C-NMR ($CDCl_3$) δ: 22.0, 24.3, 31.3, 35.1, 42.5, 45.5, 47.4, 55.2, 111.2, 111.6, 116.8, 119.4, 119.5, 119.6, 119.9, 120.0, 120.4, 121.3, 122.0, 122.1, 125.8, 126.6, 133.4, 136.7, 140.4, 145.7. HR-MS *m/z*: Calcd for $C_{26}H_{26}N_2$: 366.2096. Found:366.2106.

Ethyl *rel*-(6*S*, 6a*S*, 10a*S*)-6-Indol-3-yl-5,6,7,8,9,10,10a,6a-ocahydrobenzo[1',2'-1,5]cyclopenta[3,2-*b*]indol-10a-carboxylate (8e). mp 250-251°C (from AcOEt-hexane). IR ($CHCl_3$): 3412, 3372, 1716 cm^{-1}. ^{1}H-NMR (DMSO-d_6) δ: 1.14-1.37 (m, 3H), 1.28 (t, 3H, *J*=7.3Hz), 1.55-1.70 (m, 4H), 2.58 (d, 1H, *J*=13 Hz), 3.32-3.43 (m, 1H), 4.23 (q, 2H, *J*=7.3 Hz), 4.42 (d, 1H, *J*=10.3 Hz), 6.83 (t, 1H, *J*=7.8 Hz), 6.93-6.97 (m, 2H), 7.04 (t, 1H, *J*=7.8 Hz), 7.14 (d, 1H, *J*=7.8 Hz), 7.20-7.22 (m, 1H), 7.31 (d, 1H, *J*=2 Hz), 7.38 (d, 1H, *J*=8.3 Hz), 7.51-7.53 (m, 1H), 10.85 (br s, 1H), 10.98 (br s, 1H). ^{13}C-NMR (DMSO-d_6) δ: 14.2, 21.2, 21.8, 23.9, 33.5, 38.2, 50.9, 53.6, 60.1, 111.5, 111.8, 113.6, 118.0, 118.2,

118.5, 118.8, 119.6, 120.8, 121.1, 122.9, 123.5, 126.3, 136.8, 140.1, 144.4, 174.9. MS *m/z*: 398 (M^+). *Anal.* Calcd for $C_{26}H_{26}N_2O_2$: C, 78.36; H, 6.58; N, 7.03. Found: C, 78.10; H, 6.73; N, 6.93.

8,10,10-Trimethyl-9-10,10a-trihydroindeno[2,1-*b*]indole (9): Diisobutylaluminium hydride (1 M solution in toluene, 2 mL, 2 mmol) was added to a solution of **5l** (265 mg, 1 mmol) in THF (10 mL) at -78°C under an argon atmosphere, and the the mixture was stirred for 1 h. Then, the mixture was diluted with AcOEt, washed with brine, and dried over anhydrous $MgSO_4$. The solvent was removed, and the residue was filtered through silica gel, and the filtrate was concentrated to give crude **7**, that was used for next reaction without further purification. To a solution of crude **7** in ether (30 mL), indole (234 mg, 2 mmol) and BF_3•OEt_2 (0.3 mL, 2 mmol) were added, and the whole was stirred at rt for 3 h. Then, 10% NaOH (5 mL) was added to the mixture, and the mixture was extracted with AcOEt. The extract was washed with brine, and dried over anhydrous $MgSO_4$. The solvent was removed, and the residue was separated by flash chromatography with AcOEt-hexane=1:50 as an eluent to give 146 mg (40%) of **9**. mp 107-108°C (from MeOH). IR ($CHCl_3$): 3476 cm^{-1}. ^{1}H-NMR ($CDCl_3$) δ: 0.42 (s, 3H), 1.58 (s, 3H), 1.88 (br s, 3H), 1.95-2.04 (m, 1H), 2.20-2.35 (m, 1H), 3.20 (br s, 1H), 6.28 (s, 2H), 7.04-7.12 (m, 2H), 7.33 (d, 1H, *J*=8.3 Hz), 7.55-7.64 (m, 1H), 7.95 (br s, 1H). ^{13}C-NMR ($CDCl_3$) δ: 19.8, 24.0, 31.2, 38.0, 47.3, 54.4, 111.6, 112.4, 118.7, 119.5, 119.7, 119.8, 119.9, 125.1, 138.1, 140.2, 148.3, 152.9. MS *m/z*: 249 (M^+). *Anal.* Calcd for $C_{18}H_{19}N$: C, 86.69; H, 7.69; N, 5.62. Found: C, 86.53; H, 7.74; N, 5.56.

2-Hydroxy-3,3,5-trimethylcyclohexan-1-one (13). 2-Hydroxyisophorone (**10**)[14] (10 g) was catalytically hydrogenated over 10% Pd on C (1 g) in EtOH (100 mL) under hydrogen (1 atm). The solvent and catalyst were removed, and the residue was distilled under reduced pressure to give 9.1 g (90 %) of **13**. bp 110°C /15 mmHg. IR (neat): 3452, 1712 cm^{-1}. ^{1}H-NMR ($CDCl_3$) δ: 0.90 (s, 3H), 1.02 (d, 3H, *J*=6.3 Hz), 1.07 (s, 3H), 1.43-1.49 (m, 1H), 1.65-1.71 (m, 1H), 2.22-2.29 (m, 2H), 2.40-2.48 (m, 1H), 3.83 (s, 1H). ^{13}C-NMR ($CDCl_3$) δ: 21.9, 24.6, 27.7, 27.8, 38.3, 43.7, 44.7, 81.3, 212.8. *Anal.* Calcd for $C_9H_{16}O_2$: C, 69.18; H, 10.33. Found: C, 69.26; H, 10.46.

[Aza(2-hydroxy-3,3,5-trimethylcyclohexylidene)methyl][(4-methylphenyl)sulfonyl]amine (14). A mixture of **13** (9 g, 64 mmol) and *p*-toluenesulfonylhydrazide (12 g, 64 mmol) in the presence of camphorsulfonic acid (50 mg) in MeOH (200 mL) was stirred at rt for 15 min. The solvent was removed, the residue was crystallized from EtOH-hexane to give 15.6 g (83%) of **14**. mp 115-116°C. IR ($CHCl_3$): 3616, 3212, 1598 cm^{-1}. ^{1}H-NMR ($CDCl_3$) δ: 0.64 (s, 3H), 0.89 (s, 3H), 0.91 (d, 3H, *J*=6.3 Hz),1.22 (dd, 1H, *J*=4, 13 Hz), 1.37 (t, 1H, *J*=13 Hz), 1.61-1.71 (m,1 H), 1.83 (t, 1H, *J*=13 Hz), 2.35-2.42 (m, 1H), 2.41 (s, 3H), 3.68 (s, 1H), 7.29 (d, 2H, *J*=7.8 Hz), 7.83 (d, 2H, *J*=8.3 Hz), 8.01 (br s, 1H). ^{13}C-NMR ($CDCl_3$) δ: 21.6, 22.0, 24.8, 26.0, 27.2, 30.5, 36.7, 42.1, 78.1, 127.9, 129.6, 135.1, 144.1, 161.2. MS *m/z*: 324 (M^+). *Anal.* Calcd for $C_{16}H_{24}N_2O_3S$: C, 59.23; H, 7.46; N, 8.64. Found: C, 59.07; H, 7.37; N, 8.46.

***rel*-(1*S*, 4*R*)-2,2,4-Trimethylcyclohexan-1-ol (15).** To solution of **14** (10 g, 31 mmol) in MeOH (100 mL), $NaBH_4$ (2 g, 54 mmol) was added portionwise under ice-cooling. Then, the mixture was gradually warmed to rt over 1 h and then, heated under reflux for 30 min. The solvent was removed, and the residue was extracted with AcOEt. The extract was washed with brine and dried over anhydrous $MgSO_4$.

The solvent was removed and the residue was separated by MPLC with AcOEt:hexane=1:7 as an eluent to give 3.2g (72%) of **15**. bp 83°C /15 mmHg. IR (neat): 3424 cm^{-1}. ^{1}H-NMR ($CDCl_3$) δ: 0.86 (d, 3H, *J*=6.4 Hz), 0.92 (s, 3H), 0.94 (s, 3H), 1.15-1.23 (m, 3H), 1.39-1.46 (m, 1H), 1.52-1.67 (m, 3H), 1.73-1.82 (m, 1H), 3.41 (t, 1H, *J*=3 Hz). ^{13}C-NMR ($CDCl_3$) δ: 22.8, 25.4, 27.6, 28.0, 28.1, 29.1, 35.1, 42.2, 74.2. *Anal.* Calcd for $C_9H_{18}O$: C, 75.98; H, 12.76. Found: C, 75.82; H, 12.54.

2,2,4-Trimethylcyclohexan-1-one (16). After a mixture of PCC (15 g, 70 mmol) and celite (20 g) in CH_2Cl_2 (200 mL) was stirred for 30 min, **15** (5 g, 35 mmol) was added, and the whole was stirred for 1 h at rt. After the mixture was filtered through florisil, the filtrate was concentrated and the residue was distilled under reduced pressure to give 3.7g (76%) of **16**. bp 68°C /15 mmHg. IR (neat): 1710 cm^{-1}. ^{1}H-NMR ($CDCl_3$) δ: 0.96 (d, 3H, *J*=6.8 Hz), 1.02 (s, 3H), 1.19 (s, 3H), 1.25-1.38 (m, 2H), 1.71 (dt, 1H, *J*=13.7, 3.4 Hz), 1.94-2.14 (m, 2H), 2.19-2.25 (m, 1H), 2.60 (td, 1H, *J*=6.4, 14.7 Hz). ^{13}C-NMR ($CDCl_3$) δ: 21.6, 25.4, 25.9, 27.7, 35.6, 37.8, 44.8, 49.7, 216.5. *Anal.* Calcd for $C_9H_{16}O+1/10H_2O$: C, 76.11; H, 11.49. Found: C, 76.03; H, 11.54.

2,2,4-Trimethyl-6-(phenylselenamethyl)cyclohexan-1-one (17). *n*-BuLi (1.5 M solution in hexane, 16 mL, 24 mmol) was added to a solution of diisopropylamine (3.5 mL, 24 mmol) under an argon atmosphere at -78°C, the whole was stirred for 10 min. Then, **16** (2.8 g, 20 mmol) was added to this solution, and the mixture was stirred for 1 h. After PhSeBr (5.7 g, 24 mmol) was added, the whole was gradually raised to room temperature over 1 h. The mixture was diluted with AcOEt, washed with brine, and dried over anhydrous $MgSO_4$. The solvent was removed, and the residue was crystallized from hexane to give 4.1 g (70%) of **17**. IR ($CHCl_3$): 1698 cm^{-1}. ^{1}H-NMR ($CDCl_3$) δ: 0.89 (d, 3H, *J*=6.4 Hz), 1.09 (s, 3H), 1.25 (s, 3H), 1.35 (t, 1H, *J*=13 Hz), 1.53-1.63 (m, 1H), 1.75 (dt, 1H, *J*=3.4, 13.7 Hz), 2.01-2.20 (m, 2H), 4.45 (dd, 1H, *J*=6, 13 Hz), 7.25-7.31 (m, 3H), 7.57 (dd ,2H, *J*=1.5, 7.5 Hz). ^{13}C-NMR ($CDCl_3$) δ: 21.1, 25.7, 25.8, 28.9, 44.8, 45.7, 49.8, 50.1, 127.8, 129.0, 135.5, 212.1. HR-MS *m/z*: Calcd for $C_{15}H_{20}OSe$: 296.0679. Found: 296.0655.

4,6,6-Trimethylcyclohex-2-en-1-one (18). A mixture of **17** (3 g, 10 mmol) and MCPBA (77%, 4.5 g, 20 mmol) in CH_2Cl_2 (200 mL) was stirred at rt overnight. After the solvent was removed, the residue was dissolved in ether, and the organic layer was washed with saturated $NaHCO_3$, water, and dried over anhydrous $MgSO_4$. The solvent was removed, and the residue was separated by MPLC with AcOEt: hexane=1:20 as an eluent to give 898 mg (65%) of **18**. bp 86°C /15 mmHg. IR (neat): 1678 cm^{-1}. ^{1}H-NMR ($CDCl_3$) δ: 1.11 (d, 3H, *J*=4.4 Hz), 1.12 (s, 3H), 1.14 (s, 3H), 1.55 (dd, 1H, *J*=11, 13 Hz), 1.82 (ddd, 1H, *J*=1.5, 4.8, 13 Hz), 2.59-2.69 (m, 1H), 5.85 (dd, 1H, *J*=2.5, 10 Hz), 6.67 (dt, 1H, *J*=2, 10 Hz). ^{13}C-NMR ($CDCl_3$) δ: 20.8, 23.9, 25.1, 28.8, 41.4, 45.4, 127.1, 154.3, 204.7. *Anal.* Calcd for $C_9H_{14}O+1/6H_2O$: C, 76.55; H, 10.23. Found: C, 76.58; H, 10.26.

5,7,7-Trimethyloxepane-2,3-dione (19). To a solution of **17** (3 g, 10 mmol) and pyridine (2.4 mL, 30 mmol) in THF (100 mL), 30% H_2O_2 (5 mL) was added under ice-cooling. Then, the mixture was gradually warmed to rt, and stirred overnight. The mixture was extracted with AcOEt, and the extract was washed with brine and dried over anhydrous $MgSO_4$. The solvent was removed, and the residue was separated by MPLC with AcOEt:hexane=1:20 as an eluent to give 593 mg (43%) of **18** and 357 mg (21%) of **19**. mp 81-82°C (from pentane). IR ($CHCl_3$): 1730 cm^{-1}. ^{1}H-NMR ($CDCl_3$) δ: 1.13 (d, 3H, *J*=6.8

Hz), 1.40 (s, 3H), 1.51 (s, 3H), 1.86-2.05 (m, 2H), 2.14-2.24 (m, 1H), 2.44 (t, 1H, *J*=12 Hz), 2.68 (ddd, 1H, *J*=1.5, 3, 11 Hz). ^{13}C-NMR ($CDCl_3$) δ: 22.9, 25.2, 28.2, 32.2, 48.3, 49.5, 83.8, 166.5, 198.1. MS *m/z*: 170 (M^+). *Anal.* Calcd for $C_9H_{14}O_3$: C, 63.49; H, 8.30. Found: C, 63.37; H, 8.43.

2-(1-Hydroxy-4,6,6-trimethylcyclohex-2-enyl)-4,6,6-trimethylcyclohex-2-en-1-one (20). *n*-BuLi (1.5 M solution in hexane, 0.6 mL, 0.86 mmol) was added to a solution of diisopropylamine (0.13 mL, 0.86 mmol) under an argon atmospher at -78°C. After the mixture was stirred for 10 min, **18** (100 mg, 0.72 mmol) was added, and the whole was stirred for 1 h. Then, *N*-phenyltrifluoromethanesulfonimide (310 mg, 0.86 mmol) was added, and the mixture was gradually raised to rt over 1 h. The mixture was extracted with AcOEt, and the extract was washed with brine and dried over anhydrous $MgSO_4$. The solvent was removed and the residue was separated by MPLC with AcOEt:hexane=1:15 as an eluent to give 60 mg (30%) of **20**. mp 135-136°C (from pentane). IR ($CHCl_3$): 3396, 1648 cm^{-1}. ^{1}H-NMR ($CDCl_3$) δ: 0.75 (s, 3H), 0.97 (d, 3H, *J*=7.3 Hz), 1.04 (s, 3H), 1.09 (s, 3H), 1.11 (d, 3H, *J*=7.3 Hz), 1.18 (s, 3H), 1.31 (dd, 1H, *J*=5, 14 Hz), 1.55-1.70 (m, 2H), 1.75-1.80 (m, 1H), 2.24-2.30 (m, 1H), 2.64-2.71 (m, 1H), 5.27 (dd, 1H, *J*=2.5, 10 Hz), 5.68 (d, 1H, *J*=10 Hz), 6.51 (s, 1H), 6.58 (s, 1H). ^{13}C-NMR ($CDCl_3$) δ: 21.0, 21.3, 23.2, 24.4, 25.3, 26.6, 28.0, 28.5, 39.4, 41.8, 43.1, 45.0, 81.0, 131.5, 133.5, 134.8, 155.7, 209.4. MS *m/z*: 276 (M^+). *Anal.* Calcd for $C_{18}H_{28}O_2$: C, 78.20; H, 10.22. Found: C, 78.04; H, 10.34.

4,6,6-Trimethylcyclohexa-1,3-dienyl (Trifluoromethyl)sulfonate (21). Lithium bis(trimethylsilyl)-amide (1 M solution in THF, 8.6 mL, 8.6 mmol) was added to a solution of **18** (1 g, 7.2 mmol) in THF (50 mL) under an argon atmosphere at -15°C, and the whole was stirred for 1 h. After hexamethylphophor-amide (0.6 mL) and *N*-phenyltrifluoromethanesulfonimide (3 g, 8.6 mmol) were added, the mixture was gradually warmed to rt over 1 h. The mixture was extracted with AcOEt, and the extract was washed with brine and dried over anhydrous $MgSO_4$. The solvent was removed and the residue was separated by MPLC with AcOEt: hexane=1:100 as an eluent to give 1.4g (70%) of **21**. bp 102 °C /15 mmHg. ^{1}H-NMR ($CDCl_3$) δ: 1.12 (s, 6H), 1.80 (s, 3H), 2.24 (s, 2H), 5.54-5.56 (m, 1H), 5.80 (d, 1H, *J*=6.4 Hz). ^{13}C-NMR ($CDCl_3$) δ: 22.9, 24.7, 35.0, 46.5, 113.1, 115.8, 136.0, 153.9. *Anal.* Calcd for $C_{10}H_{13}O_3F_3S$: C, 44.44; H, 4.85. Found: C, 44.60; H, 4.84.

***tert*-Butyl 2-[(4,6,6-Trimethylcyclohexa-1,3-dienyl)carbonyl]indole-1-carboxylate (22).** To a solution of **2b**, generated from **1b** (160 mg, 0.73 mmol) in THF (20 mL) under an argon atmosphere, **21** (297 mg,1.1 mmol) and $PdCl_2(PPh_3)_2$ (26 mg, 0.03 mmol) were added at once. Then, carbon monoxide was introduced up to 10 atm, and the mixture was heated at 60°C for 20 h. After cooling, the mixture was treated with 10% NaOH (5 mL) and 30% H_2O_2 (1 mL) under ice-cooling for 10 min. The mixture was extracted with AcOEt, and the extract was washed with brine and dried over anhydrous $MgSO_4$. The solvent was removed and the residue was separated by flash chromatography with AcOEt:hexane =1:25 as an eluent to give 200 mg (75%) of **22**. mp 141-142°C (from MeOH). IR ($CHCl_3$): 1732, 1630 cm^{-1}. ^{1}H-NMR ($CDCl_3$) δ: 1.30 (s, 6H), 1.56 (s, 9H), 1.89 (br s, 3H), 2.16 (br s, 2H), 5.81 (d, 1H, *J*=5.9 Hz), 6.66 (d, 1H, *J*=5.9 Hz), 6.80 (s, 1H), 7.21 (t, 1H, *J*=7.8 Hz), 7.37 (t, 1H, *J*=8.3 Hz), 7.54 (d, 1H, *J*=7.8 Hz), 8.09 (d, 1H, *J*=8.3 Hz). ^{13}C-NMR ($CDCl_3$) δ: 24.0, 25.8, 27.8, 34.4, 46.7, 84.2, 114.6,

114.8, 118.5, 121.9, 123.1, 126.3, 127.7, 137.1, 137.8, 139.3, 142.1, 145.1, 149.5, 188.1. MS *m/z*: 365 (M^+). *Anal.* Calcd for $C_{23}H_{27}NO_3$: C, 75.58; H, 7.45; N, 3.83. Found: C, 75.36; H, 7.58; N, 3.81.

***rel*-(6a*R*, 10a*R*)-6a,7,8,10a -Tetrahydro-7,7,9-trimethylindeno[2,1-*b*]indol-6(5*H*)-one (23).** A mixture of **22** (100 mg) and TFA (1 mL) in CH_2Cl_2 (10 mL) was stirred at rt for 20 h. After 10% NaOH (5 mL) was added to the mixture, the mixture was extracted with AcOEt. The extract was washed with brine and dried over anhydrous $MgSO_4$. The solvent was removed and the residue was separated by flash chromatography with AcOEt:hexane=1:2 as an eluent to give 50 mg (70%) of **23**. mp 234-235°C (from AcOEt-hexane) (lit.,[3s] mp 230-233°C). IR (nujol): 3260, 1658 cm^{-1}. ^{1}H-NMR ($CDCl_3$) δ: 0.91 (s, 3H), 1.30 (s, 3H), 1.70 (br s, 3H), 1.76 (d, 1H, *J*=16 Hz), 1.96 (d, 1H, *J*=16 Hz), 2.89 (d, 1H, *J*=5.9 Hz), 4.05 (br s ,1H), 5.90 (br s, 1H), 7.20 (t, 1H, *J*=7.8 Hz), 7.38 (ddd, 1H, *J*=1, 6.8, 7.8 Hz), 7.45 (d, 1H, *J*=8.3 Hz), 7.80 (d, 1H, *J*=7.8 Hz), 8.63 (br s, 1H). ^{13}C-NMR ($CDCl_3$) δ: 24.1, 24.3, 29.5, 34.3, 36.6, 44.7, 60.4, 114.4, 120.8, 120.9, 122.4, 123.5, 127.1, 133.5, 139.3, 144.5, 146.1, 195.2. MS *m/z*: 265 (M+). *Anal.* Calcd for $C_{18}H_{19}NO$: C, 81.46; H, 7.22; N, 5.28. Found: C, 81.32; H, 7.28; N, 5.13.

Yuehchukene. Diisobutylaluminium hydridre (1 M solution in toluene, 0.4 mL, 0.4 mmol) was added to a solution of **25** (50 mg, 0.19 mmol) in THF (10 mL) at -78°C under an argon atmosphere, and then, the mixture was gradually warmed to rt over 1 h. The mixture was extracted with AcOEt, and the extract was washed with brine and dried over anhydrous $MgSO_4$. The solvent was removed, and the residue was filtered through silica gel, and the filtrate was concentrated to give crude alcohol (**24**), that was used for next reaction without further purification. A mixture of crude **24**, indole (47 mg, 0.4 mmol) and $Eu(OTf)_3$ (12 mg, 0.02 mmol) in THF (10 mL) was stirred at rt for 1 h. The mixture was diluted with AcOEt, and the organic layer was washed with brine and dried over anhydrous $MgSO_4$. The solvent was removed, and the residue was separated by flash chromatography with AcOEt:hexane=1:4 as an eluent to give 42 mg (60%) of **yuehchukene**.[1] amorphous powder. IR ($CHCl_3$): 3476, 3410 cm^{-1}. ^{1}H-NMR ($CDCl_3$) δ: 0.84 (s, 3H), 1.08 (s, 3H), 1.61 (d, 1H, *J*=17 Hz), 1.65 (s, 3H), 2.25 (d, 1H, *J*=17 Hz), 3.13 (t, 1H, *J*=7.8 Hz), 4.00 (br s, 1H), 4.53 (d, 1H, *J*=8.3 Hz), 5.68 (br s, 1H), 6.96-7.12 (m, 5H), 7.16 (t, 1H, *J*=7.3 Hz), 7.31 (d, 1H, *J*=7.8 Hz), 7.37 (br s, 1H), 7.40 (d, 1H, *J*=7.8 Hz), 7.56 (d, 1H, *J*=7.8 Hz), 7.89 (br s, 1H). ^{13}C-NMR ($CDCl_3$) δ: 24.1, 28.9, 29.1, 33.5, 37.5, 38.3, 41.0, 60.8, 111.2, 111.7, 118.2, 118.4, 119.3, 119.5, 120.4, 120.5, 122.0, 122.3, 122.9, 124.2, 126.8, 130.2, 136.4, 140.2, 145.2. HR-MS *m/z*: Calcd for $C_{26}H_{26}N_2$: 366.2096. Found: 366.2114.

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REFERENCES AND NOTES

1. Y. C. Kong, K. F. Cheng, R. C. Cambie, and P.G. Waterman, *J. Chem. Soc., Chem. Commun*., 1985, 47.

2. a) T. W. Leung, G. Cheng, C. H. Chui, S. K. Ho, F. Y. Lau, J. K. Tjong, T. C. Poon, J. C. Tang, W. C. Tse, K. F. Cheng, and K. C. Kong, *Chemotherapy*, 2000, **46**, 62. b) D. C. C. Wong, W. P. Fong, S. S. Lee, Y. C. Kong, K. F. Cheng, and G. Stone, *Eur. J. Pharmacol.*, 1998, **362**, 87. (c) P. C. Ng, D. D. Ho, K. H. Ng, Y. C. Kong, K. F. Cheng, and G. Stone, *Eur. J. Pharmacol.*, 1994, **264**, 1. d) K. F. Cheng, T. T. Wong, K. P. Chan, and Y. C. Kong, *Eur. J. Med. Chem.*, 1992, **27**, 121. e) D. D. Ho, C. P. Lau, K. H. Ng, Y. C. Kong, K. C. Kong, K. F. Cheng, and K. P. Chan, *Eur. J. Pharmacol.*, 1991, **205**, 209. f) M. Hammarstrom, L. Venemalm, J. Bergman, and P. Eneroth, *Am. J. Clin. Med.*, 1990, **18**, 1. g) Y. C. Kong, K. H. Ng, K. H. Wat, A. Wong, I. F. Saxena, K. F. Cheng, P. P. But, and H. T. Chang, *Planta Med*., 1985, **44**, 304. h) F. illequin, M. Koch, M. Bert, and T. Sevenet, *J. Nat. Prod*., 1979, **42**, 92.

3. a) J. Sapi and G. Massiot, " The Chemistry of Heterocyclic Compounds: Bisindole Alkaloids," Supplement to Vol. 25, part 4, ed. by J. E. Saxton, John Wiley & Sons, Ltd., Chichester, 1994, pp. 625-632. b) J. H. Sheu, C. A. Chen, and B. H. Chen, *Chem. Commun*., 1999, 203 c) J. H. Sheu, Y. K. Chen, H. F. Chung, S. F. Lin, and P. J. Sung, *J. Chem. Soc., Perkin Trans. 1*, 1998, 1959. d) K. F. Chen, M. K. Cheung, and Y. C. Kong, *Aust. J. Chem*., 1997, **50**, 349. e) K. F. Cheng, M. K. Cheng, and Y. C. Kong, *Aust. J. Chem*., 1997, **50**, 349. f) J. H. Sheu, Y. K. Chen, H. F. Chung, P. J. Sung, and S. F. Lin, *Heterocycles*, 1996, **43**, 1751. g) K. F. Cheng and M. K. Cheung, *J. Chem. Soc., Perkin Trans. 1,* 1996,1213. h) G. A. Gao and K. F. Cheng, *Synth. Commun*., 1996, **26**, 1525. i) V. Lee, M. K. Cheung, W. T. Wong, and K. F. Cheng, *Tetrahedron*, 1996, **28**, 9455. j) J. H. Sheu, Y. K. Chen, H. F. Chung, P. J. Sung, and S. F. Lin, *Heterocycles*, 1996, **43**, 1751. k) A. R. Katritzky, G. Zhang, L. Xie, and I. Hiviriga, *J. Org. Chem*., 1996, **61**, 7558. l) C. A. Harrison, R. Leineweber, C. J. Moody, and J. M. J. Williams, *J. Chem. Soc., Perkin Trans. 1*, 1995, 1127. m) C. A. Harrison, P. M. Jackson, C. J. Moody, and J. M. J. Williams, *J. Chem. Soc., Perkin Trans. 1*, 1995, 1131. n) J. Bergman and L. Venemalm, *Pure Appl. Chem.*, 1994, **66**, 2331. o) K. F. Cheng, G. A. Gao, Y. W. Yu, and Y. C. Kong, *Synth. Commun*., 1994, **24**, 65. p) J. H. Sheu, Y. K. Chen, and Y. L. V. Hong, *J. Org. Chem*., 1993, **58**, 5784. q) J. Bergman and L. Venemalm, *Tetrahedron*, 1992, **48**, 759. r) J. H. Sheu, Y. K. Chen, and Y. L. V. Hong, *Tetrahedron Lett*., 1991, **32**, 1045. s) J. P. Kutney, F. J. Lopez, S. P. Huang, H. Kurobe, R. Flogaus, K. Piotrowska, and S. J. Rettig, *Can. J. Chem*., 1991, **69**, 949. t) J. Bergman and L. Venemalm, *Tetrahedtron*, 1990, **46**, 6067. u) J. P. Kutney, F. J. Lopez, S. P. Huang, and H. Kurobe, *Heterocycles*,1989, **28**, 565. v) J. Bergman and L. Venemalm, *Tetrahedron Lett.*, 1988, **29**, 2993. w) K. F. Cheng, Y. C. Kong, and T. Y. Chan, *J. Chem. Soc., Chem. Commun.*, 1985, 48.

4. a) M. Ishikura, A. Hino, T. Yaginuma, I. Agata, and N. Katagiri, *Tetrahedron*, 2000, **56**, 193. b) M. Ishikura and I. Agata, *Recent Res. Devel. in Organic Chem*., 1997, **1**, 145. c) M. Ishikura, *Yuki Gosei Kagaku Kyokaishi,* 1995, **53**, 308.

5. M. Ishikura and M. Terashima, *J. Org. Chem.*, 1994, **59**, 2634.

6. a) M. Ishikura, *Heterocycles*, 1995, **41**, 1385. b) M. Ishikura, K. Imaizumi, and N. Katagiri, *Heterocycles*, 2000, **53**, 553.

7. a) D. L. Comins and A. Dehghani, *Tetrahedron Lett*., 1992, **33**, 6299. b) G. T. Crisp and A. G. Meyer, *J. Org. Chem*., 1992, **57**, 6972. c) J. E. MuMurry and W. J. Scott, *Tetrahedron Lett.*, 1983, **24**, 979.
8. M. Ishikura, Y. Matsuzaki, I. Agata, and N. Katagiri, *Tetrahedron*, 1998, **54**, 13929.
9. The stereochemistry of **5b** and **5b'** was determined based on NOE experiments.[5] A distinctive enhancement of 6a-H and 9-H upon irradiation of 10a-H in **5b'**.
10. R. D. Little, M. R. Masjedizadeh, O. Wallquist, and J. I. McLoughlin, *Organic Reactions*, 1995, **47**, 315.
11. The two directions of the addition can occur on the same (β-addition) and opposite sides (α-addition) of the *tert*-Bu group. In view of the hindered nature of the *tert*-Bu group (Fig.), it is conceivable that the spatial repulsion between the indole ring and *tert*-Bu group renders the β-addition slow relative to the α-addition.

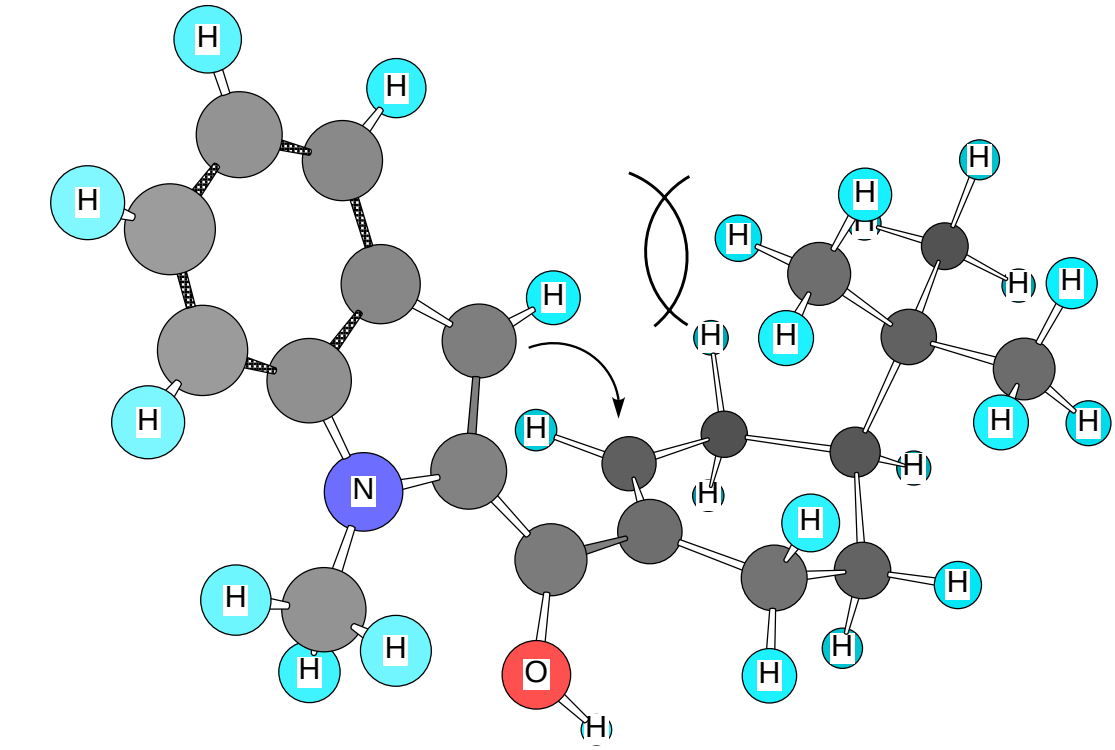
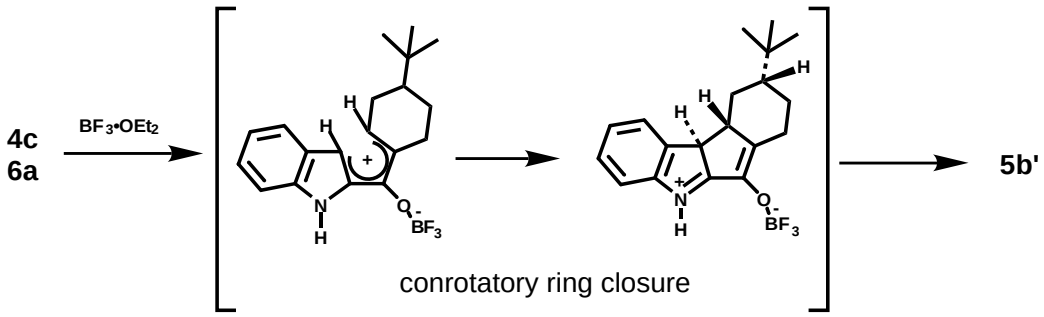


Figure Schematic representation of intramolecular Michael addition
Structure (**A**) was optimized by calculation using WinMOPAC3, Fujitsu, Ltd.

12. K. L. Habermas, S. E. Denmark, and T. K. Jones, *Organic Reactions*, 1994, **45**, 1.
13. Formation of **5b'** *via* cyclopentadienyl cation.



14. G. M. Rubotton, J. M. Gruber, H. D. Juve Jr., and D. A. Charleson, *Org. Synth*., 1990, Col. Vol. **7**, 282.
15. H. J. Reich, J. M. Renga , and I. L. Reich, *J. Am. Chem. Soc*., 1975, **97**, 5434.