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Efficient Entry into 2-Substituted Tetrahydroquinoline Systems through Alkylative Ring Expansion: Stereoselective Formal Synthesis of (±)-Martinellic Acid

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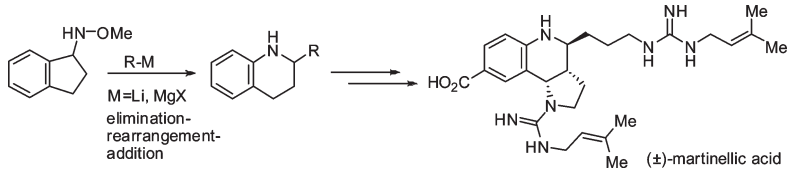

A new efficient synthesis of 2-substituted tetrahydroquinolines has been achieved by the domino reaction of *N*-indanyl(methoxy)amines, which consists of three types of reactions: elimination of an alcohol, the rearrangement of an aryl group, and the addition of an organolithium or magnesium reagent. The synthetic utility of this approach is demonstrated by the stereoselective formal synthesis of (±)- martinellic acid.

Introduction

2-Substituted tetrahydroquinoline moieties are frequently found in biologically active molecules.[1] Several of these compounds are naturally occurring. Dynemicin, a natural antitumor antibiotic, has a complex structure built on the tetrahydroquinoline system. Simple 2-alkyl and 2-arylethyl tetrahydroquinolines have been isolated from *Galipea officinalis*; a reputed folk medicine known for its multiple healing properties.[2] Perhaps the most well-known examples that comprise this molecular structure are the Martinella alkaloids, martinelline, and martinellic acid, which exhibit activities as bradykinin receptor antagonists.[3] Many relatively simple synthetic 2-substituted tetrahydroquinolines are already used or have been tested as potential drugs. Consequently, 2-substituted tetrahydroquinolines have been a significant subject of synthetic studies of biologically active compounds. In constructing the 2-substituted tetrahydroquinoline, many synthetic methods have been reported, including the hetero-Diels−Alder reaction,[4] substituent introduction to quinoline,[5] electrophilic cyclization,[6] and palladium-catalyzed annulations.[7,8]

We have developed a new methodology for the construction of 2-substituted tetrahydroquinolines from *N*-indanyl(methoxy)amines. This route involves a domino process via the elimination of methanol, rearrangement of a metal arylmethylamide, and subsequent addition of Grignard or organolithium reagents to an intermediary imine. The method described herein was successively applied to the stereoselective synthesis of a key intermediate used in the synthesis of

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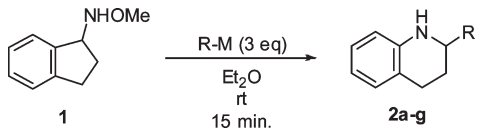
TABLE 1. Reaction of *N*-Indanyl(methoxy)amine with R-M[a]



entry	R-M	product	yield (%)[b]
1	*n*-BuLi	**2a** (R = *n*-Bu)	64
2	PhLi	**2b** (R = Ph)	68
3	EtMgBr	**2c** (R = Et)	34
4	PhMgBr	**2b** (R = Ph)	84
5	allylMgBr	**2d** (R = allyl)	92
6	$PhCH_2MgBr$	**2e** (R = CH_2Ph)	82
7	*p*-MeC_6H_4MgBr	**2f** (R = *p*-MeC_6H_4)	84
8	*p*-ClC_6H_4MgBr	**2g** (R = *p*-ClC_6H_4)	81

[a]Reaction conditions: **1** (0.3 mmol), RM (0.9 mmol) in Et_2O (6 mL) at rt. [b]Isolated yield

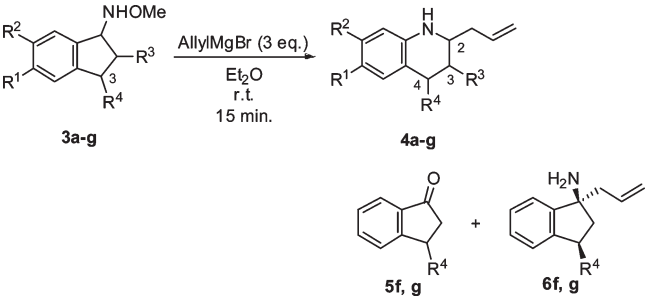
martinellic acid. We have previously demonstrated that the domino reaction of *N*-benzylalkoxyamines with Grignard or organolithium reagents gave aniline derivatives bearing a branched alkyl group.[9] In related works, the reaction of *N*-indanyl(alkoxy)amines or indanone oximes with $LiAlH_4$ or DIBALH gives rise to a reductive ring expansion that results in the formation of the tetrahydroquinoline.[10] Additionally, Yamamoto's group has reported that the organoaluminum-promoted Beckmann rearrangement of oxime sulfonate followed by either alkylation or reduction gave nitrogen-containing heterocycles.[11] This method was applied to the preparation of tetrahydroquinoline.

Results and Discussion

We first investigated the domino reaction of *N*-indanyl-(methoxy)amines **1** as preliminary experiments (Table 1). The reaction of indanylamine **1** with 3 equiv of *n*-BuLi proceeded smoothly in Et_2O at room temperature within 15 min to give the desired 2-*n*-butyltetrahydroquinoline **2a** in 64% yield (entry 1). Similarly, phenyllithium gave the corresponding product (entry 2). The treatment of **1** with either phenyl or allyl magnesium bromide afforded the desired 2-substituted tetrahydroquinolines **2b** and **2d** in 84% and 92% yields, respectively (entries 4 and 5), while 2-ethyltetrahydroquinoline **2c** was obtained in low yield (entry 3). Benzyl and *p*-substituted phenyl magnesium bromide also worked well to furnish the desired products **2e**−**g** in good yields (entries 6−8). This observation deserves particular attention, because tetrahydroquinolines carrying various substituents can be effectively synthesized in short reaction time.

To further study the scope and limitations of this process, we investigated the substituent effects in the domino reaction of *N*-indanyl(methoxy)amines **3a**−**g** with allylmagnesium bromide (Table 2). 5-Substituted indanylamines **3a**−**c** bearing electron-donating or -withdrawing groups afforded the corresponding 2-allyltetrahydroquinolines **4a**−**c** in good yields (entries 1−3). Similar results were achieved with

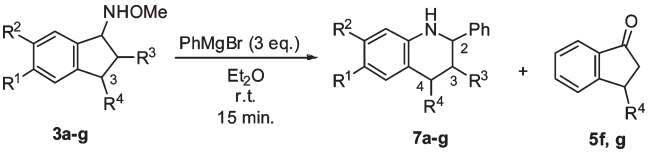
TABLE 2. Reaction of *N*-Indanyl(methoxy)amines 3a−g with AllylMgBr[a]



						yield (%)[b]		
entry	substrate	R^1	R^2	R^3	R^4	**4**	**5**	**6**
1	**3a**	OMe	H	H	H	83		
2	**3b**	Cl	H	H	H	81		
3	**3c**[c]	OH	H	H	H	81		
4	**3d**	H	Me	H	H	83		
5	**3e**[d]	H	H	Me	H	71[e]		
6	**3f**[d]	H	H	H	Me	30[f]	8	26
7	**3g**[d]	H	H	H	Ph	14[g]	8	40

[a]Reaction conditions: **3** (0.3 mmol), allylMgBr (0.9 mmol) in Et_2O (6 mL) at rt. [b]Isolated yield. [c]allylMgBr (1.2 mmol) was used. [d]Cis isomer of **3e**−**g** was used. [e]Cis/trans = 1/2.7. [f]Cis/trans = 1/3.0. [g]Cis/trans = 1/3.0.

TABLE 3. Reaction of *N*-Indanyl(methoxy)amines 3a−g with PhMgBr[a]



						yield (%)[b]	
entry	substrate	R^1	R^2	R^3	R^4	**7**	**5**
1	**3a**	OMe	H	H	H	89	
2	**3b**	Cl	H	H	H	84	
3	**3c**[c]	OH	H	H	H	87	
4	**3d**	H	Me	H	H	81	
5	**3e**[d]	H	H	Me	H	81[e]	
6	**3f**[d]	H	H	H	Me	33[f]	11
7	**3g**[d]	H	H	H	Ph	18[f]	18

[a]Reaction conditions: **3** (0.3 mmol), PhMgBr (0.9 mmol) in Et_2O (6 mL) at rt. [b]Isolated yield. [c]allylMgBr (1.2 mmol) was used. [d]Cis isomer of **3e**−**g** was used. [e]Cis/trans = 1/12. [f]Trans isomer was selectively obtained.

6- or 2-methylindanylamines **3d** and **3e** (entries 4 and 5). However, indanylamines **3f** and **3g** bearing the methyl or phenyl group at the 3-position gave the 4-substituted tetrahydroquinolines **4** in low yields, accompanied by indanones **5** and indanylamines **6** as side products (entries 6 and 7). It is noteworthy that the protection of the hydroxyl group is not necessary for this reaction system (entry 3).

We next investigated the domino reaction of *N*-indanyl-(methoxy)amines **3a**−**g** with phenylmagnesium bromide. It is one of the advantages that this reaction can introduce directly the aryl group into the 2-position of quinoline nucleus. As shown in Table 3, these reactions proceeded

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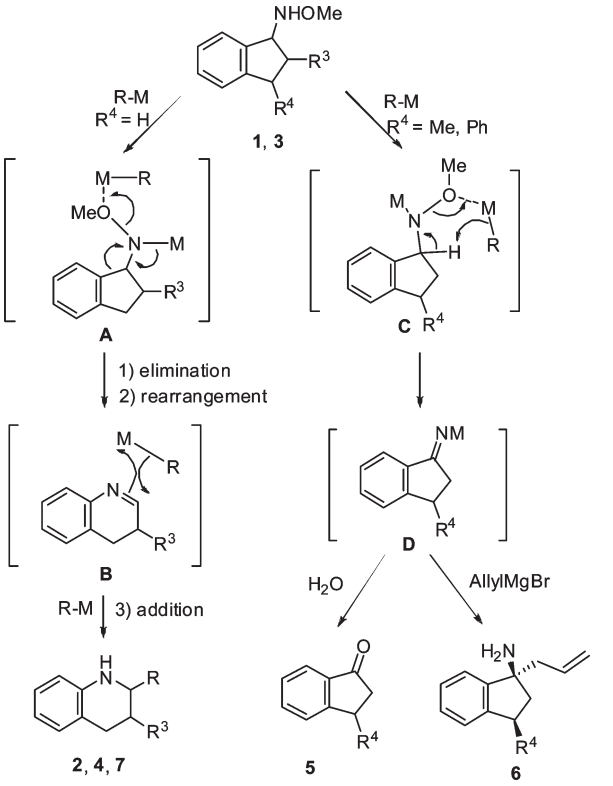
SCHEME 1. Possible Reaction Pathway

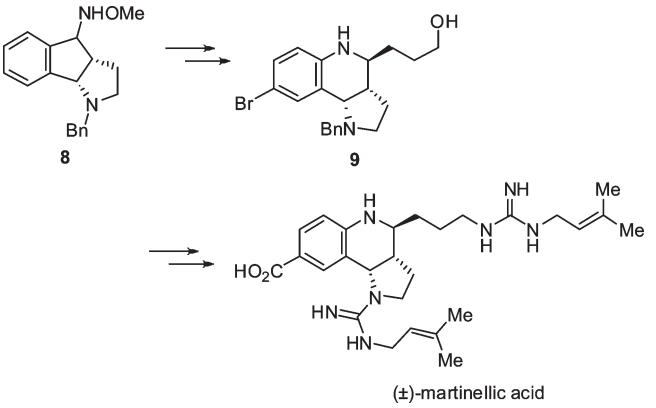


effectively to give **7a**−**g** in good yields except for 3-substituted indanylamine **3f** and **3g**.

According to our previous report on the domino reaction,[9a] we propose the possible reaction pathway as shown in Scheme 1. Initially, *N*-indanyl(methoxy)amines **1** and **3** are chelated with organolithium or Grignard reagent to generate the intermediate **A** that is converted into the imines **B** via elimination of an alkoxy group and rearrangement of an aryl group. Finally, the addition of organolithium and magnesium reagents to the imines **B** would produce 2-substituted tetrahydroquinolines **2**, **4**, and **7**. In the case of indanylamines **3f** and **3g**, the Grignard reagent would possibly attack the benzyl proton to generate the intermediate **D**, which should undergo hydrolysis to give the indanones **5**. On the other hand, the allylation of **D** could yield amino indanes **6** carrying an allyl group. Although it seems reasonable to speculate that **5** and **6** would be obtained via the route shown in Scheme 1, we are currently unable to offer a detailed explanation of the influence of the 3-substituent on this domino reaction.

To demonstrate the synthetic utility of the alkylative ring expansion, we performed an efficient formal synthesis of (±)-martinellic acid. Over the past decade, considerable effort has been devoted to the synthesis of the martinella alkaloids.[12] The pyrrolo[3,2-*c*]quinoline core of the martinella alkaloids has been prepared by several synthetic routes. Furthermore, asymmetric total synthesis of martinellines was reported by several groups.[13−16] As part of our studies

SCHEME 2. Synthetic Strategy



on the stannyl radical addition−cyclization reactions of imine derivatives, we have recently developed an asymmetric total synthesis of martinellic acid based on the RACE reaction of a chiral oxime ether.[17] However, these synthetic methods have unsatisfactory chemical yields and stereoselectivity. We have focused our efforts on the stereoselective synthesis of martinellic acid and investigated the domino reaction of tricyclic methoxyamine **8** leading to a key intermediate **9** reported by Snider and co-workers (Scheme 2).[18]

Snider succeeded in the synthesis of (±)-martinellic acid via an intermediate **9** using [3+2] dipolar cycloaddition of an azomethineylide as a key reaction.[18] However, [3+2] dipolar cycloaddition gave the undesired stereoisomer (3%), in addition to the desired 3a,4-*trans*-3a,9b-*cis*-product (57%). Recently, Lovely has reported the synthesis of (−)-martinellic acid by a similar route. Similarly, in the dipolar cycloaddition, the undesired stereoisomer was obtained as a side product (9%).[16] The tricyclic methoxyamine **8** for the domino reaction was prepared from commercially available acetal **10** (Scheme 3). Lithiation of bromoacetal **10** with *n*-BuLi and subsequent treatment with DMF gave 93% of aldehyde **11**, which was subjected to vinylation with vinylmagnesium bromide and acetylation of the resulting allyl alcohol providing **12** in 85% yield. Treatment of **12** with 10% HCl in EtOH afforded aldehyde **13**. Condensation of **13** with *N*-benzylglycine hydrochloride generated azomethine yilide, which spontaneously underwent [3+2] cycloaddition to give indenopyrrolidine **14** in 78% yield. Hydrolysis of acetate, oxidation of alcohol with MnO_2, and condensation with *O*-methylhydroxyamine hydrochloride furnished oxime ether **17**. Finally, stereoselective reduction of oxime moiety was accomplished by borane−pyridine complex and tricyclic methoxyamine **8** in 36% (99% brsm).

With the substrate for key reaction in hand, we next investigated the domino reaction of **8** with allylmagnesium bromide (Scheme 4). As expected, the reaction proceeded smoothly and stereoselectively in 30 min to give the desired pyrroloquinoline **18** in 94% yield as a sole product. The high stereoselectivity of this reaction is explained by the allylation from the less hindered convex face of the *cis*-pyrroloquinoline intermediate **E**. The bromination of **18** followed by hydroboration−oxidation of the resulting

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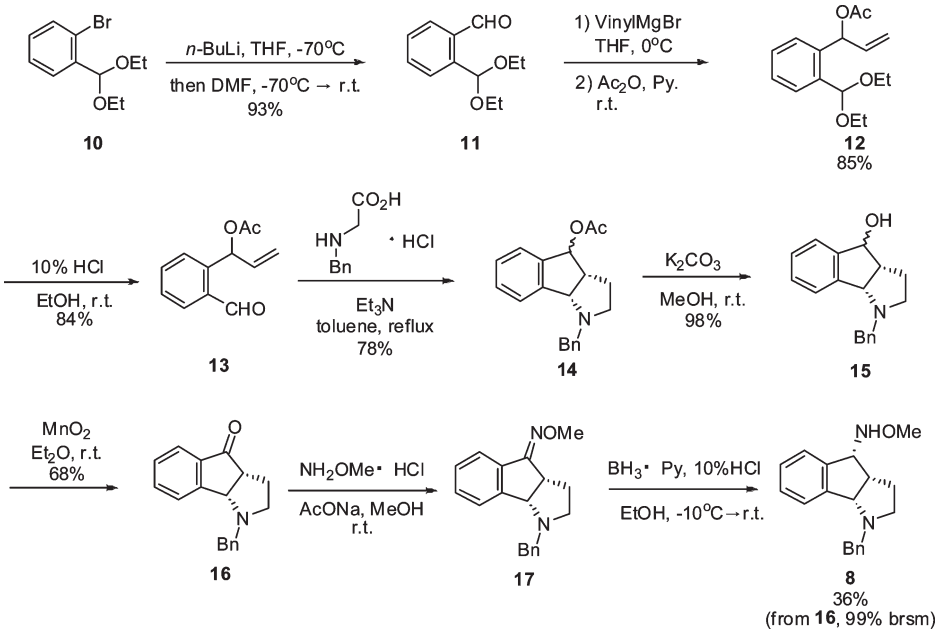
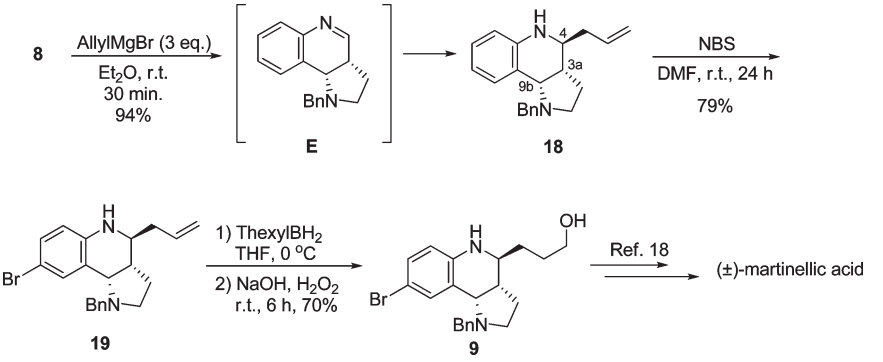
(18) Snider, B. B.; Ahn, Y.; O'Hare, S. M. *Org. Lett.* **2001**, *3*, 4217.

SCHEME 3. Synthesis of Tricyclic Methoxyamine 8



SCHEME 4. Formal Synthesis of (±)-Martinellic Acid



bromide **19** afforded pyrrolo[3,2-*c*]quinoline **9**, which is a key intermediate used in the synthesis of (±)-martinellic acid.

Conclusions

We have shown that the domino elimination−rearrangement−addition reaction of *N*-indanyl(methoxy)-amines proceeds smoothly to give the tetrahydroquinolines bearing various types of substituents. Furthermore, we have succeeded in the stereoselective formal synthesis of (±)-martinellic acid.

Experimental Section

General. Melting points are uncorrected. ^{1}H and ^{13}C NMR spectra were recorded at 300 or 500 MHz and at 75 or 125 MHz, respectively. IR spectra were recorded with FTIR apparatus. Mass spectra were obtained by EI or CI methods. Medium-pressure column chromatography (MCC) was performed with Lobar grösse B (E. Merck 310−25, Lichroprep Si60). Preparative TLC separations (PTLC) were carried out on precoated silica gel plates (E. Merck 60F_{254}). All the reagents and solvents were used as received from the manufacturer.

General Procedure for Domino Elimination−Rearrangement−Addition Reaction of 1-(Methoxyamino)indan (1) with Organometallic Reagents. To a solution of **1** (49 mg, 0.3 mmol) in Et_2O (6.0 mL) was added organometallic reagent (0.9 mmol) under an argon atmosphere at room temperature. After being stirred at the same temperature for 15 min, the reaction mixture was diluted with H_2O and extracted with $CHCl_3$. The organic phase was dried over $MgSO_4$ and concentrated under reduced pressure. Purification of the residue by PTLC (hexane:AcOEt = 5:1) afforded tetrahydroquinolines **2a**−**g**.

2-Butyl-1,2,3,4-tetrahydroquinoline (2a).[19] A colorless oil. IR (neat): 3408 cm^{-1}. ^{1}H NMR (300 MHz, $CDCl_3$): δ 6.95 (1H, br t, J = 8.0 Hz), 6.94 (1H, br d, J = 8.0 Hz), 6.59 (1H, td, J = 8.0, 1.0 Hz), 6.46 (1H, dd, J = 8.0, 1.0 Hz), 3.60 (1H, br s), 3.27−3.18 (1H, m), 2.81 (1H, ddd, J = 16.0, 11.0, 5.5 Hz), 2.71 (1H, dt, J = 16.0, 5.5 Hz), 2.00−1.91 (2H, m), 1.65−1.31 (6H, m), 0.93 (3H, t, J = 7.0 Hz). ^{13}C NMR (75 MHz, $CDCl_3$): δ 144.7, 129.2, 126.6, 121.4, 116.8, 114.0, 51.6, 36.4, 28.1, 27.9, 26.4, 22.8, 14.1. HRMS m/z: calcd for $C_{13}H_{19}N$ (M^+) 189.1516, found 189.1529.

1,2,3,4-Tetrahydro-2-phenylquinoline (2b).[19] A colorless oil. IR (neat): 3402 cm^{-1}. ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.57−7.21

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(5H, m), 6.97 (1H, br t, J = 8.0 Hz), 6.96 (1H, br d, J = 8.0 Hz), 6.64 (1H, br t, J = 8.0 Hz), 6.52 (1H, br d, J = 8.0 Hz), 4.42 (1H, dd, J = 9.0, 3.5 Hz), 4.00 (1H, br s), 2.91 (1H, br ddd, J = 16.0, 10.0, 5.5 Hz), 2.71 (1H, br dt, J = 16.0, 5.5 Hz), 2.18−1.93 (2H, m). ^{13}C NMR (75 MHz, $CDCl_3$): δ 144.7, 144.6, 129.2, 128.5, 127.3, 126.8, 126.4, 120.7, 117.0, 113.9, 56.1, 30.9, 26.2. HRMS m/z: calcd for $C_{15}H_{15}N$ (M^+) 209.1203, found 209.1203.

2-Ethyl-1,2,3,4-tetrahydroquinoline (2c).[20] A colorless oil. IR (neat): 3402 cm^{-1}. ^{1}H NMR (300 MHz, $CDCl_3$): δ 6.96 (1H, br t, J = 8.0 Hz), 6.95 (1H, br d, J = 8.0 Hz), 6.60 (1H, br t, J = 8.0 Hz), 6.50 (1H, br d, J = 8.0 Hz), 3.21−3.13 (1H, m), 2.87−2.68 (2H, m), 2.02−1.93 (1H, m), 1.66−1.49 (3H, m), 0.99 (3H, t, J = 7.0 Hz). ^{13}C NMR (75 MHz, $CDCl_3$): δ 129.2, 126.7, 121.4, 116.9, 114.0, 53.0, 29.4, 27.6, 26.4, 10.0. HRMS m/z: calcd for $C_{11}H_{15}N$ (M^+) 161.1204, found 161.1211.

1,2,3,4-Tetrahydro-2-(2-propenyl)quinoline (2d).[21] A colorless oil. IR (neat): 3402 cm^{-1}. ^{1}H NMR (300 MHz, $CDCl_3$): δ 6.95 (1H, br t, J = 8.0 Hz), 6.94 (1H, br d, J = 8.0 Hz), 6.60 (1H, br t, J = 8.0 Hz), 6.46 (1H, br d, J = 8.0 Hz), 5.93−5.73 (1H, m), 5.16 (1H, br d, J = 17.0 Hz), 5.15 (1H, br d, J = 11.0 Hz), 3.78 (1H, br s), 3.36−3.23 (1H, m), 2.92−2.74 (2H, m), 2.40−2.09 (2H, m), 2.03−1.90 (1H, m), 1.73−1.59 (1H, m). ^{13}C NMR (75 MHz, $CDCl_3$): δ 144.5, 134.9, 129.2, 126.7, 121.2, 117.9, 117.0, 114.0, 50.4, 41.1, 28.2, 26.4. HRMS m/z: calcd for $C_{12}H_{15}N$ (M^+) 173.1204, found 173.1204.

1,2,3,4-Tetrahydro-2-(phenylmethyl)quinoline (2e).[22] A colorless oil. IR (neat): 3408 cm^{-1}. ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.37−7.20 (5H, m), 6.97−6.89 (2H, m), 6.59 (1H, br t, J = 7.5 Hz), 6.39 (1H, br d, J = 7.8 Hz), 3.73 (1H, br s), 3.50 (1H, tdd, J = 8.7, 5.1, 2.7 Hz), 2.89−2.65 (4H, m), 2.07−1.96 (1H, m), 1.79−1.64 (1H, m). ^{13}C NMR (75 MHz, $CDCl_3$): δ 144.3, 138.5, 129.2, 128.6, 126.7, 126.5, 121.2, 117.1, 114.2, 52.6, 43.0, 28.2, 26.1. HRMS m/z: calcd for $C_{16}H_{17}N$ (M^+) 223.1360, found 223.1371.

1,2,3,4-Tetrahydro-2-(4-methylphenyl)quinoline (2f).[23] A colorless oil. IR (neat): 3415 cm^{-1}. ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.30−7.23 (2H, m), 7.15 (2H, br d, J = 5.1 Hz), 7.08−6.96 (2H, m), 6.64 (1H, br t, J = 7.2 Hz), 6.52 (1H, br d, J = 7.8 Hz), 4.39 (1H, dd, J = 9.3, 3.3 Hz), 3.99 (1H, br s), 2.92 (1H, ddd, J = 16.2, 10.2, 5.4 Hz), 2.73 (1H, dt, J = 16.3, 4.8 Hz), 2.35 (3H, s) 2.14−1.90 (2H, m). ^{13}C NMR (75 MHz, $CDCl_3$): δ 144.8, 141.8, 137.0, 129.24, 129.19, 126.8, 126.4, 120.8, 117.0, 113.9, 56.0, 31.0, 26.5, 21.0. HRMS m/z: calcd for $C_{16}H_{17}N$ (M^+) 223.1361, found 223.150.

1,2,3,4-Tetrahydro-2-(4-chlorophenyl)quinoline (2g).[24] A colorless oil. IR (neat): 3410 cm^{-1}. ^{1}H NMR (300 Hz, $CDCl_3$): δ 7.35−7.27 (4H, m), 7.05−6.97 (2H, m), 6.66 (1H, br t, J = 7.5 Hz), 6.55 (1H, br d, J = 7.8 Hz), 4.42 (1H, br dd, J = 9.0, 3,0 Hz), 4.00 (1H, br s), 2.91 (1H, ddd, J = 16.2, 10.2, 5.1 Hz), 2.71 (1H, dt, J = 16.2, 5.1 Hz), 2.15−2.03 (1H, m), 2.01−1.87 (1H, m). ^{13}C NMR (75 MHz, $CDCl_3$): δ 144.4, 143.3, 132.9, 129.3, 128.6, 127.9, 126.9, 120.8, 117.4, 114.0, 55.5, 30.9, 26.1. HRMS m/z: calcd for $C_{15}H_{14}{}^{35}ClN$ (M^+) 243.0814, found 243.0820.

General Procedure for Domino Elimination−Rearrangement−Addition Reaction of 1-(Methoxyamino)indans with AllylMgBr. To a solution of **3a−g** (0.3 mmol) in Et_2O (6.0 mL) was added allylmagnesium bomide (1 mol/L in THF, 0.9 mL, 0.9 mmol) under an argon atmosphere at room temperature. After being stirred at the same temperature for 15 min, the reaction mixture was diluted with H_2O and extracted with $CHCl_3$. The organic phase was dried over $MgSO_4$ and concentrated under reduced pressure. Purification of the residue by PTLC (hexane:AcOEt = 5:1 or 2:1) afforded **4a−g**, **5f**, **5g**, **6f**, and **6g**.

1,2,3,4-Tetrahydro-6-methoxy-2-(2-propenyl)quinoline (4a). A colorless oil. IR (neat): 3398 cm^{-1}. ^{1}H NMR (300 MHz, $CDCl_3$): δ 6.59 (1H, br d, J = 8.0 Hz), 6.57 (1H, br s), 6.44 (1H, d, J = 8.0 Hz), 5.90−5.76 (1H, m), 5.16 (1H, br d, J = 17.5 Hz), 5.14 (1H, br d, J = 9.5 Hz), 3.72 (3H, s), 3.28−3.19 (1H, m), 2.84 (1H, ddd, J = 17.0, 11.0, 6.0 Hz), 2.76−2.67 (1H, m), 2.37−2.28 (1H, m), 2.23−2.13 (1H, m), 2.00−1.92 (1H, m), 1.69−1.56 (1H, m). ^{13}C NMR (75 MHz, $CDCl_3$) δ 151.8, 138.5, 135.0, 122.5, 117.8, 115.2, 114.5, 112.8, 55.7, 50.8, 41.0, 28.3, 26.6. HRMS m/z: calcd for $C_{13}H_{17}NO$ (M^+) 203.1310, found 203.1314.

6-Chloro-1,2,3,4-tetrahydro-2-(2-propenyl)quinoline (4b). A colorless oil. IR (neat): 3413 cm^{-1}. ^{1}H NMR (300 MHz, $CDCl_3$): δ 6.91 (1H, br s), 6.90 (1H, br d, J = 8.0 Hz), 6.38 (1H, d, J = 8.0 Hz), 5.88−5.74 (1H, m), 5.16 (1H, br d, J = 15.5 Hz), 5.15 (1H, br d, J = 11.0 Hz), 3.87 (1H, br s), 3.32−3.23 (1H, m), 2.85−2.65 (2H, m), 2.38−2.29 (1H, m), 2.21−2.11 (1H, m), 1.99−1.91 (1H, m), 1.66−1.53 (1H, m). ^{13}C NMR (75 MHz, $CDCl_3$): δ 143.0, 134.7, 128.7, 126.5, 122.6, 121.2, 118.1, 114.9, 50.4, 40.9, 27.7, 26.2. HRMS m/z: calcd for $C_{12}H_{14}{}^{35}ClN$ (M^+) 207.0814, found 207.0821.

1,2,3,4-Tetrahydro-2-(2-propenyl)-6-quinolinol (4c). A colorless oil. IR (neat): 3602, 3367 cm^{-1}. ^{1}H NMR (300 MHz, $CDCl_3$): δ 6.49 (1H, br d, J = 8.0 Hz), 6.48 (1H, br s), 6.39 (1H, br d, J = 8.0 Hz), 5.89−5.75 (1H, m), 5.15 (1H, br d, J = 17.5 Hz), 5.14 (1H, br d, J = 9.5 Hz), 3.95 (1H, br s), 3.23−3.20 (1H, m), 2.80 (1H, ddd, J = 16.5, 11.0, 5.5 Hz), 2.67 (1H, dt, J = 16.5, 5.5 Hz), 2.36−2.28 (1H, m), 2.22−2.12 (1H, m), 1.98−1.90 (1H, m), 1.68−1.55 (1H, m). ^{13}C NMR (75 MHz, $CDCl_3$): δ 147.5, 138.4, 135.0, 123.1, 117.9, 116.0, 115.6, 113.9, 50.9, 41.0, 28.3, 26.5. HRMS m/z: calcd for $C_{12}H_{15}NO$ (M^+) 189.1153, found 189.1153.

1,2,3,4-Tetrahydro-7-methyl-2-(2-propenyl)quinoline (4d). A colorless oil. IR (neat): 3402 cm^{-1}. ^{1}H NMR (300 MHz, $CDCl_3$): δ 6.83 (1H, d, J = 7.5 Hz), 6.42 (1H, br d, J = 7.5 Hz), 6.30 (1H, br s), 5.88−5.74 (1H, m), 5.15 (1H, br d, J = 17.5 Hz), 5.14 (1H, br d, J = 10.0 Hz), 3.61 (1H, s), 3.30−3.22 (1H, m), 2.83−2.64 (2H, m), 2.41−2.10 (2H, m), 2.20 (3H, s), 1.98−1.89 (1H, m), 1.67−1.54 (1H, m). ^{13}C NMR (75 MHz, $CDCl_3$): δ 144.3, 136.3, 135.0, 129.0, 118.2, 117.9, 117.8, 114.6, 50.4, 41.1, 28.3, 26.0, 21.0. HRMS m/z: calcd for $C_{13}H_{17}N$ (M^+) 187.1360, found 187.1360.

***cis*-1,2,3,4-Tetrahydro-3-methyl-2-(2-propenyl)quinoline (4e).** A colorless oil. IR (neat): 3410 cm^{-1}. ^{1}H NMR (300 MHz, $CDCl_3$): δ 6.95 (1H, br t, J = 7.5 Hz), 6.94 (1H, br d, J = 7.5 Hz), 6.60 (1H, br t, J = 7.5 Hz), 6.46 (1H, br d, J = 7.5 Hz), 5.88−5.74 (1H, m), 5.15 (1H, br d, J = 16.0 Hz), 5.14 (1H, br d, J = 11.5 Hz), 3.38−3.21 (1H, m), 2.95 (1H, dd, J = 16.0, 6.5 Hz), 2.47 (1H, dd, J = 16.0, 5.5 Hz), 2.30−2.22 (1H, m), 2.17−2.07 (2H, m), 0.94 (3H, d, J = 7.0 Hz). ^{13}C NMR (75 MHz, $CDCl_3$): δ 143.8, 135.5, 129.8, 126.6, 120.2, 117.8, 117.1, 113.9, 53.6, 36.8, 34.5, 29.7, 14.1. HRMS m/z: calcd for $C_{13}H_{17}N$ (M^+) 187.1360, found 187.1363.

***trans*-1,2,3,4-Tetrahydro-3-methyl-2-(2-propenyl)quinoline (4e).** A colorless oil. IR (neat): 3410 cm^{-1}. ^{1}H NMR (300 MHz, $CDCl_3$): δ 6.95 (1H, br t, J = 7.5 Hz), 6.94 (1H, br d, J = 7.5 Hz), 6.59 (1H, br t, J = 7.5 Hz), 6.46 (1H, br d, J = 7.5 Hz), 5.89−5.75 (1H, m), 5.18 (1H, br d, J = 15.0 Hz), 5.14 (1H, br d, J = 10.0 Hz), 3.96 (1H, br s), 2.94 (1H, td, J = 8.0, 3.5 Hz), 2.75 (1H, dd, J = 15.0, 4.5 Hz), 2.54−2.44 (2H, m), 2.07 (1H, dt, J = 13.0, 8.0 Hz), 1.87−1.70 (1H, m), 1.03 (3H, d, J = 6.5 Hz). ^{13}C NMR (75 MHz, $CDCl_3$): δ 144.0, 135.1, 129.0, 126.7, 120.8, 118.2, 116.7, 113.5, 56.0, 38.8, 35.0, 31.3, 18.2. HRMS m/z: calcd for $C_{13}H_{17}N$ (M^+) 187.1360, found 187.1379.

1,2,3,4-Tetrahydro-4-methyl-2-(2-propenyl)quinoline (4f). The *cis*-**4f** and *trans*-**4f** were inseparable (*cis*:*trans* = 1:3). A colorless

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oil. IR (neat): 3402 cm^{-1}. ^1H NMR (300 MHz, $CDCl_3$): δ 7.12 (1/4H, br d, J = 8.0 Hz), 7.02 (3/4H, br d, J = 8.0 Hz), 6.96 (1H, br t, J = 8.0 Hz), 6.65 (1/4H, br t, J = 8.0 Hz), 6.62 (3/4H, br t, J = 8.0 Hz), 6.48 (3/4H, br d, J = 8.0 Hz), 6.46 (1/4H, br d, J = 8.0 Hz), 5.92−5.75 (1H, m), 5.17 (1H, br d, J = 17.5 Hz), 5.16 (1H, br d, J = 10.0 Hz), 3.94 (1H, br s), 3.42−3.31 (1H, m), 3.00−2.88 (1H, m), 2.39−2.25 (1H, m), 2.22−2.12 (1H, m), 1.97 (2/4H, ddd, J = 13.0, 6.0, 3.0 Hz), 1.71−1.67 (6/4H, m), 1.32 (3/4H, d, J = 7.0 Hz), 1.27 (9/4H, d, J = 7.0 Hz). ^{13}C NMR (75 MHz, $CDCl_3$): δ 143.8, 135.0, 134.9, 129.0, 126.8, 126.7, 126.5, 118.0, 117.9, 117.2, 117.0, 114.1, 113.9, 50.6, 45.9, 41.5, 41.3, 38.6, 35.3, 30.8, 30.0, 24.6, 20.2. HRMS m/z: calcd for $C_{13}H_{17}N$ (M^+) 187.1360, found 187.1370.

(1α,3α)-2,3-Dihydro-3-methyl-2-(2-propenyl)-1*H*-inden-1-amine (6f). A colorless oil. IR (neat): 3360, 3286 cm^{-1}. ^1H NMR (300 MHz, $CDCl_3$): δ 7.26−7.17 (4H, m), 5.84−5.70 (1H, m), 5.12 (1H, br d, J = 16.0 Hz), 5.11 (1H, br d, J = 11.0 Hz), 3.17−3.05 (1H, m), 2.50 (1H, dd, J = 13.0, 7.5 Hz), 2.41−2.28 (2H, m), 1.94 (2H, br s), 1.52 (1H, dd, J = 13.0, 10.0 Hz), 1.32 (3H, d, J = 7.0 Hz). ^{13}C NMR (75 MHz, $CDCl_3$): δ 146.8, 134.1, 127.4, 126.5, 123.2, 122.6, 118.6, 62.6, 50.9, 45.5, 35.7, 19.4. HRMS m/z: calcd for $C_{13}H_{17}N$ (M^+) 187.1360, found 187.1335.

1,2,3,4-Tetrahydro-4-phenyl-1-(2-propenyl)quinoline (4g). The *cis*-**4g** and *trans*-**4g** were inseparable (*cis*:*trans* = 1:3). A colorless oil. IR (neat): 3418 cm^{-1}. ^1H NMR (300 MHz, $CDCl_3$): δ 7.35−6.87 (7H, m), 6.60 (3/4H, br t, J = 8.0 Hz), 6.58 (3/4H, br d, J = 8.0 Hz), 6.53 (1/4H, br d, J = 8.0 Hz), 6.52 (1/4H, br t, J = 8.0 Hz), 5.91−5.67 (1H, m), 5.22−5.10 (2H, m), 4.19 (3/4H, t, J = 5.0 Hz), 4.14 (1/4H, dd, J = 12.0, 5.5 Hz), 3.51 (1/4H, dddd, J = 11.0, 8.0, 5.5, 3.0 Hz), 3.19 (3/4H, tt, J = 8.5, 5.5 Hz), 2.41−2.09 (2H, m), 2.00−1.95 (7/4H, m), 1.86 (1/4H, q, J = 12.0 Hz,). ^{13}C NMR (75 MHz, $CDCl_3$): δ 147.4, 145.7, 144.8, 144.6, 134.8, 134.5, 130.6, 129.7, 128.7, 128.55, 128.49, 128.1, 127.4, 127.1, 126.4, 125.9, 125.1, 122.1, 118.3, 118.0, 117.4, 117.1, 114.1, 50.9, 45.5, 44.4, 41.8, 41.2, 40.9, 39.2, 36.5. HRMS m/z: calcd for $C_{18}H_{19}N$ (M^+) 249.1517, found 249.1516.

(1α,3α)-2,3-Dihydro-3-phenyl-2-(2-propenyl)-1*H*-inden-1-amine (6g). A colorless oil. IR (neat): 3360, 3291 cm^{-1}. ^1H NMR (300 MHz, $CDCl_3$): δ 7.34−7.16 (8H, m), 6.88 (1H, br d, J = 7.5 Hz), 5.88−5.74 (1H, m), 5.15 (1H, br d, J = 16.0 Hz), 5.14 (1H, br d, J = 11.5 Hz), 4.25 (1H, t, J = 8.0 Hz), 2.74 (1H, dd, J = 12.5, 7.5 Hz), 2.51−2.38 (2H, m), 2.14 (2H, br s), 2.00 (1H, dd, J = 12.5, 10.5 Hz). ^{13}C NMR (75 MHz, $CDCl_3$): δ 145.2, 144.3, 134.0, 130.9, 128.5, 128.4, 127.6, 126.9, 126.5, 125.1, 122.7, 118.9, 93.2, 62.8, 52.5, 48.1, 45.4. HRMS m/z: calcd for $C_{18}H_{20}N$ ($M + H^+$) 250.1580, found 250.1594.

General Procedure for Domino Elimination−Rearrangement−Addition Reaction of 1-(Methoxyamino)indans with PhMgBr. To a solution of **3a−g** (0.3 mmol) in Et_2O (6.0 mL) was added phenylmagnesium bromide (3 mol/L in THF, 0.3 mL, 0.9 mmol) under an argon atmosphere at room temperature. After being stirred at the same temperature for 15 min, the reaction mixture was diluted with H_2O and extracted with $CHCl_3$. The organic phase was dried over $MgSO_4$ and concentrated under reduced pressure. Purification of the residue by PTLC (hexane:AcOEt = 5:1 or 2:1) afforded **7a−g**, **5f**, and **5g**.

1,2,3,4-Tetrahydro-6-methoxy-2-phenylquinoline (7a). A colorless oil. IR (neat): 3393 cm^{-1}. ^1H NMR (300 MHz, $CDCl_3$): δ 7.39−7.20 (5H, m), 6.62 (1H, d, J = 8.0 Hz), 6.60 (1H, br s), 6.47 (1H, br d, J = 8.0 Hz), 4.34 (1H, dd, J = 9.5, 2.5 Hz), 3.72 (3H, s), 2.91 (1H, ddd, J = 16.5, 10.5, 5.0 Hz), 2.70 (1H, dt, J = 16.5, 5.0 Hz), 2.13−1.90 (2H, m). ^{13}C NMR (75 MHz, $CDCl_3$): δ 151.8, 144.8, 138.9, 128.5, 127.3, 126.5, 122.0, 115.1, 114.6, 113.0, 56.5, 55.8, 31.1, 26.7. HRMS m/z: calcd for $C_{16}H_{17}NO$ (M^+) 239.1310, found 239.1326.

6-Chloro-1,2,3,4-Tetrahydro-2-phenylquinoline (7b). A colorless oil. IR (neat): 3419 cm^{-1}. ^1H NMR (300 MHz, $CDCl_3$): δ 7.35−7.23 (5H, m), 6.95 (1H, br s), 6.94 (1H, br d, J = 8.0 Hz), 6.43 (1H, d, J = 8.0 Hz), 4.40 (1H, dd, J = 9.0, 3.5 Hz), 4.02 (1H, br s), 2.86 (1H, ddd, J = 17.0, 10.0, 5.5 Hz), 2.67 (1H, dt, J = 17.0, 5.5 Hz), 2.14−2.05 (1H, m), 2.00−1.88 (1H, m). ^{13}C NMR (75 MHz, $CDCl_3$): δ 144.3, 143.2, 128.8, 128.6, 127.5, 126.6, 126.4, 122.3, 121.4, 114.9, 56.0, 30.4, 26.1. HRMS m/z: calcd for $C_{15}H_{14}{}^{35}ClN$ (M^+) 243.0814, found 243.0795.

1,2,3,4-Tetrahydro-2-phenyl-6-quinolinol (7c). A colorless oil. IR (neat): 3602, 3388 cm^{-1}. ^1H NMR (300 MHz, $CDCl_3$): δ 7.41−7.25 (5H, m), 6.54 (1H, br d, J = 8.0 Hz), 6.53 (1H, br s), 6.45 (1H, d, J = 8.0 Hz), 4.35 (1H, dd, J = 9.5, 3.0 Hz), 4.14 (1H, br s), 2.90 (1H, ddd, J = 16.0, 11.5, 6.5 Hz), 2.69 (1H, dt, J = 16.0, 5.0 Hz), 2.14−2.04 (1H, m), 2.02−1.91 (1H, m). ^{13}C NMR (75 MHz, $CDCl_3$): δ 147.4, 144.8, 138.9, 128.5, 127.4, 126.6, 122.5, 116.0, 115.2, 114.0, 56.6, 31.0, 26.6. HRMS m/z: calcd for $C_{15}H_{15}NO$ (M^+) 225.1153, found 225.1156.

1,2,3,4-Tetrahydro-7-methyl-2-phenylquinoline (7d). A colorless oil. IR (neat): 3415 cm^{-1}. ^1H NMR (300 MHz, $CDCl_3$): δ 7.44−7.23 (5H, m), 6.87 (1H, d, J = 7.5 Hz), 6.46 (1H, br d, J = 7.5 Hz), 6.33 (1H, br s), 4.38 (1H, dd, J = 9.0, 3.0 Hz), 3.93 (1H, br s), 2.85 (1H, ddd, J = 16.0, 10.0, 5.5 Hz), 2.67 (1H, dt, J = 16.0, 5.0 Hz), 2.23 (3H, s), 2.12−1.88 (2H, m). ^{13}C NMR (75 MHz, $CDCl_3$): δ 144.9, 144.5, 136.5, 129.1, 128.5, 127.3, 126.5, 118.0, 117.9, 114.5, 56.2, 31.1, 25.9, 21.1. HRMS m/z: calcd for $C_{16}H_{17}N$ (M^+) 223.1360, found 223.1370.

***cis*-1,2,3,4-Tetrahydro-3-methyl-2-phenylquinoline (7e).** A colorless oil. IR (neat): 3411 cm^{-1}. ^1H NMR (300 MHz, $CDCl_3$): δ 7.35−7.26 (5H, m), 7.02 (1H, br t, J = 7.5 Hz), 7.00 (1H, br d, J = 7.5 Hz), 6.65 (1H, br t, J = 7.5 Hz), 6.56 (1H, br d, J = 7.5 Hz), 4.52 (1H, d, J = 4.0 Hz), 4.14 (1H, br s), 2.97 (1H, dd, J = 16.0, 5.0 Hz), 2.50 (1H, dd, J = 16.0, 6.5 Hz), 2.34−2.29 (1H, m), 0.82 (3H, d, J = 7.0 Hz). ^{13}C NMR (75 MHz, $CDCl_3$): δ 144.2, 142.9, 129.7, 128.1, 127.2, 127.1, 126.9, 120.4, 117.1, 113.7, 59.4, 33.4, 31.9, 15.1. HRMS m/z: calcd for $C_{16}H_{17}N$ (M^+) 223.1360, found 223.1362.

***trans*-1,2,3,4-Tetrahydro-3-methyl-2-phenylquinoline (7e).** A colorless oil. IR (neat): 3420 cm^{-1}. ^1H NMR (300 MHz, $CDCl_3$): δ 7.35−7.19 (5H, m), 7.01−6.97 (2H, m), 6.63 (1H, br t, J = 7.5 Hz), 6.47 (1H, br d, J = 7.5 Hz), 3.95 (1H, br s), 3.93 (1H, d, J = 8.5 Hz), 2.79 (1H, dd, J = 16.0, 8.5 Hz), 2.59 (1H, dd, J = 16.0, 11.0 Hz), 2.13−1.98 (1H, m), 0.82 (3H, d, J = 6.5 Hz). ^{13}C NMR (75 MHz, $CDCl_3$): δ 144.5, 143.4, 129.1, 128.4, 127.6, 127.5, 126.8, 120.8, 116.9, 113.3, 63.3, 35.3, 33.8, 18.5. HRMS m/z: calcd for $C_{16}H_{17}N$ (M^+) 223.1360, found 223.1366.

***trans*-1,2,3,4-Tetrahydro-4-methyl-2-phenylquinoline (7f).** A colorless oil. IR (neat): 3391 cm^{-1}. ^1H NMR (300 MHz, $CDCl_3$): δ 7.42−7.25 (5H, m), 7.08 (1H, br t, J = 7.5 Hz), 7.01 (1H, br d, J = 7.5 Hz), 6.67 (1H, br t, J = 7.5 Hz), 6.54 (1H, br d, J = 7.5 Hz), 4.46 (1H, dd, J = 10.0, 4.0 Hz), 4.08 (1H, br s), 2.97−2.87 (1H, m), 2.03 (1H, ddd, J = 13.0, 10.0, 5.5 Hz), 1.84 (1H, dt, J = 13.0, 4.0 Hz), 1.35 (3H, d, J = 7.0 Hz). ^{13}C NMR (75 MHz, $CDCl_3$): δ 144.8, 144.0, 128.8, 128.5, 127.4, 126.9, 126.6, 126.1, 117.1, 114.0, 52.1, 38.2, 29.9, 24.1. HRMS m/z: calcd for $C_{16}H_{17}N$ (M^+) 223.1360, found 223.1370.

***trans*-1,2,3,4-Tetrahydro-2,4-diphenylquinoline (7g).** A colorless oil. IR (neat): 3391 cm^{-1}. ^1H NMR (300 MHz, $CDCl_3$): δ 7.32−7.05 (11H, m), 6.88 (1H, br d, J = 8.0 Hz), 6.64 (1H, br d, J = 8.0 Hz), 6.63 (1H, br t, J = 8.0 Hz), 4.32 (1H, dd, J = 10.0, 5.0 Hz), 4.15 (1H, t, J = 5.0 Hz), 2.30 (1H, ddd, J = 13.5, 10.0, 5.0 Hz), 2.18 (1H, dt, J = 13.5, 5.0 Hz). ^{13}C NMR (75 MHz, $CDCl_3$): δ 146.9, 144.8, 144.4, 130.5, 128.6, 128.5, 128.3, 127.6, 127.4, 126.6, 126.1, 122.2, 117.2, 114.0, 51.9, 41.7, 39.0. HRMS m/z: calcd for $C_{21}H_{19}N$ (M^+) 285.1516, found 285.1542.

2-(Diethoxymethyl)benzaldehyde (11). To a solution of bromide **10** (1.6 g, 6.2 mmol) in THF (16 mL) was added *n*-buthyllithium (1.6 mol/L in *n*-hexane, 4.3 mL, 6.8 mmol) under an argon atmosphere at −70 °C. After being stirred at the same temperature for 30 min, DMF (5.7 mL, 73.4 mmol) was

added slowly dropwise keeping the same temperature and stirring continued for 30 min. The reaction mixuture was stirred at room temperature for 30 min, poured into saturated aqueous NH_4Cl (100 mL), and extracted with Et_2O. The organic phase was washed with brine, dried over $MgSO_4$, and concentrated under reduced pressure. Purification of the residue by column chromatography on SiO_2 (*n*-hexane:AcOEt = 10:1) afforded aldehyde **11** (1.2 g, 93%) as a colorless oil. ^{1}H NMR (300 MHz, $CDCl_3$): δ 10.50 (1H, s), 7.92 (1H, br d, J = 8.0 Hz), 7.69 (1H, br d, J = 8.0 Hz), 7.58 (1H, br t, J = 8.0 Hz), 7.47 (1H, br t, J = 8.0 Hz), 5.96 (1H, s), 3.72 (1H, q, J = 7.0 Hz), 3.69 (1H, q, J = 7.0 Hz), 3.59 (1H, q, J = 7.0 Hz), 3.56 (1H, q, J = 7.0 Hz), 1.23 (6H, t, J = 7.0 Hz). The spectral data were identical with those reported in the literature.[25]

α-Ethenyl-2-(diethoxymethyl)benzenemethanol Acetate (12). To a solution of **11** (4.9 g, 23.6 mmol) in THF (34 mL) was added vinylmagnesium bromide (1 M in THF, 58.9 mL, 58.9 mmol) under an argon atmosphere at 0 °C. After being stirred at the same temperature overnight, the reaction mixture was diluted with H_2O and extracted with $CHCl_3$. The organic phase was dried over $MgSO_4$ and concentrated under reduced pressure to give the crude allyl alcohol that was subjected to the following reaction without further purification. To a solution of the crude allyl alcohol (5.6 g, 23.6 mmol) in pyridine (7.6 mL) was added Ac_2O (8.9 mL, 94.2 mmol) under a nitrogen atmosphere at room temperature. After being stirred at room temperature overnight, the reaction mixture was diluted with H_2O and extracted with $CHCl_3$. The organic phase was washed with H_2O, dried over $MgSO_4$, and concentrated under reduced pressure. Purification of the residue by column chromatography on SiO_2 (*n*-hexane:AcOEt = 10:1) afforded **12** (5.6 g, 85%) as a colorless oil. IR (neat): 1742 cm^{-1}. ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.64−7.28 (4H, m), 6.67 (1H, br d, J = 5.0 Hz), 6.02 (1H, ddd, J = 17.5, 10.5, 5.0 Hz), 5.80 (1H, s, C*H*), 5.26 (1H, dt, J = 17.5, 1.5 Hz), 5.21 (1H, dt, J = 10.5, 1.5 Hz), 3.72 (1H, q, J = 7.0 Hz), 3.69 (1H, q, J = 7.0 Hz), 3.58 (1H, q, J = 7.0 Hz), 3.52 (1H, q, J = 7.0 Hz), 2.08 (3H, s), 1.26 (3H, t, J = 7.0 Hz), 1.18 (3H, t, J = 7.0 Hz). ^{13}C NMR (75 MHz, $CDCl_3$): δ 169.8, 137.2, 136.4, 128.6, 127.7, 127.6, 126.5, 116.1, 99.4, 71.8, 62.5, 60.8, 21.1, 15.11, 15.06. HRMS *m*/*z*: calcd for $C_{16}H_{22}O_4$ (M^+) 278.1517, found 278.1533.

α-Ethenyl-2-formylbenzenemethanol Acetate (13). To a solution of **12** (165 mg, 0.6 mmol) in EtOH (5.4 mL) was added 10% HCl (1.1 mL) under a nitrogen atmosphere at room temperature. After being stirred at the same temperature for 4 h, the reaction mixture was diluted with H_2O and extracted with $CHCl_3$. The organic phase was washed with H_2O, dried over $MgSO_4$, and concentrated under reduced pressure. Purification of the residue by column chromatography on SiO_2 (*n*-hexane:AcOEt = 10:1) afforded **13** (101.6 mg, 84%) as a colorless oil. IR (neat): 1743, 1700 cm^{-1}. ^{1}H NMR (300 MHz, $CDCl_3$): δ 10.3 (1H, s), 7.88 (1H, br d, J = 8.0 Hz), 7.61 (1H, br t, J = 8.0 Hz), 7.57 (1H, br d, J = 8.0 Hz), 7.49 (1H, br t, J = 8.0 Hz), 7.05 (1H, br d, J = 5.5 Hz), 6.14−6.03 (1H, m), 5.24 (1H, br d, J = 10.5 Hz), 5.23 (1H, br d, J = 17.0 Hz), 2,13 (3H, s). ^{13}C NMR (75 MHz,, $CDCl_3$): δ 192.0, 169.4, 140.7, 136.0, 133.8, 133.1, 132.1, 128.2, 127.6, 117.0, 72.1, 20.9. HRMS *m*/*z*: calcd for $C_{10}H_9O_2$ (M^+ − 43) 161.0602, found 161.0606.

(3aα,8bα)-1,2,3,3a,4,8b-Hexahydro-1-(phenylmethyl)indeno-[1,2-*b*]pyrrol-4-ol 4-Acetate (14). To a solution of **13** (35.4 mg, 0.17 mmol) and *N*-benzylglycine hydrochloride (49.4 mg, 0.24 mmol) in toluene (3.0 mL) was added Et_3N (0.06 mL, 0.41 mmol) under a nitrogen atmosphere at room temperature. After being refluxed for 5 h, the reaction mixture was diluted with H_2O and extracted with $CHCl_3$. The organic phase was dried over $MgSO_4$ and concentrated under reduced pressure. Purification of the residue by PTLC (*n*-hexane:AcOEt = 3:1) afforded **14** (40.8 mg, 78%) as a colorless oil and an inseparable 3:2 mixture of 3a,4-*trans*-3a,8b-*cis* and 3a,4-*cis*-3a,8b-*cis* isomers. IR (neat): 1729 cm^{-1}. ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.44−7.06 (9H, m), 6.06−6.03 (1H, m), 4.40 (2/5H, d, J = 7.0 Hz), 4.23 (3/5H, d, J = 7.0 Hz), 4.06 and 3.84 (6/5H, ABq, J = 12.0 Hz), 4.06 and 3.72 (4/5H, ABq, J = 12.0 Hz), 3.53−3.42 (1H, m), 3.03−2.80 (1H, m), 2.65−2.49 (1H, m), 2.15 (9/5H, s), 2.06 (6/5H, s), 1.83−1.71 (2H, m). ^{13}C NMR (75 MHz, $CDCl_3$): δ 170.8, 145.2, 143.8, 140.4, 139.5, 139.2, 129.3, 129.0, 128.9, 128.2, 128.1, 127.7, 126.9, 126.0, 125.0, 124.8, 83.2, 75.9, 71.4, 70.6, 60.4, 59.2, 54.6, 54.1, 50.0, 45.4, 29.2, 24.8, 21.1, 20.8. HRMS *m*/*z*: calcd for $C_{20}H_{21}NO_2$ (M^+) 307.1571, found 307.1569.

(3aα,8bα)-1,2,3,3a,4,8b-Hexahydro-1-(phenylmethyl)indeno-[1,2-*b*]pyrrol-4-ol (15). To a solution of **14** (202.3 mg, 0.66 mmol) in MeOH (3.0 mL) was added K_2CO_3 (50 mg, 0.36 mmol) under a nitrogen atmosphere at room temperature. After being stirred at the same temperature for 3 h, the reaction mixture was diluted with H_2O and extracted with $CHCl_3$. The organic phase was dried over $MgSO_4$ and concentrated under reduced pressure. Purification of the residue by column chromatography on SiO_2 (*n*-hexane:AcOEt = 2:1) afforded **15** (171.3 mg, 98%) as a colorless oil and an inseparable 3:2 mixture of 3a,4-*trans*-3a,8b-*cis* and 3a,4-*cis*-3a,8b-*cis* isomers. IR (neat): 3595 cm^{-1}. ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.48 (1H, br d, J = 8.0 Hz), 7.37−7.14 (8H, m), 5.02 (2/5H, br d, J = 2.5 Hz), 4.82 (3/5H, d, J = 7.0 Hz), 4.30 (2/5H, d, J = 7.5 Hz), 4.15 and 3.37 (6/5H, ABq, J = 13.0 Hz), 4.05 and 3.66 (4/5H, ABq, J = 13.0 Hz), 3.79 (3/5H, d, J = 7.0 Hz), 3.11−3.01 (6/5H, m), 2.91−2.79 (4/5H, m), 2.54−2.42 (1H, m), 2.20−2.05 (1H, m), 1.94−1.83 (3/5H, m), 1.72−1.60 (2/5H, m). ^{13}C NMR (75 MHz, $CDCl_3$): δ 146.4, 144.7, 143.7, 142.3, 139.3, 138.5, 129.0, 128.9, 128.6, 128.5, 128.18, 128.15 127.0, 126.9, 125.6, 125.2, 125.0, 81.7, 75.0, 72.2, 71.4, 59.1, 58.2, 55.8, 54.4, 53.4, 48.7, 29.0, 22.0. HRMS *m*/*z*: calcd for $C_{18}H_{19}NO$ (M^+) 265.1466, found 265.1455.

***cis*-2,3,3a,8b-Tetrahydro-1-(phenylmethyl)indeno[1,2-*b*]pyrrol-4(1*H*)-one (16).** To a solution of **15** (1.95 g, 7.36 mmol) in Et_2O (86 mL) was added MnO_2 (2.50 g) under a nitrogen atmosphere at room temperature. After being stirred at the same temperature for 20 h, the reaction mixture was filtered through a pad of Celite and the filtrate was concentrated under reduced pressure. Purification of the residue by column chromatography on SiO_2 (*n*-hexane:AcOEt = 5:1) afforded **16** (1.32 g, 68%) as a colorless oil. IR (neat): 1714 cm^{-1}. ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.74 (1H, br d, J = 8.0 Hz), 7.60 (1H, br t, J = 8.0 Hz), 7.45 (1H, br d, J = 8.0 Hz), 7.44 (1H, br t, J = 8.0 Hz), 7.38−7.24 (5H, m), 4.44 (1H, d, J = 6.5 Hz), 4.03 and 3.81 (2H, ABq, J = 13.0 Hz), 3.31 (1H, ddd, J = 11.0, 6.5, 5.0 Hz), 2.75−2.62 (2H, m), 2.25 (1H, ddt, J = 13.0, 11.0, 6.5 Hz), 1.99 (1H, dtd, J = 13.0, 6.5, 5.0 Hz). ^{13}C NMR (75 MHz, $CDCl_3$): δ 153.4, 138.9, 136.9, 134.8, 128.9, 128.8, 128.4, 127.2, 126.7, 123.8, 100.0, 66.1, 58.2, 53.7, 51.9, 27.5. HRMS *m*/*z*: calcd for $C_{18}H_{17}NO$ (M^+) 263.1310, found 263.1296.

(3aα,4α,8bα)-1,2,3,3a,4,8b-Hexahydro-4-methoxyamino-1-(phenylmethyl)indeno[1,2-*b*]pyrrole (8). To a solution of **16** (1.7 g, 6.4 mmol) in MeOH (200 mL) were added $MeONH_2 \cdot HCl$ (1.1 g, 12.8 mmol) and AcONa (1.1 g, 12.8 mmol) under a nitrogen atmosphere at room temperature. After being stirred at the same temperature for 24 h, the reaction mixture was concentrated under reduced pressure. The residue was diluted with H_2O and extracted with $CHCl_3$. The organic phase was washed with H_2O, dried over $MgSO_4$, and concentrated under reduced pressure to give the crude oxime ether **17**, which was subjected to the following reaction without further purification. To a solution of the crude oxime ether **17** (1.87 g, 6.4 mmol) and pyridine−borane complex (2 mL, 21.1 mmol) in EtOH (15 mL) was added

(25) Chezal, J. M.; Moreau, E.; Desbois, N.; Blache, Y.; Chavignon, O.; Teulade, J. C. *Tetrahedron Lett.* **2004**, *45*, 553.

slowly 10% HCl (20 mL) at −10 °C under a nitrogen atmosphere. After the reaction mixture was stirred at room temperature for 48 h, Na_2CO_3 was added. The reaction mixture was diluted with H_2O and extracted with $CHCl_3$. The organic phase was washed with H_2O, dried over $MgSO_4$, and concentrated under reduced pressure. Purification of the residue by column chromatography on SiO_2 (*n*-hexane:AcOEt = 3:1) afforded **8** (686 mg, 36%, 99% brsm) and oxime ether **17** (1.19 g, 63%). A colorless oil. IR (neat): 3253 cm^{-1}. ^1H NMR (500 MHz, $CDCl_3$): δ 7.39−7.17 (8H, m), 7.07 (1H, br d, J = 8.0 Hz), 4.59 (1H, d, J = 8.0 Hz), 4.30 (1H, br s), 4.13 (1H, d, J = 8.0 Hz), 4.09 and 3.75 (2H, ABq, J = 13.0 Hz), 3.61 (3H, s), 3.27 (1H, dt, J = 10.0, 8.0 Hz), 3.00 (1H, ddd, J = 10.0, 6.5, 4.0 Hz), 2.58 (1H, td, J = 10.0, 6.5 Hz), 1.93−1.84 (2H, m). NOESY: NOE was observed between 3a-H (δ 3.27) and 4-H (δ 4.59), 3a-H (δ 3.27) and 8b-H (δ 4.13), 4-H (δ 4.59) and 8b-H (δ 4.13). ^{13}C NMR (125 MHz, $CDCl_3$): δ 144.4, 141.6, 139.7, 129.2, 128.3, 128.2, 127.7, 127.1, 125.5, 125.2, 71.5, 64.1, 61.4, 60.3, 55.4, 46.2, 24.0. HRMS m/z: calcd for $C_{19}H_{22}N_2O$ (M^+) 294.1731, found 294.1709.

(3aα,4*β*,9bα)-2,3,3a,4,5,9b-Hexahydro-1-(phenylmethyl)-4-(2-propenyl)-1*H*-pyrrolo-[3,2-*c*]quinoline (18). To a solution of **8** (670 mg, 2.3 mmol) in Et_2O (46 mL) was added allylmagnesium bromide (1 M in Et_2O, 0.9 mL, 0.9 mmol) under an argon atmosphere at room temperature. After being stirred at the same temperature for 30 min, the reaction mixture was diluted with H_2O and extracted with $CHCl_3$. The organic phase was washed with H_2O, dried over $MgSO_4$, and concentrated under reduced pressure. Purification of the residue by MCC (*n*-hexane:AcOEt = 5:1) afforded **18** (655 mg, 94%) as a colorless oil. IR (neat): 3415 cm^{-1}. ^1H NMR (500 MHz, $CDCl_3$): δ 7.27−7.18 (5H, m), 7.13 (1H, br d, J = 8.0 Hz), 7.07 (1H, br t, J = 8.0 Hz), 6.63 (1H, br t, J = 8.0 Hz), 6.58 (1H, br d, J = 8.0 Hz), 5.85 (1H, dtd, J = 17.5, 10.0, 5.0 Hz), 5.21 (1H, br d, J = 17.5 Hz), 5.20 (1H, br d, J = 10.0 Hz), 4.37 and 3.10 (2H, ABq, J = 13.0 Hz), 3.22 (1H, br t, J = 9.0 Hz), 3.17 (1H, d, J = 5.5 Hz), 2.88 (1H, br t, J = 8.5 Hz), 2.58−2.54 (1H, m), 2.13 (1H, q, J = 8.5 Hz), 1.99 (3H, m), 1.92−1.90 (1H, m), 1.62−1.56 (1H, m). ^{13}C NMR (125 MHz, $CDCl_3$): δ 144.8, 140.3, 135.4, 131.9, 128.5, 128.3, 128.0, 126.6, 119.2, 118.3, 116.0, 114.0, 64.1, 57.6, 51.4, 39.7, 38.4, 29.7, 25.6. HRMS m/z: calcd for $C_{21}H_{24}N_2$ (M^+) 304.1938, found 304.1925.

(3aα,4*β*,9bα)-8-Bromo-2,3,3a,4,5,9b-hexahydro-1-(phenylmethyl)-4-(2-propenyl)-1*H*-pyrrolo[3,2-*c*]quinoline (19). To a solution of **18** (91.2 mg, 0.3 mmol) in DMF (3 mL) was added *N*-bromosuccinimide (51.6 mg, 0.3 mmol) under a nitrogen atmosphere at room temperature. After being stirred at the same temperature for 24 h, the reaction mixture was diluted with H_2O and extracted with $CHCl_3$. The organic phase was washed with H_2O, dried over $MgSO_4$, and concentrated under reduced pressure. Purification of the residue by PTLC (*n*-hexane:AcOEt = 5:1) afforded **19** (88 mg, 79%) as a colorless oil. IR ($CHCl_3$): 3415 cm^{-1}. ^1H NMR (300 MHz, $CDCl_3$): δ 7.27−7.25 (5H, m), 7.20 (1H, d, J = 1.5 Hz), 7.13 (1H, dd, J = 8.0, 1.5 Hz), 6.46 (1H, d, J = 8.0 Hz), 5.83 (1H, dtd, J = 18.5, 10.0, 5.0 Hz), 5.21 (1H, br d, J = 18.5 Hz), 5.20 (1H, br d, J = 10.0 Hz), 4.31 and 3.11 (2H, ABq, J = 13.0 Hz), 4.22, (1H, br s), 3.19 (1H, br t, J = 9.0 Hz), 3.14 (1H, br d, J = 5.5 Hz), 2.88 (1H, br t, J = 8.5 Hz), 2.58−2.52 (1H, m), 2.13 (1H, q, J = 8.5 Hz), 2.05−1.84 (3H, m), 1.64−1.56 (1H, m). ^{13}C NMR (75 MHz, $CDCl_3$): δ143.8, 140.0, 135.1, 134.1, 131.0, 128.5, 128.1, 126.7, 121.2, 118.6, 115.5, 107.2, 63.7, 57.6, 51.33, 51.26, 39.4, 38.3, 25.5. HRMS m/z: calcd for $C_{21}H_{23}{}^{79}BrN_2$ (M^+) 382.1044, found 382.1057.

(3aα,4*β*,9bα)-8-Bromo-2,3,3a,4,5,9b-hexahydro-1-(phenylmethyl)-1*H*-pyrrolo[3,2-*c*]quinoline-4-propanol (9). To a solution of **19** (27.7 mg, 0.07 mmol) in THF (1 mL) was added thexylBH_2 (0.8 mol/L, 0.088 mL, 0.07 mmol) under an argon atmosphere at 0 °C. After being stirred at the same temperature for 1 h, thexylBH_2 (0.8 mol/L, 0.088 mL, 0.07 mmol) was added. After being stirred at the same temperature for 1 h, thexylBH_2 (0.8 mol/L, 0.088 mL, 0.07 mmol) was added. After being stirred at the same temperature for 1 h, MeOH (0.07 mL), aq NaOH (3 mol/L, 0.023 mL, 0.07 mmol), and 30% H_2O_2 (0.007 mL, 0.07 mmol) were added at 0 °C. After being stirred at room temperature for 3 h, the reaction was quenched by 10% HCl, and the reaction mixture was diluted with H_2O and extracted with $CHCl_3$. The organic phase was washed with H_2O, dried over $MgSO_4$, and concentrated under reduced pressure. Purification of the residue by PTLC (AcOEt) afforded **19** (19.7 mg, 70%) as a white solid. IR ($CHCl_3$): 3625, 3433 cm^{-1}. ^1H NMR (500 MHz, $CDCl_3$): δ 7.27−7.20 (6H, m), 7.14 (1H, dd, J = 8.5, 2.5 Hz), 6.48 (1H, d, J = 8.5 Hz), 4.30 (1H, d, J = 12.5 Hz), 3.71 (2H, t, J = 6.0 Hz), 3.22 (1H, br t, J = 8.5 Hz), 3.17 (1H, m), 3.15 (1H, br d, J = 12.5 Hz), 2.87 (1H, td, J = 9.0, 3.5 Hz), 2.14 (1H, br q, J = 9.0 Hz), 2.02−1.94 (2H, m), 1.80−1.65 (3H, m), 1.59 (1H, br q, J = 9.0 Hz), 1.53−1.47 (1H, m). ^{13}C NMR (125 MHz, $CDCl_3$): δ 144.0, 140.0, 134.0, 131.0, 128.6, 128.1, 126.8, 121.8, 115.8, 107.7, 63.6, 62.9, 57.9, 52.6, 51.5, 39.4, 30.0, 28.7, 25.9. HRMS m/z: calcd for $C_{21}H_{25}{}^{79}BrN_2O$ (M^+) 400.1149, found 400.1163.

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Supporting Information Available: Experimental procedure and characterization data for **1** and **3a**−**g**, and ^1H and ^{13}C NMR spectra of all obtained compounds. This material is available free of charge via the Internet at http://pubs.acs.org.