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Development of radical addition–cyclization–elimination reaction of oxime ether and its application to formal synthesis of (±)-martinelline

Okiko Miyata, Atsushi Shirai, Shintaro Yoshino, Toshiki Nakabayashi, Yoshifumi Takeda, Toshiko Kiguchi, Daisuke Fukumoto, Masafumi Ueda and Takeaki Naito*

Kobe Pharmaceutical University, 4-19-1, Motoyamakita, Higashinada, Kobe 658-8558, Japan

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Abstract—Radical addition–cyclization–elimination (RACE) reaction of oxime ether carrying unsaturated ester provides a novel method for the construction of pyrroloquinoline. Treatment of oxime ethers with Bu_3SnH and AIBN gave *N*-norpyrroloquinoline as a major product, which was also obtained by the radical reaction of the corresponding hydrazone and imine. The radical reaction of aldehyde and ketone carrying unsaturated ester proceeded stereoselectively to give *cis*-furoquinolines and *cis*-hydroxyesters. The RACE reactions by using each of Bu_3SnNMe_2, Bu_3SnD, and/or D_2O were also examined in order to propose a reaction pathway to *N*-norpyrroloquinoline. Furthermore, the synthetic utility of RACE reaction is demonstrated by preparation of a key intermediate for the synthesis of (±)-martinelline.

1. Introduction

Free-radical cyclization reactions are recognized as having a powerful effect on carbon–carbon bond forming reactions, including the construction of mono- and polycyclic compounds.[1] These processes usually occur with regio- and stereoselective control and can be modulated to form different-sized rings. They have been applied to the synthesis of a number of natural products, including terpenoids, steroids, lignans, and β-lactams.[1] We have recently developed efficient radical addition–cyclization reaction based on sulfanyl[2] and alkyl[3] radicals for the preparation of various types of carbocycles and heterocycles. We found also the efficient synthesis of substituted pyrrolidine and piperidine derivatives using stannyl[4,5c,d] radical addition–cyclization of the oxime ethers connected with either carbonyl or α,β-unsaturated carbonyl group. In order to develop new method for constructing the quinoline ring, we investigated stannyl radical addition–cyclization of oxime ethers connected with α,β-unsaturated ester.

The quinoline moiety is present as a substructure in a broad range of both natural and unnatural biologically active compounds, most notably within antimalarial agents.[6] Due to such biological importance, quinoline derivatives have become the synthetic targets of many organic and medicinal chemists.[6] As a part of our program directed toward the development of efficient radical reactions, we report here in detail radical addition–cyclization reaction of imine and ketone derivatives **1** carrying an unsaturated ester, nitrile, and amide. This method is suitable for the preparation of pyrroloquinolines **2a**,**b** (X: NH, Z: C═O), furoquinolines **2c**,**d** (X: O, Z: C═O), and substituted quinolines **3**. Furthermore, we applied this domino type of radical reaction to the synthesis of key intermediate **4** of (±)-martinelline (**5a**) (Scheme 1).[5c]

2. Results and discussion

2.1. Preparation and radical addition–cyclization–elimination reaction of oxime ethers carrying an unsaturated ester, amide, and nitrile

We first investigated the radical reaction of oxime ethers. The requisite substrates **1a–g** for the radical reactions were prepared as follows. The oxidation of benzyl alcohol **6**, prepared from commercially available methyl anthranilate by the reported procedure,[7] with MnO_2 followed by the treatment of the resulting aldehyde with benzyloxyamine hydrochloride in the presence of sodium acetate gave oxime ether **7a**, which was then N-alkylated with ethyl 4-bromocrotonate to afford the ester **1a**. Similarly, the corresponding *tert*-butyl ester **1b**, amide **1c**, and nitrile **1d** were prepared from **6**. The *O*-methyloxime ether **1e** was prepared from **6** via **7b**

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* Corresponding author. Tel.: +81 78 441 7554; fax: +81 78 441 7556; e-mail: taknaito@kobepharma-u.ac.jp

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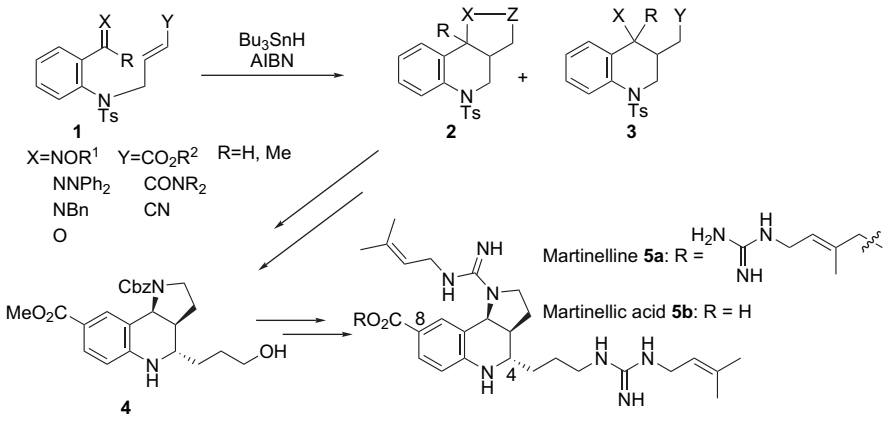
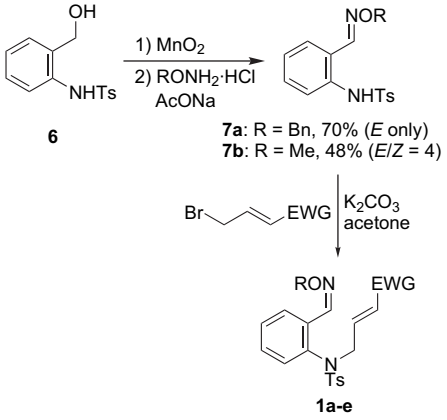


Scheme 1.

(Scheme 2, Table 1). The ketoxime ethers **1f** and **1g** were also prepared from acetophenone **8** according to similar procedure (Scheme 3). The geometrical ratios of aldoxime ethers **1a**–**g** were determined by the ^{1}H NMR spectra.

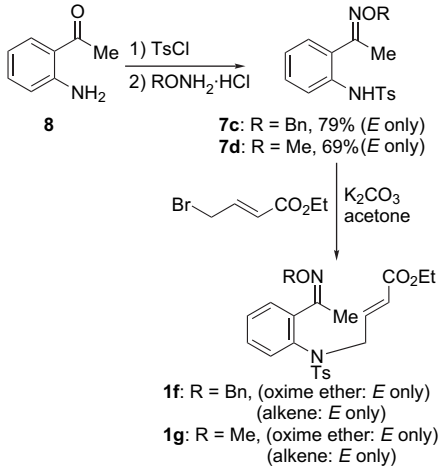


Scheme 2.

Table 1. Preparation of oxime ethers **1a**–**e**

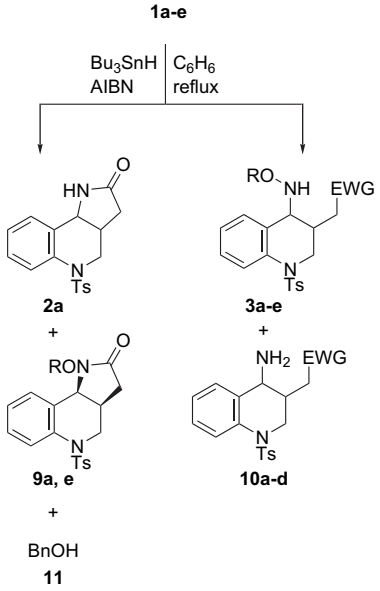
Entry	Substrate	EWG	Product	Yield (%)
1	**7a**	(*E*)-CO_2Et	**1a**	81 (oxime ether: *E* only; alkene: *E* only)
2	**7a**	(*E*)-$CO_2{}^t$Bu	**1b**	89 (oxime ether: *E* only; alkene: *E* only)
3	**7a**	(*E*)-CONHBn	**1c**	99 (oxime ether: *E* only; alkene: *E* only)
4	**7a**	(*E*/*Z*)-CN	**1d**	73 (oxime ether: *E* only; alkene: *E*/*Z*=1)
5	**7b**	(*E*)-CO_2Et	**1e**	81 (oxime ether: *E* only; alkene: *E* only)

We then investigated the radical reaction of aldoxime ethers **1a**–**e** and found an interesting radical addition–cyclization–elimination (RACE) reaction (Scheme 4, Table 2). According to our procedure developed in the radical addition–cyclization of oxime ethers, the treatment of *O*-benzyloxime ether **1a** bearing an ethoxycarbonyl group with Bu_3SnH and AIBN in refluxing benzene gave three types of products **2a**, **3a**, **9a**, and benzyl alcohol (**11**) (entry 1). Mixtures of two stereoisomers **2a** and **3a** were formed



Scheme 3.

with a low stereoselectivity but they were isolated; *cis*-isomer **9a** was also isolated. Surprisingly, a major product of the reaction was an unexpected tricyclic pyrroloquinoline



Scheme 4.

Table 2. Radical reaction of aldoxime ethers **1a–e**

Entry	Substrate	R	EWG	Yield (%) (*cis*/*trans*)				
				2a	**3a–e**	**9a**,**e**	**10b–d**	**11**
1	**1a**	Bn	(*E*)-CO_2Et	46 (1/1.3)	13 (1/1.3)	7 (1/0)	—	33
2	**1e**	Me	(*E*)-CO_2Et	56 (1/1.1)	15 (1/1.1)	2 (1/0)	—	—
3	**1b**	Bn	(*E*)-$CO_2{}^t$-Bu	14 (1/0)	29 (1/1)	—	38 (1/3.5)	14
4[a]	**1c**	Bn	(*E*)-CONHBn	—	—	—	26 (1/1.3)	—
5	(*Z*)-**1d**	Bn	(*Z*)-CN	—	24 (3/1)	—	14 (1/1)	—
6	(*E*)-**1d**	Bn	(*E*)-CN	—	14 (5/1)	—	14 (0/1)	—

[a] Compound **7a** was obtained in 8% yield in addition to **10c**.

2a, which does not carry the benzyloxy group in the molecule. The fact that the benzyl alcohol (**11**) was isolated in this radical reaction suggests that the benzyloxy group on oxime ether moiety was eliminated as benzyl alcohol in the transformation of **1a** to **2a**.

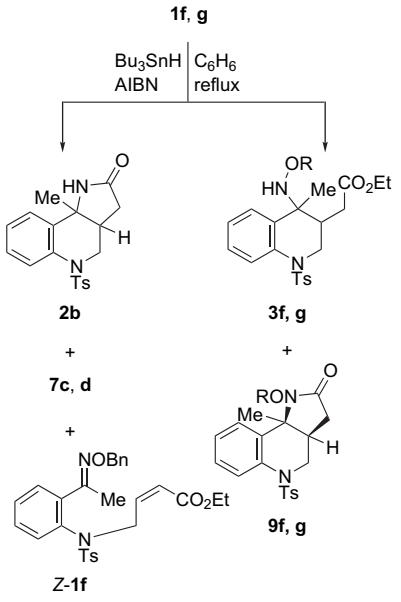
On the other hand, expected bicyclic tetrahydroquinoline **3a** and *N*-benzyloxypyrroloquinoline **9a** were obtained as minor products. The *cis*-benzyloxyamino ester **3a** was treated with TsOH in MeOH at room temperature to give *cis*-lactam **9a**. However, the *trans*-isomer **3a** did not cyclize to *trans*-**9a** under the same reaction conditions.

Similarly, *O*-methyloxime ether **1e** gave **2a**, **3e**, and **9e** under the same reaction conditions (entry 2). The yield of **2a** was improved by the use of methyloxime ether **1e** rather than benzyloxime ether **1a**. The radical reaction of oxime ether **1b** bearing the *tert*-butoxycarbonyl group gave 4-aminoquinoline **10b** as a major product in addition to **2a**, **3b**, and benzyl alcohol (**11**) (entry 3). The *N*-norpyrroloquinoline **2a** was obtained in low yield but with *cis*-selectivity. The *cis*-amino ester **10b** was converted into *cis*-*N*-norpyrroloquinoline **2a** in refluxing benzene while *trans*-isomer **2a** was not obtained from *trans*-**10b** in refluxing benzene. Similarly, amide **1c** gave 4-aminoquinoline **10c** but the desired product **2a** was not obtained (entry 4).

In the case of nitrile **1d**, readily separable *E*- and *Z*-**1d** were also subjected to the radical reaction to form bicyclic tetrahydroquinolines **3d** and **10d** in low yields accompanied with no formation of pyrroloquinoline **2a** (entries 5 and 6).

For the systematic study on our RACE, we next examined the radical reaction of ketoxime ethers **1f**,**g** (Scheme 5, Table 3). However, tricyclic products **2b** and **9f**,**g** were obtained only in low yield in addition to tosylamides **7c**,**d**, which would be formed by the elimination reaction of the alkyl group as the almost same paper reported by Bertrand.[8]

The radical reaction of oxime ethers **1** carrying unsaturated ester, amide, and nitrile can be summarized as follows. (a) In the case of oxime ethers **1a** and **1e**, the *N*-norpyrroloquinoline **2a** was obtained as a major product. (b) The oxime ether **1b** carrying *tert*-butyl ester gave amino ester **10b** with no benzyloxy group as a major product and two other products **2a** and **3b** as minor products, respectively. In this case, the formation of pyrrolidinone ring would be difficult due to the existence of a sterically bulky *tert*-butyl group. Similar trend of the difficult formation of pyrrolidinone ring was observed in the radical reaction of amide **1c**. (c) The radical reaction of nitrile **1d** proceeded inefficiently to form bicyclic



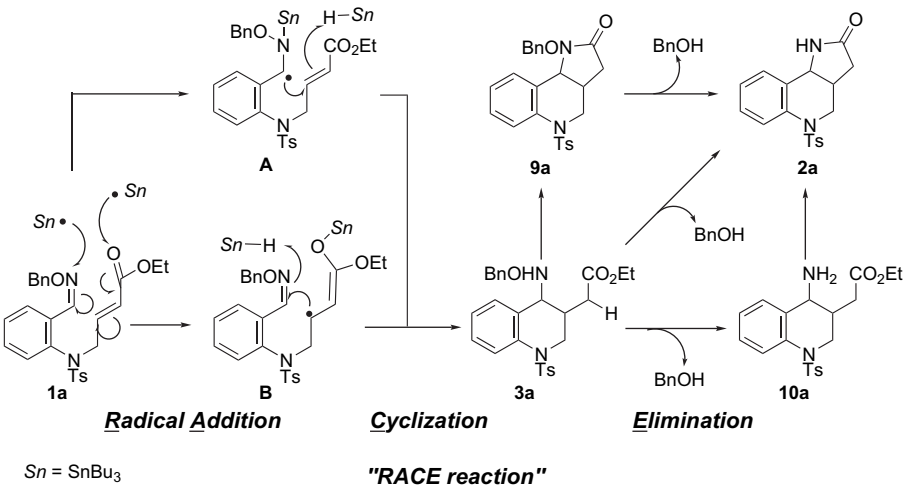
Scheme 5.

compounds **3d** and **10d** in low yields. (d) The sterically hindered ketoxime ethers **1f**,**g** cyclized but gave products **2b** and **9f**,**g** in low yield because the existence of a methyl group would interfere cyclization. Thus, we have now established novel RACE reaction of oxime ethers to form tricyclic pyrroloquinolines in only one procedure.

Considering the foregoing results, we propose a plausible reaction pathway roughly as depicted in Scheme 6. Tributylstannyl radical generated from Bu_3SnH and AIBN would add to either oxime ether or ester to give the respective intermediary radical **A** or **B**, which cyclizes to give the amino ester **3a** carrying tetrahydroquinoline core. The conversion of **3a** into debenzyloxylated *N*-norpyrroloquinoline **2a** would proceed via three possible reaction pathways. The cyclization of **3a** followed by debenzyloxylation of the resulting *N*-benzyloxypyrroloquinoline **9a** would afford the desired pyrroloquinoline **2a**. As second route, the cyclization and debenzyloxylation would occur at the same time to afford

Table 3. Radical reaction of ketoxime ethers **1f**,**g**

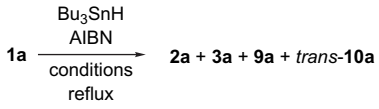
Substrate	R	Yield (%)				
		2b (*cis*/*trans*)	**3f**,**g** (*cis*/*trans*)	**7c**,**d**	**9f**,**g** (*cis*/*trans*)	(*Z*)-**1f**
1f	Bn	4 (1/1)	—	21 (**7c**)	—	2
1g	Me	5 (1/1)	5 (1/1)	20 (**7d**)	2	—



Scheme 6.

2a. Finally, the initial debenzyloxylation and subsequent cyclization would give **2a**. Thus, the radical reaction from **1a** to **2a** involves three types of reactions, which are addition, cyclization, and elimination. We designated this domino type of radical addition–cyclization–elimination reaction as 'RACE' reaction.

In order to disclose RACE reaction pathway, we next examined the additive effect in this reaction (Scheme 7, Table 4). At first, we investigated RACE reaction of oxime ether **1a** in the presence of either EtOH or BnOH, which are formed in situ in this radical reaction (entries 2 and 3). As the result, the yield of amino ester **3a** increased while the yield of *N*-norpyrroloquinoline **2a** decreased. The presence of BnOH resulted in the formation of *trans*-debenzyloxylated amino ester **10a**, which was converted into *trans*-pyrroloquinoline **2a** in refluxing benzene. We next examined the influence of Brønsted and Lewis acids, which would form a possible complex with nitrogen atom on oxime ether to affect addition reaction of tributylstannyl radical at first step (entries 4–6). Employment of TFA, *p*-TsOH, and $SnCl_4$ as an acid decreased the yield of **2a**. The presence of molecular sieves to remove moisture did not influence the yield of tricyclic compound **2a** (entry 7).



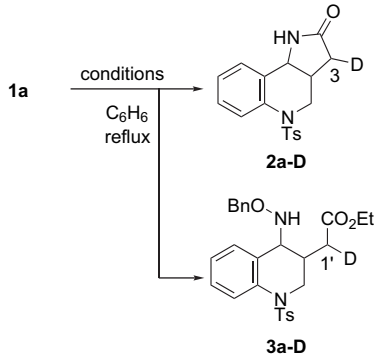
Scheme 7.

In order to clarify the reaction pathway of radical addition reaction in first step, we investigated RACE reaction using either Bu_3SnD or D_2O (Scheme 8, Table 5). The RACE reaction of oxime ether **1a** with Bu_3SnD/AIBN afforded deuterated **2a-D** and **3a-D**, the latter of which was hardly deuterated (entry 1). ^1H NMR spectra of *cis*- and *trans*-**2a-D** showed that deuterium was incorporated in 69–76% at the 3-position. On the other hand, the deuterium was incorporated only in 1-3% into 1′-position of *cis*- and *trans*-**3a-D**. The radical reaction of **1a** with Bu_3SnH followed by treatment of the resulting reaction mixture with D_2O gave

Table 4. Radical reaction of **1a** in the presence of additive

Entry	Conditions	Yield (%)			
		2a (*cis*/*trans*)	**3a** (*cis*/*trans*)	**9a**	**10a** (*trans*)
1	C_6H_6	46 (1/1.3)	13 (1/1.3)	7	—
2	C_6H_6 EtOH (5 equiv)	38 (1/1.3)	21 (1/1.5)	12	—
3	C_6H_6 BnOH (2.5 equiv)	21 (1.7/1)	24 (1/1.1)	1	9
4	C_6H_6 TFA (1.2 equiv)	33 (1/1.4)	14 (1/1.3)	3	—
5	C_6H_6 *p*-TsOH (1.2 equiv)	33 (1.1/1)	19 (1/1.3)	5	—
6	C_6H_6 $SnCl_4$ (1.2 equiv)	30 (1/1.2)	7 (1/1)	4	—
7	C_6H_6 MS (powder)	45 (1/1.1)	8 (1/1.3)	5	—

deuterated **3a-D**, in which deuterium was incorporated into 1′-position in *cis*- and *trans*-**3a-D** with low deuterium incorporation (19–34%). On the other hand, the deuterium incorporation at the 3-position in compounds of *cis*- and *trans*-**2a-D** was not detected (entry 2). Insufficient incorporation of deuterium in the compound **3a-D** under the conditions shown in entry 2 would be probably explained by the formation of BnOH and EtOH in the reaction mixture. As expected, the radical reaction of **1a** with Bu_3SnH in the presence of D_2O resulted in high deuterium incorporation (82–83%) of **3a-D** (entry 3). These deuterium experiments



Scheme 8.

Table 5. Radical reaction of **1a** with the deuterated reagents

Entry	Conditions	Deuterium incorporation (%)[a]			
		2a-D		**3a-D**	
		cis	*trans*	*cis*	*trans*
1	(1) Bu_3SnD/AIBN; (2) H_2O	69	76	3	1
2	(1) Bu_3SnH/AIBN; (2) D_2O	0	0	19	34
3	Bu_3SnH/AIBN/D_2O	2	0	82	83

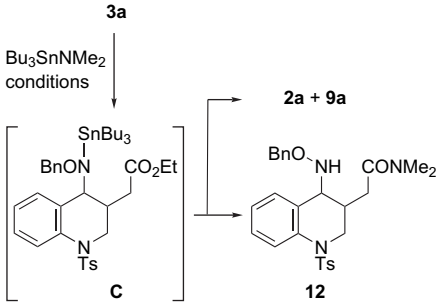
[a] Calculated by ^1H NMR.

Table 7. Reaction of **9a** with dimethylaminotributyltin

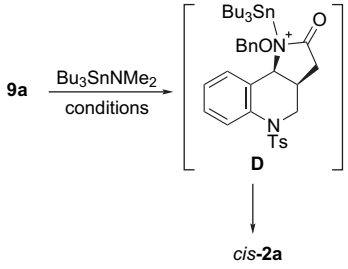
Entry	Bu_3SnNMe_2 (equiv)	Conditions	Yield (%)	
			cis-**2a**	**9a**
1	0	Bu_3SnH (2 equiv), AIBN (0.2 equiv), C_6H_6, reflux	No reaction, SM was recovered	
2	4.3	Neat, 110 °C	33	60
3	4.3	Bu_3SnH (2 equiv), AIBN (0.2 equiv), C_6H_6, reflux	83	—

suggest that the major reaction pathways to either pyrroloquinoline **2a** or amino ester **3a** are possibly not the same.

For establishment of the reaction pathway of the debenzyloxylation step, we then attempted conversion of the bicyclic amino ester **3a** and tricyclic *N*-benzyloxypyrroloquinoline **9a** into the *N*-norpyrroloquinoline **2a** (Schemes 9 and 10, Tables 6 and 7). However, reaction of **3a** and **9a** under the same radical reaction conditions did not give the desired pyrroloquinoline **2a** but recovered **3a** and **9a**, respectively (entries 1 and 5 in Table 6; entry 1 in Table 7). Therefore, we propose aminostannanes **C** and **D** instead of **3a** and **9a** as a possible intermediate for debenzyloxylation. According to the reported procedure,[9] aminostannanes **C** and **D** would



Scheme 9.



Scheme 10.

be expected to generate in situ by the reaction of **3a** and **9a** with Bu_3SnNMe_2. The reaction of *cis*-**3a** with a large amount of Bu_3SnNMe_2 proceeded in refluxing benzene to give the desired debenzyloxylated *N*-norpyrroloquinoline **2a** in low yield (entry 2, Table 6). The same reaction with 1 equiv of Bu_3SnNMe_2 did not give **2a**. When the reaction was carried out under the neat reaction conditions, the desired product **2a** was obtained in 34% yield in addition to pyrroloquinoline **9a** (28%) and amide **12** (16%) (entry 3). Similarly, *trans*-**3a** gave **2a** in 27% yield under the same neat conditions (entry 6). Reaction of *cis*- and *trans*-amino esters **3a** with Bu_3SnNMe_2 proceeded inefficiently under RACE reaction conditions (entries 4 and 7).

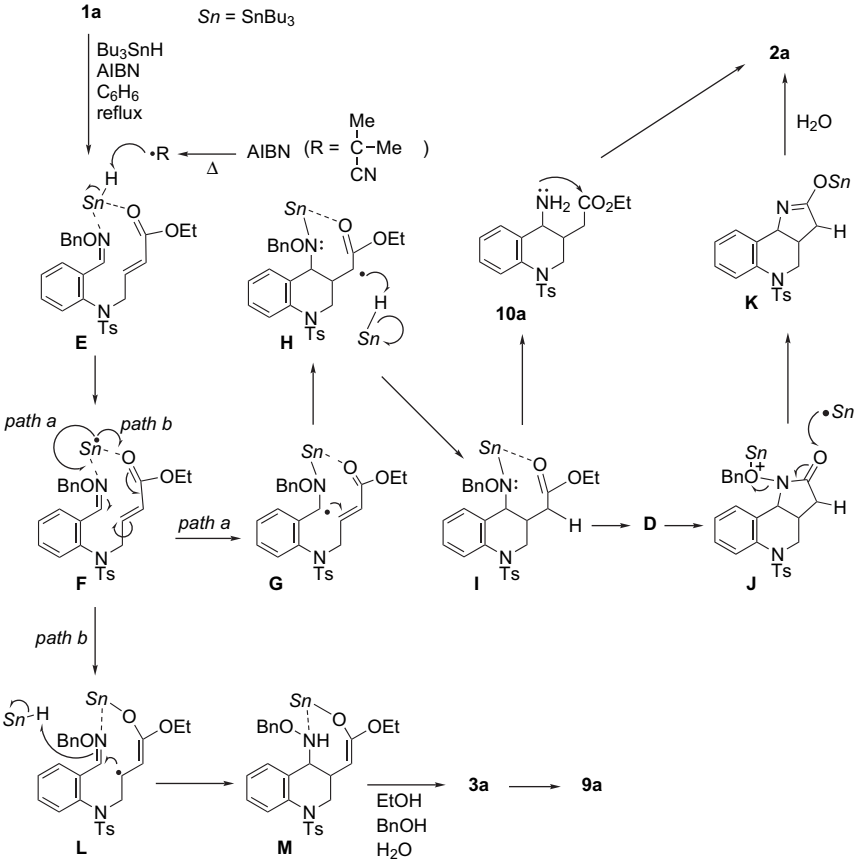
We next examined the conversion of **9a** into **2a** in the presence of Bu_3SnNMe_2 and obtained **2a** in 33% yield with recovering 60% of **9a** (entry 2, Table 7). Furthermore, **9a** was treated with Bu_3SnNMe_2 under RACE reaction conditions (Bu_3SnH/AIBN in refluxing benzene) to give the desired **2a** in good yield (entry 3). As mentioned above, we found that the debenzyloxylated *N*-norpyrroloquinoline **2a** is formed from **3a** and **9a** via aminostannanes **C** and **D** in RACE reaction.

Under the debenzyloxylation conditions (Bu_3SnNMe_2, Bu_3SnH, AIBN), amino ester *cis*-**3a** gave *N*-norpyrroloquinoline **2a** not in good yield (only 16%) but *N*-benzyloxylactam **9a** gave the corresponding **2a** in good yield (83%). This result strongly suggests not only that the reaction pathway from **9a** to **2a** would be different from that from **3a** to **2a** but also that conversion of **9a** into **2a** would proceed via radical process.

We propose possible reaction pathway for RACE reaction (Scheme 11). It is known that *O*-coordinated Ph_3SnH would more readily undergo H-atom abstraction than uncoordinated Ph_3SnH[10a] and that *O*-coordinated stannyl radicals would exist for a longer lifetime in solution compared with their uncoordinated radicals.[10] Therefore, Bu_3SnH would moderately coordinate to the ester and/or oxime ether

Table 6. Reaction of **3a** with dimethylaminotributyltin

Entry	Substrate **3a**	Bu_3SnNMe_2 (equiv)	Conditions	Yield (%)		
				2a	**9a**	**12**
1	*cis*	0	Bu_3SnH (2 equiv), AIBN (0.2 equiv), C_6H_6, reflux	No reaction, SM was recovered		
2	*cis*	19	C_6H_6, reflux	2	7	—
3	*cis*	8	Neat, 110 °C	34	28	16
4	*cis*	4	Bu_3SnH (2 equiv), AIBN (0.2 equiv), C_6H_6, reflux	16	—	65
5	*trans*	0	Bu_3SnH (2 equiv), AIBN (0.2 equiv), C_6H_6, reflux	No reaction, SM was recovered		
6	*trans*	4.7	Neat, 110 °C	27	—	50
7	*trans*	4	Bu_3SnH (2 equiv), AIBN (0.2 equiv), C_6H_6, reflux	—	—	74

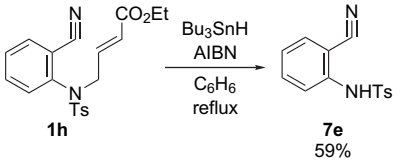


Scheme 11.

group in the substrate **1a** on RACE reaction to form the intermediate **E**. This hypothesis is supported by the improved yield (69%) of *N*-norpyrroloquinoline **2a** in RACE reaction of **1a** with Ph_3SnH, which is well known for more acidic than Bu_3SnH. Then, the reaction of **E** with AIBN generated the coordinated stannyl radical **F**, which would be converted into **2a**, **3a**, and **9a** via two possible reaction pathways, paths a and b. The addition of stannyl radical **F** to the oxime ether part forms more stable (α-stannylamino)benzyl radical **G** (path a), which cyclizes to α,β-unsaturated ester to form the α-ethoxycarbonylmethyl radical **H**. The radical **H** is trapped by Bu_3SnH to afford the intermediate **I**. The removal of the benzyloxy group in intermediate **I** followed by the cyclization of the resulting amino ester **10a** gives *N*-norpyrroloquinoline **2a**. As an alternative route, the intermediate **I** could be converted into **2a** via first cyclization followed by second removal of the benzyloxy group. The attack of stannyl radical at the lactam carbonyl group in **J** followed by the cleavage of N–O bond gives the stannyl enolate **K**, which would be converted into **2a** by work-up procedure with water. On the other hand, concomitant formation of the benzyloxyamino ester **3a** and *cis*-*N*-benzyloxypyrroloquinoline **9a** would be explained through path b based on the experimental results using either Bu_3SnD or D_2O. The addition of stannyl radical in **F** to α,β-unsaturated ester followed by the cyclization of the resulting radical **L** gives the stannyl enolate **M**, which is converted into **3a** by protonation with either BnOH and EtOH existed in the reaction mixture or water during work-up procedure. *cis*-**3a** is partially converted into *cis*-**9a** under the radical reaction conditions.

2.2. Preparation and radical reaction of unsaturated esters carrying the cyano, hydrazono, imino, and carbonyl groups

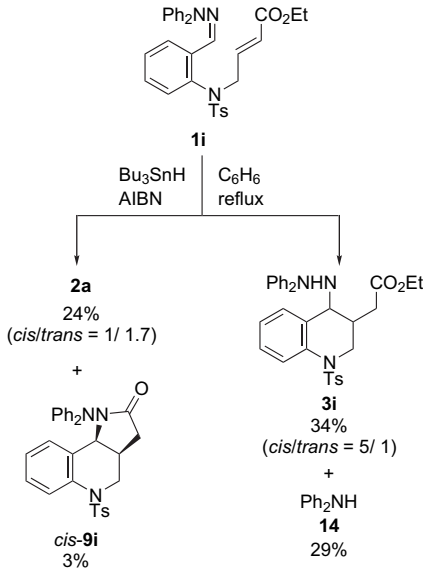
To survey the scope and limitations of our radical addition–cyclization method, we investigated RACE reaction of α,β-unsaturated esters **1h–l** carrying cyano, hydrazono, imino, and carbonyl groups. The requisite substrates **1h–l** for the radical reaction were prepared according to almost same procedure given for the preparation of oxime ethers **1a–g**. We then investigated the radical reaction of **1h–j**. Under the standard radical conditions, nitrile **1h** gave unfortunately sulfonamide **7e**[11] in 59% yield as in the case of the reactions of ketoxime ethers **1f**,**g** (Scheme 12).



Scheme 12.

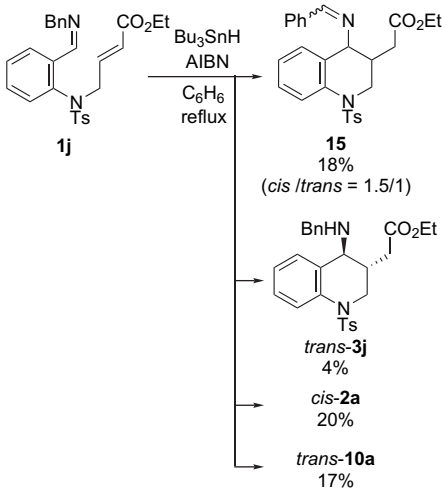
In the case of hydrazone **1i**, the radical addition–cyclization reaction proceeded smoothly to form *N*-norpyrroloquinoline **2a** (24%), bicyclic hydrazine **3i** (34%), and diphenylamine **14** (29%) with a small amount of tricyclic *N*-diphenylaminopyrroloquinoline **9i**. The fact that major product is not *N*-norpyrroloquinoline **2a** but bicyclic hydrazine **3i** is

contrast with the result found in RACE of oxime ether **1a**. It is shown that the cleavage of N–N bond in hydrazines is possible but not so easy compared with that of N–O bond in alkoxyamines (Scheme 13).



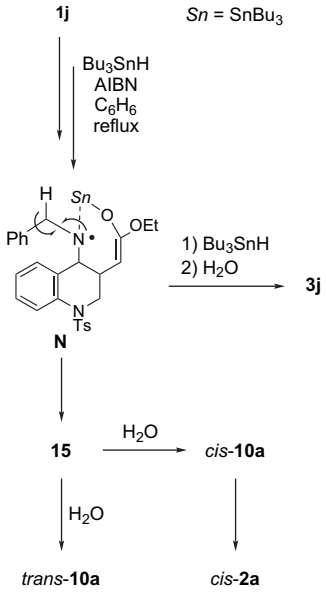
Scheme 13.

The radical reaction of imine **1j** gave *cis*-*N*-norpyrroloquinoline **2a**, bicyclic *trans*-amino ester **10a**, bicyclic imine **15**, and interestingly *trans*-benzylamino ester **3j** (Scheme 14). The *cis*-imine **15** was converted into *cis*-*N*-norpyrroloquinoline **2a** via *cis*-amino ester **10a** on standing at room temperature. On the other hand, *trans*-imine **15** gave not only the *trans*-pyrroloquinoline **2a** but also the *trans*-amino ester **10a**.



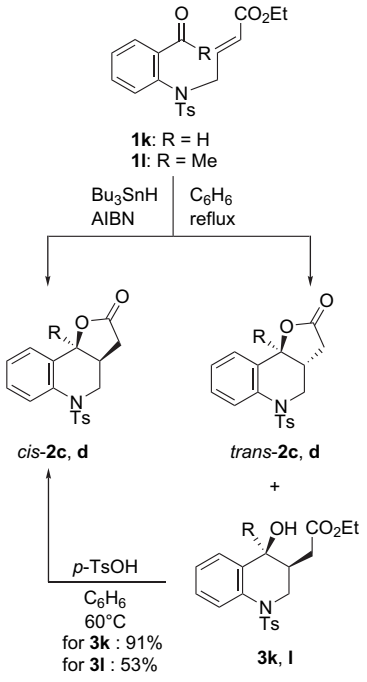
Scheme 14.

From the above result, we propose the reaction pathway of radical reaction of imine **1j** (Scheme 15). The benzylic hydrogen atom in intermediary aminyl radical **N**, formed by the addition of stannyl radical to the unsaturated ester and subsequent cyclization, was abstracted to give the imine **15**. During work-up procedure, *cis*-imine **15** was subjected to hydrolysis to form *cis*-amino ester **10a**, which was easily converted into *cis*-pyrroloquinoline **2a**. On the other hand, the formation of *trans*-pyrroloquinoline **2a** was not observed because the cyclization of *trans*-amino ester **10a** would be more difficult than that of the corresponding *cis*-stereoisomer **10a**. Furthermore, the radical **N** was reduced by Bu_3SnH to give the benzylamino ester **3j**, which was also formed by the addition of stannyl radical to oxime ether followed by cyclization.



Scheme 15.

The radical reactions of aldehyde **1k** and ketone **1l** carrying unsaturated ester proceeded smoothly to give *cis*-furoquinolines **2c**,**d** as a major product, in addition to *trans*-furoquinolines **2c**,**d** and *cis*-hydroxy ester **3k**,**l** the latter of which were treated with TsOH at 60 °C to give *cis*-**2c**,**d** (Scheme 16,



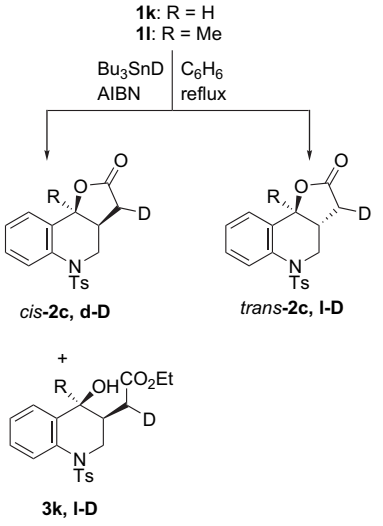
Scheme 16.

Table 8. Radical reaction of carbonyl compounds **1k**,**l**

Entry	Substrate	R	Yield (%)		
			cis-**2c**,**d**	*trans*-**2c**,**d**	**3k**,**l**
1	**1k**	H	59	3	29
2	**1l**	Me	52	6	24

Table 8). Thus, radical reactions of carbonyl compounds **1k**,**l** proceeded with high *cis*-stereoselectivity.

In order to clarify *cis*-stereoselectivity in this reaction, we examined the radical reaction using either Bu_3SnD or D_2O. The reaction of carbonyl compounds **1k**,**l** with Bu_3SnD/AIBN afforded deuterated *cis*-**2c**,**d-D**, *trans*-**2c**,**d-D**, and **3k**,**l-D** as shown in Scheme 17 and Table 9. On the other hand, when the radical reaction of **1k**,**l** with Bu_3SnH was carried out in the presence of D_2O, deuterium was not incorporated into any products, *cis*-**2c**,**d**, *trans*-**2c**,**d**, and **3k**,**l**.



Scheme 17.

This results show that the addition of stannyl radical takes place on aldehyde and ketone to give *cis*-**2c**,**d**, *trans*-**2c**,**d**, and **3k**,**l**, all of which are formed through the same route. Thus, we propose a possible intermediate **O** in which Bu_3SnH would coordinate to both the ester and formyl groups (Fig. 1). The furoquinoline **2c** is obtained by the formation of lactone ring under the reaction conditions. The fact that high *cis*-selectivity was observed in radical reaction of **1k**,**l** is explained by stronger coordination of stannane with oxygen than that with nitrogen (see Scheme 11). The radical reactions of nitrile **1h**, hydrazone **1i**, imine **1j**, and carbonyl compounds **1k**,**l** can be summarized as follows.

Table 9. Radical reaction of carbonyl compounds **1k**,**l** using Bu_3SnD

Substrate	Deuterium incorporation (%)[a]		
	cis-**2c**,**d-D**	*trans*-**2c**,**d-D**	**3k**,**l-D**
1k	95	56	66
1l	70	100	80

[a] Calculated by ^1H NMR.

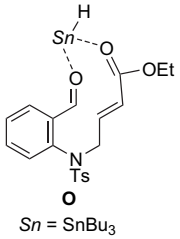


Figure 1.

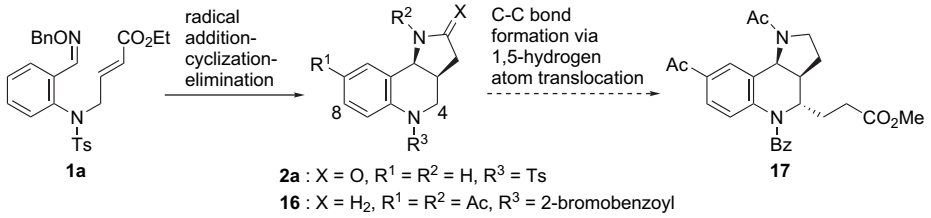
(a) Nitrile **1h** underwent fragmentation without cyclization. (b) RACE reaction of hydrazone **1i** proceeded almost similar to that of oxime ether. (c) The imine **1j** was subjected to radical addition–cyclization–oxidation even under reductive conditions to give imine **15**, which was converted into pyrroloquinoline **2a** by hydrolysis followed by cyclization. (d) The radical reaction of carbonyl compounds **1k**,**l** gave the *cis*-furoquinoline and *cis*-hydroxy ester with high cis-stereoselectivity.

2.3. A formal synthesis of (±)-martinelline

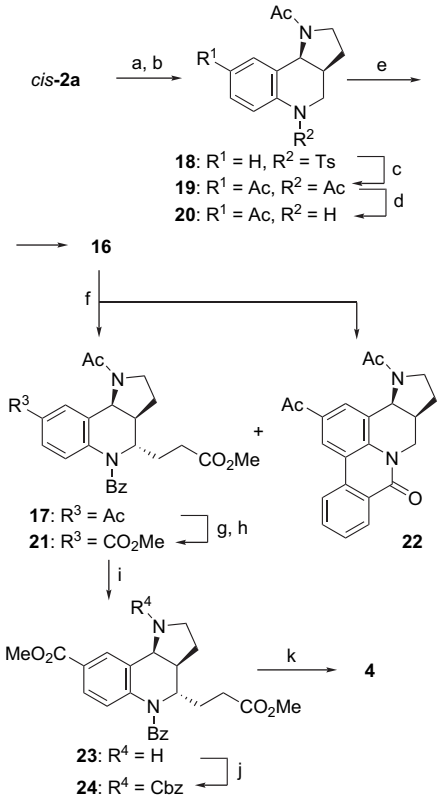
With *cis*-pyrroloquinoline **2a** in hand, we next investigated the synthetic potentiality of our RACE methodology by converting **2a** into a key intermediate **4** for the synthesis of (±)-martinelline (**5a**) (Scheme 1). Martinelline and martinellic acid were isolated from an organic extract of the *Martinella iquitosensis* root in 1995.[12] These compounds show antibiotic activity against Gram-positive and Gram-negative bacteria and affinity for several G-protein receptors, and are the first non-peptide bradykinin receptor antagonist reported to date. The pyrrolo[3,2-*c*]quinoline ring system of the martinellines core has not been reported previously in any natural product. Their biological activity and unique structure have made them the subject of intense synthetic interest.[5,13,14]

Our synthetic strategy includes two crucial radical reactions: (1) an above-mentioned RACE reaction for the construction of pyrroloquinoline ring (**1a**→**2a**); (2) *C*–*C* bond formation through a 1,5-hydrogen atom translocation for the stereoselective introduction of the side chain into the C(4)-position of pyrroloquinoline (**16**→**17**) (Scheme 18).

We examined the introduction of a carbonyl group into the C(8)-position and a C_3 unit into the C(4)-position of *cis*-**2a** possessing requisite stereostructure for the synthesis of martinelline (Scheme 19). Reduction of *cis*-**2a** with $BH_3 \cdot Me_2S$ followed by work-up with 6 M HCl to cleave the *B*–*N* bond of the resulting intermediate gave the corresponding amine, which without purification was then acetylated with AcCl in the presence of Et_3N to give amide **18** in 94% yield (two steps from *cis*-**2**). According to the known procedure, we investigated the Friedel–Crafts reaction of **18**. When **18** was treated with AcCl (3 equiv) and $AlCl_3$ (6 equiv) in refluxing 1,2-dichloroethane, we obtained fortunately the 1,5,8-triacetyl compound **19** in which the tosyl group was converted into the easily removable acetyl group.[15] Treatment of **19** with 10% aqueous NaOH in MeOH at room temperature caused selective deacetylation at the vinylogous imide system to give the 1,8-diacetyl compound **20** in 47% yield (two steps from **18**).



Scheme 18.

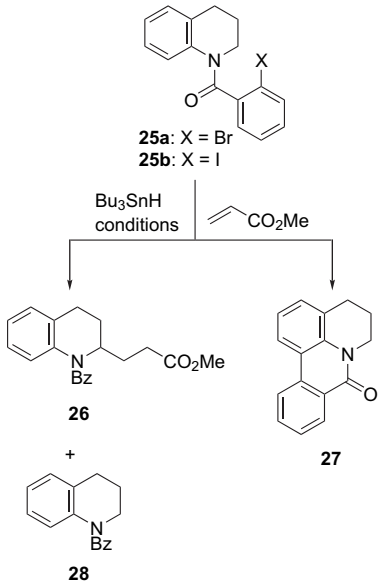


Scheme 19. Reagents: (a) $BH_3 \cdot Me_2S$, THF, reflux; (b) AcCl, Et_3N, CH_2Cl_2, 0 °C; (c) AcCl, $AlCl_3$, $ClCH_2CH_2Cl$, reflux; (d) 10% NaOH, MeOH, rt; (e) 2-bromobenzoyl chloride, Et_3N, CH_2Cl_2, rt; (f) methyl acrylate, Bu_3SnH, AIBN, benzene, reflux; (g) Br_2, 2.5% NaOH, 0 °C; (h) concd H_2SO_4, MeOH, reflux; (i) $Et_3O \cdot BF_4$, $NaHCO_3$, rt, then satd $NaHCO_3$, rt; (j) CbzCl, Et_3N, CH_2Cl_2, 0 °C; (k) $LiBH_4$, MeOH/THF, rt.

Snieckus[16] and Williams[17] have reported a diastereoselective carbon–carbon bond formation of an α-carbon adjacent to a nitrogen via a 1,5-hydrogen atom translocation and subsequent Michael-type of radical addition to methyl acrylate. This method would allow the introduction of the C_3 unit side chain into the C(4)-position adjacent to nitrogen from the less hindered convex face to afford the desired product.

As a preliminary experiment for introduction of side chain into C(4)-position, we investigated the radical reaction of *N*-(2-halogenobenzoyl)tetrahydroquinolines **25a**,**b** prepared by acylation of tetrahydroquinoline with either *o*-bromobenzoyl chloride or *o*-iodobenzoyl chloride (Scheme 20, Table 10).

According to a procedure reported by Snieckus,[16] methyl acrylate, Bu_3SnH, and AIBN were added to the solution of **25a** in toluene and then the reaction mixture was heated at 110 °C to give three products, which are the desired product



Scheme 20.

26 (22%), the tetracyclic product **27**[18a,b] (47%), and the reduced product **28**[18a,c] (26%) (entry 1). In order to improve yield of the desired product **26**, Williams procedure[17] was then applied. When a solution of Bu_3SnH and AIBN in benzene was slowly added by using a syringe pump to a solution of **25a** and methyl acrylate in refluxing benzene, the yield of desired compound **26** improved to 34% (entry 2). Under the same reaction conditions, the yield of **26** increased further by using 10 equiv of methyl acrylate (entry 3). The radical reaction of **25a** using Et_3B as a radical initiator gave **26** but only in 20% yield with recovering substrate **25a** (entry 4). Same type of radical reaction of **25b** carrying *O*-iodobenzoyl group gave similar results (entries 5 and 6).

Based on these preliminary results, we next investigated the radical reaction of **16** with methyl acrylate (Scheme 19). Amine **20** was acylated with 2-bromobenzoyl chloride in the presence of Et_3N to give the radical precursor **16** in 91% yield. When a solution of Bu_3SnH and AIBN in benzene was slowly added by using a syringe pump to a solution of **16** and methyl acrylate in refluxing benzene, the desired compound **17** was formed as a single diastereomer in 43% yield along with the pentacyclic product **22** (19%). The conversion of the C(8)-acetyl group into the methoxycarbonyl group in **17** was achieved by the conventional procedure via haloform reaction. Treatment of **17** with Br_2 in 2.5% aqueous NaOH followed by esterification of the resulting carboxylic acid gave the ester **21** in 76% yield.

Table 10. 1,5-Hydrogen transfer reaction of **25a**,**b**

Entry	Substrate	Conditions, initiator (equiv)	Methyl acrylate (equiv)	Time (h)	Products (% yield)		
					26	**27**	**28**
1	**25a**	AIBN (0.12), toluene, reflux	5	13.5	22	47	26
2[a]	**25a**	AIBN (0.1), benzene, reflux	3	6	34	46	—
3[a]	**25a**	AIBN (0.1), benzene, reflux	10	3	41	47	8
4[b]	**25a**	Et_3B (7.0), toluene, rt	5	13	20	21	—
5[a]	**25b**	AIBN (0.1), benzene, reflux	10	5	36	60	Trace
6	**25b**	Et_3B (3.5), toluene, rt	10	4	36	52	9

[a] The reaction was carried out by using a syringe pump.
[b] Starting material was recovered (<59%).

In order to convert **21** into the known intermediate **4** for martinelline synthesis, we investigated the conversion of the functional groups. Treatment of **21** with $Et_3O\cdot BF_4$ followed by hydrolysis of the resulting unstable imidate with saturated aqueous $NaHCO_3$ afforded amine **23** in 42% yield along with starting material **21** (19%). Amine **23** was reacted with CbzCl in the presence of Et_3N to give the protected compound **24** in 84% yield. Finally, the regioselective reduction of the isolated ester moiety in **24** with $LiBH_4$ in a mixture of 1/10 MeOH/THF at room temperature gave the desired alcohol **4** in 58% yield, which is a key intermediate for the synthesis of martinelline. The spectra of **4** were superimposable with those provided by Professor Ma.[13d]

3. Conclusion

We have developed an unprecedented example of the stannyl radical addition–cyclization–elimination (RACE) reaction of oxime ethers carrying unsaturated ester for constructing the pyrroloquinoline in one procedure. Additionally, the RACE reaction was applied to other imine derivatives and carbonyl compounds to afford various types of heterocycles such as substituted tetrahydroquinolines and furoquinolines.

Furthermore, we have succeeded in a formal synthesis of martinelline via the route involving two radical reactions.

4. Experimental

4.1. General

Melting points are uncorrected. ^1H and ^{13}C NMR spectra were recorded at 200, 300, or 500 MHz and at 50, 75, or 125 MHz for solution in deuteriochloroform (with tetramethylsilane as an internal reference), respectively. IR spectra were recorded using FTIR apparatus for solutions in chloroform except for KBr pellet. Mass spectra were obtained by EI method. Flash column chromatography (FCC) was preformed using E. Merck Kieselgel 60 (230–400 mesh). Medium-pressure column chromatography (MCC) was performed using Lober Größe B (E. Merck 310-25, Lichroprep Si60). Preparative TLC (PTLC) separations were carried out on precoated silica gel plates (E. Merck $60F_{254}$).

4.1.1. 4-Methyl-*N*-[[2-[(1*E*)-(phenylmethoxy)imino]-methyl]phenyl]benzenesulfonamide (7a). To a solution of *N*-[2-(hydroxymethyl)phenyl]-4-methylbenzenesulfonamide (**6**)[7] (2 g, 7.2 mmol) in CH_2Cl_2 (150 mL) was added MnO_2 (22 g, 0.25 mol) under a nitrogen atmosphere at room temperature. After being stirred for 1.5 h, the reaction mixture was filtrated through a pad of Celite and the filtrate was concentrated at reduced pressure to give the crude aldehyde. To a solution of the crude aldehyde in CH_2Cl_2/MeOH (1:1) (80 mL) were added NaOAc (500 mg, 6.2 mmol) and $BnONH_2\cdot HCl$ (1.0 g, 6.2 mmol) under a nitrogen atmosphere at room temperature. After being stirred for 1.5 h, the reaction mixture was diluted with saturated aqueous $NaHCO_3$ and extracted with CH_2Cl_2. The organic phase was washed with brine, dried over $MgSO_4$, and concentrated at reduced pressure. The residue was purified by recrystallization from EtOH to afford **7a** (1.92 g, 70%) as colorless crystals. Mp 138–140 °C (EtOH). IR ν_{max} cm^{-1}: 3154 (NH). ^1H NMR (300 MHz) δ: 8.07 (1H, s), 7.62 (1H, br d, J=8 Hz), 7.34–7.54 (8H, m), 7.23 (1H, br t, J=8 Hz), 7.05–7.14 (3H, m), 6.99 (1H, br t, J=7.5 Hz), 5.23 (2H, s), 2.32 (3H, s). ^{13}C NMR (75 MHz) δ: 151.3, 143.6, 136.9, 136.8, 136.4, 132.1, 130.5, 129.4, 129.0, 128.7, 128.3, 127.2, 123.1, 118.8, 118.3, 76.9, 21.4. HRMS (EI) *m*/*z*: Calcd for $C_{21}H_{20}N_2O_3S$ (M^+) 380.1194. Found: 380.1200. Anal. Calcd for $C_{21}H_{20}N_2O_3S\cdot 1/5H_2O$: C, 65.67; H, 5.35; N, 7.29. Found: C, 65.65; H, 5.12; N, 7.22.

4.1.2. *N*-[2-[(1*E*/*Z*)-(Methoxyimino)methyl]phenyl]-4-methylbenzenesulfonamide (7b). According to the procedure described in the preparation of **7a**, oxidation of **6** (2 g, 7.2 mmol) with MnO_2 (22 g, 250 mmol) gave crude aldehyde. Condensation of crude aldehyde with $MeONH_2\cdot HCl$ (0.52 g, 6.2 mmol) gave **7b** (873.1 mg 48%) as colorless crystals and a 4:1 mixture of *E*- and *Z*-isomers. Mp 127–131 °C (EtOH). IR ν_{max} (KBr) cm^{-1}: 3439 (NH), 1340, 1121 (NSO_2). ^1H NMR (200 MHz) δ: 10.33 (1H, br s), 7.99 (4/5H, s), 7.95–6.91 (8H+1/5H, m), 4.03 (12/5H, s), 3.84 (3/5H, s), 2.45 (3/5H, s), 2.33 (12/5H, s). ^{13}C NMR (50 MHz) δ: 150.7, 143.7, 136.6, 136.5, 132.0, 130.4, 129.6, 129.4, 127.1, 123.3, 119.0, 118.8, 62.6, 21.4. HRMS *m*/*z*: Calcd for $C_{15}H_{16}N_2O_3S$ (M^+) 304.0881. Found: 304.0872. Anal. Calcd for $C_{15}H_{16}N_2O_3S$: C, 58.94; H, 5.52; N, 8.87. Found: C, 58.99; H, 5.22; N, 8.63.

4.2. General procedure for preparation of oxime ethers 1a–e [Table 1]

To a solution of **7a** or **7b** in acetone (0.05–0.1 mmol/mL) were added ethyl 4-bromocrotonate, *tert*-butyl 4-bromocrotonate,[20] (2*E*)-4-bromo-*N*-(phenylmethyl)-2-butenamide,[19] or (*E*/*Z*)-4-bromocrotononitrile[21] (1–1.5 equiv), and K_2CO_3 (2-5 equiv) under a nitrogen atmosphere at room temperature. After disappearance of the starting material (TLC

monitoring), the reaction mixture was diluted with saturated aqueous $NaHCO_3$ and extracted with Et_2O. The organic phase was washed with brine, dried over $MgSO_4$, and concentrated at reduced pressure. The residue was purified by FCC.

4.2.1. Ethyl-(2*E*)-4-[[(4-methylphenyl)sulfonyl][2-[(phenylmethoxy)imino]methyl]phenyl]amino-2-butenoate (1a) [entry 1]. Colorless crystals. Mp 61–62 °C (AcOEt). IR ν_{max} cm^{-1}: 1717 (CO_2Et). ^1H NMR (300 MHz) δ: 8.34 (1H, s), 7.92 (1H, dd, J=8, 2 Hz), 7.53 (2H, br d, J=8 Hz), 7.20–7.44 (9H, m), 6.75 (1H, dt, J=15.5, 7 Hz), 6.73 (1H, dd, J=7.5, 1 Hz), 5.77 (1H, br d, J=15.5 Hz), 5.19 (2H, s), 4.13 (2H, q, J=7 Hz), 4.00–4.40 (2H, m), 2.42 (3H, s), 1.24 (3H, t, J=7 Hz). ^{13}C NMR (75 MHz) δ: 165.2, 145.6, 144.1, 140.9, 137.41, 137.35, 135.0, 132.9, 130.0, 129.6, 128.9, 128.8, 128.3, 128.2, 127.9, 127.2, 124.8, 76.4, 60.5, 52.8, 21.5, 14.1. HRMS (EI) m/z: Calcd for $C_{27}H_{28}N_2O_5S$ (M^+) 492.1717. Found: 492.1716. Anal. Calcd for $C_{27}H_{28}N_2O_5S$: C, 65.83; H, 5.73; N, 5.69. Found: C, 65.75; H, 5.67; N, 5.68.

4.2.2. 1,1-Dimethylethyl-(2*E*)-4-[[(4-methylphenyl)sulfonyl][2-[(1*E*)-[(phenylmethoxy)imino]methyl]phenyl]amino]-2-butenoate (1b) [entry 2]. Colorless crystals. Mp 109–110 °C (EtOH). IR ν_{max} cm^{-1}: 1709 (COO), 1357, 1163 (NSO_2). ^1H NMR (200 MHz) δ: 8.34 (1H, s), 7.93 (1H, dd, J=7, 2 Hz), 7.56–7.20 (11H, m), 6.72 (1H, dd, J=7, 2 Hz), 6.63 (1H, dt, J=16, 7 Hz), 5.69 (1H, br d, J=16 Hz), 5.19 (2H, s), 4.22 (2H, m), 2.42 (3H, s), 1.42 (9H, s). ^{13}C NMR (50 MHz) δ: 165.4, 146.8, 144.2, 140.9, 137.5, 134.8, 133.0, 130.2, 129.7, 128.9, 128.8, 127.9, 127.0, 124.8, 60.6, 52.8, 21.5, 14.0. HRMS m/z: Calcd for $C_{29}H_{33}N_2O_5S$ (M+H^+) 521.2108. Found: 521.2100. Anal. Calcd for $C_{29}H_{32}N_2O_5S$: C, 66.90; H, 6.20; N, 5.38. Found: C, 66.80; H, 6.22; N, 5.35.

4.2.3. (2*E*)-4-[[(4-Methylphenyl)sulfonyl][2-[(phenylmethoxy)imino]methyl]phenyl]amino-*N*-(phenylmethyl)-2-butanamide (1c) [entry 3]. Colorless crystals. Mp 129–133 °C (AcOEt). IR ν_{max} cm^{-1}: 3440 (NH), 1680 (CON). ^1H NMR (300 MHz) δ: 8.40 (1H, s), 7.90 (1H, d, J=7.5 Hz), 7.53 (1H, d, J=7 Hz), 7.20–7.40 (15H, m), 6.72 (1H, d, J=7.5 Hz), 6.63 (1H, dt, J=15.5, 6 Hz), 5.83 (1H, d, J=15.5 Hz), 5.69 (1H, br s), 5.14 (2H, s), 4.43 (2H, d, J=5.5 Hz), 4.24 (2H, br s), 2.42 (3H, s). ^{13}C NMR (75 MHz) δ: 164.4, 146.1, 144.1, 137.9, 137.6, 137.4, 136.8, 135.2, 133.0, 130.1, 129.7, 129.0, 128.9, 128.7, 128.4, 128.3, 127.9, 127.8, 127.6, 127.4, 127.2, 52.8, 43.6, 21.6. HRMS m/z: Calcd for $C_{32}H_{31}N_3O_4S$ (M) 553.2034. Found: 553.2041. Anal. Calcd for $C_{32}H_{31}N_3O_4S\cdot 1/2H_2O$: C, 68.31; H, 5.73; N, 7.47. Found: C, 68.48; H, 5.65; N, 7.40.

4.2.4. (2*E*)-4-[[(4-Methylphenyl)sulfonyl][2-[(1*E*)-[(phenylmethoxy)imino]methyl]phenyl]amino]-2-butenenitrile ((*E*)-1d) [entry 4]. A colorless oil. IR ν_{max} cm^{-1}: 2231 (CN), 1358, 1165 (NSO_2). ^1H NMR (200 MHz) δ: 8.28 (1H, s), 7.90 (1H, dd, J=8, 2 Hz), 7.53–7.22 (11H, m), 6.71 (1H, dd, J=8, 2 Hz), 6.54 (1H, dt, J=16, 7 Hz), 5.33 (1H, dt, J=16, 2 Hz), 5.19 (2H, s), 4.20 (2H, br d, J=7 Hz,), 2.42 (3H, s). ^{13}C NMR (75 MHz) δ: 148.0, 145.4, 144.4, 137.2, 137.0, 134.6, 132.8, 130.2, 129.7, 129.1, 128.8, 128.4, 128.3, 127.9, 127.8, 127.5, 116.0, 103.4, 76.5, 53.1, 21.5. HRMS m/z: Calcd for $C_{25}H_{24}N_3O_3S$ (M+H^+) 446.1537. Found: 446.1549.

4.2.5. (2*Z*)-4-[[(4-Methylphenyl)sulfonyl][2-[(1*E*)-[(phenylmethoxy)imino]methyl]phenyl]amino]-2-butenenitrile ((*Z*)-1d) [entry 4]. Colorless crystals. Mp 126–128 °C (EtOH). IR ν_{max} cm^{-1}: 2225 (CN), 1358, 1166 (NSO_2). ^1H NMR (200 MHz) δ: 8.51 (1H, s), 7.94 (1H, dd, J=8, 2 Hz), 7.56–7.20 (11H, m), 6.63 (1H, dd, J=8, 2 Hz), 6.45 (1H, br dt, J=11, 7 Hz), 5.26 (1H, dt, J=11, 1 Hz), 5.21 (2H, s), 4.63 (1H, br dd, J=15, 5 Hz), 4.16 (1H, br dd, J=15, 8 Hz), 2.44 (3H, s). ^{13}C NMR (75 MHz) δ: 147.6, 145.8, 144.5, 137.29, 137.26, 133.9, 133.2, 130.3, 129.7, 129.0, 128.33, 128.29, 128.0, 127.9, 127.8, 127.1, 114.4, 102.7, 76.4, 51.7, 21.5. HRMS m/z: Calcd for $C_{25}H_{24}N_3O_3S$ (M+H^+) 446.1537. Found: 446.1549. Anal. Calcd for $C_{25}H_{23}N_3O_3S$: C, 67.39; H, 5.20; N, 9.43. Found: C, 67.38; H, 5.18; N, 9.49.

4.2.6. Ethyl-(2*E*)-4-[[2-[(1*E*)-(methoxyimino)methyl]phenyl][(4-methylphenyl)sulfonyl]amino]-2-butenoate (1e) [entry 5]. Colorless crystals. Mp 149–151 °C (EtOH). IR ν_{max} cm^{-1}: 1717 (COO), 1355, 1164 (NSO_2). ^1H NMR (300 MHz) δ: 8.28 (1H, s), 7.93 (1H, dd, J=8, 1.5 Hz), 7.53 (2H, br d, J=6 Hz), 7.35–7.22 (4H, m), 6.76 (1H, dt, J=16, 7 Hz), 6.72 (1H, br d, J=8 Hz), 5.80 (1H, dt, J=16, 1 Hz), 4.34 (2H, m), 4.13 (2H, q, J=7 Hz), 3.96 (3H, s), 2.45 (3H, s), 1.25 (3H, t, J=7 Hz). ^{13}C NMR (50 MHz) δ: 165.2, 145.2, 144.1, 140.8, 137.3, 134.8, 133.0, 130.0, 129.6, 128.74, 128.65, 127.8, 127.0, 124.8, 61.9, 60.4, 52.8, 21.4, 14.0. HRMS m/z: Calcd for $C_{21}H_{24}N_2O_5S$ (M^+) 416.1404. Found: 416.1399. Anal. Calcd for $C_{21}H_{24}N_2O_5S$: C, 60.56; H, 5.81; N, 6.73. Found: C, 60.56; H, 5.81; N, 6.71.

4.2.7. 4-Methyl-*N*-[2-[1-(1*E*)-[(phenylmethoxy)imino]ethyl]phenyl]benzenesulfonamide (7c). To a solution of *N*-(2-acetylphenyl)-4-methylbenzenesulfonamide[22] (500 mg, 1.7 mmol) in EtOH/CH_2Cl_2 (1:1) (10 mL) was added $BnONH_2\cdot HCl$ (340 mg, 2.2 mmol) under a nitrogen atmosphere. After being stirred and heated at reflux for 8 h, $BnONH_2\cdot HCl$ (95 mg, 0.86 mmol) was added two for times every 10 h. The reaction mixture was diluted with water and extracted with $CHCl_3$. The organic phase was washed with brine, dried over $MgSO_4$, and concentrated at reduced pressure. The residue was purified by recrystallization from EtOH to afford **7c** (506.4 mg, 79%) as colorless crystals. Mp 129–131 °C (EtOH). IR ν_{max} cm^{-1}: 3031 (NH), 1339, 1161 (NSO_2). ^1H NMR (200 MHz) δ: 10.66 (1H, br s), 7.64–7.01 (13H, m), 5.26 (2H, s), 2.32 (3H, s), 2.07 (3H, s). ^{13}C NMR (50 MHz) δ: 156.5, 143.2, 137.1, 136.2, 135.7, 129.5, 129.2, 128.6, 128.4, 128.1, 127.0, 124.6, 123.9, 123.7, 121.0, 76.6, 21.2, 13.2. HRMS m/z: Calcd for $C_{22}H_{22}N_2O_3S$ (M^+) 394.1340. Found: 394.1359. Anal. Calcd for $C_{22}H_{22}N_2O_3S$: C, 66.98; H, 5.62; N, 7.10. Found: C, 66.99; H, 5.62; N, 7.16.

4.2.8. *N*-[2-[1-(1*E*)-(Methoxyimino)ethyl]phenyl]-4-methylbenzenesulfonamide (7d). To a solution of *N*-(2-acetylphenyl)-4-methylbenzenesulfonamide[22] (500 mg, 1.7 mmol) in EtOH (9 mL) were added $MeONH_2\cdot HCl$ (289 mg, 3.5 mmol) and pyridine (0.28 mL, 3.5 mmol) under a nitrogen atmosphere. After being stirred and heated at reflux for 15 h, the reaction mixture was diluted with water and extracted with $CHCl_3$. The organic phase was washed

with brine, dried over $MgSO_4$, and concentrated at reduced pressure. The residue was purified by recrystallization from EtOH to afford **7d** (382.1 mg, 69%) as pale yellow crystals. Mp 136–138 °C (EtOH). IR ν_{max} cm^{-1}: 3030 (NH), 1339, 1162 (NSO_2). ^1H NMR (300 MHz) δ: 10.74 (1H, br s), 7.66–7.04 (8H, m), 4.07 (3H, s), 2.35 (3H, s), 2.01 (3H, s). ^{13}C NMR (50 MHz) δ: 155.8, 143.4, 136.2, 135.6, 129.5, 129.2, 128.3, 126.9, 124.3, 124.0, 121.6, 62.3, 21.2, 12.9. HRMS *m/z*: Calcd for $C_{16}H_{18}N_2O_3S$ (M^+) 318.1037. Found: 318.1044. Anal. Calcd for $C_{16}H_{18}N_2O_3S$: C, 60.36; H, 5.70; N, 8.80. Found: C, 60.32; H, 5.68; N, 8.79.

4.2.9. Ethyl-(2*E*)-4-[[(4-Methylphenyl)sulfonyl][2-[1-(1*E*)-[(phenylmethoxy)imino]ethyl]phenyl]amino]-2-butenoate (1f). According to the procedure described in the preparation of **1a–e**, alkylation of **7c** (114 mg, 0.28 mmol) with ethyl 4-bromocrotonate (0.038 mL, 0.28 mmol) in the presence of K_2CO_3 (153 mg, 1.1 mmol) gave **1f** (135 mg, 96%) as colorless crystals. Mp 103–105 °C (EtOH). IR ν_{max} cm^{-1}: 1716 (COO), 1369, 1161 (NSO_2). ^1H NMR (200 MHz) δ: 7.56–7.17 (12H, m), 6.85 (1H, br d, *J*=7 Hz), 6.79 (1H, dt, *J*=16, 7 Hz), 5.68 (1H, dd, *J*=16, 1 Hz), 5.19 (2H, s), 4.16–4.05 (4H, m), 2.40 (3H, s), 2.18 (3H, s), 1.22 (3H, t, *J*=7 Hz). ^{13}C NMR (75 MHz) δ: 165.2, 155.1, 143.4, 142.0, 138.9, 138.1, 136.34, 136.30, 129.8, 129.6, 129.3, 128.7, 128.4, 128.1, 127.6, 127.5, 127.3, 123.8, 75.5, 60.0, 53.1, 21.2, 16.1, 13.9. HRMS *m/z*: Calcd for $C_{28}H_{31}N_2O_5S$ (M+H^+) 507.1952. Found: 507.1929. Anal. Calcd for $C_{28}H_{30}N_2O_5S$: C, 66.38; H, 5.97; N, 5.53. Found: C, 66.11; H, 5.91; N, 5.51.

4.2.10. Ethyl-(2*E*)-4-[[(4-methylphenyl)sulfonyl][2-[1-(1*E*)-(methoxyimino)ethyl]phenyl]amino]-2-butenoate (1g). According to the procedure described in the preparation of **1a–e**, alkylation of **7d** (223 mg, 0.70 mmol) with ethyl 4-bromocrotonate (0.097 mL, 0.70 mmol) in the presence of K_2CO_3 (388 mg, 2.8 mmol) gave **1g** (301 mg, 99%) as a pale yellow oil. IR ν_{max} cm^{-1}: 1717 (COO), 1351, 1162 (NSO_2). ^1H NMR (200 MHz) δ: 7.57 (2H, d, *J*=8 Hz), 7.38–7.20 (5H, m), 6.92 (1H, dt, *J*=16, 7 Hz), 6.86 (1H, d, *J*=8 Hz), 5.80 (1H, dd, *J*=16, 1 Hz), 4.35 (2H, dd, *J*=7, 1 Hz), 4.13 (2H, q, *J*=7 Hz), 3.96 (3H, s), 2.42 (3H, s), 2.16 (3H, s), 1.24 (3H, t, *J*=7 Hz). ^{13}C NMR (50 MHz) δ: 165.4, 155.0, 143.6, 142.1, 139.0, 136.7, 136.2, 129.8, 129.6, 129.4, 128.8, 128.6, 127.7, 123.9, 61.5, 60.2, 53.4, 21.3, 15.8, 14.0. HRMS *m/z*: Calcd for $C_{22}H_{27}N_2O_5S$ (M+H^+) 431.1639. Found: 431.1633.

4.2.10.1. Radical reaction of oxime ether 1a [Table 2, entry 1]. To a boiling solution of **1a** (296 mg, 0.60 mmol) in benzene (15 mL) was added a solution of Bu_3SnH (0.32 mL, 1.2 mmol) and AIBN (20 mg, 0.12 mmol) in benzene (15 mL) by syringe pump under a nitrogen atmosphere. After being stirred at reflux for 10 h, a solution of Bu_3SnH (0.32 mL, 1.2 mmol) and AIBN (20 mg, 0.12 mmol) in benzene (2 mL) was added by syringe pump. After being stirred at reflux for 17 h, the reaction mixture was extracted with hexane/MeCN. The MeCN phase was concentrated at reduced pressure. The residue was purified by MCC (hexane/AcOEt 3:1) to afford *cis*-**2a** (41 mg, 20%), *trans*-**2a** (53 mg, 26%), *cis*-**3a** (17 mg, 6%), *trans*-**3a** (22 mg, 7%), **9a** (18 mg, 7%), and benzyl alcohol (**11**) (21.6 mg, 33%). Benzyl alcohol was identical with authentic sample.

*cis-1,3,3a,4,5,9b-Hexahydro-5-[(4-methylphenyl)sulfonyl]-2H-pyrrolo[3,2-c]quinolin-2-one (cis-**2a**).* Colorless crystals. IR ν_{max} cm^{-1}: 3433 (NH), 1701 (NCO), 1354, 1166 (NSO_2). ^1H NMR (500 MHz) δ: 7.71 (1H, dd, *J*=8, 1 Hz), 7.52 (2H, br d, *J*=8 Hz), 7.31 (1H, td, *J*=7.5, 1 Hz), 7.28–7.16 (4H, m), 6.60 (1H, br s), 4.37 (1H, d, *J*=6.5 Hz), 4.20 (1H, dd, *J*=14, 5 Hz), 3.15 (1H, dd, *J*=14, 12 Hz), 2.62 (1H, dd, *J*=17.5, 9 Hz), 2.54 (1H, m), 2.40 (3H, s), 2.02 (1H, dd, *J*=17.5, 2 Hz). ^{13}C NMR (75 MHz) δ: 175.5, 144.0, 137.0, 136.4, 129.8, 128.8, 128.6, 128.2, 126.9, 126.0, 124.9, 52.0, 47.4, 34.5, 31.8, 21.5. HRMS *m/z*: Calcd for $C_{18}H_{18}N_2O_5S$ (M^+) 342.1037. Found: 342.1042. Anal. Calcd for $C_{18}H_{18}N_2O_5S \cdot 1/10H_2O$: C, 62.81; H, 5.33; N, 8.14. Found: C, 62.58; H, 5.05; N, 7.84.

*trans-1,3,3a,4,5,9b-Hexahydro-5-[(4-methylphenyl)sulfonyl]-2H-pyrrolo[3,2-c]quinolin-2-one (trans-**2a**).* Colorless crystals. IR ν_{max} cm^{-1}: 3429 (NH), 1727 (NCO), 1356, 1168 (NSO_2). ^1H NMR (500 MHz) δ: 7.82 (1H, dd, *J*=8, 0.5 Hz), 7.46–7.40 (3H, m), 7.35–7.30 (1H, br t, *J*=8 Hz), 7.21–7.17 (3H, m), 6.99 (1H, br d, *J*=7.5 Hz), 3.99 (1H, dd, *J*=11, 6 Hz), 3.58 (1H, br t, *J*=11 Hz), 3.23 (1H, d, *J*=10.5 Hz), 2.55 (1H, dd, *J*=15.5, 6.5 Hz), 2.39 (3H, s), 2.20 (1H, dd, *J*=15.5, 12.5 Hz), 2.10 (1H, m). ^{13}C NMR (75 MHz) δ: 178.1, 144.0, 135.2, 133.8, 133.5, 129.8, 128.0, 126.8, 126.6, 125.6, 121.1, 56.6, 49.4, 42.8, 36.2, 21.6. HRMS *m/z*: Calcd for $C_{18}H_{18}N_2O_5S$ (M^+) 342.1037. Found: 342.1047. Anal. Calcd for $C_{18}H_{18}N_2O_5S \cdot EtOH$: C, 61.79; H, 6.26; N, 7.14. Found: C, 61.99; H, 5.96; N, 7.10.

*Ethyl cis-1,2,3,4-tetrahydro-1-[(4-methylphenyl)sulfonyl]-4-[(phenylmethoxy)amino]quinoline-3-acetate (cis-**3a**).* A pale yellow oil. IR ν_{max} cm^{-1}: 1728 (CO_2Et), 1353, 1166 (NSO_2). ^1H NMR (500 MHz) δ: 7.90 (1H, br dd, *J*=8.5, 1 Hz), 7.55 (2H, br d, *J*=8 Hz), 7.32–7.15 (9H, m), 7.05 (1H, br t, *J*=7.5, 1 Hz), 5.14 (1H, br d, *J*=3 Hz), 4.49 and 4.39 (2H, ABq, *J*=12 Hz), 4.19–4.08 (3H, m), 3.93 (1H, br s), 3.53 (1H, dd, *J*=13, 12 Hz), 2.60 (1H, dd, *J*=15.5, 6.5 Hz), 2.34 (3H, s), 2.29 (1H, m), 1.25 (3H, t, *J*=7.5 Hz). ^{13}C NMR (75 MHz) δ: 171.7, 143.7, 137.0, 136.5, 135.7, 130.0, 129.55, 129.46, 128.5, 128.3, 127.8, 127.5, 127.1, 124.2, 122.4, 75.7, 60.5, 58.5, 46.9, 34.2, 33.1, 25.0, 23.2, 21.4, 14.1. HRMS *m/z*: Calcd for $C_{27}H_{30}N_2O_5S$ (M^+) 494.1874. Found: 494.1881.

*Ethyl trans-1,2,3,4-tetrahydro-1-[(4-methylphenyl)sulfonyl]-4-[(phenylmethoxy)amino]quinoline-3-acetate (trans-**3a**).* A pale yellow oil. IR ν_{max} cm^{-1}: 1728 (CO_2Et), 1351, 1165 (NSO_2). ^1H NMR (500 MHz) δ: 7.70–7.65 (3H, m), 7.36–7.16 (9H, m), 7.02 (1H, td, *J*=7.5, 1.5 Hz), 5.24 (1H, br s), 4.57 and 4.48 (2H, ABq, *J*=11.5 Hz), 4.20–4.13 (2H, m), 3.97–3.90 (2H, m), 3.77 (1H, br d, *J*=4.5 Hz), 2.61 (1H, m), 2.36 (3H, s), 2.31–2.28 (2H, m), 1.27 (3H, t, *J*=7.5 Hz). ^{13}C NMR (75 MHz) δ: 171.7, 143.6, 137.5, 137.3, 136.8, 130.6, 129.5, 128.4, 128.2, 127.8, 127.0, 124.6, 123.7, 121.0, 76.6, 60.9, 60.5, 46.7, 34.9, 31.0, 21.4, 14.0. HRMS *m/z*: Calcd for $C_{27}H_{30}N_2O_5S$ (M^+) 494.1874. Found: 494.1892.

*cis-1,3,3a,4,5,9b-Hexahydro-5-[(4-methylphenyl)sulfonyl]-1-(phenylmethoxy)-2H-pyrrolo[3,2-c]quinolin-2-one (**9a**).* Colorless crystals. IR ν_{max} cm^{-1}: 1713 (NCO), 1358, 1166 (NSO_2). ^1H NMR (300 MHz) δ: 7.78 (1H, br d, *J*=8 Hz),

7.67–7.45 (3H, m), 7.38 (1H, br t, J=8 Hz), 7.32–7.18 (8H, m), 4.36 (1H, d, J=7 Hz), 4.85 and 4.25 (2H, ABq, J=9.5 Hz), 4.11 (1H, dd, J=14, 4.5 Hz), 3.33 (1H, dd, J=14, 10.5 Hz), 2.56 (1H, dd, J=17, 9 Hz), 2.39 (3H, s), 2.32 (1H, m), 2.15 (1H, dd, J=17.5, 1.5 Hz). ^{13}C NMR (75 MHz) δ: 169.7, 144.1, 137.1, 136.8, 134.1, 131.8, 129.8, 129.6, 129.2, 128.7, 128.3, 126.9, 124.9, 124.4, 123.6, 77.8, 55.7, 47.8, 31.1, 26.6, 21.4. HRMS *m/z*: Calcd for $C_{25}H_{24}N_2O_4S$ (M^+) 448.1455. Found: 448.1466.

4.2.10.2. Conversion of 3a into 9a. To a solution of *cis*-**3a**/*trans*-**3a** (1:1, 76 mg, 0.155 mmol) in MeOH (1 mL) was added *p*-TsOH (29.3 mg, 0.155 mmol) under a nitrogen atmosphere at room temperature. After being stirred at room temperature for 4 h, the reaction mixture was diluted with saturated aqueous $NaHCO_3$ and was extracted with Et_2O. The organic phase was washed with brine, dried over $MgSO_4$, and concentrated at reduced pressure. The residue was purified by PTLC (hexane/AcOEt 1:1) to afford *cis*-**9a** (22 mg, 32%) and to recover *trans*-**3a** (30 mg, 37%).

4.2.11. Radical reaction of oxime ether 1e [Table 2, entry 2]. To a boiling solution of **1e** (250 mg, 0.60 mmol) in benzene (4.5 mL) was added a solution of Bu_3SnH (0.32 mL, 1.2 mmol) and AIBN (20 mg, 0.12 mmol) in benzene (4.5 mL) by syringe pump under a nitrogen atmosphere. After being stirred at reflux for 3 h, a solution of Bu_3SnH (0.32 mL, 1.2 mmol) and AIBN (20 mg, 0.12 mmol) in benzene (2 mL) was added by syringe pump. After being stirred at reflux for 4 h, the reaction mixture was extracted with hexane/MeCN. The MeCN phase was concentrated at reduced pressure. The residue was purified by MCC (hexane/AcOEt 3:1) to afford *cis*-**2a** (54 mg, 26%), *trans*-**2a** (62 mg, 30%), *cis*-**3e** (17 mg, 7%), *trans*-**3e** (22 mg, 8%), and **9e** (5.1 mg, 2%).

*Ethyl cis-1,2,3,4-tetrahydro-4-(methoxyamino)-1-[(4-methylphenyl)sulfonyl]quinoline-3-acetate (cis-**3e**)*. A pale yellow oil. IR ν_{max} cm^{-1}: 3566 (NH), 1728 (COO), 1352, 1166 (NSO_2). ^{1}H NMR (500 MHz) δ: 7.90 (1H, dd, J=7.5, 1 Hz), 7.74–7.69 (1H, m), 7.57–7.16 (5H, m), 7.08 (1H, td, J=7.5, 1 Hz), 5.06 (1H, br s), 4.17 (2H, br q, J=7 Hz), 4.12 (1H, dd, J=12.5, 4 Hz), 3.88 (1H, br d, J=4 Hz), 3.49 (1H, dd, J=12.5, 11.5 Hz), 3.29 (3H, s), 2.57 (1H, dd, J=16, 7 Hz), 2.36 (3H, s), 3.12 (1H, dd, J=16, 7 Hz), 2.29–2.23 (1H, m), 1.28 (3H, t, J=7 Hz). ^{13}C NMR (125 MHz) δ: 171.7, 143.8, 136.6, 135.8, 129.9, 129.5, 128.6, 127.7, 127.2, 124.4, 122.7, 61.2, 60.5, 58.5, 46.9, 34.3, 33.1, 21.5, 14.2. HRMS *m/z*: Calcd for $C_{21}H_{26}N_2O_5S$ (M^+) 418.1561. Found: 418.1565.

*Ethyl trans-1,2,3,4-tetrahydro-4-(methoxyamino)-1-[(4-methylphenyl)sulfonyl]quinoline-3-acetate (trans-**3e**)*. A pale yellow oil. IR ν_{max} (neat) cm^{-1}: 3262 (NH), 1736 (COO), 1341, 1160 (NSO_2). ^{1}H NMR (500 MHz) δ: 7.71 (1H, dd, J=7.5, 1 Hz), 7.67–7.65 (2H, m), 7.28–7.19 (4H, m), 7.06 (1H, td, J=7.5, 1 Hz), 5.29 (1H, br s), 4.21–4.13 (2H, m), 4.07 (1H, dd, J=12.5, 4 Hz), 3.90 (1H, dd, J=12.5, 6.5 Hz), 3.74 (1H, br d, J=4 Hz), 3.36 (3H, s), 2.61–2.57 (1H, m), 2.38 (3H, s), 2.35–2.28 (2H, m), 1.28 (3H, t, J=7 Hz). ^{13}C NMR (125 MHz) δ: 171.8, 143.7, 137.4, 136.9, 130.3, 129.6, 128.5, 127.2, 125.3, 124.1, 121.7, 62.5, 61.0, 60.7, 47.2, 35.2, 31.2, 21.5, 14.2. HRMS *m/z*: Calcd for $C_{21}H_{26}N_2O_5S$ (M^+) 418.1561. Found: 418.1563.

*cis-1,3,3a,4,5,9b-Hexahydro-1-(methoxyamino)-5-[(4-methylphenyl)sulfonyl]-2H-pyrrolo[3,2-c]quinolin-2-one (**9e**)*. Colorless crystals. Mp 169–170 °C (Et_2O). IR ν_{max} cm^{-1}: 1719 (γ-lactam), 1358, 1165 (NSO_2). ^{1}H NMR (500 MHz) δ: 7.78 (1H, dd, J=8, 1 Hz), 7.55–7.51 (3H, m), 7.39–7.36 (1H, m), 7.26–7.21 (4H, m), 4.39 (1H, d, J=7 Hz), 4.14 (1H, dd, J=14, 5 Hz), 3.43 (3H, s), 3.38 (1H, dd, J=14, 11 Hz), 2.55 (1H, dd, J=17.5, 9.5 Hz), 2.40 (3H, s), 2.38–2.36 (1H, m), 2.13 (1H, dd, J=17.5, 1.5 Hz). ^{13}C NMR (125 MHz) δ: 169.9, 144.2, 137.0, 136.9, 131.3, 129.9, 129.3, 127.0, 125.3, 124.7, 124.0, 63.8, 55.3, 47.8, 31.2, 26.4, 21.6. HRMS *m/z*: Calcd for $C_{19}H_{20}N_2O_4S$ (M^+) 372.1142. Found: 372.1142. Anal. Calcd for $C_{19}H_{20}N_2O_4S\cdot 1/4\ H_2O$: C, 60.54; H, 5.48; N, 7.43. Found: C, 60.59; H, 5.34; N, 7.44.

4.2.11.1. Radical reaction of oxime ether 1b [Table 2, entry 3]. To a boiling solution of **1b** (165 mg, 0.31 mmol) in benzene (2 mL) was added a solution of Bu_3SnH (0.17 mL, 0.62 mmol) and AIBN (10 mg, 0.062 mmol) in benzene (2.5 mL) by syringe pump under a nitrogen atmosphere. After being stirred at reflux for 4 h, a solution of Bu_3SnH (0.17 mL, 0.62 mmol) and AIBN (10 mg, 0.062 mmol) in benzene (2 mL) was added by syringe pump. After being stirred at reflux for 3 h, the reaction mixture was extracted with hexane/MeCN. The MeCN phase was concentrated at reduced pressure. The residue was purified by MCC (hexane/AcOEt 3:1) to afford *cis*-**2a** (15 mg, 14%), *cis*-**3b** (24 mg, 14.5%), *trans*-**3b** (24 mg, 14.5%), *cis*-**10b** (11 mg, 8%), *trans*-**10b** (38 mg, 30%), and benzyl alcohol (**11**). Benzyl alcohol was identical with authentic sample.

*1,1-Dimethylethyl cis-1,2,3,4-tetrahydro-1-[(4-methylphenyl)sulfonyl]-4-[(phenylmethoxy)amino]quinoline-3-acetate (cis-**3b**)*. A pale yellow oil. IR ν_{max} cm^{-1}: 3566 (NH), 1722 (COO), 1352, 1165 (NSO_2). ^{1}H NMR (200 MHz) δ: 7.89 (1H, br d, J=8 Hz), 7.55 (2H, br d, J=8 Hz), 7.35–7.01 (10H, m), 5.22 (1H, br s), 4.48 and 4.35 (2H, ABq, J=11.5 Hz), 4.11 (1H, dd, J=13, 3.5 Hz), 3.88 (1H, br d, J=3 Hz), 3.53 (1H, br t, J=11 Hz), 2.52 (1H, dd, J=18, 10 Hz), 2.33 (3H, s), 2.38–2.20 (2H, m), 2.22 (2H, br d, J=7 Hz), 1.45 (9H, s). ^{13}C NMR (50 MHz) δ: 171.1, 143.7, 137.2, 136.7, 135.9, 130.2, 129.5, 128.5, 128.4, 127.9, 127.8, 127.2, 124.2, 122.5, 80.8, 75.9, 58.6, 47.1, 35.6, 33.6, 28.1, 21.5. HRMS *m/z*: Calcd for $C_{29}H_{34}N_2O_5S$ (M^+) 522.2186. Found: 522.2180.

*1,1-Dimethylethyl trans-1,2,3,4-tetrahydro-1-[(4-methylphenyl)sulfonyl]-4-[(phenylmethoxy)amino]quinoline-3-acetate (trans-**3b**)*. A pale yellow oil. IR ν_{max} cm^{-1}: 3548 (NH), 1721 (COO), 1352, 1164 (NSO_2). ^{1}H NMR (200 MHz) δ: 7.67 (2H, br d, J=8 Hz), 7.35–6.97 (11H, m), 7.28–7.19 (4H, m), 7.06 (1H, td, J=7.5, 1 Hz), 5.28 (1H, br s), 4.59 and 4.50 (2H, ABq, J=12 Hz), 3.95 (2H, d, J=5 Hz), 3.78 (1H, br d, J=3.5 Hz), 2.63–2.61 (1H, m), 2.36 (3H, s), 1.47 (9H, s). ^{13}C NMR (50 MHz) δ: 171.1, 143.7, 137.6, 137.5, 137.0, 130.8, 129.7, 128.5, 128.4, 127.9, 127.1, 124.5, 123.7, 120.9, 80.8, 76.8, 61.1, 46.7, 36.2, 31.6, 28.1, 21.5. HRMS *m/z*: Calcd for $C_{29}H_{34}N_2O_5S$ (M^+) 522.2186. Found: 522.2179.

*1,1-Dimethylethyl cis-4-amino-1,2,3,4-tetrahydro-1-[(4-methylphenyl)sulfonyl]quinoline-3-acetate (cis-**10b**)*. A pale yellow oil. IR ν_{max} cm^{-1}: 3423, 3385 (NH), 1721 (COO), 1355, 1166 (NSO_2). ^1H NMR (500 MHz) δ: 7.87 (1H, br d, J=8.5 Hz), 7.56 (2H, br d, J=8.5 Hz), 7.25–7.17 (4H, m), 7.08 (1H, br t, J=7.5 Hz), 4.07 (1H, dd, J=13, 4 Hz), 3.76 (1H, br d, J=3.5 Hz), 3.45 (1H, dd, J=13, 11.5 Hz), 2.33 (1H, dd, J=15, 7.5 Hz), 2.36 (3H, s, 2.20 (1H, dd, J=15, 7 Hz), 2.16–2.13 (1H, m), 1.49 (9H, s). ^{13}C NMR (125 MHz) δ: 171.2, 143.8, 136.0, 135.6, 129.6, 128.0, 127.3, 127.2, 124.5, 122.8, 81.0, 49.6, 45.7, 35.3, 34.9, 28.1, 21.5. HRMS *m/z*: Calcd for $C_{22}H_{28}N_2O_4S$ (M^+) 416.1768. Found: 416.1746.

*1,1-Dimethylethyl trans-4-amino-1,2,3,4-tetrahydro-1-[(4-methylphenyl)sulfonyl]quinoline-3-acetate (trans-**10b**)*. A pale yellow oil. IR ν_{max} (neat) cm^{-1}: 3392, 3319 (NH), 1723 (COO), 1351, 1164 (NSO_2). ^1H NMR (500 MHz) δ: 7.71 (1H, dd, J=8.5, 1 Hz), 7.60 (2H, br d, J=8.5 Hz), 7.32–7.19 (4H, m), 7.10 (1H, td, J=7, 1 Hz), 4.14 (1H, dd, J=13, 4 Hz), 3.61 (1H, dd, J=13, 8.5 Hz), 3.45 (1H, br d, J=7 Hz), 2.41–2.35 (4H, m), 2.37 (3H, s), 2.17 (1H, dd, J=16, 8 Hz), 2.01–2.00 (1H, m), 1.48 (9H, s). ^{13}C NMR (125 MHz) δ: 171.2, 143.7, 136.7, 136.1, 132.6, 129.6, 128.6, 127.6, 127.2, 124.8, 122.8, 80.9, 52.5, 48.3, 37.7, 37.1, 28.1, 21.5. HRMS *m/z*: Calcd for $C_{22}H_{28}N_2O_4S$ (M^+) 416.1768. Found: 416.1788.

4.2.11.2. Conversion of *cis*-10b into *cis*-2a. After a boiling solution of *cis*-**10b** (3.3 mg, 0.008 mmol) in benzene (2 mL) was stirred under a nitrogen atmosphere for 9 h, the reaction mixture was concentrated at reduced pressure. The residue was purified by PTLC (AcOEt) to afford *cis*-**2a** (1.7 mg, 63%).

4.2.11.3. Attempted conversion of *trans*-10b into *trans*-2a. According to the procedure described in the conversion of *cis*-**10b** into *cis*-**2a**, reaction of *trans*-**10b** (33 mg, 0.079 mmol) recovered *trans*-**10b** (28 mg, 84%).

4.2.12. Radical reaction of oxime ether 1c [Table 2, entry 4]. To a boiling solution of **1c** (199.8 mg, 0.36 mmol) in benzene (2 mL) was added slowly a solution of Bu_3SnH (0.19 mL, 0.72 mmol) and AIBN (11.8 mg, 0.072 mmol) in benzene (2 mL) under a nitrogen atmosphere. After being stirred at reflux for 2 h, a solution of Bu_3SnH (0.19 mL, 0.72 mmol) and AIBN (11.8 mg, 0.072 mmol) in benzene (2 mL) was added slowly. After being stirred at reflux for 3 h, the reaction mixture was extracted with hexane/MeCN. The MeCN phase was concentrated at reduced pressure. The residue was purified by PTLC (hexane/AcOEt 1:1) to afford *cis*-**10c** (18 mg, 11%), *trans*-**10c** (23 mg, 14.5%), and **7a** (11 mg, 8%).

*cis-1,2,3,4-Tetrahydro-1-[(4-methylphenyl)sulfonyl]-4-[(phenylmethoxy)amino]-N-(phenylmethyl)quinoline-3-acetamide (cis-**10c**)*. A pale yellow oil. IR ν_{max} cm^{-1}: 3230 (NH), 1652 (CON). ^1H NMR (500 MHz) δ: 7.81 (1H, d, J=8 Hz), 7.53 (2H, d, J=8.5 Hz), 7.30–7.34 (2H, m), 7.24–7.28 (3H, m), 7.16–7.20 (3H, m), 7.10 (1H, dd, J=75, 1.5 Hz), 7.04 (1H, td, J=7.5, 1 Hz), 6.16 (1H, br s), 4.43 (1H, dd, J=15, 5.5 Hz), 4.40 (1H, dd, J=15, 5.5 Hz), 4.00 (1H, dd, J=13, 3.5 Hz), 3.70 (1H, d, J=4 Hz), 3.42 (1H, dd, J=13, 10.5 Hz), 2.30–2.39 (1H, m), 2.33 (3H, s), 2.20–2.28 (1H, m), 2.14 (1H, dd, J=14, 6 Hz). ^{13}C NMR (125 MHz) δ: 170.7, 143.9, 138.2, 135.9, 135.3, 132.8, 129.7, 129.0, 128.8, 128.0, 127.8, 127.6, 127.1, 124.5, 122.7 49.4, 46.1, 43.7, 36.1, 35.0, 21.5. HRMS *m/z*: Calcd for $C_{29}H_{34}N_2O_5S$ (M^+) 522.2186. Found: 522.2180.

*trans-1,2,3,4-Tetrahydro-1-[(4-methylphenyl)sulfonyl]-4-[(phenylmethoxy)amino]-N-(phenylmethyl)quinoline-3-acetamide (trans-**10c**)*. A pale yellow oil. IR ν_{max} cm^{-1}: 3296 (NH), 1652 (CON). ^1H NMR (500 MHz) δ: 7.62 (3H, d, J=8.5 Hz), 7.30–7.36 (2H, m), 7.21–7.30 (6H, m), 7.17 (1H, td, J=7.5, 1.5 Hz), 7.07 (1H, td, J=7.5, 1.5 Hz), 6.34 (1H, br s), 4.46 (1H, dd, J=15, 6 Hz), 4.40 (1H, dd, J=15, 5.5 Hz), 4.02 (1H, dd, J=13, 3.5 Hz), 3.76 (1H, dd, J=13, 7 Hz), 3.57 (1H, d, J=5.5 Hz), 2.37 (3H, s), 2.26 (2H, dd, J= 9, 7 Hz), 2.16–2.22 (1H, m). ^{13}C NMR (125 MHz) δ: 170.8, 143.8, 138.2, 136.9, 136.0, 131.7, 129.7, 129.1, 128.7, 127.8, 127.7, 127.5, 127.0, 124.5, 122.0, 52.4, 47.6, 43.7, 37.9, 37.6, 21.5. HRMS *m/z*: Calcd for $C_{25}H_{27}N_3O_3S$ (M^+) 449.1772. Found: 449.1780.

4.2.13. Radical reaction of oxime ether (*Z*)-1d [Table 2, entry 5]. To a boiling solution of (*Z*)-**1d** (148 mg, 0.33 mmol) in benzene (2.5 mL) was added a solution of Bu_3SnH (0.18 mL, 0.66 mmol) and AIBN (11 mg, 0.066 mmol) in benzene (2.5 mL) by syringe pump under a nitrogen atmosphere. After being stirred at reflux for 2 h, a solution of Bu_3SnH (0.18 mL, 0.66 mmol) and AIBN (11 mg, 0.066 mmol) in benzene (2 mL) was added by syringe pump. After being stirred at reflux for 3 h, the reaction mixture was extracted with hexane/MeCN. The MeCN phase was concentrated at reduced pressure. The residue was purified by MCC (hexane/AcOEt 3:1) to afford *cis*-**3d** (26.4 mg, 18%), *trans*-**3d** (8.7 mg, 6%), *cis*-**10d** (8.1 mg, 7%), and *trans*-**10d** (8.1 mg, 7%).

*cis-1,2,3,4-Tetrahydro-1-[(4-methylphenyl)sulfonyl]-4-[(phenylmethoxy)amino]quinoline-3-acetonitrile (cis-**3d**)*. A pale yellow oil. IR ν_{max} cm^{-1}: 3156 (NH), 2254 (CN), 1381, 1168 (NSO_2). ^1H NMR (200 MHz) δ: 7.93 (1H, br d, J=8 Hz), 7.53 (2H, br d, J=8 Hz), 7.36–7.01 (10H, m), 5.02 (1H, br s), 4.58 and 4.48 (2H, ABq, J=11.5 Hz), 4.16 (1H, dd, J=11.5, 4 Hz), 3.94 (1H, br d, J=4 Hz), 3.52 (1H, br t, J=11.5 Hz), 2.53 (1H, dd, J=16.5, 7.5 Hz), 2.37 (3H, s), 2.30 (1H, dd, J=16.5, 7.5 Hz), 2.00–1.92 (1H, m). ^{13}C NMR (75 MHz) δ: 144.1, 137.3, 137.0, 136.5, 130.5, 129.8, 128.9, 128.7, 128.5, 128.2, 127.0, 124.4, 123.6, 121.5, 117.7, 76.7, 60.1, 46.3, 32.0, 21.5, 18.7. HRMS *m/z*: Calcd for $C_{25}H_{25}N_3O_3S$ (M^+) 447.1615. Found: 447.1621.

*trans-1,2,3,4-Tetrahydro-1-[(4-methylphenyl)sulfonyl]-4-[(phenylmethoxy)amino)]quinoline-3-acetonitrile (trans-**3d**)*. A pale yellow oil. IR ν_{max} cm^{-1}: 3526 (NH), 2254 (CN), 1381, 1168 (NSO_2). ^1H NMR (200 MHz) δ: 7.66 (2H, br d, J=8 Hz), 7.50–7.10 (11H, m), 5.81 (1H, d), 4.77 and 4.71 (2H, ABq, J=8 Hz), 4.38 (1H, dd, J=13.5, 2.5 Hz), 3.60 (1H, br d, J=2.5 Hz), 3.23 (1H, dd, J=15, 13.5 Hz), 2.46–2.32 (2H, m), 2.41 (3H, s), 2.19 (1H, dd, J=13, 4 Hz). ^{13}C NMR (75 MHz) δ: 143.6, 138.8, 138.7, 137.0, 136.6, 129.8, 128.7, 128.55, 128.52, 128.2, 127.1, 126.1, 119.1, 117.7, 76.8, 64.5, 51.1, 35.2, 29.9, 21.5. HRMS *m/z*: Calcd for $C_{25}H_{25}N_3O_3S$ (M^+) 447.1615. Found: 447.1600.

*cis-4-Amino-1,2,3,4-tetrahydro-1-[(4-methylphenyl)sulfonyl]quinoline-3-acetonitrile (cis-**10d**)*. A pale yellow oil. IR ν_{max} cm^{-1}: 3505, 3385 (NH), 2253 (CN), 1354, 1165 (NSO_2). ^1H NMR (200 MHz) δ: 7.72–7.12 (8H, m), 4.18 (1H, dd, J=13.5, 4 Hz), 3.68 (1H, dd, J=13.5, 9 Hz), 3.59 (1H, br d, J=8 Hz), 2.51 (2H, br d, J=6 Hz), 2.40 (3H, s), 1.90–1.70 (1H, m). ^{13}C NMR (125 MHz) δ: 161.3, 144.2, 137.6, 136.1, 132.2, 131.7, 130.3, 129.8, 129.2, 127.9, 127.2, 117.0, 57.2, 56.7, 29.8, 23.1, 21.6. HRMS *m/z*: Calcd for $C_{18}H_{19}N_3O_2S$ (M^+) 341.1196. Found: 341.1175.

*trans-4-Amino-1,2,3,4-tetrahydro-1-[(4-methylphenyl)sulfonyl]quinoline-3-acetonitrile (trans-**10d**)*. A pale yellow oil. IR ν_{max} cm^{-1}: 3388, 3324 (NH), 2250 (CN), 1355, 1167 (NSO_2). ^1H NMR (200 MHz) δ: 7.91–7.22 (8H, m), 4.34 (1H, dd, J=14.5, 3 Hz), 4.10–3.92 (1H, m), 3.84 (1H, dd, J=14.5, 11 Hz), 2.73 (2H, dd, J=6, 4 Hz), 2.40 (3H, s), 1.70–1.50 (1H, m). ^{13}C NMR (50 MHz) δ: 144.2, 136.4, 135.6, 132.1, 129.8, 128.3, 128.0, 127.1, 125.3, 123.3, 117.7, 51.6, 47.8, 37.6, 21.5, 19.0. HRMS *m/z*: Calcd for $C_{18}H_{19}N_3O_2S$ (M^+) 341.1197. Found: 341.1219.

4.2.14. Radical reaction of oxime ether (*E*)-1d [Table 2, entry 6]. To a boiling solution of (*E*)-**1d** (103 mg, 0.23 mmol) in benzene (2 mL) was added a solution of Bu_3SnH (0.12 mL, 0.46 mmol) and AIBN (7.6 mg, 0.046 mmol) in benzene (2 mL) by syringe pump under a nitrogen atmosphere. After being stirred at reflux for 3 h, a solution of Bu_3SnH (0.12 mL, 0.46 mmol) and AIBN (7.6 mg, 0.046 mmol) in benzene (2 mL) was added by syringe pump. After being stirred at reflux for 3 h, the reaction mixture was extracted with hexane/MeCN. The MeCN phase was concentrated at reduced pressure. The residue was purified by MCC (hexane/AcOEt 3:1) to afford *cis*-**3d** (12.2 mg, 11.5%), *trans*-**3d** (2.2 mg, 2.5%), and *trans*-**10d** (8.4 mg, 14%).

4.2.15. Radical reaction of ketoxime ether 1f [Table 3]. To a boiling solution of **1f** (208 mg, 0.53 mmol) in benzene (4 mL) was added a solution of Bu_3SnH (0.28 mL, 1.06 mmol) and AIBN (17 mg, 0.11 mmol) in benzene (4 mL) by syringe pump under a nitrogen atmosphere. After being stirred at reflux for 3 h, a solution of Bu_3SnH (0.28 mL, 1.06 mmol) and AIBN (17 mg, 0.11 mmol) in benzene (2 mL) was added by syringe pump. After being stirred at reflux for 7 h, a solution of Bu_3SnH (0.28 mL, 1.06 mmol) and AIBN (17 mg, 0.11 mmol) in benzene (2 mL) was added by syringe pump. After being stirred at reflux for 3 h, the reaction mixture was extracted with hexane/MeCN. The MeCN phase was concentrated at reduced pressure. The residue was purified by MCC (hexane/AcOEt 5:1) to afford *cis*-**2b** (4.2 mg, 2%), *trans*-**2b** (4.2 mg, 2%), *Z*-**1f** (4.1 mg, 2%), **7c** (44.8 mg, 21%), and **1f** (78.6 mg, 36%).

*cis-1,3,3a,4,5,9b-Hexahydro-9b-methyl-5-[(4-methylphenyl)sulfonyl]-2H-pyrrolo[3,2-c]quinolin-2-one (cis-**2b**)*. A colorless solid. IR ν_{max} cm^{-1}: 3436 (NH), 1697 (γ-lactam), 1354, 1166 (NSO_2). ^1H NMR (500 MHz) δ: 7.72 (1H, br d, J=8 Hz), 7.52 (2H, br d, J=8 Hz), 7.31–7.22 (5H, m), 6.54 (1H, br s), 4.20 (1H, dd, J=14, 5 Hz), 3.15 (1H, dd, J=14, 13 Hz), 2.67 (1H, dd, J=17.5, 8.5 Hz), 2.39 (3H, s), 2.32–2.30 (1H, m), 1.96 (1H, br d, J=17.5 Hz), 1.07 (3H, s). NOESY: NOE was observed between 3a-H (δ 2.32–2.30) and 9b-Me (δ 1.07). ^{13}C NMR (125 MHz) δ: 174.3, 144.1, 137.2, 135.4, 133.6, 129.8, 128.2, 127.2, 126.7, 126.6, 125.6, 57.5, 48.3, 38.9, 33.6, 29.9, 21.5. HRMS *m/z*: Calcd for $C_{19}H_{20}N_2O_3S$ (M^+) 356.1194. Found: 356.1191.

*trans-1,3,3a,4,5,9b-Hexahydro-9b-methyl-5-[(4-methylphenyl)sulfonyl]-2H-pyrrolo[3,2-c]quinolin-2-one (trans-**2b**)*. A colorless solid. IR ν_{max} cm^{-1}: 3419 (NH), 1696 (γ-lactam), 1356, 1168 (NSO_2). ^1H NMR (500 MHz) δ: 7.94 (1H, br d, J=8 Hz), 7.63 (2H, br d, J=8 Hz), 7.28–7.24 (3H, m), 7.09 (1H, br t, J=8 Hz), 6.96 (1H, br d, J=8 Hz), 6.75 (1H, br s), 4.07 (1H, dd, J=13, 5 Hz), 3.60 (1H, dd, J=13, 10.5 Hz), 2.46–2.30 (3H, m), 2.38 (3H, s), 0.76 (3H, s). NOESY: NOE was observed between 4-Hax (δ 3.60) and 9b-Me (δ 0.76). ^{13}C NMR (125 MHz) δ: 176.8, 144.2, 135.6, 135.6, 134.1, 129.8, 128.0, 127.0, 124.0, 123.3, 121.2, 58.7, 46.4, 42.1, 32.6, 29.7, 21.6. HRMS *m/z*: Calcd for $C_{19}H_{20}N_2O_3S$ (M^+) 356.1194. Found: 356.1200.

*Ethyl-(2Z)-4-[[(4-methylphenyl)sulfonyl][2-[1-(1E)-[(phenylmethoxy)imino]ethyl]phenyl]amino]-2-butenoate (Z-**1f**)*. A colorless oil. IR ν_{max} cm^{-1}: 1709 (COO), 1352, 1191 (NSO_2). ^1H NMR (300 MHz) δ: 7.55 (2H, br d, J=8 Hz), 7.44–7.17 (10H, m), 6.72 (1H, br d, J=8 Hz), 6.41 (1H, dt, J=11.5, 6 Hz), 5.60 (1H, dd, J=11.5, 2.5 Hz), 5.22 (2H, s, 4.72 (2H, very br), 4.09 (2H, q, J=7 Hz), 2.43 (3H, s), 2.32 (3H, s), 1.23 (3H, t, J=7 Hz). ^{13}C NMR (75 MHz) δ: 165.9, 155.8, 145.7, 143.6, 139.5, 138.3, 137.7, 135.3, 129.9, 129.5, 129.0, 128.5, 128.4, 128.2, 127.7, 127.6, 127.3, 120.6, 75.8, 60.1, 51.2, 21.5, 16.7, 14.2. HRMS *m/z*: Calcd for $C_{28}H_{30}N_2O_5S$ (M^+) 506.1874. Found: 506.1888.

4.2.16. Radical reaction of ketoxime ether 1g [Table 3]. To a boiling solution of **1g** (219 mg, 0.51 mmol) in benzene (3.6 mL) was added a solution of Bu_3SnH (0.27 mL, 1.02 mmol) and AIBN (17 mg, 0.10 mmol) in benzene (4 mL) by syringe pump under a nitrogen atmosphere. After being stirred at reflux for 2 h, a solution of Bu_3SnH (0.27 mL, 1.02 mmol) and AIBN (17 mg, 0.10 mmol) in benzene (2 mL) was added by syringe pump. After being stirred at reflux for 7 h, the reaction mixture was extracted with hexane/MeCN. The MeCN phase was concentrated at reduced pressure. The residue was purified by MCC (hexane/AcOEt 5:1) to afford *cis*-**2b** (5.2 mg, 3%), *trans*-**2b** (4.4 mg, 2%), *cis*-**3g** (5.7 mg, 2.7%), *trans*-**3g** (5.0 mg, 2.4%) and **9g** (3.9 mg, 2%), **7d** (31.6 mg, 20%), and **1g** (75 mg, 34%).

*Ethyl cis-1,2,3,4-tetrahydro-4-(methoxyamino)-4-methyl-1-[(4-methylphenyl)sulfonyl]quinoline-3-acetate (cis-**3g**)*. A colorless oil. IR ν_{max} cm^{-1}: 3615 (NH), 1724 (COO), 1352, 1164 (NSO_2). ^1H NMR (500 MHz) δ: 7.86 (1H, br d, J=8 Hz), 7.52 (2H, br d, J=8 Hz), 7.47 (1H, br d, J=8 Hz), 7.28–7.17 (4H, m), 5.60 (1H, br s), 4.22 (2H, q, J=7.5 Hz), 4.19 (1H, dd, J=13.5, 4 Hz), 3.57 (1H, dd, J=13.5, 11 Hz), 3.21 (3H, s), 2.58 (1H, br d, J=15.5 Hz), 2.35 (3H, s), 2.29 (1H, dd, J=15.5, 10 Hz), 2.17–2.11 (1H, m), 1.33 (3H, t, J=7.5 Hz), 0.83 (3H, s). NOESY: NOE was observed between 2-Heq (δ 4.19) and 4-Me (δ 0.83), and 2-Hax (δ 3.57) and 1′-H (δ 2.29), 3-H (δ 2.17–2.11) and 4-Me (δ 0.83). ^{13}C NMR (125 MHz) δ: 172.6, 143.5, 136.8, 129.8, 129.4, 127.6, 127.5, 127.4, 125.2, 124.4, 121.3, 61.9, 60.8, 48.6, 32.5, 29.7, 25.2, 22.7, 21.5, 14.3. HRMS *m/z*: Calcd for $C_{22}H_{28}N_2O_5S$ (M^+) 432.1718. Found: 432.1742.

*Ethyl trans-1,2,3,4-tetrahydro-4-(methoxyamino)-4-methyl-1-[(4-methylphenyl)sulfonyl]quinoline-3-acetate (trans-**3g**).* A colorless oil. IR ν_{max} (neat) cm^{-1}: 3615 (NH), 1728 (COO), 1352, 1165 (NSO_2). ^1H NMR (500 MHz) δ: 7.93 (1H, br d, J=8 Hz), 7.58 (2H, br d, J=8 Hz), 7.35 (1H, br d, J=8 Hz), 7.24–7.12 (4H, m), 5.51 (1H, br s), 4.42 (1H, dd, J=13.5, 3.5 Hz), 4.27–4.19 (2H, m), 3.41 (1H, dd, J=13.5, 11 Hz), 3.09 (3H, s), 2.63 (1H, dd, J=15.5, 3.5 Hz), 2.58–2.52 (1H, m), 2.34 (3H, s), 2.03 (1H, dd, J=15.5, 11 Hz), 1.33 (3H, t, J=7 Hz), 1.01 (3H, s). NOESY: NOE was observed between 1′-H (δ 2.03) and 4-Me (δ 1.01), and 1′-H (δ 2.03) and 2-Hax (δ 3.41), and 2-Hax (δ 3.41) and 4-Me (δ 1.01). ^{13}C NMR (125 MHz) δ: 172.3, 143.4, 136.9, 129.4, 127.60, 127.56, 126.5, 124.9, 123.7, 121.3, 62.7, 60.8, 47.5, 32.6, 32.5, 29.7, 21.9, 21.5, 14.3. HRMS *m/z*: Calcd for $C_{22}H_{28}N_2O_5S$ (M^+) 432.1718. Found: 432.1715.

*cis-1,3,3a,4,5,9b-Hexahydro-1-(methoxyamino)-9b-methyl-5-[(4-methylphenyl)sulfonyl]-2H-pyrrolo[3,2-c]quinolin-2-one (**9g**).* Colorless solid. IR ν_{max} cm^{-1}: 1711 (γ-lactam), 1359, 1165 (NSO_2). ^1H NMR (500 MHz) δ: 7.78 (1H, dd, J=8, 1.5 Hz), 7.70 (1H, dd, J=8, 1.5 Hz), 7.46 (2H, br d, J=8 Hz), 7.37 (1H, br t, J=8 Hz), 7.27 (1H, br t, J=8 Hz), 7.22 (2H, br d, J=8 Hz), 4.19 (1H, dd, J=14, 4.5 Hz), 3.46 (3H, s), 3.28 (1H, dd, J=14, 12.5 Hz), 2.52 (1H, dd, J=17.5, 8.5 Hz), 2.39 (3H, s), 2.10–2.05 (1H, m), 1.98 (1H, br d, J=17.5 Hz), 1.12 (3H, s). NOESY: NOE was observed between 3a-H (δ 2.10–2.05) and 9b-Me (δ 1.12). ^{13}C NMR (125 MHz) δ: 168.8, 144.2, 136.9, 135.7, 129.9, 129.8, 128.8, 128.6, 127.2, 126.0, 125.3, 64.2, 59.8, 48.1, 33.4, 29.6, 23.9, 21.5. HRMS *m/z*: Calcd for $C_{20}H_{22}N_2O_4S$ (M^+) 386.1299. Found: 386.1324.

4.2.17. General procedure for radical reaction of 1a in the presence of additive [Table 4]. To a boiling solution of a mixture of **1a** (200 mg, 0.4 mmol) and additive (1.2–5.0 equiv) in solvent (2.7 mL) was added a solution of Bu_3SnH (0.21 mL, 0.8 mmol) and AIBN (13 mg, 0.08 mmol) in solvent (3 mL) by syringe pump under a nitrogen atmosphere. After being stirred at reflux for 2 h, a solution of Bu_3SnH (0.21 mL, 0.8 mmol) and AIBN (13 mg, 0.08 mmol) in solvent (2 mL) was added by syringe pump. After being stirred at reflux for 3 h, the reaction mixture was extracted with hexane/MeCN. The MeCN phase was concentrated at reduced pressure. The residue was purified by MCC (hexane/AcOEt 3:1) to afford *cis*-**2a**, *trans*-**2a**, *cis*-**3a**, *trans*-**3a**, **9a**, and *trans*-**10a** in yield shown in Table 4.

*Ethyl trans-4-amino-1,2,3,4-tetrahydro-1-[(4-methylphenyl)sulfonyl]quinoline-3-acetate (trans-**10a**).* A pale brown oil. IR ν_{max} (neat) cm^{-1}: 3384, 3313 (NH), 1732 (COO), 1352, 1166 (NSO_2). ^1H NMR (500 MHz) δ: 7.71 (1H, br d, J=8 Hz), 7.60 (2H, br d, J=8 Hz), 7.32 (1H, br d, J=8 Hz), 7.24–7.19 (3H, m), 7.11 (1H, br t, J=7.5 Hz), 4.19–4.13 (3H, m), 3.63 (1H, dd, J=13, 9 Hz), 3.51 (1H, d, J=7 Hz), 2.48 (1H, dd, J=16, 5.5 Hz), 2.38 (3H, s), 2.27 (1H, dd, J=16, 8 Hz), 2.10–2.04 (1H, m), 1.28 (3H, t, J=7 Hz). NOESY: NOE was observed between 2-Hax (δ 3.63) and 4-H (δ 3.51), and 1′-H (δ 2.27) and 4-H (δ 3.51). ^{13}C NMR (125 MHz) δ: 172.0, 143.8, 136.7, 136.1, 132.0, 129.7, 128.7, 127.9, 127.2, 124.9, 122.9, 60.8, 52.3, 48.3, 37.1, 35.9, 21.5, 14.2. HRMS *m/z*: Calcd for $C_{20}H_{24}N_2O_4S$ (M^+) 388.1455. Found: 388.1457.

4.2.18. Attempted conversion of *trans*-10a into *trans*-2a. According to the procedure described in the conversion of *cis*-**10b** into *cis*-**2a**, reaction of *trans*-**10a** (3.5 mg, 0.009 mmol) gave *trans*-**2a** (1.3 mg, 42%).

4.2.19. Radical reaction of 1a in the presence of Bu_3SnD [Table 5, entry 1]. To a boiling solution of **1a** (200 mg, 0.41 mmol) in benzene (2.0 mL) was added slowly a solution of Bu_3SnD (0.22 mL, 0.82 mmol) and AIBN (13.5 mg, 0.082 mmol) in benzene (2.1 mL) under an Ar atmosphere. After being stirred at reflux for 2 h, a solution of Bu_3SnD (0.22 mL, 0.82 mmol) and AIBN (13.5 mg, 0.082 mmol) in benzene (2.1 mL) was added slowly. After being stirred at reflux for 4 h, the reaction mixture was extracted with hexane/MeCN. The MeCN phase was concentrated at reduced pressure. The residue was purified by flash column chromatography (hexane/AcOEt 2:1) to afford *cis*-**2a-D** (D: 69%) (42 mg, 29%), *trans*-**2a-D** (D: 76%) (55 mg, 39%), *cis*-**3a-D** (D: 3%) (13 mg, 6%) and *trans*-**3a-D** (D: 1%) (18 mg, 9%).

*cis-3-d-1,3,3a,4,5,9b-Hexahydro-5-[(4-methylphenyl)sulfonyl]-2H-pyrrolo[3,2-c]quinolin-2-one (cis-**2a-D**).* Colorless crystals. IR ν_{max} cm^{-1}: 3432 (NH), 1705 (γ-lactam), 1354, 1166 (NSO_2). ^1H NMR (500 MHz) δ: 7.69 (1H, d, J=8.5 Hz), 7.50 (2H, br d, J=8.5 Hz), 7.29 (1H, td, J=8, 1.5 Hz), 7.18–7.22 (3H, m), 7.14 (1H, br d, J=8 Hz), 6.44 (1H, br s), 4.34 (1H, d, J=7 Hz), 4.17 (1H, dd, J=14, 5 Hz), 3.13 (1H, dd, J=14, 12.5 Hz), 2.57 (1/3H, d, J= 8.5 Hz), 2.50–2.55 (1H, m), 2.38 (3H, s), 1.98 (2/3H, d, J=1.5 Hz). HRMS *m/z*: Calcd for $C_{18}H_{17}DN_2O_3S$ (M^+) 343.1100. Found: 343.1116. Incorporation of D was 69% from the NMR spectrum.

*trans-3-d-1,3,3a,4,5,9b-Hexahydro-5-[(4-methylphenyl)sulfonyl]-2H-pyrrolo[3,2-c]quinolin-2-one (trans-**2a-D**).* Colorless crystals. IR ν_{max} cm^{-1}: 3429 (NH), 1705 (γ-lactam), 1356, 1167 (NSO_2). ^1H NMR (500 MHz) δ: 7.80 (1H, dd, J=8, 1 Hz), 7.39 (2H, br d, J=8.5 Hz), 7.37 (1H, br s), 7.30 (1H, br t, J=8 Hz), 7.17 (3H, br d, J=8 Hz), 6.96 (1H, d, J=7.5 Hz), 3.96 (1H, dd, J=11.5, 4.5 Hz), 3.55 (1H, t, J=12 Hz), 3.21 (1H, d, J=10 Hz), 2.50 (1/5H, br d, J=7.5 Hz), 2.36 (3H, s), 2.16 (4/5H, br d, J=12.5 Hz), 2.04–2.14 (1H, m). HRMS *m/z*: Calcd for $C_{18}H_{17}DN_2O_3S$ (M^+) 343.1100. Found: 343.1103. Incorporation of D was 76% from the NMR spectrum.

4.2.20. Radical reaction of 1a in the presence of D_2O [Table 5, entry 2]. To a boiling solution of **1a** (200 mg, 0.41 mmol) in benzene (2 mL) was added slowly a solution of Bu_3SnH (0.22 mL, 0.82 mmol) and AIBN (13.5 mg, 0.082 mmol) in benzene (2 mL) under a nitrogen atmosphere. After being stirred at reflux for 2 h, a solution of Bu_3SnH (0.22 mL, 0.82 mmol) and AIBN (13.5 mg, 0.082 mmol) in benzene (2 mL) was added slowly. After being stirred at reflux for 3 h, D_2O (1 mL) was added to it. After being stirred for 1 h, the reaction mixture was extracted with hexane/MeCN. The MeCN phase was concentrated at reduced pressure. The residue was purified by FCC (hexane/AcOEt 2:1) to afford *cis*-**2a** (23 mg, 16%), *trans*-**2a** (50.3 mg, 36%), *cis*-**3a-D** (D: 19%) (18.7 mg, 9%), and *trans*-**3a-D** (D: 34%) (27.9 mg, 14%).

4.2.21. Radical reaction of 1a in the presence of D_2O [Table 5, entry 3]. To a boiling solution of **1a** (185.2 mg, 0.38 mmol) in a mixture of benzene (2 mL) and D_2O (1.0 mL) was added slowly a solution of Bu_3SnH (0.20 mL, 0.76 mmol) and AIBN (12.5 mg, 0.076 mmol) in benzene (1.8 mL) under an Ar atmosphere. After being stirred at reflux for 2 h, a solution of Bu_3SnH (0.20 mL, 0.76 mmol) and AIBN (12.5 mg, 0.076 mmol) in benzene (1.8 mL) was added slowly. After being stirred for 2 h, the reaction mixture was extracted with hexane/MeCN. The MeCN phase was concentrated at reduced pressure. The residue was purified by FCC (hexane/AcOEt 2:1) to afford *cis*-**2a-D** (D: 2%) (16.7 mg, 13%), *trans*-**2a-D** (D: 0%) (5.3 mg, 4%), *cis*-**3a-D** (D: 82%) (18.4 mg, 10%), and *trans*-**3a-D** (D: 83%) (22.4 mg, 12%).

*A mixture of ethyl cis-1,2,3,4-tetrahydro-1-[(4-methylphenyl)sulfonyl]-4-[(phenylmethoxy)amino]quinoline-3-(1-d)-acetate (cis-**3a-D**).* A pale yellow oil. IR ν_{max} cm^{-1}: 3526 (NH), 1732 (COO), 1354, 1168 (NSO_2). ^1H NMR (500 MHz) δ: 7.89 (1H, d, J=8.5 Hz), 7.54 (2H, d, J=8.5 Hz), 7.14–7.34 (9H, m), 7.05 (1H, t, J=7.5, 1 Hz), 4.38 and 4.49 (2H, ABq, J=11.5 Hz), 4.10–4.18 (3H, m), 3.92 (1H, d, J=3.5 Hz), 3.53 (1H, t, J=12 Hz), 2.58 (3/5H, d, J=7.5 Hz), 2.37 (1/2H, d, J=12 Hz), 2.34 (3H, s), 2.26–2.32 (1H, m), 1.25 (3H, t, J=7 Hz). HRMS *m/z*: Calcd for $C_{27}H_{29}DN_2O_5S$ (M^+) 495.1937. Found: 495.1914. Incorporation of D was 82% from the NMR spectrum.

*Ethyl trans-1,2,3,4-tetrahydro-1-[(4-methylphenyl)sulfonyl]-4-[(phenylmethoxy)amino]quinoline-3-(1-d)-acetate (trans-**3a-D**).* A pale yellow oil. IR ν_{max} cm^{-1}: 3565 (NH), 1728 (COO), 1351, 1165 (NSO_2). ^1H NMR (500 MHz) δ: 7.69 (1H, d, J=8.5 Hz), 7.66 (2H, d, J=9 Hz), 7.14–7.36 (9H, m), 7.01 (1H, td, J=8, 1 Hz), 5.24 (1H, br s), 4.50 and 4.56 (2H, ABq, J=7 Hz), 4.12–4.20 (2H, m), 3.90–3.96 (2H, m), 3.78 (1H, br s), 2.58–2.64 (1H, m), 2.36 (3H, s), 2.24–2.32 (12/10H, m), 1.27 (3H, t, J=7.5 Hz). HRMS *m/z*: Calcd for $C_{27}H_{29}DN_2O_5S$ (M^+) 495.1937. Found: 495.1937. Incorporation of D was 83% from the NMR spectrum.

4.2.22. Conversion of *cis*-3a into *cis*-2a in the presence of Bu_3SnNMe_2 [Table 6, entry 2]. To a boiling solution of *cis*-**3a** (50 mg, 0.1 mmol) in benzene (3 mL) was added Bu_3SnNMe_2 (28 mg, 0.1 mmol) under a nitrogen atmosphere. After being stirred at reflux for 2 h, Bu_3SnNMe_2 (155 mg, 0.6 mmol) was added three times for every 2 h. After being stirred at reflux for 6 h, the reaction mixture was concentrated at reduced pressure. The residue was purified by FCC (hexane/AcOEt 10:1) to afford *cis*-**2a** (1.0 mg, 2%) and **9a** (3.1 mg, 7%).

4.2.23. [Table 6, entry 3]. To a solution of *cis*-**3a** (28 mg, 0.056 mmol) was added Bu_3SnNMe_2 (21 mg, 0.075 mmol) under a nitrogen atmosphere at 110 °C. After being stirred at 110 °C for 3 h, Bu_3SnNMe_2 (52 mg, 0.19 mmol) was added two times for every 1 h. After being stirred at 110 °C for 3 h, the reaction mixture was extracted with hexane/MeCN. The MeCN phase was concentrated at reduced pressure. The residue was purified by PTLC (AcOEt) to afford *cis*-**2a** (6.5 mg, 34%), **9a** (7.1 mg, 28%), and *cis*-**12** (4.5 mg, 16%).

*cis-1,2,3,4-Tetrahydro-N,N-dimethyl-1-[(4-methylphenyl)sulfonyl]-4-[(phenylmethoxy)amino]quinoline-3-acetamide (cis-**12**).* A colorless oil. IR ν_{max} cm^{-1}: 3665 (NH), 1640 (CON), 1352, 1165 (NSO_2). ^1H NMR (500 MHz) δ: 7.87 (1H, br d, J=8 Hz), 7.58 (2H, br d, J=8 Hz), 7.35–7.16 (9H, m), 7.05 (1H, br t, J=8 Hz), 4.47 and 4.44 (2H, ABq, J=12.5 Hz), 4.10 (1H, dd, J=13, 3.5 Hz), 4.03 (1H, d, J=3.5 Hz), 3.58 (1H, br t, J=13 Hz), 2.92 and 2.88 (each 3H, s), 2.58 (1H, dd, J=16, 7.5 Hz), 2.48–2.46 (1H, m), 2.34 (3H, s), 2.29 (1H, dd, J=16, 6.5 Hz). ^{13}C NMR (50 MHz) δ: 170.7, 143.7, 137.3, 136.6, 135.9, 130.2, 129.5, 128.4, 128.3, 128.2, 128.1, 127.8, 127.2, 124.1, 122.2, 75.8, 58.5, 47.6, 37.1, 35.4, 33.4, 32.8, 21.5. HRMS *m/z*: Calcd for $C_{27}H_{31}N_3O_4S$ (M^+) 493.2034. Found: 493.2031.

4.2.24. [Table 6, entry 4]. To a boiling solution of *cis*-**3a** (59 mg, 0.12 mmol) in benzene (1 mL) was added a solution of Bu_3SnH (0.063 mL, 0.24 mmol), AIBN (3.8 mg, 0.024 mmol), and Bu_3SnNMe_2 (79 mg, 0.24 mmol) in benzene (1 mL) by syringe pump under a nitrogen atmosphere. After being stirred at reflux for 4 h, Bu_3SnNMe_2 (79 mg, 0.24 mmol) was added. After being stirred at reflux for 5 h, the reaction mixture was extracted with hexane/MeCN. The MeCN phase was concentrated at reduced pressure. The residue was purified by PTLC (AcOEt) to afford *cis*-**2a** (6.4 mg, 16%) and *cis*-**12** (38 mg, 65%).

4.2.25. Conversion of *trans*-3a into *trans*-2a in the presence of Bu_3SnNMe_2 [Table 6, entry 6]. According to the procedure described in the conversion of *cis*-**3a** into *cis*-**2a** in the presence of Bu_3SnNMe_2 (Table 6, entry 3), reaction of *trans*-**3a** (50 mg, 0.10 mmol) with Bu_3SnNMe_2 (132 mg, 0.48 mmol) gave *trans*-**2a** (9.3 mg, 27%) and *trans*-**12** (25 mg, 50%).

*trans-Tetrahydro-N,N-dimethyl-1-[(4-methylphenyl)sulfonyl]-4-[(phenylmethoxy)amino]quinoline-3-acetamide (trans-**12**).* A colorless oil. IR ν_{max} cm^{-1}: 3671 (NH), 1639 (CON), 1350, 1164 (NSO_2). ^1H NMR (500 MHz) δ: 7.70 (2H, br d, J=8 Hz), 7.64 (1H, br d, J=8 Hz), 7.35–7.23 (8H, m), 7.18 (1H, br t, J=8 Hz), 7.01 (1H, br t, J=8 Hz), 4.60 and 4.51 (2H, ABq, J=12 Hz), 4.05 (1H, dd, J=13, 4.5 Hz), 3.89 (1H, dd, J=13, 3.5 Hz), 3.84 (1H, d, J=2.5 Hz), 2.96 and 2.88 (each 3H, s), 2.92–2.85 (1H, m), 2.38 (1H, dd, J=16, 9 Hz), 2.37 (3H, s), 2.18 (1H, dd, J=16, 5.5 Hz). NOESY: NOE was observed between 1′-H (δ 2.38) and 2-Heq (δ 4.05), and 1′-H (δ 2.18) and 4-H (δ 3.84), and 4-H (δ 3.84) and 2-Heq (δ 4.05). ^{13}C NMR (50 MHz) δ: 170.7, 143.6, 137.6, 137.2, 131.1, 129.7, 128.50, 128.45, 128.3, 127.8, 127.0, 124.5, 123.5, 120.5, 76.8, 61.1, 46.8, 37.2, 35.5, 33.3, 31.3, 21.5. HRMS *m/z*: Calcd for $C_{27}H_{31}N_3O_4S$ (M^+) 493.2033. Found: 493.2042.

4.2.26. [Table 6, entry 7]. According to the procedure described in the conversion of *cis*-**3a** into *cis*-**2a** in the presence of Bu_3SnNMe_2 (Table 6, entry 4), reaction of *trans*-**3a** (50 mg, 0.10 mmol) with Bu_3SnH (0.052 mL, 0.19 mmol) and Bu_3SnNMe_2 (128 mg, 0.38 mmol) in benzene (1 mL) in the presence of AIBN (3.1 mg, 0.019 mmol) gave *trans*-**12** (35 mg, 74%) as a colorless oil.

4.2.27. Conversion of 9a into *cis*-2a in the presence of Bu_3SnNMe_2 [Table 7, entry 2]. According to the procedure

described in the conversion of *cis*-**3a** into *cis*-**2a** in the presence of Bu_3SnNMe_2 (Table 6, entry 3), reaction of **9a** (50 mg, 0.11 mmol) with Bu_3SnNMe_2 (132 mg, 0.48 mmol) gave *cis*-**2a** (12 mg, 33%) and **9a** (30 mg, 60%).

4.2.28. [Table 7, entry 3]. According to the procedure described in the conversion of *cis*-**3a** into *cis*-**2a** in the presence of Bu_3SnNMe_2 (Table 6, entry 4), reaction of **9a** (50 mg, 0.11 mmol) with Bu_3SnH (0.059 mL, 0.22 mmol) and Bu_3SnNMe_2 (42 mg, 0.15 mmol) in benzene (1 mL) in the presence of AIBN (3.6 mg, 0.022 mmol) gave *cis*-**2a** (32 mg, 83%).

4.3. Radical reaction of oxime ether 1a in the presence of Ph_3SnH

According to the procedure given for radical reaction of **1a** in the presence of Bu_3SnH, reaction of **1a** (529 mg, 1.08 mmol) with Ph_3SnH (1.25 g, 4.3 mmol) in the presence of AIBN (70.5 mg, 0.43 mmol) gave *cis*-**2a** (126 mg, 34%) and *trans*-**2a** (127 mg, 35%).

4.3.1. Ethyl-(2*E*)-4-[(2-cyanophenyl)[(4-methylphenyl)-sulfonyl]amino]-2-butenoate (1h). According to the procedure given for alkylation of **7a**,**b**, reaction of *N*-[2-cyanophenyl]-4-methyl-benzenesulfonamide (**7e**)[11] (2 g, 7.34 mmol) with ethyl 4-bromocrotonate (1.2 mL, 8.8 mmol) in the presence of K_2CO_3 (4.6 g, 33 mmol) gave **1h** (2.25 g, 80%) as colorless crystals. Mp 81–83 °C (EtOH/hexane). IR ν_{max} cm^{-1}: 2234 (CN), 1716 (COO), 1360, 1165 (NSO_2). ^1H NMR (200 MHz) δ: 7.66–7.26 (8H, m), 6.82 (1H, dt, J=16, 6 Hz), 5.90 (1H, br d, J=16 Hz), 4.41 (2H, br d, J=6 Hz), 4.15 (2H, q, J=7 Hz), 2.45 (3H, s), 1.25 (3H, t, J=7 Hz). ^{13}C NMR (75 MHz) δ: 165.3, 144.6, 141.2, 140.8, 137.3, 134.0, 133.5, 131.4, 129.9, 129.0, 127.9, 124.9, 116.0, 114.4, 60.6, 51.9, 21.6, 14.1. HRMS *m*/*z*: Calcd for $C_{20}H_{20}N_2O_4S$ (M^+) 384.1142. Found: 384.1136. Anal. Calcd for $C_{20}H_{20}N_2O_4S$: C, 62.48; H, 5.24; N, 7.29. Found: C, 62.45; H, 5.29; N, 7.28.

4.3.2. Ethyl-(2*E*)-4-[[(4-methylphenyl)sulfonyl][2-[(1*E*)-(diphenylhydrazono)methyl]phenyl]amino]-2-butenoate (1i). According to the procedure described in the preparation of **7a**,**b**, oxidation of **6** (300 mg, 1.08 mmol) with MnO_2 (3.3 g, 38 mmol) gave crude aldehyde. Condensation of crude aldehyde with $Ph_2NNH_2 \cdot HCl$ (240 mg, 1.09 mmol) gave the corresponding hydrazone (288 mg 65%) as pale yellow crystals. Mp 197–198 °C (EtOH). IR ν_{max} (KBr) cm^{-1}: 3467 (NH), 1343, 1159 (NSO_2). ^1H NMR (300 MHz) δ: 8.25 (1H, dd, J=8, 2 Hz), 7.63–6.87 (18H, m), 2.44 (3H, s). ^{13}C NMR (50 MHz) δ: 144.6, 142.9, 137.5, 136.1, 132.2, 131.9, 131.2, 130.2, 129.4, 128.4, 127.8, 126.2, 124.4, 122.2, 21.5. HRMS *m*/*z*: Calcd for $C_{26}H_{23}N_3O_2S$ (M^+) 441.1510. Found: 441.1521. According to the procedure given for alkylation of **7a**,**b**, reaction of hydrazone (200 mg, 0.45 mmol) with ethyl 4-bromocrotonate (0.06 mL, 0.45 mmol) in the presence of K_2CO_3 (250 mg, 1.80 mmol) gave **1i** (192 mg, 77%) as a pale yellow oil. IR ν_{max} cm^{-1}: 1718 (COO), 1352, 1163 (NSO_2). ^1H NMR (300 MHz) δ: 8.20 (1H, dd, J=8, 1.5 Hz), 7.48–7.11 (17H, m), 6.68 (1H, dd, J=8, 1.5 Hz), 6.55 (1H, dt, J=16, 7 Hz), 5.67 (1H, br d, J=16 Hz), 4.20 (1H, m), 4.13 (2H, q, J=7 Hz), 3.88 (1H, m), 2.41 (3H, s), 1.23 (3H, t, J=7 Hz). ^{13}C NMR (50 MHz) δ: 165.2, 143.6, 143.2, 141.1, 136.6, 136.4, 135.2, 132.0, 129.6, 129.5, 128.6, 128.3, 128.2, 127.6, 126.1, 124.6, 124.2, 122.3, 60.3, 52.6, 21.4, 14.0. HRMS *m*/*z*: Calcd for $C_{32}H_{31}N_3O_4S$ (M^+) 553.2033. Found: 553.2031.

4.3.3. Ethyl-(2*E*)-4-[[(4-methylphenyl)sulfonyl][2-[(1*E*)-(phenylmethyl)imino]phenyl]amino]-2-butenoate (1j). To a solution of **6** (100 mg, 0.33 mmol) in CH_2Cl_2 (11 mL) was added MnO_2 (995 mg, 11 mmol) under nitrogen atmosphere at room temperature. After being stirred at room temperature for 2 h, the reaction mixture was filtered through a pad of Celite and the filtrate was concentrated at reduced pressure to give the crude aldehyde as a colorless solid. ^1H NMR spectrum of the residue proved the formation of desired aldehyde, which without further purification was subjected to the following reaction. To a solution of the crude aldehyde in CH_2Cl_2 (2 mL) were added $BnNH_2$ (0.039 mL, 0.36 mmol) and Al_2O_3 (100 mg, 0.98 mmol) under a nitrogen atmosphere at room temperature. After being stirred at room temperature for 1.5 h, the reaction mixture was filtered, diluted with water, and extracted with $CHCl_3$. The organic phase was washed with brine, dried over $MgSO_4$, and concentrated at reduced pressure. The residue was purified by recrystallization from EtOH to afford corresponding imine (88 mg 70%) as yellow crystals and a 2:1 mixture of *E*- and *Z*-isomers. Mp 116–119 °C (EtOH). IR ν_{max} cm^{-1}: 3690 (NH), 1383, 1169 (NSO_2). ^1H NMR (200 MHz) δ: 8.33 (2/3H, s), 8.22 (1/3H, d, J=8, 2 Hz), 7.95 (1/3H, s), 7.71–6.96 (12H+2/3H, m), 4.81 (4/3H, s), 4.39 (2/3H, s), 2.40 and 2.30 (each 3H, s). ^{13}C NMR (50 MHz) δ: 165.2, 144.5, 141.1, 140.7, 134.6, 133.9, 133.4, 131.1, 129.8, 128.9, 127.8, 124.8, 115.9, 114.4, 60.5, 51.9, 21.5, 14.0. HRMS *m*/*z*: Calcd for $C_{21}H_{20}N_2O_2S$ (M^+) 364.1244. Found: 364.1254. Anal. Calcd for $C_{21}H_{20}N_2O_2S \cdot 1/5$ EtOH: C, 68.78; H, 5.72; N, 7.50. Found: C, 68.61; H, 5.52; N, 7.40. According to the procedure given for alkylation of **7a**,**b**, reaction of imine (1.1 g, 2.9 mmol) with ethyl 4-bromocrotonate (0.40 mL, 2.9 mmol) in the presence of K_2CO_3 (1.6 g, 12 mmol) gave **1j** (1.1 g, 80%) as a pale yellow oil. IR ν_{max} cm^{-1}: 1717 (COO), 1355, 1164 (NSO_2). ^1H NMR (200 MHz) δ: 8.64 (1H, s), 8.16 (1H, dd, J=7, 2 Hz), 7.54–7.24 (11H, m), 6.80 (1H, dt, J=16, 7 Hz), 6.72 (1H, dd, J=7, 2 Hz), 5.81 (1H, br d, J=16 Hz), 4.77 (2 h, s), 4.42 (2H, m), 4.11 (2H, q, J=7 Hz), 2.39 (3H, s), 1.21 (3H, t, J=7 Hz). ^{13}C NMR (50 MHz) δ: 165.0, 158.3, 144.0, 138.9, 138.6, 135.9, 134.6, 130.8, 129.54, 129.47, 128.6, 128.2, 128.0, 127.8, 127.6, 126.7, 124.6, 65.0, 60.3, 52.8, 21.3, 13.9. HRMS *m*/*z*: Calcd for $C_{27}H_{28}N_2O_4S$ (M^+) 476.1768. Found: 476.1777.

4.3.4. Ethyl-(2*E*)-4-[[2-(hydroxymethyl)phenyl][(4-methylphenyl)sulfonyl]amino]-2-butenoate. According to the procedure given for alkylation of **7a**,**b**, reaction of **6** (200 mg, 0.72 mmol) with ethyl 4-bromocrotonate (0.12 mL, 0.86 mmol) in the presence of K_2CO_3 (398 mg, 2.9 mmol) gave the corresponding butenoate (153 mg, 55%) as colorless crystals. Mp 124–125 °C ($Et_2O/CHCl_3$). IR ν_{max} cm^{-1}: 3522 (OH), 1717 (COO), 1343, 1162 (NSO_2). ^1H NMR (200 MHz) δ: 7.63–7.11 (7H, m), 6.76 (1H, dt, J=16, 6 Hz), 6.48 (1H, dd, J=8, 1 Hz), 5.76 (1H, dt, J=16, 2 Hz), 4.91 (1H, br s), 4.55 (2H, br s), 4.13 (2H, q, J=7 Hz), 4.01 (1H, very br), 3.02 (1H, br t, J=6 Hz), 2.46 (3H, s), 1.24 (3H, t, J=7 Hz). ^{13}C NMR (50 MHz)

δ: 165.3, 144.2, 142.0, 140.8, 136.8, 134.4, 131.0, 129.6, 129.2, 128.4, 128.0, 127.4, 124.8, 60.9, 60.5, 53.0, 21.5, 14.0. HRMS *m/z*: Calcd for $C_{20}H_{23}NO_5S$ (M^+) 389.1295. Found: 389.1289. Anal. Calcd for $C_{20}H_{23}NO_5S \cdot 1/15CHCl_3$: C, 60.64; H, 5.85; N, 3.52. Found: C, 60.62; H, 5.60; N, 3.47.

4.3.5. Radical reaction of nitrile 1h [Scheme 12]. To a boiling solution of **1h** (200 mg, 0.52 mmol) in benzene (3.7 mL) was added a solution of Bu_3SnH (0.28 mL, 1.0 mmol) and AIBN (17.1 mg, 0.104 mmol) in benzene (3.7 mL) by syringe pump under a nitrogen atmosphere. After being stirred at reflux for 3 h, a solution of Bu_3SnH (0.28 mL, 1.04 mmol) and AIBN (17 mg, 0.10 mmol) in benzene (2 mL) was added by syringe pump. After being stirred at reflux for 5 h, the reaction mixture was extracted with hexane/MeCN. The MeCN phase was concentrated at reduced pressure. The residue was purified by MCC (hexane/AcOEt 3:1) to afford **7e** (83.5 mg, 59%).

4.3.6. Radical reaction of hydrazone 1i [Scheme 13]. To a boiling solution of **1i** (200 mg, 0.36 mmol) in benzene (2.5 mL) was added a solution of Bu_3SnH (0.19 mL, 0.72 mmol) and AIBN (12 mg, 0.072 mmol) in benzene (2.5 mL) by syringe pump under a nitrogen atmosphere. After being stirred at reflux for 4 h, a solution of Bu_3SnH (0.19 mL, 0.72 mmol) and AIBN (12 mg, 0.072 mmol) in benzene (2 mL) was added by syringe pump. After being stirred at reflux for 8 h, a solution of AIBN (11.8 mg, 0.072 mmol) in benzene (2 mL) was added by syringe pump. After being stirred at reflux for 1 h, the reaction mixture was extracted with hexane/MeCN. The MeCN phase was concentrated at reduced pressure. The residue was purified by MCC (hexane/AcOEt 3:1) to afford *cis*-**2a** (11 mg, 9%), *trans*-**2a** (19 mg, 15%), *cis*-**3i** (57 mg, 28%), *trans*-**3i** (11 mg, 6%), *cis*-**9i** (6.2 mg, 3%), and diphenylamine (**14**) (17 mg, 29%). Diphenylamine was identical with authentic sample.

*Ethyl cis-1,2,3,4-tetrahydro-1-[(4-methylphenyl)sulfonyl]-4-(2,2-diphenylhydrazino)quinoline-3-acetate (cis-**3i**).* Pale yellow crystals. Mp 139–140 °C (hexane/Et_2O). IR ν_{max} cm^{-1}: 3571 (NH), 1725 (COO), 1353, 1167 (NSO_2). ^1H NMR (500 MHz) δ: 7.94 (1H, br d, *J*=8.5 Hz), 7.58 (2H, br d, *J*=8.5 Hz), 7.30 (4H, br t, *J*=8.5 Hz), 7.21–7.17 (3H, m), 7.07 (2H, br t, *J*=7.5 Hz), 7.00 (4H, br d, *J*=8.5 Hz), 6.89 (1H, td, *J*=8.5, 1 Hz), 6.44 (1H, dd, *J*=7.5, 1 Hz), 4.19 (1H, ddd, *J*=12, 4, 1 Hz), 4.14–4.07 (2H, m), 4.06 (1H, br s), 3.80 (1H, t, *J*=12 Hz), 3.17 (1H, br s), 2.62 (1H, dd, *J*=16, 7 Hz), 2.31 (3H, s), 2.27 (1H, dd, *J*=16, 7 Hz), 2.24–2.20 (1H, m), 1.19 (3H, t, *J*=7.5 Hz). NOESY: NOE was observed between 1′-H (δ 2.27) and 2-Hax (δ 3.80), and 3-H (δ 2.24–2.20) and 4-H (δ 4.06). ^{13}C NMR (125 MHz) δ: 172.1, 148.9, 143.9, 136.8, 135.8, 129.61, 129.60, 129.33, 129.29, 128.6, 128.2, 127.3, 124.2, 123.5, 122.4, 121.5, 60.5, 55.3, 46.7, 33.77, 33.76, 21.5, 14.8. HRMS *m/z*: Calcd for $C_{32}H_{33}N_3O_4S$ (M^+) 555.2190. Found: 555.2187. Anal. Calcd for $C_{32}H_{33}N_3O_4S \cdot 1/3Et_2O$: C, 68.98; H, 6.31; N, 7.24. Found: C, 68.80; H, 6.03; N, 7.36.

*Ethyl trans-1,2,3,4-tetrahydro-1-[(4-methylphenyl)sulfonyl]-4-(2,2-diphenylhydrazino)quinoline-3-acetate (trans-**3i**).* A pale yellow oil. IR ν_{max} cm^{-1}: 3681 (NH), 1727 (COO), 1351, 1165 (NSO_2). ^1H NMR (500 MHz) δ: 7.76 (2H, br d, *J*=8.5 Hz), 7.68 (1H, dd, *J*=8.5, 1 Hz), 7.30–7.26 (5H, m, *J*=8.5 Hz), 7.17–7.14 (2H, m), 7.06–7.02 (6H, m), 6.91 (1H, td, *J*=8.5, 1 Hz), 6.79 (1H, dd, *J*=7.5, 1 Hz), 4.31 (1H, dd, *J*=12, 3 Hz), 4.08 (2H, m), 4.04 (1H, dd, *J*=12, 3 Hz), 3.72 (1H, br s), 2.84–2.81 (1H, m), 2.40 (3H, s), 2.37 (1H, dd, *J*=16, 7 Hz), 2.29 (1H, br s), 2.07 (1H, dd, *J*=16, 7 Hz), 1.18 (3H, t, *J*=7 Hz). NOESY: NOE was observed between 1′-H (δ 2.07) and 4-H (δ 3.72), and 1′-H (δ 2.37) and 2-H (δ 4.31). ^{13}C NMR (125 MHz) δ: 171.9, 148.4, 143.8, 137.4, 137.2, 130.8, 129.8, 129.3, 129.3, 128.8, 127.0, 123.6, 123.3, 123.1, 121.0, 119.7, 60.6, 57.4, 46.1, 34.3, 30.5, 21.6, 14.8. HRMS *m/z*: Calcd for $C_{32}H_{33}N_3O_4S$ (M^+) 555.2190. Found: 555.2188.

*cis-1,3,3a,4,5,9b-Hexahydro-5-[(4-methylphenyl)sulfonyl]-1-(diphenylamino)-2H-pyrrolo[3,2-c]quinolin-2-one (cis-**9i**).* Pale yellow crystals. Mp 230–231 °C ($CHCl_3$/hexane). IR ν_{max} cm^{-1}: 1716 (γ-lactam), 1360, 1166 (NSO_2). ^1H NMR (500 MHz) δ: 7.75 (1H, br d, *J*=8.5 Hz), 7.53 (2H, br d, *J*=8.5 Hz), 7.31–7.20 (6H, m), 7.09 (1H, dd, *J*=8.5, 1.5 Hz), 7.03–6.94 (5H, m), 6.82 (1H, br t, *J*=8.5 Hz), 6.51 (2H, br d, *J*=8.5 Hz), 4.69 (1H, d, *J*=7.5 Hz), 4.11 (1H, dd, *J*=14, 4.5 Hz), 3.49 (1H, dd, *J*=14, 10.5 Hz), 2.72 (1H, dd, *J*=17.5, 8.5 Hz), 2.55–2.51 (1H, m), 2.38 (3H, s), 2.26 (1H, dd, *J*=17.5, 2 Hz). ^{13}C NMR (125 MHz) δ: 171.3, 145.0, 144.2, 143.2, 137.3, 136.8, 132.3, 129.9, 129.6, 129.3, 128.8, 127.0, 125.2, 124.1, 123.4, 123.3, 122.7, 120.2, 118.6, 54.3, 47.7, 31.9, 28.1, 21.6. HRMS *m/z*: Calcd for $C_{30}H_{27}N_3O_3S$ (M^+) 509.1771. Found: 509.1767. Anal. Calcd for $C_{30}H_{27}N_3O_3S \cdot 1/6\ CHCl_3$: C, 68.43; H, 5.17; N, 7.94. Found: C, 68.52; H, 5.35; N, 8.01.

4.3.7. Radical reaction of imine 1j [Scheme 14]. To a boiling solution of **1j** (250 mg, 0.51 mmol) in benzene (4 mL) was added a solution of Bu_3SnH (0.27 mL, 1.0 mmol) and AIBN (17 mg, 0.10 mmol) in benzene (3.6 mL) by syringe pump under nitrogen atmosphere. After being stirred at reflux for 1 h, a solution of Bu_3SnH (0.27 mL, 1.02 mmol) and AIBN (16.7 mg, 0.102 mmol) in benzene (2 mL) was added by syringe pump. After being stirred at reflux for 2 h, the reaction mixture was extracted with hexane/MeCN. The MeCN phase was concentrated at reduced pressure. The residue was purified by MCC (hexane/AcOEt 3:1) to afford *cis*-**15** (32 mg, 11%), *trans*-**15** (21 mg, 7%), *trans*-**3j** (9.4 mg, 4%), *trans*-**10a** (43 mg, 17%), and *cis*-**2a** (34 mg, 20%).

*Ethyl cis-1,2,3,4-tetrahydro-1-[(4-methylphenyl)sulfonyl]-4-[(phenylmethylene)amino]quinoline-3-acetate (cis-**15**).* A Colorless solid. IR ν_{max} cm^{-1}: 1727 (COO), 1352, 1166 (NSO_2). ^1H NMR (200 MHz) δ: 8.16 (1H, s), 7.98 (1H, br d, *J*=8.5 Hz), 7.63–7.56 (4H, m), 7.45–6.93 (8H, m), 4.26–4.20 (2H, m), 4.13 (2H, q, *J*=7 Hz), 3.78 (1H, dd, *J*=13, 11 Hz), 2.50–2.17 (3H, m), 2.30 (3H, s), 1.23 (3H, t, *J*=7 Hz). ^{13}C NMR (75 MHz) δ: 171.7, 160.8, 143.6, 136.2, 136.1, 135.7, 131.0, 129.9, 129.5, 128.5, 128.40, 128.36, 127.3, 124.1, 122.3, 67.9, 60.6, 47.0, 34.3, 34.1, 21.5, 14.2. HRMS *m/z*: Calcd for $C_{27}H_{28}N_2O_4S$ (M^+) 476.1768. Found: 476.1762.

*Ethyl trans-1,2,3,4-tetrahydro-1-[(4-methylphenyl)sulfonyl]-4-[(phenylmethylene)amino]quinoline-3-acetate (trans-**15**).* A Colorless solid. IR ν_{max} cm^{-1}: 1728 (COO), 1351, 1165

(NSO_2). ^{1}H NMR (200 MHz) δ: 8.16 (1H, s), 7.84 (1H, br d, J=8.5 Hz), 7.68–7.59 (4H, m), 7.45–6.91 (8H, m), 4.29 (1H, dd, J=13, 4 Hz), 4.10 (2H, m), 3.97 (1H, br d, J=7 Hz), 3.76 (1H, dd, J=13, 8 Hz), 2.57–2.43 (1H, m), 2.41–2.17 (2H, m), 2.37 (3H, s), 1.23 (3H, t, J=7 Hz). ^{13}C NMR (75 MHz) δ: 171.4, 162.1, 143.7, 136.4, 136.1, 135.6, 131.1, 129.6, 129.0, 128.5, 128.4, 128.0, 127.2, 124.3, 122.5, 70.4, 60.6, 48.2, 35.41, 35.35, 21.5, 14.1. HRMS *m/z*: Calcd for $C_{27}H_{28}N_2O_4S$ (M^+) 476.1768. Found: 476.1741.

*Ethyl trans-1,2,3,4-tetrahydro-1-[(4-methylphenyl)sulfonyl]-4-[(phenylmethyl)amino]quinoline-3-acetate (trans-**3j**)*. Pale yellow crystals. Mp 83–85 °C (EtOH/hexane). IR ν_{max} (KBr) cm^{-1}: 3339 (NH), 1724 (COO), 1336, 1158 (NSO_2). ^{1}H NMR (500 MHz) δ: 7.79 (1H, br d, J=8 Hz), 7.64 (2H, br d, J=8 Hz), 7.31–7.15 (9H, m), 7.07 (1H, td, J=8, 1 Hz), 4.18–4.13 (3H, m), 3.78 (1H, dd, J=13, 7 Hz), 3.50 (1H, br d, J=5.5 Hz), 3.40 and 3.24 (2H, ABq, J=13 Hz), 2.51–2.49 (1H, m), 2.33 (1H, dd, J=16.5, 6.5 Hz), 2.24 (3H, s), 2.25 (1H, dd, J=16.5, 7.5 Hz), 1.27 (3H, t, J=7 Hz). NOESY: NOE was observed between 1′-H (δ 2.33) and 4-H (δ 3.50), and 3-H (δ 2.51–2.49) and O*CH*$_2$Ph (δ 3.40 and 3.24). ^{13}C NMR (125 MHz) δ: 172.1, 143.8, 140.1, 137.0, 136.6, 129.62, 129.57, 129.0, 128.4, 128.0, 127.2, 127.0, 124.4, 122.4, 60.7, 58.1, 49.4, 35.5, 32.2, 21.4, 14.2. HRMS *m/z*: Calcd for $C_{27}H_{30}N_2O_4S$ (M^+) 478.1925. Found: 478.1907. Anal. Calcd for $C_{27}H_{30}N_2O_4S\cdot 1/3$ EtOH: C, 67.27; H, 6.53; N, 5.67. Found: C, 67.05; H, 6.41; N, 5.53.

4.4. Ethyl-(2*E*)-4-[[2-(acetylphenyl)][(4-methylphenyl)-sulfonyl]amino]-2-butenoate (1l)

According to the procedure given for alkylation of **7a**,**b**, reaction of *N*-(2-acetylphenyl)-4-methyl-benzenesulfonamide[22] (500 mg, 1.7 mmol) with ethyl 4-bromocrotonate (0.29 mL, 2.1 mmol) in the presence of K_2CO_3 (956 mg, 6.9 mmol) gave **1l** (675.1 mg, 97%) as colorless crystals. Mp 88–91 °C (EtOH). IR ν_{max} (neat) cm^{-1}: 1717 (COO), 1699 (CO), 1350, 1164 (NSO_2). ^{1}H NMR (200 MHz) δ: 7.63 (1H, dd, J=7, 2 Hz), 7.47–7.23 (6H, m), 6.95 (1H, dt, J=16, 7 Hz), 6.79 (1H, dd, J=7, 2 Hz), 5.88 (1H, dt, J=16, 1 Hz), 4.41 (2H, br d, J=7 Hz), 4.14 (2H, q, J=7 Hz), 2.56 (3H, s), 2.42 (3H, s), 1.26 (3H, t, J=7 Hz). ^{13}C NMR (50 MHz) δ: 201.1, 165.5, 143.9, 141.6, 141.2, 136.1, 135.2, 131.4, 129.5, 129.4, 129.2, 128.5, 127.8, 124.6, 60.5, 52.8, 29.9, 21.5, 14.1. HRMS *m/z*: Calcd for $C_{21}H_{23}NO_5S$ (M^+) 401.1295. Found: 401.1302. Anal. Calcd for $C_{21}H_{23}NO_5S$: C, 62.82; H, 5.77; N, 3.49. Found: C, 62.80; H, 5.78; N, 3.47.

4.4.1. Radical reaction of aldehyde 1k [Table 8, entry 1]. To a solution of ethyl-(2*E*)-4-[[2-(hydroxymethyl)phenyl]-[(4-methylphenyl)sulfonyl]amino]-2-butenoate (250 mg, 0.64 mmol) in CH_2Cl_2 (28 mL) was added MnO_2 (1.9 g, 22 mmol) under a nitrogen atmosphere at room temperature. After being stirred at room temperature for 2 h, the reaction mixture was filtered through a pad of Celite and the filtrate was concentrated at reduced pressure to give the crude aldehyde **1k** as a colorless solid. ^{1}H NMR spectrum of the residue proved the formation of desired aldehyde, which without further purification was subjected to the following reaction. To a boiling solution of **1k** in benzene (5 mL) was added a solution of Bu_3SnH (0.38 mL, 1.4 mmol) and AIBN (23 mg, 0.14 mmol) in benzene (5 mL) by syringe pump under a nitrogen atmosphere. After being stirred at reflux for 3 h, a solution of Bu_3SnH (0.38 mL, 1.4 mmol) and AIBN (23 mg, 0.14 mmol) in benzene (2 mL) was added by syringe pump. After being stirred at reflux for 2 h, the reaction mixture was extracted with hexane/MeCN. The MeCN phase was concentrated at reduced pressure. The residue was purified by MCC (hexane/AcOEt 1:1) to afford *cis*-**2c** (130 mg, 59%), *trans*-**2c** (6 mg, 3%), and **3k** (72 mg, 29%).

*cis-1,3,3a,4,5,9b-Hexahydro-5-[(4-methylphenyl)sulfonyl]-2H-furo[3,2-c]quinolin-2-one (cis-**2c**)*. Colorless crystals. Mp 158–159 °C (EtOH). IR ν_{max} (KBr) cm^{-1}: 1780 (γ-lactone), 1348, 1167 (NSO_2). ^{1}H NMR (500 MHz) δ: 7.70 (1H, br d, J=8 Hz), 7.55 (2H, br d, J=8 Hz), 7.44 (1H, br d, J=8 Hz), 7.37 (1H, br t, J=8 Hz), 7.27–7.24 (3H, m), 5.09 (1H, d, J=6.5 Hz), 4.27 (1H, dd, J=14, 5 Hz), 3.09 (1H, dd, J=14, 12.5 Hz), 2.84 (1H, dd, J=18, 8.5 Hz), 2.67–2.64 (1H, m), 2.41 (3H, s), 2.28 (1H, dd, J=18, 2 Hz). ^{13}C NMR (125 MHz) δ: 174.5, 144.3, 136.9, 136.7, 131.0, 130.0, 129.8, 127.0, 125.9, 125.3, 124.4, 75.2, 46.5, 32.9, 32.8, 21.6. HRMS *m/z*: Calcd for $C_{18}H_{17}NO_4S$ (M^+) 343.0877. Found: 343.0889. Anal. Calcd for $C_{18}H_{17}NO_4S$: C, 62.96; H, 4.99; N, 4.08. Found: C, 62.69; H, 5.00; N, 4.03.

*trans-1,3,3a,4,5,9b-Hexahydro-5-[(4-methylphenyl)sulfonyl]-2H-furo[3,2-c]quinolin-2-one (trans-**2c**)*. Colorless solid. IR ν_{max} cm^{-1}: 1797 (γ-lactone), 1354, 1168 (NSO_2). ^{1}H NMR (500 MHz) δ: 7.83 (1H, br d, J=8 Hz), 7.41–7.35 (3H, m), 7.25–7.20 (4H, m), 4.07 (1H, dd, J=11.5, 6 Hz), 3.85 (1H, d, J=11 Hz), 3.54 (1H, br t, J=11.5 Hz), 2.75 (1H, dd, J=16, 6.5 Hz), 2.40 (3H, s), 2.36 (1H, dd, J=16, 13 Hz), 2.29–2.24 (1H, m). ^{13}C NMR (125 MHz) δ: 174.3, 144.4, 134.7, 133.4, 131.5, 129.9, 128.6, 126.8, 126.3, 125.8, 121.4, 78.1, 48.3, 42.7, 34.5, 21.6. HRMS *m/z*: Calcd for $C_{18}H_{17}NO_4S$ (M^+) 343.0877. Found: 343.0880.

*Ethyl cis-1,2,3,4-tetrahydro-4-hydroxy-1-[(4-methylphenyl)-sulfonyl]quinoline-3-acetate (**3k**)*. A colorless oil. IR ν_{max} (neat) cm^{-1}: 3507 (OH), 1732 (COO), 1349, 1164 (NSO_2). ^{1}H NMR (500 MHz) δ: 7.75 (1H, br d, J=8 Hz), 7.60 (2H, br d, J=8 Hz), 7.39 (1H, br d, J=8 Hz), 7.27–7.22 (3H, m), 7.13 (1H, td, J=8, 1 Hz), 4.23 (1H, br d, J=7.5 Hz), 4.17 (2H, q, J=7 Hz), 4.09 (1H, dd, J=13, 4 Hz), 3.65 (1H, dd, J=13, 8.5 Hz), 2.44 (1H, dd, J=16, 6.5 Hz), 2.38 (3H, s), 2.32 (1H, dd, J=16, 6.5 Hz), 2.24–2.20 (1H, m), 1.28 (3H, t, J=7 Hz). ^{13}C NMR (125 MHz) δ: 172.2, 143.9, 136.3, 135.8, 130.3, 129.7, 128.6, 128.3, 127.1, 124.7, 122.3, 70.3, 60.9, 47.9, 36.9, 35.1, 21.5, 14.2. HRMS *m/z*: Calcd for $C_{20}H_{23}NO_5S$ (M^+) 389.1296. Found: 389.1317.

4.4.2. Radical reaction of ketone 1l [Table 8, entry 2]. To a boiling solution of **1l** (224 mg, 0.56 mmol) in benzene (4 mL) was added a solution of Bu_3SnH (0.30 mL, 1.1 mmol) and AIBN (18 mg, 0.12 mmol) in benzene (4 mL) by syringe pump under a nitrogen atmosphere. After being stirred at reflux for 2 h, a solution of Bu_3SnH (0.30 mL, 1.1 mmol) and AIBN (18 mg, 0.12 mmol) in benzene (2 mL) was added by syringe pump. After being stirred at reflux for 3 h, the reaction mixture was extracted with hexane/MeCN. The MeCN phase was concentrated at reduced pressure. The residue was purified by MCC (hexane/AcOEt

3:1) to afford *cis*-**2d** (105 mg, 52%), *trans*-**2d** (12 mg, 6%), and **3l** (55 mg, 24%).

*cis-1,3,3a,4,5,9b-Hexahydro-9b-methyl-5-[(4-methylphenyl)-sulfonyl]-2H-furo[3,2-c]quinolin-2-one (cis-**2d**)*. Colorless crystals. Mp 172–175 °C (EtOH). IR ν_{max} cm^{-1}: 1773 (γ-lactone), 1358, 1166 (NSO_2). ^1H NMR (500 MHz) δ: 7.68 (1H, dd, *J*=8, 1 Hz), 7.55 (2H, br d, *J*=8 Hz), 7.49 (1H, dd, *J*=8, 1.5 Hz), 7.35 (1H, ddd, *J*=8, 7, 1.5 Hz), 7.29–7.24 (3H, m), 4.25 (1H, dd, *J*=14, 5 Hz), 3.13 (1H, dd, *J*=14, 12 Hz), 2.88 (1H, dd, *J*=18, 9 Hz), 2.54–2.48 (1H, m), 2.40 (3H, s), 2.25 (1H, dd, *J*=18, 2 Hz), 1.21 (3H, s). NOESY: NOE was observed between 3a-H (δ 2.54–2.48) and 9b-Me (δ 1.21). ^{13}C NMR (125 MHz) δ: 174.0, 144.3, 137.1, 135.6, 131.0, 129.9, 129.2, 128.6, 127.2, 126.5, 124.9, 82.0, 47.8, 32.9, 32.3, 28.5, 21.5. HRMS *m/z*: Calcd for $C_{19}H_{19}NO_4S$ (M^+) 357.1033. Found: 357.1035. Anal. Calcd for $C_{19}H_{19}NO_4S$: C, 63.85; H, 5.36; N, 3.92. Found: C, 63.71; H, 5.38; N, 3.88.

*trans-1,3,3a,4,5,9b-Hexahydro-9b-methyl-5-[(4-methylphenyl)sulfonyl]-2H-furo[3,2-c]quinolin-2-one (trans-**2d**)*. A colorless oil. IR ν_{max} cm^{-1}: 1784 (γ-lactone), 1358, 1169 (NSO_2). ^1H NMR (500 MHz) δ: 7.97 (1H, br d, *J*=8 Hz), 7.59 (2H, br d, *J*=8 Hz), 7.32–7.23 (4H, m), 7.12 (1H, br t, *J*=8 Hz), 4.13 (1H, dd, *J*=11, 5 Hz), 3.54 (1H, br dd, *J*=13, 11 Hz), 2.65–2.61 (1H, m), 2.55–2.49 (2H, m), 2.38 (3H, s), 0.80 (3H, s). NOESY: NOE was observed between 4-Hax (δ 3.54) and 9b-Me (δ 0.80). ^{13}C NMR (125 MHz) δ: 174.1, 144.4, 135.1, 134.3, 133.6, 129.8, 128.5, 127.0, 124.3, 123.3, 121.6, 81.9, 46.1, 42.6, 31.3, 21.5, 19.5. HRMS *m/z*: Calcd for $C_{19}H_{19}NO_4S$ (M^+) 357.1033. Found: 357.1029.

*Ethyl cis-1,2,3,4-tetrahydro-4-hydroxy-4-methyl-1-[(4-methylphenyl)sulfonyl]quinoline-3-acetate (**3l**)*. Colorless crystals. Mp 120–121 °C (EtOH). IR ν_{max} cm^{-1}: 3579 (OH), 1727 (COO), 1353, 1167 (NSO_2). ^1H NMR (500 MHz) δ: 7.86 (1H, dd, *J*=8, 1.5 Hz), 7.56 (2H, br d, *J*=8 Hz), 7.51 (1H, dd, *J*=8, 1.5 Hz), 7.25–7.19 (3H, m), 7.11 (1H, td, *J*=8, 1.5 Hz), 4.21 (1H, dd, *J*=13, 4.5 Hz), 4.17 (2H, q, *J*=7 Hz), 3.33 (1H, dd, *J*=13, 11.5 Hz), 2.67 (1H, dd, *J*=16, 5 Hz), 2.36 (3H, s), 2.34–2.30 (1H, m), 2.15 (1H, dd, *J*=16, 8.5 Hz), 1.28 (3H, t, *J*=7 Hz), 1.01 (3H, s). ^{13}C NMR (125 MHz) δ: 172.2, 144.0, 136.4, 135.6, 134.7, 129.6, 128.1, 127.2, 125.5, 124.5, 122.0, 71.1, 61.0, 48.4, 40.6, 32.5, 23.8, 21.5, 14.2. HRMS *m/z*: Calcd for $C_{21}H_{25}NO_5S$ (M^+) 403.1452. Found: 403.1433. Anal. Calcd for $C_{21}H_{25}NO_5S$: C, 62.51; H, 6.25; N, 3.47. Found: C, 62.56; H, 6.16; N, 3.41.

4.4.3. Conversion of 3k into *cis*-2c [Scheme 16]. To a solution of **3k** (21 mg, 0.052 mmol) in benzene (1 mL) was added *p*-TsOH·H_2O (10 mg, 0.052 mmol) under a nitrogen atmosphere. After being stirred at 60 °C for 1 h, the reaction mixture was diluted with saturated aqueous $NaHCO_3$ and extracted with Et_2O. The organic phase was washed with brine, dried over $MgSO_4$, and concentrated under reduced pressure. The residue was purified by PTLC (hexane/AcOEt 2:1) to afford *cis*-**2c** (16 mg, 91%).

4.4.4. Conversion of 3l into *cis*-2d [Scheme 16]. According to the procedure given for cyclization of **3k**, reaction of **3l** (21 mg, 0.088 mmol) with *p*-TsOH·H_2O (17 mg, 0.088 mmol) gave *cis*-**2d** (17 mg, 53%).

4.4.5. Radical reaction of aldehyde 1k in the presence of Bu_3SnD [Table 9]. To a solution of ethyl-(2*E*)-4-[[2-(hydroxymethyl)phenyl][(4-methylphenyl)sulfonyl]amino]-2-butenoate (125 mg, 0.319 mmol) in CH_2Cl_2 (14 mL) was added MnO_2 (964 mg, 11 mmol) under a nitrogen atmosphere at room temperature. After being stirred at room temperature for 2 h, the reaction mixture was filtered through a pad of Celite and the filtrate was concentrated at reduced pressure to give the crude aldehyde **1k** as a colorless solid. ^1H NMR spectrum of the residue proved the formation of desired aldehyde, which without further purification was subjected to the following reaction. To a boiling solution of crude aldehyde **1k** in benzene (2 mL) was added a solution of Bu_3SnD (0.17 mL, 0.64 mmol) and AIBN (10 mg, 0.064 mmol) in benzene (2.5 mL) by syringe pump under a nitrogen atmosphere. After being stirred at reflux for 2 h, a solution of Bu_3SnD (0.17 mL, 0.64 mmol) and AIBN (10 mg, 0.064 mmol) in benzene (2 mL) was added by syringe pump. After being stirred at reflux for 1 h, the reaction mixture was extracted with hexane/MeCN. The MeCN phase was concentrated at reduced pressure. The residue was purified by MCC (hexane/AcOEt 3:1) to afford *cis*-**2c-D** (D: 95%) (35 mg, 31%), *trans*-**2c-D** (D: 56%) (2.5 mg, 2%), and **3k-D** (D: 66%) (24 mg, 19%).

*cis-3-d-1,3,3a,4,5,9b-Hexahydro-5-[(4-methylphenyl)sulfonyl]-2H-furo[3,2-c]quinolin-2-one (cis-**2c-D**)*. Colorless crystals. IR ν_{max} (KBr) cm^{-1}: 1780 (γ-lactone), 1358, 1165 (NSO_2). ^1H NMR (300 MHz) δ: 7.70 (1H, br d, *J*=8 Hz), 7.54 (2H, br d, *J*=8 Hz), 7.44 (1H, br d, *J*=8 Hz), 7.44–7.34 (2H, m), 7.27–7.22 (3H, m), 5.08 (1H, d, *J*=6.5 Hz), 4.27 (1H, dd, *J*=14, 5 Hz), 3.09 (1H, dd, *J*=14, 12.5 Hz), 2.82 (2/5H, d, *J*=8.5 Hz), 2.67–2.59 (1H, m), 2.41 (3H, s), 2.28 (3/5H, br s). ^{13}C NMR (50 MHz) δ: 174.5, 144.3, 136.8, 136.7, 130.9, 130.0, 129.7, 126.9, 125.8, 125.2, 124.3, 75.1, 46.5, 33.2, 32.7, 21.5. HRMS *m/z*: Calcd for $C_{18}H_{16}DNO_4S$ (M^+) 344.0940. Found: 344.0942. Incorporation of D was 95% from the NMR spectrum.

*trans-3-d-1,3,3a,4,5,9b-Hexahydro-5-[(4-methylphenyl)sulfonyl]-2H-furo[3,2-c]quinolin-2-one (trans-**2c-D**)*. Colorless solid. IR ν_{max} cm^{-1}: 1789 (γ-lactone), 1358, 1168 (NSO_2). ^1H NMR (200 MHz) δ: 7.84 (1H, br d, *J*=8 Hz), 7.42–7.23 (7H, m), 4.08 (1H, dd, *J*=11.5, 6 Hz), 3.86 (1H, d, *J*=11 Hz), 3.54 (1H, br t, *J*=11.5 Hz), 2.75 (2/5H, m), 2.40 (3H, s), 2.34–2.17 (1H+3/5H, m). HRMS *m/z*: Calcd for $C_{18}H_{16}DNO_4S$ (M^+) 344.0940. Found: 344.0935. Incorporation of D was 56% from the NMR spectrum.

*Ethyl cis-1,2,3,4-tetrahydro-4-hydroxy-1-[(4-methylphenyl)-sulfonyl]quinoline-3-(1-d)-acetate (**3k-D**)*. A colorless oil. IR ν_{max} (neat) cm^{-1}: 3509 (OH), 1731 (COO), 1340, 1165 (NSO_2). ^1H NMR (200 MHz) δ: 7.74 (1H, br d, *J*=8 Hz), 7.60 (2H, br d, *J*=8 Hz), 7.41–7.08 (5H, m), 4.24–4.05 (4H, m), 3.64 (1H, dd, *J*=13, 8.5 Hz), 2.45–2.19 (1H+1H, m), 2.38 (3H, s), 1.28 (3H, t, *J*=7 Hz). ^{13}C NMR (75 MHz) δ: 172.2, 143.9, 136.3, 135.8, 130.2, 129.7, 128.5, 128.4, 127.0, 124.6, 122.1, 70.2, 60.9, 47.8, 36.9, 35.0, 21.5, 14.1. HRMS *m/z*: Calcd for $C_{20}H_{22}DNO_5S$

(M^+) 390.1358. Found: 390.1361. Incorporation of D was 66% from the NMR spectrum.

4.4.6. Radical reaction of ketone 1l in the presence of Bu_3SnD [Table 9]. To a boiling solution of **1l** (218.0 mg, 0.54 mmol) in benzene (3.6 mL) was added a solution of Bu_3SnD (0.29 mL, 1.1 mmol) and AIBN (17.7 mg, 0.11 mmol) in benzene (4 mL) by syringe pump under a nitrogen atmosphere. After being stirred at reflux for 2 h, a solution of Bu_3SnD (0.29 mL, 1.1 mmol) and AIBN (17.7 mg, 0.11 mmol) in benzene (2 mL) was added by syringe pump. After being stirred at reflux for 3 h, the reaction mixture was extracted with hexane/MeCN. The MeCN phase was concentrated at reduced pressure. The residue was purified by MCC (hexane/AcOEt 5:1) to afford *cis*-**2d-D** (D: 70%) (76 mg, 39%), *trans*-**2d-D** (D: 100%) (26 mg, 14%), and **3l-D** (D: 80%) (56 mg, 26%).

*cis-3-d-1,3,3a,4,5,9b-Hexahydro-9b-methyl-5-[(4-methylphenyl)sulfonyl]-2H-furo[3,2-c]quinolin-2-one (cis-**2d-D**).* Colorless crystals. IR ν_{max} cm^{-1}: 1769 (γ-lactone), 1351, 1168 (NSO_2). ^1H NMR (300 MHz) δ: 7.68 (1H, dd, *J*=8, 1 Hz), 7.54 (2H, br d, *J*=8 Hz), 7.48 (1H, dd, *J*=8, 1.5 Hz), 7.34 (1H, ddd, *J*=8, 7, 1.5 Hz), 7.29–7.23 (3H, m), 4.25 (1H, dd, *J*=14, 5 Hz), 3.13 (1H, dd, *J*=14, 12 Hz), 2.95–2.83 (2/5H, m), 2.55–2.48 (1H, m), 2.39 (3H, s), 2.28–2.21 (3/5H, m), 1.20 (3H, s). ^{13}C NMR (50 MHz) δ: 174.0, 144.2, 137.0, 135.5, 130.9, 129.8, 129.1, 128.5, 127.1, 126.4, 124.8, 81.9, 47.7, 39.0, 32.2, 28.4, 21.4. HRMS *m/z*: Calcd for $C_{19}H_{18}DNO_4S$ (M^+) 358.1096. Found: 358.1110. Incorporation of D was 70% from the NMR spectrum.

*trans-3-d-1,3,3a,4,5,9b-Hexahydro-9b-methyl-5-[(4-methylphenyl)sulfonyl]-2H-furo[3,2-c]quinolin-2-one (trans-**2d-D**).* A colorless oil. IR ν_{max} (neat) cm^{-1}: 1791 (γ-lactone), 1355, 1169 (NSO_2). ^1H NMR (300 MHz) δ: 7.97 (1H, br d, *J*=8 Hz), 7.59 (2H, br d, *J*=8 Hz), 7.33–7.23 (4H, m), 7.12 (1H, br t, *J*=8 Hz), 4.13 (1H, dd, *J*=11, 5 Hz), 3.61–3.47 (1H, m), 2.64–2.43 (2H, m), 2.38 (3H, s), 0.80 (3H, s). ^{13}C NMR (75 MHz) δ: 174.1, 144.4, 135.1, 134.3, 133.6, 129.8, 128.5, 127.0, 124.3, 123.2, 121.6, 81.9, 46.1, 42.5, 31.0, 21.5, 19.4. HRMS *m/z*: Calcd for $C_{19}H_{18}DNO_4S$ (M^+) 358.1096. Found: 358.1102. Incorporation of D was 100% from the NMR spectrum.

*Ethyl cis-1,2,3,4-tetrahydro-4-hydroxy-4-methyl-1-[(4-methylphenyl)sulfonyl]quinoline-3-(1-d)-acetate (**3l-D**).* Colorless crystals. IR ν_{max} cm^{-1}: 3579 (OH), 1727 (COO), 1353, 1167 (NSO_2). ^1H NMR (300 MHz) δ: 7.85 (1H, dd, *J*=8, 1.5 Hz), 7.56 (2H, br d, *J*=8 Hz), 7.50 (1H, dd, *J*=8, 1.5 Hz), 7.27–7.19 (3H, m), 7.10 (1H, td, *J*=8, 1.5 Hz), 4.23–4.07 (3H, m), 3.32 (1H, dd, *J*=13, 11.5 Hz), 2.67 (3/5H, dd, m), 2.36 (3H, s), 2.39–2.28 (1H, m), 2.18–2.10 (2/5H, m), 2.00 (1H, br s), 1.27 (3H, t, *J*=7 Hz), 1.00 (3H, s). ^{13}C NMR (75 MHz) δ: 172.5, 144.0, 136.3, 135.6, 134.7, 129.6, 128.1, 127.2, 125.5, 124.5, 122.0, 71.0, 61.0, 48.4, 40.5, 32.5, 23.7, 21.5, 14.1. HRMS *m/z*: Calcd for $C_{21}H_{24}DNO_5S$ (M^+) 404.1515. Found: 404.1522. Incorporation of D was 80% from the NMR spectrum.

4.4.7. *cis*-1-[2,3,3a,4,5,9b-Hexahydro-5-[(4-methylphenyl)sulfonyl]-1*H*-pyrrolo[3,2-*c*]quinolin-1-yl]ethanone (18). To a solution of *cis*-**2a** (1.3 g, 3.8 mmol) in THF (190 mL) was added slowly $BH_3 \cdot Me_2S$ (2.0 M in THF, 9.5 mL, 19 mmol) under a nitrogen atmosphere at room temperature. After being stirred at reflux for 9 h, 6 M aqueous HCl at 0 °C was added and the reaction mixture was stirred at room temperature for 14 h. The reaction mixture was basified with 10% aqueous NaOH at 0 °C and concentrated at reduced pressure. The residue was extracted with $CHCl_3$. The organic phase was washed with brine, dried over Na_2SO_4, and concentrated at reduced pressure. To a solution of the residue and Et_3N (0.79 mL, 5.7 mmol) in CH_2Cl_2 (25 mL) was added AcCl (0.33 mL, 4.56 mmol) at 0 °C. After being stirred at reflux for 9 h, the reaction mixture was diluted with 10% aqueous HCl at 0 °C and extracted with $CHCl_3$. The organic phase was washed with brine, dried over $MgSO_4$, and concentrated at reduced pressure. The residue was purified by MCC (AcOEt) to afford **18** (1.34 g, 94%) as colorless crystals. Mp 144–146 °C (EtOH). IR ν_{max} cm^{-1}: 1635, 1416 (NCO, NSOO). ^1H NMR (300 MHz) δ: 7.02–7.62 (16/2H, m), 4.87 (1/2H, d, *J*=8 Hz), 4.53 (1/2H, dd, *J*=15.5, 9 Hz), 3.67 (1/2H, dd, *J*=14, 6.5 Hz), 3.29–3.59 (5/2H, m), 3.26 (1/2H, d, *J*=8 Hz), 3.01 (1/2H, dd, *J*=14.5, 7 Hz), 2.84–2.93 (1/2H, m), 2.58–2.72 (1/2H, m), 2.38 (6/2H, s), 2.08 (3/2H, s), 1.79–2.05 (2/2H, m), 1.70 (3/2H, s), 1.21–1.36 (1/2H, m). ^{13}C NMR (300 MHz) δ: 170.4, 169.7, 144.1, 144.0, 137.6, 137.4, 136.5, 136.4, 132.4, 130.4, 130.05, 129.98, 129.73, 128.5, 127.8, 127.6, 127.3, 126.9, 126.7, 125.5, 125.2, 122.8, 56.7, 53.3, 48.1, 47.7, 46.7, 45.1, 41.7, 37.5, 29.8, 28.8, 22.6, 21.7, 21.6, 21.5. HRMS *m/z*: Calcd for $C_{20}H_{22}N_2O_3S$ (M^+) 370.1350. Found: 370.1349. Anal. Calcd for $C_{20}H_{22}N_2O_3S$: C, 64.84; H, 5.99; N, 7.56. Found: C, 64.88; H, 6.03; N, 7.53.

4.4.8. *cis*-1,8-Diacetyl-2,3,3a,4,5,9b-hexahydro-1*H*-pyrrolo[3,2-*c*]quinoline (20). To a solution of $AlCl_3$ (400 mg, 3 mmol) and AcCl (0.11 mL, 1.5 mmol) in $Cl(CH_2)_2Cl$ (2 mL) was added slowly a solution of **18** (185 mg, 0.5 mmol) in $Cl(CH_2)_2Cl$ (2 mL) at room temperature. After being stirred at reflux for 2.5 h, the reaction mixture was added to ice-water and extracted with $CHCl_3$. The organic phase was washed with saturated aqueous $NaHCO_3$, water and brine, dried over Na_2SO_4, and concentrated at reduced pressure. To a solution of the crude acetamide **19** in MeOH (15 mL) was added 10% aqueous NaOH (1.5 mL) under a nitrogen atmosphere at room temperature. After being stirred at reflux for 9 h, the reaction mixture was extracted with $CHCl_3$. The organic phase was washed with brine, dried over Na_2SO_4, and concentrated at reduced pressure. The residue was purified by MCC ($CHCl_3$/MeOH 20:1) to afford **20** (61.2 mg, 47%) as colorless oil. IR ν_{max} cm^{-1}: 3020, 1628 (NH, NCO, CO). ^1H NMR (300 MHz) δ: 8.23 (1H, dd, *J*=2, 1 Hz), 7.68 (1H, dd, *J*=8.5, 2 Hz), 6.47 (1H, br d, *J*=8.5 Hz), 5.51 (1H, d, *J*=7.5 Hz), 4.43 (1H, very br), 3.52–3.59 (3H, m), 3.27 (1H, dd, *J*=12.5, 3 Hz), 2.47 (3H, s), 2.46–2.59 (1H, m), 2.14 (3H, s), 1.92–2.27 (2H, m). ^{13}C NMR (200 MHz) δ: 196.8, 170.9, 147.9, 133.3, 128.3, 127.5, 120.0, 113.9, 54.0, 46.6, 41.0, 36.1, 26.6, 26.0, 22.5. HRMS *m/z*: Calcd for $C_{15}H_{18}N_2O_2$ (M^+) 258.1367. Found: 258.1374.

4.4.9. *cis*-1,8-Diacetyl-5-(2-bromobenzoyl)-2,3,3a,4,5,9b-hexahydro-1*H*-pyrrolo[3,2-*c*]quinoline (16). To a solution of **20** (156 mg, 0.61 mmol) and Et_3N (0.13 mL, 0.91 mmol)

in CH_2Cl_2 (14 mL) was added *o*-bromobenzoyl chloride (0.09 mL, 0.67 mmol) under nitrogen atmosphere at 0 °C. After being stirred at room temperature for 22.5 h, the reaction mixture was diluted with 10% aqueous HCl and extracted with $CHCl_3$. The organic phase was washed with saturated aqueous $NaHCO_3$ and brine, dried over $MgSO_4$, and concentrated at reduced pressure. The residue was purified by MCC ($CHCl_3$/MeOH 20:1) to afford **16** (243 mg, 91%) as colorless crystals. Mp 165–167 °C (AcOEt). IR ν_{max} cm^{-1}: 1646, 1682 (NCO, CO). ^1H NMR (300 MHz) δ: 8.33 (1H, br s), 7.58–7.60 (2H, m), 5.53 (1H, br s), 3.59–3.63 (3H, m), 2.97 (1H, br s), 2.56 (3H, s), 2.19 (3H, s), 2.10–2.24 (1H, br s), 1.99–2.04 (2H, br s). ^{13}C NMR (200 MHz) δ: 197.2, 171.0, 170.1, 141.4, 137.4, 134.3, 133.3, 131.1, 128.7, 127.8, 127.0, 125.0, 123.7, 119.8, 55.5, 47.1, 45.3, 41.1, 37.9, 26.5, 22.7, 22.4. HRMS *m/z*: Calcd for $C_{22}H_{21}BrN_2O_3$ (M^+) 440.0734. Found: 440.0738. Anal. Calcd for $C_{22}H_{21}BrN_2O_3$: C, 59.87; H, 4.80; N, 6.35. Found: C, 59.58; H, 4.64; N, 6.50.

4.4.10. C–C bond formation of 16 via 1,5-hydrogen atom translocation reaction. To a boiling solution of **16** (200 mg, 0.4545 mmol) and methyl acrylate (0.82 mL, 9.09 mmol) in benzene (33 mL) was added slowly a solution of Bu_3SnH (0.25 mL, 0.909 mmol) and AIBN (7.5 mg, 0.045 mmol) in benzene (33 mL) by syringe pump for 4 h under a nitrogen atmosphere. Then, a solution of AIBN (7.5 mg, 0.045 mmol) in benzene (2 mL) was added. After being stirred for 4 h at reflux, the reaction mixture was concentrated at reduced pressure. To the residue were added Et_2O (10 mL) and DBU (0.15 mL). The complex mixture was filtered through SiO_2 column chromatography and the filtrate was concentrated at reduced pressure. The residue was purified by flash column chromatography (AcOEt) to afford **17** (88.6 mg, 43%) and **22** (31.1 mg, 19%).

*4-(1,8-Diacetyl-5-benzoyl-2,3,3a,4,5,9b-hexahydro-1H-pyrrolo[3,2-c]quinoline)propanate (**17**)*. Colorless oil. IR ν_{max} cm^{-1}: 1732, 1679, 1643 (NCO, NCO, COO, CO). ^1H NMR (300 MHz) δ: 8.61 (1H, s), 7.50 (1H, d, J=8.5 Hz), 7.26–7.43 (5H, m), 6.52 (1H, d, J=8.5 Hz), 5.55 (1H, d, J=8 Hz), 4.96–4.68 (1H, m), 3.66 (3H, s), 3.58–3.66 (1H, m), 2.71–2.74 (1H, m), 2.55 (3H, s), 2.45–2.55 (1H, m), 2.17–2.37 (2H, m), 2.16 (3H, s), 1.72–1.96 (4H, m). ^{13}C NMR (200 MHz) δ: 197.3, 173.0, 171.1, 170.4, 140.3, 134.9, 134.0, 133.5, 131.2, 129.3, 128.8, 128.5, 126.9, 125.9, 55.3, 54.7, 51.8, 47.2, 43.0, 30.6, 29.6, 27.6, 26.5, 23.0. HRMS *m/z*: Calcd for $C_{26}H_{28}N_2O_5$ (M^+) 448.1996. Found: 448.1996.

*cis-1,7-Diacetyl-2,3,3a,4,5,5a-hexahydro-1,5-diazo-benzo[de]cyclopenta[b]anthracen-10-one (**22**)*. Colorless crystals. Mp 267–268 °C ($CHCl_3$/hexane). IR ν_{max} cm^{-1}: 1731, 1643 (NCO, CO). ^1H NMR (300 MHz) δ: 8.84 (1H, d, J=1.5 Hz), 8.56 (1H, s), 8.52 (1H, d, J=8 Hz), 8.40 (1H, d, J=8 Hz), 7.82 (1H, t, J=7.5 Hz), 7.64 (1H, t, J=7.5 Hz), 5.79 (1H, d, J=7.5 Hz), 5.21 (1H, dd, J=15, 2.5 Hz), 3.77 (1H, dd, J=15, 3.5 Hz), 3.48–3.66 (2H, m), 2.82–2.94 (1H, m), 2.65 (3H, s), 2.18 (3H, s), 2.10–2.21 (1H, m), 1.84–1.95 (1H, m). ^{13}C NMR (200 MHz) δ: 197.2, 171.1, 161.8, 136.3, 133.4, 133.1, 131.9, 131.7, 128.7, 128.6, 125.3, 125.1, 122.4, 122.3, 118.8, 54.4, 46.8, 40.4, 34.5, 26.7, 26.5, 22.4. HRMS *m/z*: Calcd for $C_{22}H_{20}N_2O_3$ (M^+) 360.1473. Found: 360.1484. Anal. Calcd for $C_{22}H_{20}N_2O_3 \cdot 3/2H_2O$: C, 68.20; H, 5.20; N, 7.23. Found: C, 68.32; H, 5.31; N, 7.20.

4.4.11. (3a*R*,4*R*,9b*R*)-*rel*-1-Acetyl-5-benzoyl-2,3,3a,4,5,-9b-hexahydro-4-(3-methoxy-3-oxopropyl)-1*H*-pyrrolo-[3,2-*c*]quinoline-8-carboxylic acid methyl ester (21). To a mixture of 2.5% NaOH (2 mL) and Br_2 (20 mg) was added a solution of **17** (19.8 mg, 0.044 mmol) in MeOH (1.5 mL) under a nitrogen atmosphere at 0 °C. After being stirred at room temperature for 0.5 h, 10% $Na_2S_2O_3$ was added. After being stirred at room temperature for 5 min, the reaction mixture was acidified with 10% HCl. The complex mixture was extracted with $CHCl_3$, washed with brine, dried over $MgSO_4$, and concentrated at reduced pressure. To a solution of the residue in MeOH (5 mL) was added H_2SO_4 (20 mg) at 0 °C. After being stirred under a nitrogen atmosphere at reflux for 4 h, the reaction mixture was poured into saturated aqueous $NaHCO_3$ at 0 °C and extracted with $CHCl_3$. The organic phase was washed with brine, dried over $MgSO_4$, and concentrated at reduced pressure. The residue was purified by PTLC (AcOEt) to afford **21** (15.6 mg, 76%) as colorless oil. IR ν_{max} cm^{-1}: 1722, 1640 (COO, CNO). ^1H NMR (300 MHz) δ: 8.57 (1H, s), 7.56 (1H, br d, J=8.5 Hz), 7.24–7.42 (5H, m), 6.50 (1H, d, J=8.5 Hz), 5.55 (1H, d, J=8 Hz), 4.92–5.02 (1H, m), 3.86 (3H, s), 3.66 (3H, s), 3.58–3.70 (1H, m), 2.66–2.74 (1H, m), 2.44–2.55 (1H, m), 2.25–2.38 (2H, m), 2.08–2.22 (1H, m), 2.14 (3H, s), 1.82–1.96 (1H, m), 1.56–1.76 (2H, m). ^{13}C NMR (300 MHz) δ: 173.0, 170.8, 172.2, 166.4, 140.4, 134.8, 133.7, 131.1, 129.5, 128.7, 128.4, 127.1, 125.8, 55.5, 54.9, 52.2, 51.8, 47.2, 43.4, 30.5, 30.1, 27.9, 23.0. HRMS *m/z*: Calcd for $C_{26}H_{28}N_2O_6$ (M^+) 464.1946. Found: 464.1947.

4.4.12. (3a*R*,4*R*,9b*R*)-*rel*-5-Benzoyl-2,3,3a,4,5,9b-hexahydro-4-(3-methoxy-3-oxopropyl)-1*H*-pyrrolo[3,2-*c*]-quinoline-8-carboxylic acid methyl ester (23). To a mixture of **21** (24.1 mg, 0.052 mmol) and $NaHCO_3$ (52.3 mg, 0.623 mmol) in CH_2Cl_2 (1.4 mL) was added $Et_3O \cdot BF_4$ (1.0 M in CH_2Cl_2, 0.31 mL, 0.31 mmol) under an Ar atmosphere at room temperature. After being stirred at room temperature for 50 h, saturated aqueous $NaHCO_3$ was added. After being stirred at room temperature for 15 min, the reaction mixture was extracted with $CHCl_3$, washed with brine, dried over Na_2SO_4, and concentrated at reduced pressure. The residue was purified by PTLC ($CHCl_3$/MeOH 20:1) to afford **23** (9.2 mg, 42%) and **21** (4.6 mg, 19%). Colorless oil. IR ν_{max} cm^{-1}: 1721, 1646 (COO, CNO). ^1H NMR (300 MHz) δ: 8.03 (1H, s), 7.45–7.56 (3H, m), 7.23–7.41 (3H, m), 6.48 (1H, br d, J=11 Hz), 4.94–5.03 (1H, m), 4.49 (1H, br d, J=7.5 Hz), 3.85 (3H, s), 3.64 (3H, s), 3.10–3.19 (1H, m), 2.90–3.03 (1H, m), 2.70–2.80 (1H, m), 2.40–2.53 (1H, m), 2.13–2.35 (2H, m), 1.24–2.05 (3H, s). ^{13}C NMR (300 MHz) δ: 173.2, 170.7, 166.2, 141.5, 135.0, 131.3, 131.0, 129.0, 128.7, 128.3, 126.9, 126.2, 56.0, 52.1, 51.7, 45.9, 44.1, 31.6, 30.6, 27.6. HRMS *m/z*: Calcd for $C_{24}H_{26}N_2O_5$ (M^+) 422.1840. Found: 422.1843.

4.4.13. (3a*R*,4*R*,9b*R*)-*rel*-5-Benzoyl-2,3,3a,4,5,9b-hexahydro-4-(3-methoxy-3-oxopropyl)-1*H*-pyrrolo[3,2-*c*]quinoline-8-carboxylic acid, 8-methyl 1-(phenylmethyl)-ester (24). To a solution of **23** (25.1 mg, 0.059 mmol) in CH_2Cl_2 (7 mL) were added Et_3N (0.01 mL, 0.072 mmol)

and CbzCl (0.01 mL, 0.070 mmol) under an Ar atmosphere at 0 °C. After being stirred at room temperature for 0.5 h, the reaction mixture was acidified with 10% HCl and extracted with $CHCl_3$. The organic phase was washed with saturated aqueous $NaHCO_3$ and brine, dried over $MgSO_4$, and concentrated at reduced pressure. The residue was purified by PTLC (hexane/AcOEt 1:1) to afford **24** (27.8 mg, 84%) as colorless oil. IR ν_{max} cm^{-1}: 1699, 1651 (COO, CNOO, CNO). ^1H NMR (300 MHz) δ: 8.50–8.10 (1H, very br), 7.49 (1H, br d, J=6.6 Hz), 7.12–7.34 (10H, m), 6.41 (1H, br d, J=8.5 Hz), 5.08–5.22 (3H, m), 4.83–4.92 (1H, m), 3.78 (3H, s), 3.58 (3H, s), 2.64–2.71 (1H, m), 2.37–2.48 (1H, m), 2.14–2.27 (2H, m), 1.94–2.08 (1H, m), 1.38–1.70 (2H, m), 1.12–1.30 (2H, m). ^{13}C NMR (300 MHz) δ: 175.3, 173.4, 170.6, 166.6, 156.2, 141.0, 136.7, 135.2, 133.3, 131.3, 130.1, 129.2, 129.1, 128.8, 128.7, 128.4, 127.2, 126.2, 67.7, 56.3, 56.0, 52.4, 52.0, 46.5, 45.1, 30.9, 30.2, 28.4. HRMS m/z: Calcd for $C_{32}H_{32}N_2O_7$ (M^+) 556.2207. Found: 556.2198.

4.4.14. (3a*R*,4*R*,9b*R*)-*rel*-2,3,3a,4,5,9b-Hexahydro-4-(3-hydroxypropyl)-1*H*-pyrrolo[3,2-*c*]quinoline-1,8-dicarboxylic acid, 8-methyl 1-(phenylmethyl)ester (4). To a solution of **24** (2.7 mg, 4.9 μmol) in THF (1 mL) were added $LiBH_4$ (0.5 mg, 0.023 mmol) and MeOH (0.1 mL) under a nitrogen atmosphere at room temperature. After being stirred at room temperature for 0.5 h, the reaction mixture was acidified with 1 M aqueous HCl at 0 °C and extracted with $CHCl_3$. The organic phase was washed with brine, dried over $MgSO_4$, and concentrated at reduced pressure. The residue was purified by PTLC (AcOEt) to afford **4** (1.2 mg, 58%) as colorless oil. The compound **4** was identical with the Ma's authentic sample upon comparison of their spectral data.[13d] IR ν_{max} cm^{-1}: 3365 (NH, OH), 1699 (COO, CNO). ^1H NMR (300 MHz) δ: 8.06–8.17 (1H, very br), 7.64 (1H, br d, J=8.5 Hz), 7.16–7.48 (5H, m), 6.38 (1H, d, J=8.5 Hz), 5.08–5.50 (3H, m), 5.00 (1H, very br), 3.75 (3H, s), 3.62–3.78 (2H, m), 3.46 (2H, very br), 3.33–3.36 (2H, m), 2.28–2.36 (1H, m), 1.88–1.96 (2H, m), 1.34–1.64 (2H, m). HRMS m/z: Calcd for $C_{24}H_{28}N_2O_5$ (M^+) 424.1997. Found: 424.1991.

4.4.15. 1-(2-Bromobenzoyl)-1,2,3,4-tetrahydroquinoline (25a). To a solution of tetrahydroquinoline (1.33 g, 10 mmol) and Et_3N (2.09 mL, 15 mmol) in CH_2Cl_2 (20 mL) was added slowly *o*-bromobenzoyl chloride (1.44 mL, 11 mmol) at 0 °C. After being stirred at room temperature for 1 h, the reaction mixture was diluted with 10% aqueous HCl and extracted with CH_2Cl_2. The organic phase was washed with saturated aqueous $NaHCO_3$, water and brine, dried over $MgSO_4$, and concentrated at reduced pressure. The residue was purified by recrystallization from AcOEt to afford **25a** (1.98 g, 63%) as colorless crystals. Mp 124–126 °C (AcOEt). IR ν_{max} cm^{-1}: 1637 (NCO). ^1H NMR (300 MHz) δ: 8.13 (1/2H, very br), 7.06 (1/2H, very br), 7.14–7.40 (11/2H, very br), 6.98 (1/2H, very br), 6.75 (1/2H, very br), 6.49 (1/2H, very br), 4.09 (2/2H, very br), 3.94 (2/2H, very br), 2.86 (4/2H, very br), 2.04 (4/2H, very br). ^{13}C NMR (200 MHz) δ: 168.2, 138.8, 132.9, 130.3, 129.7, 128.3, 127.3, 125.7, 125.0, 124.5, 45.4, 43.3, 27.1. HRMS m/z: Calcd for $C_{16}H_{14}BrNO$ (M^+) 315.0259. Found: 315.0268. Anal. Calcd for $C_{16}H_{14}BrNO$: C, 60.78; H, 4.46; N, 4.43. Found: C, 60.72; H, 4.37; N, 4.51.

4.4.16. 1,2,3,4-Tetrahydro-1-(2-iodobenzoyl)quinoline (25b). According to the procedure described in the preparation of **25a**, benzoylation of tetrahydroquinoline (400 mg, 3 mmol) with *o*-iodobenzoyl chloride (879 mg, 3.3 mmol) gave **25b** (1.09 g, 95%) as colorless crystals. Mp 124–126 °C (AcOEt). IR ν_{max} cm^{-1}: 1635 (NCO). ^1H NMR (300 MHz) δ: 8.12 (1/2H, very br), 7.75 (2/2H, very br), 6.90–7.50 (11/2H, very br), 6.74 (1/2H, very br), 6.46 (1/2H, very br), 3.99 (2/2H, very br), 3.46 (2/2H, very br), 2.86 (4/2H, very br), 2.01 (4/2H, very br). ^{13}C NMR (200 MHz) δ: 169.6, 142.8, 139.4, 130.2, 128.5, 125.8, 125.0, 124.7, 47.3, 43.7, 27.2. HRMS m/z: Calcd for $C_{16}H_{14}INO$ (M^+) 363.0126. Found: 363.0127. Anal. Calcd for $C_{16}H_{14}INO$: C, 52.91; H, 3.89; N, 3.86. Found: C, 52.84; H, 3.78; N, 3.87.

4.5. General procedure for C–C bond formation via 1,5-hydrogen atom translocation reaction

4.5.1. In the presence of AIBN as a radical initiator [Table 10, entry 3]. To a boiling solution of **25a** (158 mg, 0.5 mmol) and methyl acrylate (0.45 mL, 5.0 mmol) in benzene (25 mL) was added slowly a solution of Bu_3SnH (0.269 mL, 1.0 mmol) and AIBN (8.2 mg, 0.05 mmol) in benzene (25 mL) by syringe pump for 3 h under a nitrogen atmosphere. After being stirred at reflux for 3 h, the reaction mixture was concentrated at reduced pressure. To the residue were added Et_2O (10 mL) and DBU (0.15 mL). The complex mixture was filtered through SiO_2 column chromatography and the filtrate was concentrated at reduced pressure. The residue was purified by flash column chromatography (AcOEt/hexane 1:8 → 1:5 → 1:3) to afford methyl 1-benzoyl-2-(1,2,3,4-tetrahydroquinoline)propanoate **26** (66.1 mg, 41%), **27**[18a,b] (55.6 mg, 47%), and **28**[18a,c] (9.5 mg, 8%).

4.5.2. In the presence of Et_3B as a radical initiator [Table 10, entry 6]. To a solution of **25b** (120 mg, 0.33 mmol), methyl acrylate (0.3 mL, 3.3 mmol), and Bu_3SnH (0.18 mL, 0.66 mmol) in toluene (12 mL) was added Et_3B (1.0 M in Hexane, 0.82 mL, 0.82 mmol) under a nitrogen atmosphere at room temperature. After being stirred for 4 h at room temperature, the reaction mixture was concentrated at reduced pressure. To the residue were added Et_2O (6.6 mL) and DBU (0.1 mL). The complex mixture was filtered through SiO_2 column chromatography and the filtrate was concentrated at reduced pressure. The residue was purified by flash column chromatography (AcOEt/hexane 1:8 → 1:5 → 1:3) to afford methyl 1-benzoyl-2-(1,2,3,4-tetrahydroquinoline)propanoate **26** (38.4 mg, 36%), **27**[18a,b] (40.7 mg, 52%), and **28**[18a,c] (7.5 mg, 9%).

*Methyl 1-benzoyl-2-(1,2,3,4-tetrahydroquinoline)propanoate (**26**).* Colorless crystals. Mp 107–109 °C (EtOH). IR ν_{max} cm^{-1}: 1732, 1635 (COO, CO). ^1H NMR (300 MHz) δ: 7.13–7.33 (6H, m), 7.00 (1H, td, J=7.5, 1 Hz), 6.83 (1H, br t, J=7.5 Hz), 6.51 (1H, d, J=7.5 Hz), 4.90 (1H, quint, J=6.5 Hz), 3.66 (3H, s), 2.80 (2H, t, J=6.5 Hz), 2.33–2.55 (3H, m), 1.63–1.95 (3H, m). ^{13}C NMR (300 MHz) δ: 173.6, 170.0, 137.9, 136.3, 132.4, 129.9, 128.5, 127.9, 126.8, 126.0, 125.2, 51.8, 51.6, 30.8, 29.8, 28.7, 25.0. HRMS m/z: Calcd for $C_{20}H_{21}NO_3$ (M^+) 323.1520. Found: 323.1514. Anal. Calcd for $C_{20}H_{21}NO_3$: C, 74.28; H, 6.55; N, 4.33. Found: C, 74.43; H, 6.67; N, 4.28.

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References and notes

1. (a) *Radicals in Organic Synthesis*; Renaud, P., Sibi, M. P., Eds.; Wiley-VCH: Weinheim, 2001; Vols. 1 and 2; (b) Tietze, L. F.; Brasche, G.; Gericke, K. M. *Domino Reactions in Organic Synthesis*; Tietze, L. F., Brasche, G., Gericke, K. M., Eds.; Wiley-VCH: Weinheim, 2006; pp 219–279.
2. (a) Naito, T.; Honda, Y.; Miyata, O.; Ninomiya, I. *J. Chem. Soc., Perkin Trans. 1* **1995**, 19–26; (b) Miyata, O.; Nishiguchi, A.; Ninomiya, I.; Naito, T.; Aoe, K.; Okamura, K. *Tetrahedron Lett.* **1996**, *37*, 229–232; (c) Miyata, O.; Nishiguchi, A.; Ninomiya, I.; Naito, T.; Aoe, K.; Okamura, K. *Chem. Pharm. Bull.* **1996**, *44*, 1285–1287; (d) Naito, T.; Honda, Y.; Bhavakul, V.; Yamaguchi, S.; Fujiwara, A.; Miyata, O.; Ninomiya, I. *Chem. Pharm. Bull.* **1997**, *45*, 1932–1939; (e) Miyata, O.; Nishiguchi, A.; Ninomiya, I.; Aoe, K.; Okamura, K.; Naito, T. *J. Org. Chem.* **2000**, *65*, 6922–6931; (f) Miyata, O.; Ozawa, Y.; Ninomiya, I.; Naito, T. *Tetrahedron* **2000**, *56*, 6199–6207; (g) Miyata, O.; Nakajima, E.; Naito, T. *Chem. Pharm. Bull.* **2001**, *49*, 213–224; (h) Miyata, O.; Naito, T. *C. R. Acad. Sci. Paris Chim.* **2001**, *4*, 401–421; (i) Miyata, O.; Muroya, K.; Kobayashi, T.; Yamanaka, R.; Kajisa, S.; Koide, J.; Naito, T. *Tetrahedron* **2002**, *58*, 4459–4479.
3. (a) Miyabe, H.; Fujii, K.; Goto, T.; Naito, T. *Org. Lett.* **2000**, *2*, 4071–4074; (b) Miyabe, H.; Fujii, K.; Tanaka, H.; Naito, T. *Chem. Commun.* **2001**, 831–832; (c) Miyabe, H.; Tanaka, H.; Naito, T. *Tetrahedron Lett.* **1999**, *40*, 8387–8390; (d) Miyabe, H.; Ueda, M.; Fujii, K.; Nishimura, A.; Naito, T. *J. Org. Chem.* **2003**, *68*, 5618–5626; (e) Ueda, M.; Miyabe, H.; Nishimura, A.; Miyata, O.; Naito, T. *Org. Lett.* **2003**, *5*, 3835–3838; (f) Miyabe, H.; Tanaka, H.; Naito, T. *Chem. Pharm. Bull.* **2004**, *52*, 842–847.
4. (a) Naito, T.; Nakagawa, K.; Nakamura, T.; Kasei, A.; Ninomiya, I.; Kiguchi, T. *J. Org. Chem.* **1999**, *64*, 2003–2009; (b) Naito, T.; Tajiri, K.; Harimoto, T.; Ninomiya, I.; Kiguchi, T. *Tetrahedron Lett.* **1994**, *35*, 2205–2206; (c) Miyabe, H.; Torieda, M.; Inoue, K.; Tajiri, K.; Kiguchi, T.; Naito, T. *J. Org. Chem.* **1998**, *63*, 4397–4407; (d) Miyabe, H.; Torieda, M.; Ninomiya, I.; Kiguchi, T.; Naito, T. *Synlett* **1997**, 580–582; (e) Naito, T.; Torieda, M.; Tajiri, K.; Ninomiya, I.; Kiguchi, T. *Chem. Pharm. Bull.* **1996**, *44*, 624–626; (f) Naito, T.; Fukumoto, D.; Takebayashi, K.; Kiguchi, T. *Heterocycles* **1999**, *51*, 489–492; (g) Miyabe, H.; Kanehira, S.; Kume, K.; Kandori, H.; Naito, T. *Tetrahedron* **1998**, *54*, 5883–5892; (h) Kiguchi, T.; Ozaki, M.; Naito, T. *Heterocycles* **1999**, *51*, 2711–2722; (i) Kiguchi, T.; Tajiri, K.; Ninomiya, I.; Naito, T. *Tetrahedron* **2000**, *56*, 5819–5833; (j) Naito, T.; Nair, J. S.; Nishiki, A.; Yamashita, K.; Kiguchi, T. *Heterocycles* **2000**, *53*, 2611–2615; (k) Miyabe, H.; Tanaka, H.; Naito, T. *Chem. Pharm. Bull.* **2004**, *52*, 74–78; (l) Miyabe, H.; Nishiki, A.; Naito, T. *Chem. Pharm. Bull.* **2003**, *51*, 100–103.
5. Formal total synthesis of martinelline and martinellic acid, see: (a) Hadden, M.; Nieuwenhuyzen, M.; Potts, D.; Stevenson, P. J.; Thompson, N.; Walker, D. A. *Tetrahedron* **2006**, *62*, 3977–3984; (b) He, Y.; Mahmud, H.; Moningka, R.; Lovely, C. J.; Dias, H. V. R. *Tetrahedron* **2006**, *62*, 8755–8769; (c) Takeda, Y.; Nakabayashi, T.; Shirai, A.; Fukumoto, D.; Kiguchi, T.; Naito, T. *Tetrahedron Lett.* **2004**, *45*, 3481–3484; (d) Miyata, O.; Shirai, A.; Yoshino, S.; Takeda, Y.; Sugiura, M.; Naito, T. *Synlett* **2006**, 893–896; (e) Hadden, M.; Nieuwenhuyzen, M.; Osborne, D.; Stevenson, P. J.; Thompson, N. *Tetrahedron Lett.* **2001**, *42*, 6417–6419; (f) He, Y.; Moningka, R.; Mahmud, H.; Lovely, C. J. *Tetrahedron Lett.* **2005**, *46*, 1251–1254.
6. Balasubramanian, M.; Keay, J. G. *Comprehensive Heterocyclic Chemistry*; Katrizky, A. R., Rees, C. W., Scriven, E. F. V., Eds.; Pergamon: London, 1996; Vol. 5, Chapter 5.06, pp 245–300.
7. (a) Hewson, A. T.; Hughes, K.; Richardson, S. K.; Sharpe, D. A.; Wadsworth, A. H. *J. Chem. Soc., Perkin Trans. 1* **1991**, 1565–1569; (b) Hechavarria Fonseca, M.; Eibler, E.; Zabel, M.; Konig, B. *Tetrahedron: Asymmetry* **2003**, *14*, 1989–1994.
8. (a) Bertrand, M. P.; Escoubet, S.; Gastaldi, S.; Timokhin, V. I. *Chem. Commun.* **2002**, 216–217; (b) Escoubet, S.; Gastaldi, S.; Timokhin, V. I.; Bertrand, M. P.; Siri, D. *J. Am. Chem. Soc.* **2004**, *126*, 12343–12352.
9. Jones, K.; Lappert, M. F. *J. Chem. Soc.* **1965**, 1944–1951.
10. (a) Dimopoulos, P.; Athlan, A.; Manaviazar, S.; George, J.; Walters, M.; Lazarides, L.; Aliev, A. E.; Hale, K. J. *Org. Lett.* **2005**, *7*, 5369–5372; (b) Nativi, C.; Taddei, M. *J. Org. Chem.* **1988**, *53*, 820–826.
11. Corsaro, A.; Chiacchio, U.; Caramella, P.; Purrello, G. *J. Heterocycl. Chem.* **1984**, *21*, 949–952.
12. Witherup, K. M.; Ransom, R. W.; Graham, A. C.; Bernard, A. M.; Salvatore, M. J.; Lumma, W. C.; Anderson, P. S.; Pitzenberger, S. M.; Varga, S. L. *J. Am. Chem. Soc.* **1995**, *117*, 6682–6685.
13. Total synthesis of martinelline and martinellic acid, see: (a) Snider, B. B.; Ahn, Y.; O'Hare, S. M. *Org. Lett.* **2001**, *3*, 4217–4220; (b) Powell, D. A.; Batey, R. A. *Org. Lett.* **2002**, *4*, 2913–2916; (c) Ma, D.; Xia, C.; Jiang, J.; Zhang, J. *Org. Lett.* **2001**, *3*, 2189–2191; (d) Xia, C.; Heng, L.; Ma, D. *Tetrahedron Lett.* **2002**, *43*, 9405–9409; (e) Ma, D.; Xia, C.; Jiang, J.; Zhang, J.; Tang, W. *J. Org. Chem.* **2003**, *68*, 442–451; (f) Ikeda, S.; Shibuya, M.; Iwabuchi, Y. *Chem. Commun.* **2007**, 504–506; (g) Badarinarayana, V.; Lovely, C. J. *Tetrahedron Lett.* **2007**, *48*, 2607–2610.
14. Synthesis of the pyrroloquinoline core, see: (a) Gurjar, M. K.; Pal, S.; Rama Rao, A. V. *Heterocycles* **1997**, *45*, 231–234; (b) Ho, T. C. T.; Jones, K. *Tetrahedron* **1997**, *53*, 8287–8294; (c) Batey, R. A.; Simoncic, P. D.; Lin, D.; Smyj, R. P.; Lough, A. J. *Chem. Commun.* **1999**, 651–652; (d) Hadden, M.; Stevenson, P. J. *Tetrahedron Lett.* **1999**, *40*, 1215–1218; (e) Lovely, C. J.; Mahmud, H. *Tetrahedron Lett.* **1999**, *40*, 2079–2082; (f) Snider, B. B.; Ahn, Y.; Foxman, B. M. *Tetrahedron Lett.* **1999**, *40*, 3339–3342; (g) Frank, K. E.; Aubé, J. *J. Org. Chem.* **2000**, *65*, 655–666; (h) Nieman, J. A.; Ennis, M. D. *Org. Lett.* **2000**, *2*, 1395–1397; (i) Nyerges, M.; Fejes, I.; Toke, L. *Tetrahedron Lett.* **2000**, *41*, 7951–7954; (j) Snider, B. B.; O'Hare, S. M. *Tetrahedron Lett.* **2001**, *42*, 2455–2458; (k) Mahmud, H.; Lovely, C. J.; Dias, H. V. R. *Tetrahedron* **2001**, *57*, 4095–4105; (l) Hadden, M.; Nieuwenhuyzen, M.; Potts, D.; Stevenson, P. J.; Thompson, N. *Tetrahedron* **2001**,

57, 5615–5624; (m) Batey, R. A.; Powell, D. A. *Chem. Commun.* **2001**, 2362–2363; (n) Hamada, Y.; Kunimune, I.; Hara, O. *Heterocycles* **2002**, *56*, 97–100; (o) He, Y.; Mahmud, H.; Wayland, B. R.; Dias, H. V. R.; Lovely, C. J. *Tetrahedron Lett.* **2002**, *43*, 1171–1174; (p) Malassene, R.; Sanchez-Bajo, L.; Toupet, L.; Hurvois, J.-P.; Moinet, C. *Synlett* **2002**, 1500–1504; (q) Nyerges, M.; Fejes, I.; Toke, L. *Synthesis* **2002**, 1823–1828; (r) Hara, O.; Sugimoto, K.; Makino, K.; Hamada, Y. *Synlett* **2004**, 1625–1627; (s) Hara, O.; Sugimoto, K.; Makino, K.; Hamada, Y. *Tetrahedron* **2004**, *60*, 9381–9390; (t) Yadav, J. S.; Subba, R. B. V.; Sunitha, V.; Srinivasa, R. K.; Ramakrishna, K. V. S. *Tetrahedron Lett.* **2004**, *45*, 7947–7950; (u) Nyerges, M. *Heterocycles* **2004**, *63*, 1685–1712; (v) Shaw, J. T.; Masse, C. E.; Ng, P. Y. *Org. Lett.* **2006**, *8*, 3999–4002.

15. (a) Astill, B. D.; Boekelheide, V. *J. Am. Chem. Soc.* **1955**, *77*, 4079–4084; (b) Jiang, Y.; Ma, D. *Tetrahedron Lett.* **2002**, *43*, 7013–7015.
16. Beaulieu, F.; Arora, J.; Veith, U.; Taylor, N. J.; Chapell, B. J.; Snieckus, V. *J. Am. Chem. Soc.* **1996**, *118*, 8727–8728.
17. Williams, L.; Booth, S. E.; Undheim, K. *Tetrahedron* **1994**, *50*, 13697–13708.
18. (a) Nagarajan, K.; Nair, M. D.; Pillai, P. M. *Tetrahedron* **1967**, *23*, 1683–1690; (b) Harayama, T.; Sato, T.; Hori, A.; Abe, H.; Takeuchi, Y. *Heterocycles* **2005**, *66*, 527–530; (c) Crabb, T. A.; Soilleux, S. L. *J. Chem. Soc., Perkin Trans. 1* **1985**, 1381–1385.
19. (a) Kunz, H.; Dombo, B. *Angew. Chem., Int. Ed. Engl.* **1988**, *27*, 711–713; (b) Elliott, M.; Farnham, A. W.; Janes, N. F.; Johnson, D. M.; Pulman, D. A. *Pestic. Sci.* **1987**, *18*, 229–238.
20. (a) Orsini, F.; Pelizzoni, F.; Ricca, G. *Synth. Commun.* **1982**, *12*, 1147–1154; (b) Salamonczyk, G. M.; Han, K.; Guo, Z.; Sih, C. J. *J. Org. Chem.* **1996**, *61*, 6893–6900.
21. (a) Kirsop, P.; Storey, J. M. D.; Harrison, W. T. A. *Acta Crystallogr.* **2004**, *9*, 1636–1638; (b) Sarrazin, L.; Mauze, B. *Synth. Commun.* **1996**, 3179–3191; (c) Bailey, W. J.; Bello, J. *J. Org. Chem.* **1955**, *20*, 525–529.
22. (a) Carril, M.; SanMartin, R.; Dominguez, E.; Tellitu, I. *Tetrahedron* **2006**, *63*, 690–702; (b) Carril, M.; SanMartin, R.; Churruca, F.; Tellitu, I.; Dominguez, E. *Org. Lett.* **2005**, *7*, 4787–4789.