Tetrahedron 68 (2012) 9962–9972

Contents lists available at SciVerse ScienceDirect

Tetrahedron

journal homepage: www.elsevier.com/locate/tet

Regio- and enantioselective synthesis of functionalized tetrahydroquinolines by palladium-catalyzed cyclization of 2-amidophenylmalonates with allylic bisacetates

Masahiro Yoshida *, Yohei Maeyama, Kozo Shishido

Graduate School of Pharmaceutical Sciences, The University of Tokushima, 1-78-1 Sho-machi, Tokushima 770-8505, Japan

ARTICLE INFO

Article history:
Received 22 August 2012
Received in revised form 12 September 2012
Accepted 14 September 2012
Available online 25 September 2012

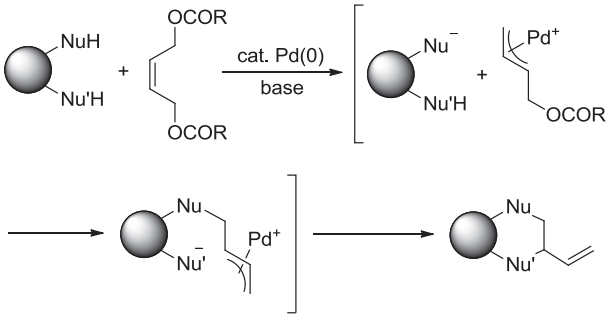
Keywords:
Cascade reactions
Cyclizations
Palladium
Enantioselective reactions
Tetrahydroquinolines

ABSTRACT

A palladium-catalyzed cyclization of 2-amidophenylmalonates with allylic bisacetates is described. Tetrahydroquinolines having a vinyl group at the 3- or 2-position were produced, in which the regioselectivity of the resulting products was altered depending on the substituent on the amino group. The product was transformed to the azabicyclo[3.3.1]nonene via the ring-closing metathesis. Enantioselective reactions also successfully proceeded in the presence of (*S*)-BINAP to give the optically active tetrahydroquinoline with high enantioselectivity.

1. Introduction

Palladium-catalyzed allylic substitution with nucleophiles have received considerable attention and have been extensively studied due to their versatile and specific reactivities.[1] 2-Butene-1,4-diol derivatives, such as the dicarbonate and diacetate are known as useful substrates for palladium-catalyzed reactions with nucleophiles. For example, 1,4-diacyloxy-2-butene reacts with a bis-nucleophile that contains two nucleophilic parts within the molecule, to afford the cyclized product via successive double allylic substitutions (Scheme 1). A variety of classes of cyclic molecules, such as quinoxalines,[2] benzoxazines,[3] piperidines,[4] morpholines,[4,5] benzodioxanes,[6] oxazolidinones,[7] pyrroles,[8] and dihydrofurans[9] have been synthesized using this methodology. During the course of our studies on the palladium-catalyzed cascade cyclizations using bis-nucleophiles,[10] we focused on the nucleophilic activity of 2-amidophenylmalonates toward the 1,4-diacyloxybut-2-ene. It is expected that substituted tetrahydroquinolines, common structures in many biologically active compounds,[11] could be constructed in one step by introducing nucleophilic nitrogen and carbon moieties within the molecule. Herein, we describe in full detail the palladium-catalyzed reaction of 2-amidophenylmalonates **1** with 1,4-diacetoxybut-2-ene **2**, in which the substituted tetrahydroquinoline **3** or **4** having a vinyl group at the 3- or 2-position has been constructed regioselectively and enantioselectively depending on the substrate and reaction conditions (Scheme 2).[12]



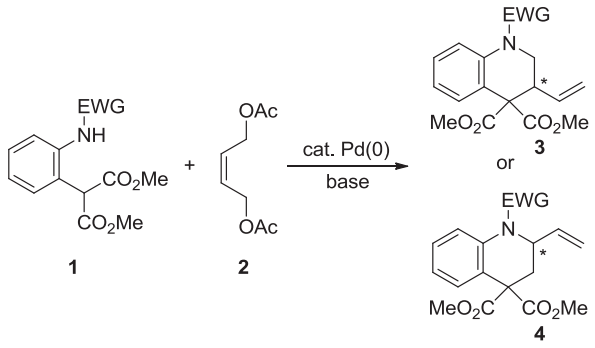
Scheme 1.

2. Results and discussion

The 2-amidophenylmalonates **1** for the cyclization reactions were synthesized as follows (Scheme 3). The nucleophilic aromatic substitution of 2-fluoronitrobenzene (**5a**) with dimethyl malonate in the presence of ^{t}BuOK afforded the substituted product **6a** in 66%

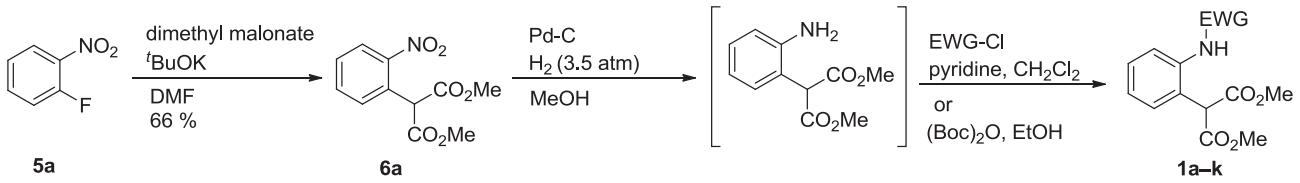
* Corresponding author. Tel./fax: +81 88 6337294; e-mail addresses: yoshi@tokushima-u.ac.jp, yoshida@ph.tokushima-u.ac.jp (M. Yoshida).

0040-4020/$ – see front matter © 2012 Elsevier Ltd. All rights reserved.
http://dx.doi.org/10.1016/j.tet.2012.09.075



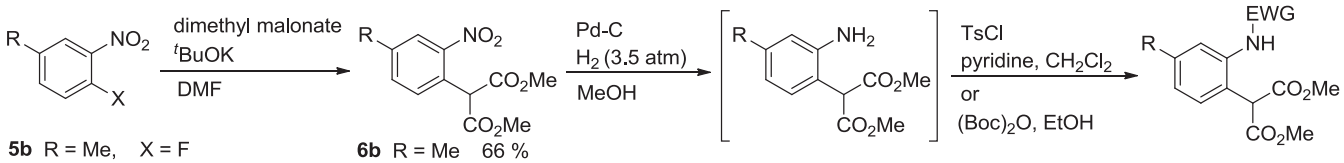
Scheme 2.

Having identified a useful set of reaction conditions, we next conducted the reactions using the 2-amidophenylmalonates **1b**–**k** having various electron-withdrawing groups on the amino group (Table 2). Sulfonamide-type substrates **1b** and **1c** having a benzenesulfonyl- and a 2-naphthalenesulfonyl group successfully reacted with **2** in the presence of the palladium catalyst to produce the 3-vinyltetrahydroquinolines **3b** and **3c** in 89% and 55% yield, respectively (entries 1 and 2). Similar results were obtained in the reaction of 4-nitrobenzenesulfonyl (Ns)- and 3,5-dimethylbenzenesulfonyl-substituted substrates to afford the corresponding products **3d** and **3e** in 80% and 82% yield, respectively (entries 3 and 4). On the other hand, it is interesting to note that the 2-vinyltetrahydroquinoline **4i** was produced predominantly when the benzyloxycarbonyl (Cbz)-substituted substrate **1i** was used (entry 5). Although the yield of the resulting product



EWG-Cl = *p*-Toluenesulfonyl chloride
Benzenesulfonyl chloride
2-Naphtalenesulfonyl chloride
4-Nitrobenzenesulfonyl chloride
3,5-Dimethylbenzenesulfonyl chloride
4-Methoxybenzenesulfonyl chloride
4-Trifluoromethylbenzenesulfonyl chloride
4-Cyanobenzenesulfonyl chloride
Benzyloxycarbonyl chloride
Methoxycarbonyl chloride

1a	EWG = *p*-Toluenesulfonyl (Ts)	68% (2 steps)
1b	EWG = Benzenesulfonyl	68% (2 steps)
1c	EWG = 2-Naphtalenesulfonyl	63% (2 steps)
1d	EWG = 4-Nitrobenzenesulfonyl (Ns)	80% (2 steps)
1e	EWG = 3,5-Dimethylbenzenesulfonyl	61% (2 steps)
1f	EWG = 4-Methoxybenzenesulfonyl	34% (2 steps)
1g	EWG = 4-Trifluoromethylbenzenesulfonyl	56% (2 steps)
1h	EWG = 4-Cyanobenzenesulfonyl	63% (2 steps)
1i	EWG = Benzyloxycarbonyl (Cbz)	68% (2 steps)
1j	EWG = Methoxycarbonyl	72% (2 steps)
1k	EWG = *t*-Buthoxycarbonyl (Boc)	88% (2 steps)



5b R = Me, X = F
5c R = OMe, X = Cl

6b R = Me 66 %
6c R = OMe 20 %

1l	R = Me,	EWG = Ts	62% (2 steps)
1m	R = OMe	EWG = Ts	64% (2 steps)
1n	R = Me	EWG = Boc	81% (2 steps)
1o	R = OMe	EWG = Boc	63% (2 steps)

Scheme 3.

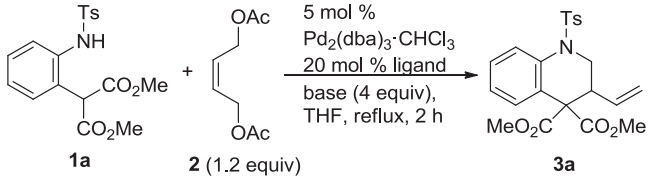
yield. After the reduction of the nitro group in **6a**, the resulting amino moiety was protected with various electron-withdrawing groups to produce the 2-amidophenylmalonates **1a**–**k** in moderate to good yields. The substrates **1l**–**o** having a methyl and methoxy group at the aromatic 5-position were also prepared from the corresponding 2-fluoro- and 2-chloronitrobenzenes **5b** and **5c** by following the same procedure.

The initial reactions for the synthesis of tetrahydroquinolines were attempted using the tosyl-substituted 2-amidophenylmalonate **1a** and (*Z*)-1,4-diacetoxy-2-butene (**2**) (Table 1). When **1a** and **2** were subjected to the reaction with 5 mol % $Pd_2(dba)_3 \cdot CHCl_3$, 20 mol % DPPE, and ^{t}BuOK in THF under reflux for 2 h, the 3-vinyltetrahydroquinoline **3a** was obtained in 27% yield (Table 1, entry 1). The yield of **3a** was improved to 79% with K_2CO_3 (entry 5) by changing the base (entries 2–5). After experimenting with various ligands (entries 6–9), we found that the yield of **3a** could be increased to 86% yield when DPPP was used as the ligand (entry 8).

4i was low (27%), it was improved to 74% by carrying out the reaction in the presence of (±)-BINAP as the ligand (entry 6). Similar reactivity was observed from the reactions of other carbamate-type substrates. Thus, compounds **1j** and **1k**, containing a methoxycarbonyl and a *tert*-butoxycarbonyl (Boc) group, were regioselectively transformed to the corresponding 2-vinyltetrahydroquinolines **4j** and **4k** in 66% and 82% yield, respectively (entries 7 and 8). From these results, it has been made clear that the regioselectivity of the reaction is altered depending on the electron-withdrawing group on the amine.

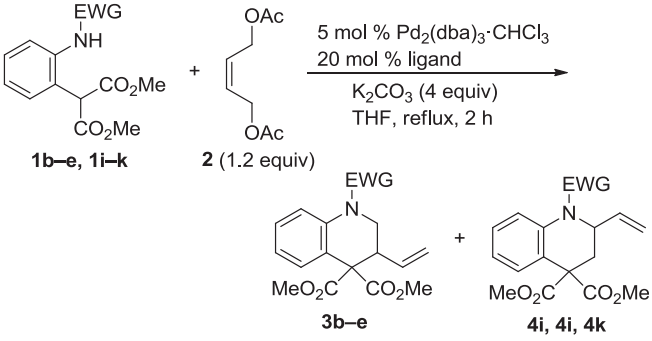
The reactions of substituted amidophenylmalonates **1l**–**o** are summarized in Scheme 4. When the tosylamides **1l** and **1m**, which have a methyl and a methoxy group on the aromatic ring, were subjected to the reactions with **2**, the 3-vinyltetrahydroquinolines **3l** and **3m** were obtained in 86% and 92% yield, respectively. Similarly, the reactions of the carbamates **1n** and **1o** also proceeded to produce the corresponding 2-vinyltetrahydroquinolines **4n** and **4o** in 71% and 85% yield, respectively.

Table 1
Effect of base and ligand



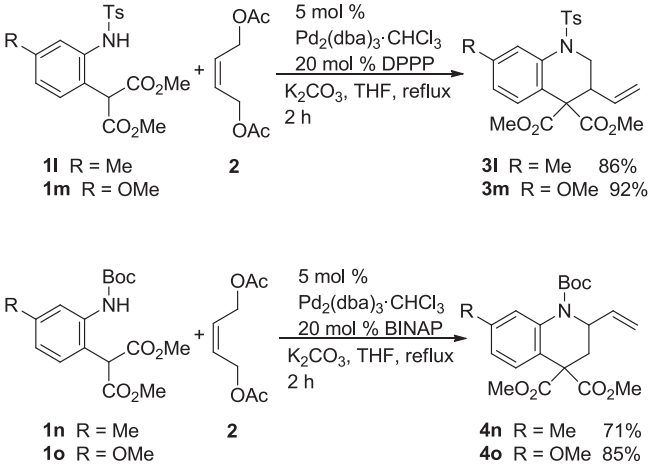
Entry	Base	Ligand	Yield of **3a** (%)
1	^{t}BuOK	DPPE	27
2	Et_3N	DPPE	22
3	K_3PO_4	DPPE	58
4	Cs_2CO_3	DPPE	60
5	K_2CO_3	DPPE	79
6	K_2CO_3	DPPF	61
7	K_2CO_3	DPPB	68
8	K_2CO_3	DPPP	86
9	K_2CO_3	(±)-BINAP	36

Table 2
Reactions using various substrates **1b–e**, **1i–k** with **2**



Entry	EWG	Yields (%)	
		3	**4**
1[a]	Benzenesulfonyl (**1b**)	89	—
2[a]	2-Naphthalenesulfonyl (**1c**)	55	—
3[a]	4-Nitrobenzensulfonyl (Ns) (**1d**)	80	
4[a]	3,5-Dimethylbenzenesulfonyl (**1e**)	82	
5[a]	Benzyloxycarbonyl (Cbz) (**1i**)	7	27
6[b]	Benzyloxycarbonyl (Cbz) (**1i**)	14	74
7[b]	Methoxycarbonyl (**1j**)	—	66
8[b]	*tert*-Butoxycarbonyl (Boc) (**1k**)	—	82

[a] DPPP was used as the ligand.
[b] (±)-BINAP was used as the ligand.



Scheme 4.

A plausible mechanism for the cyclization is shown in Scheme 5. By reacting with the palladium catalyst, 1,4-diacetoxybut-2-ene **2** is transformed to the π-allylpalladium complex **7**, which is further subjected to the reaction with the 2-amidophenylmalonates. In the case of the sulfonamide-type substrate, the aza-anion **8** was selectively generated because of the strong electron-withdrawing character of the sulfonyl group.[13] As a result, the nucleophilic attack of the sulfonamide initially occurs to afford the intermediate **9**, which is successively subjected to the intramolecular nucleophilic attack of the malonate moiety in the presence of palladium to produce the 3-vinyltetrahydroquinoline **3**. On the other hand, the malonate anion **10** would be predominantly produced in the case of the carbamate-type substrate,[13] which would lead to the formation of the 2-vinyltetrahydroquinoline **4** via the intermediate **11**.[14]

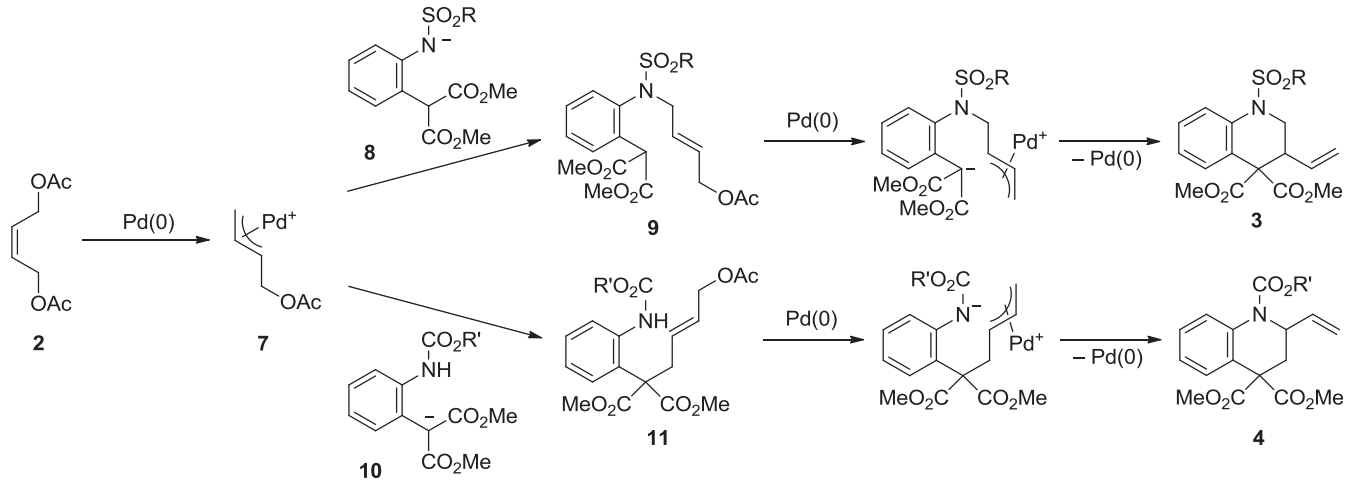
We next attempted the reactions using various allylic bisacetates (Scheme 6). When (*E*)-1,4-diacetoxy-2-butene (**12**) was treated with the tosylamide **1a** and the *tert*-butoxy carbamate **1k**, the corresponding products **3a** and **4k** were obtained in 81% and 57% yield, respectively. Similarly, 1,2-diacetoxy-3-butene (**13**) reacted with **1a** and **1k** to give the corresponding products **3a** and **4k** in 81% and 82% yield, respectively. Although the reason for the difference of the chemical yield derived from allylic bisacetates **12** and **13** is not clear, these results imply that the reactions occurred via the common π-allylpalladium intermediate **7**, regardless of the stereo- and regiochemistry of the allylic bisacetates.

The availability of tetrahydroquinolines containing a vinyl group offers new opportunities to synthesize a variety of structurally complex molecules that cannot be easily accessed by an alternative protocol. An example toward the synthesis of azabicyclo[3.3.1]nonene derivative is shown in Scheme 7. The nosyl group of the 3-vinyltetrahydroquinoline **3d** was removed by thiophenol with K_2CO_3 to afford the amine **14**, which was subjected to the reaction with allyl bromide leading to the diene **15**. When **15** was subjected to the reaction with Grubb's II catalyst, ring-closing metathesis uneventfully proceeded to produce the azabicyclo[3.3.1]nonene **16** in 90% yield.

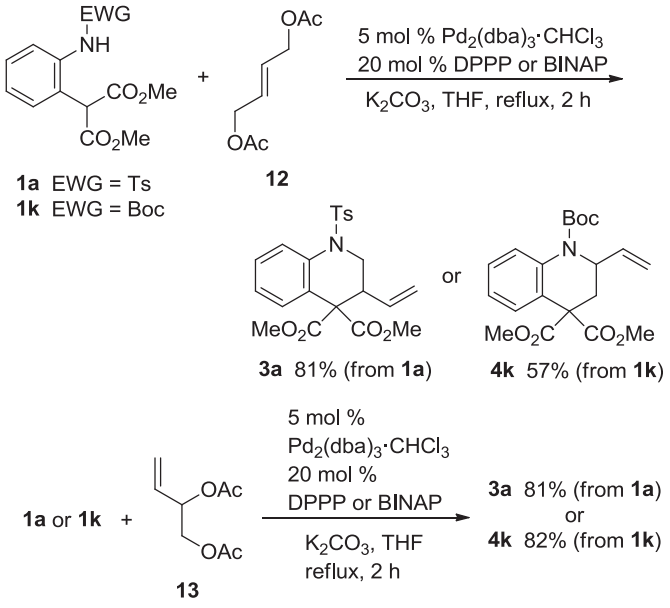
We next turned our attention to the application of this process to an enantioselective reaction. Although various palladium-catalyzed enantioselective cyclizations of allylic bisacetates or biscarbonates with nucleophiles are known,[2–9] few examples of the production of the optically active compounds with high enantiomeric excess have been reported. In the reaction described herein, an asymmetric center is formed via the achiral π-allylpalladium intermediate **17**, and it is anticipated that the enantiocontrolled cyclization could be achieved by a chiral palladium catalyst (Scheme 8).

To achieve this enantioselective process, we first examined the reactions of **1a** with **2** under various conditions (Table 3, Fig. 1). The reactions were carried out in the presence of 5 mol % $Pd_2(dba)_3\cdot CHCl_3$, 20 mol % chiral ligand, and K_2CO_3 in THF under reflux. The enantiomeric excess was not observed from the reaction using (*R*,*R*)-DACH-phenyl Trost ligand (23% yield with 0% ee, entry 1), but the optically active 3-vinyltetrahydroquinoline (−)-**3a** was formed in 36% yield with 56% ee when (*S*)-BINAP was used (entry 2). Similar results were obtained in the case of (*S*)-DM-BINAP and (*S*)-tol-BINAP, in which (−)-**3a** was produced in 49% ee and 43% ee, respectively (entries 3 and 4).[15]

Attempts for the enantioselective cyclization using various sulfonamide-substituted substrates **1b**,**d**,**f**–**h** with **2** in the presence of (*S*)-BINAP are summarized in Table 4. When benzenesulfonyl-substituted substrate **1b** was subjected to the reaction, the cyclized product (−)-**3b** was obtained in 60% yield with 57% ee (entry 1). The substrate **1f** having a 4-methoxybenzenesulfonyl group also reacted with **2** to give the product (−)-**3f** in 55% ee (entry 2). When reactions with 4-trifluoromethyl- and 4-cyanobenzenesulfonyl-substituted substrates **1g** and **1h** were carried out, the enantiomeric excess of the resulting products (−)-**3g** and (−)-**3h** were improved to 65% and

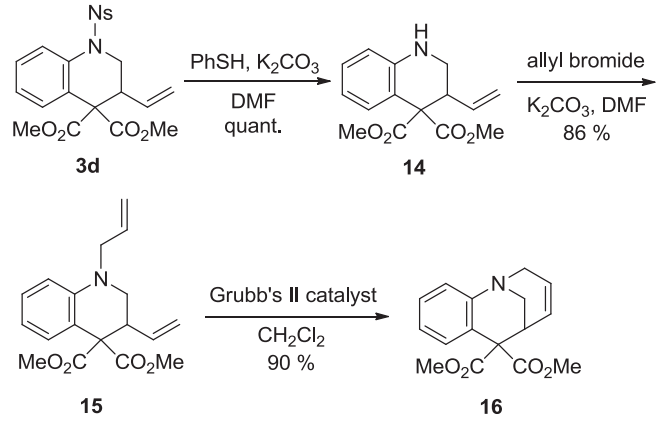


Scheme 5.

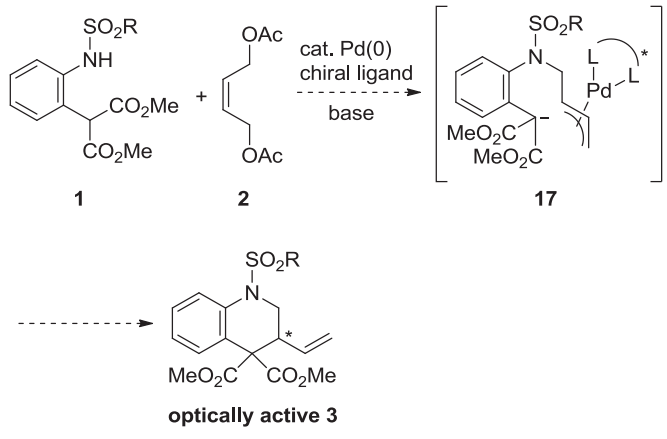


Scheme 6.

76%, respectively (entries 3 and 4). Furthermore, it was found that the cyclized product (−)-**3d** was produced in 50% yield with 99% ee from the reaction with 4-nitrobenzenesulfonyl-substituted substrate **1d** (entry 5).

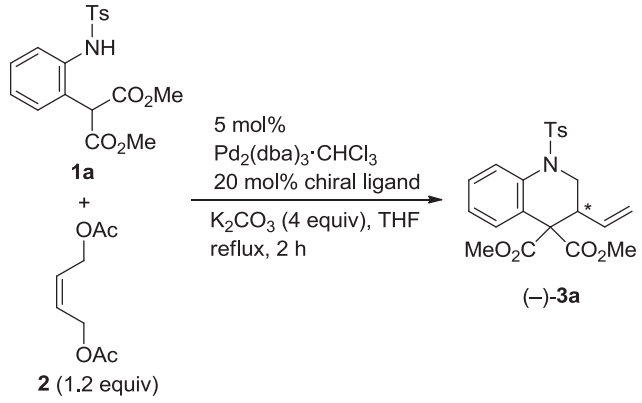


Scheme 7.



Scheme 8.

Table 3
Enantioselective cyclization of **1a** with **2**



Entry	Chiral ligand	Yield (%)	ee (%)[a]
1	(*R*,*R*)-DACH-phenyl Trost ligand	23	0
2	(*S*)-BINAP	36	56
3	(*S*)-DM-BINAP	38	49
4	(*S*)-tol-BINAP	31	43

[a] Enantiomeric excess were determined by HPLC using a chiral column (CHIRALPAK AS-H).

Further optimization of reaction conditions using 4-nitrobenzenesulfonyl-substituted substrate **1d** is shown in Table 5.

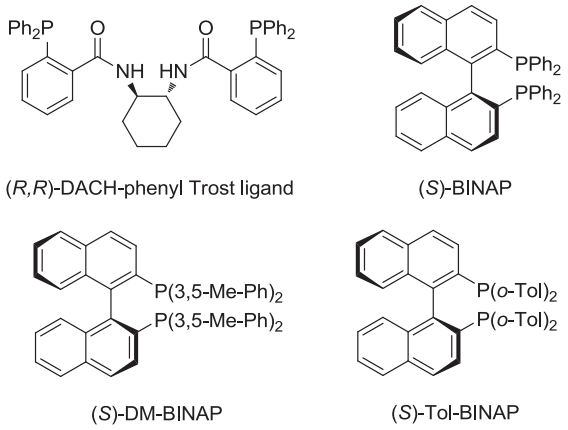
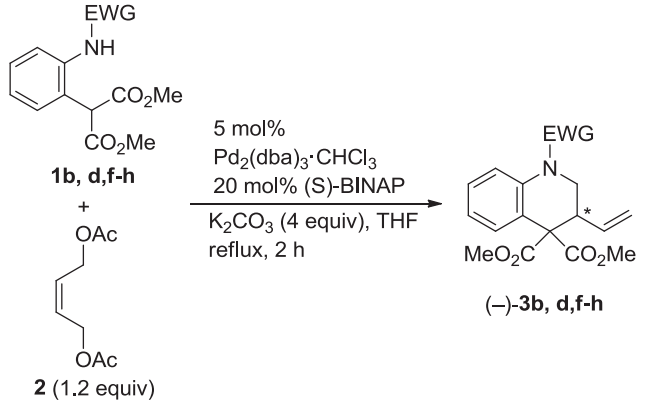


Fig. 1. Structure of chiral ligands.

Table 4
Enantioselective cyclization using **1b**,**d**,**f**–**h** in the presence of (*S*)-BINAP



Entry	EWG	Yield (%)	ee (%)[a]
1	Benzenesulfonyl (**1b**)	60	57
2	4-Methoxybenzensulfonyl (**1f**)	31	55
3	4-Trifluoromethylbenzenesulfonyl (**1g**)	69	65
4	4-Cyanobenzenesulfonyl (**1h**)	93	76
5	4-Nitrobenzensulfonyl (Ns) (**1d**)	50	99

[a] Enantiomeric excess were determined by HPLC using a chiral column (CHIRALPAK AS-H).

After the examinations using various bases, solvents, and reaction temperatures (entries 1–9), it was made clear that the optically active 3-vinyltetrahydroquinoline (−)-**3d** was formed in 79% yield with 99% ee when the reaction was carried out in the presence of K_2CO_3 in dioxane at 80 °C (entry 8). During the course of this optimization study, we found the regioisomer of (−)-**3d** was selectively produced by the choice of base. Thus, when K_3PO_4 and KOH were employed in the reactions, the optically active 2-vinyltetrahydroquinoline (+)-**4d** was obtained predominantly in 46% yield with 92% ee and 52% yield with 83% ee, respectively (entries 3 and 4). Although the reason is not clear, it is interesting that the regioselectivity was controlled depending on the base.

3. Conclusion

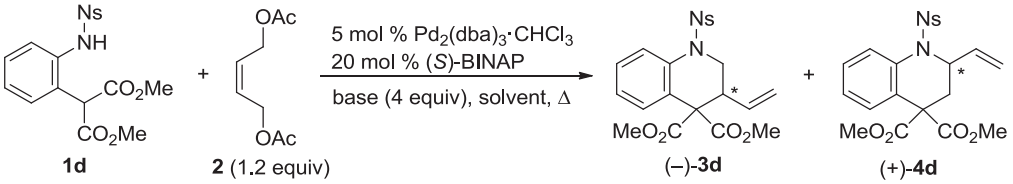
In summary, the studies described above have resulted in the regioselective synthesis of vinyltetrahydroquinolines by a palladium-catalyzed cyclization of the 2-amidophenylmalonates and 1,4-diacetoxy-2-butene. The regioselectivity of the reaction can be altered depending on the substituent on the amino group, in which substituted tetrahydroquinolines having a vinyl group at the 3- or 2-position were, respectively, produced in a highly regioselective manner. The resulting product was successfully transformed to the azabicyclo[3.3.1]nonene via the ring-closing metathesis. Enantioselective reactions proceeded to give the optically active tetrahydroquinoline with high enantioselectivity. Biologically active compounds having tetrahydroquinoline structures have been reported,[11] and this methodology could provide a new and significant protocol for the synthesis of these compounds.

4. Experimental section

4.1. General

All nonaqueous reactions were carried out under a positive atmosphere of argon in dried glassware unless otherwise indicated. Materials were obtained from commercial suppliers and used without further purification except when otherwise noted. Solvents were dried and distilled according to the standard protocols. The phrase ‘residue upon workup’ refers to the residue obtained when the organic layer was separated and dried over anhydrous $MgSO_4$ and the solvent was evaporated under reduced pressure.

Table 5
Optimization of the reaction conditions using **1d** with **2**



Entry	Base	Solvent	Temp (°C)	(−)-**3d**		(+)-**4d**	
				Yield (%)	ee (%)[a]	Yield (%)	ee (%)[b]
1	$CaCO_3$	THF	Reflux	30	86	—	—
2	Na_2CO_3	THF	Reflux	29	96	—	—
3	K_3PO_4	THF	Reflux	17	98	46	92
4	KOH	THF	Reflux	—	—	52	83
5	K_2CO_3	DMSO	100	Trace	—	—	—
6	K_2CO_3	DMF	100	62	86	—	—
7	K_2CO_3	Dioxane	100	73	99	—	—
8	K_2CO_3	Dioxane	80	79	99	—	—
9	K_2CO_3	Dioxane	60	75	99	—	—

[a] Enantiomeric excess were determined by HPLC using a chiral column (CHIRALPAK AS-H).
[b] Enantiomeric excess were determined by HPLC using a chiral column (CHIRALPAK AD).

4.2. General procedure for the synthesis of 2-amidophenylmalonates

Synthesis of **6a**: To a stirred solution of dimethyl malonate (1.10 mL, 9.52 mmol) in DMF (20 mL) was added ^{t}BuOK (1.30 g, 11.9 mmol) at rt. After stirring was continued for 10 min at 90 °C, the resulting mixture was cooled to rt, and 2-fluoronitrobenzene (**5a**) (0.50 mL, 4.76 mmol) was added. The mixture was heated at 90 °C for 2 h, and then stored for 16 h at rt. The resulting solution was diluted with water and extracted with Et_2O. The combined extracts were washed with saturated aqueous NaCl. The residue upon workup was chromatographed on silica gel with hexane/AcOEt (80:20, v/v) as eluent to give the 2-nitrophenyl malonate **6a** (1.00 g, 83%) as light yellow prisms.

*4.2.1. Dimethyl 2-(2-nitrophenyl)malonate (**6a**).* Yield 83%; light yellow prisms; mp: 53.0–55.0 °C [benzene/hexane (1:1)]; IR (KBr) 1738, 1529, 1436, 1349 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 3.81 (s, 6H), 5.34 (s, 1H), 7.51–7.56 (m, 2H), 7.66 (t, J=7.6 Hz, 1H), 8.08 (dd, J=0.8, 7.6 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 53.1 (CH_3), 54.1 (CH), 125.2 (CH), 127.9 (Cq), 129.3 (CH), 131.3 (CH), 133.6 (CH), 148.7 (Cq), 167.6 (Cq); HRMS (ESI) m/z calcd for $C_{11}H_{11}NO_6Na$ [M^++Na^+] 276.0484, found 276.0486.

*4.2.2. Dimethyl 2-(4-methyl-2-nitrophenyl)malonate (**6b**).* Yield 66%; colorless needles; mp: 97.1–97.8 °C [AcOEt/hexane (1:1)]; IR (KBr) 2956, 1733, 1533, 1439, 1294, 1248, 1204, 1008 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 2.45 (s, 3H), 3.80 (s, 6H), 5.29 (s, 1H), 7.38 (d, J=8.0 Hz, 1H), 7.46 (d, J=8.0 Hz, 1H), 7.88 (s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 21.2 (CH_3), 53.4 (CH_3), 54.1 (CH), 125.2 (Cq), 125.9 (CH), 131.4 (CH), 134.6 (CH), 140.4 (Cq), 148.8 (Cq), 168.1 (Cq); HRMS (ESI) m/z calcd for $C_{12}H_{13}NO_6Na$ [M^++Na^+] 290.0641, found 290.0643.

*4.2.3. Dimethyl 2-(4-methoxy-2-nitrophenyl)malonate (**6c**).* Yield 20%; colorless needles; mp: 92.6–93.4 °C [AcOEt/hexane (1:1)]; IR (KBr) 2957, 1737, 1625, 1536, 1440, 1241, 1165 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 3.80 (s, 6H), 3.89 (s, 3H), 5.27 (s, 1H), 7.18 (dd, J=2.8, 8.8 Hz, 1H), 7.42 (d, J=8.8 Hz, 1H), 7.57 (d, J=2.8 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 53.0 (CH_3), 53.4 (CH), 55.8 (CH_3), 110.1 (CH), 119.6 (Cq), 119.7 (CH), 132.2 (CH), 149.3 (Cq), 159.7 (Cq), 167.9 (Cq); HRMS (ESI) m/z calcd for $C_{12}H_{14}NO_7$ [M^++H^+] 284.0770, found 284.0770.

4.3. General procedure for the synthesis of sulfonamides

Synthesis of **1a**: To a stirred suspension of Pd–C (49.0 mg, 10 wt %) in MeOH was added nitrobenzene **6a** (490 mg, 1.94 mmol) at rt, and stirring was continued for 2 h at the same temperature under 3.5 atm of hydrogen gas. The reaction mixture was filtered and concentrated in vacuo. The resulting crude amine was dissolved in CH_2Cl_2 (10 mL), and treated with TsCl (553 mg, 2.90 mmol) and pyridine (0.94 mL, 11.6 mmol) at rt. After stirring was continued for 2 h at the same temperature, the resulting solution was diluted with water and extracted with CH_2Cl_2. The combined extracts were washed with saturated aqueous NaCl. The residue upon work up was chromatographed on silica gel with hexane/AcOEt (75:25, v/v) as eluent to give the 2-amidophenylmalonate **1a** (498 mg, 68%, two steps) as colorless needles.

*4.3.1. Dimethyl 2-[2-(4-methylphenylsulfonamido)phenyl]malonate (**1a**).* Yield 68% (two steps); colorless needles; mp: 147.2–149.1 °C [AcOEt/hexane (1:1)]; IR (KBr) 3263, 1746, 1598, 1495, 1438, 1336, 1282, 1228, 1164, 1093 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 2.41 (s, 3H), 3.76 (s, 6H), 4.91 (s, 1H), 7.02–7.04 (m, 1H), 7.18–7.22 (m, 2H), 7.26–7.27 (m, 1H), 7.38–7.40 (m, 2H), 7.43 (br s, NH), 7.68 (d, J=8.0 Hz, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 21.5 (CH_3), 53.1 (CH_3), 53.9 (CH), 125.4 (CH), 126.7 (CH), 127.3 (CH), 128.5 (Cq), 129.2 (CH), 129.6 (CH), 131.2 (CH), 135.1 (Cq), 136.9 (Cq), 143.7 (Cq), 168.8 (Cq); HRMS (ESI) m/z calcd for $C_{18}H_{19}NO_6NaS$ [M^++Na^+] 400.0831, found 400.0834.

*4.3.2. Dimethyl 2-[2-(phenylsulfonamido)phenyl]malonate (**1b**).* Yield 68% (two steps); colorless prisms; mp: 98.1–100.1 °C [AcOEt/hexane (1:1)]; IR (KBr) 3211, 2956, 1736, 1602, 1452, 1276, 1172, 1093, 1006 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 3.76 (s, 6H), 4.89 (s, 1H), 7.02–7.06 (m, 1H), 7.18–7.23 (m, 2H), 7.37–7.41 (m, 1H), 7.46–7.51 (m, 2H), 7.54 (s, NH), 7.55–7.60 (m, 1H), 7.82 (dd, J=1.6, 10.2 Hz, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 53.1 (CH_3), 54.0 (CH), 125.4 (CH), 126.8 (CH), 127.2 (CH), 128.5 (Cq), 129.1 (CH), 129.2 (CH), 131.3 (CH), 132.9 (CH), 135.0 (Cq), 139.9 (Cq), 168.7 (Cq); HRMS (ESI) m/z calcd for $C_{17}H_{17}NO_6NaS$ [M^++Na^+] 386.0674, found 386.0669.

*4.3.3. Dimethyl 2-[2-(naphthalene-2-sulfonamido)phenyl]malonate (**1c**).* Yield 63% yield (two steps); colorless prisms; mp: 114.0–115.5 °C [AcOEt/hexane (1:1)]; IR (KBr) 3284, 2953, 1740, 1627, 1593, 1497, 1456, 1282, 1162, 1095 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 3.66 (s, 6H), 4.84 (s, 1H), 7.09–7.11 (m, 1H), 7.15–7.21 (m, 2H), 7.37–7.40 (m, 1H), 7.58–7.67 (m, 3H), 7.79 (dd, J=2.0, 8.8 Hz, 1H), 7.89 (s, NH), 7.91–7.95 (m, 2H), 8.36 (s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 53.0 (CH_3), 53.7 (CH), 122.4 (CH), 125.9 (CH), 126.9 (CH), 127.5 (CH), 127.8 (CH), 128.6 (CH), 128.7 (CH), 128.9 (CH), 129.2 (CH), 129.3 (CH), 129.4 (CH), 131.1 (CH), 132.0 (Cq), 134.8 (Cq), 134.9 (Cq), 136.7 (Cq), 168.6 (Cq); HRMS (ESI) m/z calcd for $C_{21}H_{19}NO_6NaS$ [M^++Na^+] 436.0831, found 436.0828.

*4.3.4. Dimethyl 2-[2-(4-nitrophenylsulfonamido)phenyl]malonate (**1d**).* Yield 80% (two steps); colorless needles; mp: 137.1–138.2 °C [AcOEt/hexane (1:1)]; IR (KBr) 3249, 1740, 1532, 1350, 1167 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 3.77 (s, 6H), 4.77 (s, 1H), 7.11 (dd, J=1.6, 7.4 Hz, 1H), 7.20–7.28 (m, 2H), 7.36 (dd, J=1.6, 7.4 Hz, 1H), 8.03 (d, J=8.8 Hz, 2H), 8.10 (br s, NH), 8.33 (d, J=8.8 Hz, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 53.3 (CH_3), 54.8 (CH), 124.3 (CH), 124.7 (CH), 127.1 (CH), 127.8 (Cq), 128.6 (CH), 129.7 (CH), 131.9 (CH), 134.7 (Cq), 145.9 (Cq), 150.2 (Cq), 168.7 (Cq); HRMS (ESI) m/z calcd for $C_{17}H_{17}N_2O_8S$ [M^++H^+] 409.0706, found 409.0708.

*4.3.5. Dimethyl 2-[2-(3,5-dimethylphenylsulfonamido)phenyl]malonate (**1e**).* Yield 61% (two steps); colorless needles; mp: 127.9–128.5 °C [AcOEt/hexane (1:1)]; IR (KBr) 3254, 2954, 1740, 1436, 1334, 1157 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 2.34 (s, 6H), 3.76 (s, 6H), 4.85 (s, 1H), 7.04–7.07 (m, 1H), 7.17 (br s, NH), 7.20–7.22 (m, 2H), 7.39–7.49 (m, 4H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 21.1 (CH_3), 53.0 (CH_3), 53.8 (CH), 124.7 (CH), 125.7 (CH), 126.7 (CH), 128.6 (Cq), 129.1 (CH), 131.1 (CH), 134.5 (CH), 135.2 (Cq), 139.1 (Cq), 139.7 (Cq), 168.7 (Cq); HRMS (ESI) m/z calcd for $C_{19}H_{22}NO_6S$ [M^++H^+] 392.1168, found 392.1165.

*4.3.6. Dimethyl 2-[2-(4-methoxyphenylsulfonamido)phenyl]malonate (**1f**).* Yield 34% (two steps); colorless prisms; mp: 112.7–113.2 °C [AcOEt/hexane (1:1)]; IR (KBr) 3251, 1739, 1596, 1498, 1261, 1156 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 3.76 (s, 6H), 3.85 (s, 3H), 4.89 (s, 1H), 6.92 (d, J=8.8 Hz, 2H), 7.04–7.07 (m, 1H), 7.18–7.23 (m, 2H), 7.28 (br s, NH), 7.39–7.42 (m, 1H), 7.72 (d, J=8.8 Hz, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 53.0 (CH_3), 53.6 (CH_3), 55.5 (CH), 114.2 (CH), 125.8 (CH), 126.8 (CH), 128.7 (Cq), 129.1 (CH), 129.5 (CH), 131.1 (CH), 131.2 (Cq), 135.1 (Cq), 163.1 (Cq), 168.7 (Cq); HRMS (ESI) m/z calcd for $C_{18}H_{19}NO_7NaS$ [M^++Na^+] 416.0780, found 416.0781.

*4.3.7. Dimethyl 2-[2-(4-(trifluoromethyl)phenylsulfonamido)phenyl]malonate (**1g**).* Yield 56% (two steps); colorless needles; mp: 124.9–125.5 °C (AcOEt/hexane 1:1); IR (KBr) 3248, 1741, 1406, 1324,

1170, 1063 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 3.75 (s, 6H), 4.78 (s, 1H), 7.12 (dd, J=2.0, 7.4 Hz, 1H), 7.20–7.28 (m, 2H), 7.38 (dd, J=2.0, 7.4 Hz, 1H), 7.75 (d, J=8.0 Hz, 2H), 7.89 (br s, NH), 7.96 (d, J=8.0 Hz, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 53.2 (CH_3), 54.3 (CH), 124.5 (Cq), 125.3 (CH), 126.2 (q, J=3.3 Hz, CF_3), 127.0 (CH), 127.8 (CH ×4), 128.2 (Cq), 129.5 (CH), 131.6 (CH), 134.7 (Cq), 143.6 (Cq), 168.7 (Cq); HRMS (ESI) m/z calcd for $C_{18}H_{16}NO_6NaSF_3$ [M^++Na^+] 454.0548, found 454.0550.

*4.3.8. Dimethyl 2-[2-(4-cyanophenylsulfonamido)phenyl]malonate (**1h**).* Yield 63% (two steps); colorless oil; IR (KBr): 3247, 1739, 1437, 1339, 1164 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 3.77 (s, 6H), 4.77 (s, 1H), 7.08 (dd, J=2.0, 7.2 Hz, 1H), 7.20–7.26 (m, 2H), 7.36 (dd, J=2.0, 7.2 Hz, 1H), 7.79 (d, J=8.4 Hz, 2H), 7.95 (d, J=8.4 Hz, 2H), 8.01 (br s, NH); ^{13}C NMR (100 MHz, $CDCl_3$) δ 53.2 (CH_3), 54.4 (CH), 116.5 (Cq), 117.2 (Cq), 125.1 (CH), 127.1 (CH), 127.9 (CH), 128.2 (Cq), 129.5 (CH), 131.7 (CH), 132.9 (CH), 134.5 (Cq), 144.1 (Cq), 168.7 (Cq); HRMS (ESI) m/z calcd for $C_{18}H_{15}N_2O_6S$ [M^+−H^+] 387.0651, found 387.0653.

*4.3.9. Dimethyl 2-[4-methyl-2-(4-methylphenylsulfonamido)phenyl] malonate (**1l**).* Yield 62% (two steps); colorless prisms; mp: 137.9–139.2 °C [AcOEt/hexane (1:1)]; IR (KBr): 3267, 2955, 1758, 1736, 1586, 1508, 1434, 1261, 1159, 1092 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 2.22 (s, 3H), 2.42 (s, 3H), 3.74 (s, 6H), 4.80 (s, 1H), 6.88 (s, 1H), 7.00 (d, J=8.0 Hz, 1H), 7.24 (d, J=8.0 Hz, 1H), 7.27 (d, J=8.4 Hz, 2H), 7.38 (s, NH), 7.69 (d, J=8.4 Hz, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 21.0 (CH_3), 21.5 (CH_3), 53.0 (CH_3), 53.6 (CH), 125.3 (Cq), 126.1 (CH), 127.3 (CH), 127.5 (CH), 129.6 (CH), 130.8 (CH), 134.8 (Cq), 137.0 (Cq), 139.4 (Cq), 143.6 (Cq), 168.9 (Cq); HRMS (ESI) m/z calcd for $C_{19}H_{22}NO_6S$ [M^++H^+] 392.1168, found 392.1169.

*4.3.10. Dimethyl 2-[4-methoxy-2-(4-methylphenylsulfonamido)phenyl]malonate (**1m**).* Yield 64% (two steps); colorless prisms; mp: 138.1–139.9 °C [AcOEt/hexane (1:1)]; IR (KBr): 3267, 3011, 1754, 1730, 1615, 1506, 1271, 1197, 1159 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 2.41 (s, 3H), 3.67 (s, 3H), 3.75 (s, 6H), 4.73 (s, 1H), 6.67 (d, J=2.4 Hz, 1H), 6.70 (dd, J=2.8, 8.4 Hz, 1H), 7.25 (d, J=8.4 Hz, 1H), 7.28 (d, J=8.4 Hz, 2H), 7.68 (br s, NH), 7.73 (d, J=8.4 Hz, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 21.5 (CH_3), 53.0 (CH_3), 53.6 (CH), 55.2 (CH_3), 110.2 (CH), 112.2 (CH), 119.6 (Cq), 127.4 (CH), 129.6 (CH), 132.0 (CH), 136.3 (Cq), 137.0 (Cq), 143.7 (Cq), 159.9 (Cq), 169.0 (Cq); HRMS (ESI) m/z calcd for $C_{19}H_{22}NO_7S$ [M^++H^+] 408.1117, found 408.1118.

4.4. General procedure for the synthesis of carbamate

Synthesis of **1i**: To a stirred suspension of Pd–C (25.0 mg, 10 wt %) in MeOH was added nitrobenzene **6a** (249 mg, 0.985 mmol) at rt, and stirring was continued for 2 h at the same temperature under 3.5 atm of hydrogen gas. The reaction mixture was filtered and concentrated in vacuo. The resulting crude amine was dissolved in CH_2Cl_2 (5 mL), and treated with CbzCl (0.170 mL, 1.18 mmol) and pyridine (0.160 mL, 1.97 mmol) at 0 °C. After stirring was continued for 5 h at the same temperature, the resulting solution was diluted with water and extracted with CH_2Cl_2. The combined extracts were washed with saturated aqueous NaCl. The residue upon workup was chromatographed on silica gel with hexane/AcOEt (80:20, v/v) as eluent to give the 2-amidophenylmalonate **1i** (238 mg, 68%, two steps) as colorless oil.

*4.4.1. Dimethyl 2-[2-(benzyloxycarbonylamino)phenyl]malonate (**1i**).* Yield 68% (two steps); colorless oil; IR (neat) 3343, 2954, 1731, 1590, 1518, 1455, 1221, 1155, 1041 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 3.67 (s, 6H), 4.67 (s, 1H), 5.20 (s, 2H), 7.15 (t, J=7.6 Hz, 1H), 7.24 (d, J=7.6 Hz, 1H), 7.29–7.43 (m, 6H), 7.67 (s, 1H), 7.97 (br s, NH); ^{13}C NMR (100 MHz, $CDCl_3$) δ 53.0 (CH_3), 56.0 (CH), 66.9 (CH_2), 125.3 (CH), 125.8 (Cq), 128.1 (CH), 128.3 (CH), 128.5 (CH ×4), 129.4 (CH), 131.1 (CH), 136.3 (Cq), 136.5 (Cq), 154.2 (Cq), 169.1 (Cq); HRMS (ESI) m/z calcd for $C_{19}H_{19}NO_6Na$ [M^++Na^+] 380.1110, found 380.1113.

*4.4.2. Dimethyl 2-[2-(methoxycarbonylamino)phenyl]malonate (**1j**).* Yield 72% (two steps); yellow oil; IR (neat) 3347, 2956, 1731, 1590, 1518, 1236, 1114, 1066 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 3.757 (s, 3H), 3.763 (s, 6H), 4.70 (s, 1H), 7.16 (t, J=7.6 Hz, 1H), 7.26 (d, J=7.6 Hz, 2H), 7.37 (dt, J=1.6, 7.6 Hz, 1H), 7.68 (br s, NH); ^{13}C NMR (100 MHz, $CDCl_3$) δ 52.3 (CH_3), 53.0 (CH_3), 55.7 (CH), 125.2 (CH), 125.5 (Cq), 129.3 (CH ×2), 131.0 (CH), 136.5 (Cq), 154.7 (Cq), 169.0 (Cq); HRMS (ESI) m/z calcd for $C_{13}H_{15}NO_6Na$ [M^++Na^+] 304.0797, found 304.0793.

*4.4.3. Dimethyl 2-[2-(tert-butoxycarbonylamino)phenyl]malonate (**1k**).* Yield 88% (two steps); colorless oil; IR (neat) 3352, 2980, 1731, 1589, 1514, 1454, 1241, 1155, 1024 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 1.50 (s, 9H), 3.77 (s, 6H), 4.70 (s, 1H), 7.13 (t, J=7.6 Hz, 1H), 7.26 (d, J=7.6 Hz, 1H), 7.34 (t, J=7.6 Hz, 1H), 7.55 (br s, NH), 7.63 (d, J=7.6 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 28.2 (CH_3), 53.0 (CH_3), 55.7 (CH), 80.2 (Cq), 124.9 (CH), 125.9 (CH), 126.2 (Cq), 129.1 (CH), 130.9 (CH), 136.8 (Cq), 153.5 (Cq), 169.1 (Cq); HRMS (ESI) m/z calcd for $C_{16}H_{22}NO_6$ [M^++H^+] 324.1447, found 324.1447.

*4.4.4. Dimethyl 2-[2-(tert-butoxycarbonylamino)-4-methylphenyl] malonate (**1n**).* Yield 81% (two steps); colorless oil; IR (neat) 3356, 2979, 1731, 1618, 1583, 1241, 1157, 1051 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 1.50 (s, 9H), 2.34 (s, 3H), 3.76 (s, 6H), 4.66 (s, 1H), 6.94 (d, J=6.8 Hz, 1H), 7.13 (d, J=6.8 Hz, 1H), 7.47 (s, 1H), 7.53 (br s, NH); ^{13}C NMR (100 MHz, $CDCl_3$) δ 21.1 (CH_3), 28.3 (CH_3), 52.9 (CH_3), 55.5 (CH), 80.1 (Cq), 123.1 (Cq), 125.8 (CH), 126.3 (CH), 130.7 (CH), 136.6 (Cq), 139.4 (Cq), 153.5 (Cq), 169.3 (Cq); HRMS (ESI) m/z calcd for $C_{17}H_{23}NO_6Na$ [M^++Na^+] 360.1423, found 360.1425.

*4.4.5. Dimethyl 2-[2-(tert-butoxycarbonylamino)-4-methoxyphenyl] malonate (**1o**).* Yield 63% (two steps); colorless prisms; mp: 97.8–99.1 °C [AcOEt/hexane (1:1)]; IR (KBr) 3325, 2977, 1729, 1619, 1584, 1533, 1242, 1160 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 1.50 (s, 9H), 3.76 (s, 6H), 3.81 (s, 3H), 4.62 (s, 1H), 6.66 (dd, J=2.8, 8.4 Hz, 1H), 7.13 (d, J=8.4 Hz, 1H), 7.26 (d, J=2.8 Hz, 1H), 7.64 (br s, NH); ^{13}C NMR (100 MHz, $CDCl_3$) δ 28.2 (CH_3), 52.9 (CH_3), 55.1 (CH), 55.3 (CH_3), 80.2 (Cq), 110.3 (CH), 110.9 (CH), 117.7 (Cq), 131.7 (CH), 138.0 (Cq), 153.3 (Cq), 160.1 (Cq), 169.3 (Cq); HRMS (ESI) m/z calcd for $C_{17}H_{24}NO_7$ [M^++H^+] 354.1553, found 354.1552.

4.5. General procedure for the synthesis of 3-vinyltetrahydroquinoline

Synthesis of **3a** (Table 1, entry 8): To a stirred solution of sulfonamide **1a** (30.0 mg, 0.0795 mmol) and (*Z*)-1,4-diacetoxy-2-butene (**2**) (16.4 mg, 0.0954 mmol) in THF (2 mL) were added $Pd_2(dba)_3 \cdot CHCl_3$ (4.10 mg, 3.95 μmol), DPPP (6.50 mg, 15.8 μmol), and K_2CO_3 (43.7 mg, 0.318 mmol) at rt, and stirring was continued for 30 min at the same temperature. The reaction mixture was then allowed to heat to 80 °C, and stirred for 2 h. After filtration of the reaction mixture using small amount of silica gel followed by concentration, the residue was chromatographed on silica gel with hexane/AcOEt (80:20, v/v) as eluent to give the 3-vinyltetrahydroquinoline **3a** (29.3 mg, 86%) as colorless prisms.

*4.5.1. Dimethyl-1-(4-methylphenylsulfonyl)-3-vinyl-2,3-dihydroquinoline-4,4(1H)-dicarboxylate (**3a**).* Yield 86%; colorless prisms; mp: 111.7–113.8 °C [AcOEt/hexane (2:1)]; IR (KBr) 2953, 1746, 1721, 1489, 1361, 1240, 1178, 1099, 1028 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 2.39 (s, 3H), 2.98 (dt, J=4.0, 9.0 Hz, 1H), 3.56 (s, 3H), 3.64 (s, 3H), 3.99 (dd, J=9.0, 13.2 Hz, 1H), 4.09 (dd, J=4.0, 13.2 Hz, 1H), 5.10 (dd, J=0.8, 17.2 Hz, 1H), 5.15 (dd, J=0.8, 10.4 Hz, 1H), 5.86 (ddd, J=9.0, 10.4,

17.2 Hz, 1H), 7.09 (dt, *J*=0.8, 7.8 Hz, 1H), 7.23 (d, *J*=8.8 Hz, 2H), 7.27 (dt, *J*=1.2, 7.8 Hz, 1H), 7.33 (dd, *J*=1.2, 7.8 Hz, 1H), 7.57 (d, *J*=8.8 Hz, 2H), 7.82 (dd, *J*=0.8, 7.8 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 21.4 (CH_3), 43.0 (CH), 47.6 (CH_2), 52.5 (CH_3), 52.7 (CH_3), 60.8 (Cq), 119.0 (CH_2), 122.6 (CH), 124.0 (CH), 124.5 (Cq), 127.2 (CH), 128.6 (CH), 129.6 (CH), 131.1 (CH), 134.2 (CH), 136.3 (Cq), 136.5 (Cq), 143.8 (Cq), 169.2 (Cq), 169.9 (Cq); HRMS (ESI) *m*/*z* calcd for $C_{22}H_{24}NO_6S$ [M^++H^+] 430.1324, found 430.1320.

*4.5.2. Dimethyl-1-(phenylsulfonyl)-3-vinyl-2,3-dihydroquinoline-4,4(1H)-dicarboxylate (**3b**).* Yield 89%; colorless prisms; mp: 93.5–94.7 °C [AcOEt/hexane (2:1)]; IR (KBr) 2954, 1738, 1490, 1356, 1241, 1172, 1091 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 2.94 (dt, *J*=3.6, 9.0 Hz, 1H), 3.56 (s, 3H), 3.63 (s, 3H), 3.99 (dd, *J*=9.0, 13.2 Hz, 1H), 4.11 (dd, *J*=3.6, 13.2 Hz, 1H), 5.09 (d, *J*=17.2 Hz, 1H), 5.15 (d, *J*=10.4 Hz, 1H), 5.85 (ddd, *J*=9.0, 10.4, 17.2 Hz, 1H), 7.11 (dt, *J*=1.6, 7.6 Hz, 1H), 7.29 (dt, *J*=1.6, 7.6 Hz, 1H), 7.33 (dd, *J*=1.6, 7.6 Hz, 1H), 7.45 (t, *J*=8.4 Hz, 2H), 7.56 (dt, *J*=1.6, 7.6 Hz, 1H), 7.69 (dd, *J*=1.2, 8.4 Hz, 2H), 7.83 (dd, *J*=1.2, 8.4 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 43.1 (CH), 47.6 (CH_2), 52.6 (CH_3), 52.8 (CH_3), 60.9 (Cq), 119.1 (CH_2), 122.8 (CH), 124.2 (CH), 124.6 (Cq), 127.1 (CH), 128.6 (CH), 129.1 (CH), 131.1 (CH), 132.9 (CH), 134.1 (CH), 136.2 (Cq), 139.5 (Cq), 169.2 (Cq), 169.9 (Cq); HRMS (ESI) *m*/*z* calcd for $C_{21}H_{21}NO_6NaS$ [M^++Na^+] 438.0987, found 438.0990.

*4.5.3. Dimethyl-1-(naphthalen-2-ylsulfonyl)-3-vinyl-2,3-dihydroquinoline-4,4(1H)-dicarboxylate (**3c**).* Yield 55%; colorless prisms; mp: 127.5–128.4 °C [AcOEt/hexane (2:1)]; IR (KBr) 1774, 1351, 1241, 1165, 1070 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 2.94 (dt, *J*=4.0, 9.0 Hz, 1H), 3.37 (s, 3H), 3.44 (s, 3H), 4.03 (dd, *J*=9.0, 13.2 Hz, 1H), 4.18 (dd, *J*=4.0, 13.2 Hz, 1H), 5.03 (d, *J*=17.2 Hz, 1H), 5.12 (dd, *J*=1.2, 10.2 Hz, 1H), 5.83 (ddd, *J*=9.0, 10.2, 17.2 Hz, 1H), 7.11 (dt, *J*=1.2, 7.6 Hz, 1H), 7.29–7.33 (m, 2H), 7.57–7.65 (m, 3H), 7.86–7.92 (m, 4H), 8.28 (s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 43.0 (CH), 47.8 (CH_2), 52.5 (CH_3), 52.6 (CH_3), 60.8 (Cq), 119.2 (CH_2), 122.3 (CH), 123.0 (CH), 124.3 (CH), 124.8 (Cq), 127.6 (CH), 127.8 (CH), 128.6 (CH), 128.7 (CH), 129.0 (CH), 129.3 (CH ×2), 131.1 (CH), 132.1 (Cq), 134.1 (CH), 134.9 (Cq), 136.2 (Cq), 136.4 (Cq), 169.1 (Cq), 169.8 (Cq); HRMS (ESI) *m*/*z* calcd for $C_{25}H_{23}NO_6NaS$ [M^++Na^+] 488.1144, found 488.1146.

*4.5.4. Dimethyl 1-(4-nitrophenylsulfonyl)-3-vinyl-2,3-dihydroquinoline-4,4(1H)-dicarboxylate (**3d**).* Yield 80%; colorless prisms; mp: 164.2–165.4 °C [AcOEt/hexane (2:1)]; IR (KBr) 1734, 1532, 1351, 1247, 1173 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 3.00 (dt, *J*=4.4, 9.4 Hz, 1H), 3.55 (s, 3H), 3.63 (s, 3H), 3.99 (dd, *J*=9.4, 13.2 Hz, 1H), 4.15 (dd, *J*=4.4, 13.2 Hz, 1H), 5.12 (d, *J*=17.2 Hz, 1H), 5.18 (d, *J*=10.4 Hz, 1H), 5.81 (ddd, *J*=9.4, 10.4, 17.2 Hz, 1H), 7.16 (dt, *J*=1.2, 7.6 Hz, 1H), 7.32 (dt, *J*=1.2, 7.6 Hz, 1H), 7.36 (dd, *J*=1.2, 7.6 Hz, 1H), 7.80 (dd, *J*=1.2, 7.6 Hz, 1H), 7.84 (d, *J*=9.2 Hz, 2H), 8.27 (d, *J*=9.2 Hz, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 43.2 (CH), 47.9 (CH_2), 52.6 (CH_3), 52.9 (CH_3), 60.8 (Cq), 119.5 (CH_2), 122.7 (CH), 124.3 (CH), 125.0 (CH), 125.2 (Cq), 128.4 (CH), 128.9 (CH), 131.3 (CH), 133.7 (CH), 135.5 (Cq), 144.9 (Cq), 150.3 (Cq), 168.9 (Cq), 169.6 (Cq); HRMS (ESI) *m*/*z* calcd for $C_{21}H_{20}N_2O_{8}$-NaS [M^++Na^+] 483.0838, found 483.0835.

*4.5.5. Dimethyl 1-(3,5-dimethylphenylsulfonyl)-3-vinyl-2,3-dihydroquinoline-4,4(1H)-dicarboxylate (**3e**).* Yield 82%; colorless oil; IR (KBr) 2953, 1735, 1490, 1355, 1246, 1163 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 2.31 (s, 6H), 2.95 (dt, *J*=4.0, 9.0 Hz, 1H), 3.58 (s, 3H), 3.65 (s, 3H), 4.00 (dd, *J*=9.0, 13.2 Hz, 1H), 4.08 (dd, *J*=4.0, 13.2 Hz, 1H), 5.07 (d, *J*=17.0 Hz, 1H), 5.15 (d, *J*=10.4 Hz, 1H), 5.85 (ddd, *J*=9.0, 10.4, 17.0 Hz, 1H), 7.10 (t, *J*=7.6 Hz, 1H), 7.16 (s, 1H), 7.28–7.29 (m, 3H), 7.36 (d, *J*=7.6 Hz, 1H), 7.77 (d, *J*=7.6 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 21.1 (CH_3), 43.0 (CH), 47.7 (CH_2), 52.5 (CH_3), 52.7 (CH_3), 60.9 (Cq), 118.9 (CH_2), 122.8 (CH), 124.0 (CH), 124.4 (Cq), 124.7 (CH), 128.6 (CH), 131.2 (CH), 134.4 (CH), 134.6 (CH), 136.5 (Cq), 139.2 (Cq), 139.4 (Cq), 169.3 (Cq), 170.0 (Cq); HRMS (ESI) *m*/*z* calcd for $C_{23}H_{26}NO_6S$ [M^++H^+] 444.1481, found 444.1476.

*4.5.6. Dimethyl-7-methyl-1-(4-methylphenylsulfonyl)-3-vinyl-2,3-dihydroquinoline-4,4(1H)-dicarboxylate (**3l**).* Yield 86%; yellow oil; IR (neat) 2953, 1733, 1614, 1572, 1504, 1252, 1165, 1091 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 2.34 (s, 3H), 2.39 (s, 3H), 2.94 (dt, *J*=4.0, 9.0 Hz, 1H), 3.56 (s, 3H), 3.62 (s, 3H), 3.96 (dd, *J*=9.0, 13.2 Hz, 1H), 4.08 (dd, *J*=4.0, 13.2 Hz, 1H), 5.08 (dd, *J*=0.8, 17.2 Hz, 1H), 5.14 (dd, *J*=0.8, 10.4 Hz, 1H), 5.83 (ddd, *J*=9.0, 10.4, 17.2 Hz, 1H), 6.92 (dd, *J*=2.0, 8.0 Hz, 1H), 7.23 (t, *J*=7.6 Hz, 3H), 7.57 (d, *J*=8.4 Hz, 2H), 7.65 (s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 21.4 (CH_3), 21.5 (CH_3), 42.9 (CH), 47.7 (CH_2), 52.5 (CH_3), 52.7 (CH_3), 60.6 (Cq), 118.9 (CH_2), 121.5 (Cq), 123.1 (CH), 125.2 (CH), 127.2 (CH), 129.6 (CH), 130.9 (CH), 134.3 (CH), 136.2 (Cq), 136.7 (Cq), 138.7 (Cq), 140.7 (Cq), 169.4 (Cq), 170.1 (Cq); HRMS (ESI) *m*/*z* calcd for $C_{23}H_{26}NO_6S$ [M^++H^+] 444.1481, found 444.1481.

*4.5.7. Dimethyl-7-methoxy-1-(4-methylphenylsulfonyl)-3-vinyl-2,3-dihydroquinoline-4,4(1H)-dicarboxylate (**3m**).* Yield 92%; colorless oil; IR (neat) 2953, 1733, 1612, 1507, 1254, 1166 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 2.39 (s, 3H), 2.97 (dt, *J*=3.6, 8.8 Hz, 1H), 3.58 (s, 3H), 3.62 (s, 3H), 3.79 (s, 3H), 4.02 (dd, *J*=8.8, 13.2 Hz, 1H), 4.10 (dd, *J*=3.6, 13.2 Hz, 1H), 5.10 (d, *J*=17.2 Hz, 1H), 5.14 (d, *J*=10.2 Hz, 1H), 5.81 (ddd, *J*=8.8, 10.2, 17.2 Hz, 1H), 6.67 (dd, *J*=2.8, 8.4 Hz, 1H), 7.23–7.27 (m, 3H), 7.37 (d, *J*=2.8 Hz, 1H), 7.69 (d, *J*=8.4 Hz, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 21.5 (CH_3), 42.7 (CH), 47.7 (CH_2), 52.5 (CH_3), 52.7 (CH_3), 55.3 (CH_3), 60.2 (Cq), 106.9 (CH), 111.0 (CH), 115.9 (Cq), 118.9 (CH_2), 127.2 (CH), 129.7 (CH), 132.2 (CH), 134.3 (CH), 136.7 (Cq), 137.5 (Cq), 143.9 (Cq), 159.4 (Cq), 169.7 (Cq), 170.2 (Cq); HRMS (ESI) *m*/*z* calcd for $C_{23}H_{26}NO_7S$ [M^++H^+] 460.1431, found 460.1433.

4.6. General procedure for the synthesis of 2-vinyltetrahydroquinoline

Synthesis of **4i** (Table 2, entry 6): To a stirred solution of carbamate **1i** (31.3 mg, 0.0876 mmol) and (*Z*)-1,4-diacetoxy-2-butene (**2**) (18.1 mg, 0.105 mmol) in THF (2 mL) were added $Pd_2(dba)_3 \cdot CHCl_3$ (4.50 mg, 4.38 μmol), (±)-BINAP (11.0 mg, 17.5 μmol), and K_2CO_3 (48.0 mg, 0.350 mmol) at rt, and stirring was continued for 30 min at the same temperature. The reaction mixture was then allowed to heat to 80 °C, and stirred for 2 h. After filtration of the reaction mixture using small amount of silica gel followed by concentration, the residue was chromatographed on silica gel with hexane/AcOEt (80:20, v/v) as eluent to give the 2-vinyltetrahydroquinoline **4i** (26.7 mg, 74%) and the 3-vinyltetrahydroquinoline **3i** (5.10 mg, 14%).

*4.6.1. 1-Benzyl 4,4-dimethyl 2-vinyl-2,3-dihydroquinoline-1,4,4-tricarboxylate (**4i**).* Yield 74%; colorless oil; IR (neat) 2953, 1732, 1712, 1644, 1604, 1585, 1321, 1130, 1036 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 2.16 (dd, *J*=9.2, 13.6 Hz, 1H), 3.01 (dd, *J*=8.0, 13.6 Hz, 1H), 3.51 (s, 3H), 3.86 (s, 3H), 4.96 (ddd, *J*=6.4, 10.4, 16.9 Hz, 1H), 5.08 (d, *J*=10.4 Hz, 1H), 5.16 (d, *J*=12.4 Hz, 1H), 5.18 (d, *J*=10.4 Hz, 1H), 5.23 (d, *J*=12.4 Hz, 1H), 5.70 (ddd, *J*=8.0, 9.2, 10.4), 7.07 (dd, *J*=1.2, 7.8 Hz, 1H), 7.14 (dt, *J*=1.2, 7.6 Hz, 1H), 7.26–7.33 (m, 6H), 7.51 (d, *J*=8.0 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 38.4 (CH_2), 52.9 (CH_3), 53.0 (CH_3), 53.4 (CH), 57.6 (Cq), 67.5 (CH_2), 115.5 (CH_2), 124.8 (CH), 125.6 (CH), 126.5 (CH), 127.87 (CH), 127.94 (CH), 128.1 (CH), 128.3 (CH), 131.2 (Cq), 135.7 (Cq), 136.2 (Cq), 136.8 (CH), 154.2 (Cq), 169.8 (Cq), 170.0 (Cq); HRMS (ESI) *m*/*z* calcd for $C_{23}H_{23}NO_6Na$ [M^++Na^+] 432.1423, found 432.1421.

*4.6.2. 1-Benzyl 4,4-dimethyl 3-vinyl-2,3-dihydroquinoline-1,4,4-tricarboxylate (**3i**).* Yield 14%; colorless oil; IR (neat) 2953, 1734, 1494, 1435, 1391, 1329, 1260, 1151, 1028 cm^{-1}; ^{1}H NMR (400 MHz,

$CDCl_3$) δ 3.25 (ddd, J=4.0, 7.2, 9.6 Hz, 1H), 3.63 (s, 3H), 3.75 (s, 3H), 3.86 (dd, J=4.0, 13.0 Hz, 1H), 4.18 (dd, J=7.2, 13.0 Hz, 1H), 5.10 (dd, J=1.2, 9.6 Hz, 1H), 5.18 (d, J=12.4 Hz, 1H), 5.19 (d, J=12.4 Hz, 1H), 5.25 (d, J=12.4 Hz, 1H), 5.86 (dt, J=9.6, 17.0 Hz, 1H), 7.10 (dt, J=1.2, 7.2 Hz, 1H), 7.28–7.42 (m, 7H), 7.74 (d, J=7.6 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 45.1 (CH), 46.5 (CH_2), 52.6 (CH_3), 52.9 (CH_3), 61.1 (Cq), 67.7 (CH_2), 119.2 (CH_2), 123.7 (CH), 124.0 (CH), 124.8 (Cq), 128.04 (CH), 128.07 (CH), 128.11 (CH), 128.5 (CH), 130.2 (CH), 134.2 (CH), 136.1 (Cq), 137.5 (Cq), 154.4 (Cq), 169.4 (Cq), 170.1 (Cq); HRMS (ESI) m/z calcd for $C_{23}H_{24}NO_6$ [M^++H^+] 410.1604, found 410.1605.

*4.6.3. Trimethyl 2-vinyl-2,3-dihydroquinoline-1,4,4-tricarboxylate (**4j**).* Yield 66%; yellow oil; IR (neat) 2954, 1732, 1644, 1604, 1493, 1440, 1257, 1197, 1079 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 2.19 (dd, J=9.2, 13.6 Hz, 1H), 3.01 (dd, J=8.0, 13.6 Hz, 1H), 3.65 (s, 3H), 3.69 (s, 3H), 3.86 (s, 3H), 4.94 (tddd, J=1.2, 6.0, 8.0, 9.2 Hz, 1H), 5.09 (td, J=1.2, 10.4 Hz, 1H), 5.20 (td, J=1.2, 17.2 Hz, 1H), 5.69 (ddd, J=6.0, 10.4, 17.2 Hz, 1H), 7.08 (dd, J=1.6, 7.8 Hz, 1H), 7.14 (dt, J=1.2, 7.8 Hz, 1H), 7.32 (dt, J=1.6, 7.8 Hz, 1H), 7.49 (dd, J=1.2, 7.8 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 38.4 (CH_2), 53.0 (CH_3 ×2), 53.1 (CH_3), 53.4 (CH), 57.6 (Cq), 115.5 (CH_2), 124.8 (CH), 125.9 (CH), 126.4 (CH), 128.2 (CH), 130.9 (Cq), 135.9 (Cq), 136.9 (CH), 154.9 (Cq), 169.9 (Cq), 170.1 (Cq); HRMS (ESI) m/z calcd for $C_{17}H_{19}NO_6Na$ [M^++Na^+] 356.1110, found 356.1107.

*4.6.4. 1-tert-Butyl 4,4-dimethyl 2-vinyl-2,3-dihydroquinoline-1,4,4-tricarboxylate (**4k**).* Yield 82%; colorless needles; mp: 103.9–105.6 °C [AcOEt/hexane (2:1)]; IR (KBr) 2980, 1740, 1694, 1491, 1250, 1160, 1132, 1071 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.46 (s, 9H), 2.13 (dd, J=8.0, 13.6 Hz, 1H), 2.99 (dd, J=8.0, 13.6 Hz, 1H), 3.68 (s, 3H), 3.87 (s, 3H), 4.86 (tddd, J=1.2, 6.4, 8.0, 9.6 Hz, 1H), 5.07 (td, J=1.2, 10.4 Hz, 1H), 5.17 (td, J=1.2, 17.2 Hz, 1H), 5.68 (ddd, J=6.4, 10.4, 17.2 Hz, 1H), 7.04 (dd, J=1.6, 7.6 Hz, 1H), 7.10 (dt, J=1.6, 7.6 Hz, 1H), 7.29 (dt, J=0.8, 7.6 Hz, 1H), 7.49 (dd, J=0.8, 7.6 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 28.2 (CH_3), 38.8 (CH_2), 53.00 (CH_3), 53.03 (CH_3), 53.2 (CH), 57.8 (Cq), 81.0 (Cq), 115.1 (CH_2), 124.4 (CH), 125.4 (CH), 126.8 (CH), 127.9 (CH), 131.3 (Cq), 136.4 (Cq), 137.4 (CH), 153.3 (Cq), 170.1 (Cq), 170.3 (Cq); HRMS (ESI) m/z calcd for $C_{20}H_{25}NO_6Na$ [M^++Na^+] 398.1580, found 398.1582.

*4.6.5. 1-tert-Butyl 4,4-dimethyl 7-methyl-2-vinyl-2,3-dihydroquinoline-1,4,4-tricarboxylate (**4n**).* Yield 71%; colorless prisms; mp: 104.5–105.9 °C [AcOEt/hexane (2:1)]; IR (KBr) 2986, 1746, 1732, 1703, 1504, 1436, 1256, 1147, 1067 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.47 (s, 9H), 2.12 (dd, J=9.6, 13.4 Hz, 1H), 2.34 (s, 3H), 2.96 (dd, J=8.0, 13.4 Hz, 1H), 3.68 (s, 3H), 3.85 (s, 3H), 4.85 (ddd, J=6.4, 8.0, 9.6 Hz, 1H), 5.06 (d, J=10.0 Hz, 1H), 5.16 (d, J=17.2 Hz, 1H), 5.67 (ddd, J=6.4, 10.0, 17.2 Hz, 1H), 6.92 (s, 2H), 7.35 (s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 21.3 (CH_3), 28.2 (CH_3), 38.6 (CH_2), 52.9 (CH_3), 53.0 (CH_3), 53.2 (CH), 57.4 (Cq), 80.9 (Cq), 115.0 (CH_2), 125.1 (CH), 125.3 (CH), 127.2 (CH), 128.1 (Cq), 136.1 (Cq), 137.4 (CH), 137.8 (Cq), 153.3 (Cq), 170.3 (Cq), 170.4 (Cq); HRMS (ESI) m/z calcd for $C_{21}H_{27}NO_6Na$[M^++Na^+] 412.1736, found 412.1739.

*4.6.6. 1-tert-Butyl 4,4-dimethyl 7-methoxy-2-vinyl-2,3-dihydroquinoline-1,4,4-tricarboxylate (**4o**).* Yield 85%; colorless prisms; mp: 92.7–93.6 °C [AcOEt/hexane (2:1)]; IR (KBr) 2978, 2953, 1739, 1614, 1505, 1168, 1047 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.48 (s, 9H), 2.18 (dd, J=9.2, 13.6 Hz, 1H), 2.95 (dd, J=7.6, 13.4 Hz, 1H), 3.69 (s, 3H), 3.80 (s, 3H), 3.84 (s, 3H), 4.89 (ddd, J=5.6, 7.6, 9.2 Hz, 1H), 5.06 (dd, J=1.2, 10.4 Hz, 1H), 5.15 (dd, J=1.2, 17.0 Hz, 1H), 5.67 (ddd, J=5.6, 10.4, 17.0 Hz, 1H), 6.66 (dd, J=2.8, 8.6 Hz, 1H), 6.98 (d, J=8.6 Hz, 1H), 7.13 (d, J=2.8 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 28.2 (CH_3), 38.3 (CH_2), 52.9 (CH_3), 53.0 (CH_3), 53.2 (CH), 55.3 (CH_3), 56.9 (Cq), 81.1 (Cq), 110.3 (CH), 112.0 (CH), 115.2 (CH_2), 122.7 (Cq), 126.6 (CH), 137.2 (CH), 137.4 (Cq), 153.1 (Cq), 159.1 (Cq), 170.4 (Cq), 170.5 (Cq); HRMS (ESI) m/z calcd for $C_{21}H_{28}NO_7$ [M^++H^+] 406.1866, found 406.1870.

4.7. Dimethyl 3-vinyl-2,3-dihydroquinoline-4,4(1*H*)-dicarboxylate (14)

To a stirred solution of 3-vinyltetrahydroquinoline **3d** (48.7 mg, 0.106 mmol) in DMF (2 mL) was added K_2CO_3 (43.8 mg, 0.317 mmol) and thiophenol (10.0 μL, 0.127 mmol) at 0 °C, and stirring was continued for 13 h at rt. The resulting solution was filtered using small amount of silica gel and concentrated in vacuo. The residue was chromatographed on silica gel with hexane/AcOEt (80:20, v/v) as eluent to give the amine **14** (29.1 mg, quant.) as yellow oil; IR (neat) 3410, 2952, 1730, 1608, 1503, 1226 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 3.21–3.25 (m, 1H), 3.29 (dd, J=5.8, 11.4 Hz, 1H), 3.65 (dd, J=3.2, 11.4 Hz, 1H), 3.69 (s, 3H), 3.73 (s, 3H), 3.98 (br s, NH), 5.07 (dd, J=1.6, 10.0 Hz, 1H), 5.16 (dd, J=1.6, 17.2 Hz, 1H), 5.95 (dt, J=10.0, 17.2 Hz, 1H), 6.52 (dd, J=1.2, 8.0 Hz, 1H), 6.69 (dt, J=1.2, 8.0 Hz, 1H), 7.08 (dt, J=1.2, 8.0 Hz, 1H), 7.33 (dd, J=1.2, 8.0 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 43.1 (CH), 43.7 (CH_2), 52.3 (CH_3), 52.6 (CH_3), 59.9 (Cq), 114.6 (CH), 116.8 (CH), 117.1 (CH_2), 128.7 (CH), 132.36 (CH), 136.3 (CH), 144.0 (Cq), 170.4 (Cq), 171.1 (Cq); HRMS (ESI) m/z calcd for $C_{15}H_{17}NO_4Na$ [M^++Na^+] 298.1055, found 298.1060.

4.8. Dimethyl 1-allyl-3-vinyl-2,3-dihydroquinoline-4,4(1*H*)-dicarboxylate (15)

To a stirred solution of amine **14** (82.6 mg, 0.300 mmol) in DMF (2 mL) was added K_2CO_3 (124 mg, 0.900 mmol) and allyl bromide (0.0770 mL, 0.900 mmol) at rt. The reaction mixture was then allowed to heat to 80 °C, and stirred for 2 h. The resulting solution was filtered using small amount of silica gel and concentrated in vacuo. The residue was chromatographed on silica gel with hexane/AcOEt (80:20, v/v) as eluent to give the allylamine **15** (80.9 mg, 86%) as colorless oil; IR (neat) 1734, 1604, 1504, 1231 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 3.19–3.30 (m, 2H), 3.58 (dd, J=3.2, 11.2 Hz, 1H), 3.69 (s, 3H), 3.74 (s, 3H), 3.83 (dd, J=4.8, 17.4 Hz, 1H), 3.93 (dd, J=4.8, 17.4 Hz, 1H), 5.07–5.20 (m, 4H), 5.76–5.85 (m, 1H), 5.97 (dt, J=10.0, 16.8 Hz, 1H), 6.63 (d, J=8.0 Hz, 1H), 6.67 (t, J=8.0 Hz, 1H), 7.15 (dt, J=1.6, 8.0 Hz, 1H), 7.28 (dd, J=1.6, 8.0 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 43.6 (CH), 50.7 (CH_2), 52.4 (CH_3), 52.6 (CH_3), 53.8 (CH_2), 60.7 (Cq), 111.6 (CH), 115.8 (CH), 116.2 (Cq), 116.3 (CH_2), 117.5 (CH_2), 129.0 (CH), 131.8 (CH), 132.9 (CH), 136.2 (CH), 144.4 (Cq), 170.4 (Cq), 171.1 (Cq); HRMS (ESI) m/z calcd for $C_{18}H_{21}NO_4Na$ [M^++Na^+] 338.1368, found 338.1368.

4.9. Dimethyl 2-benzo-1-azabicyclo[3.3.1]-6-nonene-4,4-dicarboxylate (16)

To a stirred solution of allylamine **15** (11.0 mg, 0.0349 mmol) in CH_2Cl_2 (2 mL) was added Grubbs' second catalyst (1.50 mg, 1.74 μmol) at rt. After being refluxed for 1 h, the reaction mixture was evaporated. The residue was chromatographed on silica gel with hexane/AcOEt (70:30, v/v) as eluent to give the **16** (9.00 mg, 90%) as colorless prisms; mp: 157.5–158.8 °C [AcOEt/hexane (4:1)]; IR (neat) 1730, 1481, 1262, 1223 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 3.15 (s, 1H), 3.32 (dd, J=2.8, 13.6 Hz, 1H), 3.54 (s, 1H), 3.57–3.59 (m, 1H), 3.77 (s, 3H), 3.79 (s, 3H), 4.00 (dd, J=1.2, 18.2 Hz, 1H), 5.58–5.62 (m, 1H), 5.75 (dd, J=2.8, 9.8 Hz, 1H), 7.08 (t, J=8.0 Hz, 1H), 7.09 (d, J=8.0 Hz, 1H), 7.27 (t, J=8.0 Hz, 1H), 7.60 (d, J=8.0 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 31.5 (CH), 48.1 (CH_2), 52.7 (CH_3), 53.0 (CH_3), 57.0 (CH_2), 60.4 (Cq), 123.0 (CH), 123.8 (Cq), 125.6 (CH), 126.0 (CH), 128.8 (CH), 129.2 (CH), 132.9 (CH), 150.4 (Cq), 170.3 (Cq), 170.6 (Cq); HRMS (ESI) m/z calcd for $C_{16}H_{18}NO_4$ [M^++H^+] 288.1236, found 288.1239.

4.10. General procedure for the enantioselective cyclization of 2-amidophenylmalonates

Synthesis of (−)-**3d** (Table 5, entry 8): To a stirred solution of sulfonamide **1d** (35.0 mg, 0.0857 mmol) and (*Z*)-1,4-diacetoxy-2-butene (**2**) (17.7 mg, 0.103 mmol) in dioxane (2 mL) were added $Pd_2(dba)_3\cdot CHCl_3$ (4.40 mg, 4.29 μmol), (*S*)-(−)-BINAP (10.7 mg, 17.1 μmol), and K_2CO_3 (47.0 mg, 0.343 mmol) at rt, and stirring was continued for 30 min at the same temperature. The reaction mixture was then allowed to heat to 80 °C, and stirred for 2 h. After filtration of the reaction mixture using small amount of silica gel followed by concentration, the residue was chromatographed on silica gel with hexane/AcOEt (80:20, v/v) as eluent to give the optically active 3-vinyltetrahydroquinoline (−)-**3d** (31.3 mg, 79%, 99% ee) as colorless prisms.

*4.10.1. (−)-Dimethyl 1-(4-nitrophenylsulfonyl)-3-vinyl-2,3-dihydroquinoline-4,4(1H)-dicarboxylate [(−)-**3d**].* Yield 79%, 99% ee; yellow oil; $[\alpha]_D^{26}$ −17.3 (*c* 1.50 in $CHCl_3$). Enantiomeric excess was determined by HPLC analysis [CHIRALCEL AS-H column, hexane/^{i}PrOH (8:2 v/v), 0.5 mL/min, λ=254 nm, retention time 30.9 min and 37.6 min]. Other spectral data coincides with those of the racemic **3d**.

*4.10.2. (+)-Dimethyl 1-(4-nitrophenylsulfonyl)-2-vinyl-2,3-dihydroquinoline-4,4(1H)-dicarboxylate [(+)-**4d**].* Yield 52%, 83% ee (Table 5, entry 4); colorless oil; $[\alpha]_D^{26}$ +62.4 (*c* 0.87 in $CHCl_3$); IR (neat) 1736, 1531, 1351, 1250, 1172 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 2.48 (d, *J*=5.6 Hz, 2H), 3.55 (s, 3H), 3.74 (s, 3H), 5.09–5.13 (m, 1H), 5.10 (d, *J*=10.8 Hz, 1H), 5.23 (d, *J*=17.2 Hz, 1H), 5.64 (ddd, *J*=5.6, 10.8, 17.2 Hz, 1H), 7.21 (dt, *J*=1.2, 7.8 Hz, 1H), 7.25–7.28 (m, 2H), 7.36 (dt, *J*=1.2, 7.8 Hz, 1H), 7.82 (d, *J*=9.2 Hz, 2H), 8.26 (d, *J*=9.2 Hz, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 34.4 (CH_2), 53.2 (CH_3), 53.3 (CH_3), 55.4 (CH), 55.7 (Cq), 117.5 (CH_2), 124.2 (CH), 125.0 (CH), 125.7 (CH), 126.8 (Cq), 128.7 (CH), 129.1 (CH), 129.9 (CH), 134.2 (Cq), 135.1 (CH), 145.0 (Cq), 150.3 (Cq), 169.8 (Cq), 170.0 (Cq); HRMS (ESI) *m*/*z* calcd for $C_{21}H_{21}N_2O_8S$ [M^++H^+] 461.1019, found 461.1017. Enantiomeric excess was determined by HPLC analysis [CHIRALCEL AD column, hexane/^{i}PrOH (9:1 v/v), 0.5 mL/min, λ=254 nm, retention time 46.4 min and 56.4 min].

*4.10.3. (−)-Dimethyl 1-(4-methoxyphenylsulfonyl)-3-vinyl-2,3-dihydroquinoline-4,4(1H)-dicarboxylate [(−)-**3f**].* Yield 31%, 55% ee; colorless prisms; mp: 97.0–97.8 °C [AcOEt/hexane (2:1)]; $[\alpha]_D^{26}$ −13.5 (*c* 0.72 in $CHCl_3$); IR (KBr) 2953, 1733, 1596, 1497, 1354, 1261, 1161 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 2.98 (dt, *J*=4.0, 9.0 Hz, 1H), 3.57 (s, 3H), 3.64 (s, 3H), 3.83 (s, 3H), 3.96 (dd, *J*=9.0, 13.2 Hz, 1H), 4.09 (dd, *J*=4.0, 13.2 Hz, 1H), 5.10 (d, *J*=17.6 Hz, 1H), 5.15 (d, *J*=10.2 Hz, 1H), 5.86 (ddd, *J*=9.0, 10.2, 17.6 Hz, 1H), 6.89 (d, *J*=8.8 Hz, 2H), 7.09 (dt, *J*=1.2, 7.6 Hz, 1H), 7.28 (dt, *J*=1.2, 7.6 Hz, 1H), 7.32 (dd, *J*=1.2, 7.6 Hz, 1H), 7.61 (d, *J*=8.8 Hz, 2H), 7.84 (dd, *J*=1.2, 7.6 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 43.0 (CH), 47.6 (CH_2), 52.5 (CH_3), 52.7 (CH_3), 55.6 (CH_3), 60.9 (Cq), 114.2 (CH), 119.0 (CH_2), 122.8 (CH), 124.0 (CH), 124.6 (Cq), 128.6 (CH), 129.3 (CH), 131.0 (CH), 131.1 (Cq), 134.3 (CH), 136.4 (Cq), 163.2 (Cq), 169.2 (Cq), 169.9 (Cq); HRMS (ESI) *m*/*z* calcd for $C_{22}H_{23}NO_7NaS$ [M^++Na^+] 468.1093, found 468.1093. Enantiomeric excess was determined by HPLC analysis [CHIRALCEL AS-H column, hexane/^{i}PrOH (8:2 v/v), 0.5 mL/min, λ=254 nm, retention time 67.9 min and 89.3 min].

*4.10.4. (−)-Dimethyl 1-(4-(trifluoromethyl)phenylsulfonyl)-3-vinyl-2,3-dihydroquinoline-4,4(1H)-dicarboxylate [(−)-**3g**].* Yield 69%, 65% ee; colorless oil; $[\alpha]_D^{27}$ −13.6 (*c* 0.42 in $CHCl_3$); IR (KBr) 1736, 1324, 1248, 1173, 1063 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 2.93 (dt, *J*=4.0, 8.8 Hz, 1H), 3.53 (s, 3H), 3.62 (s, 3H), 3.98 (dd, *J*=8.8, 13.2 Hz, 1H), 4.13 (dd, *J*=4.0, 13.2 Hz, 1H), 5.09 (dd, *J*=0.8, 17.6 Hz, 1H), 5.16 (dd, *J*=0.8, 10.2 Hz, 1H), 5.84 (ddd, *J*=8.8, 10.2, 17.6 Hz, 1H), 7.15 (dt, *J*=1.2, 7.8 Hz, 1H), 7.29–7.35 (m, 2H), 7.70 (d, *J*=8.0 Hz, 2H), 7.79 (d, *J*=8.0 Hz, 2H), 7.84 (dd, *J*=1.2, 7.8 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 43.2 (CH), 47.8 (CH_2), 52.5 (CH_3), 52.8 (CH_3), 60.9 (Cq), 119.3 (CH_2), 123.0 (CH), 124.8 (CH), 125.3 (Cq), 126.2 (q, *J*=33 Hz, CF_3), 127.7 (CH ×4), 128.8 (CH), 131.2 (CH), 133.9 (CH), 135.8 (Cq ×2), 142.9 (Cq), 169.0 (Cq), 169.7 (Cq); HRMS (ESI) *m*/*z* calcd for $C_{22}H_{20}NO_6NaSF_6$ [M^++Na^+] 506.0861, found 506.0861. Enantiomeric excess was determined by HPLC analysis [CHIRALCEL AS-H column, hexane/^{i}PrOH (9:1 v/v), 0.5 mL/min, λ=254 nm, retention time 19.4 min and 22.8 min].

*4.10.5. (−)-Dimethyl 1-(4-cyanophenylsulfonyl)-3-vinyl-2,3-dihydroquinoline-4,4(1H)-dicarboxylate [(−)-**3h**].* Yield 93%, 76% ee; colorless prisms; mp: 138.9–139.9 °C [AcOEt/hexane (2:1)]; IR (KBr): 1734, 1489, 1363, 1249, 1168 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 2.97 (dt, *J*=4.0, 9.2 Hz, 1H), 3.56 (s, 3H), 3.66 (s, 3H), 3.98 (dd, *J*=9.2, 13.2 Hz, 1H), 4.12 (dd, *J*=4.0, 13.2 Hz, 1H), 5.11 (d, *J*=17.2 Hz, 1H), 5.17 (d, *J*=10.4 Hz, 1H), 5.82 (ddd, *J*=9.2, 10.4, 17.2 Hz, 1H), 7.15 (dt, *J*=1.2, 7.8 Hz, 1H), 7.31 (dt, *J*=1.6, 7.8 Hz, 1H), 7.36 (dd, *J*=1.6, 7.8 Hz, 1H), 7.72–7.79 (m, 5H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 43.2 (CH), 47.9 (CH_2), 52.6 (CH_3), 53.0 (CH_3), 60.8 (Cq), 116.7 (Cq), 117.1 (Cq), 119.4 (CH_2), 122.7 (CH), 124.9 (CH), 125.1 (Cq), 127.8 (CH), 128.9 (CH), 131.3 (CH), 132.8 (CH), 133.7 (CH), 135.6 (Cq), 143.4 (Cq), 168.9 (Cq), 169.7 (Cq); HRMS (ESI) *m*/*z* calcd for $C_{22}H_{20}N_2O_6NaS$ [M^++Na^+] 463.0940, found 463.0939. Enantiomeric excess was determined by HPLC analysis [CHIRALCEL AS-H column, hexane/^{i}PrOH (8:2 v/v), 0.5 mL/min, λ=254 nm, retention time 45.2 min and 56.6 min].

Acknowledgements

This study was supported in part by a Grant-in-Aid for the Encouragement of Young Scientists (B) from the Japan Society for the Promotion of Science (JSPS), Uehara Memorial Foundation, Takeda Science Foundation and the Program for Promotion of Basic and Applied Research for Innovations in the Bio-oriented Industry (BRAIN). We are grateful to Dr. Tatsusada Yoshida for helpful suggestions about p*K*a calculations.

Supplementary data

Supplementary data associated with this article can be found in the online version at http://dx.doi.org/10.1016/j.tet.2012.09.075.

References and notes

1. (a) Tsuji, J. *Palladium Reagents and Catalysts: New Perspectives for the 21st Century*; Wiley: New York, NY, 2004, pp 431; (b) Davis, J. A. In *Comprehensive Organometallic Chemistry II*; Able, E. W., Stone, F. G. A., Wilkinson, G., Eds.; Pergamon: Oxford, 1995; Vol. 9, p 291; (c) Godleski, S. A. In *Comprehensive Organic Synthesis*; Trost, B. M., Fleming, I., Eds.; Pergamon: New York, NY, 1991; Vol. 3, p 585.
2. (a) Massacret, M.; Lhoste, P.; Sinou, D. *Eur. J. Org. Chem.* **1999**, 129; (b) Yang, S.-C.; Shue, Y.-J.; Liu, P.-C. *Organometallics* **2002**, *21*, 2013; (c) Yang, S.-C.; Liu, P.-C.; Feng, W.-H. *Tetrahedron Lett.* **2004**, *45*, 4951.
3. (a) Yamazaki, A.; Achiwa, I.; Achiwa, K. *Tetrahedron: Asymmetry* **1996**, *7*, 403; (b) Massacret, M.; Lakhmiri, R.; Lhoste, P.; Nguefack, C.; Abdelouahab, F. B. B.; Fadel, R.; Sinou, D. *Tetrahedron: Asymmetry* **2000**, *11*, 3561; (c) Yang, S.-C.; Lai, H.-C.; Tsai, Y.-C. *Tetrahedron Lett.* **2004**, *45*, 2693.
4. (a) Tsuda, T.; Kiyoi, T.; Saegusa, T. *J. Org. Chem.* **1990**, *55*, 3388; (b) Uozumi, Y.; Tanahashi, A.; Hayashi, T. *J. Org. Chem.* **1993**, *58*, 6826; (c) Yamazaki, A.; Achiwa, K. *Tetrahedron: Asymmetry* **1995**, *6*, 1021; (d) Nakano, H.; Yokoyama, J.; Fujita, R.; Hongo, H. *Tetrahedron Lett.* **2002**, *43*, 7761.
5. (a) Thorey, C.; Wilken, J.; Hénin, F.; Martens, J.; Mehler, T.; Muzart, J. *Tetrahedron Lett.* **1995**, *36*, 5527; (b) Ito, K.; Imahayashi, Y.; Kuroda, T.; Eno, S.; Saito, B.; Katsuki, T. *Tetrahedron Lett.* **2004**, *45*, 7277.
6. Massacret, M.; Goux, C.; Lhoste, P.; Sinou, D. *Tetrahedron Lett.* **1994**, *35*, 6093.
7. (a) Hayashi, T.; Yamamoto, A.; Ito, Y. *Tetrahedron Lett.* **1987**, *28*, 4837; (b) Hayashi, T.; Yamamoto, A.; Ito, Y. *Tetrahedron Lett.* **1988**, *29*, 99; (c) Moreno-Mañas, M.; Morral, L.; Pleixats, R.; Villarroya, S. *Eur. J. Org. Chem.* **1999**, 181; (d) Tanimori, S.; Kirihata, M. *Tetrahedron Lett.* **2000**, *41*, 6785.

8. Murahashi, S.-I.; Shimamura, T.; Moritani, I. *J. Chem. Soc., Chem. Commun.* **1974**, 931.
9. (a) Hayashi, T.; Yamamoto, A.; Ito, Y. *Tetrahedron Lett.* **1988**, *29*, 669; (b) Hayashi, T.; Ohno, A.; Lu, A. S.-J.; Matsumoto, Y.; Fukuyo, E.; Yanagi, K. *J. Am. Chem. Soc.* **1994**, *116*, 4221; (c) Sakamoto, M.; Shimizu, I.; Yamamoto, A. *Bull. Chem. Soc. Jpn.* **1996**, *69*, 1065; (d) Nomura, N.; Tsurugi, K.; Okada, M. *Angew. Chem., Int. Ed.* **2001**, *40*, 1932; (e) Murakami, H.; Matsui, Y.; Ozawa, F.; Yoshifuji, M. *J. Organomet. Chem.* **2006**, *691*, 3151; (f) Tanimori, S.; Kato, Y.; Kirihata, M. *Synthesis* **2006**, 865.
10. (a) Yoshida, M.; Higuchi, M.; Shishido, K. *Tetrahedron Lett.* **2008**, *49*, 1678; (b) Yoshida, M.; Higuchi, M.; Shishido, K. *Org. Lett.* **2009**, *11*, 4752; (c) Yoshida, M.; Higuchi, M.; Shishido, K. *Tetrahedron* **2010**, *66*, 2675; (d) Yoshida, M.; Sugimura, C.; Shishido, K. *Org. Lett.* **2011**, *13*, 3482; (e) Yoshida, M.; Ohno, S.; Shishido, K. *Chem.—Eur. J.* **2012**, *18*, 1604; (f) Yoshida, M. *Chem. Pharm. Bull.* **2012**, *60*, 285.
11. Katrizky, A.; Rachwal, S.; Rachwal, B. *Tetrahedron* **1996**, *52*, 15031 and references therein.
12. Preliminary studies have been published: Yoshida, M.; Maeyama, Y.; Shishido, K. *Tetrahedron Lett.* **2010**, *51*, 6008.
13. The p*K*a values of the tosylamide and the malonate moiety in **1a**, using the *ChemAxon*'s p*K*a calculation method, are 7.37 and 10.17, respectively. On the other hand, the p*K*a value of the *tert*-butoxy carbamate group in **1f** is 11.68.
14. For examples showing the difference in reactivity between sulfonamides and carbamates, see: (a) Ishikawa, T.; Aikawa, T.; Watanabe, S.; Saito, S. *Org. Lett.* **2006**, *8*, 3881; (b) Chataingner, I.; Panel, C.; Gérard, H.; Piettre, S. R. *Chem. Commun.* **2007**, 3288.
15. When Boc-substituted substrate **1k** was subjected to the reaction in the presence of chiral ligand, the enantiomeric excess was not observed in the resulting product **4k**.