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Asymmetric Synthesis of Dihydronaphthoquinones Containing Adjacent Stereocenters via a Sulfa-Michael Addition Triggered Ring-Expansion Approach

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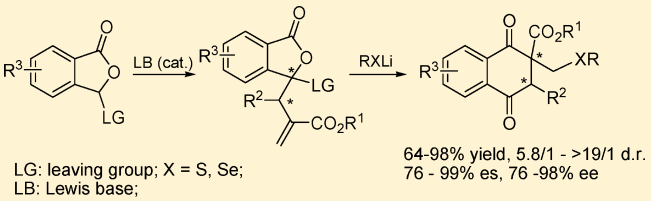
Supporting Information

ABSTRACT: A novel asymmetric synthetic approach for the construction of enantioenriched functionalized dihydroquinones incorporating adjacent quaternary and tertiary stereocenters has been reported, in which enantioenriched 3-allylic phthalides engaged in an unprecedented sulfa-Michael addition-triggered stereoselective ring-expansion reaction, and furnished the desired sulfur-incoporated dihydronaphthoquinones with high stereoselectivity.



INTRODUCTION

Dihydronaphthoquinones are frequently occurring structural motifs spread across many biologically active natural products and pharmaceutical compounds,[1] in particular, the frameworks bearing adjacent stereocenters embodied in a range of biological relevant dihydronaphthoquinone compounds (Figure 1).[1e−h] Therefore, the availability of efficient methods for the asymmetric synthesis of structurally diverse dihydroquinones bearing adjacent stereocenters is highly attractive to the discovery of biologically interesting agents. However, to our best knowledge, the asymmetric approach for the preparation of enantioenriched functionalized dihydroquinones incorporating adjacent quaternary and tertiary stereocenters is unexploited.

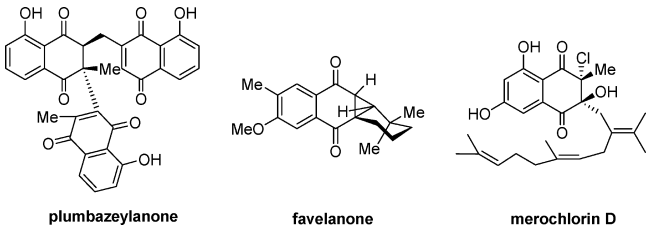


Figure 1. Bioactive molecules that incorporate a dihydronaphthoquinone framework bearing adjacent stereocenters.

Sulfa-Michael addition (SMA) is one of the most important C−S bond formations and has found wide application in organic synthesis and in biological processes, which provides a diversity of organosulfur compounds.[2] In particular, combining with appropriate reaction partners, SMA triggered tandem protocols demonstrated great potential in the rapid and efficient assembly of complex functionalized sulfur-incorporated compounds.[2f,3] Phthalides are frequently found in naturally occurring substances which exhibit a broad spectrum of biological activities[4] and also act as useful building blocks in organic synthesis, particularly for the synthesis of functionalized naphthalenes, anthracenes, and naphthacene natural products via an annulation approach.[5] Nevertheless, these motifs have seldom been employed in an asymmetric cascade transformation to construct enantiomerically pure chiral compounds. Recently, we have developed a Lewis base catalyzed asymmetric allylic alkylation (AAA) reaction to access enantioenriched 3-allylic-3-cyano substituted phthalides, which underwent further intramolecular acylcyanation to provide enantioenriched densely functionalized nitriles bearing dihydronaphthoquinone moieties.[6,7] On the basis of these, we envision that a general tandem protocol in which enantioenriched 3-allylic phthalides containing a leaving group at the 3-position would engage in an SMA triggered stereoselective ring-expansion reaction, and thereby furnish enantioenriched sulfur-incoporated dihydronaphthoquinones possessing contiguous quaternary and tertiary stereocenters, could be established (Scheme 1), all of which would preserve the stereochemical integrity of the chiral allylic phthalides. Herein, we report our preliminary results.

RESULTS AND DISCUSSION

To achieve this goal, two requirements need to be met: (1) devising appropriate 3-allylic phthalides containing a leaving group which can undergo further SMA triggered tandem sequences and (2) developing efficient asymmetric approaches to prepare enantioenriched 3-allylic phthalides bearing contiguous quaternary and tertiary stereocenters, and enabling SMA triggered tandem reaction stereoselectively. Keeping these in mind, we started the initial investigation to assess the feasibility of this tandem reaction by treating racemic 3-allylic

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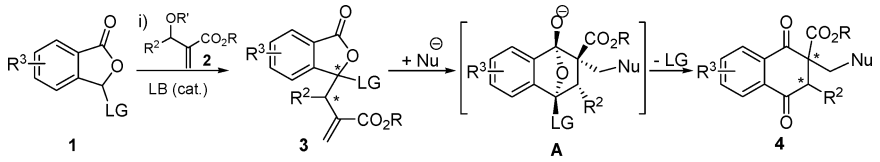
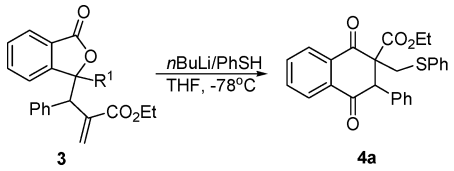
Scheme 1. Synthetic Strategy



LG: leaving group; Nu: sulfur nucleophiles; LB: Lewis base;

phthalides containing different leaving groups such as cyano, phenylsulfanyl, and phenylsulfinyl groups with lithium thiophenolate in situ generated from thiophenol and *n*-butyllithium at −78 °C in THF (Scheme 2). It turned out that the type of leaving group is crucial to the accomplishment of this transformation. 3-Allylic-3-cyano substituted phthalide **3a** gave the desired product **4a** in near quantitative yield with promising diastereoselectivity, while phthalides possessing phenylsulfanyl and phenylsulfinyl groups provided the desired product **4a** in 14% yield.

Scheme 2. Initial Investigation



3a (R^1 = CN): 2h, 99% yield (**4a**), d.r. = 6/1;
3aa (R^1 = SPh): 10h, nd;
3ab (R^1 = SO_2Ph): 10h, 14% yield (**4a**), d.r. = 3/1;

With these preliminary results, the further studies were focused on the development of a catalytic enantioselective route to construct 3-allylic-3-cyano substituted phthalides bearing contiguous quaternary and tertiary stereocenters. Recently, Lu et al. reported an elegant work to prepare enantioenriched 3-allylic-3-carboxylate phthalides by utilizing a Lewis base catalyzed asymmetric AAA reaction of Morita−Baylis−Hillman (MBH) carbonates.[8] In a similar strategy, our group demonstrated a facile route to access enantioenriched 3-allylic-3-cyano substituted phthalides bearing a single quaternary stereocenter.[6] However, an asymmetric catalytic approach to prepare the aforementioned motifs with both high enantioselectivities and diastereoselectivity has not been developed.[9] Keeping these surveys in mind, our efforts were focused on screening effective catalysts and conditions for the enantioselective allylic alkylation reaction between 3-cyano phthalide **1** and substituted MBH carbonate **2** to afford 3,3-disubstituted phthalide **3** (Table 1). A focused catalyst survey showed that a bifunctional phosphine catalyst was found to be superior in stereochemical control, which furnished the desired product **3a** in excellent yield with 99% ee. On the basis of these, the scope of the catalytic enantioselective allylic alkylation of various 3-cyano phthalides **1** with MBH carbonates **2** was examined, and results are shown in Table 1. In general, excellent to high yields and enantioselectivities were observed for a broad range of phthalides and MBH carbonates. For examples, treatment of unsubstituted 3-cyano phthalide (R^3 = H) with a range of MBH carbonates **2** containing aryl moieties provided the desired products **3b**−**3h** in excellent yields with remarkable stereocontrol under optimized reaction conditions, regardless of the substituent pattern and electronic nature on the aromatic ring (R^2) of MBH carbonates. 2-Naphthyl substituted MBH carbonate can also react with phthalide to furnish the congested product **3i** in 93% yield and 97% ee correspondingly. Notably, the reaction between alkyl substituted MBH carbonate and phthalide proceeded smoothly and gave alkyl substituted product **3j** in good yield and excellent enantioselectivity, albeit with diminished diastereoselectivity. In addition, phthalides with various substituents were well tolerated. Both electron-rich and electron-deficient group substituted phthalides provided the desired products **3k**−**3q** in excellent yields and stereoselectivities irrespective of substituent patterns. Disubstituted phthalide can also serve as a suitable substrate to give the desired product **3r** with the similar chemical yield and stereoselectivity to that of the monosubstituted analogue. Additionally, the absolute configuration of the product **3f** was determined on the basis of X-ray crystal structural analyses.[10]

Next, we directed our efforts to probing the stereoselective SMA triggered tandem reaction, choosing enantioenriched 3-allylic phthalide **3a** as model substrate. The results are summarized in Table 2. Treatment of chiral phthalide **3a** with lithium thiophenolate in situ generated from thiophenol and *n*-butyllithium at −78 °C in THF provided the desired functionalized dihydroquinones **4a** incorporating contiguous quaternary and tertiary stereocenters in excellent yield and enantioselectivity, albeit with moderate diastereoselectivity (Table 2, entry 1).[11] The surveys on solvents indicated that THF was the best solvent with regard to the yield and stereoselectivity (Table 2, entries 2−6). Further reducing the temperature had little influence on this tandem process (Table 2, entry 7), whereas elevating the temperature led to an obvious deterioration in the enantioselectivity of this transformation (Table 2, entry 8). Gratifyingly, the addition of $MgBr_2{\cdot}Et_2O$ resulted in a significant increase in diastereoselectivity and gave the desired product in 90% yield with excellent enantio- and diastereocontrol (98% ee and d.r. > 19/1) (Table 2, entry 9).[12]

With these optimized reaction conditions, SMA triggered tandem reactions with a variety of enantioenriched allylic phthalides were examined, and the results are depicted in Table 3. Substituents (R^2) with different electronic nature on the aromatic ring, such as methoxy and halogen, were tolerated, and both substituent pattern and electronic nature (R^2) on the aromatic ring have few effects on the chemical outcome and enantioselectivity of this transformation. For example, all reactions provided the desired products in good yields with excellent stereoselectivities (**4a**−**4i**). With regard to the diastereoselectivities, most of the cases provided the excellent selectivities (**4a**−**4c**, **4e**−**4g**), while substrates with electron-withdrawing groups at the *para*-position on the aromatic core delivered the desired product **4d** with decreased diastereoselectivities, presumably due to the susceptibility of the resultant dihydroquinones to racemization at the α-position. The naphthyl-substituted compound also provided the correspond-

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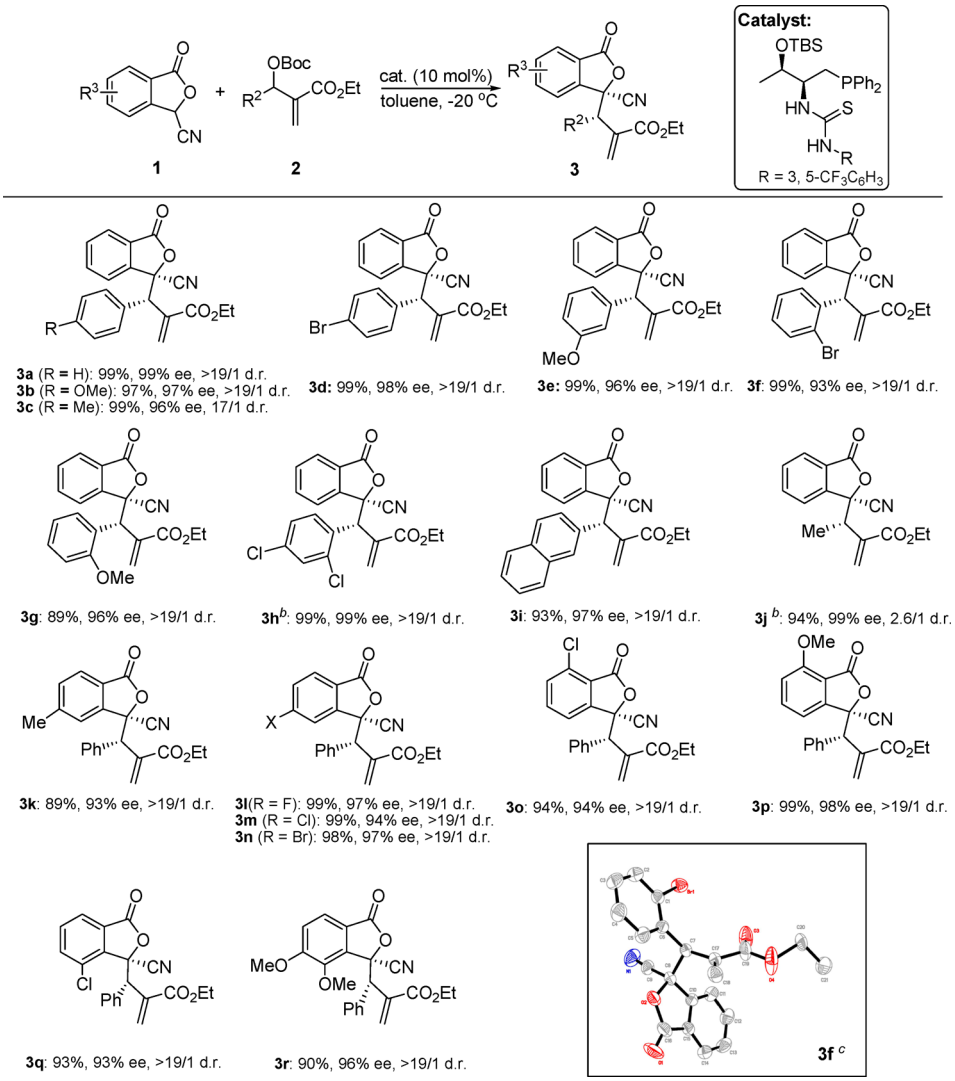
Table 1. Development of Asymmetric Catalytic Allylic Alkylation To Prepare Functionalized 3-Cyano Phthalide 3[a]



[a]Performed with **1** (0.2 mmol), **2** (0.24 mmol), and catalyst (10 mol %) in toluene (2.0 mL) at −20 °C. Yields shown are of isolated products. ee values were determined by chiral HPLC analysis. d.r. values were determined by ^{1}H NMR analysis. [b]Run at −30 °C. [c]X-ray structure of compound **3f**.

ing product **4i** in comparably good yield and enantioselectivity. When a substrate with an alkyl substituent was employed, the desired product **4j** was obtained in 64% yield with moderate stereoselectivity. Notably, substrates with *ortho*-substituent patterns can provide the desired products **4f**–**4g** in excellent yields and stereoselectivities in the absence of a Lewis acid, and the absolute configuration of the product **4f** was determined on the basis of X-ray crystal structural analyses.[10] Subsequently, substrates with different substituents (R^3) on the aromatic ring of phthalides were surveyed. It turned out that the chemical outcome and stereoselectivity rather relied upon the substituent patterns and electronic nature on the aromatic ring of phthalides. Phthalide bearing an electron-donating group at the 4-position provided the desired product **4k** in good yield with an excellent es value and remarkable diastereoselectivity, whereas substrates possessing electron-withdrawing groups at the 4-position furnished functionalized dihydronaphthoquinones in good to high yields with excellent enantioselectivities, but moderate diastereoselectivities were obtained (**4l**–**4n**). The reactions of 2-methoxyl substituted and 4,5-methoxyl disubstituted phthalides did not give any desired products (**4p** and **4r**), whereas 2-chloro-substituted and 5-chloro-substituted analogues provided products in high yields with high stereoselection (**4o** and **4q**), which indicated that the electronic nature of the substituent may exert more influence on the chemical outcome of this transformation than substituent patterns.

This tandem process is equally applicable to analogues of thiophenolate. For examples, substituted thiophenolates and benzyl thiolate can act as suitable nucleophiles to trigger this tandem reaction, respectively, and provide the desired products (**4s**–**4u**) in good yields with high enantioselectivities and moderate to high diastereoselectivities (Table 4, entries 1–3). Organoselenide is a class of important chemical feedstock which can be elaborated in a variety of synthetically transformations. Under the modified reaction conditions, the desired organoselenium compound **4v** incorporating a chiral dihydroquinone moiety can be obtained in comparable yield and stereoselectivity to that of the thiolate analogue (Table 4, entry 4), which further extends the application of this tandem

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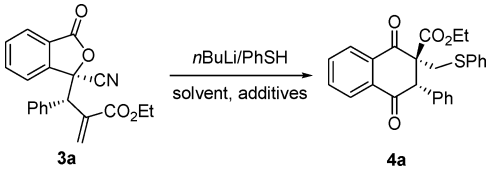
Table 2. Screening of Tandem Reaction for Dihydroquinones 4a[a]



3a 4a

entry	solvent	T (°C)	t (h)	yield (%)[b]	d.r.[c]	es (%)[d]
1	THF	−78	2	99	6/1	98
2	ether	−78	2	88	6.8/1	97
3	toluene	−78	2	89	6.6/1	93
4	DCM	−78	2	3	6.3/1	
5[e]	THF/CH_3CN	−78	2	99	5.6/1	99
6[f]	THF/HMPA	−78	2	81	5/1	96
7	THF	−90	2	99	6/1	99
8	THF	−40	2	99	5/1	92
9[g]	THF	−78	2.5	90	>19/1	98

[a]Reactions were performed with **3a** (0.2 mmol) in the mole ratio of **3a**/PhSH/*n*BuLi = 1/1.3/1.2 in solvent (2 mL) at −78 °C. Enantioenriched **3a** was employed (d.r. > 19/1). [b]Isolated yields. [c]Determined by ^{1}H NMR analysis. [d]es = (product ee/starting material ee) × 100%. ee values were determined by chiral HPLC analysis. [e]THF/CH_3CN = 2/1. [f]HMPA (4 equiv) was added. [g]$MgBr_2{\cdot}Et_2O$ (0.4 mmol) was added, and the reaction was carried out in the mole ratio of **3a**/PhSH/*n*BuLi = 1/1.5/1.5.

protocol to prepare diverse enantiomerically pure dihydroquinone derivates and has the potential to be further elaborated in a variety of synthetically useful transformations. The synthetic utility of enantioenriched sulfur-incoporated dihydronaphthoquinone was illustrated finally (Scheme 3). The treatment of compound **4a** with *m*-CPBA in CH_2Cl_2 afforded sulfone **5** in 84% yield with almost intact stereoselectivities.[13]

CONCLUSION

In conclusion, we have developed a novel asymmetric synthetic approach for the preparation of enantioenriched functionalized dihydroquinones incorporating adjacent quaternary and tertiary stereocenters first, in which a Lewis base catalyzed AAA reaction and an unprecedented SMA triggered stereoselective ring-expansion reaction were involved. In this novel protocol, enantioenriched 3-allylic phthalides engaged in an SMA triggered tandem reaction, which furnished enantioenriched sulfur-incoporated dihydronaphthoquinones possessing contiguous quaternary and tertiary stereocenters with high stereoselectivty in the presence of $MgBr_2{\cdot}Et_2O$. The broad scope and versatility of the process were demonstrated. Further studies on extending this strategy to related processes as well as the synthetic applications of this transformation are underway in our laboratory.

EXPERIMENTAL SECTION

General Procedure for the Allylic Alkylation Reaction of MBH Adducts 2 with Phthalides 1. To a dried 10 mL reaction tube under a N_2 atmosphere were added catalyst (10 mol %), and phthalide **1** (0.2 mmol), and toluene (2.0 mL). After stirring at the −20 °C for 5 min, to the solution was added MBH carbonates **2** (0.24 mmol). The reaction was monitored by TLC. Upon completion, the reaction mixture was concentrated *in vacuo*. The crude mixture was purified by column chromatography (silica gel, EtOAc/Petroleum ether (60−90 °C)) to provide the following compounds.

*Ethyl 2-((S)-((S)-1-Cyano-3-oxo-1,3-dihydroisobenzofuran-1-yl)-(phenyl)methyl)acrylate (Table 1, **3a**).* The residue was purified by column chromatography (silica gel, EtOAc/Petroleum ether) to afford the title compound (69 mg, 99% yield, d.r. > 19/1) as a white solid, mp: 98−99 °C. The ee value was determined to be 99% by chiral HPLC analysis (Chiralpak AS-H, 20/80 isopropanol/hexanes, λ = 254 nm at 30 °C, flow rate = 0.5 mL/min, t_R(major) = 15.9 min, t_R(minor) = 19.3 min). $[\alpha]_D^{25}$ = −66.2 (*c* = 1.00, $CHCl_3$). ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.93 (d, *J* = 7.5 Hz, 1H), 7.70 (t, *J* = 7.4 Hz, 1H), 7.65 (t, *J* = 7.4 Hz, 1H), 7.59 (d, *J* = 6.9 Hz, 2H), 7.50−7.36 (m, 3H), 7.32 (d, *J* = 7.6 Hz, 1H), 6.42 (s, 1H), 6.16 (s, 1H), 4.92 (s, 1H), 4.07−3.87 (m, 2H), 1.09 (t, *J* = 7.1 Hz, 3H). ^{13}C NMR (125 MHz, $CDCl_3$): δ 167.2, 165.9, 144.9, 136.2, 136.1, 134.9, 131.4, 130.1, 129.5, 129.1, 128.6, 126.2, 125.1, 123.9, 115.7, 79.4, 61.5, 51.8, 14.1; HRMS (ESI): calcd. for $C_{21}H_{18}NO_4$ ($[M + H]^+$): 348.1230, found 348.1231.

*Ethyl 2-((3-Oxo-1-(phenylthio)-1,3-dihydroisobenzofuran-1-yl)-(phenyl)methyl)acrylate (Scheme 2, **3aa**).* The residue was purified by column chromatography (silica gel, EtOAc/Petroleum ether) to afford the title compound (83 mg, 96% yield, d.r. > 19/1) as a white solid, mp: 118−120 °C (DABCO was used as catalyst). ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.83 (d, *J* = 7.4 Hz, 2H), 7.65 (d, *J* = 7.7 Hz, 1H), 7.55 (t, *J* = 7.5 Hz, 1H), 7.43 (t, *J* = 7.5 Hz, 2H), 7.41−7.34 (m, 2H), 7.24 (t, *J* = 7.0 Hz, 1H), 7.09 (d, *J* = 6.8 Hz, 3H), 6.98 (t, *J* = 7.6 Hz, 2H), 6.16 (s, 1H), 5.99 (s, 1H), 5.35 (s, 1H), 3.90 (q, *J* = 7.1 Hz, 2H), 1.04 (t, *J* = 7.1 Hz, 3H). ^{13}C NMR (125 MHz, $CDCl_3$): δ 169.1, 166.5, 149.1, 138.4, 138.2, 136.7, 133.5, 130.1, 129.9, 129.4, 129.8, 128.6, 128.4, 127.8, 126.6, 124.3, 123.9, 98.3, 61.1, 51.1, 14.3; HRMS (ESI): calcd. for $C_{26}H_{23}O_4$ S ($[M + H]^+$): 431.1312, found 431.1299.

*Ethyl 2-((3-Oxo-1-(phenylsulfonyl)-1,3-dihydroisobenzofuran-1-yl)(phenyl)methyl)acrylate (Scheme 2, **3ab**).* The residue was purified by column chromatography (silica gel, EtOAc/Petroleum ether) to afford the title compound (43 mg, 64% yield, d.r. > 19/1) as a white solid, mp: 118−119 °C (DABCO was used as catalyst). ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.86 (d, *J* = 7.8, 1H), 7.58 (t, *J* = 7.5, 3H), 7.50 (t, *J* = 7.4, 1H), 7.38 (d, *J* = 7.5, 1H), 7.31 (t, *J* = 7.8, 3H), 7.13 (d, *J* = 7.4, 2H), 7.05−6.93 (m, 3H), 6.51 (s, 1H), 6.44 (s, 1H), 5.72 (s, 1H), 4.31−4.14 (m, 2H), 1.31 (t, *J* = 7.1, 3H). ^{13}C NMR (125 MHz, $CDCl_3$): δ 167.8, 166.1, 144.6, 136.6, 136.4, 134.5, 134.4, 134.2, 130.6, 130.2, 129.8, 129.2, 129.2, 128.7, 128.3, 127.5, 126.2, 125.2, 101.7, 61.4, 45.4, 14.1; HRMS (ESI): calcd. for $C_{26}H_{23}O_6S$ ($[M + H]^+$): 463.1210, found 463.1218.

*Ethyl 2-((S)-((S)-1-Cyano-3-oxo-1,3-dihydroisobenzofuran-1-yl)(4-methoxyphenyl)methyl)acrylate (Table 1, **3b**).* The residue was purified by column chromatography (silica gel, EtOAc/Petroleum ether) to afford the title compound (73 mg, 97% yield, d.r. > 19/1) as a white solid, mp: 97−99 °C. The ee value was determined to be 97% by chiral HPLC analysis (Chiralpak AD-H, 10/90 isopropanol/hexanes, λ = 254 nm at 30 °C, flow rate = 0.5 mL/min, t_R(major) = 39.2 min, t_R(minor) = 24.8 min). $[\alpha]_D^{25}$ = −56.2 (*c* = 1.00, $CHCl_3$). ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.95 (d, *J* = 7.5 Hz, 1H), 7.72 (td, *J* = 7.5, 1.2 Hz, 1H), 7.67 (td, *J* = 7.5, 0.8 Hz, 1H), 7.55−7.48 (m, 2H), 7.29 (d, *J* = 7.0 Hz, 1H), 7.01−6.93 (m, 2H), 6.43 (s, 1H), 6.20 (s, 1H), 4.83 (s, 1H), 4.05−3.94 (m, 2H), 3.86 (s, 3H), 1.13 (t, *J* = 7.1 Hz, 3H). ^{13}C NMR (125 MHz, $CDCl_3$): δ 167.2, 166.0, 159.7, 145.1, 136.4, 134.8, 131.3, 130.8, 129.3, 127.8, 126.2, 125.0, 124.0, 115.7, 114.3, 79.6, 61.3, 55.3, 51.3, 14.0; The ee value was 98% (99%es), t_R(major) = 10.8 min, t_R(minor) = 15.0 min(Chiralpak AD-H, 20/80 isopropanol/hexanes, λ = 254 nm at 30 °C, flow rate = 0.5 mL/min); HRMS (ESI): calcd. for $C_{22}H_{20}NO_5$ ($[M + H]^+$): 378.1336, found 378.1335.

*Ethyl 2-((S)-((S)-1-Cyano-3-oxo-1,3-dihydroisobenzofuran-1-yl)(p-tolyl)methyl)acrylate (Table 1, **3c**).* The residue was purified by column chromatography (silica gel, EtOAc/Petroleum ether) to afford the title compound (71 mg, 98% yield, d.r. = 17/1) as a white solid, mp: 120−122 °C. The ee value was determined to be 96% by chiral HPLC analysis (Chiralpak AS-H, 5/95 isopropanol/hexanes, λ = 254 nm at 30 °C, flow rate = 0.5 mL/min, t_R(major) = 32.1 min, t_R(minor) = 47.4 min). $[\alpha]_D^{25}$ = −91.6 (*c* = 1.00, $CHCl_3$). ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.92 (d, *J* = 7.5 Hz, 1H), 7.70 (td, *J* = 7.6, 1.0 Hz, 1H), 7.64 (td, *J* = 7.5, 0.6 Hz, 1H), 7.46 (d, *J* = 8.1 Hz, 2H), 7.31 (d, *J* = 7.7 Hz, 1H), 7.23 (d, *J* = 7.9 Hz, 2H), 6.40 (s, 1H), 6.16 (s, 1H), 4.86 (s, 1H), 4.03−3.91 (m, 2H), 2.39 (s, 3H), 1.10 (t, *J* = 7.1

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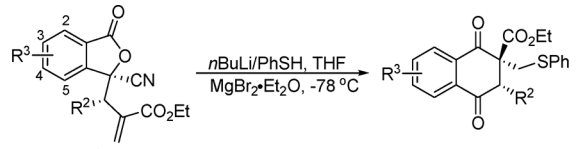
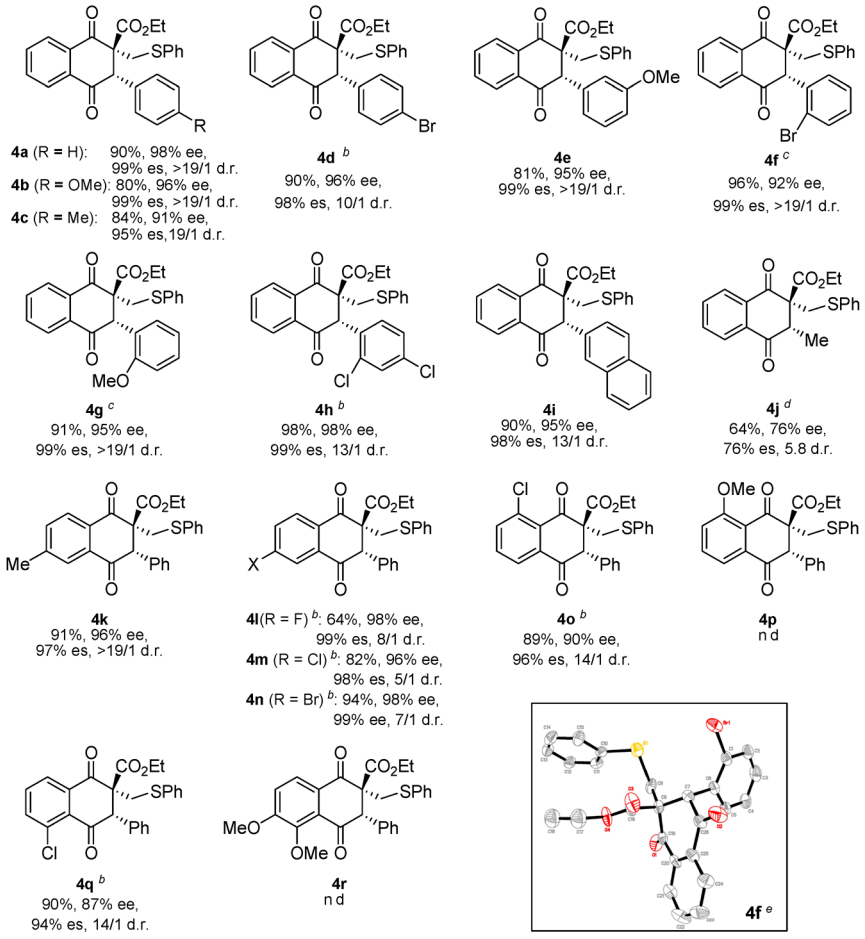
Table 3. Scope of Tandem Reactions for Functionalized Dihydroquinones[a]





[a]Reactions were performed with **3** (0.2 mmol) and $MgBr_2 \cdot Et_2O$ (0.4 mmol) in the mole ratio of **3**/PhSH/*n*BuLi = 1/1.5/1.5 in THF (2 mL) at −78 °C. Diastereomeric pure **3** were employed (d.r. > 19/1). Yields shown are of isolated products. ee values were determined by chiral HPLC analysis. es = (product ee/starting material ee) × 100%. d.r. values were determined by ^{1}H NMR analysis. [b]$MgBr_2 \cdot Et_2O$ (0.6 mmol) was added. [c]Without addition of $MgBr_2 \cdot Et_2O$. [d]**3j** (d.r. = 2.6/1) was used. [e]X-ray structure of compound **4f**.

Hz, 3H). ^{13}C NMR (125 MHz, $CDCl_3$): δ 167.2, 165.9, 145.1, 138.5, 136.2, 134.8, 133.0, 131.3, 129.8, 129.7, 129.4, 128.8, 126.1, 125.0, 124.0, 115.7, 79.5, 61.4, 51.5, 21.2, 14.0; HRMS (ESI): calcd. for $C_{22}H_{20}NO_4$ ($[M + H]^+$): 362.1387, found 362.1377.

*Ethyl 2-((S)-(4-Bromophenyl)((S)-1-cyano-3-oxo-1,3-dihydroisobenzofuran-1-yl)methyl)acrylate (Table 1, **3d**).* The residue was purified by column chromatography (silica gel, EtOAc/Petroleum ether) to afford the title compound (85 mg, 99% yield, d.r. > 19/1) as a white solid, mp: 87−88 °C. The ee value was determined to be 98% by chiral HPLC analysis (Chiralpak AD-H, 10/90 isopropanol/hexanes, λ = 254 nm at 30 °C, flow rate = 0.5 mL/min, t_R(major) = 39.0 min, t_R(minor) = 22.2 min). $[\alpha]_D^{25}$ = −34.2 (c = 1.00, $CHCl_3$). ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.93 (d, J = 7.6 Hz, 1H), 7.74 (t, J = 7.5 Hz, 1H), 7.67 (t, J = 7.5 Hz, 1H), 7.57 (d, J = 8.4 Hz, 2H), 7.49 (d, J = 8.4 Hz, 2H), 7.43 (d, J = 7.7 Hz, 1H), 6.39 (s, 1H), 6.07 (s, 1H), 4.96 (s, 1H), 4.02−3.88 (m, 2H), 1.09 (t, J = 7.1 Hz, 3H). ^{13}C NMR (125 MHz, $CDCl_3$): δ 167.0, 165.7, 144.6, 135.5, 135.4, 135.1, 132.2, 131.5, 131.1, 130.5, 126.3, 125.0, 123.8, 122.9, 115.4, 79.0, 61.5, 51.1, 14.0; HRMS (ESI): calcd. for $C_{21}H_{17}BrNO_4$ ($[M + H]^+$): 426.0335, found 426.0333.

*Ethyl 2-((S)-((S)-1-Cyano-3-oxo-1,3-dihydroisobenzofuran-1-yl)(3-methoxyphenyl)methyl)acrylate (Table 1, **3e**).* The residue was purified by column chromatography (silica gel, EtOAc/Petroleum ether) to afford the title compound (75 mg, 99% yield, d.r. > 19/1) as a white solid, mp: 143−144 °C. The ee value was determined to be 96% by chiral HPLC analysis (Chiralpak AS-H, 10/90 isopropanol/hexanes, λ = 254 nm at 30 °C, flow rate = 0.5 mL/min, t_R(major) = 31.1 min, t_R(minor) = 46.3 min). $[\alpha]_D^{25}$ = −80.8 (c = 1.00, $CHCl_3$). ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.93 (d, J = 7.5 Hz, 1H), 7.71 (t, J = 7.2 Hz, 1H), 7.65 (t, J = 7.4 Hz, 1H), 7.34 (t, J = 7.8 Hz, 2H), 7.18 (d, J = 7.7 Hz, 1H), 7.12 (d, J = 1.8 Hz, 1H), 6.94 (dd, J = 8.2, 2.2 Hz, 1H), 6.41 (s, 1H), 6.17 (s, 1H), 4.89 (s, 1H), 4.04−3.91 (m, 2H), 3.84 (s, 3H), 1.10 (t, J = 7.1 Hz, 3H). ^{13}C NMR (125 MHz, $CDCl_3$): δ 167.2, 165.9, 159.9, 144.9, 137.6, 135.9, 134.9, 131.4, 130.2, 130.0, 126.2, 125.0, 124.0, 121.7, 115.6, 115.2, 113.9, 79.3, 61.4, 55.3, 51.7, 14.0; HRMS (ESI): calcd. for $C_{22}H_{20}NO_5$ ($[M + H]^+$): 378.1336, found 378.1332.

*Ethyl 2-((2-Bromophenyl)(1-cyano-3-oxo-1,3-dihydroisobenzofuran-1-yl)methyl)acrylate (Table 1, **3f**).* The residue was purified by column chromatography (silica gel, EtOAc/Petroleum ether) to afford the title compound (84 mg, 99% yield, d.r. > 19/1) as a white

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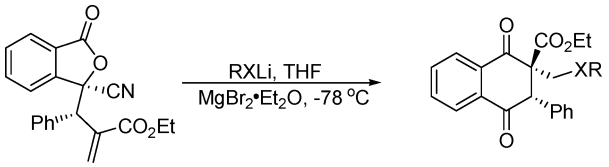
Table 4. Scope of Tandem Reactions[a]

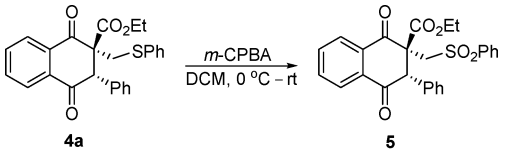


3a 4

entry	R	X	t (h)	yield (%)[b]	d.r.[c]	es (%)[d]
1	4-MeOC$_6$H$_5$	S	2	3	80 (**4s**)	10/1
2	2-BrC$_6$H$_5$	S	2	12	63 (**4t**)	4.5/1
3	PhCH$_2$	S	2	2	83 (**4u**)	7.5/1
4	Ph	Se	2.5	12	64 (**4v**)	>19/1

[a]Reactions were performed with **3a** (0.2 mmol) and $MgBr_2{\cdot}Et_2O$ (0.4 mmol) in the mole ratio of **3a**/PhSH/*n*BuLi = 1/1.5/1.5 in THF (2 mL) at −78 °C. Enantioenriched **3a** was employed (d.r. > 19/1). [b]Isolated yields. [c]Determined by ^{1}H NMR analysis. [d]es = (product ee/starting material ee) × 100%. ee values were determined by chiral HPLC analysis.

Scheme 3. Synthetic Transformation



4a 98% ee, d.r.>19/1 **5** 84% yield, 96% ee, d.r.>19/1

solid, mp: 109−110 °C. The ee value was determined to be 93% by chiral HPLC analysis (Chiralpak AS-H, 5/95 isopropanol/hexanes, λ = 254 nm at 30 °C, flow rate = 0.5 mL/min, t_R(major) = 45.6 min, t_R(minor) = 55.6 min). $[\alpha]_D^{25}$ = −133.4 (c = 1.00, $CHCl_3$). ^{1}H NMR (500 MHz, $CDCl_3$): δ 8.08 (dd, J = 7.8, 1.2 Hz, 1H), 7.92 (d, J = 7.6 Hz, 1H), 7.74 (t, J = 7.5 Hz, 1H), 7.70−7.59 (m, 2H), 7.49 (dd, J = 11.2, 4.1 Hz, 1H), 7.42 (d, J = 7.7 Hz, 1H), 7.27 (dd, J = 15.3, 1.3 Hz, 1H), 6.51 (s, 1H), 6.06 (s, 1H), 5.44 (s, 1H), 3.97−3.87 (m, 2H), 1.06 (t, J = 7.1 Hz, 3H). ^{13}C NMR (125 MHz, $CDCl_3$): δ 167.0, 165.1, 144.5, 136.2, 134.9, 134.8, 133.6, 131.7, 131.4, 130.1, 130.0, 128.1, 126.1, 126.0, 124.9, 124.6, 115.5, 78.6, 61.3, 51.1, 13.9; HRMS (ESI): calcd. for $C_{21}H_{17}BrNO_4$ ([M + H]$^+$): 426.0335, found 426.0331.

*Ethyl 2-((S)-((S)-1-Cyano-3-oxo-1,3-dihydroisobenzofuran-1-yl)(2-methoxyphenyl)methyl)acrylate (Table 1, **3g**).* The residue was purified by column chromatography (silica gel, EtOAc/Petroleum ether) to afford the title compound (64 mg, 89% yield, d.r. > 19/1) as a white solid, mp: 117−118 °C. The ee value was determined to be 96% by chiral HPLC analysis (Chiralpak AS-H, 20/80 isopropanol/hexanes, λ = 254 nm at 30 °C, flow rate = 0.5 mL/min, t_R(major) = 25.6 min, t_R(minor) = 38.2 min). $[\alpha]_D^{25}$ = −560.0 (c = 0.50, $CHCl_3$). ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.95−7.87 (m, 2H), 7.70 (t, J = 7.3 Hz, 1H), 7.63 (t, J = 7.4 Hz, 1H), 7.42 (d, J = 7.7 Hz, 1H), 7.39−7.33 (m, 1H), 7.09 (t, J = 7.5 Hz, 1H), 6.88 (d, J = 8.2 Hz, 1H), 6.37 (s, 1H), 6.03 (s, 1H), 5.47 (s, 1H), 3.99−3.68 (m, 2H), 3.68 (s, 3H), 1.07 (t, J = 7.1 Hz, 3H). ^{13}C NMR (125 MHz, $CDCl_3$): δ 167.4, 165.6, 156.8, 145.2, 136.1, 134.6, 131.1, 130.3, 129.5, 129.0, 125.9, 125.3, 125.1, 124.3, 120.9, 115.8, 110.7, 79.0, 61.0, 55.3, 44.4, 14.0; HRMS (ESI): calcd. for $C_{22}H_{20}NO_5$ ([M + H]$^+$): 378.1336, found 378.1335.

*Ethyl 2-((R)-((S)-1-Cyano-3-oxo-1,3-dihydroisobenzofuran-1-yl)(2,4-dichlorophenyl)methyl)acrylate (Table 1, **3h**).* The residue was purified by column chromatography (silica gel, EtOAc/Petroleum ether) to afford the title compound (83 mg, 99% yield, d.r. > 19/1) as a white solid, mp: 132−133 °C. The ee value was determined to be 99% by chiral HPLC analysis (Chiralpak AS-H, 10/90 isopropanol/hexanes, λ = 254 nm at 30 °C, flow rate = 0.5 mL/min, t_R(major) = 18.4 min, t_R(minor) = 20.2 min). $[\alpha]_D^{25}$ = −84.2 (c = 1.00, $CHCl_3$). ^{1}H NMR (500 MHz, $CDCl_3$): δ 8.06 (d, J = 8.5 Hz, 1H), 7.92 (d, J = 7.6 Hz, 1H), 7.81−7.74 (m, 1H), 7.67 (t, J = 7.5 Hz, 1H), 7.57 (d, J = 7.8 Hz, 1H), 7.47 (d, J = 2.1 Hz, 1H), 7.43 (dd, J = 8.5, 2.2 Hz, 1H), 6.44 (s, 1H), 5.94 (s, 1H), 5.49 (s, 1H), 3.97−3.85 (m, 2H), 1.06 (t, J = 7.1 Hz, 3H). ^{13}C NMR (125 MHz, $CDCl_3$): δ 166.8, 165.0, 144.1, 135.6, 135.1, 135.0, 134.4, 133.6, 132.1, 131.5, 130.6, 130.0, 127.8, 126.1, 124.9, 124.4, 115.4, 78.2, 61.4, 47.9, 13.9; HRMS (ESI): calcd. for $C_{21}H_{16}Cl_2NO_4$ ([M + H]$^+$): 416.0451, found 416.0436.

*Ethyl 2-((S)-((S)-1-Cyano-3-oxo-1,3-dihydroisobenzofuran-1-yl)(naphthalen-2-yl)methyl)acrylate (Table 1, **3i**).* The residue was purified by column chromatography (silica gel, EtOAc/Petroleum ether) to afford the title compound (74 mg, 93% yield, d.r. > 19/1) as a white solid, mp: 147−148 °C. The ee value was determined to be 97% by chiral HPLC analysis (Chiralpak AD-H, 10/90 isopropanol/hexanes, λ = 254 nm at 30 °C, flow rate = 0.5 mL/min, t_R(major) = 47.2 min, t_R(minor) = 34.2 min). $[\alpha]_D^{25}$ = −540.8 (c = 1.00, $CHCl_3$). ^{1}H NMR (500 MHz, $CDCl_3$): δ 8.15 (s, 1H), 7.97−7.84 (m, 4H), 7.71−7.65 (m, 2H), 7.61 (dd, J = 8.5, 1.8 Hz, 1H), 7.58−7.50 (m, 2H), 7.37 (d, J = 7.6 Hz, 1H), 6.43 (s, 1H), 6.19 (s, 1H), 5.13 (s, 1H), 4.02−3.90 (m, 2H), 1.09 (t, J = 7.1 Hz, 3H). ^{13}C NMR (125 MHz, $CDCl_3$): δ 167.3, 166.0, 145.0, 136.0, 134.9, 133.7, 133.3, 133.0, 131.4, 130.5, 128.8, 128.6, 128.3, 127.6, 127.0, 126.7, 126.6, 126.2, 125.1, 124.0, 115.7, 79.3, 61.4, 51.9, 14.0; The ee value was 98% (99% es), t_R(major) = 10.8 min, t_R(minor) = 15.0 min (Chiralpak AD-H, 20/80 isopropanol/hexanes, λ = 254 nm at 30 °C, flow rate = 0.5 mL/min); HRMS(ESI) calcd. for $C_{25}H_{20}NO_4$ ([M + H]$^+$) 398.1387, found 398.1360.

*Ethyl 2-((S)-((S)-1-Cyano-6-methyl-3-oxo-1,3-dihydroisobenzofuran-1-yl)(phenyl)methyl)acrylate (Table 1, **3k**).* The residue was purified by column chromatography (silica gel, EtOAc/Petroleum ether) to afford the title compound (72 mg, 99% yield, d.r. > 19/1) as a colorless oil. The ee value was determined to be 93% by chiral HPLC analysis (Chiralpak AS-H, 5/95 isopropanol/hexanes, λ = 254 nm at 30 °C, flow rate = 0.5 mL/min, t_R(major) = 30.1 min, t_R(minor) = 46.7 min). $[\alpha]_D^{25}$ = −218.0 (c = 0.50, $CHCl_3$). ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.80 (d, J = 7.8 Hz, 1H), 7.58 (d, J = 6.7 Hz, 2H), 7.47−7.36 (m, 4H), 7.08 (s, 1H), 6.40 (s, 1H), 6.14 (s, 1H), 4.89 (s, 1H), 4.03−3.92 (m, 2H), 2.46 (s, 3H), 1.10 (t, J = 7.1 Hz, 3H). ^{13}C NMR (125 MHz, $CDCl_3$): δ 167.3, 166.0, 146.6, 145.5, 136.2, 136.0, 132.4, 129.9, 129.5, 128.9, 128.6, 125.9, 124.2, 122.4, 115.8, 79.1, 61.4, 51.8, 22.1, 13.9; HRMS (ESI): calcd. for $C_{22}H_{20}NO_4$ ([M + H]$^+$): 362.1387, found 362.1385.

*Ethyl 2-((S)-((S)-1-Cyano-6-fluoro-3-oxo-1,3-dihydroisobenzofuran-1-yl)(phenyl)methyl)acrylate (Table 1, **3l**).* The residue was purified by column chromatography (silica gel, EtOAc/Petroleum ether) to afford the title compound (72 mg, 99% yield, d.r. > 19/1) as a white solid, mp: 78−79 °C. The ee value was determined to be 97% by chiral HPLC analysis (Chiralpak AS-H, 5/95 isopropanol/hexanes, λ = 254 nm at 30 °C, flow rate = 0.5 mL/min, t_R(major) = 34.3 min, t_R(minor) = 50.3 min). $[\alpha]_D^{25}$ = −140.0 (c = 1.00, $CHCl_3$). ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.93 (dd, J = 8.4, 4.6 Hz, 1H), 7.57 (d, J = 6.7 Hz, 2H), 7.49−7.38 (m, 3H), 7.35 (td, J = 8.4, 1.7 Hz, 1H), 6.94 (dd, J = 7.3, 1.3 Hz, 1H), 6.46 (s, 1H), 6.18 (s, 1H), 4.87 (s, 1H), 4.13−3.92 (m, 2H), 1.13 (t, J = 7.1 Hz, 3H). ^{13}C NMR (126 MHz, $CDCl_3$): δ 165.9, 165.8, 166.5 (d, J = 260.0 Hz), 147.7 (d, J = 10.2 Hz), 135.8, 135.6, 130.2, 129.4, 129.1, 128.8, 128.6 (d, J = 10.2 Hz), 121.1 (d, J = 2.0 Hz), 119.7 (d, J = 24.0 Hz), 115.1, 111.7 (d, J = 25.7 Hz), 78.7, 61.6, 51.8, 14.0; HRMS (ESI): calcd. for $C_{21}H_{17}FNO_4$ ([M + H]$^+$): 366.1136, found 366.1133.

*Ethyl 2-((S)-((S)-6-Chloro-1-cyano-3-oxo-1,3-dihydroisobenzofuran-1-yl)(phenyl)methyl)acrylate (Table 1, **3m**).* The residue was purified by column chromatography (silica gel, EtOAc/Petroleum ether) to afford the title compound (76 mg, 99% yield, d.r. > 19/1) as a white solid, mp: 111−112 °C. The ee value was determined to be 94% by chiral HPLC analysis (Chiralpak AS-H, 5/95 isopropanol/hexanes, λ = 254 nm at 30 °C, flow rate = 0.5 mL/min, t_R(major) = 29.6 min, t_R(minor) = 48.1 min). $[\alpha]_D^{25}$ = −69.4 (c = 1.00, $CHCl_3$). ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.85 (d, J = 8.2 Hz, 1H), 7.62 (d, J = 8.2 Hz, 1H), 7.57 (d, J = 7.4 Hz, 2H), 7.49−7.38 (m, 3H), 7.25 (s, 1H), 6.44 (s, 1H), 6.16 (s, 1H), 4.88 (s, 1H), 4.12−3.94 (m, 2H), 1.14 (t, J = 7.1 Hz, 3H). ^{13}C NMR (125 MHz, $CDCl_3$): δ 166.0, 165.8, 146.4, 141.8, 135.8, 135.7, 132.1, 130.3, 129.4, 129.1, 128.8, 127.2, 124.5,

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123.4, 115.1, 78.8, 61.6, 51.8, 14.0; HRMS (ESI): calcd. for $C_{21}H_{17}ClNO_4$ ([M + H]$^+$): 382.0841, found 382.0833.

*Ethyl 2-((S)-((S)-6-Bromo-1-cyano-3-oxo-1,3-dihydroisobenzofuran-1-yl)(phenyl)methyl)acrylate (Table 1, **3n**).* The residue was purified by column chromatography (silica gel, EtOAc/Petroleum ether) to afford the title compound (83 mg, 98% yield, d.r. > 19/1) as a white solid, mp: 112−123 °C. The ee value was determined to be 99% by chiral HPLC analysis (Chiralpak AS-H, 5/95 isopropanol/hexanes, λ = 254 nm at 30 °C, flow rate = 0.5 mL/min, t_R(major) = 25.9 min, t_R(minor) = 42.3 min). $[\alpha]_D^{25}$ = −64.4 (c = 1.00, $CHCl_3$). ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.78 (s, 2H), 7.56 (d, J = 6.6 Hz, 2H), 7.49−7.37 (m, 4H), 6.44 (s, 1H), 6.15 (s, 1H), 4.87 (s, 1H), 4.14−3.92 (m, 2H), 1.14 (t, J = 7.1 Hz, 3H). ^{13}C NMR (125 MHz, $CDCl_3$): δ 166.2, 165.8, 146.4, 135.8, 135.7, 135.0, 130.3, 130.2, 129.4, 129.1, 128.8, 127.5, 127.3, 123.9, 120.0, 115.1, 78.7, 61.6, 51.9, 14.0; HRMS (ESI): calcd. For $C_{21}H_{17}BrNO_4$ ([M + H]$^+$): 426.0335, found 426.0337.

*Ethyl 2-((S)-((S)-4-Chloro-1-cyano-3-oxo-1,3-dihydroisobenzofuran-1-yl)(phenyl)methyl)acrylate (Table 1, **3o**).* The residue was purified by column chromatography (silica gel, EtOAc/Petroleum ether) to afford the title compound (72 mg, 94% yield, d.r. > 19/1) as a white solid, mp: 119−120 °C. The ee value was determined to be 94% by chiral HPLC analysis (Chiralpak OD-H, 20/80 isopropanol/hexanes, λ = 254 nm at 30 °C, flow rate = 0.5 mL/min, t_R(major) = 17.1 min, t_R(minor) = 26.9 min). $[\alpha]_D^{25}$ = −267.0 (c = 1.00, $CHCl_3$). ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.66−7.54 (m, 4H), 7.46−7.37 (m, 3H), 7.23 (d, J = 7.0 Hz, 1H), 6.45 (s, 1H), 6.17 (s, 1H), 4.92 (s, 1H), 4.06−3.92 (m, 2H), 1.11 (t, J = 7.1 Hz, 3H). ^{13}C NMR (125 MHz, $CDCl_3$): δ 165.8, 164.1, 147.0, 135.9, 135.8, 135.8, 133.9, 132.7, 130.4, 129.4, 129.1, 128.7, 122.4, 121.8, 115.2, 78.2, 61.5, 51.7, 14.0; HRMS (ESI): calcd. for $C_{21}H_{17}ClNO_4$ ([M + H]$^+$): 382.0841, found 382.0844.

*Ethyl 2-((S)-((S)-1-Cyano-4-methoxy-3-oxo-1,3-dihydroisobenzofuran-1-yl)(phenyl)methyl)acrylate (Table 1, **3p**).* The residue was purified by column chromatography (silica gel, EtOAc/Petroleum ether) to afford the title compound (76 mg, 99% yield, d.r. > 19/1) as a white solid, mp: 101−102 °C. The ee value was determined to be 98% by chiral HPLC analysis (Chiralpak AS-H, 20/80 isopropanol/hexanes, λ = 254 nm at 30 °C, flow rate = 0.5 mL/min, t_R(major) = 32.9 min, t_R(minor) = 37.4 min). $[\alpha]_D^{25}$ = −27.6 (c = 1.00, $CHCl_3$). ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.64 (t, J = 8.0 Hz, 1H), 7.60 (d, J = 6.9 Hz, 2H), 7.45−7.34 (m, 3H), 7.04 (d, J = 8.3 Hz, 1H), 6.91 (d, J = 7.6 Hz, 1H), 6.40 (s, 1H), 6.14 (s, 1H), 4.94 (s, 1H), 4.07−3.94 (m, 5H), 1.11 (t, J = 7.1 Hz, 3H). ^{13}C NMR (125 MHz, $CDCl_3$): δ 165.9, 165.2, 158.7, 147.3, 137.2, 136.4, 135.9, 130.2, 129.4, 128.9, 128.5, 115.7, 115.3, 112.9, 112.4, 78.5, 61.4, 56.3, 51.6, 14.0; HRMS (ESI): calcd. for $C_{22}H_{20}NO_5$ ([M + H]$^+$): 378.1336, found 378.1332.

*Ethyl 2-((S)-((S)-7-Chloro-1-cyano-3-oxo-1,3-dihydroisobenzofuran-1-yl)(phenyl)methyl)acrylate (Table 1, **3q**).* The residue was purified by column chromatography (silica gel, EtOAc/Petroleum ether) to afford the title compound (71 mg, 93% yield, d.r. > 19/1) as a white solid, mp: 107−108 °C. The ee value was determined to be 93% by chiral HPLC analysis (Chiralpak OD-H, 10/90 isopropanol/hexanes, λ = 254 nm at 30 °C, flow rate = 0.5 mL/min, t_R(major) = 27.1 min, t_R(minor) = 66.9 min). $[\alpha]_D^{25}$ = −154.6 (c = 1.00, $CHCl_3$). ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.84 (d, J = 7.5 Hz, 1H), 7.76 (d, J = 7.8 Hz, 1H), 7.69 (d, J = 7.4 Hz, 2H), 7.63 (t, J = 7.7 Hz, 1H), 7.45 (t, J = 7.4 Hz, 2H), 7.39 (t, J = 7.3 Hz, 1H), 6.35 (s, 1H), 5.89 (s, 1H), 5.57 (s, 1H), 3.89 (q, J = 7.1 Hz, 2H), 1.07 (t, J = 7.1 Hz, 3H). ^{13}C NMR (125 MHz, $CDCl_3$): δ 166.1, 165.5, 141.0, 137.0, 136.0, 135.1, 133.1, 133.0, 130.8, 129.1, 128.4, 127.9, 124.5, 113.5, 79.0, 61.4, 48.6, 14.0; HRMS (ESI): calcd. for $C_{21}H_{17}ClNO_4$ ([M + H]$^+$): 382.0841, found 382.0841.

*Ethyl 2-((S)-((S)-1-Cyano-6,7-dimethoxy-3-oxo-1,3-dihydroisobenzofuran-1-yl)(phenyl)methyl)acrylate (Table 1, **3r**).* The residue was purified by column chromatography (silica gel, EtOAc/Petroleum ether) to afford the title compound (72 mg, 90% yield, d.r. > 19/1) as a white solid, mp: 79−80 °C. The ee value was determined to be 96% by chiral HPLC analysis (Chiralpak AS-H, 20/80 isopropanol/hexanes, λ = 254 nm at 30 °C, flow rate = 0.5 mL/min, t_R(major) = 33.5 min, t_R(minor) = 37.5 min). $[\alpha]_D^{25}$ = −134.8 (c = 1.00, $CHCl_3$). ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.68 (d, J = 7.5 Hz, 2H), 7.58 (d, J = 8.3 Hz, 1H), 7.42 (t, J = 7.5 Hz, 2H), 7.36 (t, J = 7.3 Hz, 1H), 7.15 (d, J = 8.3 Hz, 1H), 6.28 (s, 1H), 5.81 (s, 1H), 5.43 (s, 1H), 4.15 (s, 3H), 3.98 (s, 3H), 3.96−3.85 (m, 2H), 1.08 (t, J = 7.1 Hz, 3H). ^{13}C NMR (125 MHz, $CDCl_3$): δ 167.0, 165.7, 157.8, 144.0, 137.7, 137.2, 135.8, 131.8, 129.2, 128.9, 128.1, 121.7, 118.0, 115.9, 115.6, 77.7, 61.2, 61.0, 56.6, 49.6, 13.9; HRMS (ESI): calcd. for $C_{23}H_{22}NO_6$ ([M + H]$^+$): 408.1442, found 408.1444.

General Procedure of Tandem Reaction for Functionalized Dihydroquinones 4. To a solution of the $MgBr_2{\cdot}Et_2O$ (0.4 mmol) and PhSH (0.3 mmol) in THF (1 mL) was added nBuLi (0.3 mmol) at −78 °C. After stirring at −78 °C for 20 min, compound **3** (0.2 mmol) in THF (1 mL) was added dropwise. The reaction was monitored by TLC. Upon completion, the mixture was poured into saturated ammonium chloride (10 mL) and then extracted with ethyl acetate (4 × 20 mL). Combined organic layers were washed with brine and dried over Na_2SO_4, filtered, and concentrated *in vacuo*. The crude mixture was purified by column chromatography (silica gel, EtOAc/Petroleum ether (60−90 °C)) to provide the desired product **4**.

*Ethyl (2R,3S)-1,4-Dioxo-3-phenyl-2-((phenylthio)methyl)-1,2,3,4-tetrahydronaphthalene-2-carboxylate (Table 3, **4a**).* The residue was purified by column chromatography (silica gel, EtOAc/Petroleum ether) to afford the title compound (77 mg, 90% yield, d.r. > 19/1) as a white solid, mp: 112−114 °C. The ee value was determined to be 98% (99% es) by chiral HPLC analysis (Chiralpak AD-H, 10/90 isopropanol/hexanes, λ = 254 nm at 30 °C, flow rate = 0.5 mL/min, t_R(major) = 48.9 min, t_R(minor) = 60.9 min). $[\alpha]_D^{25}$ = −253 (c = 1.00, $CHCl_3$). ^{1}H NMR (500 MHz, $CDCl_3$): δ 8.17 (dd, J = 5.9, 3.0 Hz, 1H), 8.08 (dd, J = 5.8, 3.1 Hz, 1H), 7.84−7.76 (m, 2H), 7.32 (d, J = 7.3 Hz, 2H), 7.27−7.16 (m, 6H), 7.08 (d, J = 6.8 Hz, 2H), 5.07 (s, 1H), 3.95 (d, J = 13.7 Hz, 1H), 3.91−3.85 (m, 1H), 3.75−3.68 (m, 1H), 3.09 (d, J = 13.7 Hz, 1H), 0.92 (t, J = 7.1 Hz, 3H). ^{13}C NMR (125 MHz, $CDCl_3$): δ 192.7, 192.6, 168.5, 135.0, 135.0, 134.8, 134.5, 134.4, 133.6, 131.0, 129.2, 129.1, 128.8, 128.2, 127.9, 127.1, 126.9, 65.5, 62.6, 59.1, 35.9, 13.5; HRMS (ESI): calcd. for $C_{26}H_{23}O_4S$ ([M + H]$^+$): 431.1312, found 431.1309.

*Ethyl (2R,3S)-3-(4-Methoxyphenyl)-1,4-dioxo-2-((phenylthio)-methyl)-1,2,3,4-tetrahydronaphthalene-2-carboxylate (Table 3, **4b**).* The residue was purified by column chromatography (silica gel, EtOAc/Petroleum ether) to afford the title compound (74 mg, 80% yield, d.r. > 19/1) as a white solid, mp: 70−72 °C. The ee value was determined to be 96% (99% es) by chiral HPLC analysis (Chiralpak AD-H, 10/90 isopropanol/hexanes, λ = 254 nm at 30 °C, flow rate = 0.5 mL/min, t_R(major) = 56.9 min, t_R(minor) = 72.2 min). $[\alpha]_D^{25}$ = −291.6 (c = 1.00, $CHCl_3$). ^{1}H NMR (500 MHz, $CDCl_3$): δ 8.18−8.11 (m, 1H), 8.07−8.01 (m, 1H), 7.81−7.73 (m, 2H), 7.33−7.28 (m, 2H), 7.24−7.19 (m, 2H), 7.19−7.14 (m, 1H), 6.97 (d, J = 8.8 Hz, 2H), 6.72 (d, J = 8.8 Hz, 2H), 4.98 (s, 1H), 3.90 (d, J = 13.7 Hz, 1H), 3.89−3.81 (m, 1H), 3.74 (s, 3H), 3.73−3.68 (m, 1H), 3.09 (d, J = 13.6 Hz, 1H), 0.89 (t, J = 7.1 Hz, 3H). ^{13}C NMR (125 MHz, $CDCl_3$): δ 192.9, 192.8, 168.5, 159.3, 135.1, 134.9, 134.8, 134.5, 134.4, 130.9, 130.3, 128.8, 127.9, 127.1, 126.9, 125.5, 114.6, 65.6, 62.5, 58.3, 55.2, 35.9, 13.5; HRMS (ESI): calcd. for $C_{27}H_{25}O_5S$ ([M + H]$^+$): 461.1417, found 461.1417.

*Ethyl (2R,3S)-1,4-Dioxo-2-((phenylthio)methyl)-3-(p-tolyl)-1,2,3,4-tetrahydronaphthalene-2-carboxylate (Table 3, **4c**).* The residue was purified by column chromatography (silica gel, EtOAc/Petroleum ether) to afford the title compound (75 mg, 84% yield, d.r. > 19/1) as a white solid, mp: 91−92 °C. The ee value was determined to be 91% (95% es) by chiral HPLC analysis (Chiralpak AD-H, 10/90 isopropanol/hexanes, λ = 254 nm at 30 °C, flow rate = 0.5 mL/min, t_R(major) = 39.6 min, t_R(minor) = 42.9 min). $[\alpha]_D^{25}$ = −280.8 (c = 1.00, $CHCl_3$). ^{1}H NMR (500 MHz, $CDCl_3$): δ 8.18−8.10 (m, 1H), 8.08−8.02 (m, 1H), 7.83−7.68 (m, 2H), 7.30 (d, J = 7.5 Hz, 2H), 7.21 (t, J = 7.3 Hz, 2H), 7.19−7.13 (m, 1H), 7.00 (d, J = 7.8 Hz, 2H), 6.94 (d, J = 7.8 Hz, 2H), 5.00 (s, 1H), 3.91 (d, J = 13.7 Hz, 1H), 3.88−3.82 (m, 1H), 3.71−3.65 (m, 1H), 3.08 (d, J = 13.7 Hz, 1H), 2.25 (s, 3H), 0.89 (t, J = 7.1 Hz, 3H). ^{13}C NMR (125 MHz, $CDCl_3$): δ 192.8, 192.7, 168.5, 138.0, 135.1, 134.9, 134.5, 134.3, 130.9, 130.5, 129.9, 129.0,

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128.8, 127.9, 127.1, 126.8, 65.5, 62.5, 58.8, 35.9, 21.0, 13.5; HRMS (ESI): calcd. for $C_{27}H_{25}O_4S$ ([M + H]$^+$): 445.1468, found 445.1456.

*Ethyl (2R,3S)-3-(4-Bromophenyl)-1,4-dioxo-2-((phenylthio)-methyl)-1,2,3,4-tetrahydronaphthalene-2-carboxylate (Table 3, **4d**).* The residue was purified by column chromatography (silica gel, EtOAc/Petroleum ether) to afford the title compound (91 mg, 90% yield, d.r. = 10/1) as a white solid, mp: 102−104 °C. The ee value was determined to be 96% (98% es) by chiral HPLC analysis (Chiralpak AD-H, 10/90 isopropanol/hexanes, λ = 254 nm at 30 °C, flow rate = 0.5 mL/min, t_R(major) = 60.2 min, t_R(minor) = 65.3 min). $[\alpha]_D^{25}$ = −268.4 (c = 1.00, $CHCl_3$). ^{1}H NMR (500 MHz, $CDCl_3$): δ 8.19−8.09 (m, 1H), 8.09−7.98 (m, 1H), 7.78 (dd, J = 8.9, 5.4 Hz, 2H), 7.30 (dd, J = 15.8, 7.8 Hz, 4H), 7.20 (m, 3H), 6.93 (d, J = 8.3 Hz, 2H), 5.01 (s, 1H), 3.91 (d, J = 13.8 Hz, 1H), 3.89−3.81 (m, 1H), 3.75−3.68 (m, 1H), 3.07 (d, J = 13.8 Hz, 1H), 0.91 (t, J = 7.1 Hz, 3H). ^{13}C NMR (125 MHz, $CDCl_3$): δ 192.4, 192.0, 168.3, 135.1, 134.7, 134.6, 134.5, 134.3, 132.6, 132.3, 131.0, 130.8, 128.9, 127.9, 127.2, 127.0, 122.4, 65.4, 62.7, 58.4, 35.8, 13.5; HRMS (ESI): calcd. for $C_{26}H_{22}BrO_4S$ ([M + H]$^+$): 509.0417, found 509.0414.

*Ethyl (2R,3S)-3-(3-Methoxyphenyl)-1,4-dioxo-2-((phenylthio)-methyl)-1,2,3,4-tetrahydronaphthalene-2-carboxylate (Table 3, **4e**).* The residue was purified by column chromatography (silica gel, EtOAc/Petroleum ether) to afford the title compound (75 mg, 81% yield, d.r. > 19/1) as a white solid, mp: 103−105 °C. The ee value was determined to be 95% (99% es) by chiral HPLC analysis (Chiralpak AD-H, 10/90 isopropanol/hexanes, λ = 254 nm at 30 °C, flow rate = 0.5 mL/min, t_R(major) = 63.4 min, t_R(minor) = 77.3 min). $[\alpha]_D^{25}$ = −258.6 (c = 1.00, $CHCl_3$). ^{1}H NMR (500 MHz, $CDCl_3$): δ 8.18−8.12 (m, 1H), 8.08−8.01 (m, 1H), 7.81−7.72 (m, 2H), 7.34−7.28 (m, 2H), 7.21 (t, J = 7.3 Hz, 2H), 7.16 (t, J = 7.2 Hz, 1H), 7.09 (t, J = 8.0 Hz, 1H), 6.75 (dd, J = 8.3, 1.7 Hz, 1H), 6.67 (s, 1H), 6.57 (d, J = 7.7 Hz, 1H), 5.01 (s, 1H), 3.93 (d, J = 13.7 Hz, 1H), 3.87−3.81 (m, 1H), 3.70−3.63 (m, 1H), 3.67 (s, 3H), 3.09 (d, J = 13.7 Hz, 1H), 0.88 (t, J = 7.1 Hz, 3H). ^{13}C NMR (125 MHz, $CDCl_3$): δ 192.5, 192.4, 168.4, 159.9, 135.1, 135.0, 134.9, 134.8, 134.5, 134.4, 130.9, 130.1, 128.8, 127.9, 127.1, 126.8, 120.9, 115.3, 113.7, 65.5, 62.6, 59.1, 55.1, 35.9, 13.4; HRMS (ESI): calcd. for $C_{27}H_{25}O_5S$ ([M + H]$^+$): 461.1417, found 461.1411.

*Ethyl (2R,3R)-3-(2-Bromophenyl)-1,4-dioxo-2-((phenylthio)-methyl)-1,2,3,4-tetrahydronaphthalene-2-carboxylate (Table 3, **4f**).* The residue was purified by column chromatography (silica gel, EtOAc/Petroleum ether) to afford the title compound (98 mg, 96% yield, d.r. > 19/1) as a white solid, mp: 83−84 °C. The ee value was determined to be 92% (99% es) by chiral HPLC analysis (Chiralpak AD-H, 20/80 isopropanol/hexanes, λ = 254 nm at 30 °C, flow rate = 0.5 mL/min, t_R(major) = 24.3 min, t_R(minor) = 36.3 min). $[\alpha]_D^{25}$ = −282.8 (c = 1.00, $CHCl_3$). ^{1}H NMR (500 MHz, $CDCl_3$): δ 8.14−8.10 (m, 1H), 8.08 (dd, J = 5.6, 3.3 Hz, 1H), 7.79−7.74 (m, 2H), 7.66 (dd, J = 5.9, 3.4 Hz, 1H), 7.31−7.27 (m, 2H), 7.20 (dd, J = 10.1, 4.7 Hz, 2H), 7.17−7.12 (m, 1H), 7.08 (dd, J = 5.9, 3.5 Hz, 2H), 6.90−6.78 (m, 1H), 5.86 (s, 1H), 3.93 (d, J = 13.7 Hz, 1H), 3.90−3.83 (m, 1H), 3.78−3.72 (m, 1H), 3.18 (d, J = 13.8 Hz, 1H), 0.90 (t, J = 7.1 Hz, 3H). ^{13}C NMR (125 MHz, $CDCl_3$): δ 192.9, 191.5, 168.4, 135.4, 135.1, 134.7, 134.5, 134.4, 134.3, 133.2, 130.5, 129.5, 128.8, 128.5, 128.4, 127.7, 127.38 127.2, 126.7, 65.1, 62.7, 57.2, 36.1, 13.4; HRMS (ESI): calcd. for $C_{26}H_{22}BrO_4S$ ([M + H]$^+$): 509.0417, found 509.0407.

*Ethyl (2R,3S)-3-(2-Methoxyphenyl)-1,4-dioxo-2-((phenylthio)-methyl)-1,2,3,4-tetrahydronaphthalene-2-carboxylate (Table 3, **4g**).* The residue was purified by column chromatography (silica gel, EtOAc/Petroleum ether) to afford the title compound (84 mg, 91% yield, d.r. > 19/1) as a white solid, mp: 66−68 °C. The ee value was determined to be 95% (99% es) by chiral HPLC analysis (Chiralpak AD-H, 10/90 isopropanol/hexanes, λ = 254 nm at 30 °C, flow rate = 0.5 mL/min, t_R(major) = 48.0 min, t_R(minor) = 72.2 min). $[\alpha]_D^{25}$ = −316.8 (c = 1.00, $CHCl_3$). ^{1}H NMR (500 MHz, $CDCl_3$): δ 8.09 (dd, J = 5.7, 3.3 Hz, 1H), 7.97 (dd, J = 5.5, 3.3 Hz, 1H), 7.70 (dd, J = 5.7, 3.3 Hz, 2H), 7.28 (d, J = 7.5 Hz, 3H), 7.25−7.17 (m, 3H), 7.14 (t, J = 7.2 Hz, 1H), 6.88 (t, J = 7.0 Hz, 1H), 6.71 (d, J = 7.9 Hz, 1H), 5.22 (s, 1H), 3.94 (d, J = 13.6 Hz, 1H), 3.84−3.79 (m, 1H), 3.61−3.55 (m, 1H), 3.32 (s, 3H), 2.95 (d, J = 13.5 Hz, 1H), 0.80 (t, J = 7.1 Hz, 3H). ^{13}C NMR (125 MHz, $CDCl_3$): δ 194.0, 191.8, 169.2, 156.7, 135.8, 135.1, 134.9, 133.8, 133.6, 130.7, 129.7, 128.7, 127.2, 126.6, 126.0, 123.6, 121.1, 110.8, 64.1, 62.3, 53.8, 36.23 29.7, 13.4; HRMS (ESI): calcd. for $C_{27}H_{25}O_5S$ ([M + H]$^+$): 461.1417, found 461.1417.

*Ethyl (2R,3R)-3-(2,4-Dichlorophenyl)-1,4-dioxo-2-((phenylthio)-methyl)-1,2,3,4-tetrahydronaphthalene-2-carboxylate (Table 3, **4h**).* The residue was purified by column chromatography (silica gel, EtOAc/Petroleum ether) to afford the title compound (98 mg, 98% yield, d.r. = 13/1) as a colorless oil. The ee value was determined to be 98% (99% es) by chiral HPLC analysis (Chiralpak AD-H, 10/90 isopropanol/hexanes, λ = 254 nm at 30 °C, flow rate = 0.5 mL/min, t_R(major) = 29.9 min, t_R(minor) = 34.9 min). $[\alpha]_D^{25}$ = −294.0 (c = 1.00, $CHCl_3$). ^{1}H NMR (500 MHz, $CDCl_3$): δ 8.14−8.09 (m, 1H), 8.05 (d, J = 6.0, 1H), 7.77 (dd, J = 9.1, 5.7, 2H), 7.45 (s, 1H), 7.25 (d, J = 8.6, 2H), 7.20 (t, J = 7.3, 2H), 7.16 (d, J = 7.1, 1H), 7.05 (d, J = 7.8, 1H), 6.84 (s, 1H), 5.77 (s, 1H), 3.92 (d, J = 13.8, 1H), 3.90−3.84 (m, 1H), 3.83−3.73 (m, 1H), 3.17 (d, J = 13.8, 1H), 0.93 (t, J = 7.0, 3H). ^{13}C NMR (125 MHz, $CDCl_3$): δ 192.7, 191.2, 168.3, 135.2, 135.0, 134.6, 134.2, 134.1, 130.9, 130.5, 129.8, 128.8, 128.7, 127.9, 127.3, 127.2, 126.8, 126.5, 64.9, 62.8, 53.8, 36.1, 13.4; HRMS (ESI): calcd. for $C_{26}H_{21}Cl_2O_4S$ ([M + H]$^+$): 499.0532, found 499.0534.

*Ethyl (2S,3R)-1,4-Dioxo-3-((phenylthio)methyl)-1,2,3,4-tetrahydro-[2,2′-binaphthalene]-3-carboxylate (Table 3, **4i**).* The residue was purified by column chromatography (silica gel, EtOAc/Petroleum ether) to afford the title compound (87 mg, 90% yield, d.r. = 13/1) as a white solid, mp: 62−63 °C. The ee value was determined to be 95% (98% es) by chiral HPLC analysis (Chiralpak AS-H, 5/95 isopropanol/hexanes, λ = 254 nm at 30 °C, flow rate = 0.5 mL/min, t_R(major) = 53.4 min, t_R(minor) = 62.7 min). $[\alpha]_D^{25}$ = −319.0 (c = 1.00, $CHCl_3$). ^{1}H NMR (500 MHz, $CDCl_3$): δ 8.18−8.13 (m, 1H), 8.13−8.07 (m, 1H), 7.81−7.76 (m, 2H), 7.74 (dd, J = 6.1, 3.0, 1H), 7.69−7.62 (m, 2H), 7.55 (s, 1H), 7.46−7.39 (m, 2H), 7.31−7.26 (m, 2H), 7.20−7.09 (m, 4H), 5.21 (s, 1H), 3.95 (d, J = 13.8, 1H), 3.89 (dq, J = 10.7, 7.1, 1H), 3.73 (dq, J = 10.8, 7.1, 1H), 3.13 (d, J = 13.8, 1H), 0.92 (t, J = 7.1, 3H). ^{13}C NMR (125 MHz, $CDCl_3$): δ 192.7, 192.5, 168.5, 135.0, 134.9, 134.8, 134.5, 134.5, 133.3, 132.7, 131.0, 129.1, 129.0, 128.8, 128.1, 127.9, 127.5, 127.2, 126.9, 126.5, 126.4, 126.2, 65.7, 62.6, 59.2, 36.0, 13.5; HRMS (ESI): calcd. for $C_{30}H_{25}O_4$ S ([M + H]$^+$): 481.1468, found 481.1461.

*Ethyl 3-Methyl-1,4-dioxo-2-((phenylthio)methyl)-1,2,3,4-tetrahydronaphthalene-2-carboxylate (Table 3, **4j**).* The residue was purified by column chromatography (silica gel, EtOAc/Petroleum ether) to afford the title compound (47 mg, 64% yield, d.r. = 5.8/1) as a white solid, mp: 73−75 °C. The ee value was determined to be 76% (76% es) by chiral HPLC analysis (Chiralpak OD-H, 10/90 isopropanol/hexanes, λ = 254 nm at 30 °C, flow rate = 0.5 mL/min, t_R(major) = 39.6 min, t_R(minor) = 42.9 min). $[\alpha]_D^{25}$ = −105.2 (c = 1.00, $CHCl_3$). ^{1}H NMR (500 MHz, $CDCl_3$): δ 8.11 (d, J = 7.8 Hz, 1H), 7.86 (d, J = 7.7 Hz, 1H), 7.75 (td, J = 7.7, 1.1 Hz, 1H), 7.66 (td, J = 7.6, 1.0 Hz, 1H), 7.35−7.29 (m, 2H), 7.25−7.14 (m, 3H), 3.99−3.76 (m, 4H), 3.55 (d, J = 14.0 Hz, 1H), 1.16 (d, J = 7.4 Hz, 3H), 1.00 (t, J = 7.1 Hz, 3H). ^{13}C NMR (125 MHz, $CDCl_3$): δ 196.5, 193.1, 169.1, 134.9, 134.8, 134.0, 133.6, 133.5, 130.8, 128.9, 127.0, 65.5, 62.4, 47.2, 35.0, 13.6, 13.1; HRMS (ESI): calcd. for $C_{21}H_{21}O_4S$ ([M + H]$^+$): 369.1155, found 369.1162.

*Ethyl (2R,3S)-6-Methyl-1,4-dioxo-3-phenyl-2-((phenylthio)-methyl)-1,2,3,4-tetrahydronaphthalene-2-carboxylate (Table 3, **4k**).* The residue was purified by column chromatography (silica gel, EtOAc/Petroleum ether) to afford the title compound (81 mg, 91% yield, d.r. > 19/1) as a white solid, mp: 96−97 °C. The ee value was determined to be 96% (97% es) by chiral HPLC analysis (Chiralpak AD-H, 10/90 isopropanol/hexanes, λ = 254 nm at 30 °C, flow rate = 0.5 mL/min, t_R(major) = 41.1 min, t_R(minor) = 65.7 min). $[\alpha]_D^{25}$ = −335.2 (c = 1.00, $CHCl_3$). ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.97 (d, J = 7.9 Hz, 1H), 7.94 (s, 1H), 7.56 (d, J = 7.8 Hz, 1H), 7.30 (d, J = 7.3 Hz, 2H), 7.25−7.12 (m, 6H), 7.05 (d, J = 6.7 Hz, 2H), 5.02 (s, 1H), 3.94 (d, J = 13.7 Hz, 1H), 3.89−3.82 (m, 1H), 3.72−3.66 (m, 1H), 3.05 (d, J = 13.7 Hz, 1H), 2.47 (s, 3H), 0.90 (t, J = 7.1 Hz, 3H). ^{13}C NMR (125 MHz, $CDCl_3$): δ 192.9, 192.3, 168.6, 146.4, 135.3, 135.1, 134.7, 133.7, 132.2, 131.0, 129.2, 129.1, 128.8, 128.1, 128.1, 127.3,

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126.8, 65.5, 62.5, 59.2, 35.9, 21.9, 13.5; HRMS (ESI): calcd. for $C_{27}H_{25}O_4S$ ([M + H]$^+$): 445.1468, found 445. 1468.

*Ethyl (2R,3S)-6-Fluoro-1,4-dioxo-3-phenyl-2-((phenylthio)-methyl)-1,2,3,4-tetrahydronaphthalene-2-carboxylate (Table 3, **4l**).* The residue was purified by column chromatography (silica gel, EtOAc/Petroleum ether) to afford the title compound (57 mg, 64% yield, d.r. = 8/1) as a white solid, mp: 119−121 °C. The ee value was determined to be 98% (99% es) by chiral HPLC analysis (Chiralpak OD-H, 5/95 isopropanol/hexanes, λ = 254 nm at 30 °C, flow rate = 0.5 mL/min, t_R(major) = 24.3 min, t_R(minor) = 26.8 min). $[\alpha]_D^{25}$ = −247.0 (c = 1.00, $CHCl_3$). ^{1}H NMR (500 MHz, $CDCl_3$): δ 8.10 (dd, J = 8.6, 5.2 Hz, 1H), 7.78 (dd, J = 8.5, 2.6 Hz, 1H), 7.42 (td, J = 8.3, 2.6 Hz, 1H), 7.31−7.27 (m, 2H), 7.26−7.14 (m, 6H), 7.04 (d, J = 6.8 Hz, 2H), 5.04 (s, 1H), 3.92 (d, J = 13.8 Hz, 1H), 3.90−3.85 (m, 1H), 3.75−3.68 (m, 1H), 3.08 (d, J = 13.8 Hz, 1H), 0.93 (t, J = 7.1 Hz, 3H). ^{13}C NMR (126 MHz, $CDCl_3$): δ 191.4, 191.2, 168.5, 166.7 (d, J = 259.7 Hz), 137.8 (d, J = 7.2 Hz), 134.8, 133.2, 131.0, 130.5 (d, J = 9.0 Hz), 129.3, 129.1, 129.0, 128.9, 128.6, 128.3, 127.0, 121.8 (d, J = 21.8 Hz), 114.3 (d, J = 23.0 Hz), 65.6, 62.7, 59.0, 35.8, 13.5; HRMS (ESI): calcd. for $C_{26}H_{22}FO_4S$ ([M + H]$^+$): 449.1217, found 449.1217.

*Ethyl (2R,3S)-6-Chloro-1,4-dioxo-3-phenyl-2-((phenylthio)-methyl)-1,2,3,4-tetrahydronaphthalene-2-carboxylate (Table 3, **4m**).* The residue was purified by column chromatography (silica gel, EtOAc/Petroleum ether) to afford the title compound (76 mg, 82% yield, d.r. = 5/1) as a white solid, mp: 128−129 °C. The ee value was determined to be 96% (98% es) by chiral HPLC analysis (Chiralpak AD-H, 10/90 isopropanol/hexanes, λ = 254 nm at 30 °C, flow rate = 0.5 mL/min, t_R(major) = 28.7 min, t_R(minor) = 41.8 min). $[\alpha]_D^{25}$ = −289.0 (c = 1.00, $CHCl_3$). ^{1}H NMR (500 MHz, $CDCl_3$): δ 8.09 (d, J = 2.0 Hz, 1H), 8.00 (d, J = 8.3 Hz, 1H), 7.70 (dd, J = 8.3, 2.1 Hz, 1H), 7.28 (d, J = 7.0 Hz, 2H), 7.26−7.14 (m, 6H), 7.03 (d, J = 6.8 Hz, 2H), 5.04 (s, 1H), 3.92 (d, J = 13.8 Hz, 1H), 3.89−3.84 (m, 1H), 3.74−3.68 (m, 1H), 3.07 (d, J = 13.8 Hz, 1H), 0.93 (t, J = 7.1 Hz, 3H). ^{13}C NMR (125 MHz, $CDCl_3$): δ 191.6, 191.3, 168.4, 142.0, 136.1, 134.8, 134.5, 133.1, 132.5, 131.0, 130.6, 130.3, 129.7, 129.3, 129.1, 129.0, 128.9, 128.6, 128.3, 127.8, 127.0, 65.7, 62.8, 59.1, 35.8, 13.5; HRMS (ESI): calcd. for $C_{26}H_{22}ClO_4S$ ([M + H]$^+$): 465.0922, found 465.0922.

*Ethyl (2R,3S)-6-Bromo-1,4-dioxo-3-phenyl-2-((phenylthio)-methyl)-1,2,3,4-tetrahydronaphthalene-2-carboxylate (Table 3, **4n**).* The residue was purified by column chromatography (silica gel, EtOAc/Petroleum ether) to afford the title compound (96 mg, 94% yield, d.r. = 7/1) as a white solid, mp: 122−123 °C. The ee value was determined to be 98% (99% es) by chiral HPLC analysis (Chiralpak AD-H, 10/90 isopropanol/hexanes, λ = 254 nm at 30 °C, flow rate = 0.5 mL/min, t_R(major) = 32.6 min, t_R(minor) = 53.6 min). $[\alpha]_D^{25}$ = −219.0 (c = 1.00, $CHCl_3$). ^{1}H NMR (500 MHz, $CDCl_3$): δ 8.26 (d, J = 1.8 Hz, 1H), 7.91 (d, J = 8.3 Hz, 1H), 7.87 (dd, J = 8.3, 1.9 Hz, 1H), 7.30−7.27 (m, 2H), 7.25−7.14 (m, 6H), 7.06−6.99 (m, 2H), 5.04 (s, 1H), 3.91 (d, J = 13.8 Hz, 1H), 3.89−3.84 (m, 1H), 3.74−3.68 (m, 1H), 3.07 (d, J = 13.8 Hz, 1H), 0.93 (t, J = 7.1 Hz, 3H). ^{13}C NMR (125 MHz, $CDCl_3$): δ 191.8, 191.3, 168.3, 137.5, 135.9, 134.8, 133.1, 132.9, 131.0, 130.8, 130.7, 130.6, 129.3, 129.1, 129.0, 128.9, 128.8, 128.3, 127.0, 65.7, 62.8, 59.1, 35.8, 13.5; HRMS (ESI): calcd. for $C_{26}H_{22}BrO_4S$ ([M + H]$^+$): 509.0417, found 509.0419.

*Ethyl (2R,3S)-8-Chloro-1,4-dioxo-3-phenyl-2-((phenylthio)-methyl)-1,2,3,4-tetrahydronaphthalene-2-carboxylate (Table 3, **4o**).* The residue was purified by column chromatography (silica gel, EtOAc/Petroleum ether) to afford the title compound (83 mg, 89% yield, d.r. = 14/1) as a white solid, mp: 100−101 °C. The ee value was determined to be 90% (96% es) by chiral HPLC analysis (Chiralpak AD-H, 10/90 isopropanol/hexanes, λ = 254 nm at 30 °C, flow rate = 0.5 mL/min, t_R(major) = 47.6 min, t_R(minor) = 64.1 min). $[\alpha]_D^{25}$ = −400.7 (c = 0.90, $CHCl_3$). ^{1}H NMR (500 MHz, $CDCl_3$): δ 8.11 (d, J = 7.7 Hz, 1H), 7.76 (d, J = 7.8 Hz, 1H), 7.64 (t, J = 7.9 Hz, 1H), 7.35 (d, J = 7.4 Hz, 2H), 7.27−7.21 (m, 5H), 7.19 (t, J = 7.2 Hz, 1H), 7.07 (d, J = 6.6 Hz, 2H), 5.08 (s, 1H), 3.86−3.80 (m, 1H), 3.74 (d, J = 13.9 Hz, 1H), 3,50−3.44 (m, 1H), 3.00 (d, J = 13.9 Hz, 1H), 0.83 (t, J = 7.1 Hz, 3H). ^{13}C NMR (125 MHz, $CDCl_3$): δ 192.0, 190.9, 168.6, 137.0, 136.9, 134.7, 134.1, 133.7, 133.5, 132.5, 131.3, 130.5, 129.2, 129.1, 129.0, 128.9, 128.4, 127.1, 126.9, 65.6, 62.4, 58.4, 35.4, 13.4; HRMS (ESI): calcd. for $C_{26}H_{22}ClO_4$ S ([M + H]$^+$): 465.0922, found 465.0922.

*Ethyl (2R,3S)-5-Chloro-1,4-dioxo-3-phenyl-2-((phenylthio)-methyl)-1,2,3,4-tetrahydronaphthalene-2-carboxylate (Table 3, **4q**).* The residue was purified by column chromatography (silica gel, EtOAc/Petroleum ether) to afford the title compound (84 mg, 90% yield, d.r. = 14/1) as a white solid, mp: 100−101 °C. The ee value was determined to be 87% (94% es) by chiral HPLC analysis (Chiralpak AD-H, 10/90 isopropanol/hexanes, λ = 254 nm at 30 °C, flow rate = 0.5 mL/min, t_R(major) = 51.4 min, t_R(minor) = 54.5 min). $[\alpha]_D^{25}$ = −206.2 (c = 1.00, $CHCl_3$). ^{1}H NMR (500 MHz, $CDCl_3$): δ 8.02 (d, J = 7.5 Hz, 1H), 7.76 (d, J = 7.8 Hz, 1H), 7.63 (t, J = 7.7 Hz, 1H), 7.28 (d, J = 7.2 Hz, 2H), 7.25−7.14 (m, 6H), 7.06 (d, J = 6.4 Hz, 2H), 5.03 (s, 1H), 3.90−3.84 (m, 2H), 3.77−3.71 (m, 1H), 3.06 (d, J = 13.7 Hz, 1H), 0.93 (t, J = 6.9 Hz, 3H). ^{13}C NMR (125 MHz, $CDCl_3$): δ 192.0, 190.4, 168.1, 138.4, 137.1, 135.6, 134.9, 133.9, 133.2, 131.0, 130.8, 129.3, 129.2, 128.9, 128.3, 127.0, 126.6, 65.2, 62.7, 60.1, 36.0, 13.5; HRMS (ESI): calcd. for $C_{26}H_{22}ClO_4S$ ([M + H]$^+$): 465.0922, found 465.0922.

*Ethyl (2R,3S)-2-(((4-Methoxyphenyl)thio)methyl)-1,4-dioxo-3-phenyl-1,2,3,4-tetrahydronaphthalene-2-carboxylate (Table 4, **4s**).* The residue was purified by column chromatography (silica gel, EtOAc/Petroleum ether) to afford the title compound (87 mg, 94% yield, d.r. = 10/1) as a white solid, mp: 89−90 °C. The ee value was determined to be 92% (96% es, starting material **3a** (ee = 96%) was employed) by chiral HPLC analysis (Chiralpak OD-H, 10/90 isopropanol/hexanes, λ = 254 nm at 30 °C, flow rate = 0.5 mL/min, t_R(major) = 24.7 min, t_R(minor) = 27.5 min). $[\alpha]_D^{25}$ = −242.6 (c = 1.00, $CHCl_3$). ^{1}H NMR (500 MHz, $CDCl_3$): δ 8.14 (dd, J = 5.9, 3.0 Hz, 1H), 8.05 (dd, J = 5.8, 3.0 Hz, 1H), 7.81−7.72 (m, 2H), 7.26 (d, J = 8.5 Hz, 2H), 7.20 (q, J = 6.2 Hz, 3H), 7.05 (d, J = 6.6 Hz, 2H), 6.76 (d, J = 8.6 Hz, 2H), 5.06 (s, 1H), 3.92−3.84 (m, 1H), 3.82 (d, J = 13.9 Hz, 1H), 3.77 (s, 3H), 3.74−3.66 (m, 1H), 3.00 (d, J = 13.9 Hz, 1H), 0.91 (t, J = 7.1 Hz, 3H). ^{13}C NMR (125 MHz, $CDCl_3$): δ 192.8, 192.7, 168.5, 159.3, 134.9, 134.8, 134.5, 134.3, 134.1, 133.7, 129.2, 129.1, 128.1, 127.9, 127.1, 125.3, 114.4, 65.6, 62.5, 59.1, 55.3, 37.4, 13.5; HRMS (ESI): calcd. for $C_{27}H_{25}O_5$ S ([M + H]$^+$): 461.1417, found 461.1415.

*Ethyl (2R,3S)-2-(((2-Bromophenyl)thio)methyl)-1,4-dioxo-3-phenyl-1,2,3,4-tetrahydronaphthalene-2-carboxylate (Table 4, **4t**).* The residue was purified by column chromatography (silica gel, EtOAc/Petroleum ether) to afford the title compound (65 mg, 63% yield, d.r. = 4.5/1) as a colorless oil. The ee value was determined to be 93% (97% es, starting material **3a** (ee = 96%) was employed) by chiral HPLC analysis (Chiralpak AD-H, 10/90 isopropanol/hexanes, λ = 254 nm at 30 °C, flow rate = 0.5 mL/min, t_R(major) = 42.2 min, t_R(minor) = 70.0 min). $[\alpha]_D^{25}$ = −223.4 (c = 1.00, $CHCl_3$). ^{1}H NMR (500 MHz, $CDCl_3$): δ 8.17−8.14 (m, 1H), 8.10−8.07 (m, 1H), 7.81−7.77 (m, 2H), 7.51 (d, J = 7.9 Hz, 1H), 7.30 (d, J = 8.1 Hz, 1H), 7.22−7.16 (m, 4H), 7.10−7.01 (m, 3H), 5.06 (s, 1H), 3.96 (d, J = 13.2 Hz, 1H), 3.94−3.88 (m, 1H), 3.87−3.79 (m, 1H), 3.04 (d, J = 13.3 Hz, 1H), 0.95 (t, J = 7.1 Hz, 3H). ^{13}C NMR (125 MHz, $CDCl_3$): δ 192.4, 168.4, 136.1, 135.0, 134.8, 134.5, 134.4, 133.5, 133.1, 131.4, 129.2, 129.1, 128.2, 127.9, 127.7, 127.2, 125.8, 65.4, 62.8, 59.3, 35.1, 13.5; HRMS (ESI): calcd. for $C_{26}H_{22}BrO_4S$ ([M + H]$^+$): 509.0417, found 509.0411.

*Ethyl (2R,3S)-2-((Benzylthio)methyl)-1,4-dioxo-3-phenyl-1,2,3,4-tetrahydronaphthalene-2-carboxylate (Table 4, **4u**).* The residue was purified by column chromatography (silica gel, EtOAc/Petroleum ether) to afford the title compound (74 mg, 83% yield, d.r. = 7.5/1) as a white solid, mp: 48−49 °C. The ee value was determined to be 92% (96% es, starting material **3a** (ee = 96%) was employed) by chiral HPLC analysis (Chiralpak AS-H, 10/90 isopropanol/hexanes, λ = 254 nm at 30 °C, flow rate = 0.5 mL/min, t_R(major) = 31.4 min, t_R(minor) = 35.0 min). $[\alpha]_D^{25}$ = −213.2 (c = 1.00, $CHCl_3$). ^{1}H NMR (500 MHz, $CDCl_3$): δ 8.16−8.12 (m, 1H), 8.10−8.05 (m, 1H), 7.77 (dd, J = 5.7, 3.4 Hz, 2H), 7.25−7.18 (m, 6H), 7.13 (d, J = 7.0 Hz, 2H), 7.08 (d, J = 6.9 Hz, 2H), 4.95 (s, 1H), 4.11−4.02 (m, 2H), 3.58 (d, J = 13.3 Hz, 1H), 3.53 (d, J = 13.3 Hz, 1H), 3.40 (d, J = 13.2 Hz, 1H), 2.60 (d, J = 13.2 Hz, 1H), 1.04 (t, J = 7.1 Hz, 3H). ^{13}C NMR (125 MHz, $CDCl_3$):

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δ 192.7, 192.6, 168.9, 137.5, 135.0, 134.9, 134.6, 134.4, 133.7, 129.2, 129.1, 128.8, 128.5, 128.2, 127.8, 127.2, 127.1, 65.6, 62.8, 59.3, 37.5, 32.6, 13.7; HRMS (ESI): calcd. for $C_{27}H_{25}O_4S$ ([M + H]$^+$): 445.1468, found 445.1461.

*Ethyl (2R,3S)-1,4-Dioxo-3-phenyl-2-((phenylselanyl)methyl)-1,2,3,4-tetrahydronaphthalene-2-carboxylate (Table 4, **4v**).* The residue was purified by column chromatography (silica gel, EtOAc/Petroleum ether) to afford the title compound (62 mg, 64% yield, d.r. > 19/1) as a white solid, mp: 116−117 °C. The ee value was determined to be 96% (98% es, starting material **3a** (ee = 98%) was employed) by chiral HPLC analysis (Chiralpak AD-H, 10/90 isopropanol/hexanes, λ = 254 nm at 30 °C, flow rate = 0.5 mL/min, t_R(major) = 36.3 min, t_R(minor) = 46.5 min). $[\alpha]_D^{25}$ = −279.6 (*c* = 1.00, $CHCl_3$). ^{1}H NMR (500 MHz, $CDCl_3$): δ 8.17−8.10 (m, 1H), 8.09−8.03 (m, 1H), 7.80−7.73 (m, 2H), 7.47−7.38 (m, 2H), 7.25−7.14 (m, 6H), 7.02 (d, *J* = 6.9 Hz, 2H), 5.02 (s, 1H), 3.87−3.80 (m, 2H), 3.64−3.58 (m, 1H), 3.00 (d, *J* = 13.0 Hz, 1H), 0.86 (t, *J* = 7.1 Hz, 3H). ^{13}C NMR (125 MHz, $CDCl_3$): δ 193.1, 192.6, 168.6, 134.9, 134.8, 134.7, 134.4, 133.7, 133.6, 129.3, 129.2, 129.1, 129.0, 128.2, 127.9, 127.4, 127.1, 65.6, 62.5, 60.1, 29.4, 13.4; HRMS (ESI): calcd. for $C_{26}H_{23}O_4Se$ ([M + H]$^+$): 479.0756, found 479.0758.

*Ethyl (2R,3S)-1,4-Dioxo-3-phenyl-2-(phenylsulfonylmethyl)-1,2,3,4-tetrahydronaphthalene-2-carboxylate (Scheme 3, **5**).* To a stirred solution of **4a** (0.2 mmol) in DCM (2 mL) was added *m*-CPBA (0.44 mmol, 75.9 mg) portionwise at 0 °C for 15 min.[14] Reaction mixture was stirred at this temperature for 30 min, then warmed to room temperature, and stirred for 5 h. After completion, the reaction was diluted with DCM (8 mL) and washed with 5% aqueous K_2CO_3 (8 mL) and 5% $NaHCO_3$ (10 mL) solution. Then, the aqueous layer was extracted with DCM (3 × 10 mL), the combined organic layers were dried over anhydrous Na_2SO_4, and the solvent was evaporated *in vacuo*. The crude mixture was purified by column chromatography (silica gel, EtOAc/Petroleum ether) to provide compound **5** (77 mg, 84% yield, d.r. > 19/1) as a white solid, mp: 151−152 °C. The ee value was determined to be 96% by chiral HPLC analysis (Chiralpak AD-H, 20/80 isopropanol/hexanes, λ = 254 nm at 30 °C, flow rate = 0.5 mL/min, t_R(major) = 49.0 min, t_R(minor) = 83.3 min). $[\alpha]_D^{25}$ = −189.0 (*c* = 1.00, $CHCl_3$). ^{1}H NMR (500 MHz, $CDCl_3$): δ 8.17−8.11 (m, 1H), 8.07 (dd, *J* = 9.3, 3.5 Hz, 1H), 7.82−7.74 (m, 4H), 7.63 (t, *J* = 7.4 Hz, 1H), 7.51 (t, *J* = 7.7 Hz, 2H), 7.24−7.18 (m, 3H), 7.10 (d, *J* = 6.9 Hz, 2H), 5.34 (s, 1H), 4.31 (d, *J* = 14.9 Hz, 1H), 4.11 (dq, *J* = 10.9, 7.2 Hz, 1H), 4.02 (dq, *J* = 10.8, 7.1 Hz, 1H), 3.40 (d, *J* = 14.9 Hz, 1H), 1.07 (t, *J* = 7.1 Hz, 3H). ^{13}C NMR (125 MHz, $CDCl_3$): δ 191.4, 190.7, 167.3, 140.4, 135.4, 134.5, 134.2, 133.9, 133.8, 133.3, 130.2, 129.9, 129.4, 129.3, 129.2, 128.3, 128.0, 127.7, 127.4, 63.4, 62.9, 59.3, 55.8, 13.5; HRMS (ESI): calcd. for $C_{26}H_{23}O_6S$ ([M + H]$^+$): 463.1210, found 463.1209.

■ ASSOCIATED CONTENT

Ⓢ Supporting Information

NMR and HPLC spectra of products **3ab**, **3ab**, **3a−3i**, **3k−3r**, **4a−4o**, **4q**, **4s−4v**, and **5**, as well as X-ray structures of compound **3f** and compound **4f**. This material is available free of charge via the Internet at http://pubs.acs.org.

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Notes

The authors declare no competing financial interest.

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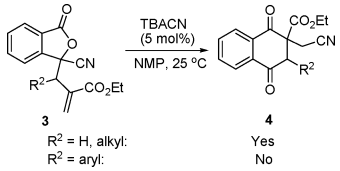

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(10) See the Supporting Information for X-ray structures. CCDC 1041921 (**3f**) and 1041922 (**4f**) contain the supplementary crystallographic data for this paper.
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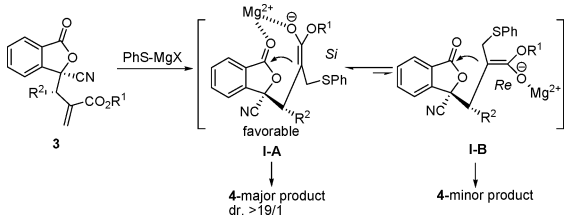
(12) The explicit mechanism of magnesium cation improved selectivity in this reaction remains unclear at this stage. However, we assume that the magnesium cation should coordinate favorably to both the oxygen atom of the lactone and the enolate units of intermediate **I-A** to fix a chelating structure that may contribute the present high diastereoselectivity in this tandem process.



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