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# Highly Enantioselective Synthesis of Naphthoquinones and Pyranonaphthoquinones Catalyzed by Bifunctional Chiral Bis-Squaramides

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A variety of enantioenriched naphthoquinones have been synthesized in high yields and excellent enantioselectivities (up to >99% ee) using a bifunctional chiral bis-squaramide catalyzed conjugate addition of 2-hydroxy-1,4-naphthoquinone to 2-enoylpyridines. Some of the Michael products have been successfully converted into various enantioenriched pyranonaphthoquinone derivatives. The protocol is further extended to the synthesis of various 4-hydroxycoumarin derivatives under mild conditions.

## Introduction

Naphthoquinone and pyranonaphthoquinone derivatives are important building blocks used in the synthesis of a wide range of natural products (Figure 1).[1] They possess a variety of pharmacological activities, such as anti-inflammatory, molluscicidal, leishmanicidal, antitumor and anti-HIV activities.[2] The structural feature of these compounds exhibit redox properties that regulate various catalytic organic transformations.[3] One way to approach these molecules in enantiopure form is through asymmetric Michael addition using 2-hydroxy-1,4-naphthoquinone as Michael donor. Towards this, few α,β-unsaturated carbonyl compounds are used as coupling partners in Michael addition through asymmetric organocatalysis,[4] either involving iminium catalysis[5] or by bifunctional hydrogen bonding catalysis.[6] We have also recently used cinchona derived thiourea (urea) bifunctional catalysts[7] to synthesize enantiopure compounds in high yields and excellent enantioselctivities.[8]

The role of cinchona-based thiourea (urea) bifunctional hydrogen bonding catalysts to realize these transformations in higher enantioselectivities has made them privileged catalysts in last few decades.[9] Indeed a large number of asymmetric organic transformations have been promoted by cinchona derived thiourea (urea) bifunctional catalysts to achieve high chiral induction. Very recently, a new class of H-bonding chiral squaramide organocatalysts has been introduced by Rawal *et al.*;[10a] where the two hydrogen atoms are reasonably far away than those present in thiourea catalysts to carry out a variety of asymmetric transformations.[10-11] These squaramide catalysts are supposed to be better catalysts in dual H-bonding activation under mild reaction conditions and are least explored in catalysis.

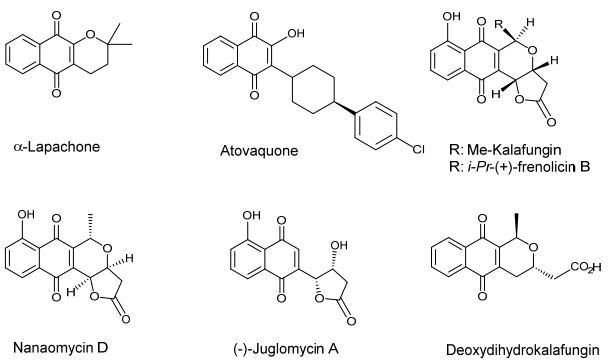



**Fig. 1** Selected examples of natural products containing a 1,4-naphthoquinone structural motif.

The efficient catalytic activity of squaramide catalysts made us see its application in the synthesis of naphthoquinone and pyranonaphthoquinone derivatives using 2-enoylpyridines[12-15] as a Michael acceptor in the presence of 2-hydroxy-1,4-naphthoquinone[16] as Michael donor. Delightfully, the resulting Michael adducts were obtained in excellent yields and enantioselectivities (up to 97% and up to >99%, respectively). Further, we extended the catalytic protocol in the enantioselective synthesis of 4-hydroxycoumarins, 4-hydroxy-1-methyl-2(1H)-quinolone and 4-hydroxy-6-methyl-2-pyrone derivatives in high yields and excellent enantioselectivities.

## Results and discussion

A systematic study was initiated with the model reaction of 2-hydroxy-1,4-naphthoquinone (**1**) and 2-enoylpyridine (**2a**) in the presence of 10 mol% quinine derived thiourea-catalyst (**3a**) using toluene as solvent at room temperature (Table 1). As per our assumption, the desired Michael adduct was formed in high yields and we isolated it as its acyl derivative (**4a**) (95%) in moderate enantioselectivity (60%) (Table 1, entry 1). Encouraged by these initial findings, various cinchona-alkaloid derived urea and thiourea catalysts (**3b-h,** Figure 2) have also been screened. As summarized in table 1 (entries 2-8), the high yields for all catalysts clearly indicate that both urea and thiourea derived catalysts afforded the Michael adduct (**4a**) in moderate enantioselectivities (58-73%) and excellent yields (92-96%). Interestingly, switching from a thiourea catalyst to quinine-derived squaramide catalyst (**5a**) under similar reaction

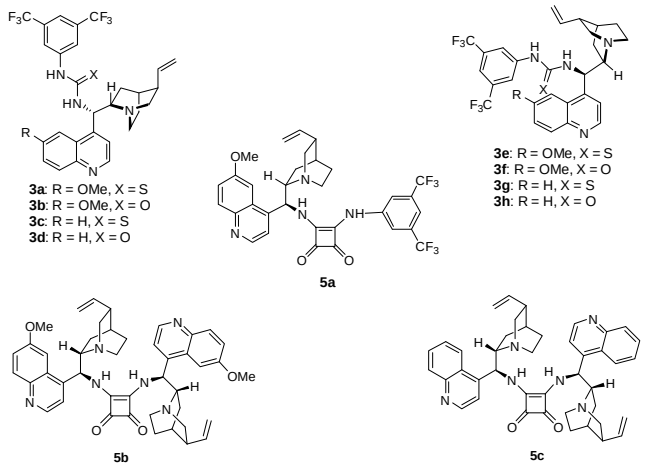
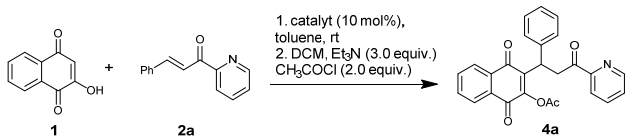



**Fig. 2** Cinchona alkaloid derived (thio)urea and squaramide catalysts.

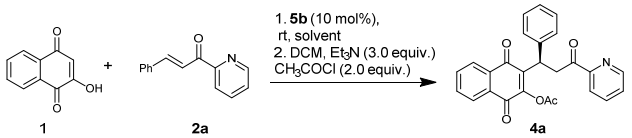
**Table 1** Catalyst Screening [a]




| Entry | Catalyst | Yield (%) | ee (%) |
|---|---|---|---|
| 1 | **3a** | 95 | 60 |
| 2 | **3b** | 95 | 73 |
| 3 | **3c** | 93 | 58 |
| 4 | **3d** | 94 | 65 |
| 5[c] | **3e** | 92 | 67 |
| 6[c] | **3f** | 95 | 71 |
| 7[c] | **3g** | 94 | 70 |
| 8[c] | **3h** | 96 | 70 |
| 9 | **5a** | 93 | 92 |
| 10 | **5b** | 95 | 98 |
| 11 | **5c** | 95 | 96 |

[a]Reactions were carried out on 0.12 mmol of **2a** and 0.1 mmol of **1** in 1 mL of toluene at rt using 10 mol% of catalyst ; after complete conversion of **1** the acetylation was performed (1hour) unless noted otherwise. [b]Determined by HPLC using Diacel chiralpak IA column.[c] Opposite enantiomer as major was obtained.

**Table 2** Solvent study [a]




| Entry | Solvent | Time (h) | Yield (%) | ee (%)[b] |
|---|---|---|---|---|
| 1 | toluene | 48 | 95 | 98 |
| 2 | xylene | 48 | 94 | 96 |
| 3 | $CH_2Cl_2$ | 48 | 92 | 96 |
| 4 | DCE | 48 | 93 | 95 |
| 5 | $CHCl_3$ | 48 | 94 | 95 |
| 6 | THF | 48 | 94 | 96 |
| 7 | 1,4-dioxane | 48 | 90 | 96 |
| 8 | EtOAc | 48 | 91 | 96 |
| 9 | MeOH | 40 | 90 | 53 |

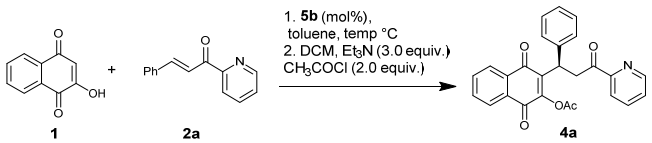
[a]Reactions were carried out on 0.12 mmol of **2a** and 0.1 mmol of **1** in 1 mL of solvent at rt using 10 mol% of catalyst **5b**; after complete conversion of **1** the acetylation was performed (1hour) unless noted otherwise. [b]Determined by HPLC using Diacel chiralpak IA column.

conditions, we obtained the Michael adduct (**4a**) in excellent yield (93%) and enantioselectivity (92%) (Table 1, entry 9). In order to further screen the squaramide catalysts, $C_2$-symmetric bis-quinine (**5b**) and $C_2$-symmetric bis-cinchonidine (**5c**) squaramides were used.[17] Both the catalysts afforded the products in enhanced enantioselectivities up to 98% (Table1 entries 10, 11) in fairly good yields. These optimization studies led us to choose $C_2$-symmetric bis-quinine (**5b**) catalyst as the catalyst of choice for the further studies.

Solvent screening (Table 2) revealed that formation of Michael adduct (**4a**) was equally good in a wide range of solvents of different polarity, except methanol. In methanol, the product **4a** was obtained in good yield, but a significant decrease in enantioselectivity was observed (53%) (Table 2, entry 9) which may be due to the hydrogen bonding nature of the solvent leading to a competition with substrate molecules to be activated by catalyst through hydrogen bonding. Ultimately, we found toluene to be the best solvent for further studies (Table 2, entry 1).

Then we looked into the effect of catalyst loading and temperature variation (Table 3) in the reaction of 2-hydroxy-1,4-naphthoquinone (**1**) and 2-enoylpyridine (**2a**) using catalyst **5b** in toluene. We found that decreasing the catalyst loading from 10 mol% to 5 mol% drastically prolonged the reaction time from 48 hours to 98 hours (Table 3, entries 1, 2) whereas, the yields and enantioselectivities remained unchanged. In general, the enantioselective reactions are highly affected by reaction temperature and increasing the reaction temperature leads to a decrease in enantioselectivity. Whereas, the present study shows that increasing the reaction temperature from room temperature to 40 °C significantly reduced reaction time, without affecting the yield and enantioselectivity of product **4a** (Table 3, entry 3). Formation of Michael adduct **4a** could be completed within 4 hours at 85 °C in equivalently good yields and enantioselectivities (entry 5). To make the protocol more feasible and useful we chose 40 °C (entry 3) as an optimum reaction temperature to explore the substrate scope.

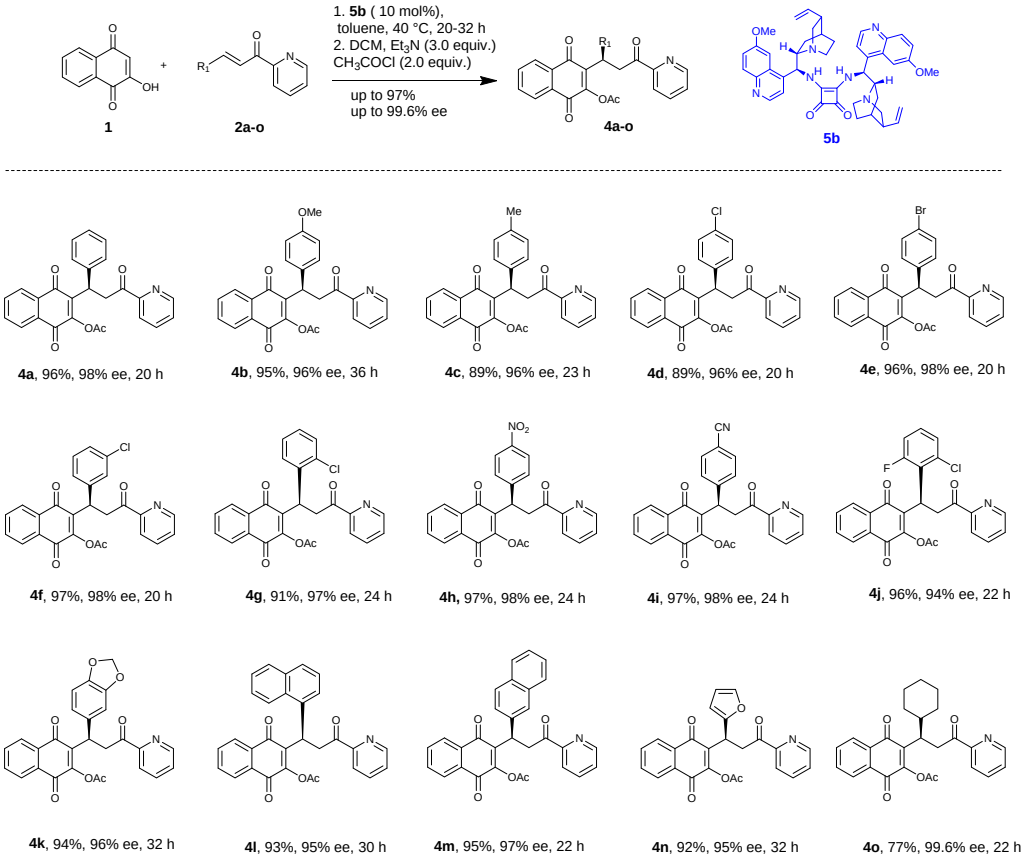
**Table 3** Catalyst loading and temperature study[a]




| Entry | (mol%) | Temp (° C) | Time (h) | Yield (%) | ee (%)b |
|---|---|---|---|---|---|
| 1 | 10 | rt | 48 | 95 | 98 |
| 2 | 5 | rt | 98 | 95 | 98 |
| 3 | 10 | 40 | 20 | 96 | 98 |
| 4 | 10 | 60 | 10 | 95 | 96 |
| 5 | 10 | 85 | 4 | 95 | 96 |
| 6 | 5 | 85 | 7 | 94 | 95 |
| 7[c] | 2 | 85 | 24 | 82 | 94 |
| 8 | 5 | 40 | 36 | 94 | 98 |
| 9[c] | 2 | 40 | 50 | 70 | 97 |

[a]Reactions were carried out on 0.12 mmol of **2a** and 0.1 mmol of **1** in 1 mL of toluene at rt using 10 mol% of catalyst **5b**; after complete conversion of **1** the acetylation was performed (1hour) unless noted otherwise. [b]Determined by HPLC using Diacel chiralpak IA colum. [c]Reaction performed at 0.5 M concentration

**Table 4** Substrates scope of enantioselective Michael addition[a]

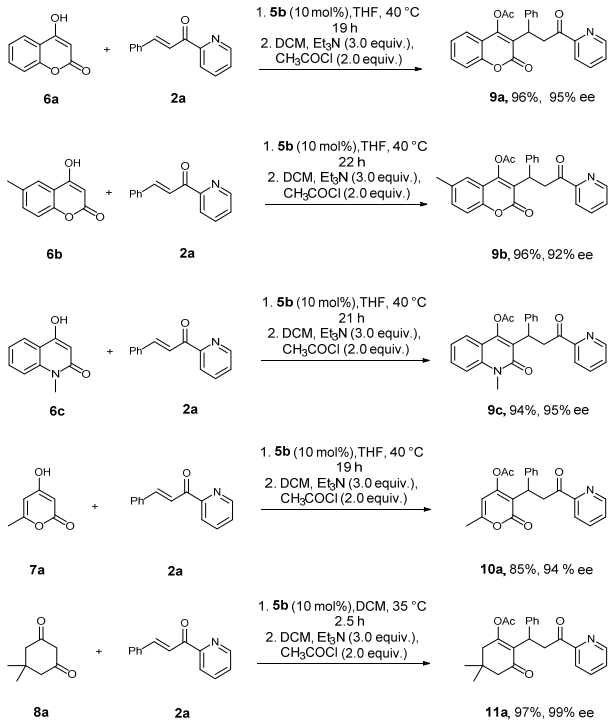



[a]Reactions were carried out on 0.12 mmol of **2a** and 0.1 mmol of **1** in 1 mL of toluene at 40 °C using 10 mol% of catalyst **5b**; after complete conversion of **1** the acetylation was performed (1hour) unless noted otherwise.

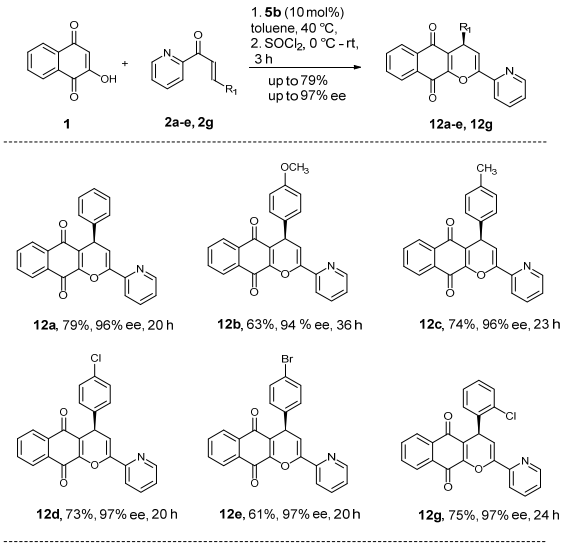
With optimal reaction conditions in hand (Table 3, entry 3), we investigated the scope of 2-enoylpyridines (**2a-o**) for the synthesis of Michael adducts of 2-hydroxy-1,4-naphthoquinone (**1**). From the results summarized in table 4, it is clearly evident that the electronic nature of the substituents present in phenyl ring did not show any significant effect on enantioselectivity of the product. Notably, 2-enoylpyridines having electron donating and withdrawing groups on the phenyl ring reacted

smoothly with 2-hydroxy-1,4-naphthoquinone and afforded desired Michael adducts (**4b-i**) in good yields and excellent enantioselectivities (Table 4, **4b-i**). Notably, multiply substituted substrates **2j** and **2k** reacted smoothly and afforded the corresponding desired Michael adducts **4j** and **4k**, respectively, in good level of enantioselectivities. The sterically demanding substrates 1-napthyl (**2l**), 2-napthyl (**2m**) and 2-furyl (**2n**) substituted 2-enoylpyridines also work in a similar manner and corresponding Michael adducts (**4l, 4m** and **4n** respectively) were formed in excellent yields and enantioselectivities. It was worth noting that cyclohexyl β-substituted 2-enoylpyridine (**2o**) yielded Michael adduct (**4o**) with >99% ee and good yield (77%).

To further explore the versatility of this catalytic system, a few cyclic 1,3-dicarbonyls such as 4-hydroxycoumarin derivatives (**6a-b**, Scheme 1), as well as other analogues such as 4-hydroxy-1-methyl-2(1H)-quinolone (**6c**) 4-hydroxy-6-methyl-2-pyrone (**7a**) and dimedone (**8a**) were also used as Michael donors with electrophile (**2a**) under the optimized reaction conditions employing THF and DCM as solvents instead of toluene to overcome the solubility issue associated with these substrates. Interestingly, in all cases the Michael addition reaction proceeded efficiently and corresponding Michael adducts were obtained in excellent yields and enantioselectivities (Scheme 1). Notably, in the case of dimedone (**8a**) the Michael adduct (**11**) formed within 2.5 hours in excellent yield (97%) and enantioselectivity (99%).

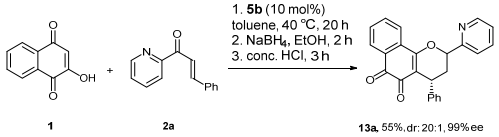



**Scheme 1** Extended substrate scope to 4-hydroxycoumarin derivatives, 4-hydroxy-1-methyl-2(1H)-quinolone, 4-hydroxy-6-methyl-2-pyrone and dimedone.




**Scheme 2** Synthesis of enantioenriched pyranonaphthoquinone derivatives.

Next, we investigated the possible synthetic utility of our catalytic protocol in the enantioselective synthesis of pyranonaphthoquinone derivatives from the Michael adduct (Scheme 2) in one pot. After formation of the Michael adduct under optimized reaction conditions, the solvent was removed and in the same reaction pot thionyl chloride was added, which leads to the formation of pyranonaphthoquinone in high yield and excellent ee (96%). A variety of pyranonaphthoquinones have been successfully synthesized in good yield and excellent enantioselectivities following this method. Furthermore the obtained enantiopure Michael adduct transformed to β-lapachone derivative (1,2-pyranonaphthoquinone)[18-19] in excellent ee (99%, Scheme 4).




**Scheme 3** Synthesis of enantioenriched β-lapacone derivative.

The absolute configuration of product **4d** was unambiguously established as ***R*** by a single-crystal X-ray diffraction analysis (CCDC 1030663). Based on the configuration of product **4d**, a transition state model has been proposed (Figure 3). We envisioned that the chiral squaramide catalyst acts in a synergistic fashion. NH-group of squaramide catalyst interacts via hydrogen bonding interaction with nitrogen and carbonyl oxygen of 2-enoylpyridine and leads to increased electrophilicity of β-position of 2-enoylpyridine. Meanwhile, the 2-hydroxy 1,4-naphthoquinone is activated by the basic quinuclidine nitrogen atom of catalyst and the subsequent addition of nucleophile to the *Si*- face of the 2-enoylpyridine afforded ***R*** configuration of product (**4d**).

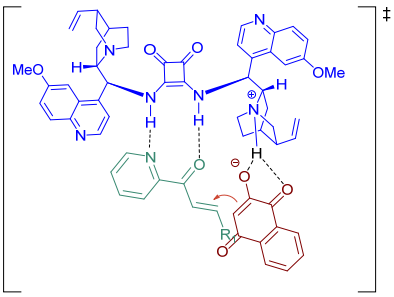


**Fig. 3.** Proposed transition state model.

## Conclusions

In summary, we have developed an efficient and operationally simple protocol for the synthesis of various naphthoquinones using cinchona-based bis-squaramide catalysts. Several naphthoquinone derivatives were obtained in excellent yields (up to 97%) and enantioselectivities (up to >99% ee) under optimized reaction conditions in short reaction time. The catalytic protocol can also be applied in the synthesis of variety of 4-hydroxycoumarin derivatives in excellent yields and enantioselectivities. In addition, the Michael adduct of 2-hydroxy-1,4-naphthoquinone and 2-enoylpyridine were further utilized to synthesise pyranonaphthoquinone derivatives in high yields and enantioselectivities. The stereochemical outcome of the reaction was established by single crystal X-ray analysis and a proposed transition state model has been discussed.

## Acknowledgements

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## Experimental section

### General methods

All reactions were carried out under an atmosphere of nitrogen in oven dried glassware with magnetic stirring. All solvents were purified and dried according to standard methods prior to use. Catalysts **3a-h** and **5a-c** were prepared according to procedure reported in the literature.[7c,17a,20] 2-hydroxy-1,4-naphthoquinone (**1**), 4-hydroxycoumarin (**6a**), 4-hydroxy-6-methyl-2-pyrone (**7a**), dimedone (**8a**) are commercially available and used without further purification. 6-methyl-4-hydroxycoumarin (**6b**), 4-hydroxy-1-methyl-2(1H)-quinolone (**6c**), and β-substituted 2-enoylpyridines (**2a-o**) were prepared by earlier reported methods.[12c,13a] $^1$H spectra were recorded on 400 or 500 or 700 MHz in CDCl3 and $^{13}$C NMR spectra were recorded on 100 or 125 or 175 MHz in CDCl3 using TMS or residual protio solvent signals as internal standard. Data for $^1$H NMR are recorded as follows: chemical shift (δ, ppm), multiplicity (s = singlet, d = doublet, t = triplet, q = quartet, m = multiplet or unresolved, coupling constant(s) in Hz, integration). Data for $^{13}$C NMR are reported in terms of chemical shift (δ, ppm). High resolution mass spectra (HRMS) were obtained by the ESI (Q-TOF) ionization sources. IR spectra were measured with Bruker FT/IR Vector 22 spectrometer. Optical rotations were measured on a commercial automatic polarimeter and reported as follows: [α] TD (c = g/100 mL, solvent). Routine monitoring of reactions were performed using precoated silica gel TLC plates from E-Merck. All the chromatographic separations were carried out by using silica gel (Acme's, 100-200 mesh). Melting points were recorded by using a melting point apparatus and are uncorrected. The enantioselectivity was determined by chiral HPLC analysis using Diacel chiralpak IA, IC and ADH columns with a 200 UV-detector by using iso-propanol and n-hexane as eluents at 25 °C

### General procedure for the conjugate addition of 2-hydroxy 1,4-naphthoquinone to β-substituted 2-enoylpyridines

The 2-hydroxy1,4-naphthoquinone **1** (0.1 mmol) was added to a mixture of β-substituted 2-enoylpyridine **2** (0.12 mmol) and the catalyst **5b** (7.26 mg, 0.01 mmol) in toluene (1.0 mL) at room temperature. The reaction mixture was stirred at 40 °C and the progress of the reaction was monitored by TLC (40% ethyl acetate in hexane). After complete conversion of 2-hydroxy1,4-naphthoquinone, evaporate the solvent and dissolve the reaction mixture in $CH_2Cl_2$ (1.5 mL) was added triethylamine (41.7 µL, 0.3 mmol) to the reaction mixture at room temperature. After stirring for 10 min, acetyl chloride (14.2 µL, 0.2 mmol) was added, and stirring was maintained for 50 min. The crude product was purified over silica gel by column chromatography (25% ethyl acetate in hexane). Enantiomeric excess of the Michael adduct was determined by chiral HPLC analysis.

**(*R*)-1,4-dioxo-3-(3-oxo-1-phenyl-3-(pyridin-2-yl)propyl)-1,4-dihydronaphthalen-2-yl acetate (4a):** The compound **4a** was obtained as a yellow semisolid in 96% yield (40.8 mg) and 98% ee. The optical purity was determined by chiral HPLC on Daicel Chiralpak IA column [*n*-hexane/2-propanol 80:20]; flow rate 1 mL/min; λ = 254 nm; $t_R$(minor) = 13.84 min, $t_R$(major) = 16.99 min; $[\alpha]_D^{25}$ = +31.8 (*c* 0.16 in $CHCl_3$); $^1$H NMR (500 MHz, $CDCl_3$): δ 8.69 (bs, 1H), 8.12 (d, *J* = 7.4 Hz, 1H), 8.05 – 7.98 (m, 2H), 7.86 – 7.63 (m, 3H), 7.54 – 7.12 (m, 7H), 5.23 (t, *J* = 6.7 Hz, 1H), 4.27 – 4.24 (m, 2H), 2.33 (s, 2H); $^{13}$C NMR (125 MHz, $CDCl_3$): δ 199.3, 184.2, 178.3, 167.6, 152.9, 151.2, 148.9, 140.2, 140.0, 137.0, 134.2, 133.7, 132.1, 130.7, 128.6, 128.1, 127.4, 127.0, 126.9, 126.4, 121.9, 40.7, 36.5, 20.4; IR (film): 2924, 1778, 1698, 1675, 1633, 1594 cm$^{-1}$; HRMS (ES+) calc. for $C_{26}H_{20}NO_5$ $[M+H]^+$: 426.1341, found: 426.1342

**(*R*)-3-(1-(4-methoxyphenyl)-3-oxo-3-(pyridin-2-yl)propyl)-1,4-dioxo-1,4-dihydronaphthalen-2-yl acetate (4b):** The compound **4b** was obtained as a light brown semisolid in 95% yield (43.2 mg) and 96% ee. The optical purity was determined by chiral HPLC on Daicel Chiralpak IA column [*n*-hexane/2-propanol 80:20]; flow rate 1 mL/min; λ =

254 nm; $t_R$(minor) = 21.56 min, $t_R$(major) = 28.07 min; $[\alpha]_D^{25}$ = -9.6 (*c* 0.7 in $CHCl_3$); $^1$H NMR (400 MHz, $CDCl_3$): δ 8.65 (d, *J* = 4.3 Hz, 1H), 8.10 – 8.04 (m, 1H), 8.01 (dd, *J* = 7.2, 1.6 Hz, 1H), 7.95 (d, *J* = 7.8 Hz, 1H), 7.78 (td, *J* = 7.7, 1.5 Hz, 1H), 7.72 – 7.62 (m, 2H), 7.47 – 7.40 (m, 1H), 7.35 (d, *J* = 8.6 Hz, 2H), 6.81 (d, *J* = 8.6 Hz, 2H), 5.11 (t, *J* = 7.7 Hz, 1H), 4.22 – 4.14 (m, 2H), 3.73 (s, 3H), 2.32 (s, 3H); $^{13}$C NMR (100 MHz, $CDCl_3$): δ 199.3, 184.3, 178.4, 167.7, 158.4, 152.9, 150.9, 148.9, 140.1, 136.9, 134.1, 133.7, 132.2, 132.1, 130.7, 129.2, 127.3, 126.9, 126.4, 121.9, 113.9, 55.2, 40.9, 35.8, 20.4; IR (film): 2924, 2853, 1778, 1698, 1675, 1594 cm$^{-1}$; HRMS (ES+) calc. for $C_{27}H_{22}NO_6$ $[M+H]^+$: 456.1447, found: 456. 1447

**(*R*)-1,4-dioxo-3-(3-oxo-3-(pyridin-2-yl)-1-(p-tolyl)propyl)-1,4-dihydronaphthalen-2-yl acetate (4c):** The compound **4c** was obtained as a yellow semisolid in 89% yield (39.0 mg) and 96% ee. The optical purity was determined by chiral HPLC on Daicel Chiralpak IA column [*n*-hexane/2-propanol 80:20]; flow rate 1 mL/min; λ = 254 nm; $t_R$(minor) = 13.43 min, $t_R$(major) = 19.94 min; $[\alpha]_D^{25}$ = -2.2 (*c* 1.9 in $CHCl_3$); $^1$H NMR (400 MHz, $CDCl_3$): δ 8.65 (d, *J* = 4.3 Hz, 1H), 8.11 – 7.98 (m, 2H), 7.96 (d, *J* = 7.8 Hz, 1H), 7.78 (td, *J* = 7.7, 1.5 Hz, 1H), 7.71 – 7.62 (m, 2H), 7.47 – 7.41 (m, 1H), 7.32 (d, *J* = 8.0 Hz, 2H), 7.08 (d, *J* = 7.9 Hz, 2H), 5.14 (t, *J* = 7.7 Hz, 1H), 4.20 (d, *J* = 7.7 Hz, 2H), 2.31 (s, 3H), 2.27 (s, 3H); $^{13}$C NMR (100 MHz, $CDCl_3$): δ 199.3, 184.2, 178.4, 167.6, 152.9, 151.0, 148.9, 140.1, 137.1, 136.9, 136.5, 134.1, 133.7, 132.1, 130.7, 129.2, 127.9, 127.3, 127.0, 126.4, 121.9, 40.7, 36.2, 21.0, 20.4; IR (film): 2973, 2916, 1777, 1674, 1594 cm$^{-1}$; HRMS (ES+) calc. for $C_{27}H_{22}NO_5$ $[M+H]^+$: 440.1492, found: 440.1508

**(*R*)-3-(1-(4-chlorophenyl)-3-oxo-3-(pyridin-2-yl)propyl)-1,4-dioxo-1,4-dihydronaphthalen-2-yl acetate (4d):** The compound **4d** was obtained as a pale yellow semisolid (recrystallization afforded a pale yellow solid, mp: 110 – 112 °C) in 96% yield (44.1 mg) and 98% ee. The optical purity was determined by chiral HPLC on Daicel Chiralpak IA column [*n*-hexane/2-propanol 80:20]; flow rate 1 mL/min; λ = 254 nm; $t_R$(minor) = 14.96 min, $t_R$(major) = 21.59 min; $[\alpha]_D^{25}$ = +22.5 (*c* 0.16 in $CHCl_3$); $^1$H NMR (400 MHz, $CDCl_3$): δ 8.64 (d, *J* = 4.3 Hz, 1H), 8.10 – 8.04 (m, 1H), 8.03 – 7.98 (m, 1H), 7.95 (d, *J* = 7.8 Hz, 1H), 7.78 (td, *J* = 7.7, 1.5 Hz, 1H), 7.73 – 7.61 (m, 2H), 7.42-7.46 (m, , 1H), 7.36 (d, *J* = 8.4 Hz, 2H), 7.23 (d, *J* = 8.5 Hz, 2H), 5.13 (t, *J* = 7.6 Hz, 1H), 4.21 (dd, *J* = 18.5, 6.8 Hz, 1H), 4.17 – 4.08 (m, 1H), 2.32 (s, 3H); $^{13}$C NMR (100 MHz, $CDCl_3$): δ 199.0, 184.1, 178.2, 167.6, 152.8, 151.2, 148.9, 139.4, 139.2, 138.7, 137.0, 134.2, 133.8, 132.7, 132.0, 130.6, 129.5, 128.6, 127.4, 127.0, 126.5, 121.9, 40.56, 36.09, 33.83, 31.93, 31.65, 20.4; IR (film): 3026, 2851, 1777, 1674, 1588 cm$^{-1}$; HRMS (ES+) calc. for $C_{26}H_{19}ClNO_5$ $[M+H]^+$: 460.0946, found: 460.0948

**(*R*)-3-(1-(4-bromophenyl)-3-oxo-3-(pyridin-2-yl)propyl)-1,4-dioxo-1,4-dihydronaphthalen-2-yl acetate (4e):** The compound **4e** was obtained as a yellow semisolid in 97% yield (48.9 mg) and 98% ee. The optical purity was determined by chiral HPLC on Daicel Chiralpak IA column [*n*-hexane/2-propanol 80:20]; flow rate 1 mL/min; λ = 254 nm; $t_R$(minor) = 16.06 min, $t_R$(major) = 24.13 min; $[\alpha]_D^{25}$ = +15.18 (*c* 2.4 in THF); $^1$H NMR (400 MHz, $CDCl_3$): δ 8.65 (d, *J* = 4.3 Hz, 1H), 8.09 – 8.00 (m, 2H), 7.96 (d, *J* = 7.8 Hz, 1H), 7.79 (td, *J* = 7.7, 1.5 Hz, 1H), 7.74 – 7.63 (m, 2H), 7.48 – 7.42 (m, 1H), 7.39 (d, *J* = 8.5 Hz, 2H), 7.30 (d, *J* = 8.5 Hz, 2H), 5.11 (t, *J* = 7.6 Hz, 1H), 4.21 (dd, *J* = 18.5, 6.8 Hz, 1H), 4.12 (dd, *J* = 18.5, 8.4 Hz, 1H), 2.32 (s, 3H); $^{13}$C NMR (100 MHz, $CDCl_3$): δ 199.0, 184.1, 178.2, 167.6, 152.8, 151.2, 148.9, 139.3, 139.3, 137.0, 134.2, 133.8, 132.0, 131.6, 130.6, 129.9, 127.4, 127.0, 126.5, 121.9, 120.8, 40.5, 36.1, 20.4; IR (film): 3054, 2924, 2853, 1778, 1698, 1634, 1594 cm$^{-1}$; HRMS (ES+) calc. for $C_{26}H_{19}BrNO_5$ $[M+H]^+$: 504.0447, found: 504.0448

**(*R*)-3-(1-(3-chlorophenyl)-3-oxo-3-(pyridin-2-yl)propyl)-1,4-dioxo-1,4-dihydronaphthalen-2-yl acetate (4f):** The compound **4f** was obtained as a yellow semisolid in 96% yield (44.1 mg) and 98% ee. The optical purity was determined by chiral HPLC on Daicel Chiralpak IA column [*n*-hexane/2-propanol 80:20]; flow rate 1 mL/min; λ = 254 nm; $t_R$(minor) = 11.85 min, $t_R$(major) = 14.01 min; $[\alpha]_D^{25}$ = +33.25 (*c* 0.29 in $CHCl_3$); $^1$H NMR (400 MHz, $CDCl_3$): δ 8.65 (d, *J* = 4.3 Hz, 1H), 8.14 – 8.06 (m, 1H), 8.05 – 7.98 (m, 1H), 7.95 (d, *J* = 7.8 Hz, 1H), 7.79 (td, *J* = 7.7, 1.4 Hz, 1H), 7.74 – 7.63 (m, 2H), 7.45 (dd, *J* = 8.8, 7.2 Hz, 2H), 7.32 – 7.11 (m, 3H), 5.15 (t, *J* = 7.6 Hz, 1H), 4.24 – 4.05 (m, 2H), 2.31 (s, 3H); $^{13}$C NMR (100 MHz, $CDCl_3$): δ 198.9, 184.0, 178.2, 167.5, 152.7, 151.3, 148.9, 142.2, 139.4, 137.0, 134.3, 134.2, 133.8, 132.0, 130.7, 129.8, 128.1, 127.5, 127.1, 127.0, 126.5, 121.9, 40.4, 36.1, 20.4; IR (film): 2926, 2851, 1778, 1676, 1594 cm$^{-1}$; HRMS (ES+) calc. for $C_{26}H_{19}ClNO_5$ $[M+H]^+$: 460.0946, found: 460.0952

**(*S*)-3-(1-(2-chlorophenyl)-3-oxo-3-(pyridin-2-yl)propyl)-1,4-dioxo-1,4-dihydronaphthalen-2-yl acetate (4g):** The compound **4g** was obtained as a yellow semisolid in 91% yield (41.8 mg) and 97% ee. The optical purity was determined by chiral HPLC on Daicel Chiralpak IA column [*n*-hexane/2-propanol 80:20]; flow rate 1 mL/min; λ = 254 nm; $t_R$(minor) = 11.70 min, $t_R$(major) = 18.38 min; $[\alpha]_D^{25}$ = +34.4 (*c* 0.12 in $CHCl_3$); $^1$H NMR (400 MHz, $CDCl_3$): δ 8.65 (d, *J* = 4.3 Hz, 1H), 8.11 – 7.92 (m, 3H), 7.81 (t, *J* = 7.6 Hz, 1H), 7.66-7.71 (m, 2H), 7.50 – 7.41 (m, 2H), 7.33 (d, *J* = 7.5 Hz, 1H), 7.21 – 7.05 (m, 2H), 5.45 (t, *J* = 7.7 Hz, 1H), 4.21 – 3.89 (m, 2H), 2.11 (s, 3H). $^{13}$C NMR (100 MHz, $CDCl_3$): δ 198.6, 184.1, 178.1, 167.4, 152.8, 151.9, 148.9, 138.7, 138.0, 137.0, 134.2, 134.0, 133.7, 132.1, 130.7, 129.8, 129.1, 128.1, 127.4, 127.0, 126.8, 126.5, 122.0, 40.4, 34.9, 20.2; IR (film): 2972, 1777, 1681, 1593 cm$^{-1}$; HRMS (ES+) calc. for $C_{26}H_{19}ClNO_5$ $[M+H]^+$: 460.0946, found: 460.0946

**(*R*)-3-(1-(4-nitrophenyl)-3-oxo-3-(pyridin-2-yl)propyl)-1,4-dioxo-1,4-dihydronaphthalen-2-yl acetate (4h):** The compound **4h** was obtained as a yellow semisolid in 97% yield (45.6 mg) and 98% ee. The optical purity was determined by chiral HPLC on Daicel Chiralpak IA column [*n*-hexane/2-propanol 80:20]; flow rate 1 mL/min; λ = 254 nm; $t_R$(minor) = 30.36 min, $t_R$(major) = 36.39 min; $[\alpha]_D^{25}$ = +46.8 (*c* 2.3 in DCM); $^1$H NMR (400 MHz, $CDCl_3$): δ 8.65 (d, *J* = 4.2 Hz, 1H), 8.12 (d, *J* = 8.6 Hz, 2H), 8.08 – 8.00 (m, 2H), 7.96 (d, *J* = 7.8 Hz, 1H), 7.81 (t, *J* = 7.2 Hz, 1H), 7.75 – 7.66 (m, 2H), 7.59 (d,

$J$ = 8.6 Hz, 2H), 7.50 – 7.44 (m, 1H), 5.32 – 5.12 (m, 1H), 4.32 (dd, $J$ = 18.5, 7.1 Hz, 1H), 4.16 – 4.04 (m, 1H), 2.34 (s, 3H); $^{13}$C NMR (100 MHz, $CDCl_3$): δ 198.6, 183.9, 178.0, 167.6, 152.6, 151.6, 149.0, 147.9, 146.7, 138.6, 137.1, 134.4, 134.0, 131.9, 130.6, 129.0, 127.6, 127.0, 126.6, 123.7, 122.0, 40.1, 36.5, 20.4; IR (film): 2924, 2854, 1779, 1699, 1677, 1636, 1595, 1520, 1346, 1289cm$^{-1}$; HRMS (ES+) calc. for $C_{26}H_{18}N_2O_7$ $[M+Na]^+$: 493.1006, found: 493.1004

**(*R*)-3-(1-(4-cyanophenyl)-3-oxo-3-(pyridin-2-yl)propyl)-1,4-dioxo-1,4-dihydronaphthalen-2-yl acetate (4i):** The compound **4i** was obtained as a yellow semisolid in 92% yield (43.6 mg) and 98% ee. The optical purity was determined by chiral HPLC on Daicel Chiralpak IA column [*n*-hexane/2-propanol 80:20]; flow rate 1 mL/min; λ = 254 nm; $t_R$(minor) = 27.22 min, $t_R$(major) = 35.05 min; $[\alpha]_D^{25}$ = +45.18 (*c* 2.2 in THF); $^1$H NMR (400 MHz, $CDCl_3$) : δ 8.66 (d, $J$ = 4.1 Hz, 1H), 8.12 – 8.00 (m, 2H), 7.97 (d, $J$ = 7.7 Hz, 1H), 7.81 (t, $J$ = 7.3 Hz, 1H), 7.76 – 7.41 (m, 7H), 5.19 (t, $J$ = 7.4 Hz, 1H), 4.28 (dd, $J$ = 18.5, 7.0 Hz, 1H), 4.09 (dd, $J$ = 18.5, 8.0 Hz, 1H), 2.33 (s, 3H); $^{13}$C NMR (100 MHz, $CDCl_3$): δ 198.6, 183.9, 178.0, 167.6, 152.6, 151.6, 149.0, 145.8, 138.7, 137.1, 134.4, 134.0, 132.3, 131.9, 130.6, 128.9, 127.6, 127.0, 126.6, 122.0, 118.7, 110.8, 40.1, 36.7, 20.4; IR (film): 2924, 2854, 2227, 1779, 1699, 1677, 1635, 1287, 1169 cm$^{-1}$; HRMS (ES+) calc. for $C_{27}H_{19}N_2O_5$ $[M+H]^+$: 451.1294, found: 451.1290

**(*S*)-3-(1-(2-chloro-6-fluorophenyl)-3-oxo-3-(pyridin-2-yl)propyl)-1,4-dioxo-1,4-dihydronaphthalen-2-yl acetate (4j)**: The compound **4j** was obtained as a yellow semisolid in 96% yield (45.8 mg) and 94% ee. The optical purity was determined by chiral HPLC on Daicel Chiralpak IA column [*n*-hexane/2-propanol 80:20]; flow rate 1 mL/min; λ = 254 nm; $t_R$(minor) = 12.70 min, $t_R$(major) = 17.92 min; $[\alpha]_D^{25}$ = +42.9 (*c* 2.3 in THF); $^1$H NMR (500 MHz, $CDCl_3$): δ 8.71 (bs, 1H), 8.08 – 8.05 (m, 3H), 7.87 – 7.51 (m, 5H), 7.21 – 7.16 (m, 2H), 6.94 – 6.90 (m, 1H), 5.45 (bs, 1H), 4.31 (bs, 1H), 2.13 (s, 3H); $^{13}$C NMR (125 MHz, $CDCl_3$): δ 198.3, 183.8, 177.9, 167.1, 160.9, 152.8, 152.2, 149.0, 137.7, 134.2, 133.7, 132.1, 130.6, 128.7, 128.6, 127.4, 127.0, 126.5, 125.8, 122.0, 114.8, 114.6, 39.8, 33.1, 20.0; IR (film): 2924, 1779, 1700, 1677, 1594 cm$^{-1}$; HRMS (ES+) calc. for $C_{26}H_{18}ClFNO_5$ $[M+H]^+$: 478.0858, found: 478.0856

**(*R*)-3-(1-(benzo[d][1,3]dioxol-5-yl)-3-oxo-3-(pyridin-2-yl)propyl)-1,4-dioxo-1,4-dihydronaphthalen-2-yl acetate (4k):** The compound **4k** was obtained as a light brown semisolid in 94% yield (44.1 mg) and 96% ee. The optical purity was determined by chiral HPLC on Daicel Chiralpak IA column [*n*-hexane/2-propanol 80:20]; flow rate 1 mL/min; λ = 254 nm; $t_R$(minor) = 21.51 min, $t_R$(major) = 25.85 min; $[\alpha]_D^{25}$ = +6.2 (*c* 0.1 in $CHCl_3$); $^1$H NMR (500 MHz, $CDCl_3$) δ 8.71 (bs, 1H), 8.14 (d, $J$ = 7.4 Hz, 1H), 8.09 – 7.98 (m, 2H), 7.89 – 7.69 (m, 3H), 7.52 (bs, 1H), 6.99 (s, 1H), 6.94 (d, $J$ = 7.6 Hz, 1H), 6.75 (d, $J$ = 7.7 Hz, 1H), 5.92 (d, $J$ = 1.6 Hz, 2H), 5.13 (bs, 1H), 4.21 (bs, 2H), 2.38 (s, 3H); $^{13}$C NMR (125 MHz, $CDCl_3$) δ 198.9, 184.3, 178.3, 167.6, 150.9, 148.7, 147.7, 146.4, 139.8, 137.3, 134.2, 133.9, 133.7, 132.1, 130.7, 127.5, 127.0, 126.4, 122.0, 121.3, 108.8, 108.3, 101.0, 40.8, 36.0, 20.1; IR (film): 2924, 2854, 1778, 1698, 1674, 1633, 1593 cm$^{-1}$; HRMS (ES+) calc. for $C_{27}H_{20}NO_7$ $[M+H]^+$: 470.1240, found: 470.1242

**(*R*)-3-(1-(naphthalen-1-yl)-3-oxo-3-(pyridin-2-yl)propyl)-1,4-dioxo-1,4-dihydronaphthalen-2-yl acetate (4l):** The compound **4l** was obtained as a yellow semisolid in 93% yield (44.2 mg) and 95% ee. The optical purity was determined by chiral HPLC on Daicel Chiralpak IA column [*n*-hexane/2-propanol 80:20]; flow rate 1 mL/min; λ = 254 nm; $t_R$(minor) = 15.77 min, $t_R$(major) = 23.66 min; $[\alpha]_D^{25}$ = +20.18 (*c* 2.2 in THF); $^1$H NMR (400 MHz, $CDCl_3$): δ 8.65 (d, $J$ = 3.5 Hz, 1H), 8.19 (d, $J$ = 8.3 Hz, 1H), 8.09 (d, $J$ = 7.7 Hz, 1H), 8.04 – 7.59 (m, 8H), 7.57 – 7.32 (m, 4H), 5.97 (t, $J$ = 7.4 Hz, 1H), 4.36 – 4.10 (m, 2H), 2.10 (s, 3H); $^{13}$C NMR (100 MHz, $CDCl_3$): δ 199.1, 184.3, 178.1, 167.3, 152.9, 152.1, 148.9, 139.7, 137.0, 136.4, 134.2, 134.0, 133.7, 132.1, 131.5, 130.7, 129.0, 127.8, 127.4, 127.1, 126.5, 126.4, 125.6, 125.3, 125.2, 123.2, 122.0, 41.5, 33.3, 20.2; IR (film): 3053, 2853, 2924, 1778, 1698, 1676, 1633, 1594 cm$^{-1}$; HRMS (ES+) calc. for $C_{30}H_{22}NO_5$ $[M+H]^+$: 476.1498, found: 476.1490

**(*R*)-3-(1-(naphthalen-2-yl)-3-oxo-3-(pyridin-2-yl)propyl)-1,4-dioxo-1,4-dihydronaphthalen-2-yl acetate (4m):** The compound **4m** was obtained as a yellow semisolid in 95% yield (45.1 mg) and 97% ee. The optical purity was determined by chiral HPLC on Daicel Chiralpak IA column [*n*-hexane/2-propanol 80:20]; flow rate 1 mL/min; λ = 254 nm; $t_R$(minor) = 17.79 min, $t_R$(major) = 21.87 min; $[\alpha]_D^{25}$ = +52.13 (*c* 2.2 in THF); $^1$H NMR (400 MHz, $CDCl_3$): δ 8.68 (d, $J$ = 4.2 Hz, 1H), 8.03 – 8.08 (m, 3H), 7.90 (s, 1H), 7.84 – 7.60 (m, 6H), 7.57 – 7.33 (m, 4H), 5.35 (t, $J$ = 7.6 Hz, 1H), 4.39 – 4.24 (m, 2H), 2.27 (s, 3H); $^{13}$C NMR (100 MHz, $CDCl_3$): δ 199.2, 184.2, 178.4, 167.6, 152.9, 151.2, 148.9, 139.9, 137.6, 137.0, 134.1, 133.7, 133.4, 132.3, 132.1, 130.7, 128.3, 127.8, 127.6, 127.4, 127.0, 126.5, 126.4, 126.1, 125.7, 122.0, 40.7, 36.6, 20.4; IR (film): 3055, 2924, 2854, 1778, 1698, 1675, 1632, 1594 cm$^{-1}$; HRMS (ES+) calc. for $C_{30}H_{22}NO_5$ $[M+H]^+$: 476.1498, found: 476.1499

**(*S*)-3-(1-(furan-2-yl)-3-oxo-3-(pyridin-2-yl)propyl)-1,4-dioxo-1,4-dihydronaphthalen-2-yl acetate:** The compound **4n** was obtained as a light brown semisolid in 92% yield (38.2 mg) and 95% ee. The optical purity was determined by chiral HPLC on Daicel Chiralpak IA column [*n*-hexane/2-propanol 80:20]; flow rate 1 mL/min; λ = 254 nm; $t_R$(minor) = 13.16 min, $t_R$(major) = 17.46 min; $[\alpha]_D^{25}$ = +40.74 (*c* 0.1 in $CHCl_3$); $^1$H NMR (400 MHz, $CDCl_3$): δ 8.66 (d, $J$ = 4.3 Hz, 1H), 8.17 – 8.10 (m, 1H), 8.03 (dd, $J$ = 8.7, 7.1 Hz, 1H), 7.96 (d, $J$ = 7.8 Hz, 1H), 7.79 (td, $J$ = 7.7, 1.5 Hz, 1H), 7.75 – 7.65 (m, 2H), 7.48 – 7.42 (m, 1H), 7.26 (d, $J$ = 6.3 Hz, 1H), 6.27 (dd, $J$ = 3.0, 1.9 Hz, 1H), 6.20 (d, $J$ = 3.1 Hz, 1H), 5.29 – 5.19 (m, 1H), 4.23 (dd, $J$ = 18.7, 6.4 Hz, 1H), 4.11 – 4.02 (m, 1H), 2.29 (s, 3H); $^{13}$C NMR (100 MHz, $CDCl_3$): δ 198.7, 183.6, 178.3, 167.4, 153.1, 152.8, 151.5, 148.9, 141.6, 137.7, 136.9, 134.2, 133.7, 132.0, 130.8, 127.4, 127.1, 126.5, 121.9, 110.4, 106.2, 39.6, 30.4, 20.3. IR (film): 2925, 2854, 1779, 1698, 1677, 1593 cm$^{-1}$; HRMS (ES+) calc. for $C_{24}H_{18}NO_6$ $[M+H]^+$: 416.1134, found: 416.1130

**(*R*)-3-(1-cyclohexyl-3-oxo-3-(pyridin-2-yl)propyl)-1,4-dioxo-1,4-dihydronaphthalen-2-yl acetate (4o):** The

compound **4o** was obtained as a pale yellow semisolid in 77% yield (3.2 mg) and 99.6% ee. The optical purity was determined by chiral HPLC on Daicel Chiralpak IA column [*n*-hexane/2-propanol 95:5]; flow rate 1 mL/min; λ = 254 nm; $t_R$(minor) = 19.09 min, $t_R$(major) = 23.66 min; $[\alpha]_D^{25}$ = -26.2 (*c* 1.5 in THF); $^1$H NMR (400 MHz, $CDCl_3$): δ 8.61 (t, *J* = 8.5 Hz, 1H), 8.12 (t, *J* = 7.2 Hz, 1H), 8.03 (d, *J* = 6.9 Hz, 1H), 7.89 (t, *J* = 7.9 Hz, 1H), 7.81 – 7.59 (m, 3H), 7.49 – 7.32 (m, 1H), 3.87 – 3.68 (m, 2H), 3.55 (d, *J* = 5.0 Hz, 1H), 2.34 (s, 3H), 2.00 (d, *J* = 12.2 Hz, 1H), 1.58-1.80 (m, 4H), 1.37 – 0.82 (m, 6H); $^{13}$C NMR (100 MHz, $CDCl_3$): δ 200.2, 184.4, 177.9, 167.9, 152.9, 148.6, 141.5, 137.0, 134.0, 133.6, 132.2, 130.8, 127.1, 127.0, 126.4, 121.9, 40.6, 39.9, 31.7, 31.7, 26.3, 26.2, 26.2, 20.5; IR (film): 2926, 2851, 1777, 1698, 1674, 1631, 1595 cm$^{-1}$; HRMS (ES+) calc. for $C_{26}H_{26}NO_5$ $[M+H]^+$: 432.1811, found: 432.1818

**General procedure for the conjugate addition of 4-hydroxycoumarins (6a-b) to 2-enoylpyridine (2a)**

The 4-hydroxycoumarin **6** (0.1 mmol) was added to a mixture of 2-enoylpyridine **2a** (0.12 mmol) and the catalyst **5b** (7.26 mg, 0.01 mmol) in THF (1.0 mL) at room temperature. The reaction mixture was stirred at 40 °C and the progress of the reaction was monitored by TLC (40% ethyl acetate in hexane). After complete conversion of 4-hydroxycoumarin, evaporate the solvent and dissolve the reaction mixture in $CH_2Cl_2$ (1.5 mL) was added triethylamine (41.7 µL, 0.3 mmol) to the reaction mixture at room temperature. After stirring for 10 min, acetyl chloride (14.2 µL, 0.2 mmol) was added, and stirring was maintained for 50 min. The crude product was purified over silica gel by column chromatography (25% ethyl acetate in hexane). Enantiomeric excess of the Michael adduct was determined by chiral HPLC analysis.

**(+)-2-oxo-3-(3-oxo-1-phenyl-3-(pyridin-2-yl)propyl)-2H-chromen-4-yl acetate (9a):** The compound **9a** was obtained as a colorless semisolid in 96% yield (39.7 mg) and 95% ee. The optical purity was determined by chiral HPLC on Daicel Chiralpak IA column [*n*-hexane/2-propanol 80:20]; flow rate 1 mL/min; λ = 254 nm; $t_R$(minor) = 14.21 min, $t_R$(major) = 18.98 min; $[\alpha]_D^{25}$ = +73.5 (*c* 2.1 in DCM); $^1$H NMR (400 MHz, $CDCl_3$): δ 8.67 (d, *J* = 4.0 Hz, 1H), 7.96 (d, *J* = 7.8 Hz, 1H), 7.85 – 7.64 (m, 1H), 7.55 – 7.37 (m, 4H), 7.36 – 7.01 (m, 6H), 5.04 (t, *J* = 7.2 Hz, 1H), 4.36 (dd, *J* = 18.4, 6.9 Hz, 1H), 4.13 (dd, *J* = 18.4, 7.6 Hz, 1H), 2.44 (s, 3H); $^{13}$C NMR (100 MHz, $CDCl_3$): δ 199.6, 167.1, 161.1, 155.3, 153.0, 152.4, 148.9, 140.5, 136.9, 131.8, 128.4, 128.0, 127.2, 126.8, 124.1, 123.0, 121.9, 121.9, 116.7, 116.0, 39.7, 37.0, 20.6; IR (film): 3059, 2925, 2853, 1778, 1722, 1626, 1608, 1582 cm$^{-1}$; HRMS (ES+) calc. for $C_{25}H_{20}NO_5$ $[M+H]^+$: 414.1341, found: 414. 1347

**(+)-6-methyl-2-oxo-3-(3-oxo-1-phenyl-3-(pyridin-2-yl)propyl)-2H-chromen-4-yl acetate (9b):** The compound **9b** was obtained as a colourless semisolid in 96% yield (41.0 mg) and 92% ee. The optical purity was determined by chiral HPLC on Daicel Chiralpak IA column [*n*-hexane/2-propanol 70:30]; flow rate 1 mL/min; λ = 254 nm; $t_R$(minor) = 9.41 min, $t_R$(major) = 12.25 min; $[\alpha]_D^{25}$ = +76.08 (*c* 2.0 in $CHCl_3$); $^1$H NMR (400 MHz, $CDCl_3$): δ 8.67 (d, *J* = 4.3 Hz, 1H), 7.96 (d, *J* = 7.8 Hz, 1H), 7.77 (td, *J* = 7.7, 1.4 Hz, 1H), 7.49 – 7.11 (m, 8H), 7.06 (s, 1H), 5.03 (t, *J* = 7.2 Hz, 1H), 4.37 (dd, *J* = 18.4, 7.0 Hz, 1H), 4.10 (dd, *J* = 18.4, 7.5 Hz, 1H), 2.45 (s, 3H), 2.35 (s, 3H); $^{13}$C NMR (100 MHz, $CDCl_3$): δ 199.7, 167.2, 161.2, 155.3, 153.1, 150.6, 148.9, 140.6, 136.8, 133.9, 132.9, 128.3, 128.0, 127.2, 126.7, 122.6, 121.9, 121.7, 116.4, 115.7, 39.7, 37.0, 21.0, 20.6; IR (film): 3058, 2924, 2853, 1777, 1721, 1628, 1582 cm$^{-1}$; HRMS (ES+) calc. for $C_{26}H_{22}NO_5$ $[M+H]^+$: 428.1498, found: 428.1492

**Procedure for the conjugate addition of 4-hydroxy-1-methyl-2(1H)-quinolone (6c) to 2-enoylpyridine (2a)**

The 4-hydroxy-1-methyl-2(1H)-quinolone **6c** (0.1 mmol) was added to a mixture of 2-enoylpyridine **2a** (0.12 mmol) and the catalyst **5b** (7.26 mg, 0.01 mmol) in THF (1.0 mL) at room temperature. The reaction mixture was stirred for 21 hours at 40 °C (the progress of the reaction was monitored by TLC 60% ethyl acetate in hexane). After complete conversion of 4-hydroxy-1-methyl-2(1H)-quinolone, evaporate the solvent and dissolve the reaction mixture in $CH_2Cl_2$ (1.5 mL) was added triethylamine (41.7 µL, 0.3 mmol) to the reaction mixture at room temperature. After stirring for 10 min, acetyl chloride (14.2 µL, 0.2 mmol) was added, and stirring was maintained for 50 min. The crude product was purified over silica gel by column chromatography (40% ethyl acetate in hexane). Enantiomeric excess of the Michael adduct was determined by chiral HPLC analysis.

**(+)-1-methyl-2-oxo-3-(3-oxo-1-phenyl-3-(pyridin-2-yl)propyl)-1,2-dihydroquinolin-4-yl acetate (9c):** The compound **9c** was obtained as a colourless semisolid in 94% yield (40.0 mg) and 95% ee. The optical purity was determined by chiral HPLC on Daicel Chiralpak ADH column [*n*-hexane/2-propanol 80:20]; flow rate 1 mL/min; λ = 254 nm; $t_R$(minor) = 16.68 min, $t_R$(major) = 19.77 min; $[\alpha]_D^{25}$ = +65.6 (*c* 2.2 in $CHCl_3$); $^1$H NMR (500 MHz, $CDCl_3$): δ 8.71 (d, *J* = 3.9 Hz, 1H), 8.00 (d, *J* = 7.7 Hz, 1H), 7.81 (t, *J* = 7.5 Hz, 1H), 7.58 – 7.42 (m, 5H), 7.35 (d, *J* = 8.5 Hz, 1H), 7.30 – 7.15 (m, 4H), 5.23 (t, *J* = 6.9 Hz, 1H), 4.60 (d, *J* = 10.7 Hz, 1H), 4.04 (d, *J* = 14.7 Hz, 1H), 3.69 (s, 3H), 2.46 (s, 3H); $^{13}$C NMR (125 MHz, $CDCl_3$): δ 200.0, 167.9, 162.0, 153.3, 151.9, 148.9, 141.6, 138.9, 136.8, 130.7, 128.1, 128.0, 127.1, 126.3, 126.0, 123.2, 122.1, 121.8, 116.3, 114.2, 39.7, 37.1, 29.9, 20.7; IR (film): 3057, 2924, 2853, 1769, 1697, 1643, 1597 cm$^{-1}$; HRMS (ES+) calc. for $C_{26}H_{23}N_2O_4$ $[M+H]^+$: 427.1658, found: 427.1657

**Procedure for the conjugate addition of 4-hydroxy-6-methyl-2-pyrone (7a) to 2-enoylpyridine (2a)**

The 4-hydroxy-6-methyl-2-pyrone **7a** (0.1 mmol) was added to a mixture of 2-enoylpyridine **2a** (0.12 mmol) and the catalyst **5b** (7.26 mg, 0.01 mmol) in THF (1.0 mL) at room temperature. The reaction mixture was stirred for 19 hours at 40 °C (the progress of the reaction was monitored by TLC 60% ethyl acetate in hexane). After complete conversion of 4-hydroxy-6-methyl-2-pyrone, evaporate the solvent and dissolve the reaction mixture in $CH_2Cl_2$ (1.5 mL) was added triethylamine (41.7 µL, 0.3 mmol) to the reaction mixture at room temperature. After stirring for 10 min, acetyl chloride (14.2 µL, 0.2 mmol) was added, and stirring was maintained for 50 min.

The crude product was purified over silica gel by column chromatography (40% ethyl acetate in hexane).

**(−)-6-methyl-2-oxo-3-(3-oxo-1-phenyl-3-(pyridin-2-yl)propyl)-2H-pyran-4-yl acetate (10a):** The compound **10a** was obtained as a colourless semisolid in 85% yield (32.0 mg) and 94% ee. The optical purity was determined by chiral HPLC on Daicel Chiralpak IA column [*n*-hexane/2-propanol 80:20]; flow rate 1 mL/min; λ = 254 nm; $t_R$(minor) = 11.64 min, $t_R$(major) = 17.55 min; $[\alpha]_D^{25}$ = -2.0 (*c* 0.5 in $CHCl_3$); $^1$H NMR (500 MHz, $CDCl_3$): δ 8.70 (s, 1H), 8.00 (s, 1H), 7.89 – 7.09 (m, 7H), 5.96 (s, 1H), 4.96 (s, 1H), 4.30 (dd, *J* = 17.3, 8.3 Hz, 1H), 4.11 (d, *J* = 14.8 Hz, 1H), 2.31 (s, 3H), 2.20 (s, 3H); $^{13}$C NMR (125 MHz, $CDCl_3$): δ 199.7, 167.2, 163.5, 160.3, 158.8, 153.0, 148.9, 147.9, 141.3, 137.0, 128.3, 127.9, 127.3, 126.6, 122.0, 116.4, 102.4, 39.9, 36.0, 21.1, 19.8; IR (film): 3023, 2898, 2840, 1777, 1694, 1578, 1448, 1403 cm$^{-1}$; HRMS (ES+) calc. for $C_{22}H_{20}NO_5$ $[M+H]^+$: 378.1336, found: 378.1361

**Procedure for the Conjugate Addition of Dimedone (8a) to 2-Enoylpyridine (2a):**

The dimedone **8a** (0.1 mmol) was added to a mixture of 2-enoylpyridine **2a** (0.12 mmol) and the catalyst **5b** (7.26 mg, 0.01 mmol) in DCM (1.0 mL) at room temperature. The reaction mixture was stirred for 2.5 hours at 35 °C (the progress of the reaction was monitored by TLC 40% ethyl acetate in hexane). After complete conversion of dimedone, triethylamine (41.7 µL, 0.3 mmol) was added to the reaction mixture at room temperature. After stirring for 10 min, acetyl chloride (14.2 µL, 0.2 mmol) was added, and stirring was maintained for 50 min. The crude product was purified over silica gel by column chromatography (25% ethyl acetate in hexane).

**(+)-5,5-dimethyl-3-oxo-2-(3-oxo-1-phenyl-3-(pyridin-2-yl)propyl)cyclohex-1-en-1-yl acetate (11a):** The compound **11a** was obtained as a colourless semisolid in 97% yield (37.9 mg) and 99% ee. The optical purity was determined by chiral HPLC on Daicel Chiralpak IA column [*n*-hexane/2-propanol 80:20]; flow rate 1 mL/min; λ = 254 nm; $t_R$(minor) = 8.73 min, $t_R$(major) = 12.89 min, $[\alpha]_D^{25}$ = +76.5 (*c* 0.57 in $CHCl_3$); $^1$H NMR (400 MHz, $CDCl_3$): δ 8.66 (d, *J* = 4.0 Hz, 1H), 7.96 (d, *J* = 7.8 Hz, 1H), 7.79 (t, *J* = 7.2 Hz, 1H), 7.50 – 7.01 (m, 6H), 4.85 (t, *J* = 7.5 Hz, 1H), 4.12 (dd, *J* = 17.6, 6.6 Hz, 1H), 3.86 (dd, *J* = 17.6, 8.5 Hz, 1H), 2.51 (d, *J* = 17.7 Hz, 1H), 2.38 (d, *J* = 17.7 Hz, 1H), 2.33 – 2.19 (m, 2H), 2.09 (s, 3H), 1.03 (s, 3H), 1.01 (s, 3H); $^{13}$C NMR (100 MHz, $CDCl_3$): δ 200.0, 198.3, 167.4, 163.7, 153.2, 148.8, 142.2, 137.0, 129.4, 128.1, 127.5, 127.1, 126.0, 121.9, 51.5, 42.8, 40.1, 35.1, 32.6, 28.0, 27.9, 20.9; HRMS (ES+) calc. for $C_{24}H_{26}NO_4$ $[M+H]^+$ : 392.1856, found: 392.1875

**General procedure for the synthesis of enantioenriched pyranonaphthoquinones (12a-e, 12g)**

The 2-hydroxy1,4-naphthoquinone **1** (0.1 mmol) was added to a mixture of β-substituted 2-enoylpyridine **2** (0.12 mmol) and the catalyst **5b** (7.26 mg, 0.01 mmol) in toluene (1.0 mL) at room temperature. The reaction mixture was stirred 40 °C and the progress of the reaction was monitored by TLC (40% ethyl acetate in hexane). After complete conversion of 2-hydroxy1,4-naphthoquinone, evaporate the solvent and $SOCl_2$ (0.5 mL) was added slowly to the reaction mixture at 0 °C, and allow the reaction mixture to warm to room temperature and stirring was maintained for 3 hours at rt. The reaction mixture was pour into cold water and neutralized with solid $NaHCO_3$ and extracted with $CH_2Cl_2$ thrice. The combined organic layers were dried over anhydrous $NaSO_4$, filtered and concentrated under reduced pressure. The product was purified by column chromatography over silica gel. Enantiomeric excess of the pyranonaphthoquinones were determined by chiral HPLC analysis.

**(*R*)-4-phenyl-2-(pyridin-2-yl)-4H-benzo[g]chromene-5,10-dione (12a):** The compound **12a** was obtained as a yellow semisolid in 79% yield (28.8 mg) and 96% ee. The optical purity was determined by chiral HPLC on Daicel Chiralpak IA column [*n*-hexane/2-propanol 90:10]; flow rate 1 mL/min; λ = 254 nm; $t_R$(minor) = 17.13 min, $t_R$(major) = 20.44 min, $[\alpha]_D^{25}$ = +186.0 (*c* 0.25 in $CHCl_3$); $^1$H NMR (500 MHz, $CDCl_3$): δ 8.62 (bs, 1H), 8.24 – 7.96 (m, 3H), 7.93 – 7.59 (m, 3H), 7.54 – 7.14 (m, 6H), 6.67 (bs, 1H), 4.95 (d, *J* = 3.7 Hz, 1H); $^{13}$C NMR (125 MHz, $CDCl_3$): δ 183.8, 178.5, 150.7, 149.7, 149.1, 146.1, 145.6, 143.2, 137.3, 134.3, 133.5, 131.9, 130.8, 128.8, 128.5, 127.3, 126.4, 123.7, 122.1, 119.5, 106.1, 36.0; IR (film): 3028, 2936, 1668, 1620, 1493, 1453, 1323, 1200, 1105, 1004 cm$^{-1}$; HRMS (ES+) calc. for $C_{24}H_{16}NO_3$ $[M+H]^+$ : 366.1125, found: 366.1097

**(*R*)-4-(4-methoxyphenyl)-2-(pyridin-2-yl)-4H-benzo[g]chromene-5,10-dione (12b):** The compound **12b** was obtained as a light brown semisolid in 63% yield (24.9 mg) and 94% ee. The optical purity was determined by chiral HPLC on Daicel Chiralpak IA column [*n*-hexane/2-propanol 80:20]; flow rate 1 mL/min; λ = 254 nm; $t_R$(minor) = 17.13 min, $t_R$(major) = 18.87 min, $[\alpha]_D^{25}$ = +305.7 (*c* 0.15 in $CHCl_3$); $^1$H NMR (500 MHz, $CDCl_3$): δ 8.63 (bs, 1H), 8.23 – 7.66 (m, 6H), 7.39 – 7.31 (m, 3H), 6.85 (d, *J* = 8.5 Hz, 2H), 6.66 (bs, 1H), 4.90 (d, *J* = 4.0 Hz, 1H), 3.77 (s, 3H); $^{13}$C NMR (125 MHz, $CDCl_3$): δ 183.9, 178.6, 158.8, 150.4, 149.8, 149.1, 146.1, 137.3, 135.5, 134.3, 133.5, 131.9, 130.8, 129.6, 126.4, 126.3, 123.7, 122.3, 119.5, 114.1, 106.1, 55.2, 35.1; IR (film): 2920, 2835, 1672, 1620, 1510, 1368, 1329, 1250, 1203, 1108, 1006 cm$^{-1}$; HRMS (ES+) calc. for $C_{25}H_{18}NO_4$ $[M+H]^+$ : 396.1230, found: 396.1226

**(*R*)-2-(pyridin-2-yl)-4-(p-tolyl)-4H-benzo[g]chromene-5,10-dione (12c):** The compound **12c** was obtained as a yellow semisolid in 74% yield (28.0 mg) and 96% ee. The optical purity was determined by chiral HPLC on Daicel Chiralpak IA column [*n*-hexane/2-propanol 80:20]; flow rate 1 mL/min; λ = 254 nm; $t_R$(minor) = 10.59 min, $t_R$(major) = 16.91 min, $[\alpha]_D^{25}$ = +179.7 (*c* 0.10 in $CHCl_3$); $^1$H NMR (500 MHz, $CDCl_3$): δ 8.61 (s, 1H), 8.26 – 7.94 (m, 3H), 7.89-7.78 (m, 3H), 7.48 – 7.20 (m, 3H), 7.13 (d, *J* = 7.5 Hz, 2H), 6.64 (bs, 1H), 4.91 (d, *J* = 4.5 Hz, 1H), 2.30 (s, 3H); $^{13}$C NMR (125 MHz, $CDCl_3$): δ 183.8, 178.6, 150.6, 149.8, 149.1, 146.1, 140.3, 137.2, 137.0, 134.2, 133.4, 131.9, 130.8, 129.4, 128.4, 126.4, 126.3, 123.7, 122.3, 119.5, 106.2, 35.6, 21.0. IR (film): 2973, 2914, 1673, 1621, 1328, 1233, 1004 cm$^{-1}$; HRMS (ES+) calc. for $C_{25}H_{18}NO_3$ $[M+H]^+$ : 380.1281, found: 380.1293

**(*R*)-4-(4-chlorophenyl)-2-(pyridin-2-yl)-4H-benzo[g]chromene-5,10-dione (12d):** The compound **12d** was obtained as a yellow semisolid in 73% yield (29.2 mg) and 97% ee. The optical purity was determined by chiral HPLC on Daicel Chiralpak IC column [*n*-hexane/2-propanol 80:20]; flow rate 1 mL/min; λ = 254 nm; $t_R$(minor) = 9.76 min, $t_R$(major) = 14.02 min, $[\alpha]_D^{25}$ = +100.0 (*c* 0.33 in $CHCl_3$); $^1$H NMR (500 MHz, $CDCl_3$): δ 8.61 (d, *J* = 3.1 Hz, 1H), 8.21 – 8.15 (m, 1H), 8.07 – 7.97 (m, 2H), 7.87 (t, *J* = 7.6 Hz, 1H), 7.78 – 7.70 (m, 2H), 7.37 (d, *J* = 8.4 Hz, 2H), 7.35 – 7.29 (m, 2H), 7.28 (d, *J* = 3.5 Hz, 1H), 6.60 (d, *J* = 4.5 Hz, 1H), 4.92 (d, *J* = 4.7 Hz, 1H); $^{13}$C NMR (125 MHz, $CDCl_3$): δ 183.7, 178.4, 150.7, 149.5, 149.2, 146.4, 141.7, 137.3, 134.4, 133.6, 133.1, 131.8, 130.7, 129.9, 128.9, 126.4, 126.4, 123.9, 121.7, 119.6, 105.4, 35.5; IR (film): 2898, 2840, 1670, 1623, 1482, 1330, 1251, 1203, 1004 cm$^{-1}$ HRMS (ES+) calc. for $C_{24}H_{15}ClNO_3$ $[M+H]^+$ : 400.0735, found: 400.0732

**(*R*)-4-(4-bromophenyl)-2-(pyridin-2-yl)-4H-benzo[g]chromene-5,10-dione (12e):** The compound **12e** was obtained as a yellow semisolid in 61% yield (27.0 mg) and 97% ee. The optical purity was determined by chiral HPLC on Daicel Chiralpak IA column [*n*-hexane/2-propanol 90:10]; flow rate 1 mL/min; λ = 254 nm; $t_R$(major) = 20.53 min, $t_R$(minor) = 21.99 min, $[\alpha]_D^{25}$ = +148.3 (*c* 0.18 in $CHCl_3$); $^1$H NMR (500 MHz, $CDCl_3$): δ 8.61 (bs, 1H), 8.23 – 7.95 (m, 3H), 7.90 – 7.66 (m, 3H), 7.45 (d, *J* = 8.0 Hz, 2H), 7.36 – 7.23 (m, 3H), 6.60 (bs, 1H), 4.91 (d, *J* = 3.8 Hz, 1H); $^{13}$C NMR (125 MHz, $CDCl_3$): δ 183.7, 178.4, 150.7, 150.3, 149.4, 149.2, 149.1, 146.3, 142.2, 137.5, 134.4, 133.6, 131.8, 131.7, 130.7, 130.3, 126.5, 126.4, 123.9, 121.6, 121.3, 119.6, 105.5, 35.6; IR (film): 2993, 1673, 1621, 1580, 1329, 1249, 1203, 1111, 1008 cm$^{-1}$ HRMS (ES+) calc. for $C_{24}H_{16}BrNO_3$ $[M+2H]^+$ : 446.0211, found: 446.0221

**(*S*)-4-(2-chlorophenyl)-2-(pyridin-2-yl)-4H benzo[g]chromene-5,10-dione (12g):** The compound **12g** was obtained as a yellow semisolid in 75% yield (30.0 mg) and 97% ee. The optical purity was determined by chiral HPLC on Daicel Chiralpak IA column [*n*-hexane/2-propanol 90:10]; flow rate 1 mL/min; λ = 254 nm; $t_R$(minor) = 16.84 min, $t_R$(major) = 22.16 min, $[\alpha]_D^{25}$ = +114.2 (*c* 0.19 in $CHCl_3$); $^1$H NMR (500 MHz, $CDCl_3$): δ 8.61 (bs, 1H), 8.22 (d, *J* = 5.0 Hz, 1H), 8.08 – 7.96 (m, 2H), 7.94 – 7.50 (m, 3H), 7.48 – 7.06 (m, 5H), 6.63 (bs, 1H), 5.45 (bs, 1H); $^{13}$C NMR (125 MHz, $CDCl_3$): δ 183.45, 178.37, 151.92, 149.37, 148.92, 145.67, 140.57, 137.79, 134.53, 133.69, 132.87, 131.78, 130.83, 129.98, 128.47, 127.53, 126.55, 126.52, 124.00, 121.05, 119.76, 105.13, 33.39; IR (film): 2995, 1670, 1620, 1450, 1373, 1328, 1205, 1004 cm$^{-1}$ HRMS (ES+) calc. for $C_{24}H_{15}ClNO_3$ $[M+H]^+$ : 400.0735, found: 400.0730

**Procedure for the synthesis of enantioenriched 1,2-pyranonaphthoquinone (13a)**

The 2-hydroxy1,4-naphthoquinone **1** (0.1 mmol) was added to a mixture of β-substituted 2-enoylpyridine **2a** (0.12 mmol) and the catalyst **5b** (7.26 mg, 0.01 mmol) in toluene (1.0 mL) at room temperature. The reaction mixture was stirred 40 °C and the progress of the reaction was monitored by TLC (40% ethyl acetate in hexane). After complete conversion of 2-hydroxy1,4-naphthoquinone, evaporate the solvent and dissolved in ethanol (2.0 mL), then sodium borohydride (28 mg, 0.74 mmol) was added slowly to the reaction mixture at 0 °C, and allow the reaction mixture to warm to room temperature and stirring was maintained for 2 hours at rt. Then concentrated hydrochloric acid (about 35%, 3.0 mL) was added dropwise and the mixture was stirred at room temperature for 3 hours. The reaction mixture was pour into cold water and neutralized with solid $NaHCO_3$ and extracted with $CH_2Cl_2$ thrice. The combined organic layers were dried over anhydrous $NaSO_4$, filtered and concentrated under reduced pressure. The product was purified by column chromatography over silica gel. Enantiomeric excess of the 1,2-pyranonaphthoquinone was determined by chiral HPLC analysis.

**(*4R*)-4-phenyl-2-(pyridin-2-yl)-3,4-dihydro-2H-benzo[h]chromene-5,6-dione (13a):** The compound **13a** was obtained as orange solid in 55% yield (20 mg, mp: 190 – 192 °C), >20:1 dr and 99% ee. The optical purity was determined by chiral HPLC on Daicel Chiralpak ADH column [*n*-hexane/2-propanol 80:20]; flow rate 1 mL/min; λ = 254 nm; $t_R$(major) = 19.29 min, $t_R$(minor) = 22.79 min, $[\alpha]_D^{25}$ = -20.0 (*c* 0.12 in $CHCl_3$); $^1$H NMR (700 MHz, $CDCl_3$): δ 8.59 (d, *J* = 4.4 Hz, 1H), 8.18 – 8.05 (m, 1H), 8.00 (d, *J* = 7.6 Hz, 1H), 7.81 (td, *J* = 7.7, 1.7 Hz, 1H), 7.74 (td, *J* = 7.7, 1.3 Hz, 1H), 7.62 – 7.58 (m, 2H), 7.30 – 7.29 (m, 1H), 7.23 – 7.11 (m, 5H), 5.44 (dd, *J* = 10.9, 2.2 Hz, 1H), 4.26 (dd, *J* = 10.5, 7.0 Hz, 1H), 2.84 (ddd, *J* = 14.4, 7.0, 2.4 Hz, 1H), 2.31 – 2.25 (m, 1H); $^{13}$C NMR (175 MHz, $CDCl_3$): δ δ 179.2, 178.2, 163.5, 157.8, 149.4, 143.0, 137.1, 135.0, 132.1, 131.1, 130.3, 128.9, 128.5, 126.9, 126.3, 124.5, 123.3, 120.2, 117.8, 80.4, 39.0, 37.8; IR (film): 2898, 2848, 1649, 1594, 1567, 1381, 1286, 1164, 1095 cm$^{-1}$; HRMS (ES+) calc. for $C_{24}H_{18}NO_3$ $[M+H]^+$ : 368.1281, found: 368.1289

## Notes and references

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† Electronic Supplementary Information (ESI) available: The Copies of NMR spectra and HPLC chromatograms of all new compounds and crystal data of **4d**. CCDC 1030663 contains supplementary crystallographic data for the structure **4d**. See DOI: 10.1039/b000000x/

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