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Enantioselective Cascade Double Michael Addition of 3-Nitro-2*H*-Chromenes and Acyclic Enones: Efficient Synthesis of Functionalized Tricyclic Chroman Derivatives

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An efficient protocol for the asymmetric construction of enantiomerically enriched tetrahydro-6*H*-benzo[*c*]chromenes, tetrahydro-6*H*-benzo[*c*]thiochromene or hexahydrophenanthrene and their derivatives have been developed. The corresponding products were obtained by the cascade double Michael addition of 3-nitro-2*H*-chromenes and its derivatives with α,β-unsaturated ketones catalyzed by a combination of a quinine-derived primary amine and benzoic acid. Through this methodology, the desired products could be obtained in moderate to good yield (up to 90%), with excellent diastereoselectivities (up to >25:1 dr) and moderate to excellent enantioselectivities (up to 95% *ee*).

Introduction

Chroman derivatives as an important class of compounds, were widely found in natural compounds and synthetic analogues exhibiting various biological activities,[1] and great progress in the synthesis of those kinds of skeletons via an organocatalytic cascade reaction has been made in recent years.[2] Among various kinds of the chroman skeletons, the tricyclic compounds, tetrahydro-6*H*-benzo[*c*]chromene system occurs widely in a variety of natural products exhibiting various biological activities, such as Nabilone, (+)-Conicol, secretase inhibitors, the cannabinoid receptor CB1 and so on (Figure 1).[3] At the same time its similar structure tetrahydro-6*H*-benzo[*c*]thiochromen or hexahydrophenanthrene constitutes the basic skeleton of many naturally occurring and synthetic compounds possessing a number of interesting biological properties (Figure 1).[4]

In this regard, the tetrahydro-6*H*-benzo[*c*]chromene, tetrahydro-6*H*-benzo[*c*]thiochromene and hexahydrophenanthrene derivatives have received much attention in synthetic endeavors, and recently several elegant approaches have been established for the asymmetric construction of these highly valuable heterocyclic architectures (Scheme 1). Few years ago, Hong and co-workers successively reported an organocatalytic domino condensation of 2-((*E*)-2- nitrovinyl) benzene-1,4-diol and α,β-unsaturated aldehydes to synthesis skeleton of hexahydro-6*H*-benzo[*c*]chromenes.[5] Later, groups of Li and Wang also synthesis skeleton of tetrahydro-6*H*-benzo[*c*]chromene derivatives through an organocatalytic cascade reaction of 2-hydroxychalcones[6] or (*E*)-2-hydroxyaryl-2-oxobut-3-enoate[7] derivatives with α,β-unsaturated aldehydes. In addition, Hong and co-workers also reported the asymmetric synthesis of the tetrahydro-6*H*-benzo[*c*]chromen-6-ones[8] and hexahydrophenanthrene[9] derivatives through the organocatalytic cascade reactions. Of course, other groups also have done a lot of good works in the synthesis of these highly valuable heterocyclic architectures.[10] Although excellent works have been done for the

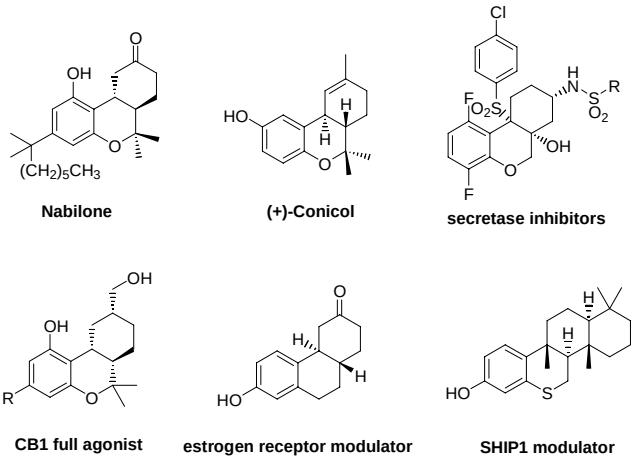

Figure 1. Representative examples of biologically active compounds containing tetrahydro-6*H*-benzo[*c*]chromenes or hexahydrophenanthrene core.

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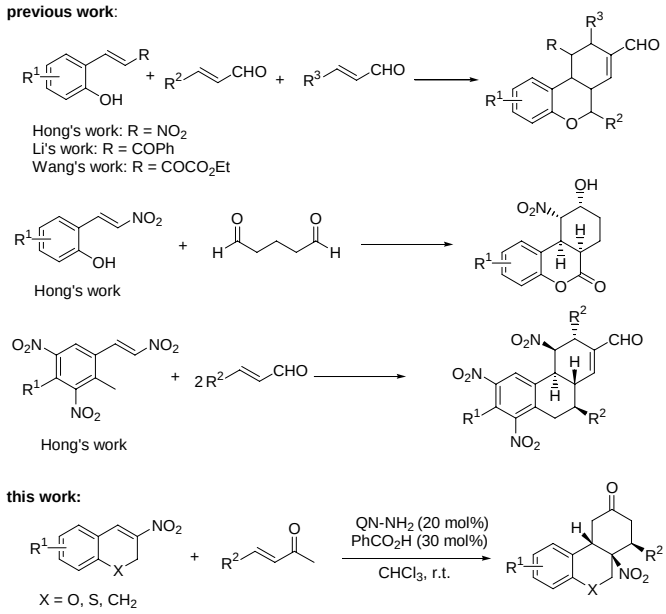
asymmetric construction of these valuable heterocyclic architectures, some improvements still need to be made. For example, the substrate scopes of the reactions were still limited, especially for the hexahydrophenanthrene. and as far as we know, the directly asymmetric synthesis of tetrahydro-6*H*-benzo[*c*]thiochromenes has not been reported yet.

3-Nitro-2*H*-chromenes, which can be easily prepared from salicylaldehyde and nitroethylene[11] are valuable intermediates for the synthesis of chroman derivatives, and recently many complex compounds has been constructed by the 3-nitro-2*H*-chromenes and its derivatives.[12] Herein, we would like to present the first asymmetric organocatalytic cascade Michael/Michael cycloaddition reaction of 3-nitro-2*H*-chromenes and α,β-unsaturated ketones to provide the tetrahydro-6*H*-benzo[*c*]chromenes in moderate to good yield, with excellent diastereoselectivities and moderate enantioselectivities. Moreover, the tetrahydro-6*H*-benzo[*c*]thiochromene and hexahydrophenanthrene could also be obtained under this asymmetric catalytic system.



Scheme 1. Cascade organocatalytic reactions for the synthesis of tetrahydro-6*H*-benzo[*c*]chromene or hexahydrophenanthrene derivatives.

Results and discussion

In recently years, quinine or quinidine alkaloid-derived primary amine with an organic protonic acid was proved to be a powerful catalyst to activate unsaturated ketones to complete chiral induction.[13] With this in mind, we firstly examine the cascade Michael/Michael reaction of 3-nitro-2*H*-chromene **1a** and α,β-unsaturated ketones **2a**, using 20 mol% quinine-derived primary amine **I** as catalyst and 30 mol% benzoic acid **A1** as an additive (Table 1, entry 1). We were pleased that the reaction proceeded smoothly to provide the desired product **3a** in moderate yield (63%) with good enantioselectivity (73% *ee*) and excellent diastereoselectivity (96:4 dr). Then cinchonidine-derived primary amine **II** was also used as the catalyst, and the same enantiomer product was obtained with the same enantioselectivity and slightly lower yield and diastereoselectivity (Table 1, entry 2). In consideration of the tiny gap of the result, quinine-derived primary amine **I** was selected for further optimization. Then several commonly used solvent or mixed solvent were screened to further improve the reaction efficiency (Table 3, entries 3–8). Chloroform was found to be the most optimal solvent, affording the desired product **3a** in 67% yield with 99:1 dr and 77% *ee* (Table 1, entry 7). Meanwhile, when THF was used as the solvent, no product was observed after 96 h. Afterwards, except the benzoic acid, different benzoic acid derivatives were also used as the additives to explore the influence of protonic acid on the reactivity of this transformation, but no better results were obtained (Table 1, entry 10–13). To our surprise, when no additive was added into the reaction, the opposite enantiomer product was obtained, at the same time the yield and enantioselectivity were reduced dramatically (Table 1, entry 9). This result indicate that the additives play an important role in the cascade Michael/Michael reaction, and it was more like a kind of cocatalyst than just the role of protonic acid to adjust the pH. We also investigated the effect of temperature. When the temperature of the reaction was changed from room temperature to 40 °C, the same yield was obtained, but the enantioselectivity and diastereoselectivity became lower (Table 1, entry 14). After select the benzoic acid **A1** as an additive and chloroform as the solvent, the quinidine-derived primary amine **III** was used as the catalyst for this cascade reaction, and the opposite enantiomer was obtained. Surprisingly, although the similar diastereoselectivity was obtained, both the yield and enantioselectivity were lower than its pseudoenantiomer, quinine-derived primary amine, as the catalyst (Table 1, entry 15). Moreover, other primary amines such as 1,2-diphenylethylenediamine (**IV**), 1,2-diaminocyclohexane (**V**), and *L*-proline (**VI**) were also used as the catalysts, but no better results were obtained (Table 1, entries 16–18). Overall, the quinine-derived primary amine **I** as catalyst and 30 mol% **A1** as an additive turn out to be the optimal catalytic system for the synthesis of tetrahydro-6*H*-benzo[*c*]chromene in chloroform at room temperature.

Having established the optimal reaction conditions, the scope of the organocatalytic cascade Michael/Michael addition reaction was explored by varying the 3-nitro-2*H*-chromenes **1** and α,β-unsaturated ketones **2** as summarized in Table 2. The reactions proceeded smoothly to give the corresponding adducts in moderate to good yields with good to excellent diastereoselectivities and moderate to good enantioselectivities.

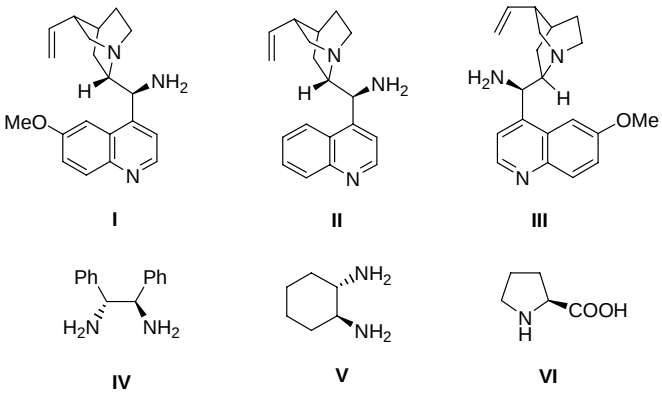
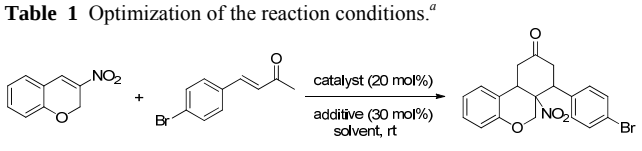


Figure 2. The screened catalysts and additives.

Table 1 Optimization of the reaction conditions.[a]



1a 2a 3a

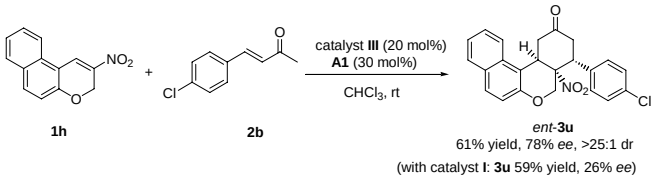
Entry	Catalyst	Additive	Solvent	Yield[b] (%)	dr[c]	*ee*[d] (%)
1	**I**	A1	CH_2Cl_2	63	25:1	73
2	**II**	A1	CH_2Cl_2	62	20:1	73
3	**I**	A1	PhMe	77	>25:1	71
4	**I**	A1	xylene	73	20:1	69
5	**I**	A1	CH_3CN	33	4:1	67
6	**I**	A1	THF	trace	–	–
7	**I**	A1	$CHCl_3$	67	>25:1	77
8	**I**	A1	$CHCl_3$/ PhMe(1:1)	70	25:1	73
9[f]	**I**	–	$CHCl_3$	28	20:1	10
10	**I**	A2	$CHCl_3$	61	>25:1	76
11	**I**	A3	$CHCl_3$	49	>25:1	67
12	**I**	A4	$CHCl_3$	69	>25:1	74
13	**I**	A5	$CHCl_3$	66	>25:1	76
14[e]	**I**	A1	$CHCl_3$	67	20:1	74
15[f]	**III**	A1	$CHCl_3$	58	>25:1	56
16	**IV**	A1	$CHCl_3$	39	>25:1	69
17[f]	**V**	A1	$CHCl_3$	49	25:1	49
18	**VI**	A1	$CHCl_3$	trace	–	–

[a] Unless noted otherwise, Reactions were carried out with **1a** (0.21 mmol), **2a** (0.20 mmol), catalyst loading (20 mol%) and additive (30 mol%) in solvent (1.0 mL) at room temperature for 96 h. [b] Isolated yield after column chromatography purification. [c] Determined by NMR spectroscopy analysis [d] Determined by chiral HPLC analysis. [e] The reaction was performed at 40 °C [f] The opposite enantiomer.

Firstly, different substituents of α,β-unsaturated ketones were explored. Even similar results were obtained, but there are still some slightly difference between electron-donating substituents and electron-withdrawing substituents. Products with electron-donating substituents on the *ortho*, *meta* or *para* position of α,β-unsaturated ketones obtain the good enantioselectivities, which were better than products with other substituents (Table 3, entries 3–4, 8 and 10–11). Moreover, when the α,β-unsaturated ketones with nitro-group on the *para* position was used as the substrate, the lowest enantioselectivity was obtained (Table 3, entry 5). Although good enantioselectivity of product with methoxy group on the *ortho* position of α,β-unsaturated ketone was obtained, the diastereoselectivity of product **3h** was only 10:1 (Table 3, entry 8). At the same time, excellent diastereoselectivity (>25:1) was obtained by all of other products, which represent that the electron-donating substituent on the *ortho* position of α,β-unsaturated ketone could lower the diastereoselectivity of the product. As for the yields, the yield of product **3l** (90%) was obvious better than other products, this might indicate that the reactivity of α, β-unsaturated ketones derived from fused ring was higher for this reaction.

Next, different substituents or atoms on the 3-nitro-2*H*-chromenes were explored. When the substrates with electron-withdrawing substituents on the R^1 group were used (Table 3, entries 13–16), excellent diastereoselectivities and moderate enantioselectivities were obtained, but the yield of products were obvious lower. On the other hand, When the substrates with electron-donating substituents on the R^1 group were used (Table 3, entries 17 and 18), the yield of the products were much better, which indicate that, just like the α,β-unsaturated ketones, the reactivity of 3-nitro-2*H*-chromenes with electron-donating substituents was also higher. To evaluate the synthetic potential of this reaction system, the oxygen atom of 3-nitro-2*H*-chromene was replaced by a methylene or a sulfur atom, which provide an easy acess to the hexahydrophenanthrene (Table 3, entry 19) or tetrahydro-6*H*-benzo[*c*]thiochromene (Table 3, entry 20). The desired products **3s** and **3t** can be obtained in moderate yields (64% and 74%) with high to excellent enantioselectivities (81% and 95% *ee*) and excellent diastereoselectivities (>25:1 dr).

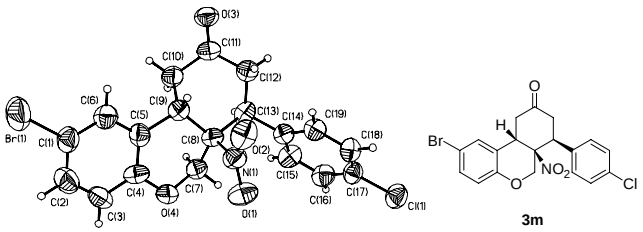
During the exploration of the scope of this cascade Michale/Michael reaction, 2-nitro-3*H*-benzo[*f*]chromene (**1h**) was also used as the substrate to afford the tetrahydro-1*H*-dibenzo[*c*,*f*]chromen-2-one (**3u**). Firstly, the reaction was taken under optimal reaction conditions and the quinine-derived primary amine **I** was used as the catalyst. To our surprise, very low enantioselectivity was obtained (26% *ee*). After a series of analysis, we believe that the fused ring structure of substrate **1h** have a special steric effect between the catalyst **I** and additive **A1**. So the opposite enantiomer of the catalyst **I**, quinidine-derived primary amine **III**, was used as the catalyst to provide a different steric effect for the reaction, and the enantioselectivity of enantiomer product *ent*-**3u** was enhanced to 78% *ee*.



1h 2b *ent*-**3u**
61% yield, 78% *ee*, >25:1 dr
(with catalyst **I**: **3u** 59% yield, 26% *ee*)

Scheme 2. The reaction of 2-nitro-3*H*-benzo[*f*]chromene with 4-(4-chlorophenyl)but-3-en-2-one under different catalysts.

To determine the absolute configuration of the cascade reaction products, structure of **3m** was assigned unambiguously by single-crystal X-ray analysis to be (6a*R*,7*S*,10a*S*),[14] and the ORTEP structure is shown in Figure 1.



3m

Figure 2. X-ray crystal structure of **3m.**

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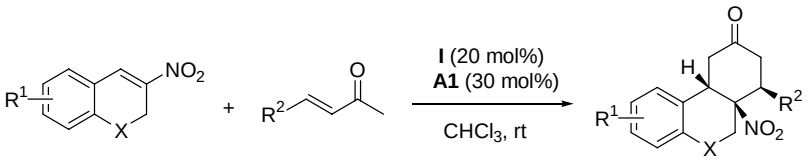
Table 2 Substrate scope of the asymmetric cascade Michael/Michael addition[a]



1a-i **2a-l** **3a-t**

Entry	R^1	X	R^2	Product	Yield[b] (%)	dr[c] (%)	*ee*[d] (%)
1	H (**1a**)	O	4-BrC_6H_4 (**2a**)	**3a**	67	>25:1	77
2	H (**1a**)	O	4-ClC_6H_4 (**2b**)	**3b**	67	>25:1	77
3	H (**1a**)	O	4-MeC_6H_4 (**2c**)	**3c**	57	>25:1	79
4	H (**1a**)	O	4-$MeOC_6H_4$ (**2d**)	**3d**	75	>25:1	81
5	H (**1a**)	O	4-$O_2NC_6H_4$ (**2e**)	**3e**	66	>25:1	74
6	H (**1a**)	O	Ph (**2f**)	**3f**	61	>25:1	78
7	H (**1a**)	O	2-BrC_6H_4 (**2g**)	**3g**	85	>25:1	75
8	H (**1a**)	O	2-$MeOC_6H_4$ (**2h**)	**3h**	78	10:1	80
9	H (**1a**)	O	3-$O_2NC_6H_4$ (**2i**)	**3i**	64	>25:1	77
10	H (**1a**)	O	3,4-$(MeO)_2C_6H_3$ (**2j**)	**3j**	69	>25:1	83
11	H (**1a**)	O	4-$(CH_3)_2NC_6H_4$ (**2k**)	**3k**	78	>25:1	83
12	H (**1a**)	O	1-naphthyl (**2l**)	**3l**	90	>25:1	79
13	6-Br (**1b**)	O	4-ClC_6H_4 (**2b**)	**3m**	53	>25:1	78
14	6-Cl (**1c**)	O	4-ClC_6H_4 (**2b**)	**3n**	59	>25:1	73
15	6,8-Br_2 (**1d**)	O	4-ClC_6H_4 (**2b**)	**3o**	45	>25:1	65
16	6,8-Cl_2 (**1e**)	O	4-ClC_6H_4 (**2b**)	**3p**	54	>25:1	68
17	8-MeO (**1f**)	O	4-ClC_6H_4 (**2b**)	**3q**	80	>25:1	73
18	8-EtO (**1g**)	O	4-ClC_6H_4 (**2b**)	**3r**	81	>25:1	71
19	H (**1h**)	CH_2	4-BrC_6H_4 (**2a**)	**3s**	64	>25:1	81
20	H (**1i**)	S	4-BrC_6H_4 (**2a**)	**3t**	74	>25:1	95

[a] Unless noted otherwise, reactions were carried out with **1** (0.21 mmol), **2** (0.20 mmol) catalyst **I** (20 mol%) and additive (30 mol%) in CH_3Cl (1.0 mL) at room temperature for 96 h. [b] Isolated yield after column chromatography purification. [c] Determined by NMR spectroscopy analysis [d] Determined by chiral HPLC analysis.

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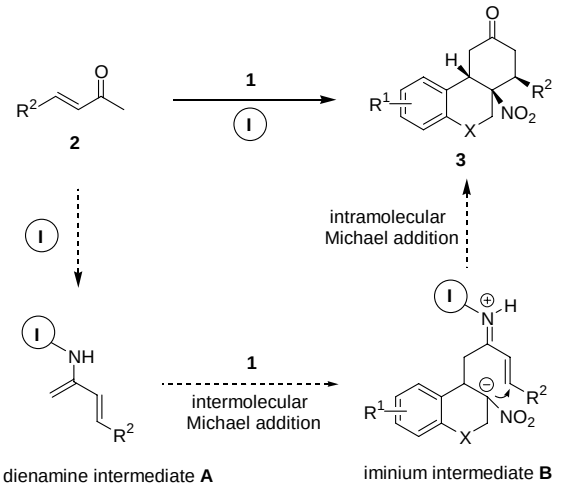

Figure 3. Proposed reaction mechanism.

Inspired by the previous study of this catalytic system,[13a,13b,13f] a possible transition state model is proposed and shown in Figure 3. The activated dienamine ion intermediate **A** was first generated by the intercept of the primary amine catalyst to unsaturated ketone **2**. Then an intermolecular Michael addition was initiated between the prochiral carbon nucleophile **A** and 3-nitro-2*H*-chromene **1**. The resulting intermediate **B** would further selectively engage itself in an intramolecular, iminium-catalyzed conjugate addition. Thus the tricyclic chroman derivatives were obtained through the cascade double Michael addition.

Conclusions

In summary, we have successfully developed an efficient protocol for the construction of enantiomerically enriched tetrahydro-6*H*-benzo[*c*]chromenes, tetrahydro-6*H*-benzo[*c*]thiochromene and hexahydrophenanthrene *via* the asymmetric organocatalytic cascade Michael/Michael reaction of 3-nitro-2*H*-chromenes and α, β-unsaturated ketones, which is catalyzed by a combination of a quinine-derived primary amine and benzoic acid. Through this new methodology, the corresponding chiral tricyclic chroman derivatives could be obtained in moderate to good yield (up to 90%) with excellent diastereoselectivities (up to >25:1 dr) and moderate to excellent enantioselectivities (up to 95% *ee*). The structure was confirmed by single crystal X-ray analysis of cascade adduct **3m**. Further studies on organocatalytic enantioselective synthesis of pharmaceutical intermediates or biologically active compounds are ongoing in our laboratory.

Experimental

General information

Commercially available compounds were used without further purification. Column chromatography was carried out using silica gel (200–300 mesh). Melting points were measured with a XT-4 melting point apparatus without correction. The ^{1}H NMR spectra were recorded with a Bruker Avance 400 MHz spectrometer, while ^{13}C NMR spectra were recorded at 100 MHz. Infrared spectra were obtained with a Nicolet Magna IR-560 spectrometer. The high resolution ESI-MS spectra were obtained with Bruker APEX IV Fourier transform mass spectrometer. Optical rotations were measured with a Krüss P8000 polarimeter at the indicated concentration with unit g per 100 mL. The enantiomeric excesses of the products were determined by chiral HPLC using Agilent 1200 LC instrument on Daicel Chiralpak AD-H or IB columns.

Materials

The substrates **1**[11c,15] and **2**[13g] were synthesized following the reported procedures.

General procedure for the enantioselective Michael addition reaction

A mixture of 3-nitro-2*H*-chromene **1** (0.21 mmol), α,β-unsaturated ketone **2** (0.20 mmol), catalyst **I** (13.0 mg, 0.04 mmol, 20 mol%) and benzoic acid (7.4 mg, 0.06 mmol, 30 mol%) in chloroform (1.0 mL) was stirred at room temperature for 96 h. Then the mixture was concentrated and purified by silica gel column chromatography (with ethyl acetate–petroleum ether as the eluent) to afford the desired products **3**.

(6a*R*,7*S*,10a*S*)-7-(4-bromophenyl)-6a-nitro-7,8,10,10a-tetrahydro-6*H*-benzo[*c*]chromen-9(6a*H*)-one (**3a**). The product **3a** was obtained according to the general procedure as a white solid (54.2 mg, 67% yield), m.p. 66–71 °C. HPLC (Daicel Chiralpak AD-H column, *n*-hexane–2-propanol 80:20, flow rate 1.0 mL/min, detection at 254 nm): t_{major} = 16.4 min, t_{minor} = 15.2 min, 77% *ee*; $[\alpha]_D^{20}$ = –4.2 (*c* 2.3, CH_2Cl_2); ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.51–7.48 (m, 2H, ArH), 7.23–7.18 (m, 2H, ArH), 7.09–7.06 (m, 2H, ArH), 7.01 (dt, J_1 = 1.2 Hz, J_2 = 7.6 Hz, 1H, ArH), 6.93 (d, J = 8.0 Hz, 1H, ArH), 4.58 (d, J = 11.6 Hz, 1H, CH), 4.30–4.23 (m, 2H, CH + CH), 3.54 (dd, J_1 = 4.6 Hz, J_2 = 13.0 Hz, 1H, CH), 3.41–3.30 (m, 2H, CH_2), 2.88 (dd, J_1 = 8.2 Hz, J_2 = 16.6 Hz, 1H, CH), 2.54 (dd, J_1 = 4.4 Hz, J_2 = 16.0 Hz, 1H, CH) ppm; ^{13}C NMR (100 MHz, $CDCl_3$): δ 205.8, 152.2, 134.4, 132.2, 129.9, 129.1, 128.4, 123.0, 122.6, 120.2, 117.5, 87.2, 65.2, 43.4, 42.8, 41.4, 39.1 ppm; IR (KBr): $\tilde{\nu}$ 1717, 1585, 1543, 1488, 1456, 1409, 1340, 1276, 1259, 1228, 1075, 837, 751, 506 cm^{-1}; HRMS (ESI): *m/z* calcd. for $C_{19}H_{16}BrNNaO_4$ $[M + Na]^+$ 424.01549, found 424.01628.

(6a*R*,7*S*,10a*S*)-7-(4-chlorophenyl)-6a-nitro-7,8,10,10a-tetrahydro-6*H*-benzo[*c*]chromen-9(6a*H*)-one (3b). The product **3b** was obtained according to the general procedure as a white solid (47.6 mg, 67% yield), m.p. 170–173 °C. HPLC (Daicel Chiralpak AD-H column, hexane–2-propanol 80:20, flow rate 1.0 mL/min, detection at 254 nm): t_{major} = 15.2 min, t_{minor} = 13.2 min, 77% *ee*; $[\alpha]_D^{20}$ = –1.4 (*c* 1.9, CH_2Cl_2); ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.34 (d, *J* = 8.0 Hz, 2H, ArH), 7.23–7.19 (m, 2H, ArH), 7.14 (d, *J* = 8.4 Hz, 2H, ArH), 7.02 (t, *J* = 7.6 Hz, 1H, ArH), 6.93 (d, *J* = 8.0 Hz, 1H, ArH), 4.58 (d, *J* = 11.6 Hz, 1H, CH), 4.30–4.24 (m, 2H, CH+CH),3.55 (dd, J_1 = 4.4 Hz, J_2 = 12.8 Hz, 1H, CH), 3.41–3.01 (m, 2H, CH_2) 2.89 (dd, J_1 = 8.2 Hz, J_2 = 16.6 Hz, 1H, CH), 2.54 (dd, J_1 = 4.4 Hz, J_2 = 15.6 Hz, 1H, CH) ppm; ^{13}C NMR (100 MHz, $CDCl_3$): δ 205.9, 152.2, 134.8, 133.9, 129.5, 129.3, 129.0, 128.4, 122.5, 120.2, 117.5, 87.3, 65.2, 43.4, 42.7, 41.5, 39.0 ppm; IR (KBr): $\tilde{\nu}$ 1724, 1689, 1546, 1489, 1456, 1280, 1249, 1229, 1125, 1093, 1068, 1014, 839, 811, 7753, 707, 666, 541, 514 cm^{-1}; HRMS (ESI): *m/z* calcd. for $C_{19}H_{16}ClNNaO_4$ $[M + Na]^+$ 380.06601, found 380.06605.

(6a*R*,7*S*,10a*S*)-6a-nitro-7-(p-tolyl)-7,8,10,10a-tetrahydro-6*H*-benzo[*c*]chromen-9(6a*H*)-one (3c). The product **3c** was obtained according to the general procedure as a white solid (38.6 mg, 57% yield), m.p. 63–68 °C. HPLC (Daicel Chiralpak AD-H column, *n*-hexane–2-propanol 80:20, flow rate 1.0 mL/min, detection at 254 nm): t_{major} = 12.1 min, t_{minor} = 10.7 min, 79% *ee*; $[\alpha]_D^{20}$ = +7.6 (*c* 1.6, CH_2Cl_2); ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.21–7.15 (m, 4H, ArH), 7.06 (d, *J* = 8.0 Hz, 2H, ArH) 7.00 (dt, J_1 = 1.2 Hz, J_2 = 7.6 Hz, 1H, ArH), 6.92 (d, *J* = 8.0 Hz, ArH, 1H) 4.66 (dd, J_1 = 1.0 H, J_2 = 11.8 Hz, 1H, CH), 4.31–4.25 (m, 2H, CH+CH), 3.50 (dd, J_1 = 4.0 Hz, J_2 = 12.8 Hz, 1H, CH), 3.39 (dd, J_1 = 12.8 H, J_2 = 15.6 Hz, 1H, CH), 3.31 (dd, J_1 = 5.4 H, J_2 = 16.6 Hz, 1H, CH), 2.84 (dd, J_1 = 8.8 Hz, J_2 = 16.6 Hz, 1H, CH), 2.56 (dd, J_1 = 4.0 Hz, J_2 = 15.6 Hz, 1H, CH), 2.34 (s, 3H, CH_3) ppm; ^{13}C NMR (100 MHz, $CDCl_3$): δ 206.5, 152.4, 138.7, 132.4, 129.8, 128.9, 128.5, 128.0, 122.4, 120.4, 117.5, 87.8, 68.2, 43.9, 43.3, 41.7, 38.5, 21.1 ppm; IR (KBr): $\tilde{\nu}$ 2313, 1715, 1585, 1544, 1514, 1489, 1456, 12776, 1228, 1218, 1070, 819, 751, 503 cm^{-1}; HRMS (ESI): *m/z* calcd. for $C_{20}H_{20}NO_4$ $[M + H]^+$ 338.13868, found 338.13912.

(6a*R*,7*S*,10a*S*)-7-(4-methoxyphenyl)-6a-nitro-7,8,10,10a-tetrahydro-6*H*-benzo[*c*]chromen-9(6a*H*)-one (3d). The product **3d** was obtained according to the general procedure as a white solid (53.3 mg, 75% yield), m.p. 53–59 °C. HPLC (Daicel Chiralpak AD-H column, *n*-hexane–2-propanol 80:20, flow rate 1.0 mL/min, detection at 254 nm): t_{major} = 18.0 min, t_{minor} = 16.4 min, 81% *ee*; $[\alpha]_D^{20}$ = +7.9 (*c* 1.5, CH_2Cl_2); ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.22–7.17 (m, 2H, ArH), 7.12–7.08 (m, 2H, ArH), 7.00 (td, J_1 = 1.2 Hz, J_2 = 7.6 Hz, 1H, ArH), 6.93–6.86 (m, 3H,ArH), 4.64 (dd, J_1 = 0.8 Hz, J_2 = 12.0 Hz, 1H, CH), 4.31–4.24 (m, 2H, CH+CH), 3.79 (s, 3H, CH_3), 3.49 (dd, J_1 = 4.0 Hz, J_2 = 12.8 Hz, 1H, CH), 3.37 (dd, J_1 = 12.8 H, J_2 = 15.8 Hz, 1H, CH), 3.31 (dd, J_1 = 5.6 H, J_2 = 16.4 Hz, 1H, CH), 2.85 (dd, J_1 = 9.0 Hz, J_2 = 16.4 Hz, 1H, CH), 2.56 (dd, J_1 = 4.0 Hz, J_2 = 15.8 Hz, 1H, CH) ppm; ^{13}C NMR (100 MHz, $CDCl_3$): δ (100 MHz, $CDCl_3$): δ 206.5, 159.7, 152.4, 129.2, 128.9, 128.5, 127.3, 122.4, 120.4, 117.4, 114.4, 87.8, 65.2, 55.2, 43.8, 42.9, 41.8, 38.5 ppm; IR (KBr): $\tilde{\nu}$ 1716, 1610, 1543, 1513, 1489, 1457, 1251, 1228, 1218, 1181, 1069, 1028, 835, 752, 510 cm^{-1}; HRMS (ESI): *m/z* calcd. for $C_{20}H_{20}NO_5$ $[M + H]^+$ 354.13360, found 354.13367; calcd. for $C_{20}H_{19}NNaO_5$ $[M + Na]^+$ 376.11554, found 376.11514.

(6a*R*,7*S*,10a*S*)-6a-nitro-7-(4-nitrophenyl)-7,8,10,10a-tetrahydro-6*H*-benzo[*c*]chromen-9(6a*H*)-one (3e). The product **3e** was obtained according to the general procedure as a white solid (48.7 mg, 66% yield), m.p. 206–216 °C. HPLC (Daicel Chiralpak AD-H column, *n*-hexane–2-propanol 80:20, flow rate 1.0 mL/min, detection at 254 nm): t_{major} = 37.5 min, t_{minor} = 31.0 min, 74% *ee*; $[\alpha]_D^{20}$ = –11.9 (*c* 1.4, CH_2Cl_2); ^{1}H NMR (400 MHz, acetone-d_6): δ 8.25 (d, *J* = 8.8 Hz, 2H, ArH), 7.58 (d, *J* = 8.4 Hz, 2H, ArH), 7.38 (d, *J* = 7.6 Hz, 1H, ArH), 7.21–7.17 (m, 1H, ArH), 7.01–6.98 (m, 1H, ArH), 6.86 (d, *J* = 8.0 Hz, 1H, ArH), 5.06 (dd, J_1 = 2.4 Hz, J_2 = 12.8 Hz, 1H, CH), 4.73–4.66 (m, 2H, CH+CH), 4.07 (dd, J_1 = 4.4 Hz, J_2 = 11.2 Hz, 1H, CH), 3.35 (dd, J_1 = 11.2 Hz, J_2 = 16.4 Hz, 1H, CH), 3.12 (dd, J_1 = 5.2 Hz, J_2 = 17.2 Hz, 1H, CH), 2.96 (dd, J_1 = 12.8 Hz, J_2 = 17.2 Hz, 1H, CH), 2.73 (dd, J_1 = 4.4 Hz, J_2 = 16.4 Hz, 1H, CH) ppm; ^{13}C NMR (100 MHz, acetone-d_6): δ 206.8, 154.3, 149.8, 146.3, 131.7, 131.2, 130.4, 125.5, 123.8, 123.1, 118.7, 92.0, 66.7, 46.8, 45.4, 42.7, 37.9 ppm; IR (KBr): $\tilde{\nu}$ 1731, 1714, 1681, 1546, 1519, 1493, 1351, 1275, 1073, 857, 851, 765, 750, 695 cm^{-1}; HRMS (ESI): *m/z* calcd. For $C_{19}H_{16}N_2NaO_6$ $[M + Na]^+$ 391.09006, found 391.08874.

(6a*R*,7*S*,10a*S*)-6a-nitro-7-phenyl-7,8,10,10a-tetrahydro-6*H*-benzo[*c*]chromen-9(6a*H*)-one (3f). The product **3f** was obtained according to the general procedure as a white solid (39.5 mg, 61% yield), m.p. 166–170 °C. (HPLC on Daicel Chiralpak AD-H column, *n*-hexane–2-propanol 80:20, flow rate 1.0 mL/min, detection at 254 nm): t_{major} = 15.1 min, t_{minor} = 12.0 min, 78% *ee*. $[\alpha]_D^{20}$ = +12.2 (*c* 1.7, CH_2Cl_2); ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.39–7.33 (m, 3H, ArH), 7.22–7.17 (m, 4H, ArH), 7.00 (t, *J* = 7.6 Hz, 1H, ArH), 6.92 (d, *J* = 8.0 Hz, 1H, ArH), 4.66 (d, *J* = 11.6 Hz, 1H, ArH), 4.31–4.26 (m, 2H, CH+CH), 3.54 (dd, J_1 = 4.0 Hz, J_2 = 12.8 Hz, 1H, CH), 3.41 (dd, J_1 = 12.8 Hz, J_2 = 15.8 Hz, 1H, CH), 3.31 (dd, J_1 = 5.6 Hz, J_2 = 16.4 Hz, 1H, CH), 2.85 (dd, J_1 = 9.0 Hz, J_2 = 16.4 Hz, 1H, CH), 2.57 (dd, J_1 = 4.0 Hz, J_2 = 15.8 Hz, 1H, CH) ppm; ^{13}C NMR (100 MHz, $CDCl_3$): δ 206.4, 152.3, 135.4, 129.1, 128.9, 128.8, 128.5, 128.1, 122.4, 120.3, 117.4, 87.7, 65.2, 43.8, 43.5, 41.5, 38.5 ppm; IR (KBr): $\tilde{\nu}$ 1726, 1690, 1681, 1547, 1489, 1455, 1422, 1341, 1278, 1249, 1227, 1217, 1065, 757, 702, 542, 515 cm^{-1}; HRMS (ESI): *m/z* calcd. for $C_{19}H_{17}NNaO_4$ $[M + H]^+$ 346.10498, found 346.10497.

(6a*S*,7*S*,10a*S*)-7-(2-bromophenyl)-6a-nitro-7,8,10,10a-tetrahydro-6*H*-benzo[*c*]chromen-9(6a*H*)-one (3g). The product 3g was obtained according to the general procedure as white solid (68 mg, 85% yield), m.p. 116–122 °C. HPLC (Daicel Chiralpak AD-H column, *n*-hexane–2-propanol 80:20, flow rate 1.0 mL/min, detection at 254 nm): t_{major} = 21.5 min, t_{minor} = 12.1 min, 75% *ee*; $[\alpha]_D^{20}$ = +93.1 (*c* 2.9, CH_2Cl_2); ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.65 (dd, J_1 = 1.6 Hz, J_2 = 8.0 Hz, 1H, ArH), 7.32 (td, J_1 = 1.2 Hz, J_2 = 7.6 Hz, 1H, ArH), 7.24–7.16 (m, 3H, ArH), 7.07 (dd, J_1 = 1.6 Hz, J_2 = 7.6 Hz, 1H, ArH), 7.01–6.97 (m, 1H, ArH), 6.89–6.87 (m, 1H, ArH), 5.06 (dd, J_1 = 2.0 Hz, J_2 = 12.8 Hz, 1H, CH), 4.51 (dd, J_1 = 2.6 Hz, J_2 = 13.6 Hz, 1 H, CH), 4.20 (d, *J* = 12.4 Hz, 1H, CH), 4.06 (dd, J_1 = 3.2 Hz, J_2 = 14.0 Hz, 1H, CH), 3.35 (dd, J_1 = 14.0 Hz, J_2 = 17.2 Hz, 1H, CH), 3.12 (dd, J_1 = 4.4 Hz, J_2 = 17.6 Hz, 1H, CH), 2.78 (dd, J_1 = 13.6 Hz, J_2 = 17.6 Hz, 1H, CH), 2.50 (dd, J_1 = 3.2 Hz, J_2 = 17.2 Hz, 1H, CH) ppm; ^{13}C NMR (100 MHz, $CDCl_3$): δ 206.3, 152.7, 135.1, 133.5, 130.3, 128.9, 128.8, 128.7, 127.7, 125.2, 122.2, 119.5, 117.5, 91.0, 65.2, 44.8, 41.7, 41.4, 36.3 ppm; IR (KBr): $\tilde{\nu}$ 1723, 1586, 1543, 1489, 1342, 1247, 1215, 1067, 1023, 908, 756, 725, 671, 608, 543, 508, 463 cm^{-1}; HRMS (ESI): *m/z* calcd. for $C_{19}H_{16}BrNNaO_4$ $[M + Na]^+$ 424.01549, found 424.01482.

(6a*R*,7*S*,10a*S*)-7-(2-methoxyphenyl)-6a-nitro-7,8,10,10a-tetrahydro-6*H*-benzo[*c*]chromen-9(6a*H*)-one (3h). The product **3h** was obtained according to the general procedure as a white solid (55.3 mg, 78% yield), m.p. 149–152 °C. HPLC (Daicel Chiralpak AD-H column, *n*-hexane–2-propanol 80:20, flow rate 1.0 mL/min, detection at 254 nm): t_{major} = 24.8 min, t_{minor} = 12.1 min, 80% *ee*; $[\alpha]_D^{20}$ = +95.4 (*c* 1.8, CH_2Cl_2); ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.33–7.28 (m, 1H, ArH), 7.17–7.12 (m, 2H, ArH), 7.00–6.90 (m, 4H, ArH), 6.85 (d, J = 8.4 Hz, 1H, ArH), 5.03 (d, J = 12.4 Hz, 1H, CH), 4.47 (dd, J_1 =2.4 Hz, J_2 = 13.6 Hz, 1H, CH), 4.14 (d, J = 10.4 Hz, 1H, CH), 3.91 (d, J = 11.6 Hz, 1H, CH), 3.85 (s, 3H, OCH_3), 3.41 (t, J = 15.2 Hz, 1H, CH), 3.06 (dd, J_1 = 4.2 Hz, J_2 = 17.6 Hz, 1H, CH), 2.69 (dd, J_1 = 13.6 Hz, J_2 = 17.6 Hz, 1H, CH), 2.46 (dd, J_1 = 2.8 Hz, J_2 = 17.2 Hz, 1H, CH) ppm; ^{13}C NMR (100 MHz, $CDCl_3$): δ 205.5, 157.6, 156.5, 152.6, 129.8, 128.9, 128.7, 123.9, 121.9, 121.5, 117.3, 111.2, 110.6, 90.8, 77.2, 65.0, 55.2, 45.3, 41.0, 36.1 ppm; IR (KBr): $\tilde{\nu}$ 1724, 1539, 1491, 1459, 1250, 1234, 1214, 1064, 1026, 753, 727, 488 cm^{-1}; HRMS (ESI): *m/z* calcd. for $C_{20}H_{20}NO_5$ $[M + H]^+$ 354.13360, found 354.13361.

(6a*R*,7*S*,10a*S*)-6a-nitro-7-(3-nitrophenyl)-7,8,10,10a-tetrahydro-6*H*-benzo[*c*]chromen-9(6a*H*)-one (3i). The product 3i was obtained according to the general procedure as a white solid (47.4 mg, 64% yield), m. p. 72–76 °C. (HPLC on Daicel Chiralpak AD-H column, *n*-hexane–2-propanol 80:20, flow rate 1.0 mL/min, detection at 254nm): t_{major} = 25.8 min, t_{minor} = 21.4 min, 77% *ee*; $[\alpha]_D^{20}$ = +6.1 (*c* 1.8, CH_2Cl_2); ^{1}H NMR (400 MHz, acetone-d_6): δ 8.25 (d, J = 7.6 Hz, 1H, ArH), 8.14 (s, 1H, ArH), 7.75–7.68 (m, 2H, ArH), 7.38 (d, J = 7.6 Hz, 1H, ArH), 7.18 (t, J = 7.6 Hz, 1H, ArH), 6.99 (t, J = 7.6 Hz, 1H, ArH), 6.86 (d, J = 8.4 Hz, 1H, ArH), 5.06 (d, J = 12.8 Hz, 1H, CH), 4.72–4.65 (m, 2H, CH+CH), 4.09 (dd, J_1 = 4.0 Hz, J_2 = 11.4 Hz, 1H, CH), 3.40 (dd, J_1 = 11.4 Hz, J_2 = 16.4 Hz, 1H, CH), 3.13 (dd, J_1 = 4.8 Hz, J_2 = 17.2 Hz, 1H, CH), 2.97 (dd, J_1 = 13.0 Hz, J_2 = 17.2 Hz, 1H, CH), 2.74 (dd, J_1 = 4.0 Hz, J_2 = 16.4 Hz, 1H, CH) ppm; ^{13}C NMR (100 MHz, acetone-d_6): δ 206.9, 154.3, 150.2, 141.0, 136.5, 132.1, 131.2, 130.4, 125.2, 125.1, 123.8, 123.0, 118.7, 92.0, 66.6, 46.7, 45.2, 42.8, 37.9 ppm; IR (KBr): $\tilde{\nu}$ 1718, 1528, 1489, 1457, 1347, 1250, 1220, 1069, 810, 758, 730, 687 cm^{-1}; HRMS (ESI): *m/z* calcd. for $C_{19}H_{16}N_2NaO_6$ $[M + Na]^+$ 391.09006, found 391.08919.

(6a*R*,7*S*,10a*S*)-7-(3,4-dimethoxyphenyl)-6a-nitro-7,8,10,10a-tetrahydro-6*H*-benzo[*c*]chromen-9(6a*H*)-one (3j). The product **3j** was obtained according to the general procedure as a white solid (53.2 mg, 69% yield), m. p. 78–83 °C. HPLC (Daicel Chiralpak IB column, *n*-hexane–2-propanol 65:35, flow rate 1.0 mL/min, detection at 254 nm): t_{major} = 36.6 min, t_{minor} = 21.0 min, 83% *ee*; $[\alpha]_D^{20}$ = +8.3 (*c* 1.7, CH_2Cl_2); ^{1}H NMR (400 MHz, acetone-d_6): δ 7.35 (d, J = 7.6 Hz, 1H, ArH), 7.16 (t, J = 7.6 Hz, 1H, ArH), 6.97 (t, J = 7.4 Hz, 1H, ArH), 6.90 (d, J = 8.0 Hz, 1H, ArH), 6.83 (d, J = 8.0 Hz, 1H, ArH), 6.79–6.75 (m, 2H, ArH), 5.03 (dd, J_1 = 1.8 Hz, J_2 = 12.8 Hz, 1H, CH), 4.63 (d, J = 12.4 Hz, 1H, CH), 4.56 (dd, J_1 = 4.0 Hz, J_2 = 12.8 Hz, 1H, CH), 3.79 (s, 6H, OCH_3+OCH_3), 3.74 (dd, J_1 = 4.4 Hz, J_2 = 10.8 Hz, 1H, CH), 3.25 (dd, J_1 = 10.8 Hz, J_2 = 16.4 Hz, 1H, CH), 3.07 (dd, J_1 = 5.2 Hz, J_2 = 17.2 Hz, 1H, CH), 2.89 (dd, J_1 = 12.8 Hz, J_2 = 16.8 Hz, 1H, CH), 2.64 (dd, J_1 = 4.4 Hz, J_2 = 16.4 Hz, 1H, CH) ppm; ^{13}C NMR (100 MHz, acetone-d_6): δ 207.8, 154.4, 151.4, 151.2, 131.2, 131.0, 130.3, 123.6, 123.5, 122.4, 118.7, 114.0, 113.6, 91.9, 66.9, 57.1, 57.0, 47.0, 45.7, 43.6, 37.9 ppm; IR (KBr): $\tilde{\nu}$ 1720, 1587, 1544, 1518, 1491, 1460, 1347, 1246, 1147, 1072, 1023, 811, 759, 640, 476 cm^{-1}; HRMS (ESI): *m/z* calcd. for $C_{21}H_{22}NO_6$ $[M + H]^+$ 384.14416, found 384.14378; calcd. for $C_{21}H_{21}NNaO_6$ $[M + Na]^+$ 406.12611, found 406.12592.

(6a*R*,7*S*,10a*S*)-7-(4-(dimethylamino)phenyl)-6a-nitro-7,8,10,10a-tetrahydro-6*H*-benzo[*c*]chromen-9(6a*H*)-one (3k). The product **3k** was obtained according to the general procedure as a white solid (56.8 mg, 78% yield), m.p.: 67–71 °C. HPLC (Daicel Chiralpak IB column, *n*-hexane–2-propanol 65:35, flow rate 1.0 mL/min, detection at 254 nm): t_{major} = 21.0 min, t_{minor} = 16.7 min, 83% *ee*; $[\alpha]_D^{20}$ = +14.0 (*c* 1.1, CH_2Cl_2); ^{1}H NMR (400 MHz, acetone-d_6): δ 7.35 (d, J = 7.6 Hz, 1H, ArH), 7.18–7.14 (m, 1H, ArH), 7.02 (d, J = 8.4 Hz, 2H, ArH), 6.96 (t, J = 7.6 Hz, 1H, ArH), 6.83 (d, J = 8.4 Hz, 1H, ArH), 6.68 (d, J = 8.8 Hz, 2H, ArH), 5.00 (dd, J_1 = 2.0 Hz, J_2 = 12.4 Hz, 1H, CH), 4.66 (d, J = 12.4 Hz, 1H, CH), 4.55–4.50 (m, 1H, CH), 3.67 (dd, J_1 = 4.4 Hz, J_2 = 10.4 Hz, 1H, CH), 3.18 (dd, J_1 = 10.4 Hz, J_2 = 16.4 Hz, 1H, CH), 3.06 (dd, J_1 = 5.2 Hz, J_2 = 16.8 Hz, 1H, CH), 2.93 (s, 6H, $2CH_3$), 2.90–2.80 (m, 1H, CH), 2.62 (dd, J_1 = 4.4 Hz, J_2 = 16.4 Hz, 1H, CH) ppm; ^{13}C NMR (100 MHz, acetone-d_6): δ 207.8, 154.4, 152.4, 131.2, 130.7, 130.2, 125.7, 123.8, 123.5, 118.7, 114.1, 91.9, 67.1, 47.1, 45.6, 43.8, 41.3, 37.9 ppm; IR (KBr): $\tilde{\nu}$ 1709, 1611, 1548, 1523, 1488, 1348, 1225, 1042, 943, 823, 763, 613, 567, 525, 424 cm^{-1}; HRMS (ESI): *m/z* calcd. for $C_{21}H_{23}N_2O_4$ $[M + H]^+$ 367.16523, found 367.16423.

(6a*R*,7*S*,10a*S*)-7-(naphthalen-1-yl)-6a-nitro-7,8,10,10a-tetrahydro-6*H*-benzo[*c*]chromen-9(6a*H*)-one (3l). The product **3l** was obtained according to the general procedure as a white solid (67.6 mg, 90% yield), m.p.: 99–102 °C. HPLC (Daicel Chiralpak AD-H column, *n*-hexane–2-propanol 80:20, flow rate 1.0 mL/min, detection at 254 nm): t_{major} = 45.2 min, t_{minor} = 16.0 min, 79% *ee*; $[\alpha]_D^{20}$ = +121.0 (*c* 2.6, CH_2Cl_2); ^{1}H NMR (400 MHz, acetone-d_6): δ 8.37 (d, J = 8.4 Hz, 1H, ArH), 7.97 (d, J = 8.0 Hz, 1H, ArH), 7.91 (d, J = 8.0 Hz, 1H, ArH), 7.64–7.55 (m, 2H, ArH), 7.48 (t, J = 7.6 Hz, 1H, ArH), 7.41–7.38 (m, 2H, ArH), 7.15 (t, J = 8.0 Hz, 1H, ArH), 6.98 (t, J = 7.6 Hz, 1H, ArH), 6.81 (d, J = 8.4 Hz, 1H, ArH), 4.98 (dd, J_1 = 1.6 Hz, J_2 = 12.4 Hz, 1H, CH), 4.90–4.80 (m, 3H, CH+CH_2), 3.48 (dd, J_1 = 11.6 Hz, J_2 = 16.4 Hz, 1H, CH), 3.19–3.07 (m, 2H, CH_2), 2.68 (dd, J_1 = 3.6 Hz, J_2 = 16.8 Hz, 1H, ArH) ppm; ^{13}C NMR (100 MHz, acetone-d_6): δ 207.9, 154.4, 135.9, 135.5, 133.8, 131.3, 131.0, 130.7, 130.3, 128.4, 127.8, 127.4, 126.7, 124.7, 123.7, 123.2, 118.6, 93.6, 67.3, 47.0, 44.1, 38.8, 37.9 ppm; IR (KBr): $\tilde{\nu}$ 1722, 1586, 1544, 1491, 1459, 1343, 1275, 1259, 1230, 1214, 1070, 802, 780, 753 cm^{-1}; HRMS (ESI): *m/z* calcd. for $C_{23}H_{19}NNaO_4$ $[M + Na]^+$ 396.12063, found 396.12062.

(6a*R*,7*S*,10a*S*)-2-bromo-7-(4-chlorophenyl)-6a-nitro-7,8,10,10a-tetrahydro-6*H*-benzo[*c*]chromen-9(6a*H*)-one (3m). The product **3m** was obtained according to the general procedure as a white solid (46.6 mg, 53% yield), m.p. 163–166 °C. HPLC (Daicel Chiralpak IB column, *n*-hexane–2-propanol 65:35, flow rate 1.0 mL/min, detection at 254nm): t_{major} = 22.0 min, t_{minor} = 17.6 min, 78% *ee*; $[\alpha]_D^{20}$ = +10.1 (*c* 0.67, CH_2Cl_2); ^{1}H NMR (400 MHz, acetone-d_6): δ 7.58 (d, J = 2.4 Hz, 1H, ArH), 7.42–7.39 (m, 2H, ArH), 7.32 (dd, J_1 = 2.4 Hz, J_2 = 8.8 Hz, 1H, ArH), 7.28–7.25 (m, 2H, ArH), 6.82 (d, J = 8.8 Hz, 1H, ArH), 5.07 (dd, J_1 = 2.4 Hz, J_2 = 12.8 Hz, 1H, CH), 4.74 (dd, J_1 = 2.4 Hz, J_2 = 12.8 Hz, 1H, CH), 4.65 (dd, J_1 = 4.6Hz, J_2 = 12.8 Hz, 1H, CH), 3.92–3.88 (m, 1H, CH), 3.24–3.18 (m, 1H, CH), 3.12 (dd, J_1 = 5.2 Hz, J_2 = 17.2 Hz, 1H, CH), 2.94 (dd, J_1 = 13.0 Hz, J_2 = 17.2 Hz, 1H, CH), 2.84–2.69 (m, 1H, CH) ppm; ^{13}C NMR (100 MHz, acetone-d_6): δ 206.8, 153.6, 137.7, 135.7, 133.7, 133.3, 131.9, 130.7, 126.0,

120.8, 115.2, 91.7, 67.0, 46.8, 45.4, 43.2, 37.5 ppm; IR (KBr): $\tilde{\nu}$ 1723, 1547, 1479, 1409, 1339, 1279, 1251, 1092, 1067, 1014, 830, 813, 749, 692, 613, 510 cm^{-1}; HRMS (ESI): *m/z* calcd. for $C_{19}H_{15}BrClNNaO_4$ $[M + Na]^+$ 457.97652, found 457.97672.

(6a*R*,7*S*,10a*S*)-2-chloro-7-(4-chlorophenyl)-6a-nitro-7,8,10,10a-tetrahydro-6*H*-benzo[*c*]chromen-9(6a*H*)-one (3n). The product **3n** was obtained according to the general procedure as a white solid (46.2 mg, 59% yield), m.p. 192–196 °C. HPLC (Daicel Chiralpak IB column, *n*-hexane–2-propanol 65:35, flow rate 1.0 mL/min, detection at 254 nm): t_{major} = 21.6 min, t_{minor} = 16.6 min, 73% *ee*; $[\alpha]_D^{20}$ = +11.8 (*c* 1.4, CH_2Cl_2); ^{1}H NMR (400 MHz, acetone-d_6): δ 7.44 (d, J = 2.8 Hz, 1H, ArH), 7.40 (*d*, J = 8.4 Hz, 2H, ArH), 7.26 (d, J = 8.8 Hz, 2H, ArH), 7.19 (dd, J_1 = 2.4 Hz, J_2 = 8.8 Hz, 1H, ArH), 6.87 (d, J = 8.8 Hz, 1H, ArH), 5.06 (dd, J_1 = 2.0 Hz, J_2 = 12.4 Hz, 1H, CH), 4.74 (*J* = 12.8 Hz, 1H, CH), 4.66–4.62 (m, 1H, CH), 3.90 (dd, J_1 = 4.4 Hz, J_2 = 10.4 Hz, 1H, CH), 3.21 (dd, J_1 = 10.4 Hz, J_2 = 16.8 Hz, 1H, CH), 3.12 (dd, J_1 = 4.8 Hz, J_2 = 17.2 Hz, 1H, CH), 2.94 (dd, J_1 = 12.8 Hz, J_2 = 17.2 Hz, 1H, CH), 2.71 (dd, J_1 = 4.4 Hz, J_2 = 16.4 Hz, 1H, CH) ppm; ^{13}C NMR (100 MHz, acetone-d_6): δ 206.8, 153.2, 137.8, 135.7, 131.9, 130.8, 130.7, 130.4, 128.0, 125.5, 120.4, 91.7, 67.1, 46.8, 45.4, 43.2, 37.6 ppm; IR (KBr): $\tilde{\nu}$ 1722, 1540, 1488, 1411, 1339, 1250, 1089, 1010, 844, 817, 749, 690, 638, 613, 505, 423 cm^{-1}; HRMS (ESI): *m/z* calcd. for $C_{19}H_{15}Cl_2NNaO_4$ $[M + Na]^+$ 414.02703, found 414.02719.

(6a*R*,7*S*,10a*S*)-2,4-dibromo-7-(4-chlorophenyl)-6a-nitro-7,8,10,10a-tetrahydro-6*H*-benzo[*c*]chromen-9(6a*H*)-one (3o). The product **3o** was obtained according to the general procedure as a white solid (46.9 mg, 45% yield), m.p. 205–208 °C. HPLC (Daicel Chiralpak IB column, *n*-hexane–2-propanol 65:35, flow rate 1.0 mL/min, detection at 254 nm): t_{major} = 20.0 min, t_{minor} = 17.6 min, 65% *ee*; $[\alpha]_D^{20}$ = +1.5 (*c* 1.6, CH_2Cl_2); ^{1}H NMR (400 MHz, acetone-d_6): δ 7.62 (s, 2H, ArH), 7.41 (d, J = 8.4 Hz, 2H, ArH), 7.27 (d, J = 8.8 Hz, 2H, ArH), 5.23 (dd, J_1 = 2.0 Hz, J_2 = 12.4 Hz, 1H, CH), 4.89 (d, J = 12.8 Hz, 1H, CH), 4.73–4.68 (m, 1H, CH), 3.95 (dd, J_1 = 4.4 Hz, J_2 = 9.8 Hz, 1H, CH), 3.23–3.11 (m, 2H, CH_2), 2.99 (dd, J_1 = 13.2 Hz, J_2 = 17.2 Hz, 1H, CH), 2.84–2.74 (m, 1H, CH) ppm; ^{13}C NMR (100 MHz, acetone-d_6): δ 206.5, 150.6, 137.6, 135.9, 135.8, 133.3, 131.9, 130.7, 127.3, 115.1, 113.2, 91.7, 67.8, 46.8, 45.4, 43.2, 37.6 ppm; IR (KBr): $\tilde{\nu}$ 1722, 1548, 1461, 1412, 1276, 1262, 1245, 1227, 1170, 1090, 1064, 1013, 866, 825, 750, 725, 671, 609, 531, 472 cm^{-1}; HRMS (ESI): *m/z* calcd. for $C_{19}H_{14}Br_2ClNNaO_4$ $[M + Na]^+$ 535.88703, found 535.88661.

(6a*R*,7*S*,10a*S*)-2,4-dichloro-7-(4-chlorophenyl)-6a-nitro-7,8,10,10a-tetrahydro-6*H*-benzo[*c*]chromen-9(6a*H*)-one (3p). The product **3p** was obtained according to the general procedure as a white solid (46.4 mg, 54% yield), m.p. 211–220 °C. HPLC (Daicel Chiralpak IB column, *n*-hexane–2-propanol 65:35, flow rate 1.0 mL/min, detection at 254 nm): t_{major} = 19.7 min, t_{minor} = 16.6 min, 68% *ee*; $[\alpha]_D^{20}$ = +2.1 (*c* 2.0, CH_2Cl_2); ^{1}H NMR (400 MHz, acetone-d_6): δ 7.45 (d, J = 2.4 Hz, 1H, ArH), 7.41 (d, J = 8.8 Hz, 2H, ArH), 7.36 (d, J = 2.4 Hz, 1H, ArH), 7.27 (d, J = 8.4 Hz, 2H, ArH), 5.23 (dd, J_1 = 2.0 Hz, J_2 = 12.4 Hz, 1H, CH), 4.89 (d, J = 12.4 Hz, 1H, CH), 4.72–4.68 (m, 1H, CH), 3.96 (dd, J_1 = 4.6 Hz, J_2 = 9.8 Hz, 1H, CH), 3.23–3.11 (m, 2H, CH_2), 2.99 (dd, J_1 = 12.8 Hz, J_2 = 17.2 Hz, 1H, CH), 2.77 (dd, J_1 = 4.6 Hz, J_2 = 16.8 Hz, 1H, CH) ppm; ^{13}C NMR (100 MHz, acetone-d_6): δ 206.5, 149.2, 137.6, 135.8, 132.0, 130.8, 130.4, 129.7, 127.8, 127.0, 124.2, 91.7, 67.7, 46.8, 45.4, 43.2, 37.7 ppm; IR (KBr): $\tilde{\nu}$ 1724, 1549, 1469, 1412, 1248, 1226, 1091, 1066, 1035, 1013, 864, 846, 825, 620, 535 cm^{-1}; HRMS (ESI): *m/z* calcd. for $C_{19}H_{14}Cl_3NNaO_4$ $[M + H]^+$ 447.98806, found 447.98771.

(6a*R*,7*S*,10a*S*)-7-(4-chlorophenyl)-4-methoxy-6a-nitro-7,8,10,10a-tetrahydro-6*H*-benzo[*c*]chromen-9(6a*H*)-one (3q). The product **3q** was obtained according to the general procedure as a white solid (62.1 mg, 80% yield), m.p. 201–205 °C. HPLC (Daicel Chiralpak AD-H column (*n*-hexane–2-propanol 80:20, flow rate 1.0 mL/min, detection at 254 nm): t_{major} = 19.8 min, t_{minor} = 24.7 min, 73% *ee*; $[\alpha]_D^{20}$ = –17.6 (*c* 2.4, CH_2Cl_2); ^{1}H NMR (400 MHz, acetone-d_6): δ 7.40 (d, J = 8.4 Hz, 2H, ArH), 7.27 (d, J = 8.4 Hz, 2H, ArH), 6.93–6.88 (m, 2H, ArH), 6.86–6.82 (m, 1H, ArH), 5.05 (dd, J_1 = 2.0 Hz, J_2 = 12.4 Hz, 1H, CH), 4.64 (d, J = 12.4 Hz, 1H, CH), 4.60–4.56 (m, 1H, CH), 3.87 (dd, J_1 = 4.4 Hz, J_2 = 10.8 Hz, 1H, CH), 3.77 (s, 3H, CH_3), 3.24 (dd, J_1 = 10.8 Hz, J_2 = 16.4 Hz, 1H, CH), 3.08 (dd, J_1 = 4.8 Hz, J_2 = 17.2 Hz, 1H, CH), 2.91 (dd, J_1 = 12.8 Hz, J_2 = 17.2 Hz, 1H, CH), 2.67 (dd, J_1 = 4.4 Hz, J_2 = 16.4 Hz, 1H, CH) ppm; ^{13}C NMR (100 MHz, acetone-d_6): δ 207.2, 150.5, 144.1, 137.9, 135.7, 131.9, 130.7, 124.0, 123.3, 122.3, 112.4, 91.8, 66.7, 57.0, 47.0, 45.3, 43.1, 37.8 ppm; IR (KBr): $\tilde{\nu}$ 1727, 1547, 1481, 1411, 1334, 1262, 1220, 1081, 1064, 1015, 829, 816, 788, 741, 666, 537 cm^{-1}; HRMS (ESI): *m/z* calcd. for $C_{20}H_{18}ClNNaO_5$ $[M + Na]^+$ 410.07657, found 410.07655.

(6a*R*,7*S*,10a*S*)-7-(4-chlorophenyl)-4-ethoxy-6a-nitro-7,8,10,10a-tetrahydro-6*H*-benzo[*c*]chromen-9(6a*H*)-one (3r). The product **3r** was obtained according to the general procedure as a white solid (64.7 mg, 81% yield), m.p. 76–80 °C. HPLC (Daicel Chiralpak AD-H column, *n*-hexane–2-propanol 80:20, flow rate 1.0 mL/min, detection at 254 nm): t_{major} = 14.7 min, t_{minor} = 22.3 min, 71% *ee*; $[\alpha]_D^{20}$ = –16.2 (*c* 2.3, CH_2Cl_2); ^{1}H NMR (400 MHz, acetone-d_6): δ 7.42–7.38 (m, 2H, ArH), 7.28–7.25 (m, 2H, ArH), 6.92–6.86 (m, 2H, ArH), 6.83–6.78 (m, 1H, ArH), 5.06 (dd, J_1 = 2.4 Hz, J_2 = 12.4 Hz, 1H, CH), 4.63 (d, J = 12.4 Hz, 1H, CH), 4.60–4.56 (m, 1H, CH), 4.03–3.96 (m, 2H, CH_2), 3.86 (dd, J_1 = 4.4 Hz, J_2 = 10.8 Hz, 1H, CH), 3.24 (dd, J_1 = 10.4 Hz, J_2 = 16.4 Hz, 1H, CH), 3.07 (dd, J_1 = 4.8 Hz, J_2 = 17.2 Hz, 1H, CH), 2.90 (dd, J_1 = 13.2 Hz, J_2 = 17.2 Hz, 1H, CH), 2.68 (dd, J_1 = 4.4 Hz, J_2 = 16.4 Hz, 1H, CH), 1.34 (t, J = 6.8 Hz, 3H, CH_3) ppm; ^{13}C NMR (100 MHz, acetone-d_6): δ 207.3, 149.7, 144.3, 137.9, 135.6, 131.9, 130.6, 124.0, 123.3, 122.3, 113.6, 91.8, 66.7, 65.8, 47.0, 45.3, 43.1, 37.8, 16.1 ppm; IR (KBr): $\tilde{\nu}$ 1715, 1586, 1544, 1487, 1473, 1338, 1261, 1212, 1091, 1013, 829, 764, 750 cm^{-1}; HRMS (ESI): *m/z* calcd. for $C_{21}H_{20}ClNNaO_5$ $[M + Na]^+$ 424.09222, found 424.09249.

(1*S*,4a*S*,10a*R*)-1-(4-bromophenyl)-10a-nitro-1,4,4a,9,10,10a-hexahydrophenanthren-3(2*H*)-one (3s). The product **3s** was obtained according to the general procedure as white solid (50.9 mg, 64% yield), m.p. 74–78 °C. HPLC (Daicel Chiralpak AD-H column, *n*-hexane–2-propanol 80:20, flow rate 1.0 mL/min, detection at 254 nm): t_{major} = 12.9 min, t_{minor} = 15.0 min, 81% *ee*; $[\alpha]_D^{20}$ = +9.3 (*c* 1.8, CH_2Cl_2); ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.49–7.42 (m, 2H, ArH), 7.18–7.06 (m, 4H, ArH), 6.97 (d, J = 8.8 Hz, 2H, ArH), 4.26 (dd, J_1 = 5.2 Hz, J_2 = 13.2 Hz, 1H, CH), 3.56 (dd, J_1 = 6.0 Hz, J_2 = 6.8 Hz, 1H, CH), 3.04 (dd, J_1 = 6.8 Hz, J_2 = 16.8 Hz, 1H, CH), 3.00–2.84 (m, 4H), 2.78 (dd, J_1 = 5.6 Hz, J_2 = 16.8 Hz, 1H, CH), 2.58 (dd, J_1 = 13.2 Hz, J_2 = 17.2 Hz, 1H, CH), 2.52–2.42 (m, 1H, CH) ppm; ^{13}C NMR (100 MHz, $CDCl_3$): δ 207.0, 136.1, 135.0, 132.6, 132.1, 129.7, 129.1, 128.5, 127.2, 126.9, 122.7, 92.5, 49.4, 47.2, 42.0, 38.6, 28.0, 25.3 ppm.

IR (KBr): $\tilde{\nu}$ 1715, 1537, 1489, 1453, 1441, 1409, 1351, 12776, 1226, 1120, 1109, 1076, 1009, 908, 832, 806, 753, 735, 649, 613, 516, 446 cm^{-1}; HRMS (ESI): *m/z* calcd. for $C_{20}H_{18}BrNNaO_3$ $[M + Na]^+$ 422.03623, found 422.03681.

(6a*R*,7*S*,10a*S*)-7-(4-bromophenyl)-6a-nitro-7,8,10,10a-tetrahydro-6*H*-benzo[*c*]thiochromen-9(6a*H*)-one (3t). The product **3t** was obtained according to the general procedure as a white solid (62.1 mg, 74% yield), m.p. 180–182 °C. HPLC (Daicel Chiralpak AD-H column, *n*-hexane–2-propanol 80:20, flow rate 1.0 mL/min, detection at 254 nm): t_{major} = 16.3 min, t_{minor} = 27.4 min, 95% *ee*; $[\alpha]_D^{20}$ = +37.6 (*c* 1.9, CH_2Cl_2); ^1H NMR (400 MHz, $CDCl_3$): δ 7.46 (d, *J* = 8.8 Hz, 2H, ArH), 7.21–7.12 (m, 4H, ArH), 6.97 (d, *J* = 8.4 Hz, 2H, ArH), 4.16 (dd, J_1 = 6.8 Hz, J_2 = 10.8 Hz, 1H, CH), 3.95 (dd, J_1 = 6.0 Hz, J_2 = 7.6 Hz, 1H, CH), 3.63 (d, *J* = 14.0 Hz, 1H, CH), 3.56 (d, *J* = 14.0 Hz, 1H, CH), 3.08 (dd, J_1 = 7.8 Hz, J_2 = 17.4 Hz, 1H, CH), 2.90–2.78 (m, 3H, CH+CH_2) ppm; ^{13}C NMR (400 MHz, $CDCl_3$): δ 206.0, 135.5, 134.6, 132.3, 131.5, 129.9, 129.6, 127.70, 127.69, 126.4, 123.1, 92.4, 47.3, 46.2, 42.0, 40.8, 33.1 ppm; IR (KBr): $\tilde{\nu}$ 1705, 1548, 1489, 1411, 1276, 1230, 1077, 1010, 830, 7748, 732, 612, 568, 515, 483, 446 cm^{-1}; HRMS (ESI): *m/z* calcd. for $C_{19}H_{16}BrNNaO_3S$ $[M + Na]^+$ 439.99265, found 439.99310.

(4*S*,4a*R*,12c*S*)-4-(4-chlorophenyl)-4a-nitro-3,4,4a,5-tetrahydro-1*H*-dibenzo[*c*,*f*]chromen-2(12c*H*)-one (e*nt*-3u). The product *ent*-**3u** was obtained according to the general procedure using catalyst **III** as a white solid (49.4 mg, 61% yield), m.p. 206–211 °C. HPLC (Daicel Chiralpak AD-H column, *n*-hexane–2-propanol 80:20, flow rate 1.0 mL/min, detection at 254 nm): t_{major} = 21.9 min, t_{minor} = 32.8 min, 78% *ee*; ^1H NMR (400 MHz, acetone-d_6): δ 8.16 (d, *J* = 8.4 Hz, 1H, ArH), 7.84 (d, *J* = 8.0 Hz, 1H, ArH), 7.75 (d, *J* = 8.8 Hz, 1H, ArH), 7.57 (t, *J* = 7.6 Hz, 1H, ArH), 7.44–7.33 (m, 5H, ArH), 7.04 (d, *J* = 8.8 Hz, 1H, ArH), 5.27–5.20 (m, 2H, CH_2), 5.00 (d, *J* = 12.4 Hz, 1H, CH), 3.92 (dd, J_1 = 4.6 Hz, J_2 = 9.8 Hz, 1H, CH), 3.44 (dd, J_1 = 9.8 Hz, J_2 = 16.6 Hz, 1H, CH), 3.31 (dd, J_1 = 4.2 Hz, J_2 = 18.0 Hz, 1H, CH), 2.89 (dd, J_1 = 13.6 Hz, J_2 = 18.0 Hz, 1H, CH), 2.81 (d, J_1 = 4.6 Hz, J_2 = 16.6 Hz, 1H, CH) ppm; ^{13}C NMR (100 MHz, acetone-d_6): δ 206.8, 151.8, 138.0, 135.7, 133.5, 132.0, 131.7, 131.4, 130.7, 130.3, 129.1, 125.8, 123.5, 120.1, 114.5, 91.7, 66.5, 45.8, 45.7, 43.3, 34.5 ppm; IR (KBr): $\tilde{\nu}$ 1720, 1620, 1599, 1543, 1471, 1413, 1343, 1233, 1112, 1014, 821, 763, 442 cm^{-1}; HRMS (ESI): *m/z* calcd. for $C_{23}H_{19}ClNO_4$ $[M + H]^+$ 408.09971, found 408.10005; *m/z* calcd. for $C_{23}H_{18}ClNNaO_4$ $[M + Na]^+$ 430.08166, found 430.08193.

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14. Crystallographic data for compound-**3m** (CCDC-1406419) has been provided as CIF file in supporting information.

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