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Stereoselective Cascade Formal Nucleophilic Substitution and Mannich Reaction of Ethyl 2-Aroyl-1-chlorocyclopropanecarboxylates

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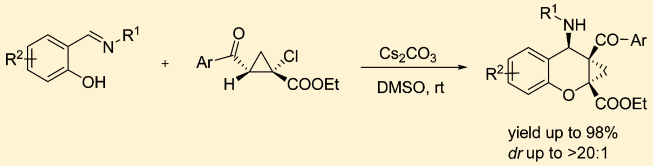
Supporting Information

ABSTRACT: A highly regio- and diastereoselective cascade formal nucleophilic substitution and Mannich reaction of ethyl 2-aroyl-1-chlorocyclopropanecarboxylates with salicylaldimines is described. Under basic conditions, ethyl 2-aroyl-1-chlorocyclopropanecarboxylate is easily converted into a cyclopropene intermediate via simple 1,2-elimination of hydrogen chloride. The highly reactive cyclopropene quickly combines with salicylaldimine through regioselective oxa-addition to the strained C═C bond and subsequent diastereoselective addition to C═N bond, constructing C−O and C−C bonds at one time. This provides a highly stereoselective novel methodology for synthesis of conformationally constrained *cis*-tetrahydrocyclopropa[*b*]chromene derivatives.

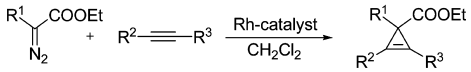


INTRODUCTION

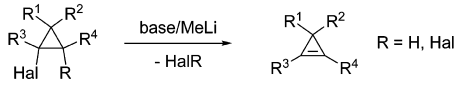
The chemistry of cyclopropenes has attracted increasing interest of chemists in the past decades[1] for their remarkable reactivity that extends far beyond chemical properties typical for common alkenes.[2] Thus, much effort has been taken to develop new methodologies for generation of diversely substituted cyclopropenes.[3] The most widely used approaches involve [2 + 1] cycloaddition of carbenoids to alkynes catalyzed by the transition metals like rhodium complexes (Scheme 1, Route A),[3b,d] and 1,2-elimination of H−X, X−X (X = halogen) from halogenated cyclopropane precursors in the presence of strong base (*t*-BuOK or KOH) and lithium methide, respectively (Scheme 1, Route B).[3c,e,h] Rhodium complex-catalyzed reactions have been widely applied in the preparation of cyclopropene compounds, including optically active ones.[4]

Scheme 1. Two Most Important Routes to Cyclopropene Core

Route A: [2+1] cycloaddition



Route B: 1,2-elimination



An alternative preparation of cyclopropene compounds was successfully achieved through route B in this decade, and three kinds of cyclopropenes differing in structure have been investigated in detail (Figure 1).[3c,e,5] Large-scale preparation of 3,3-disubstituted cyclopropenes type I and type II (Figure 1) was achieved by Rubin's group.[3c,e] These compounds are stable to long-term storage, while cyclopropenes possessing an electron-withdrawing group on C═C bond are extremely unstable and difficult to be isolated (Figure 1, type III).[5e]

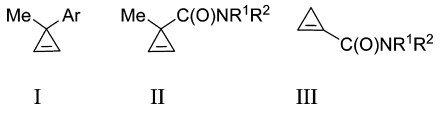


Figure 1. Three types of cyclopropenes in formal nucleophilic substitution.

The chemical properties for various cyclopropenes have been well reviewed.[1] Among the reported reactions, addition reactions were diverse including 1,2-addition of H−H,[4e] H−C,[2h,j] H−N,[5b,c,e] H−O,[5d,f,g] H−S,[5d] H−M,[2t,6] and C−M[7] moieties across C═C bond of cyclopropenes. Recently, a facile 1,2-hydrofluorination process was observed between a cyclopropene IV intermediate bearing two electron-withdrawing groups and HF_2^- or $H_2F_3^-$ during our investigation of the reaction between ethyl 2-aroyl-1-chlorocyclopropanecarboxylates and KF or KHF_2 (Scheme 2).[8] This observation revealed that aroyl group at C-2 site made the dehydrochlorination of monochlorinated cyclopropane much easier under weakly basic conditions. This provided a useful preparative way to a novel kind of cyclopropene intermediates bearing two electron-withdrawing groups at their C═C bond under mild conditions.

In fact, cyclopropenes with the structure like cyclopropene IV possessing two electron-withdrawing groups at C═C bond and without substitution at C-3 were rarely reported.[9] Inspired

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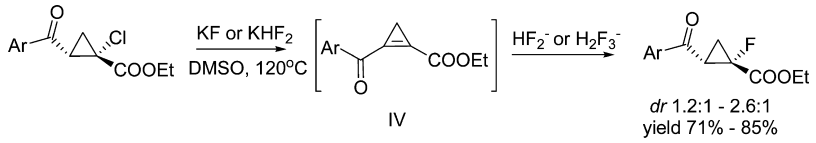
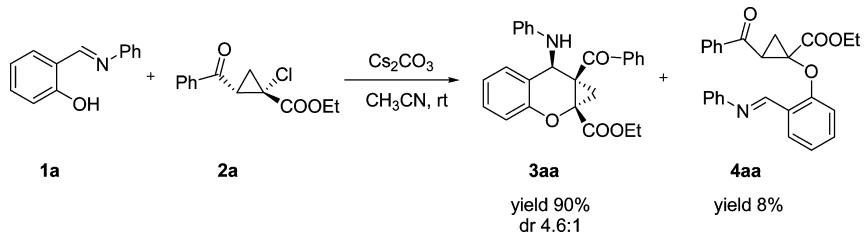
Scheme 2. Our Previous Work Based on Cyclopropene with Two Electron-Withdrawing Groups at C=C bond



Scheme 3. Reaction between 1a and 2a



by the successful addition of H−F species to C=C bond of the cyclopropene IV, we focused our attention on investigation of their chemical behaviors. In view of their structural feature, we realized that cyclopropenes IV could be employed to react with donor−acceptor species to get polycyclic structural diversity compounds. At this point, a relevant reaction should be noted between stable 3,3-disubstituted cyclopropene and salicylaldehyde, in which a Rh-catalyzed hydroacylation occurred rather than cascade oxa-addition/aldol reaction.[2h] Herein, we wish to introduce an efficient base-promoted cascade oxa-addition/Mannich reaction between salicylaldimine and the cyclopropene IV generated in situ, which afforded valuable *cis*-tetrahydrocyclopropa[*b*]chromene skeleton widely existing in glutamate receptor ligand, such as PHCCC and CPCCOEt.[10]

RESULTS AND DISCUSSION

As part of our ongoing work, we chose salicylaldimine **1** as the donor−acceptor species to test the possibility of the cascade reaction process based on the cyclopropene intermediate IV derived from ethyl 2-aroyl-1-chlorocyclopropanecarboxylates **2**. Initially, we carried out the reaction between 2-((phenylimino)-methyl)phenol **1a** and ethyl 2-benzoyl-1-chlorocyclopropanecarboxylate **2a** in the presence of Cs_2CO_3 in CH_3CN at room temperature (Scheme 3). Gratifyingly, the reaction proceeded smoothly, giving the desired product **3aa** in 90% yield with 4.6:1 dr value. The stereochemistry for this process was analyzed by NMR spectroscopy, and the major isomer was assigned to be *cis*-**3aa**. This assignment was also supported by single crystal X-ray analysis and NOESY analysis.[11] Further experiment demonstrated that the product **3aa** was stable under the reaction conditions. Thus, the unusual predominant formation of *cis*-**3aa** with much larger steric hindrance clearly indicated this process was kinetically controlled since no intramolecular hydrogen bonding exists between N−H and C=O groups of cis-isomer, which was confirmed by single-crystal X-ray diffraction analysis. It should be mentioned that a little amount of **4aa** (in 8% yield) yielded through a simple oxa-addition was also detected, which could not be separated easily from **3aa** by silica gel column chromatography.

This preliminary result encouraged us to evaluate the reaction parameters suitable for this cascade reaction. The above reaction of **1a** with **2a** was chosen as the model to optimize the reaction conditions including the bases and solvents. All the results are summarized in Table 1. Apparently, all of the inorganic bases listed in Table 1 could promote this reaction, but their property had a great influence on the reaction. Common bases like K_2CO_3 or K_3PO_4 showed inferior catalytic activity and gave low conversions after 12 h (Table 1, entries 1−2). In contrast, Cs_2CO_3 gave the desired product **3aa** in 90% yield possibly owing to its high solubility in acetonitrile (Table 1, entry 3). On the other hand, strong bases such as NaOH, KOH, or *t*-BuOK obviously accelerated the consumption rate of **2a** but declined the yields of **3aa** significantly (Table 1, entries 4−6). A similar result was observed in the case of DBU; only 15% yield of **3aa** was obtained accompanied with 28% yield of **4aa**, although the starting material **2a** was consumed completely within 1 h (Table 1, entry 7). The above low yields could be attributed to much faster 1,2-elimination of **2a** and subsequent decomposition of the cyclopropene intermediate generated in situ under the strong basic conditions. In addition, when common organic bases such as Et_3N and DIPEA were used, the reaction could not proceed readily, possibly because of their weak ability to abstract hydrogen chloride from **2a** at room temperature (Table 1, entries 8−9). On the basis of the above observations, Cs_2CO_3 was chosen as the most promising base to optimize the reaction media.

Table 1. Optimization of the Cascade Reaction between 1a and 2a[a]

entry	base	solvent	time (h)	cony (%)[b]	yield of **3aa** (%)	dr[c]	yield of **4aa** (%)
1	K_2CO_3	CH_3CN	12	44	26	3.0:1	15
2	K_3PO_4	CH_3CN	12	36	20	2.4:1	13
3	Cs_2CO_3	CH_3CN	6	100	90	4.6:1	8
4	NaOH	CH_3CN	2	100	19	3.3:1	5
5	KOH	CH_3CN	2	100	50	6.1:1	1
6	*t*-BuOK	CH_3CN	2	100	29	2.9:1	13
7	DBU	CH_3CN	1	100	15	2.5:1	28
8	Et_3N	CH_3CN	12	0	0	–	0
9	DIPEA	CH_3CN	12	0	0	–	0
10	Cs_2CO_3	THF	8	90	12	5.0:1	59
11	Cs_2CO_3	acetone	8	95	60	5.9:1	22
12	Cs_2CO_3	DMF	3	100	95	6.4:1	2
13	Cs_2CO_3	DMSO	2	100	92	6.4:1	0

[a]Reactions were carried out using a 0.2 mmol of **1a**, 0.2 mmol of **2a**, and 0.4 mmol of base in 1 mL of solvent at room temperature for the given time. [b]Conversions were based on the recovery of **2a**. [c]Diastereomeric ratios (*cis*:*trans*) determined by ^1H NMR of the crude product.

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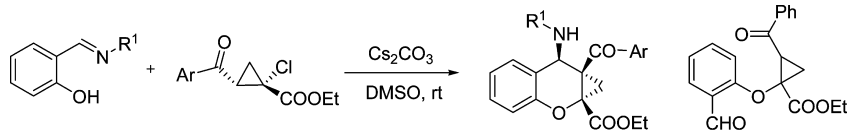
Table 2. Scope of the Cascade Reaction between 1 and 2[a]

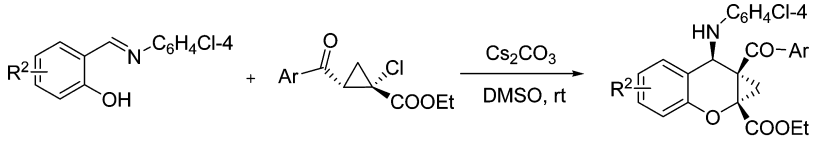


1a-1g 2a-2h 3 5a

entry	substrate 1	substrate 2	product	time (h)	yield (%)	dr[b]
1	**1a** (R^1 = Ph)	**2a** (Ar = Ph)	**3aa**	2	92	6.4:1
2	**1a**	**2b** (Ar = 4-MeC_6H_4)	**3ab**	2	91	8.9:1
3	**1a**	**2c** (Ar = 4-$MeOC_6H_4$)	**3ac**	2	94	10.5:1
4	**1a**	**2d** (Ar = 4-ClC_6H_4)	**3ad**	2	87	3.7:1
5	**1a**	**2e** (Ar = 4-BrC_6H_4)	**3ae**	2	85	3.4:1
6	**1a**	**2f** (Ar = 2-thienyl)	**3af**	2	90	7.9:1
7	**1a**	**2g** (Ar = 1-naphthyl)	**3ag**	2	98	2.9:1
8	**1a**	**2h** (Ar = 4-PhC_6H_4)	**3ah**	2	98	6.7:1
9	**1b** (R^1 = 4-ClC_6H_4)	**2a**	**3ba**	2	95	12.7:1
10	**1c** (R^1 = 4-BrC_6H_4)	**2a**	**3ca**	2	95	18.0:1
11	**1d** (R^1= 4-$MeOC_6H_4$)	**2a**	**3da**	2	97	2.4:1
12	**1e** (R^1 = benzyl)	**2a**	**5a**	2	80	8.3:1
13	**1f** (R^1 = *n*-butyl)	**2a**	**5a**	2	82	8.7:1
14	**1g** (R^1 = Ts)	**2a**	**3ga**	2	56	>20:1

[a]Reactions were carried out using a 0.2 mmol of **1**, 0.2 mmol of **2**, and 0.4 mmol of Cs_2CO_3 in 1 mL of DMSO at room temperature for the given time. [b]Diastereomeric ratios (*cis*:*trans*) determined by ^{1}H NMR of the crude products.

Table 3. Scope of the Cascade Reaction between 1 and 2[a]



1b, 1h-1n 2a-2h 3

entry	substrate 1	substrate 2	product	time (h)	yield (%)	dr[b]
1	**1b** (R^2 = H)	**2a**	**3ba**	2	95	12.7:1
2	**1b**	**2b**	**3bb**	2	98	14.5:1
3	**1b**	**2c**	**3bc**	2	96	12.6:1
4	**1b**	**2d**	**3bd**	2	73	10.6:1
5	**1b**	**2e**	**3be**	2	76	10.3:1
6	**1b**	**2f**	**3bf**	2	86	13.6:1
7	**1b**	**2g**	**3bg**	2	96	6.5:1
8	**1b**	**2h**	**3bh**	2	94	9.4:1
9	**1h** (R^2 = 4-Me)	**2a**	**3ha**	2	93	17.4:1
10	**1i** (R^2 = 4-OMe)	**2a**	**3ia**	2	89	16.7:1
11	**1j** (R^2 = 4-*t*-Bu)	**2a**	**3ja**	2	95	17.0:1
12	**1k** (R^2 = 4-Cl)	**2a**	**3ka**	2	96	15.8:1
13	**1l** (R^2 = 6-Me)	**2a**	**3la**	2	95	0.84:1
14	**1m** (R^2 = 4,6-di-Me)	**2a**	**3ma**	2	97	0.98:1
15[c]	**1n**	**2a**	**3na**	2	96	1.36:1

[a]Reactions were carried out using a 0.2 mmol of **1**, 0.2 mmol of **2**, and 0.4 mmol of Cs_2CO_3 in 1 mL of DMSO at room temperature for the given time. [b]Diastereomeric ratio (*cis*:*trans*) determined by ^{1}H NMR of the crude product. [c]**1n** refers to 2-((4-chlorophenylimino)methyl)naphthalen-1-ol.

In view of this reaction feature, various aprotic polar solvents were mainly assessed (Table 1, entries 10−13). In THF, the consumption of **2a** was sluggish and the yield of **4aa** was elevated to 59% (Table 1, entry 10). Similar result was observed in acetone (Table 1, entry 11). To our delight, this reaction proceeded very well in both DMF and DMSO, providing **3aa** in excellent yields with good dr values. It should be emphasized that only the employment of DMSO as the solvent could avoid the formation of simple oxa-addition product **4aa**. Further experiments clearly demonstrated that the oxa-addition product **4aa** yielded in THF could be completely converted into **3aa** by removing THF and stirring the residue in DMSO at room temperature.[12] Thus, in the perspective of isolation step, we chose DMSO rather than DMF as the optimum solvent to carry out the following reactions.

After systematical optimization of the reaction parameters, the generality of this cascade reaction was then explored. First, the scope of ethyl 2-aroyl-1-chlorocyclopropanecarboxylates **2** was investigated under the optimized reaction conditions (Table 2, entries 1−8). Substrates **2b** and **2c** with electron-

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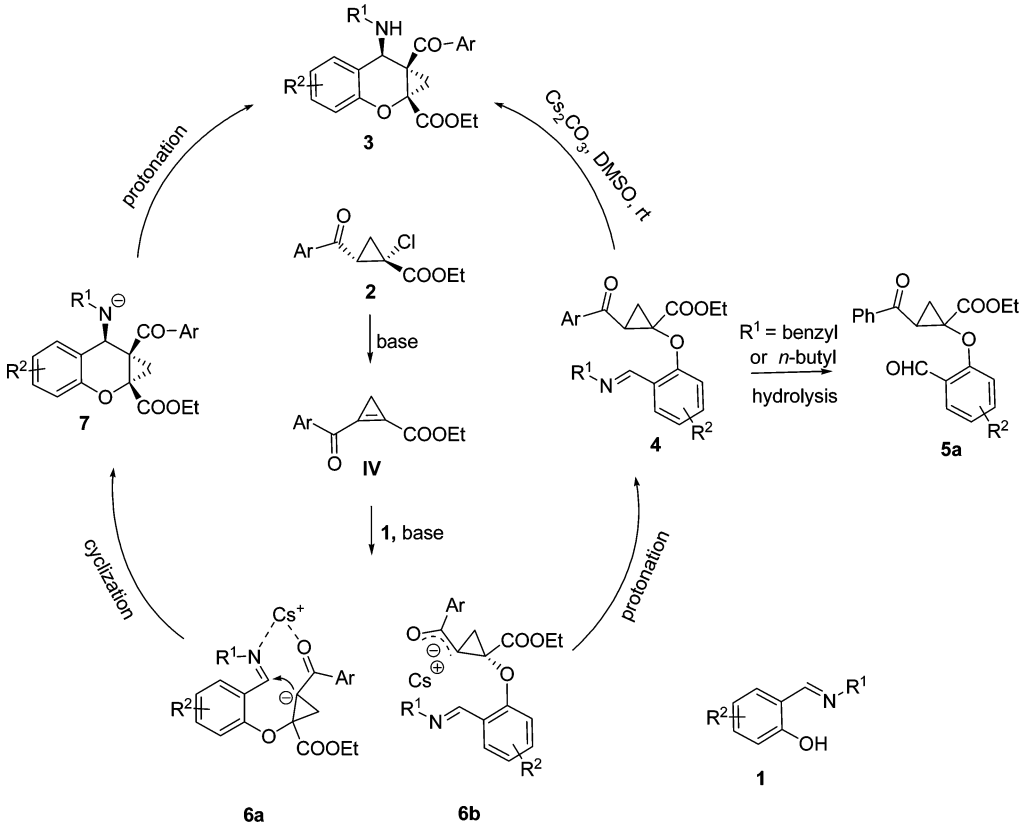
Scheme 4. Proposed Reaction Mechanism for the Cascade Reaction between 1 and 2



donating groups on aromatic ring gave the desired products **3ab** and **3ac** in excellent yields with better diastereoselectivities in comparison with **3aa** (Table 2, entries 2−3). Substrates with electron-withdrawing Cl or Br groups afforded the corresponding products **3ad** or **3ae** uneventfully, but both the yields and the diastereoselectivities declined (Table 2, entries 4−5). Substrates **2f**−**2h** with 2-thienyl, 1-naphthyl or biphenyl groups were also tolerated in this reaction, furnishing high yields of products **3af**−**3ah**, respectively (Table 2, entries 6−8). It is noteworthy that an obvious decline in diastereomeric ratio (2.9:1) appeared in the case of **2g** because of the steric hindrance of bulky 1-naphthyl group.

Next, the role of substituent R^1 on salicylaldimine **1** in the reaction was probed. As shown in Table 2, three kinds of R^1 groups including aryl, alkyl, and *p*-toluenesulfonyl have been investigated for this purpose. In the cases of aryl groups, the electronic property exerted little influence on the product yields but had great effect on the diastereomeric ratios (Table 2, entries 9−11). The dr values observed in the above reactions ranged from 2.4:1 to 18.0:1. Up to 18.0:1 dr value was achieved when R^1 was an electron-withdrawing 4-bromophenyl group (Table 2, entry 10). The lowest dr value 2.4:1 appeared in the case of 4-methoxyphenyl group (Table 2, entry 11). Next, the reactivity of salicylaldimines **1e** and **1f** derived from aliphatic benzylamine and *n*-butylamine was examined. In these cases, a formal substitution product **5a** instead of the desired product **3ea** or **3fa** was obtained in good yields with 8.3:1 and 8.7:1 dr values, respectively (Table 2, entries 12−13), which was yielded via simple oxa-addition of **1e** or **1f** to cyclopropene intermediate IV and subsequent hydrolysis during workup process. Finally, **1g** with a *p*-toluenesulfonyl group was used to assess the effect of strong electron-withdrawing group on the reaction. As expected, the highest dr value (>20:1) was observed in this case (Table 2, entry 14), indicating that the quick intramolecular nucleophilic attack onto C═N bond favored the formation of cis-isomer. The relatively low yield was resulted from a competitive hydrolysis of **1g** in the reaction system. Thus, anhydrous treatment of the reagent and solvent was beneficial to the formation of **3ga**.

Since the substituent R^1 group had a remarkable effect on the diastereoselectivity, the reaction of salicylaldimines **1b** with various ethyl 2-aroy-1-chlorolcyclopropanecarboxylates **2** and the reaction of **1h**−**n** with **2a** were further investigated. The results are summarized in Table 3. In comparison with **1a**, the diastereoselectivities were much higher for **1b**, while the electronic property of Ar groups for **2** had less effect on the diastereoselectivities in these cases (Table 3, entries 1−8). In addition, the effect of R^2 group on salicylaldimines **1** was also estimated. Substituents at para position of phenolic hydroxyl group including Me, MeO, *t*-Bu and Cl were all tolerated in this reaction, and afforded the desired products in excellent yields and dr values despite of their electronic property and bulk (Table 3, entries 9−12). A sharp decline in the diastereoselectivity was observed when a methyl group was introduced into ortho position of phenolic hydroxyl group, although the reaction yield still kept up to 97% (Table 3, entries 13−14). Similar result was obtained for 2-((4-chlorophenylimino)-methyl)naphthalen-1-ol (**1n**) (Table 3, entry 15).

On the basis of these observations, a possible reaction mechanism was proposed as shown in Scheme 4. The reaction was initiated by 1,2-elimination of hydrogen chloride from the substrate **2**, and the formed reactive cyclopropene IV quickly combined with the cesium salt of salicylaldimine **1** via simple oxa-addition. The adduct **6** was then converted into polycyclic

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intermediate **7** through intramolecular nucleophilic attack onto C═N bond, and **7** was next protonated into the final product **3**. On the other hand, **6** could be directly converted into a simple oxa-addition product **4** by abstracting a proton from the reaction system, and the latter was easily hydrolyzed into **5a** when R^1 was alphatic benzyl or *n*-butyl group during workup process. As depicted in structure **6a**, the preferential formation of *cis*-**3** could be rationalized by suggesting the existence of a concerted coordination role of N and O atoms with cesium ion. In fact, the marked increases in diastereomeric ratios of **3** caused by both electron-donating role of Ar group on **2** and electron-withdrawing role of R^1 group on **1** clearly indicated that the intramolecular nucleophilic attack on C═N bond from the concerted coordination state **6a** was much favored relative to the nonconcerted state **6b** in these instances. The sharp decline in diastereoselectivity in the cases of **1l**, **1m**, and **1n** could be ascribed to the large steric hindrance resulted from the introduction of R^2 like Me at 6-site, which disfavored formation of the concerted coordinating state **6a**.

CONCLUSION

We have developed a cascade base-promoted formal nucleophilic substitution and Mannich addition between salicylaldimines and ethyl 2-aroyl-1-chlorocyclopropanecarboxylates. This transformation is based on the reactive cyclopropenes with two electron-withdrawing groups at C═C bond generated via a facile stereoconvergent 1,2-elimination of ethyl 2-aroyl-1-chlorocyclopropanecarboxylates. This reaction is tolerant to the steric hindrance and electronic property of the reactants and can be easily performed under very mild conditions. This method provides an efficient and practical synthesis of conformationally constrained *cis*-tetrahydrocyclopropa[*b*]chromenes.

EXPERIMENTAL SECTION

General Experimental Methods. Reactions were monitored by TLC analysis using silica gel 60 Å F-254 thin layer plates. Flash column chromatography was performed on silica gel 60 Å, 10−40 μm. ^{1}H NMR spectra were recorded at 400 MHz. Chemical shifts are reported in ppm from tetramethylsilane with the solvent resonance as the internal standard ($CDCl_3$, δ = 7.26). Data are reported as follows: chemical shift, multiplicity (s: singlet, d: doublet, t: triplet, q: quartet, m: multiplet, br: broad), coupling constants (Hz) and integration. ^{13}C NMR spectra were recorded at 100 MHz with complete proton decoupling. Chemical shifts are reported in ppm from the tetramethylsilane with the solvent resonance as internal standard ($CDCl_3$, δ = 77.0). IR spectra were recorded on an infrared spectrometer. Melting point was recorded on a melting point detector. HRMS was measured on a TOF-Q mass spectrometer equipped with an ESI source.

Typical Procedure for the Synthesis of *cis*-Tetrahydrocyclopropa[*b*]chromene 3aa. To a solution of **1a** (0.2 mmol) and **2a** (0.2 mmol) in 1 mL of DMSO was added Cs_2CO_3 (0.4 mmol), and the mixture was stirred at room temperature. The reaction was followed by thin layer chromatography until all the substrate **2a** disappeared. The mixture was then washed with water and extracted with CH_2Cl_2 for three times to remove DMSO. Combined extracts were dried over anhydrous Na_2SO_4 and concentrated under reduced pressure. The residue was purified by silica gel column chromatography using petroleum ether/ethyl acetate (5:1) as the eluent to afford 76 mg of compound **3aa** in 92% yield. Unless otherwise specified, all other products **3** were synthesized according to this typical procedure.

(1aS*,7R*,7aR*)-Ethyl 7a-benzoyl-7-(phenylamino)-1,1a,7,7a-tetrahydrocyclopropa[*b*]chromene-1a-carboxylate (3aa). Yellow solid (76 mg, 92% yield): mp 101.9−102.8 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.80−7.78 (m, 2H), 7.53−7.49 (m, 1H), 7.38−7.29 (m, 3H), 7.21 (dt, *J* = 8.2, 4.2 Hz, 2H), 7.09 (dd, *J* = 8.4, 7.4 Hz, 2H), 7.03 (td, *J* = 7.5, 1.2 Hz, 1H), 6.71 (t, *J* = 7.3 Hz, 1H), 6.51 (d, *J* = 7.7 Hz, 2H), 5.14 (s, 1H), 4.17−3.99 (m, 2H), 2.38 (d, *J* = 6.8 Hz, 1H), 2.03 (d, *J* = 6.8 Hz, 1H), 1.13 (t, *J* = 7.1 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 194.2, 168.8, 152.3, 146.1, 136.1, 133.1, 129.4, 129.2, 128.7, 128.5, 126.8, 125.6, 123.3, 118.9, 118.5, 114.5, 64.4, 62.0, 54.8, 43.4, 21.5, 13.8; IR (film) ν 3355, 3065, 3006, 2979, 2946, 2921, 1743, 1672, 1589, 1514, 1487, 1450, 1423, 1399, 1371, 1350, 1334, 1312, 1291, 1250, 1169, 1140, 1091, 1071, 1047, 1009, 961, 922, 852, 817, 761, 746, 724, 700 cm^{-1}; HRMS (ESI) *m*/*z* calcd for $C_{26}H_{23}NO_4Na$ [M + Na]$^+$ 436.1525, found 436.1504.

(1aS*,7R*,7aR*)-Ethyl 7a-(4-methylbenzoyl)-7-(phenylamino)-1,1a,7,7a-tetrahydrocyclopropa[*b*]chromene-1a-carboxylate (3ab). Yellow solid (78 mg, 91% yield): mp 164.4−165.5 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.69 (d, *J* = 8.2 Hz, 2H), 7.33−7.29 (m, 1H), 7.24−7.19 (m, 2H), 7.15 (d, *J* = 8.0 Hz, 2H), 7.11−7.07 (m, 2H), 7.03 (td, *J* = 7.5, 1.2 Hz, 1H), 6.71 (t, *J* = 7.3 Hz, 1H), 6.53 (d, *J* = 7.7 Hz, 2H), 5.12 (s, 1H), 4.16−3.98 (m, 2H), 3.90 (s, 1H), 2.39 (s, 3H), 2.37 (d, *J* = 6.8 Hz, 1H), 2.01 (d, *J* = 6.8 Hz, 1H), 1.12 (t, *J* = 7.1 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 193.6, 168.9, 152.4, 146.3, 144.0, 133.6, 129.3, 129.2, 128.8, 126.7, 125.9, 123.2, 118.8, 118.5, 114.5, 64.4, 62.0, 54.8, 43.5, 21.7, 21.7, 13.8; IR (film) ν 3414, 3041, 2997, 2962, 2853, 1739, 1671, 1605, 1510, 1481, 1453, 1434, 1371, 1355, 1313, 1289, 1233, 1168, 1132, 1098, 1050, 1021, 959, 851, 828, 763, 744, 691 cm^{-1}; HRMS (ESI) *m*/*z* calcd for $C_{27}H_{25}NO_4Na$ [M + Na]$^+$ 450.1682, found 450.1665.

(1aS*,7R*,7aR*)-Ethyl 7a-(4-methoxybenzoyl)-7-(phenylamino)-1,1a,7,7a-tetrahydrocyclopropa[*b*]chromene-1a-carboxylate (3ac). Yellow solid (83 mg, 94% yield): mp 151.1−152.5 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.78 (d, *J* = 8.9 Hz, 2H), 7.33−7.29 (m, 1H), 7.25−7.18 (m, 2H), 7.09 (dd, *J* = 8.5, 7.4 Hz, 2H), 7.02 (td, *J* = 7.5, 1.2 Hz, 1H), 6.82 (d, *J* = 9.0 Hz, 2H), 6.70 (t, *J* = 7.3 Hz, 1H), 6.53 (dd, *J* = 8.5, 0.8 Hz, 2H), 5.11 (s, 1H), 4.15−3.98 (m, 2H), 3.90 (s, 1H), 3.83 (s, 3H), 2.35 (d, *J* = 6.7 Hz, 1H), 2.00 (d, *J* = 6.7 Hz, 1H), 1.12 (t, *J* = 7.1 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 192.4, 168.9, 163.5, 152.4, 146.3, 131.0, 129.3, 129.2, 129.0, 126.8, 125.9, 123.2, 118.7, 114.4, 113.7, 64.4, 61.9, 55.5, 54.8, 43.4, 21.6, 13.8; IR (film) ν 3395, 3099, 3058, 3015, 2962, 2921, 2846, 1746, 1655, 1599, 1506, 1484, 1457, 1426, 1371, 1349, 1310, 1262, 1224, 1180, 1140, 1052, 1024, 985, 919, 853, 804, 762, 745 cm^{-1}; HRMS (ESI) *m*/*z* calcd for $C_{27}H_{25}NO_5Na$ [M + Na]$^+$ 466.1631, found 466.1625.

(1aS*,7R*,7aR*)-Ethyl 7a-(4-chlorobenzoyl)-7-(phenylamino)-1,1a,7,7a-tetrahydrocyclopropa[*b*]chromene-1a-carboxylate (3ad). Yellow solid (78 mg, 87% yield): mp 148.4−149.5 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.71−7.68 (m, 2H), 7.34−7.30 (m, 3H), 7.26−7.19 (m, 2H), 7.12−7.09 (m, 2H), 7.04 (td, *J* = 7.5, 1.2 Hz, 1H), 6.73 (t, *J* = 7.3 Hz, 1H), 6.54 (d, *J* = 7.7 Hz, 2H), 5.10 (s, 1H), 4.16−3.99 (m, 2H), 3.92 (s, 1H), 2.35 (d, *J* = 6.7 Hz, 1H), 2.03 (d, *J* = 6.8 Hz, 1H), 1.14 (t, *J* = 7.1 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 193.3, 168.8, 152.5, 146.1, 139.4, 134.6, 130.0, 129.4, 129.3, 128.7, 126.6, 125.7, 123.4, 119.0, 118.5, 114.4, 64.6, 62.1, 54.8, 43.4, 22.0, 13.9; IR (film) ν 3375, 3054, 2979, 2930, 2898, 1722, 1658, 1595, 1488, 1453, 1396, 1370, 1316, 1272, 1228, 1186, 1137, 1090, 1061, 1013, 967, 914, 882, 858, 838, 793, 766, 753, 728, 693 cm^{-1}; HRMS (ESI) *m*/*z* calcd for $C_{26}H_{22}ClNO_4Na$ [M + Na]$^+$ 470.1135, found 470.1107.

(1aS*,7R*,7aR*)-Ethyl 7a-(4-bromobenzoyl)-7-(phenylamino)-1,1a,7,7a-tetrahydrocyclopropa[*b*]chromene-1a-carboxylate (3ae). Yellow solid (84 mg, 85% yield): mp 157.8−159.5 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.63−7.60 (m, 2H), 7.47−7.45 (m, 2H), 7.34−7.29 (m, 1H), 7.25 (d, *J* = 7.4 Hz, 1H), 7.20 (dd, *J* = 8.1, 1.0 Hz, 1H), 7.13−7.09 (m, 2H), 7.04 (td, *J* = 7.5, 1.1 Hz, 1H), 6.74 (t, *J* = 7.3 Hz, 1H), 6.54 (d, *J* = 7.9 Hz, 2H), 5.09 (s, 1H), 4.15−3.99 (m, 2H), 3.94 (s, 1H), 2.35 (d, *J* = 6.7 Hz, 1H), 2.03 (d, *J* = 6.8 Hz, 1H), 1.14 (t, *J* = 7.1 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 193.6, 168.8, 152.5, 146.1, 135.0, 131.7, 130.1, 129.4, 129.3, 128.2, 126.5, 125.7, 123.4, 119.0, 118.5, 114.4, 64.6, 62.1, 54.8, 43.4, 22.1, 13.9; IR (film) ν 3410, 3089, 3057, 3019, 2983, 2903, 2869, 1743, 1670, 1590, 1491, 1457, 1430, 1397, 1372, 1345, 1309, 1292, 1243, 1191, 1178, 1138, 1096,

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1071, 1056, 1016, 986, 912, 885, 862, 754, 692 cm^{-1}; HRMS (ESI) *m/z* calcd for $C_{26}H_{22}BrNO_4Na$ $[M + Na]^+$ 514.0630, found 514.0638.

(1aS*,7R*,7aR*)-Ethyl 7-(phenylamino)-7a-(thiophene-2-carbonyl)-1,1a,7,7a-tetrahydrocyclopropa[*b*]chromene-1a-carboxylate (3af). Yellow solid (75 mg, 90% yield): mp 134.5−135.8 °C; ^1H NMR (400 MHz, $CDCl_3$) δ 7.57 (dd, *J* = 4.9, 1.0 Hz, 1H), 7.38 (d, *J* = 3.4 Hz, 1H), 7.35−7.28 (m, 2H), 7.22 (dd, *J* = 8.1, 0.9 Hz, 1H), 7.13−7.09 (m, 2H), 7.06 (td, *J* = 7.5, 1.1 Hz, 1H), 6.97 (dd, *J* = 4.9, 3.9 Hz, 1H), 6.72 (t, *J* = 7.3 Hz, 1H), 6.59 (d, *J* = 7.7 Hz, 2H), 5.10 (s, 1H), 4.13−3.97 (m, 2H), 3.97 (s, 1H), 2.45 (d, *J* = 6.7 Hz, 1H), 2.00 (d, *J* = 6.7 Hz, 1H), 1.10 (t, *J* = 7.1 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 186.2, 168.7, 152.7, 146.2, 143.1, 134.2, 132.7, 129.4, 129.2, 128.0, 126.6, 125.9, 123.4, 118.8, 118.6, 114.3, 64.3, 62.0, 54.7, 44.5, 21.9, 13.7; IR (film) ν 3363, 3080, 3025, 2999, 2981, 2954, 2920, 1742, 1648, 1598, 1499, 1457, 1411, 1373, 1341, 1293, 1244, 1192, 1120, 1095, 1058, 1012, 973, 924, 863, 799, 769, 749, 733, 691 cm^{-1}; HRMS (ESI) *m/z* calcd for $C_{24}H_{21}NO_4SNa$ $[M + Na]^+$ 442.1089, found 442.1099.

(1aS*,7R*,7aR*)-Ethyl 7a-(1-naphthoyl)-7-(phenylamino)-1,1a,7,7a-tetrahydrocyclopropa[*b*]chromene-1a-carboxylate (3ag). Yellow solid (91 mg, 98% yield): mp 144.0−145.8 °C; ^1H NMR (400 MHz, $CDCl_3$) δ 8.43−8.41 (m, 1H), 7.95 (d, *J* = 8.2 Hz, 1H), 7.85−7.83 (m, 1H), 7.78 (dd, *J* = 7.2, 0.9 Hz, 1H), 7.52−7.46 (m, 2H), 7.35−7.21 (m, 4H), 7.09−7.02 (m, 3H), 6.72 (t, *J* = 7.3 Hz, 1H), 6.48 (d, *J* = 7.8 Hz, 2H), 5.03 (s, 1H), 4.28−4.01 (m, 3H), 2.55 (d, *J* = 6.7 Hz, 1H), 2.16 (d, *J* = 6.8 Hz, 1H), 1.15 (t, *J* = 7.1 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 197.5, 169.0, 153.5, 146.2, 134.1, 133.8, 133.1, 130.6, 129.2, 128.9, 128.8, 128.2, 127.9, 127.7, 126.5, 126.2, 125.7, 123.8, 123.4, 119.0, 118.4, 114.7, 66.3, 62.2, 55.5, 45.9, 24.0, 13.9; IR (film) ν 3367, 3091, 3053, 3000, 2965, 2921, 2897, 2871, 1725, 1657, 1600, 1507, 1482, 1453, 1439, 1374, 1350, 1326, 1309, 1263, 1223, 1172, 1145, 1111, 1090, 1065, 1051, 1023, 946, 915, 875, 805, 779, 751, 730, 695 cm^{-1}; HRMS (ESI) *m/z* calcd for $C_{30}H_{25}NO_4Na$ $[M + Na]^+$ 486.1682, found 486.1678.

(1aS*,7R*,7aR*)-Ethyl 7a-(biphenylcarbonyl)-7-(phenylamino)-1,1a,7,7a-tetrahydrocyclopropa[*b*]chromene-1a-carboxylate (3ah). Yellow solid (96 mg, 98% yield): mp 146.5−146.6 °C; ^1H NMR (400 MHz, $CDCl_3$) δ 7.88 (d, *J* = 8.3 Hz, 2H), 7.64−7.59 (m, 4H), 7.52−7.48 (m, 2H), 7.45−7.41 (m, 1H), 7.37−7.33 (m, 1H), 7.30−7.24 (m, 2H), 7.12 (t, *J* = 7.9 Hz, 2H), 7.06 (td, *J* = 7.5, 1.1 Hz, 1H), 6.74 (t, *J* = 7.3 Hz, 1H), 6.58 (d, *J* = 8.0 Hz, 2H), 5.18 (s, 1H), 4.20−4.03 (m, 2H), 3.99 (s, 1H), 2.44 (d, *J* = 6.7 Hz, 1H), 2.08 (d, *J* = 6.7 Hz, 1H), 1.16 (t, *J* = 7.1 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 193.7, 168.9, 152.5, 146.2, 145.7, 139.7, 134.9, 129.4, 129.3, 129.3, 129.0, 128.4, 127.3, 127.1, 126.7, 125.8, 123.3, 118.9, 118.5, 114.5, 64.6, 62.1, 54.9, 43.6, 21.9, 13.9; IR (film) ν 3388, 3054, 3032, 2983, 2932, 2906, 2871, 1735, 1674, 1600, 1500, 1454, 1401, 1372, 1311, 1287, 1243, 1180, 1136, 1095, 1058, 1014, 968, 912, 857, 755, 695 cm^{-1}; HRMS (ESI) *m/z* calcd for $C_{32}H_{27}NO_4Na$ $[M + Na]^+$ 512.1838, found 512.1842.

(1aS*,7R*,7aR*)-Ethyl 7a-benzoyl-7-(4-chlorophenylamino)-1,1a,7,7a-tetrahydrocyclopropa[*b*]chromene-1a-carboxylate (3ba). Yellow solid (85 mg, 95% yield): mp 138.2−139.1 °C; ^1H NMR (400 MHz, $CDCl_3$) δ 7.79 (dd, *J* = 8.2, 1.1 Hz, 2H), 7.54−7.51 (m, 1H), 7.37 (t, *J* = 7.8 Hz, 2H), 7.33−7.28 (m, 1H), 7.18−7.16 (m, 2H), 7.03−6.99 (m, 3H), 6.40 (d, *J* = 8.8 Hz, 2H), 5.10 (s, 1H), 4.17−3.99 (m, 2H), 3.93 (s, 1H), 2.35 (d, *J* = 6.8 Hz, 1H), 2.01 (d, *J* = 6.8 Hz, 1H), 1.12 (t, *J* = 7.1 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 193.3, 168.7, 151.9, 144.7, 135.9, 133.3, 129.6, 129.0, 128.7, 128.6, 126.9, 124.8, 123.4, 123.3, 118.6, 115.6, 64.2, 62.1, 54.9, 43.0, 20.9, 13.8; IR (film) ν 3354, 3067, 3029, 3003, 2979, 2950, 1743, 1673, 1592, 1514, 1489, 1450, 1423, 1404, 1370, 1351, 1333, 1312, 1290, 1250, 1169, 1140, 1083, 1046, 1010, 961, 923, 853, 819, 760, 748, 701 cm^{-1}; HRMS (ESI) *m/z* calcd for $C_{26}H_{22}ClNO_4Na$ $[M + Na]^+$ 470.1135, found 470.1139.

(1aS*,7R*,7aR*)-Ethyl 7-(4-chlorophenylamino)-7a-(4-methylbenzoyl)-1,1a,7,7a-tetrahydrocyclopropa[*b*]chromene-1a-carboxylate (3bb). Yellow solid (90 mg, 98% yield): mp 144.8−146.5 °C; ^1H NMR (400 MHz, $CDCl_3$) δ 7.69 (d, *J* = 8.2 Hz, 2H), 7.30 (td, *J* = 8.0, 1.6 Hz, 1H), 7.17 (t, *J* = 7.4 Hz, 4H), 7.03−6.98 (m, 3H), 6.43−6.40 (m, 2H), 5.07 (s, 1H), 4.06 (ddq, *J* = 38.8, 10.8, 7.1 Hz, 2H), 3.94 (s, 1H), 2.38 (s, 3H), 2.33 (d, *J* = 6.8 Hz, 1H), 1.99 (d, *J* = 6.8 Hz, 1H), 1.11 (t, *J* = 7.1 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 193.4, 168.7, 152.0, 144.8, 144.2, 133.3, 129.5, 129.3, 129.0, 128.8, 126.9, 125.0, 123.3, 123.3, 118.6, 115.5, 64.2, 62.0, 54.9, 43.2, 21.7, 21.1, 13.8; IR (film) ν 3386, 3034, 2981, 2963, 2925, 2871, 1735, 1673, 1601, 1495, 1455, 1403, 1373, 1314, 1289, 1242, 1178, 1136, 1091, 1061, 1018, 970, 911, 859, 818, 761, 732 cm^{-1}; HRMS (ESI) *m/z* calcd for $C_{27}H_{24}ClNO_4Na$ $[M + Na]^+$ 484.1292, found 484.1286.

(1aS*,7R*,7aR*)-Ethyl 7-(4-chlorophenylamino)-7a-(4-methoxybenzoyl)-1,1a,7,7a-tetrahydrocyclopropa[*b*]chromene-1a-carboxylate (3bc). Yellow solid (92 mg, 96% yield): mp 147.5−148.9 °C; ^1H NMR (400 MHz, $CDCl_3$) δ 7.77 (d, *J* = 8.9 Hz, 2H), 7.32−7.28 (m, 1H), 7.18−7.16 (m, 2H), 7.03−6.98 (m, 3H), 6.82 (d, *J* = 9.0 Hz, 2H), 6.43−6.41 (m, 2H), 5.06 (d, *J* = 7.0 Hz, 1H), 4.14−3.98 (m, 2H), 3.95 (d, *J* = 8.2 Hz, 1H), 3.83 (s, 3H), 2.32 (d, *J* = 6.8 Hz, 1H), 1.98 (d, *J* = 6.8 Hz, 1H), 1.11 (t, *J* = 7.1 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 192.2, 168.7, 163.6, 152.1, 144.9, 131.0, 129.5, 129.0, 128.8, 126.9, 125.1, 123.3, 123.2, 118.6, 115.5, 113.8, 64.2, 62.0, 55.5, 54.9, 43.1, 21.1, 13.8; IR (film) ν 3408, 3064, 3039, 3983, 2958, 2900, 2843, 1743, 1657, 1602, 1507, 1455, 1420, 1354, 1317, 1250, 1170, 1132, 1092, 1021, 959, 936, 914, 845, 818, 794, 964, 736, 698 cm^{-1}; HRMS (ESI) *m/z* calcd for $C_{27}H_{24}ClNO_5Na$ $[M + Na]^+$ 500.1241, found 500.1235.

(1aS*,7R*,7aR*)-Ethyl 7a-(4-chlorobenzoyl)-7-(4-chlorophenylamino)-1,1a,7,7a-tetrahydrocyclopropa[*b*]chromene-1a-carboxylate (3bd). Yellow solid (70 mg, 73% yield): mp 129.8−131.2 °C; ^1H NMR (400 MHz, $CDCl_3$) δ 7.72−7.68 (m, 2H), 7.32−7.28 (m, 3H), 7.17 (t, *J* = 7.9 Hz, 2H), 7.04−7.00 (m, 3H), 6.45−6.42 (m, 2H), 5.05 (s, 1H), 4.15−3.98 (m, 3H), 2.32 (d, *J* = 6.8 Hz, 1H), 2.01 (d, *J* = 6.8 Hz, 1H), 1.12 (t, *J* = 7.1 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 193.1, 168.6, 152.1, 144.6, 140.0, 130.0, 129.6, 129.1, 128.8, 126.8, 124.9, 123.6, 123.4, 118.6, 115.5, 64.4, 62.2, 54.8, 43.0, 21.4, 13.9; IR (film) ν 3378, 3070, 3038, 2983, 2927, 2872, 1735, 1674, 1591, 1494, 1457, 1423, 1400, 1373, 1314, 1288, 1240, 1182, 1138, 1091, 1062, 1014, 970, 910, 857, 840, 819, 761, 731 cm^{-1}; HRMS (ESI) *m/z* calcd for $C_{26}H_{21}Cl_2NO_4Na$ $[M + Na]^+$ 504.0746, found 504.0751.

(1aS*,7R*,7aR*)-Ethyl 7a-(4-bromobenzoyl)-7-(4-chlorophenylamino)-1,1a,7,7a-tetrahydrocyclopropa[*b*]chromene-1a-carboxylate (3be). Yellow solid (80 mg, 76% yield): mp 136.6−138.5 °C; ^1H NMR (400 MHz, $CDCl_3$) δ 7.63−7.60 (m, 2H), 7.48−7.45 (m, 2H), 7.32−7.28 (m, 1H), 7.19−7.15 (m, 2H), 7.04−7.00 (m, 3H), 6.46−6.42 (m, 2H), 5.04 (s, 1H), 4.12−3.97 (m, 3H), 2.31 (d, *J* = 6.8 Hz, 1H), 2.00 (d, *J* = 6.8 Hz, 1H), 1.12 (t, *J* = 7.1 Hz, 3H); ^{13}C NMR (400 MHz, $CDCl_3$) δ 193.3, 168.6, 152.1, 144.6, 134.8, 131.8, 130.1, 129.6, 129.1, 128.4, 126.7, 124.9, 123.6, 123.4, 118.6, 115.5, 64.4, 62.2, 54.8, 43.0, 21.4, 13.9; IR (film) ν 3377, 3069, 3036, 2983, 2927, 2872, 2855, 1734, 1675, 1588, 1494, 1457, 1423, 1398, 1373, 1314, 1288, 1239, 1181, 1138, 1091, 1069, 1012, 968, 910, 858, 819, 760, 732 cm^{-1}; HRMS (ESI) *m/z* calcd for $C_{26}H_{21}BrClNO_4Na$ $[M + Na]^+$ 548.0240, found 548.0248.

(1aS*,7R*,7aR*)-Ethyl 7-(4-chlorophenylamino)-7a-(thiophene-2-carbonyl)-1,1a,7,7a-tetrahydrocyclopropa[*b*]-chromene-1a-carboxylate (3bf). Yellow solid (78 mg, 86% yield): mp 128.6−130.0 °C; ^1H NMR (400 MHz, $CDCl_3$) δ 7.59−7.58 (m, 1H), 7.40 (d, *J* = 3.6 Hz, 1H), 7.34−7.30 (m, 1H), 7.21 (dd, *J* = 19.8, 7.7 Hz, 2H), 7.06−7.01 (m, 3H), 6.99−6.97 (m, 1H), 6.51−6.48 (m, 2H), 5.06 (s, 1H), 4.12−3.97 (m, 3H), 2.41 (d, *J* = 6.8 Hz, 1H), 1.98 (d, *J* = 6.8 Hz, 1H), 1.09 (t, *J* = 7.1 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 186.1, 168.5, 152.4, 144.8, 142.9, 134.5, 132.8, 129.6, 129.0, 128.1, 126.7, 125.2, 123.4, 123.3, 118.6, 115.4, 64.2, 62.1, 54.8, 44.2, 21.5, 13.8; IR (film) ν 3377, 3092, 3062, 2982, 2922, 2851, 1746, 1632, 1596, 1516, 1487, 1455, 1412, 1375, 1353, 1315, 1263, 1240, 1173, 1086, 1051, 1021, 951, 924, 902, 864, 852, 809, 762, 720, 668 cm^{-1}; HRMS (ESI) *m/z* calcd for $C_{24}H_{20}ClNO_4SNa$ $[M + Na]^+$ 476.0700, found 476.0688.

(1aS*,7R*,7aR*)-Ethyl 7a-(1-naphthoyl)-7-(4-chlorophenylamino)-1,1a,7,7a-tetrahydrocyclopropa[*b*]chromene-1a-carboxylate (3bg). Yellow solid (96 mg, 96% yield): mp 120.8−122.2 °C; ^1H NMR (400 MHz, $CDCl_3$) δ 8.39 (dd, *J* = 6.9, 2.3 Hz, 1H), 7.97 (d, *J* = 8.2 Hz, 1H), 7.85−7.79 (m, 2H), 7.52−7.45 (m, 2H),

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7.37−7.30 (m, 2H), 7.22−7.20 (m, 1H), 7.12 (d, J = 7.0 Hz, 1H), 7.02 (td, J = 7.5, 1.1 Hz, 1H), 6.97−6.95 (m, 2H), 6.32 (d, J = 8.8 Hz, 2H), 4.99 (d, J = 5.4 Hz, 1H), 4.30−4.03 (m, 3H), 2.53 (d, J = 6.8 Hz, 1H), 2.13 (d, J = 6.8 Hz, 1H), 1.16 (t, J = 7.1 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 197.2, 168.8, 152.9, 144.7, 134.1, 133.6, 133.2, 130.6, 129.2, 129.0, 128.5, 128.3, 128.0, 126.6, 126.6, 126.0, 123.7, 123.5, 123.4, 118.5, 115.7, 66.0, 62.3, 55.5, 45.5, 23.1, 13.9; IR (film) ν 3407, 3049, 2980, 2960, 2924, 1722, 1658, 1596, 1498, 1456, 1400, 1372, 1315, 1290, 1268, 1232, 1205, 1178, 1141, 1093, 1061, 1018, 947, 908, 862, 811, 782, 761, 731 cm^{-1}; HRMS (ESI) m/z calcd for $C_{30}H_{24}ClNO_4Na$ [M + Na]$^+$ 520.1292, found 520.1287.

(1aS*,7R*,7aR*)-Ethyl 7a-(biphenylcarbonyl)-7-(4-chlorophenylamino)-1,1a,7,7a-tetrahydrocyclopropa[*b*]chromene-1a-carboxylate (3bh). Yellow solid (98 mg, 94% yield): mp 182.8−183.4 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.86 (d, J = 8.5 Hz, 2H), 7.64−7.59 (m, 4H), 7.51−7.47 (m, 2H), 7.45−7.41 (m, 1H), 7.36−7.31 (m, 1H), 7.23−7.20 (m, 2H), 7.07−7.01 (m, 3H), 6.46 (d, J = 8.9 Hz, 2H), 5.12 (s, 1H), 4.19−4.02 (m, 3H), 2.40 (d, J = 6.8 Hz, 1H), 2.04 (d, J = 6.8 Hz, 1H), 1.15 (t, J = 7.1 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 193.5, 168.7, 152.1, 145.9, 144.7, 139.6, 134.6, 129.6, 129.3, 129.1, 129.0, 128.4, 127.2, 127.1, 126.9, 125.0, 123.5, 123.3, 118.6, 115.6, 64.3, 62.1, 55.0, 43.2, 21.3, 13.9; IR (film) ν 3391, 3063, 3035, 2991, 2969, 2923, 2852, 1725, 1669, 1602, 1500, 1452, 1404, 1372, 1321, 1295, 1269, 1239, 1176, 1132, 1110, 1091, 1068, 1021, 961, 915, 859, 844, 822, 798, 777, 756, 696 cm^{-1}; HRMS (ESI) m/z calcd for $C_{32}H_{26}ClNO_4Na$ [M + Na]$^+$ 546.1448, found 546.1456.

(1aS*,7R*,7aR*)-Ethyl 7a-benzoyl-7-(4-bromophenylamino)-1,1a,7,7a-tetrahydrocyclopropa[*b*]chromene-1a-carboxylate (3ca). Yellow solid (93 mg, 95% yield): mp 137.6−138.2 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.79 (d, J = 7.3 Hz, 2H), 7.53 (t, J = 7.4 Hz, 1H), 7.46−7.23 (m, 3H), 7.15 (dd, J = 14.0, 8.5 Hz, 4H), 7.02 (t, J = 7.5 Hz, 1H), 6.36 (d, J = 8.8 Hz, 2H), 5.10 (s, 1H), 4.08 (ddq, J = 39.1, 10.8, 7.1 Hz, 2H), 2.34 (d, J = 6.8 Hz, 1H), 2.01 (d, J = 6.8 Hz, 1H), 1.12 (t, J = 7.1 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 193.9, 168.7, 151.9, 145.1, 135.9, 133.3, 131.9, 129.7, 128.7, 128.6, 127.0, 124.7, 123.3, 118.6, 110.6, 64.2, 62.1, 54.8, 43.0, 20.9, 13.8; IR (film) ν 3413, 3091, 3055, 2995, 2968, 2925, 1743, 1675, 1601, 1508, 1482, 1451, 1433, 1393, 1370, 1355, 1311, 1287, 1231, 1170, 1133, 1097, 1049, 1016, 959, 933, 853, 819, 796, 765, 745, 690 cm^{-1}; HRMS (ESI) m/z calcd for $C_{26}H_{22}BrNO_4Na$ [M + Na]$^+$ 514.0630, found 514.0618.

(1aS*,7R*,7aR*)-Ethyl 7a-benzoyl-7-(4-methoxyphenylamino)-1,1a,7,7a-tetrahydrocyclopropa[*b*]chromene-1a-carboxylate (3da). Yellow solid (86 mg, 97% yield): mp 125.8−127.3 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.81 (d, J = 7.4 Hz, 2H), 7.52 (t, J = 7.4 Hz, 1H), 7.37 (t, J = 7.7 Hz, 2H), 7.29 (dd, J = 11.3, 4.1 Hz, 1H), 7.14 (dd, J = 22.4, 7.8 Hz, 2H), 6.98 (t, J = 7.4 Hz, 1H), 6.65 (d, J = 8.9 Hz, 2H), 6.40 (d, J = 8.8 Hz, 2H), 5.02 (s, 1H), 4.09 (dddd, J = 25.0, 10.7, 7.2, 3.6 Hz, 2H), 3.69 (s, 3H), 2.34 (d, J = 6.7 Hz, 1H), 2.01 (d, J = 6.8 Hz, 1H), 1.14 (t, J = 7.1 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 194.3, 168.8, 153.2, 151.9, 140.1, 136.1, 133.0, 129.3, 128.7, 128.5, 127.0, 125.4, 123.1, 118.4, 116.8, 114.7, 64.4, 62.0, 56.6, 55.6, 43.4, 21.0, 13.8; IR (film) ν 3422, 3064, 3007, 2980, 2955, 2901, 2831, 1738, 1679, 1594, 1513, 1480, 1454, 1413, 1350, 1310, 1283, 1233, 1175, 1130, 1095, 1061, 1026, 962, 933, 911, 874, 846, 819, 798, 769, 747, 693 cm^{-1}; HRMS (ESI) m/z calcd for $C_{27}H_{25}NO_5Na$ [M + Na]$^+$ 466.1631, found 466.1622.

Ethyl 2-benzoyl-1-(2-formylphenoxy)-cyclopropanecarboxylate (5a). Colorless liquid (54 mg, 80% yield): ^{1}H NMR (400 MHz, $CDCl_3$) δ 10.08 (s, 1H), 7.99 (d, J = 7.5 Hz, 2H), 7.79 (dd, J = 7.7, 1.6 Hz, 1H), 7.61 (t, J = 7.3 Hz, 1H), 7.50 (t, J = 7.7 Hz, 2H), 7.43−7.36 (m, 1H), 7.03 (t, J = 7.5 Hz, 1H), 6.92 (d, J = 8.4 Hz, 1H), 4.39−4.27 (m, 2H), 3.71 (dd, J = 9.1, 7.6 Hz, 1H), 2.33 (dd, J = 7.6, 5.7 Hz, 1H), 2.12 (dd, J = 9.1, 5.6 Hz, 1H), 1.26 (t, J = 7.1 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 191.2, 189.2, 169.7, 159.5, 137.3, 135.0, 133.6, 128.8, 128.6, 128.3, 128.1, 125.4, 122.0, 114.3, 63.8, 62.6, 33.4, 19.9, 14.1; HRMS (ESI) m/z calcd for $C_{20}H_{18}O_5Na$ [M + Na]$^+$ 361.1052, found 361.1048.

(1aS*,7R*,7aR*)-Ethyl 7a-benzoyl-7-(4-methylphenylsulfonamido)-1,1a,7,7a-tetrahydrocyclopropa[*b*]chromene-1a-carboxylate (3ga). White solid (55 mg, 56% yield): mp 97.5−98.3 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.71 (d, J = 7.4 Hz, 2H), 7.53 (t, J = 7.4 Hz, 1H), 7.44 (d, J = 8.2 Hz, 2H), 7.35 (t, J = 7.8 Hz, 2H), 7.25 (t, J = 8.3 Hz, 2H), 7.00 (d, J = 7.9 Hz, 1H), 6.97 (t, J = 7.5 Hz, 1H), 6.94 (d, J = 8.1 Hz, 1H), 5.46 (d, J = 8.3 Hz, 1H), 5.18 (d, J = 8.3 Hz, 1H), 4.17−4.05 (m, 2H), 2.24 (s, 3H), 2.02 (d, J = 7.3 Hz, 1H), 1.98 (d, J = 7.4 Hz, 1H), 1.15 (t, J = 7.1 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 193.5, 168.1, 150.8, 143.1, 137.2, 134.4, 133.5, 130.3, 129.3, 129.0, 128.4, 126.9, 123.5, 122.7, 118.4, 63.7, 62.2, 53.5, 42.1, 21.4, 18.8, 13.9; IR (film) ν 3270, 3063, 2982, 2927, 1735, 1674, 1594, 1487, 1453, 1424, 1374, 1339, 1245, 1226, 1189, 1160, 1091, 1054, 1022, 994, 972, 915, 862, 756, 729; HRMS (ESI) m/z calcd for $C_{27}H_{25}NO_6SNa$ [M + Na]$^+$ 514.1301, found 514.1296.

(1aS*,7R*,7aR*)-Ethyl 7a-benzoyl-7-(4-chlorophenylamino)-5-methyl-1,1a,7,7a-tetrahydrocyclopropa[*b*]chromene-1a-carboxylate (3ha). Yellow liquid (86 mg, 93% yield): ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.79 (d, J = 7.8 Hz, 2H), 7.52 (t, J = 7.3 Hz, 1H), 7.36 (t, J = 7.7 Hz, 1H), 7.12−6.98 (m, 5H), 6.40 (d, J = 8.7 Hz, 2H), 5.06 (s, 1H), 4.07 (ddq, J = 41.0, 10.8, 7.1 Hz, 2H), 3.93 (s, 1H), 2.32 (d, J = 6.8 Hz, 1H), 2.27 (s, 3H), 1.99 (d, J = 6.8 Hz, 1H), 1.12 (t, J = 7.1 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 194.1, 168.7, 149.7, 144.7, 135.9, 133.2, 132.8, 130.1, 129.0, 128.7, 128.5, 127.3, 124.5, 123.3, 118.3, 115.4, 64.3, 62.0, 54.8, 43.1, 21.0, 20.8, 13.8; IR (neat) ν 3383, 3059, 3030, 2983, 2926, 2865, 1735, 1676, 1596, 1497, 1449, 1421, 1400, 1373, 1316, 1289, 1240, 1183, 1137, 1092, 1064, 1018, 973, 949, 912, 818, 754, 732, 698 cm^{-1}; HRMS (ESI) m/z calcd for $C_{27}H_{24}ClNO_4Na$ [M + Na]$^+$ 484.1292, found 484.1285.

(1aS*,7R*,7aR*)-Ethyl 7a-benzoyl-7-(4-chlorophenylamino)-5-methoxy-1,1a,7,7a-tetrahydrocyclopropa[*b*]chromene-1a-carboxylate (3ia). Yellow solid (85 mg, 89% yield): mp 155.6−156.8 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.75 (d, J = 7.4 Hz, 2H), 7.51 (t, J = 7.4 Hz, 1H), 7.35 (t, J = 7.7 Hz, 2H), 7.11 (d, J = 8.8 Hz, 1H), 7.01 (d, J = 8.7 Hz, 2H), 6.84 (dd, J = 8.8, 2.9 Hz, 1H), 6.72 (d, J = 2.9 Hz, 1H), 6.43 (d, J = 8.8 Hz, 2H), 5.01 (s, 1H), 4.05 (ddq, J = 38.3, 10.8, 7.1 Hz, 2H), 3.93 (s, 1H), 3.71 (s, 3H), 2.34 (d, J = 6.8 Hz, 1H), 2.00 (d, J = 6.8 Hz, 1H), 1.10 (t, J = 7.1 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 194.1, 168.8, 155.4, 146.1, 144.7, 136.0, 133.2, 129.1, 128.6, 128.5, 126.2, 123.5, 119.2, 115.6, 114.5, 111.9, 64.6, 62.0, 55.7, 55.2, 43.1, 21.7, 13.8; IR (film) ν 3400, 3068, 2988, 2958, 2900, 2876, 2830, 1735, 1661, 1594, 1500, 1452, 1430, 1400, 1353, 1320, 1301, 1280, 1256, 1208, 1179, 1136, 1106, 1086, 1067, 1047, 1017, 967, 933, 886, 857, 812, 754, 699, 673 cm^{-1}; HRMS (ESI) m/z calcd for $C_{27}H_{24}ClNO_5Na$ [M + Na]$^+$ 500.1241, found 500.1255.

(1aS*,7R*,7aR*)-Ethyl 7a-benzoyl-5-*tert*-butyl-7-(4-chlorophenylamino)-1,1a,7,7a-tetrahydrocyclopropa[*b*]chromene-1a-carboxylate (3ja). Yellow solid (96 mg, 95% yield): mp 164.2−166.8 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.81 (d, J = 7.3 Hz, 2H), 7.53 (t, J = 7.4 Hz, 1H), 7.38 (t, J = 7.7 Hz, 2H), 7.32 (dd, J = 8.6, 2.3 Hz, 1H), 7.10−7.08 (m, 2H), 7.01 (d, J = 8.8 Hz, 2H), 6.41 (d, J = 8.8 Hz, 2H), 5.10 (s, 1H), 4.18−4.00 (m, 2H), 3.87 (s, 1H), 2.32 (d, J = 6.8 Hz, 1H), 2.02 (d, J = 6.8 Hz, 1H), 1.23 (s, 9H), 1.13 (t, J = 7.1 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 194.0, 168.7, 149.2, 146.1, 144.8, 135.9, 133.2, 128.9, 128.7, 128.5, 126.5, 123.9, 123.6, 123.5, 117.9, 116.1, 64.2, 62.0, 55.5, 42.9, 34.3, 31.4, 20.5, 13.8; IR (film) ν 3367, 3164, 3086, 3067, 2961, 2931, 2866, 1727, 1663, 1597, 1516, 1496, 1451, 1412, 1377, 1325, 1295, 1325, 1295, 1256, 1233, 1189, 1134, 1081, 1025, 956, 863, 818, 753, 705, 676 cm^{-1}; HRMS (ESI) m/z calcd for $C_{30}H_{30}ClNO_4Na$ [M + Na]$^+$ 526.1761, found 526.1769.

(1aS*,7R*,7aR*)-Ethyl 7a-benzoyl-5-chloro-7-(4-chlorophenylamino)-1,1a,7,7a-tetrahydrocyclopropa[*b*]chromene-1a-carboxylate (3ka). Yellow solid (93 mg, 96% yield): mp 132.7−134.1 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.73 (d, J = 7.6 Hz, 2H), 7.52 (t, J = 7.3 Hz, 1H), 7.35 (t, J = 7.7 Hz, 2H), 7.28−7.22 (m, 2H), 7.12 (d, J = 8.6 Hz, 1H), 7.03 (d, J = 8.7 Hz, 2H), 6.43 (d, J = 8.7 Hz, 2H), 5.00 (s, 1H), 4.06 (ddq, J = 35.0, 10.8, 7.2 Hz, 2H), 3.96 (s, 1H), 2.39 (d, J = 6.9 Hz, 1H), 2.01 (d, J = 6.9 Hz, 1H), 1.11 (t, J = 7.1 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 193.9, 168.4, 151.2, 144.3, 135.8, 133.4, 129.4, 129.2, 128.6, 128.3, 127.2, 126.5, 123.8, 119.9, 115.5, 64.7, 62.2, 54.6, 42.9, 22.1, 13.8; IR (film) ν 3373, 3062, 3032, 2984, 2932, 2872, 1735, 1674, 1597, 1492, 1449, 1407, 1373, 1324, 1276, 1245, 1191, 1137, 1093, 1016, 970, 910, 861, 819, 752, 734, 691 cm^{-1}; HRMS (ESI) m/z calcd for $C_{26}H_{21}Cl_2NO_4Na$ [M + Na]$^+$ 504.0746, found 504.0752.

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(1aS*,7R*,7aR*)-Ethyl 7a-benzoyl-7-(4-chlorophenylamino)-3-methyl-1,1a,7,7a-tetrahydrocyclopropa[*b*]chromene-1a-carboxylate (3la). Yellow solid (88 mg, 95% yield): mp 125.3−127.1 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.69 (d, J = 7.4 Hz, 2H), 7.50 (t, J = 7.4 Hz, 1H), 7.33 (t, J = 7.7 Hz, 2H), 7.20 (d, J = 7.1 Hz, 1H), 7.06−7.04 (m, 3H), 6.96 (t, J = 7.5 Hz, 1H), 6.46 (d, J = 8.8 Hz, 2H), 4.91 (s, 1H), 4.10−3.95 (m, 2H), 3.91 (s, 1H), 2.48 (s, 3H), 2.44 (d, J = 6.6 Hz, 1H), 1.99 (d, J = 6.6 Hz, 1H), 1.10 (t, J = 7.1 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 194.2, 168.9, 151.3, 144.8, 136.3, 133.1, 130.7, 129.1, 128.6, 128.5, 128.0, 125.9, 123.4, 123.2, 122.7, 115.4, 64.7, 62.0, 55.2, 43.8, 23.3, 15.6, 13.8; IR (film) ν 3374, 3069, 2966, 2924, 2854, 1744, 1675, 1596, 1509, 1466, 1372, 1316, 1291, 1171, 1145, 1094, 1020, 959, 865, 816, 748, 698 cm^{-1}; HRMS (ESI) m/z calcd for $C_{27}H_{24}ClNO_4Na$ $[M + Na]^+$ 484.1292, found 484.1279.

(1aS*,7R*,7aR*)-Ethyl 7a-benzoyl-7-(4-chlorophenylamino)-3,5-dimethyl-1,1a,7,7a-tetrahydrocyclopropa[*b*]chromene-1a-carboxylate (3ma). Yellow solid (92 mg, 97% yield): mp 133.7−134.1 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.69 (d, J = 7.3 Hz, 2H), 7.50 (t, J = 7.4 Hz, 1H), 7.32 (t, J = 7.8 Hz, 2H), 7.06−7.01 (m, 3H), 6.88 (s, 1H), 6.47 (d, J = 8.8 Hz, 2H), 4.88 (s, 1H), 4.02 (ddq, J = 21.6, 10.8, 7.2 Hz, 2H), 3.92 (s, 1H), 2.44 (s, 3H), 2.41 (d, J = 6.6 Hz, 1H), 2.26 (s, 3H), 1.98 (d, J = 6.5 Hz, 1H), 1.09 (t, J = 7.1 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 194.4, 169.0, 149.2, 144.9, 136.3, 133.1, 132.1, 131.3, 129.1, 128.6, 128.4, 127.6, 125.7, 123.6, 123.2, 115.2, 64.8, 61.9, 55.2, 43.9, 23.5, 20.9, 15.5, 13.8; IR (film) ν 3396, 3005, 2981, 2963, 2925, 2863, 1720, 1678, 1598, 1507, 1400, 1373, 1352, 1330, 1297, 1278, 1211, 1185, 1136, 1094, 1013, 956, 937, 856, 816, 799, 759, 713, 688 cm^{-1}; HRMS (ESI) m/z calcd for $C_{28}H_{26}ClNO_4Na$ $[M + Na]^+$ 498.1448, found 498.1453.

(7R*,7aR*,8aS*)-Ethyl 7a-benzoyl-7-(4-chlorophenylamino)-7,7a,8,8a-tetrahydrobenzo[*h*]cyclopropa[*b*]chromene-8a-carboxylate (3na). Yellow solid (96 mg, 96% yield): mp 221.2−222.2 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.45 (d, J = 7.8 Hz, 1H), 7.87 (d, J = 7.4 Hz, 2H), 7.82 (d, J = 7.2 Hz, 1H), 7.61−7.52 (m, 3H), 7.49 (d, J = 8.4 Hz, 1H), 7.39 (t, J = 7.7 Hz, 2H), 7.20 (d, J = 8.5 Hz, 1H), 6.99 (d, J = 8.7 Hz, 2H), 6.38 (d, J = 8.7 Hz, 2H), 5.33 (d, J = 9.7 Hz, 1H), 4.19−4.02 (m, 2H), 3.90 (d, J = 10.0 Hz, 1H), 2.39 (d, J = 6.7 Hz, 1H), 2.08 (d, J = 6.8 Hz, 1H), 1.15 (t, J = 7.1 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 194.0, 168.6, 146.6, 144.8, 136.0, 134.3, 133.2, 129.0, 128.7, 128.6, 127.5, 122.7, 122.2, 117.5, 115.4, 64.5, 62.1, 54.7, 42.4, 20.1, 13.8; IR (film) ν 3389, 3061, 3029, 2995, 2956, 2926, 1740, 1674, 1596, 1511, 1445, 1403, 1378, 1350, 1319, 1298, 1271, 1244, 1208, 1176, 1148, 1093, 1073, 1042, 1010, 986 956, 857, 813, 749, 698 cm^{-1}; HRMS (ESI) m/z calcd for $C_{30}H_{24}ClNO_4Na$ $[M + Na]^+$ 520.1292, found 520.1286.

■ ASSOCIATED CONTENT

Ⓢ Supporting Information

Detailed information for the effect of solvent DMSO. Copies of ^{1}H, ^{13}C NMR spectra for all compounds. Copies of NOE spectra for **3bb**, **3bd**, **3be** and **3ga**. X-ray structure of **3ad** and crystal data of **3ad** in CIF format. This material is available free of charge via the Internet at http://pubs.acs.org.

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Notes

The authors declare no competing financial interest.

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(11) See Supporting Information for details on the single crystal X-ray analysis of **3ad**, and NOE analysis of **3bb**, **3bd**, **3be**, and **3ga**. The stereochemistry of other products are assigned by analogy.
(12) See Supporting Information for the details about the effect of DMSO on the reaction.