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Concise Synthesis of 2-Benzazepine Derivatives and Their Biological Activity

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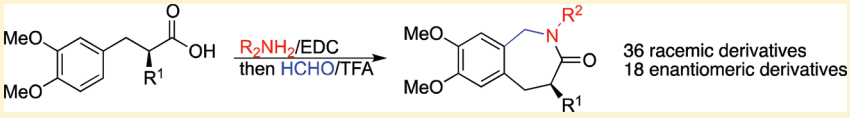
Supporting Information



ABSTRACT: 2-Benzazepines, which are potentially good candidates for new drug therapies to treat skin wounds, were readily prepared from substituted cinnamylamide via an intramolecular Friedel–Crafts reaction. With few steps and effective reactions, the procedure enables a rapid derivatization of 2-benzazepines. Moreover, optically active 4-substituted-2-benzazepines were prepared from chiral α-substituted cinnamylamides, which were readily prepared by asymmetric α-alkylation of chiral cinnamyl oxazolidinone amides. We have easily prepared a library of more than 20 derivatives and examined the biological activity of the compounds.

INTRODUCTION

Benzazepine possesses a 7-membered aza-heterocyclic ring-fused aromatic unit, a framework that is often observed among bioactive natural products and pharmaceuticals.[1] For example, paullones show cyclin-dependent kinase (CDK) inhibitory activity and sirtuin 1 (SIRT1) inhibitory activity.[1k−m] 2-Benzazepine derivatives have been investigated as mimics of peptides containing the RGD motif, which is a well-known antagonist of integrin-mediated adhesion and signal transduction in cells.[2] Syntheses of 2-benzazepine have been performed by lactamization,[3] transition metal-mediated cyclizations such as the Heck reaction,[4] and ring-closure metathesis reaction.[5] Most of these methods require several steps and the use of precious and hazardous transition metal catalysts. Therefore, a new transition metal-free methodology is desired to synthesize 2-benzazepine derivatives.

Recently, we prepared and derivatized 2-benzazepines via the 7-endo selective radical cyclization of (*o*-bromobenzyl)-methacrylamide[6] and found that the 2-benzazepine derivatives promoted epithelial cell migration without proliferation.[7] Thus, 2-benzazepine derivatives are good candidates for new drug therapies to treat skin wounds. Although radical cyclization provides a convenient synthesis of 2-benzazepine derivatives, it is usually very difficult to remove unwanted byproducts, derived from tin hydride, from the crude reaction mixture. In addition, tin compounds are usually toxic, and thus their use should be avoided in the preparation of bioactive compounds. Therefore, we initiated the development of a less toxic method to prepare 2-benzazepine derivatives. A new synthesis based on C–H activation is fascinating because this approach can avoid the use of precious transition metal catalysts as well as expensive aryl halides. We assumed that an intramolecular Friedel–Crafts reaction would be a good candidate for this purpose.[8] In this paper, we present a new method to prepare 2-benzazepines via an intramolecular Friedel–Crafts reaction and report the synthesis of a library of 2-benzazepines using this facile derivatization method. In addition, asymmetric 2-benzazepine derivatives are examined with respect to their biological activity.

RESULTS AND DISCUSSION

We attempted the synthesis of 2-benzazepine derivatives using commercially available 3,4-dimethoxyphenyl propionic acids. Treatment of the acid with thionyl chloride followed by methylamine resulted in the formation of the cyclization precursor *N*-(methyl)-3-(3,4-dimethoxy)phenylpropionamides **1**.[9] An exposure of the compounds **1** to paraformaldehyde in presence of trifluoroacetic acid gave the desired 2-benzazepines **2.** Table 1 shows the results.

For example, 7,8-dimethoxy-2-benzazepine **2a** was prepared rapidly in 88% yield from 3-(3,4-dimethoxy)phenylpropionic acid using the two-step sequence (entry 1). The isolated **2a** contained a single isomer and suggested that the cyclization occurred in a highly regioselective manner. *N*-Ethyl-2-benzazepine **2b** was prepared in 92% yield (entry 2), while *N*-isopropyl-2-benzazepine **2c** was isolated in only 49% yield (entry 3). Steric hindrance from the *N*-*i*Pr group most probably contributed to the lower yield of **2c**. The cyclization from 3,4-methylenedioxyphenyl propionic acid also progressed smoothly, and the desired 2-benzazepines **2d**–**2f** were obtained in good yields (entries 4–6).

We examined the introduction of various alkyl groups at the C4 position of the 4-unsubstituted-2-benzazepines **2** (Scheme 1). 4-Unsubstituted-2-benzazepines **2** underwent smooth alkylation by treatment with LDA followed by various alkyl halides, giving **3** and **4** in good yields. For example, the

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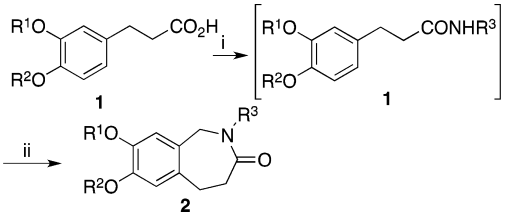
Table 1. Preparation of 4-Substituted-2-Benzazepines 2 via an Intramolecular Friedel–Crafts Reaction[a]

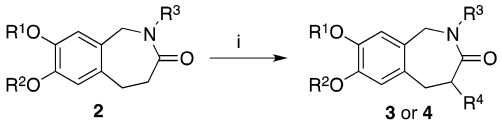


entry	R^1	R^2	R^3	**2**; yield (%)[b]
1	Me	Me	Me	**2a**; 88
2	Me	Me	Et	**2b**; 92
3	Me	Me	*i*Pr	**2c**; 49
4		$-CH_2-$	Me	**2d**; 72
5		$-CH_2-$	Et	**2e**; 83
6		$-CH_2-$	*n*Pr	**2f**; 87

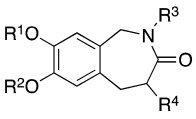
[a]Reagents and conditions: (i) $SOCl_2$, THF, reflux, then R^3NH_2, $NaHCO_3$, or R^3NH_2, EDCl; (ii) $(CH_2O)_n$, TFA, CH_2Cl_2. [b]Isolated yields.

methylation of *N*-methyl-2-benzazepine **2a** gave *N*-methyl-4-methyl-2-benzazepine **3a** in 82% yield. We prepared 36 derivatives of **3** and **4** via this simple manipulation.

Scheme 1. C4 Alkylation of Benzazepines 2



Reagents and conditions: i, LDA, THF, -78 °C then R^4X.

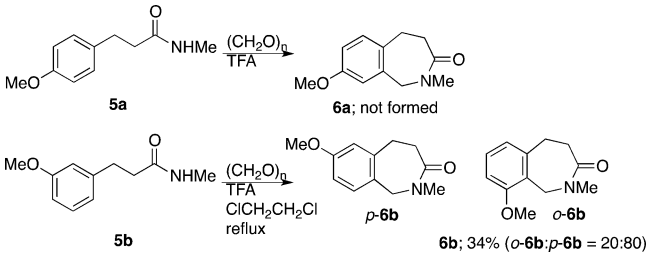


3; R^1, R^2 = Me
4; R^1, R^2 = $-CH_2-$

3a; R^1, R^2 = Me, R^3 = Me, R^4 = Me; 82%
3b; R^1, R^2 = Me, R^3 = Me, R^4 = Et; 57%
3c; R^1, R^2 = Me, R^3 = Me, R^4 = Pr; 52%
3d; R^1, R^2 = Me, R^3 = Me, R^4 = Bu; 59%
3e; R^1, R^2 = Me, R^3 = Me, R^4 = nC_5H_{11}; 59%
3f; R^1, R^2 = Me, R^3 = Me, R^4 = Bn; 72%
3g; R^1, R^2 = Me, R^3 = Et, R^4 = Me; 71%
3h; R^1, R^2 = Me, R^3 = Et, R^4 = Et; 80%
3i; R^1, R^2 = Me, R^3 = Et, R^4 = Pr; 72%
3j; R^1, R^2 = Me, R^3 = Et, R^4 = Bu; 75%
3k; R^1, R^2 = Me, R^3 = Et, R^4 = nC_5H_{11}; 51%
3l; R^1, R^2 = Me, R^3 = Et, R^4 = Bn; 77%
3m; R^1, R^2 = Me, R^3 = iPr, R^4 = Me; 61%
3n; R^1, R^2 = Me, R^3 = iPr, R^4 = Et; 62%
3o; R^1, R^2 = Me, R^3 = iPr, R^4 = Pr; 59%
3p; R^1, R^2 = Me, R^3 = iPr, R^4 = Bu; 63%
3q; R^1, R^2 = Me, R^3 = iPr, R^4 = nC_5H_{11}; 57%
3r; R^1, R^2 = Me, R^3 = iPr, R^4 = Bn; 58%
4a; R^1, R^2 = $-CH_2-$, R^3 = Me, R^4 = Me; 84%
4b; R^1, R^2 = $-CH_2-$, R^3 = Me, R^4 = Et; 71%
4c; R^1, R^2 = $-CH_2-$, R^3 = Me, R^4 = Pr; 82%
4d; R^1, R^2 = $-CH_2-$, R^3 = Me, R^4 = Bu; 77%
4e; R^1, R^2 = $-CH_2-$, R^3 = Me, R^4 = nC_5H_{11}; 44%
4f; R^1, R^2 = $-CH_2-$, R^3 = Me, R^4 = Bn; 85%
4g; R^1, R^2 = $-CH_2-$, R^3 = Et, R^4 = Me; 81%
4h; R^1, R^2 = $-CH_2-$, R^3 = Et, R^4 = Et; 83%
4i; R^1, R^2 = $-CH_2-$, R^3 = Et, R^4 = Pr; 69%
4j; R^1, R^2 = $-CH_2-$, R^3 = Et, R^4 = Bu; 52%
4k; R^1, R^2 = $-CH_2-$, R^3 = Et, R^4 = nC_5H_{11}; 44%
4l; R^1, R^2 = $-CH_2-$, R^3 = Et, R^4 = Bn; 81%
4m; R^1, R^2 = $-CH_2-$, R^3 = Pr, R^4 = Me; 82%
4n; R^1, R^2 = $-CH_2-$, R^3 = Pr, R^4 = Et; 76%
4o; R^1, R^2 = $-CH_2-$, R^3 = Pr, R^4 = Pr; 72%
4p; R^1, R^2 = $-CH_2-$, R^3 = Pr, R^4 = Bu; 66%
4q; R^1, R^2 = $-CH_2-$, R^3 = Pr, R^4 = nC_5H_{11}; 68%
4r; R^1, R^2 = $-CH_2-$, R^3 = Pr, R^4 = Bn; 87%

The present cyclization depends on the methoxy substituents on the aromatic ring. The formation of 2-benzazepines was examined for monomethoxy substituted precursors (Scheme 2). Treatment of 4-methoxyphenylpropionic amide **5a**, which

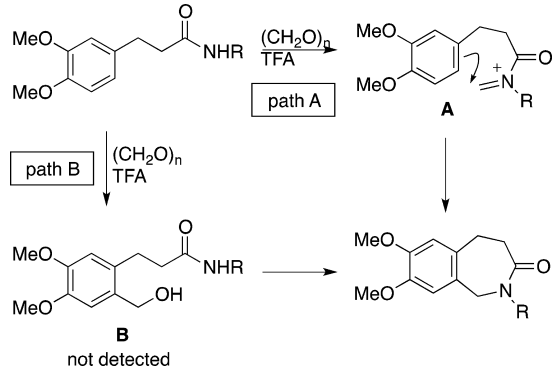
Scheme 2. Reaction of Different Methoxy-Substituted Amides 5



was prepared from the corresponding acid and amine, with formalin and TFA failed to provide benzazepine **6a**, whereas 3-methoxyphenylpropionic amide **5b** underwent the cyclization to give **6b** in 27% yield. The yield of **6b** was improved to 34% when the reaction was carried out at higher temperature. *p*-**6b** was formed as the major isomer and the ratio between *o*-**6b** and *p*-**6b** was 20:80.

These results clearly indicate that cyclization requires a methoxy substituent in the para-position of the cyclized aromatic carbon. When two electron-donating substituents are on the benzene ring, cyclization occurs smoothly to afford the desired 2-benzazepines in good yield. On the basis of these results, we assume a reaction mechanism as depicted in Scheme 3. First, the iminium cation **A** is generated from the

Scheme 3. Plausible Reaction Mechanisms



propionamide and paraformaldehyde. The intermediate **A** undergoes intramolecular Friedel–Crafts reaction via a nucleophilic attack of the aromatic ring, thereby affording the 2-benzazepines in good yield (path A). This may be regarded as a Pictet–Spengler reaction using amide derivatives.[10] The Pictet–Spengler reaction is usually applied to primary and secondary amines, and amides are not commonly used for intramolecular cyclization. Alternatively, 2-benzazepines can be formed via intermolecular hydroxymethylation followed by dehydration (path B); however, we have never detected any intermediate benzyl alcohol **B**. Thus, we believe that the Picktet–Spengler-type intramolecular Friedel–Crafts reaction (path A) is the most possible mechanism for the reaction.

Although we achieved an effective construction of 2-benzazepine derivatives from commercially available com-

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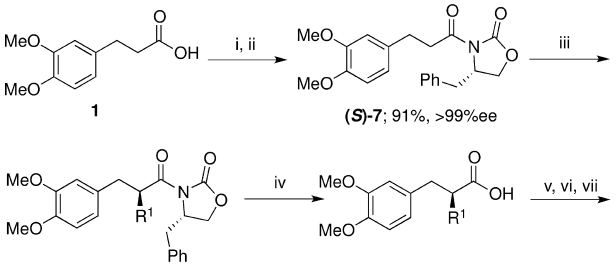
pounds under transition metal-free conditions, it was difficult to obtain chiral 2-benzazepines using this method. To synthesize chiral 2-benzazepine derivatives, the asymmetric alkylation of 4-unsubstituted-2-benzazepines **2** is essential. However, asymmetric alkylation reactions employing chiral additives such as sparteine afforded only racemic products. Therefore, we thought that the synthesis of chiral 4-substituted-2-benzazepines via intramolecular Friedel–Crafts reaction of chiral precursors should be practical, and specifically the asymmetric alkylation of chiral oxazolidinone amides was attractive. Therefore, the necessary chiral cyclization precursors were prepared from 3,4-dimethoxyphenyl propionic acid **1**.

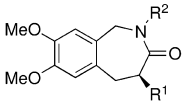
The chiral oxazolidinones[11] were introduced to **1** via the usual method to give (*S*)-**7** in 91% yield (Scheme 4).[12] The

Scheme 4. Preparation of (*S*)-4-Substituted-2-Benzazepines (*S*)-3[a]



(*S,S*)-**8a**; R^1= Me, 69%, 92%de
(*S,S*)-**8b**; R^1= CH_2=$CHCH_2$-, 58%, 98%de
(*S,S*)-**8c**; R^1= Bn, 71%, >99%de

(*S*)-**9a**; R^1= Me, 87%, 92%ee
(*S*)-**9b**; R^1= CH_2=$CHCH_2$-, 91%, 98%ee
(*S*)-**9c**; R^1= Bn, 93%, >99%ee



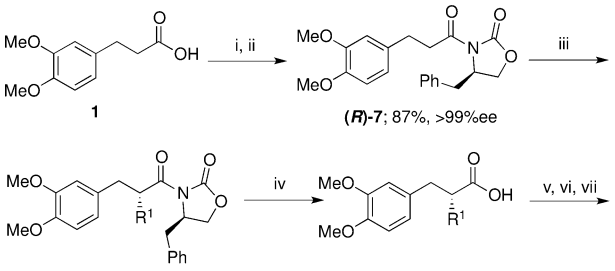
(*S*)-**3a**; R^1 =Me, R^2 = Me, 62%, 90%ee
(*S*)-**3g**; R^1 =Me, R^2 = Et, 74%, 89%ee
(*S*)-**3s**; R^1 =Me, R^2 = nPr, 78%, 91%ee
(*S*)-**3t**; R^1= CH_2=$CHCH_2$-, R^2 = Me, 61%, 97%ee
(*S*)-**3u**; R^1= CH_2=$CHCH_2$-, R^2 = Et, 60%, 97%ee
(*S*)-**3v**; R^1= CH_2=$CHCH_2$-, R^2 = nPr, 74%, 96%ee
(*S*)-**3f**; R^1=Bn, R^2 = Me, 67%, 96%ee
(*S*)-**3l**; R^1=Bn, R^2 = Et, 61%, 98%ee
(*S*)-**3w**; R^1=Bn, R^2 = nPr, 68%, 98%ee

[a]Reagents and conditions: (i) *t*-BuCOCl, Et_3N, THF, −78 °C; (ii) (*S*)-oxazolidinone, THF, −78 °C to rt; (iii) LDA, THF, −78 °C, then R^1X; (iv) LiOH, H_2O_2, THF–H_2O, 0 °C to rt; (v) $SOCl_2$, THF, reflux; (vi) R^2NH_2; (vii) $(CH_2)_n$, TFA, CH_2Cl_2.

following asymmetric alkylation was performed with various alkyl halides and LDA in THF, thereby giving (*S,S*)-**8** in 58–71% yield.[13] For example, the reaction of (*S*)-**7** with benzyl bromide provided (*S,S*)-**8c** in 71% yield with greater than 99% diastereoselectivity. In this alkylation, bulky alkyl halides such as benzyl bromide offered high diastereoselectivity. The obtained alkylated products (*S,S*)-**8** underwent hydrolysis in the presence of LiOH and H_2O_2[14] to give the chiral carboxylic acids (*S*)-**9** in 87–93% yields without any significant loss in enantiomeric excess. Intramolecular Friedel–Crafts reaction was performed under the previously described conditions to afford the desired chiral 2-benzazepines (*S*)-**3** in 60–78% isolated yield. Chiral HPLC analyses revealed that the enantiomeric excesses of most of the products exceeded 90%, and the optical purities obtained during alkylation were maintained during the intramolecular Friedel–Crafts reaction.

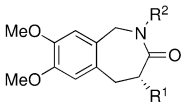
A series of (*R*)-4-substituted-2-benzazepine (*R*)-**3** were prepared in good yields starting with the (*R*)-oxazolidinones (Scheme 5). Importantly, all the reactions were performed via simple and quick manipulations, and each compound was prepared within a short period.

Scheme 5. Preparation of (*R*)-4-Substituted-2-Benzazepines (*R*)-3[a]



(*R,R*)-**8a**; R^1= Me, 57%, 92%de
(*R,R*)-**8b**; R^1= CH_2=$CHCH_2$-, 76%, 98%de
(*R,R*)-**8c**; R^1= Bn, 81%, >99%de

(*R*)-**9a**; R^1= Me, 87%, 92%ee
(*R*)-**9b**; R^1= CH_2=$CHCH_2$-, 92%, 98%ee
(*R*)-**9c**; R^1= Bn, 96%, >99%ee



(*R*)-**3a**; R^1 =Me, R^2 = Me, 73%, 88%ee
(*R*)-**3g**; R^1 =Me, R^2 = Et, 71%, 89%ee
(*R*)-**3s**; R^1 =Me, R^2 = nPr, 88%, 89%ee
(*R*)-**3t**; R^1= CH_2=$CHCH_2$-, R^2 = Me, 78%, 96%ee
(*R*)-**3u**; R^1= CH_2=$CHCH_2$-, R^2 = Et, 84%, 97%ee
(*R*)-**3v**; R^1= CH_2=$CHCH_2$-, R^2 = nPr, 66%, 96%ee
(*R*)-**3w**; R^1=Bn, R^2 = Me, 74%, 94%ee
(*R*)-**3l**; R^1=Bn, R^2 = Et, 71%, 98%ee
(*R*)-**3w**; R^1=Bn, R^2 = nPr, 84%, 99%ee

[a]Reagents and conditions: (i) *t*-BuCOCl, Et_3N, THF, −78 °C; (ii) (*R*)-oxazolidinone, THF, −78 °C to rt; (iii) LDA, THF, −78 °C, then R^1X; (iv) LiOH, H_2O_2, THF–H_2O, 0 °C to rt; (v) $SOCl_2$, THF, reflux; (vi) R^2NH_2; (vii) $(CH_2)_n$, TFA, CH_2Cl_2.

With 36 racemic and 18 optically active 2-benzazepines **3** in hand, we next examined the biological activity of the 2-benzazepine derivatives using an in vitro wound healing assay with HaCat cells, derived from skin keratinocytes. Figure 1 shows typical results in the assay for racemic 2-benzazepines **3**. DMSO is a negative control that does not stimulate cell migration, and the compound **10** is a positive control that promotes cell migration.[6] Cell migration was significantly promoted when 30 μM of compounds **3g**, **3h**, and **3i** were employed in the assay. Their activities are as high as or slightly

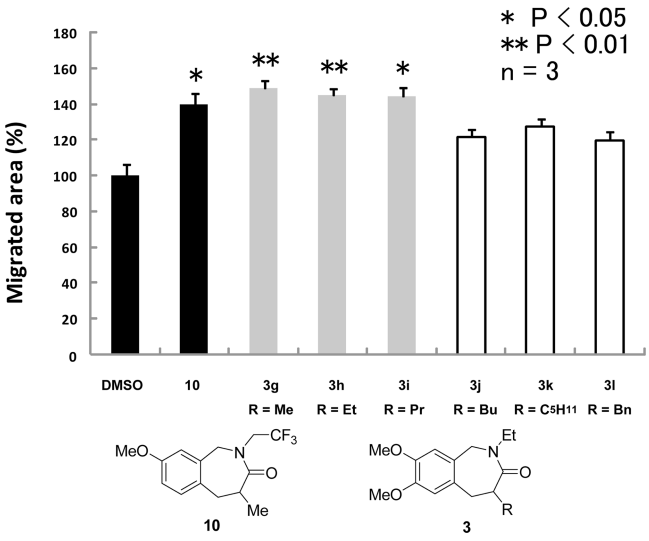


Figure 1. Effects of 2-benazepines **10** and **3** on the migration of HaCat cells. The extent of cell migration into the wound area was determined via an in vitro wound healing assay with the compound at 30 μM, and it is expressed as a percentage of cell migration measured for cultures incubated with DMSO (control). The data are means ± SEM for three independent determinations. *P < 0.05, **P < 0.01 versus control.

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higher than the compound **10**. However, the activity was sensitive to the steric size of the C4 substituent, and the migration decreased when the C4 substituent became bulkier than the butyl group.

Since the compounds **3** are racemic mixtures, we wondered which enantiomer would promote cell migration. To answer this question, we examined the effects of each enantiomer of **3g** on cell migration. Figure 2 shows the results. This figure clearly

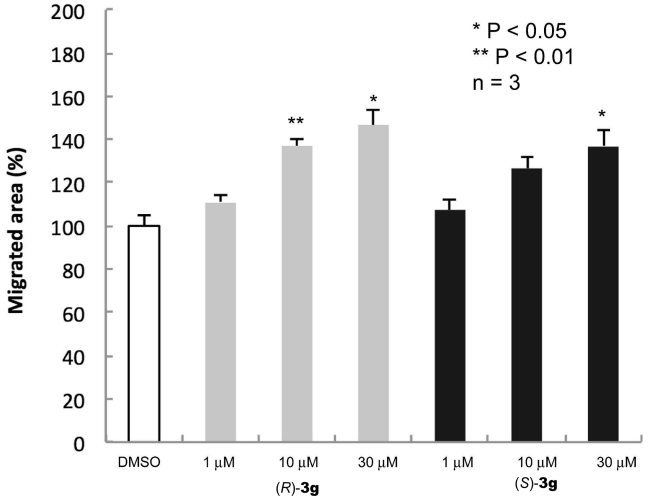

Figure 2. Effects of the enantiomers of (*S*)-**3g** and (*R*)-**3g** on HaCat cell migration. The extent of cell migration into the wound area was determined with each enantiomer at 1−30 μM, and it is expressed as a percentage of cell migration measured for cultures incubated with DMSO (control). Data are means ± SEM for three independent determinations. *P < 0.05, **P < 0.01 versus control.

indicated that both enantiomers are almost equally active. Therefore, this biological activity is insensitive to the absolute configuration at the C4 position of the 2-benzazepines.

In conclusion, we have synthesized 2-benzazepine derivatives rapidly using an intramolecular Friedel−Crafts reaction that conveniently provides racemic derivatives. The method is very simple and useful because 2-benzazepines can be constructed in two steps from commercially available 3,4-dimethoxyphenyl propionic acid. It must be mentioned that all the steps are performed without using transition metal catalysts or expensive aryl halide reagents. The Friedel−Crafts reaction is also applicable to the synthesis of asymmetric derivatives, and we have prepared both enantiomers of 18 derivatives in sufficient enantiomer excess. Further biological assays are underway in our research group and will be reported in due course.

EXPERIMENTAL SECTION

Preparation of 7,8-Dimethoxy-2-methyl-4,5-dihydro-1*H*-benzo[c]azepin-3(2*H*)-one (2a). Thionyl chloride (0.65 mL, 9.0 mmol) was added to a solution of 3-(3,4-dimethoxyphenyl)propanoic acid (0.631 g, 3.00 mmol) in THF (30 mL) in a 100 mL round-bottom flask, and the solution was heated at reflux for 4 h. The volatile contents were then removed using a rotary evaporator under reduced pressure. CH_2Cl_2 (30 mL) was added to the residue. A solution of saturated aqueous $NaHCO_3$ (10 mL) and aqueous $MeNH_2$ (40%, 1.1 mL, 13 mmol, 4.2 equiv) were placed separately in a 100 mL three-necked round-bottom flask and cooled at 0 °C. The CH_2Cl_2 solution, containing propanoyl chloride, was added slowly to the aqueous solution at 0 °C, and the reaction mixture was stirred for 1 h at 0 °C. Saturated aqueous $NaHCO_3$ (30 mL) was then added to the reaction mixture, and the resulting solution was extracted with CH_2Cl_2 (15 mL × 3). The organic phases were combined and dried with Na_2SO_4. After filtration, the filtrate was concentrated using a rotary evaporator under reduced pressure to give crude *N*-methyl-propanamide (0.681 g), which was used without further purification. The *N*-methyl-propanamide (0.536 g) was dissolved in CH_2Cl_2 (50 mL), paraformaldehyde (0.332 g, 11.1 mmol), and trifluoroacetic acid (1.85 mL, 24.2 mmol), and the reaction mixture was stirred at room temperature for 24 h. Then saturated aqueous $NaHCO_3$ (50 mL) was added to the mixture, and the resulting solution was extracted with CH_2Cl_2 (15 mL × 3). The organic phases were combined and dried with Na_2SO_4. After filtration, the filtrate was concentrated using a rotary evaporator under reduced pressure to give crude **2a**, which was purified by flash chromatography (silica gel/hexane then hexane/EtOAc 1:3) to give **2a** in 88% yield (two steps, 0.489 g, 2.08 mmol). Pale yellow oil: ^{1}H NMR (500 MHz, $CDCl_3$) δ 6.64 (s, 1 H), 6.57 (s, 1 H), 4.43 (s, 2 H), 3.87 (s, 3 H), 3.85 (s, 3 H), 3.10 (t, J = 6.6 Hz, 2 H), 3.05 (s, 3 H), 2.91 (t, J = 7.1 Hz, 2 H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 173.1, 147.9, 146.0, 129.0, 125.8, 112.9, 111.8, 55.4, 55.3, 53.3, 34.5, 32.9, 27.8; IR (neat) ν 3435, 2909, 1628, 1256 cm^{-1}; HRMS (ESI M + H) m/z 236.1294, calcd for $C_{13}H_{18}NO_3$ 236.1287.

The following compounds **2** were prepared in a similar manner.

2-Ethyl-7,8-dimethoxy-4,5-dihydro-1*H*-benzo[c]azepin-3(2*H*)-one (2b). Yellow oil: ^{1}H NMR (500 MHz, $CDCl_3$) δ 6.63 (s, 1 H), 6.57 (s, 1 H), 4.42 (s, 2 H), 3.87 (s, 3 H), 3.85 (s, 3 H), 3.52 (q, J = 7.1 Hz, 2 H), 3.10 (t, J = 6.9 Hz, 2 H), 2.89 (t, J = 6.9 Hz, 2 H), 1.10 (t, J = 7.2 Hz, 3 H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 172.3, 147.6, 145.9, 128.8, 126.3, 112.6, 111.3, 55.2, 55.0, 50.9, 41.7, 32.8, 27.7, 12.7; IR (neat) ν 2934, 1632, 1518, 1204 cm^{-1}; HRMS (ESI M + H) m/z 250.1443, calcd for $C_{14}H_{20}NO_3$ 250.1443.

2-Isopropyl-7,8-dimethoxy-4,5-dihydro-1*H*-benzo[c]azepin-3(2*H*)-one (2c). Yellow oil: ^{1}H NMR (500 MHz, $CDCl_3$) δ 6.61 (s, 1 H), 6.56 (s, 1 H), 4.90 (dt, J = 13.6, 6.8 Hz, 1 H), 4.34 (s, 2 H), 3.87 (s, 3 H), 3.85 (s, 3 H), 3.10 (t, J = 6.7 Hz, 2 H), 2.90 (t, J = 6.7 Hz, 2 H), 1.09 (d, J = 6.8 Hz, 6H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 173.2, 148.1, 146.5, 129.5, 127.3, 113.1, 111.6, 56.0, 55.7, 45.1, 44.5, 33.7, 28.5, 20.3; IR (neat) ν 2972, 1628, 1456, 1250 cm^{-1}; HRMS (ESI M + H) m/z 264.1598, calcd for $C_{15}H_{22}NO_3$ 264.1600.

6-Methyl-8,9-dihydro-5*H*-[1,3]dioxolo[4′,5′:4,5]benzo[1,2-c]-azepin-7(6*H*)-one (2d). White solid: mp 150.0−151.0 °C; ^{1}H NMR (500 MHz, $CDCl_3$) δ 6.62 (s, 1 H), 6.57 (s, 1 H), 5.93 (s, 2 H), 4.37 (s, 2 H), 3.05 (t, J = 6.8 Hz, 2 H), 3.04 (s, 3 H), 2.88 (t, J = 6.8 Hz, 2 H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 173.3, 147.4, 145.5, 131.3, 127.5, 110.3, 109.0, 101.1, 54.0, 35.3, 33.8, 28.9; IR ($CHCl_3$) ν 2903, 1643, 1503, 1227 cm^{-1}; HRMS (ESI M + H) m/z 220.0973, calcd for $C_{12}H_{14}NO_3$ 220.0974.

6-Ethyl-8,9-dihydro-5*H*-[1,3]dioxolo[4′,5′:4,5]benzo[1,2-c]-azepin-7(6*H*)-one (2e). White solid: mp 106.0−107.0 °C; ^{1}H NMR (500 MHz, $CDCl_3$) δ 6.61 (s, 1 H), 6.58 (s, 1 H), 5.93 (s, 2 H), 4.36 (s, 2 H), 3.50 (q, J = 7.2 Hz, 2 H), 3.06 (t, J = 6.9 Hz, 2 H), 2.86 (t, J = 7.2 Hz, 2 H), 1.09 (t, J = 7.2 Hz, 3 H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 172.9, 147.4, 145.6, 131.3, 128.3, 110.3, 108.7, 101.2, 51.9, 42.7, 34.0, 29.0, 13.6; IR ($CHCl_3$) ν 2901, 1640, 1487, 1233 cm^{-1}: HRMS (ESI M + H) m/z 234.1116, calcd for $C_{13}H_{16}NO_3$ 234.1130.

6-Propyl-8,9-dihydro-5*H*-[1,3]dioxolo[4′,5′:4,5]benzo[1,2-c]-azepin-7(6*H*)-one (2f). White solid: mp 108.0−109.0 °C; ^{1}H NMR (500 MHz, $CDCl_3$) δ 6.61 (s, 1 H), 6.56 (s, 1 H), 5.93 (s, 2 H), 4.36 (s, 2 H), 3.42 (t, J = 7.3 Hz, 2 H), 3.06 (t, J = 6.2 Hz, 2 H), 2.87 (dd, J = 8.6, 5.1 Hz, 2 H), 1.60−1.41 (m, 2 H), 0.83 (t, J = 7.4 Hz, 3 H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 173.3, 147.3, 145.5, 131.2, 128.1, 110.3, 108.7, 101.1, 52.4, 49.6, 33.9, 29.1, 21.6, 11.3; IR ($CHCl_3$) ν 2901, 1640, 1487, 1231 cm^{-1}: HRMS (ESI M + H) m/z 248.1296, calcd for $C_{14}H_{18}NO_3$ 248.1287.

Preparation of 7,8-Dimethoxy-2,4-dimethyl-4,5-dihydro-1*H*-benzo[c]azepin-3(2*H*)- one (3a). An LDA solution in THF (0.33 M, 2.6 mL, 0.86 mmol) was added to a solution of **2a** (0.123 g, 0.524 mmol) in THF (2 mL) at −78 °C, and the mixture was stirred for 30 min at the same temperature. Iodomethane (0.28 mL, 4.5 mmol, 4.5 equiv) was then slowly added to the solution. The reaction mixture was stirred for 2 h at the same temperature and then allowed to warm to the room temperature for 30 min. Saturated aqueous NH_4Cl (5

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mL) was added to the mixture, and THF was removed under reduced pressure using a rotary evaporator. Saturated brine (20 mL) was then added to the residue, and the resulting aqueous solution was extracted with EtOAc (20 mL × 3). The organic phases were combined and dried over Na_2SO_4. After filtration, the filtrate was concentrated under reduced pressure. The oily residue was purified by flash chromatography (silica gel/hexane then hexane/EtOAc 1:3), to give **3a** in 82% yield (0.107 g, 0.431 mmol). White solid: mp 168.0−168.6 °C; ^{1}H NMR (500 MHz, $CDCl_3$) δ 6.60 (s, 1 H), 6.56 (s, 1 H), 5.17 (d, J = 16.3 Hz, 1 H), 3.87 (s, 3 H), 3.84 (s, 3 H), 3.72 (d, J = 16.4 Hz, 1 H), 3.38 (tt, J = 12.7, 6.4 Hz, 1 H), 3.05 (s, 3 H), 2.95 (dd, J = 17.1, 4.1 Hz, 1 H), 2.84 (dd, J = 17.0, 13.0 Hz, 1 H), 1.25 (d, J = 6.5 Hz, 3 H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 175.6, 148.4, 146.5, 129.7, 126.2, 113.5, 112.0, 56.1, 56.0, 53.7, 37.7, 35.3, 34.8, 17.6; IR ($CHCl_3$) ν 2967, 1526, 1348, 1258 cm^{-1}. Anal. Calcd. for $C_{14}H_{19}NO_3$: C, 67.45; H, 7.68; N, 5.62. Found: C, 67.27; H, 7.70; N, 5.60.

The following compounds **3** were prepared in a similar manner.

2-Ethyl-7,8-dimethoxy-4-methyl-4,5-dihydro-1*H*-benzo[c]-azepin-3(2*H*)-one (3b). Yellow solid: mp 89.5−90.0 °C; ^{1}H NMR (500 MHz, $CDCl_3$) δ 6.60 (s, 1 H), 6.56 (s, 1 H), 5.19 (d, J = 16.3 Hz, 1 H), 3.87 (s, 3 H), 3.84 (s, 3 H), 3.72 (d, J = 16.4 Hz, 1 H), 3.27−3.06 (m, 1 H), 3.04 (s, 3 H), 3.00 (dd, J = 3.3, 16.1 Hz, 1 H), 2.79 (dd, J = 13.4, 16.8 Hz, 1 H), 2.04−1.92 (m, 1 H), 1.50−1.37 (m, 1 H), 1.01 (t, J = 7.4 Hz, 3 H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 175.0, 148.3, 146.4, 129.6, 126.1, 113.6, 112.0, 56.0, 55.9, 53.5, 42.0, 35.6, 35.0, 25.1, 12.4; IR ($CHCl_3$) ν 2936, 1643, 1522, 1261 cm^{-1}; HRMS (ESI M + H) m/z 264.1602, calcd for $C_{15}H_{22}NO_3$ 264.1600.

7,8-Dimethoxy-2-methyl-4-propyl-4,5-dihydro-1*H*-benzo[c]-azepin-3(2*H*)-one (3c). Yellow solid: mp 88.4−88.9 °C; ^{1}H NMR (500 MHz, $CDCl_3$) δ 6.60 (s, 1 H), 6.56 (s, 1 H), 5.19 (d, J = 16.3 Hz, 1 H), 3.87 (s, 3 H), 3.84 (s, 3 H), 3.72 (d, J = 16.4 Hz, 1 H), 3.22 (dd, J = 12.4, 7.1 Hz, 1 H), 3.03 (s, 3 H), 2.99 (dd, J = 17.2, 3.6 Hz, 1 H), 2.80 (dd, J = 13.5, 16.7 Hz, 1 H), 2.03−1.89 (m, 1 H), 1.55−1.27 (m, 3 H), 0.95 (t, J = 7.1 Hz, 3 H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 175.1, 148.4, 146.5, 129.7, 126.2, 113.6, 112.0, 56.1, 55.9, 53.6, 40.0, 35.9, 35.1, 34.3, 20.9, 14.3; IR ($CHCl_3$) ν 2936, 1643, 1522, 1261 cm^{-1}; HRMS (ESI M + H) m/z 278.1765, calcd for $C_{16}H_{24}NO_3$ 278.1756.

4-Butyl-7,8-dimethoxy-2-methyl-4,5-dihydro-1*H*-benzo[c]-azepin-3(2*H*)-one (3d). Yellow solid: mp 102.5−103.0 °C; ^{1}H NMR (500 MHz, $CDCl_3$) δ 6.60 (s, 1 H), 6.56 (s, 1 H), 5.18 (d, J = 16.3 Hz, 1 H), 3.87 (s, 3 H), 3.84 (s, 3 H), 3.71 (d, J = 16.4 Hz, 1 H), 3.20 (dd, J = 12.3, 7.3 Hz, 1 H), 3.03 (s, 3 H), 2.99 (dd, J = 17.2, 3.8 Hz, 1 H), 2.80 (dd, J = 16.8, 13.4 Hz, 1 H), 2.14−1.83 (m, 1 H), 1.49−1.23 (m, 5 H), 0.92 (t, J = 6.9 Hz, 3 H); ^{13}C NMR (68 MHz, $CDCl_3$) δ 175.1, 148.6, 146.6, 129.8, 126.3, 113.8, 112.3, 55.9, 55.8, 53.4, 40.1, 35.8, 34.8, 31.7, 29.8, 22.7, 13.7; IR ($CHCl_3$) ν 2953, 1651, 1522, 1256 cm^{-1}. Anal. Calcd. for $C_{17}H_{25}NO_3$: C, 70.07; H, 8.65; N, 4.81. Found: C, 69.83; H, 8.57; N, 4.83.

7,8-Dimethoxy-2-methyl-4-pentyl-4,5-dihydro-1*H*-benzo[c]-azepin-3(2*H*)-one (3e). Yellow solid: mp 113.7−114.2 °C; ^{1}H NMR (500 MHz, $CDCl_3$) δ 6.60 (s, 1 H), 6.56 (s, 1 H), 5.19 (d, J = 16.2 Hz, 1 H), 3.87 (s, 3 H), 3.84 (s, 3 H), 3.71 (d, J = 15.8 Hz, 1 H), 3.20 (br, 1 H), 3.04 (s, 3 H), 2.99 (d, J = 16.9 Hz, 1 H), 2.80 (t, J = 14.9 Hz, 1 H), 2.17−1.76 (m, 1 H), 1.50−1.20 (m, 7 H), 1.00−0.77 (m, 3 H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 175.2, 148.4, 146.4, 129.7, 126.1, 113.6, 112.0, 56.0, 55.9, 53.6, 40.2, 35.9, 35.1, 32.1, 32.0, 27.5, 22.6, 14.1; IR ($CHCl_3$) ν 2953, 1651, 1522, 1252 cm^{-1}. Anal. Calcd. for $C_{18}H_{27}NO_3$: C, 70.79; H, 8.91; N, 4.59. Found: C, 70.59; H, 8.85; N, 4.52.

4-Benzyl-7,8-dimethoxy-2-methyl-4,5-dihydro-1*H*-benzo[c]-azepin-3(2*H*)-one (3f). White solid: mp 162.5−163.0 °C; ^{1}H NMR (500 MHz,) δ 7.34−7.16 (m, 5 H), 6.54 (s, 1 H), 6.54 (s, 1 H), 5.16 (d, J = 16.3 Hz, 1 H), 3.85 (s, 3 H), 3.81 (s, 3 H), 3.70 (d, J = 16.4 Hz, 1 H), 3.54 (dq, J = 7.9, 5.4 Hz, 1 H), 3.35 (dd, J = 14.0, 5.8 Hz, 1 H), 3.05 (s, 3 H), 2.97 (dd, J = 17.0, 4.0 Hz, 1 H), 2.85 (dd, J = 16.9, 13.1 Hz, 1 H), 2.69 (dd, J = 14.0, 8.0 Hz, 1 H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 174.7, 148.4, 146.5, 140.2, 129.3, 128.4, 128.4, 126.2, 125.9, 113.6, 112.0, 56.1, 55.9, 53.6, 42.1, 38.0, 35.3, 34.9; IR ($CHCl_3$) ν 2934, 1651, 1522, 1252 cm^{-1}. Anal. Calcd. for $C_{20}H_{23}NO_3$: C, 73.82; H, 7.12; N, 4.30. Found: C, 74.12; H, 7.19; N, 4.33.

2-Ethyl-7,8-dimethoxy-4-methyl-4,5-dihydro-1*H*-benzo[c]-azepin-3(2*H*)-one (3g). White solid: mp 125.0−125.5 °C; ^{1}H NMR (500 MHz, $CDCl_3$) δ 6.59 (s, 1 H), 6.58 (s, 1 H), 5.10 (d, J = 16.4 Hz, 1 H), 3.87 (s, 3 H), 3.84 (s, 3 H), 3.79 (d, J = 16.5 Hz, 1 H), 3.52 (q, J = 7.1 Hz, 2 H), 3.46−3.27 (m, 1 H), 2.93 (dd, J = 17.1, 4.1 Hz, 1 H), 2.85 (dd, J = 16.9, 12.9 Hz, 1 H), 1.25 (d, J = 6.5 Hz, 3 H), 1.07 (t, J = 7.2 Hz, 3 H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 174.9, 148.2, 146.5, 129.6, 126.9, 113.3, 111.6, 56.0, 55.8, 51.4, 42.6, 37.7, 34.7, 17.5, 13.5; IR ($CHCl_3$) ν 2970, 2932, 1636, 1250 cm^{-1}. Anal. Calcd. for $C_{15}H_{21}NO_3$: C, 68.42; H, 8.04; N, 5.32. Found: C, 68.25; H, 8.05; N, 5.26.

2,4-Diethyl-7,8-dimethoxy-4,5-dihydro-1*H*-benzo[c]azepin-3(2*H*)-one (3h). White solid: mp 118.8−119.2 °C; ^{1}H NMR (500 MHz, $CDCl_3$) δ 6.60 (s, 1 H), 6.58 (s, 1 H), 5.12 (d, J = 16.4 Hz, 1 H), 3.86 (s, 3 H), 3.84 (s, 3 H), 3.80 (d, J = 16.5 Hz, 1 H), 3.62−3.43 (m, 2 H), 3.08 (ddd, J = 17.3, 9.7, 5.5 Hz, 1 H), 2.99 (dd, J = 17.0, 3.4 Hz, 1 H), 2.81 (dd, J = 16.9, 13.3 Hz, 1 H), 2.06−1.92 (m, 1 H), 1.50−1.36 (m, 1 H), 1.06 (t, J = 7.2 Hz, 3 H), 1.01 (t, J = 7.4 Hz, 3 H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 174.3, 148.1, 146.4, 129.5, 126.9, 113.4, 111.6, 56.0, 55.8, 51.4, 42.4, 42.0, 35.5, 25.0, 13.5, 12.3; IR ($CHCl_3$) ν 2934, 1636, 1520, 1248 cm^{-1}. Anal. Calcd. for $C_{16}H_{23}NO_3$: C, 69.29; H, 8.36; N, 5.05. Found: C, 69.20; H, 8.26; N, 5.01.

2-Ethyl-7,8-dimethoxy-4-propyl-4,5-dihydro-1*H*-benzo[c]-azepin-3(2*H*)-one (3i). Pale yellow solid: mp 107.8−108.3 °C; ^{1}H NMR (500 MHz, $CDCl_3$) δ 6.59 (s, 1 H), 6.56 (s, 1 H), 5.11 (d, J = 16.4 Hz, 1 H), 3.86 (s, 3 H), 3.84 (s, 3 H), 3.78 (d, J = 16.5 Hz, 1 H), 3.52 (q, J = 7.1 Hz, 2 H), 3.21−3.13 (m, 1 H), 2.97 (dd, J = 17.1, 3.5 Hz, 1 H), 2.82 (dd, J = 16.9, 13.3 Hz, 1 H), 1.96 (tdd, J = 10.1, 8.9, 5.6 Hz, 1 H), 1.52−1.26 (m, 3 H), 1.06 (t, J = 7.2 Hz, 3 H), 0.96 (t, J = 7.2 Hz, 3 H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 174.4, 148.2, 146.5, 129.7, 127.0, 113.5, 111.6, 56.0, 55.8, 51.4, 42.5, 40.0, 35.9, 34.2, 20.9, 14.2, 13.6; IR ($CHCl_3$) ν 2932, 1643, 1518, 1248 cm^{-1}. Anal. Calcd. for $C_{17}H_{25}NO_3$: C, 70.07; H, 8.65; N, 4.81. Found: C, 69.94; H, 8.65; N, 4.72.

4-Butyl-2-ethyl-7,8-dimethoxy-4,5-dihydro-1*H*-benzo[c]-azepin-3(2*H*)-one (3j). White solid: mp 95.5−96.0 °C; ^{1}H NMR (500 MHz, $CDCl_3$) δ 6.59 (s, 1 H), 6.56 (s, 1 H), 5.11 (d, J = 16.4 Hz, 1 H), 3.86 (s, 3 H), 3.84 (s, 3 H), 3.78 (d, J = 16.5 Hz, 1 H), 3.52 (q, J = 7.1 Hz, 2 H), 3.20−3.11 (m, 1 H), 2.98 (dd, J = 17.1, 3.4 Hz, 1 H), 2.82 (dd, J = 16.8, 13.3 Hz, 1 H), 2.15−1.82 (m, 1 H), 1.46−1.30 (m, 5 H), 1.06 (t, J = 7.1 Hz, 3 H), 0.92 (t, J = 6.9 Hz, 3 H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 174.33, 148.04, 146.32, 129.50, 126.84, 113.33, 111.51, 55.88, 55.69, 51.29, 42.33, 40.09, 35.77, 31.65, 29.86, 22.77, 13.92, 13.44; IR ($CHCl_3$) ν 2932, 1640, 1520, 1254 cm^{-1}. Anal. Calcd. for $C_{18}H_{27}NO_3$: C, 70.79; H, 8.91; N, 4.59. Found: C, 70.64; H, 8.99; N, 4.60.

2-Ethyl-7,8-dimethoxy-4-pentyl-4,5-dihydro-1*H*-benzo[c]-azepin-3(2*H*)-one (3k). White solid: mp 95.0−95.5 °C; ^{1}H NMR (500 MHz, $CDCl_3$) δ 6.59 (s, 1 H), 6.56 (s, 1 H), 5.11 (d, J = 16.4 Hz, 1 H), 3.86 (s, 3 H), 3.84 (s, 3 H), 3.78 (d, J = 16.5 Hz, 1 H), 3.52 (q, J = 7.1 Hz, 2 H), 3.21−3.11 (m, 1 H), 2.97 (dd, J = 17.1, 3.4 Hz, 1 H), 2.82 (dd, J = 16.9, 13.3 Hz, 1 H), 1.96 (dq, J = 15.3, 7.5 Hz, 1 H), 1.41−1.19 (m, 7 H), 1.06 (t, J = 7.1 Hz, 3 H), 0.90 (t, J = 6.6 Hz, 3 H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 174.6, 148.3, 146.6, 129.8, 127.1, 113.6, 111.7, 56.1, 55.9, 51.6, 42.6, 40.4, 36.0, 32.1, 32.1, 27.6, 22.7, 14.2, 13.7; IR ($CHCl_3$) ν 2930, 1643, 1520, 1250 cm^{-1}. Anal. Calcd. for $C_{19}H_{29}NO_3$: C, 71.44; H, 9.15; N, 4.38. Found: C, 71.18; H, 9.07; N, 4.31.

4-Benzyl-2-ethyl-7,8-dimethoxy-4,5-dihydro-1*H*-benzo[c]-azepin-3(2*H*)-one (3l). White solid: mp 181.5−182.0 °C; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.33−7.27 (m, 4 H), 7.21 (dd, J = 9.2, 4.3 Hz, 1 H), 6.54 (s, 1 H), 6.53 (s, 1 H), 5.09 (d, J = 16.4 Hz, 1 H), 3.85 (s, 3 H), 3.81 (s, 3 H), 3.77 (d, J = 16.5 Hz, 1 H), 3.62−3.40 (m, 3 H), 3.36 (dd, J = 14.0, 5.5 Hz, 1 H), 2.95 (dd, J = 17.0, 3.8 Hz, 1 H), 2.85 (dd, J = 16.9, 13.1 Hz, 1 H), 2.69 (dd, J = 14.1, 8.3 Hz, 1 H), 1.07 (t, J = 7.1 Hz, 3 H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 173.8, 148.1, 146.4, 140.1, 129.2, 129.1, 128.2, 126.7, 125.9, 113.4, 111.5, 55.9, 55.7, 51.3, 42.5, 41.9, 37.8, 34.7, 13.4; IR ($CHCl_3$) ν 2930, 1638, 1520, 1248 cm^{-1}. Anal. Calcd. for $C_{21}H_{25}NO_3$: C, 74.31; H, 7.42; N, 4.13. Found: C, 74.29; H, 7.38; N, 4.08.

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2-Isopropyl-7,8-dimethoxy-4-methyl-4,5-dihydro-1*H*-benzo[c]azepin-3(2*H*)-one (3m). White solid: mp 103.5−104.0 °C; ^{1}H NMR (500 MHz, $CDCl_3$) δ 6.57 (s, 1 H), 6.56 (s, 1 H), 4.95 (m, J = 6.8 Hz, 1 H), 4.83 (d, J = 16.6 Hz, 1 H), 3.88 (d, J = 17.0 Hz, 1 H), 3.86 (s, 3 H), 3.84 (s, 3 H), 3.38−3.29 (m, 1 H), 2.94−2.84 (m, 2 H), 1.25 (d, J = 6.5 Hz, 3 H), 1.17 (d, J = 6.8 Hz, 3 H), 0.96 (d, J = 6.8 Hz, 3 H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 174.8, 148.0, 146.4, 129.6, 127.5, 113.1, 111.3, 56.0, 55.7, 44.8, 44.3, 37.7, 34.8, 20.8, 20.0, 17.5; IR ($CHCl_3$) ν 2972, 1636, 1520, 1250 cm^{-1}. Anal. Calcd. for $C_{16}H_{23}NO_3$: C, 69.29; H, 8.36; N, 5.05. Found: C, 69.13; H, 8.47; N, 5.02.

4-Ethyl-2-isopropyl-7,8-dimethoxy-4,5-dihydro-1*H*-benzo[c]azepin-3(2*H*)-one (3n). White solid: mp 127.5−128.0 °C; ^{1}H NMR (500 MHz, $CDCl_3$) δ 6.58 (s, 1 H), 6.56 (s, 1 H), 4.96 (m, J = 6.8 Hz, 1 H), 4.86 (d, J = 16.6 Hz, 1 H), 3.88 (d, J = 17.6 Hz, 1 H), 3.86 (s, 3 H), 3.84 (s, 3 H), 3.10−3.03 (m, 1 H), 2.97 (dd, J = 17.1, 2.9 Hz, 1 H), 2.82 (dd, J = 16.8, 13.5 Hz, 1 H), 2.08−1.91 (m, 1 H), 1.49−1.36 (m, 1 H), 1.17 (d, J = 6.8 Hz, 3 H), 1.01 (t, J = 7.4 Hz, 3 H), 0.95 (d, J = 6.8 Hz, 3 H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 174.2, 147.9, 146.4, 129.6, 127.5, 113.2, 111.3, 55.9, 55.7, 44.7, 44.1, 42.0, 35.5, 24.9, 20.8, 20.0, 12.3; IR ($CHCl_3$) ν 2934, 1636, 1520, 1248 cm^{-1}. Anal. Calcd. for $C_{17}H_{25}NO_3$: C, 70.07; H, 8.65; N, 4.81. Found: C, 69.75; H, 8.74; N, 4.82.

2-Isopropyl-7,8-dimethoxy-4-propyl-4,5-dihydro-1*H*-benzo[c]azepin-3(2*H*)-one (3o). White solid: mp 113.5−114.0 °C; ^{1}H NMR (500 MHz, $CDCl_3$) δ 6.57 (s, 1 H), 6.56 (s, 1 H), 4.95 (m, J = 6.8 Hz, 1 H), 4.86 (d, J = 16.6 Hz, 1 H), 3.88 (d, J = 17.0 Hz, 1 H), 3.86 (s, 3H), 3.84 (s, 3 H), 3.22−3.08 (m, 1 H), 2.96 (dd, J = 17.0, 3.1 Hz, 1 H), 2.83 (dd, J = 16.8, 13.3 Hz, 1 H), 2.05−1.90 (m, 1 H), 1.50−1.30 (m, 3 H), 1.17 (d, J = 6.8 Hz, 3 H), 0.96 (dd, J = 8.2, 7.1 Hz, 6 H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 174.4, 148.0, 146.5, 129.7, 127.6, 113.3, 111.4, 56.0, 55.8, 44.9, 44.3, 40.1, 35.9, 34.2, 20.9 (2C), 20.2, 14.3; IR ($CHCl_3$) ν 2955, 1638, 1520, 1248 cm^{-1}; HRMS (ESI M + H) m/z 306.2069, calcd for $C_{18}H_{28}NO_3$ 306.2068.

4-Butyl-2-isopropyl-7,8-dimethoxy-4,5-dihydro-1*H*-benzo[c]azepin-3(2*H*)-one (3p). White solid: mp 99.3−99.8 °C; ^{1}H NMR (500 MHz, $CDCl_3$) δ 6.57 (s, 1 H), 6.55 (s, 1 H), 4.96 (m, J = 6.8 Hz, 1 H), 4.85 (d, J = 16.6 Hz, 1 H), 3.88 (d, J = 16.4 Hz, 1 H), 3.86 (s, 3 H), 3.84 (s, 3 H), 3.17−3.10 (m, 1 H), 2.96 (dd, J = 17.1, 3.1 Hz, 1 H), 2.83 (dd, J = 16.9, 13.3 Hz, 1 H), 2.18−1.83 (m, 1 H), 1.54−1.32 (m, 5 H), 1.17 (d, J = 6.8 Hz, 3 H), 0.94 (d, J = 6.9 Hz, 3 H), 0.92 (t, J = 7.0 Hz, 3 H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 174.4, 148.0, 146.4, 129.7, 127.6, 113.3, 111.4, 56.0, 55.7, 44.8, 44.2, 40.3, 35.9, 31.7, 30.0, 22.9, 20.8, 20.1, 14.0; IR ($CHCl_3$) ν 2932, 1634, 1520, 1252 cm^{-1}. Anal. Calcd. for $C_{19}H_{29}NO_3$: C, 71.44; H, 9.15; N, 4.38. Found: C, 71.33; H, 9.18; N, 4.34.

2-Isopropyl-7,8-dimethoxy-4-pentyl-4,5-dihydro-1*H*-benzo[c]azepin-3(2*H*)-one (3q). Pale yellow oil: ^{1}H NMR (500 MHz, $CDCl_3$) δ 6.57 (s, 1 H), 6.55 (s, 1 H), 4.96 (m, J = 6.8 Hz, 1 H), 4.85 (d, J = 16.6 Hz, 1 H), 3.88 (d, J = 16.6 Hz, 1 H), 3.86 (s, 3 H), 3.84 (s, 3 H), 3.19−3.10 (m, 1 H), 2.96 (dd, J = 17.0, 3.1 Hz, 1 H), 2.83 (dd, J = 16.8, 13.3 Hz, 1 H), 2.22−1.80 (m, 1 H), 1.48−1.23 (m, 7 H), 1.17 (d, J = 6.8 Hz, 3 H), 0.94 (d, J = 6.8 Hz, 3 H), 0.90 (t, J = 6.7 Hz, 3 H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 174.4, 148.0, 146.4, 129.7, 127.6, 113.3, 111.4, 56.0, 55.7, 44.8, 44.2, 40.4, 35.9, 32.0, 32.0, 27.4, 22.5, 20.9, 20.1, 14.0; IR (neat) ν 2930, 1638, 1520, 1250 cm^{-1}; HRMS (ESI M + H) m/z 334.2389, calcd for $C_{20}H_{32}NO_3$ 334.2382.

4-Benzyl-2-isopropyl-7,8-dimethoxy-4,5-dhydro-1*H*-benzo[c]azepin-3(2*H*)-one (3r). White solid: mp 157.5−158.0 °C; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.34−7.27 (m, 4 H), 7.24−7.16 (m, 1 H), 6.53 (s, 1 H), 6.50 (s, 1 H), 4.97 (dt, J = 13.6, 6.8 Hz, 1 H), 4.84 (d, J = 16.6 Hz, 1 H), 3.87 (d, J = 16.8 Hz, 1 H), 3.84 (s, 3 H), 3.80 (s, 3 H), 3.48 (ddd, J = 13.0, 9.2, 4.8 Hz, 1 H), 3.37 (dd, J = 14.1, 5.2 Hz, 1 H), 3.00−2.78 (m, 2 H), 2.70 (dd, J = 14.1, 8.6 Hz, 1 H), 1.18 (d, J = 6.8 Hz, 3 H), 0.96 (d, J = 6.8 Hz, 3 H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 173.9, 147.9, 146.4, 140.2, 129.2, 129.2, 128.2, 127.4, 126.0, 113.3, 111.3, 55.9, 55.7, 44.8, 44.4, 42.0, 37.8, 34.6, 20.8, 20.0; IR ($CHCl_3$) ν 2932, 1634, 1520, 1248 cm^{-1}. Anal. Calcd. for $C_{22}H_{27}NO_3$: C, 74.76; H, 7.70; N, 3.96. Found: C, 74.59; H, 7.86; N, 3.90.

6,8-Dimethyl-8,9-dihydro-5*H*-[1,3]dioxolo[4′,5′:4,5]benzo-[1,2-c]azepin-7(6*H*)-one (4a). White solid: mp 122.0−122.5 °C; ^{1}H NMR (500 MHz, $CDCl_3$) δ 6.57 (s, 1 H), 6.55 (s, 1 H), 5.92 (s, 2 H), 5.07 (d, J = 16.2 Hz, 1 H), 3.70 (d, J = 16.3 Hz, 1 H), 3.35 (m, J = 6.3 Hz, 1 H), 3.03 (s, 3 H), 2.93 (dd, J = 17.1, 4.4 Hz, 1 H), 2.79 (dd, J = 17.1, 12.8 Hz, 1 H), 1.24 (d, J = 6.6 Hz, 3 H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 175.2, 147.2, 145.2, 131.0, 127.2, 110.3, 108.7, 101.0, 53.5, 37.9, 35.1, 34.9, 17.6; IR ($CHCl_3$) 2899, 1645, 1227, 1028 cm^{-1}. Anal. Calcd. for $C_{13}H_{15}NO_3$: C, 66.94; H, 6.48; N, 6.00. Found: C, 66.74; H, 6.65; N, 5.88.

8-Ethyl-6-methyl-8,9-dihydro-5*H*-[1,3]dioxolo[4′,5′:4,5]-benzo[1,2-c]azepin-7(6*H*)-one (4b). Pale yellow solid: mp 102.5−103.0 °C; ^{1}H NMR (500 MHz, CDCl3) δ 6.58 (s, 1 H), 6.55 (s, 1 H), 5.92 (s, 2 H), 5.09 (d, J = 16.2 Hz, 1 H), 3.70 (d, J = 16.3 Hz, 1 H), 3.09 (td, J = 12.7, 5.5 Hz, 1 H), 3.02 (s, 3 H), 2.98 (dd, J = 16.9, 4.0 Hz, 1 H), 2.75 (dd, J = 17.0, 13.1 Hz, 1 H), 2.04−1.87 (m, 1 H), 1.54−1.33 (m, 1 H), 1.00 (t, J = 7.4 Hz, 3 H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 174.7, 147.2, 145.2, 131.0, 127.3, 110.4, 108.7, 101.0, 53.5, 42.2, 35.9, 34.9, 25.3, 12.3; IR ($CHCl_3$) ν 2876, 1643, 1487, 1225 cm^{-1}. Anal. Calcd. for $C_{14}H_{17}NO_3$: C, 68.00; H, 6.93; N, 5.66. Found: C, 67.77; H, 7.06; N, 5.57.

6-Methyl-8-propyl-8,9-dihydro-5*H*-[1,3]dioxolo[4′,5′:4,5]-benzo[1,2-c]azepin-7(6*H*)-one (4c). Pale yellow oil: ^{1}H NMR (500 MHz, $CDCl^3$) δ 6.58 (s, 1 H), 6.55 (s, 1 H), 5.92 (s, 2 H), 5.09 (d, J = 16.2 Hz, 1 H), 3.71 (d, J = 16.3 Hz, 1 H), 3.25−3.15 (m, 1 H), 3.02 (s, 3 H), 2.96 (dd, J = 17.1, 4.3 Hz, 1 H), 2.76 (dd, J = 16.8, 12.9 Hz, 1 H), 2.04−1.85 (m, 1 H), 1.52−1.28 (m, 3 H), 0.95 (t, J = 7.1 Hz, 3 H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 175.0, 147.3, 145.3 131.2, 127.4, 110.6, 108.8, 101.1, 53.7, 40.3, 36.3, 35.1, 34.5, 21.0, 14.3; IR (neat) ν 2930, 1647, 1487, 1236 cm^{-1}; HRMS (ESI M + H) m/z 262.1456, calcd for $C_{15}H_{20}NO_3$ 262.1443.

8-Butyl-6-methyl-8,9-dihydro-5*H*-[1,3]dioxolo[4′,5′:4,5]-benzo[1,2-c]azepin-7(6*H*)-one (4d). Pale yellow oil: ^{1}H NMR (500 MHz, $CDCl_3$) δ 6.58 (s, 1 H), 6.55 (s, 1 H), 5.92 (s, 2 H), 5.09 (d, J = 16.2 Hz, 1 H), 3.70 (d, J = 16.3 Hz, 1 H), 3.17 (m, J = 6.0 Hz, 1 H), 3.02 (s, 3 H), 2.97 (dd, J = 17.1, 4.3 Hz, 1 H), 2.76 (dd, J = 16.8, 12.9 Hz, 1 H), 2.01−1.88 (m, 1 H), 1.48−1.24 (m, 5 H), 0.92 (t, J = 7.0 Hz, 3 H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 175.0, 147.3, 145.3, 131.2, 127.4, 110.6, 108.8, 101.1, 53.7, 40.5, 36.3, 35.1, 32.1, 30.1, 23.0, 14.1; IR (neat) ν 2930, 1649, 1487, 1229 cm^{-1}; HRMS (ESI M + H) m/z 276.1609, calcd for $C_{16}H_{22}NO_3$ 276.1600.

6-Methyl-8-pentyl-8,9-dihydro-5*H*-[1,3]dioxolo[4′,5′:4,5]-benzo[1,2-c]azepin-7(6*H*)-one (4e). Pale yellow solid: mp 66.0−66.5 °C; ^{1}H NMR (500 MHz, $CDCl_3$) δ 6.58 (s, 1 H), 6.55 (s, 1 H), 5.92 (s, 2 H), 5.09 (d, J = 16.2 Hz, 1 H), 3.69 (d, J = 16.3 Hz, 1 H), 3.22−3.12 (m, 1 H), 3.01 (s, 3 H), 2.97 (dd, J = 17.1, 4.3 Hz, 1 H), 2.76 (dd, J = 16.8, 12.9 Hz, 1 H), 2.04−1.80 (m, 1 H), 1.46−1.24 (m, 7 H), 0.89 (t, J = 6.5 Hz, 3 H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 174.9, 147.2, 145.3, 131.1, 127.3, 110.5, 108.7, 101.0, 53.5, 40.5, 36.3, 35.0, 32.3, 32.0, 27.5, 22.6, 14.1; IR ($CHCl_3$) ν 2926, 1647, 1487, 1225 cm^{-1}; HRMS (ESI M + H) m/z 290.1762, calcd for $C_{17}H_{24}NO_3$ 290.1756.

8-Benzyl-6-methyl-8,9-dihydro-5*H*-[1,3]dioxolo-[4′,5′:4,5benzo[1,2-c]azepin-7(6*H*)-one (4f). Pale yellow oil: ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.36−7.26 (m, 4 H), 7.24−7.16 (m, 1 H), 6.53 (s, 2 H), 5.90 (d, J = 3.2 Hz, 2 H),5.06 (d, J = 16.3 Hz, 1 H), 3.67 (d, J = 16.4 Hz, 1 H), 3.54−3.45 (m, 1 H), 3.33 (dd, J = 13.9, 5.9 Hz, 1 H), 3.03 (s, 3 H), 2.94 (dd, J = 17.0, 4.2 Hz, 1 H), 2.81 (dd, J = 17.0, 13.0 Hz, 1 H), 2.67 (dd, J = 14.0, 7.9 Hz, 1 H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 174.3, 147.2, 145.3, 140.1, 130.6, 129.2, 128.3, 127.1, 126.1, 110.5, 108.7, 101.0, 53.5, 42.3, 38.0, 35.2, 35.1; IR (neat) ν 2891, 1645, 1487, 1231 cm^{-1}: HRMS (ESI M + H) m/z 310.1436, calcd for $C_{19}H_{20}NO_3$ 310.1443.

6-Ethyl-8-methyl-8,9-dihydro-5*H*-[1,3]dioxolo[4′,5′:4,5]-benzo[1,2-c]azepin-7(6*H*)-one (4g). White solid: mp 160.4−160.8 °C; ^{1}H NMR (500 MHz, $CDCl_3$) δ 6.57 (s, 1 H), 6.56 (s, 1 H), 5.92 (s, 2 H), 5.02 (d, J = 16.4 Hz, 1 H), 3.76 (d, J = 16.4 Hz, 1 H), 3.63−3.38 (m, 2 H), 3.38−3.15 (m, 1 H), 2.91 (dd, J = 17.1, 4.2 Hz, 1 H), 2.81 (dd, J = 17.0, 12.9 Hz, 1 H), 1.23 (d, J = 6.5 Hz, 3 H), 1.06 (t, J = 7.2 Hz, 3 H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 174.7, 147.0, 145.3, 130.9, 128.0, 110.2, 108.3, 101.0, 51.4, 42.5, 38.0, 34.8, 17.6, 13.5; IR

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($CHCl_3$) ν 2899, 1647, 1476, 1233 cm^{-1}. Anal. Calcd. for $C_{14}H_{17}NO_3$: C, 68.00; H, 6.93; N, 5.66. Found: C, 67.82; H, 7.02; N, 5.72.

6,8-Diethyl-8,9-dihydro-5*H*-[1,3]dioxolo[4′,5′:4,5]benzo[1,2-c]azepin-7(6*H*)-one (4h). Yellow solid: mp 88.5−89.0 °C; ^{1}H NMR (500 MHz, $CDCl_3$) δ 6.57 (s, 1 H), 6.56 (s, 1 H), 5.92 (s, 2 H), 5.03 (d, J = 16.4 Hz, 1 H), 3.77 (d, J = 16.4 Hz, 1 H), 3.50 (m, J = 7.1 Hz, 2 H), 3.05 (m, J = 6.3 Hz, 1 H), 2.96 (dd, J = 17.1, 3.7 Hz, 1 H), 2.77 (dd, J = 16.9, 13.2 Hz, 1 H), 2.04−1.88 (m, 1 H), 1.51−1.34 (m, 1 H), 1.06 (t, J = 7.2 Hz, 3 H), 1.00 (t, J = 7.4 Hz, 3 H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 174.1, 147.0, 145.3, 131.0, 128.1, 110.4, 108.4, 101.0, 51.4, 42.4, 42.2, 35.9, 25.2, 13.6, 12.3; IR ($CHCl_3$) ν 2930, 1641, 1487, 1223 cm^{-1}. Anal. Calcd. for $C_{15}H_{19}NO_3$: C, 68.94; H, 7.33; N, 5.36. Found: C, 68.73; H, 7.41; N, 5.31.

6-Ethyl-8-propyl-8,9-dihydro-5*H*-[1,3]dioxolo[4′,5′:4,5]benzo[1,2-c]azepin-7(6*H*)-one (4i). Yellow oil: ^{1}H NMR (500 MHz, $CDCl_3$) δ 6.57 (s, 1 H), 6.56 (s, 1 H), 5.92 (s, 2 H), 5.03 (d, J = 16.4 Hz, 1 H), 3.77 (d, J = 16.4 Hz, 1 H), 3.50 (m, J = 6.9 Hz, 2 H), 3.15 (m, J = 5.9 Hz, 1 H), 2.94 (dd, J = 17.0, 3.8 Hz, 1 H), 2.78 (dd, J = 17.0, 13.1 Hz, 1 H), 2.08−1.88 (m, 1 H), 1.49−1.29 (m, 3 H), 1.06 (t, J = 7.2 Hz, 3 H), 0.95 (t, J = 7.2 Hz, 3 H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 174.3, 147.1, 145.3, 131.0, 128.1, 110.4, 108.4, 101.0, 51.5, 42.5, 40.2, 36.2, 34.3, 20.9, 14.2, 13.6; IR (neat) ν 2932, 1643, 1485, 1234 cm^{-1}; HRMS (ESI M + H) m/z 276.1599, calcd for $C_{16}H_{22}NO_3$ 276.1600.

8-Butyl-6-ethyl-8,9-dihydro-5*H*-[1,3]dioxolo[4′,5′:4,5]benzo[1,2-c]azepin-7(6*H*)-one (4j). Yellow oil: ^{1}H NMR (500 MHz, $CDCl_3$) δ 6.57 (s, 1 H), 6.56 (s, 1 H), 5.92 (s, 2 H), 5.03 (d, J = 16.4 Hz, 1 H), 3.76 (d, J = 16.4 Hz, 1 H), 3.50 (m, J = 7.0 Hz, 2 H), 3.18−3.08 (m, 1 H), 2.95 (dd, J = 17.1, 3.8 Hz, 1 H), 2.78 (dd, J = 17.0, 13.2 Hz, 1 H), 2.00−1.90 (m, 1 H), 1.46−1.28 (m, 5 H), 1.06 (t, J = 7.2 Hz, 3 H), 0.92 (t, J = 7.0 Hz, 3 H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 174.4, 147.1, 145.3, 131.1, 128.1, 110.4, 108.4, 101.0, 51.5, 42.5, 40.5, 36.3, 31.9, 30.0, 22.9, 14.1, 13.6; IR (neat) ν 2957, 1649, 1489, 1233 cm^{-1}; HRMS (ESI M + H) m/z 290.1769, calcd for $C_{17}H_{24}NO_3$ 290.1756.

6-Ethyl-8-pentyl-8,9-dihydro-5*H*-[1,3]dioxolo[4′,5′:4,5]benzo[1,2-c]azepin-7(6*H*)-one (4k). Yellow oil: ^{1}H NMR (500 MHz, $CDCl_3$) δ 6.57 (s, 1 H), 6.56 (s, 1 H), 5.92 (s, 2 H), 5.03 (d, J = 16.4 Hz, 1 H), 3.76 (d, J = 16.4 Hz, 1 H), 3.50 (m, J = 7.1 Hz, 2 H), 3.20−3.04 (m, 1 H), 2.94 (dd, J = 17.1, 3.8 Hz, 1 H), 2.78 (dd, J = 17.0, 13.1 Hz, 1 H), 1.98−1.90 (m, 1 H), 1.45−1.28 (m, 7 H), 1.05 (t, J = 7.2 Hz, 3 H), 0.89 (t, J = 6.6 Hz, 3 H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 174.3, 147.1, 145.3, 131.1, 128.1, 110.4, 108.4, 101.0, 51.5, 42.5, 40.5, 36.2, 32.2, 32.0, 27.5, 22.6, 14.1, 13.6; IR (neat) ν 2928, 1645, 1487, 1231 cm^{-1}; HRMS (ESI M + H) m/z 304.1931, calcd for $C_{18}H_{26}NO_3$ 304.1913.

8-Benzyl-6-ethyl-8,9-dihydro-5*H*-[1,3]dioxolo[4′,5′:4,5]benzo[1,2-c]azepin-7(6*H*)-one (4l). Pale yellow oil: ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.37−7.23 (m, 4 H), 7.23−7.13 (m, 1 H), 6.52 (s, 1 H), 6.49 (s, 1 H), 5.86 (d, J = 5.0 Hz, 2 H), 4.97 (d, J = 16.4 Hz, 1 H), 3.72 (d, J = 16.5 Hz, 1 H), 3.56 (dq, J = 14.3, 7.2 Hz, 1 H), 3.49−3.39 (m, 2 H), 3.33 (dd, J = 14.0, 5.5 Hz, 1 H), 2.90 (dd, J = 17.0, 4.0 Hz, 1 H), 2.80 (dd, J = 16.9, 13.0 Hz, 1 H), 2.67 (dd, J = 14.0, 8.1 Hz, 1 H), 1.05 (t, J = 7.2 Hz, 3 H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 173.8, 147.1, 145.3, 140.1, 130.6, 129.3, 128.3, 127.9, 126.1, 110.4, 108.3, 101.0, 51.4, 42.7, 42.3, 37.9, 35.1, 13.5; IR (neat) ν 2889, 1641, 1487, 1233 cm^{-1}; HRMS (ESI M + H) m/z 324.1617, calcd for $C_{20}H_{22}NO_3$ 324.1600.

8-Methyl-6-propyl-8,9-dihydro-5*H*-[1,3]dioxolo[4′,5′:4,5]benzo[1,2-c]azepin-7(6*H*)-one (4m). White solid: mp 139.0−139.5 °C; ^{1}H NMR (500 MHz, $CDCl_3$) δ 6.56 (s, 1 H), 6.55 (s, 1 H), 5.92 (s, 2 H), 5.03 (d, J = 16.3 Hz, 1 H), 3.74 (d, J = 16.4 Hz, 1 H), 3.58−3.46 (m, 1 H), 3.40−3.26 (m, 2 H), 2.91 (dd, J = 17.1, 4.1 Hz, 1 H), 2.82 (dd, J = 17.1, 12.8 Hz, 1 H), 1.54−1.41 (m, 2 H), 1.23 (d, J = 6.5 Hz, 3 H), 0.81 (t, J = 7.4 Hz, 3 H); ^{13}C NMR (126 MHz,) δ 175.0, 147.0, 145.3, 130.9, 127.9, 110.2, 108.4, 101.0, 51.9, 49.5, 38.1, 34.8, 21.6, 17.6, 11.2; IR ($CHCl_3$) ν 2930, 1643, 1485, 1229 cm^{-1}. Anal. Calcd. for $C_{15}H_{19}NO_3$: C, 68.94; H, 7.33; N, 5.36. Found: C, 68.61; H, 7.33; N, 5.40.

8-Ethyl-6-propyl-8,9-dihydro-5*H*-[1,3]dioxolo[4′,5′:4,5]benzo[1,2-c]azepin-7(6*H*)-one (4n). Pale yellow oil: ^{1}H NMR (500 MHz, $CDCl_3$) δ 6.56 (s, 1 H), 6.55 (s, 1 H), 5.91 (s, 2 H), 5.04 (d, J = 16.4 Hz, 1 H), 3.74 (d, J = 16.5 Hz, 1 H), 3.50 (dt, J = 13.5, 7.4 Hz, 1 H), 3.33 (dt, J = 13.7, 7.1 Hz, 1 H), 3.12−3.00 (m, 1 H), 2.95 (dd, J = 17.0, 3.6 Hz, 1 H), 2.77 (dd, J = 17.0, 13.2 Hz, 1 H), 2.03−1.89 (m, 1 H), 1.55−1.35 (m, 3 H), 1.00 (t, J = 7.4 Hz, 3 H), 0.80 (t, J = 7.4 Hz, 3 H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 174.5, 147.0, 145.3, 130.9, 128.0, 110.3, 108.4, 101.0, 51.8, 49.3, 42.2, 36.0, 25.2, 21.6, 12.3, 11.2; IR (neat) ν 2874, 1643, 1487, 1244 cm^{-1}; HRMS (ESI M + H) m/z 276.1610, calcd for $C_{16}H_{22}NO_3$ 276.1600.

6,8-Dipropyl-8,9-dihydro-5*H*-[1,3]dioxolo[4′,5′:4,5]benzo[1,2-c]azepin-7(6*H*)-one (4o). Yellow oil: ^{1}H NMR (500 MHz, $CDCl_3$) δ 6.57 (s, 1 H), 6.54 (s, 1 H), 5.92 (d, J = 1.5 Hz, 2 H), 5.04 (d, J = 16.4 Hz, 1 H), 3.74 (d, J = 16.4 Hz, 1 H), 3.49 (dt, J = 13.7, 7.4 Hz, 1 H), 3.34 (dt, J = 13.7, 7.1 Hz, 1 H), 3.18−3.13 (m, 1 H), 2.94 (dd, J = 17.1, 3.7 Hz, 1 H), 2.79 (dd, J = 17.0, 13.1 Hz, 1 H), 1.99−1.90 (m, 1 H), 1.51−1.43 (m, 5 H), 0.95 (t, J = 7.2 Hz, 3 H), 0.80 (t, J = 7.4 Hz, 3 H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 174.6, 147.0, 145.3, 131.0, 128.0, 110.3, 108.4, 101.0, 51.8, 49.3, 40.1, 36.3, 34.3, 21.6, 20.9, 14.2, 11.2; IR (neat) ν 2957, 1645, 1487, 1235 cm^{-1}; HRMS (ESI M + H) m/z 290.1754, calcd for $C_{17}H_{24}NO_3$ 290.1756.

8-Butyl-6-propyl-8,9-dihydro-5*H*-[1,3]dioxolo[4′,5′:4,5]benzo[1,2-c]azepin-7(6*H*)-one (4p). Yellow oil: ^{1}H NMR (500 MHz, $CDCl_3$) δ 6.57 (s, 1 H), 6.54 (s, 1 H), 5.92 (d, J = 1.2 Hz, 2 H), 5.04 (d, J = 16.4 Hz, 1 H), 3.74 (d, J = 16.5 Hz, 1 H), 3.50 (dt, J = 14.9, 7.5 Hz, 1 H), 3.33 (dt, J = 13.8, 7.1 Hz, 1 H), 3.18−3.10 (m, 1 H), 2.95 (dd, J = 17.1, 3.7 Hz, 1 H), 2.79 (dd, J = 17.0, 13.2 Hz, 1 H), 1.98−1.92 (m, 1 H), 1.51−1.29 (m, 7 H), 0.92 (t, J = 7.0 Hz, 3 H), 0.80 (t, J = 7.4 Hz, 3 H); ^{13}C NMR (126 MHz,) δ 174.5, 147.0, 145.2, 130.9, 128.0, 110.3, 108.4, 100.9, 51.8, 49.3, 40.3, 36.3, 31.9, 29.9, 22.8, 21.6, 14.0, 11.1; IR (neat) ν 2928, 1643, 1487, 1229 cm^{-1}; HRMS (ESI M + H) m/z 304.1923, calcd for $C_{18}H_{26}NO_3$ 304.1913.

8-Pentyl-6-propyl-8,9-dihydro-5*H*-[1,3]dioxolo[4′,5′:4,5]benzo[1,2-c]azepin-7(6*H*)-one (4q). Pale yellow oil: ^{1}H NMR (500 MHz, $CDCl_3$) δ 6.57 (s, 1 H), 6.54 (s, 1 H), 5.92 (d, J = 1.3 Hz, 2 H), 5.04 (d, J = 16.3 Hz, 1 H), 3.74 (d, J = 16.4 Hz, 1 H), 3.50 (dt, J = 13.7, 7.5 Hz, 1 H), 3.33 (dt, J = 13.7, 7.1 Hz, 1 H), 3.21−3.02 (m, 1 H), 2.94 (dd, J = 17.1, 3.7 Hz, 1 H), 2.78 (dd, J = 17.0, 13.2 Hz, 1 H), 2.05−1.75 (m, 1 H), 1.51−1.29 (m, 9 H), 0.89 (t, J = 6.6 Hz, 3 H), 0.80 (t, J = 7.4 Hz, 3 H); ^{13}C NMR (126 MHz,) δ 174.6, 147.0, 145.2, 131.0, 128.0, 110.3, 108.4, 101.0, 51.8, 49.3, 40.4, 36.3, 32.1, 32.0, 27.4, 22.6, 21.6, 14.1, 11.2; IR (neat) ν 2926, 1645, 1487, 1227 cm^{-1}; HRMS (ESI M + H) m/z 318.2069, calcd for $C_{19}H_{28}NO_3$ 318.2069.

8-Benzyl-6-propyl-8,9-dihydro-5*H*-[1,3]dioxolo[4′,5′:4,5]benzo[1,2-c]azepin-7(6*H*)-one (4r). Yellow solid: mp 103.5−104.0 °C; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.34−7.27 (m, 4 H), 7.25−7.15 (m, 1 H), 6.52 (s, 1 H), 6.52 (s, 1 H), 5.90 (s, 1 H), 5.89 (s, 1 H), 5.02 (d, J = 16.4 Hz, 1 H), 3.72 (d, J = 16.5 Hz, 1 H), 3.55 (dt, J = 13.7, 7.6 Hz, 1 H), 3.51−3.42 (m, 1 H), 3.34 (dd, J = 14.2, 5.6 Hz, 2 H), 3.29 (dd, J = 13.7, 6.9 Hz, 1 H), 2.93 (dd, J = 17.1, 3.9 Hz, 1 H), 2.83 (dd, J = 17.0, 12.9 Hz, 1 H), 2.67 (dd, J = 14.0, 8.0 Hz, 1 H), 1.47 (m, J = 7.3 Hz, 2 H), 0.80 (t, J = 7.4 Hz, 3 H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 174.0, 146.9, 145.2, 140.1, 130.4, 129.2, 128.2, 127.8, 126.0, 110.3, 108.3, 100.9, 51.7, 49.5, 42.2, 37.9, 35.2, 21.5, 11.1; IR ($CHCl_3$) ν 2928, 1643, 1487, 1231 cm^{-1}. Anal. Calcd. for $C_{21}H_{23}NO_3$: C, 74.75; H, 6.87; N, 4.15. Found: C, 74.46; H, 6.96; N, 4.08.

Preparation of 3-(4-Methoxyphenyl)-*N*-methylpropanamide (5a). EDCI (2.063 g, 30.6 mmol) was added to a solution of 3-(4-methoxyphenyl)propionic acid (1.814 g, 10.06 mmol) and methylamine hydrochloride (2.06 g, 10.6 mmol) in CH_2Cl_2 (40 mL) at room temperature. Et_3N (6.25 mL, 45.1 mmol) was then added to the solution, and the reaction mixture was stirred at room temperature for 6 h. Aqueous HCl (1 M, 100 mL) was added to the reaction mixture, and the organic phase was separated. The aqueous phase was extracted with CH_2Cl_2 (40 mL × 3). The organic phases were combined and dried over Na_2SO_4 and filtered. The filtrate was concentrated in vacuo, and the residue was purified by flash chromatography (silica gel/hexane then hexane/EtOAc 7:1 to 1:3) to give **5a** in 41% yield (804.6 mg, 4.16 mmol). White solid: mp 87.5−88.0 °C;^{1}H NMR (500 MHz, $CDCl_3$) δ 7.11 (dd, J = 8.8, 2.3 Hz, 2 H), 6.82 (d, J = 8.7 Hz, 2 H), 5.31 (s, 1 H), 3.78 (s, 3 H), 2.90 (t, J = 7.7 Hz, 2 H), 2.76 (d, J = 4.9

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Hz, 3 H), 2.42 (t, J = 8.8 Hz, 2 H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 172.9, 158.1, 133.0, 129.4, 114.0, 55.4, 38.9, 31.0, 26.4; HRMS (FAB M + H) m/z 194.1177, calcd for $C_{11}H_{16}NO_2$ 194.1181.

Compound **5b** was prepared in a similar manner.

3-(3-Methoxyphenyl)-*N*-methylpropanamide (5b). Colorless oil: ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.20 (dd, J = 8.9, 7.5 Hz, 1 H), 6.78 (d, J = 7.5 Hz, 1 H), 6.76–6.72 (m, 2 H), 5.36 (s, 1 H), 3.78 (s, 3 H), 2.94 (t, J = 7.8 Hz, 2 H), 2.77 (d, J = 4.9 Hz, 2 H), 2.45 (d, J = 7.8 Hz, 2 H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 172.9, 158.1, 133.0, 129.4, 114.0, 55.4, 38.9, 31.0, 26.4; HRMS (FAB M + H) m/z 194.1175, calcd for $C_{11}H_{16}NO_2$ 194.1181.

Preparation of 6b. Paraformaldehyde (0.0653 g, 2.17 mmol) and TFA (0.41 mL, 5.4 mmol) were added to a solution of 3-(3-methoxyphenyl)-*N*-methylpropanamide **5b** (0.103 g, 0.531 mmol) in $ClCH_2CH_2Cl$ (11 mL) at room temperature, and the reaction mixture was stirred at room temperature for 4 h. Saturated aqueous $NaHCO_3$ (15 mL) was then added, and the resulting biphasic mixture was extracted with CH_2Cl_2 (3 × 50 mL). The organic phases were combined and dried over Na_2SO_4. After filtration, the filtrate was concentrated using a rotary evaporator, and the residue was purified by flash chromatography (silica gel/hexane then hexane/EtOAc 3:1 to 1:3) to give **6b** in 34% yield (0.0373 g, 0.182 mmol). *o*-**6b** and *p*-**6b** were separated by preparative recycle HPLC apparatus.

9-Methoxy-2-methyl-4,5-dihydro-1*H*-benzo[c]azepin-3(2*H*)-one (*o*-6b). Pale yellow oil: ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.16 (t, J = 8.0 Hz, 1 H), 6.75 (d, J = 7.7 Hz, 1 H), 6.72 (d, J = 8.2 Hz, 1 H), 4.64 (s, 2 H), 3.82 (s, 3 H), 3.12 (t, J = 6.9 Hz, 2 H), 3.03 (s, 3 H), 2.88 (t, J = 6.9 Hz, 2 H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 173.9, 156.3, 140.0, 128.4, 123.9, 122.4, 108.1, 55.8, 44.7, 35.8, 34.0, 29.1; HRMS (FAB M + H) m/z 206.1189, calcd for $C_{12}H_{16}NO_2$ 206.1181.

7-Methoxy-2-methyl-4,5-dihydro-1*H*-benzo[c]azepin-3(2*H*)-one (*p*-6b). White solid: mp 107.0–107.5 °C; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.00 (d, J = 8.2 Hz, 1 H), 6.69 (d, J = 2.5 Hz, 1 H), 6.67 (dd, J = 8.2, 2.7 Hz, 1 H), 4.43 (s, 2 H), 3.78 (s, 3 H), 3.14 (t, J = 6.5 Hz, 2 H), 3.04 (s, 3 H), 2.91 (t, J = 6.5 Hz, 2 H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 173.5, 159.4, 139.1, 130.1, 126.7, 115.7, 111.4, 55.8, 53.9, 35.2, 33.6, 29.1; HRMS (ESI M + H) m/z 206.1177, calcd for $C_{12}H_{16}NO_2$ 206.1181.

(*S*)-4-Benzyl-3-(3-(3,4-dimethoxyphenyl)propanoyl)-oxazolidin-2-one (*S*-7). Et_3N (1.66 mL, 11.9 mmol) and pivaloyl chloride (1.28 mL, 10.4 mmol) were added to a solution of 3-(3,4-dimethoxyphenyl)propanoic acid (2.102 g, 9.999 mmol) in THF (50 mL) at −78 °C, and the reaction mixture was stirred at the same temperature for 1 h. LDA (1.0 M, 12.0 mL) was slowly added to a solution of (*S*)-4-benzyloxazolidin-2-one (1.952 g, 11.0 mmol) in THF (50 mL) at −78 °C. The former reaction mixture was then transferred via a cannula to the latter solution at −78 °C, and the resulting mixture was stirred at the same temperature for 1 h and then at room temperature for 24 h. Saturated aqueous NH_4Cl (20 mL) was added to the reaction mixture. THF was removed using a rotary evaporator under reduced pressure. Saturated aqueous $NaHCO_3$ (50 mL) was added to the residue. The resulting mixture was extracted with EtOAc (50 mL × 3). The organic phases were combined, dried over Na_2SO_4, and filtered. The filtrate was then concentrated under reduced pressure, and the residue was purified by flash chromatography (silica gel/hexane then hexane/EtOAc 3:1) to afford *S*-7 in 91% yield (3.361 g, 9.099 mmol). White solid: mp 91.5–92.0 °C; $[\alpha]_D$ +47.8° (c = 0.99, $CHCl_3$); the enantiomeric purity was determined by HPLC analysis (230 nm, 40 °C) t_R 37.0 min (major); t_R 34.9 min (minor) [CHIRALPAK IC (2.1 mm × 250 mm) (from Daicel Chemical Ind., Ltd.) hexane/*i*-PrOH, 85/15, 1.00 mL/min] as >99% ee; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.36–7.24 (m, 3 H), 7.17 (d, J = 6.9 Hz, 2 H), 6.83–6.78 (m, 3 H), 4.67 (ddd, J = 12.9, 6.9, 3.4 Hz, 1 H), 4.19 (dd, J = 9.1, 6.5 Hz, 1 H), 4.16 (dd, J = 9.1, 3.4 Hz, 1 H), 3.89 (s, 3 H), 3.86 (s, 3 H), 3.34–3.19 (m, 3 H), 3.01 (dd, J = 13.8 Hz, 6.4 Hz, 1 H), 2.93 (dd, J = 13.8, 6.7 Hz, 1 H), 2.75 (dd, J = 13.4, 9.5 Hz, 1 H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 172.4, 153.4, 148.8, 147.4, 135.1, 133.0, 129.4, 128.9, 127.3, 120.4, 111.9, 111.2, 66.1, 55.9, 55.8, 55.0, 37.7, 37.3, 29.9; IR ($CHCl_3$) ν 2936, 1643, 907, 725 cm^{-1}. Anal. Calcd. for $C_{21}H_{23}NO_5$: C, 68.28; H, 6.28; N, 3.79. Found: C, 68.19; H, 6.38; N, 3.77.

R-7 was prepared in a similar manner.

(*R*)-4-Benzyl-3-(3-(3,4-dimethoxyphenyl)propanoyl)-oxazolidin-2-one (*R*-7). White solid: mp 91.5–92.0 °C; $[\alpha]_D$ −47.3° (c = 0.99, $CHCl_3$); the enantiomeric purity was determined by HPLC analysis (230 nm, 40 °C) t_R 35.2 min (major); t_R 38.2 min (minor) [CHIRALPAK IC (2.1 mm × 250 mm) (from Daicel Chemical Ind., Ltd.) hexane/*i*-PrOH, 85/15, 1.00 mL/min] as >99% ee; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.35–7.26 (m, 3 H), 7.17 (d, J = 6.8 Hz, 2 H), 6.84–6.79 (m, 3 H), 4.67 (ddd, J = 12.9, 7.0, 3.4 Hz, 1 H), 4.19 (dd, J = 9.2, 7.0 Hz, 1 H), 4.15 (dd, J = 9.0, 3.3 Hz, 1 H), 3.88 (s, 3 H), 3.86 (s, 3 H), 3.36–3.17 (m, 3 H), 3.00 (dd, J = 14.1, 6.7 Hz, 1 H), 2.95 (dd, J = 14.0, 7.0 Hz, 1 H), 2.75 (dd, J = 13.4, 9.5 Hz, 1 H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 172.5, 153. 4, 148.9, 147.5, 135.2, 133.1, 129.4, 128.9, 127.4, 120.5, 111.9, 111.3, 66.2, 55.9, 55.9, 55.1, 37.8, 37.3, 30.0; IR ($CHCl_3$) ν 2936, 1778, 1258, 1028 cm^{-1}. Anal. Calcd. for $C_{21}H_{23}NO_5$: C, 68.28; H, 6.28; N, 3.79. Found: C, 68.02; H, 6.37; N, 3.81.

(*S*)-4-Benzyl-3-((*S*)-3-(3,4-dimethoxyphenyl)-2-methylpropanoyl)oxazolidin-2-one (*S,S*-8a). Under a nitrogen atmosphere, LDA (1.0 M, 5.5 mL, 5.5 mmoL) was added slowly to a solution of (*S*)-7 (1.853 g, 5.016 mmol) in THF (50 mL) at −78 °C, and the reaction mixture was then stirred at the same temperature for 30 min. Iodomethane (1.40 mL, 22.5 mmol) was added to the reaction mixture, and the resulting solution was stirred at −78 °C for 2 h and then at room temperature for 30 min. Saturated aqueous NH_4Cl (20 mL) was added to the reaction mixture. THF was removed under reduced pressure. Saturated brine (20 mL) was then added to the residue, and the resulting aqueous solution was extracted with EtOAc (50 mL × 3). The organic phases were combined, dried over Na_2SO_4, and filtered. The filtrate was concentrated under reduced pressure. The residue was purified by flash chromatography (silica gel/hexane then hexane/EtOAc 4:1) to afford *S,S*-**8a** in 69% yield (1.334 g, 3.480 mmol). Colorless oil: $[\alpha]_D$ +103.7° (c = 1.01, $CHCl_3$); HPLC analysis indicated diastereomeric ratio was 96/4; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.36–7.28 (m, 3 H), 7.20 (d, J = 6.9 Hz, 2 H), 6.79–6.75 (m, 3 H), 4.52 (dddd, J = 9.9, 7.7, 3.2, 2.4 Hz, 1 H), 4.15–4.05 (m, 2 H), 3.99 (t, J = 8.4 Hz, 1 H), 3.87 (s, 3 H), 3.85 (s, 3 H), 3.24 (dd, J = 13.3, 3.3 Hz, 1 H), 2.98 (dd, J = 13.4, 7.8 Hz, 1 H), 2.75 (dd, J = 13.4, 9.6 Hz, 1 H), 2.65 (dd, J = 13.4, 7.3 Hz, 1 H), 1.25 (d, J = 6.8 Hz, 3 H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 176.3, 152.9, 148.5, 147.3, 135.1, 131.6, 129.2, 128.7, 127.1, 120.9, 112.0, 110.8, 65.8, 55.6, 55.8, 55.1, 39.4, 39.3, 37.6, 16.8; IR (neat) ν 2934, 1773, 1694, 1234, 1026, 727 cm^{-1}; HRMS (ESI M + H) m/z 384.1808, calcd for $C_{22}H_{26}NO_5$ 384.1811.

Other compounds **8** were prepared in a similar manner.

(*R*)-4-Benzyl-3-((*R*)-3-(3,4-dimethoxyphenyl)-2-methylpropanoyl)oxazolidin-2-one (*R,R*-8a). Pale yellow oil: $[\alpha]_D$ −87.9° (c = 3.28, $CHCl_3$); HPLC analysis indicated diastereomeric ratio was 96/4; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.37–7.26 (m, 3 H), 7.20 (d, J = 6.9 Hz, 2 H), 6.81–6.73 (m, 3 H), 4.52 (dddd, J = 9.8, 7.7, 3.3, 2.5 Hz, 1 H), 4.13–4.08 (m, 2 H), 4.03–3.95 (t, J = 8.4 Hz, 1 H), 3.87 (s, 3 H), 3.85 (s, 3 H), 3.24 (dd, J = 13.4, 3.3 Hz, 1 H), 2.98 (dd, J = 13.4, 7.8 Hz, 1 H), 2.75 (dd, J = 13.4, 9.6 Hz, 1 H), 2.65 (dd, J = 13.4, 7.3 Hz, 1 H), 1.25 (d, J = 6.8 Hz, 3 H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 176.5, 153.1, 148.6, 147.5, 135.2, 131.8, 129.4, 128.9, 127.3, 121.1, 112.2, 110.9, 66.0, 55.8, 55.8, 55.4, 39.6, 39.5, 37.8, 17.0; IR (neat) ν 2932, 1775, 1695, 1236, 729 cm^{-1}; HRMS (ESI M + H) m/z 384.1825, calcd for $C_{22}H_{26}NO_5$ 384.1811.

(*S*)-4-Benzyl-3-((*S*)-2-(3,4-dimethoxybenzyl)pent-4-enoyl)-oxazolidin-2-one (*S,S*-8b). Pale yellow oil: $[\alpha]_D$ +107.3° (c = 0.98, $CHCl_3$); HPLC analysis indicated diastereomeric ratio was 99/1; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.35–7.27 (m, 3 H), 7.19 (d, J = 6.9 Hz, 2 H), 6.80–6.70 (m, 3 H), 5.92–5.80 (m, 1 H), 5.13 (dq, J = 17.0, 1.5 Hz, 1 H), 5.08 (ddd, J = 11.1, 1.9, 0.9 Hz, 1 H), 4.46 (dddd, J = 10.0, 7.7, 3.3, 2.4 Hz, 1 H), 4.39–4.29 (m, 1 H), 4.03 (dd, J = 9.0, 2.4 Hz, 1 H), 3.87 (s, 3 H), 3.86 (dd, J = 9.3, 6.9 Hz, 1 H), 3.84 (s, 3 H), 3.23 (dd, J = 13.3, 3.3 Hz, 1 H), 2.90 (dd, J = 13.5, 8.9 Hz, 1 H), 2.78 (dd, J = 13.5, 6.5 Hz, 1 H), 2.65 (dd, J = 13.4, 9.9 Hz, 1 H), 2.60–2.50 (m, 1 H), 2.40–2.31 (m, 1 H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 175.3,

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153.1, 148.6, 147.5, 135.3, 135.1, 131.4, 129.4, 128.8, 127.2, 121.0, 117.3, 112.1, 110.9, 65.8, 55.8, 55.8, 55.4, 43.9, 38.0, 37.9, 36.3; IR (neat) ν 2934, 1775, 1236, 1028 cm^{-1}; HRMS (ESI M + H) m/z 410.1968, calcd for $C_{24}H_{28}NO_5$ 410.1967.

(*R*)-4-Benzyl-3-((*R*)-2-(3,4-dimethoxybenzyl)pent-4-enoyl)-oxazolidin-2-one (*R*,*R*-8b). Pale yellow oil: $[\alpha]_D$ −105.5° (c= 1.05, $CHCl_3$); HPLC analysis indicated diastereomeric ratio was 99/1; ^1H NMR (500 MHz, $CDCl_3$) δ 7.35−7.24 (m, 3 H), 7.19 (d, J = 7.0 Hz, 2 H), 6.82−6.69 (m, 3 H), 5.86 (ddt, J = 17.1, 10.1, 7.0 Hz, 1 H), 5.13 (d, J = 17.1 Hz, 1 H), 5.08 (d, J = 10.2 Hz, 1 H), 4.49−4.43 (m, 1 H), 4.36−4.30 (m, 1 H), 4.03 (dd, J = 9.0, 2.3 Hz, 1 H), 3.86 (s, 1 H), 3.86 (dd, J = 9.3, 6.9 Hz, 1 H), 3.83 (s, 1 H), 3.23 (dd, J = 13.4, 3.1 Hz, 1 H), 2.90 (dd, J = 13.5, 8.9 Hz, 1 H), 2.78 (dd, J = 13.5, 6.5 Hz, 1 H), 2.65 (dd, J = 13.3, 9.9 Hz, 1 H), 2.58−2.51 (m, 1 H), 2.38−2.33 (m, 1 H); ^{13}C NMR (126 MHz,) δ 175.5, 153.2, 148.7, 147.6, 135.4, 135.2, 131.5, 129.5, 129.0, 127.4, 121.1, 117.4, 112.2, 111.0, 65.9, 55.9, 55.9, 55.6, 44.0, 38.1, 38.1, 36.4; IR (neat) ν 2916, 1775, 1695, 1516, 1236 cm^{-1}; HRMS (ESI M + H) m/z 410.1960, calcd for $C_{24}H_{28}NO_5$ 410.1967.

(*S*)-4-Benzyl-3-((*S*)-2-benzyl-3-(3,4-dimethoxyphenyl)-propanoyl)oxazolidin-2-one (*S*,*S*-8c). Pale yellow oil: $[\alpha]_D$ +85.7° (c = 0.97, $CHCl_3$); HPLC analysis indicated diastereomeric ratio was >99/1; ^1H NMR (500 MHz, $CDCl_3$) δ 7.30−7.18 (m, 8 H), 6.94 (dd, J = 7.0, 2.4 Hz, 2 H), 6.81−6.73 (m, 3 H), 4.70−4.62 (m, 1 H), 4.44−4.38 (m, 1 H), 3.93 (dd, J = 9.0, 2.5 Hz, 1 H), 3.86 (s, 3 H), 3.83 (s, 3 H), 3.81 (t, J = 7.7 Hz, 1 H), 3.11 (dd, J = 13.4, 9.1 Hz, 1 H), 2.95 (dd, J = 13.5, 8.9 Hz, 1 H), 2.90 (dd, J = 14.6, 3.3 Hz, 1 H), 2.87 (dd, J = 13.4, 6.0 Hz, 1 H), 2.80 (dd, J = 13.4, 6.6 Hz, 1 H), 2.42 (dd, J = 13.5, 9.1 Hz, 1 H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 175.2, 152.8, 148.6, 147.5, 138.9, 134.9, 131.2, 129.3, 129.2, 128.7, 128.3, 127.1, 126.4, 121.0, 112.0, 110.9, 65.5, 55.8, 55.7, 54.9, 46.1, 38.4, 38.1, 37.4; IR (neat) ν 2946, 1775, 1236, 1028 cm^{-1}; HRMS (ESI M + H) m/z 460.2097, calcd for $C_{28}H_{30}NO_5$ 460.2124.

(*R*)-4-Benzyl-3-((*R*)-2-benzyl-3-(3,4-dimethoxyphenyl)-propanoyl)oxazolidin-2-one (*R*,*R*-8c). Pale yellow oil: $[\alpha]_D$ −86.9° (c = 1.16, $CHCl_3$); HPLC analysis indicated diastereomeric ratio was >99/1; ^1H NMR (500 MHz, $CDCl_3$) δ 7.31−7.18 (m, 8 H), 6.94 (dd, J = 6.9, 2.5 Hz, 2 H), 6.81−6.71 (m, 3 H), 4.66 (tt, J = 8.9, 6.3 Hz, 1 H), 4.44−4.39 (m, 1 H), 3.93 (dd, J = 9.0, 2.4 Hz, 1 H), 3.86 (s, 3 H), 3.84 (s, 3 H), 3.81 (d, J = 8.6 Hz, 1 H), 3.11 (dd, J = 13.4, 9.2 Hz, 1 H), 2.95 (dd, J = 13.3, 8.7 Hz, 2 H), 2.91 (dd, J = 13.2, 3.1 Hz, 1 H), 2.87 (dd, J = 13.4, 6.0 Hz, 1 H), 2.80 (dd, J = 13.4, 6.6 Hz, 1 H), 2.42 (dd, J = 13.5, 9.1 Hz, 1 H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 175.4, 152.9, 148.7, 147.5, 138.9, 135.0, 131.3, 129.3, 129.3, 128.8, 128.4, 127.2, 126.5, 121.0, 112.1, 110.9, 65.6, 55.9, 55.8, 55.0, 46.2, 38.5, 38.2, 37.5; IR (neat) ν 2936, 1775, 1260, 1028 cm^{-1}; HRMS (ESI M + H) m/z 460.2108, calcd for $C_{28}H_{30}NO_5$ 460.2124.

Preparation of (*S*)-3-(3,4-Dimethoxyphenyl)-2-methylpropanoic Acid (*S*-9a). H_2O_2 (30% in water, 0.40 mL, 3.9 mmol) and LiOH (0.025 g, 1.04 mmol) in water (1 mL) were added to a solution of (*S*,*S*)-8a (0.154 g, 0.400 mmol) in THF (3 mL) at 0 °C. The reaction mixture was allowed to warm to room temperature and then stirred for 4 h. Aqueous 30% $Na_2S_2O_3$ (2 mL) was added slowly to the mixture at 0 °C, and THF was removed using a rotary evaporator under reduced pressure. 3 N HCl aq (10 mL) was added to the residue, and the aqueous mixture was extracted with EtOAc (20 mL × 3). The organic phases were combined, dried over Na_2SO_4, and filtered. The filtrate was then concentrated under reduced pressure, and the crude product was purified by flash chromatography (silica gel/hexane then hexane/EtOAc 1:1) to give ***S*-9a** in 87% yield (0.078 g, 0.35 mmol). Pale yellow oil: $[\alpha]_D$ +14.8° (c = 2.23, $CHCl_3$); the enantiomeric purity was determined by HPLC analysis (230 nm, 40 °C) t_R 23.2 min (major); t_R 16.8 min (minor) [CHIRALPAK IC (2.1 mm × 250 mm) (from Daicel Chemical Ind., Ltd.) hexane/*i*-PrOH, 80/20, 1.00 mL/min] as 92% ee; ^1H NMR (500 MHz, $CDCl_3$) δ 6.79 (d, J = 8.1 Hz, 1 H), 6.73 (dd, J = 10.9, 2.7 Hz, 2 H), 3.86 (s, 6 H), 3.01 (dd, J = 13.6, 6.7 Hz, 1 H), 2.74 (m, J = 7.0 Hz, 1 H), 2.63 (dd, J = 13.6, 7.8 Hz, 1 H), 1.18 (d, J = 6.9 Hz, 3 H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 182.4, 148.8, 147.6, 131.6, 121.0, 112.2, 111.2, 55.9, 55.8, 41.5, 39.0, 16.5; IR (neat) ν 3650−3450, 2938, 1705, 1261, 905 cm^{-1}; HRMS (ESI M − H) m/z 223.0969, calcd for $C_{12}H_{15}O_4$ 223.0970.

Other compounds **9** were prepared in a similar manner.

(*R*)-3-(3,4-Dimethoxyphenyl)-2-methylpropanoic Acid (*R*-9a). Pale yellow oil: $[\alpha]_D$ −18.8° (c = 2.54, $CHCl_3$); the enantiomeric purity was determined by HPLC analysis (230 nm, 40 °C) t_R 24.4 min (major); t_R 15.7 min (minor) [CHIRALPAK IC (2.1 mm × 250 mm) (from Daicel Chemical Ind., Ltd.) hexane/*i*-PrOH, 80/20, 1.00 mL/min] as 92% ee; ^1H NMR (500 MHz, $CDCl_3$) δ 6.81−6.69 (m, 3 H), 3.86 (s, 6 H), 3.01 (m, J = 6.9 Hz, 1 H), 2.73 (dd, J = 14.1, 7.0 Hz, 1 H), 2.62 (dd, J = 13.6, 7.9 Hz, 1 H), 1.17 (d, J = 6.9 Hz, 3 H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 182.5, 148.8, 147.6, 131.6, 121.0, 112.2, 111.2, 55.8, 55.7, 41.5, 38.9, 16.5; IR (neat) ν 3600−3000, 2936, 1703, 1514, 1260, 1140 cm^{-1}; HRMS (ESI M − H) m/z 223.0968, calcd for $C_{12}H_{15}O_4$ 223.0970.

(*S*)-2-(3,4-Dimethoxybenzyl)pent-4-enoic Acid (*S*-9b). Pale yellow oil: $[\alpha]_D$ +23.5° (c = 1.11, $CHCl_3$); the enantiomeric purity was determined by HPLC analysis (230 nm, 40 °C) t_R 22.8 min (major); t_R 14.2 min (minor) [CHIRALPAK IC (2.1 mm × 250 mm) (from Daicel Chemical Ind., Ltd.) hexane/*i*-PrOH, 80/20, 1.00 mL/min] as 97% ee.; ^1H NMR (500 MHz, $CDCl_3$) δ 6.78 (d, J = 8.1 Hz, 1 H), 6.74−6.71 (m, 2 H), 5.79 (ddt, J = 17.1, 10.1, 7.0 Hz, 1 H), 5.13−5.05 (m, 2 H), 3.85 (s, 6 H), 2.93 (td, J = 10.2, 4.9 Hz, 1 H), 2.84−2.68 (m, 2 H), 2.42−2.26 (m, 2 H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 181.1, 148.7, 147.5, 134.8, 131.3, 120.9, 117.4, 112.1, 111.1, 55.8, 55.7, 47.2, 36.9, 35.6; IR (neat) 3400−3000, 2936, 1705, 1260, 1140 cm^{-1}; HRMS (ESI M − H) m/z 249.1132, calcd for $C_{14}H_{17}O_4$ 249.1127.

(*R*)-2-(3,4-Dimethoxybenzyl)pent-4-enoic Acid (*R*-9b). Pale yellow oil: $[\alpha]_D$ −16.5° (c = 1.03, $CHCl_3$); the enantiomeric purity was determined by HPLC analysis (230 nm, 40 °C) t_R 12.3 min (major); t_R 24.5 min (minor) [CHIRALPAK IC (2.1 mm × 250 mm) (from Daicel Chemical Ind., Ltd.) hexane/*i*-PrOH, 80/20, 1.00 mL/min] as 98% ee; ^1H NMR (500 MHz, $CDCl_3$) δ 6.79 (d, J = 8.1 Hz, 1 H), 6.76−6.68 (m, 2 H), 5.79 (ddt, J = 17.1, 10.2, 7.0 Hz, 1 H), 5.16−5.04 (m, 2 H), 3.86 (s, 3 H), 3.85 (s, 3 H), 2.98−2.90 (m, 1 H), 2.79−2.72 (m, 2 H), 2.41−2.26 (m, 2 H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 180.9, 148.6, 147.5, 134.8, 131.2, 120.8, 117.3, 112.0, 111.0, 55.7, 55.6, 47.1, 36.9, 35.5; IR (neat) ν 3400−3000, 2936, 1732, 1705, 1236 cm^{-1}; HRMS (ESI M − H) m/z 249.1130, calcd for $C_{14}H_{17}O_4$ 249.1127.

(*S*)-2-Benzyl-3-(3,4-dimethoxyphenyl)propanoic Acid (*S*-9c). Pale yellow oil: $[\alpha]_D$ +5.8° (c = 1.17, $CHCl_3$); the enantiomeric purity was determined by HPLC analysis (230 nm, 40 °C) t_R 27.7 min (major); t_R 33.6 min (minor) [CHIRALPAK IC (2.1 mm × 250 mm) (from Daicel Chemical Ind., Ltd.) hexane/*i*-PrOH, 82/18, 0.70 mL/min] as >99% ee; ^1H NMR (500 MHz, $CDCl_3$) δ 7.31−7.15 (m, 5 H), 6.77 (d, J = 8.2 Hz, 1 H), 6.71 (dd, J = 8.1, 2.0 Hz, 1 H), 6.67 (d, J = 1.9 Hz, 1 H), 3.85 (s, 3 H), 3.83 (s, 3 H), 3.11−2.90 (m, 3 H), 2.88−2.64 (m, 2 H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 181.0, 148.8, 147.7, 138.8, 131.3, 128.9, 128.5, 126.5, 120.9, 112.1, 111.3, 55.8, 55.8, 49.4, 37.6, 37.4; IR (neat) 3300, 3000, 2936, 1705, 1260, 727 cm^{-1}; HRMS (ESI M − H) m/z 299.1294, calcd for $C_{18}H_{19}O_4$ 299.1283.

(*R*)-2-Benzyl-3-(3,4-dimethoxyphenyl)propanoic Acid (*R*-9c). Colorless oil: $[\alpha]_D$ −6.2° (c = 0.98, $CHCl_3$); the enantiomeric purity was determined by HPLC analysis (230 nm, 40 °C) t_R 31.4 min (major); t_R 28.4 min (minor) [CHIRALPAK IC (2.1 mm × 250 mm) (from Daicel Chemical Ind., Ltd.) hexane/*i*-PrOH, 82/18, 0.70 mL/min] as >99% ee; ^1H NMR (500 MHz, $CDCl_3$) δ 7.31−7.15 (m, 5 H), 6.77 (d, J = 8.2 Hz, 1 H), 6.71 (dd, J = 8.1, 2.0 Hz, 1 H), 6.67 (d, J = 1.9 Hz, 1 H), 3.85 (s, 3 H), 3.83 (s, 3 H), 2.97−2.93 (m, 3 H), 2.84−2.74 (m, 2 H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 181.0, 148.8, 147.6, 138.8, 131.2, 128.9, 128.5, 126.5, 120.9, 112.1, 111.2, 55.8, 55.8, 49.4, 37.6, 37.4; IR (neat) ν 3500−3000, 2936, 1705, 1260, 1028 cm^{-1}; HRMS (ESI M − H) m/z 299.1299, calcd for $C_{18}H_{19}O_4$ 299.1283.

Preparation of (*S*)-7,8-Dimethoxy-2,4-dimethyl-4,5-dihydro-1*H*-benzo[c]azepin-3(2*H*)-one (*S*-3a). A solution of **9a** (0.116 g, 0.516 mmol) and $SOCl_2$ (0.11 mL, 1.5 mmol) in THF (5 mL) was heated at reflux for 4 h. THF and excess amounts of $SOCl_2$ were then evaporated under reduced pressure. CH_2Cl_2 (5 mL) was added to the residue, and this solution was added slowly to a biphasic mixture of

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CH_2Cl_2 (3 mL), saturated aqueous $NaHCO_3$ (3 mL), and an aqueous solution of $MeNH_2$ (40%, 0.20 mL, 2.3 mmol) at 0 °C. This reaction mixture was stirred for 2 h. Saturated aqueous $NaHCO_3$ (5 mL) was added to the mixture, and the reaction mixture was extracted with CH_2Cl_2 (10 mL × 3). The organic phases were combined, dried over Na_2SO_4, and filtered. The filtrate was then concentrated under reduced pressure to give *N*-methyl-propanamide (0.127 g), which was used for the next step without further purification.

A solution of *N*-methyl-propanamide (0.091 g) paraformaldehyde (0.047 g, 1.58 mmol), and trifluoroacetic acid (0.3 mL, 3.9 mmol) in CH_2Cl_2 (8 mL) was stirred at room temperature for 18 h. Saturated aqueous $NaHCO_3$ (20 mL) was then added to the reaction mixture, and the resulting biphasic mixture was extracted with CH_2Cl_2 (10 mL × 3). The organic phases were combined, dried over Na_2SO_4, and filtered. The filtrate was then concentrated under reduced pressure, and the residue was purified by flash chromatography (silica gel/hexane then hexane/EtOAc 1:3) to give ***S*-3a** in 62% yield (0.058 g, 0.23 mmol). White solid: mp 197.5−198.0 °C; $[\alpha]_D$ +100.7° (*c* = 1.01, $CHCl_3$); the enantiomeric purity was determined by HPLC analysis (230 nm, 40 °C) t_R 18.6 min (major); t_R 16.7 min (minor) [CHIRALPAK IC (2.1 mm × 250 mm) (from Daicel Chemical Ind., Ltd.) hexane/*i*-PrOH, 60/40, 1.00 mL/min] as 90% ee; ^{1}H NMR (500 MHz, $CDCl_3$) δ 6.60 (s, 1 H), 6.56 (s, 1 H), 5.17 (d, *J* = 16.3 Hz, 1 H), 3.87 (s, 3 H), 3.84 (s, 3 H), 3.72 (d, *J* = 16.4 Hz, 1 H), 3.45−3.34 (m, 1 H), 3.05 (s, 3 H), 2.95 (dd, *J* = 17.1, 4.1 Hz, 1 H), 2.84 (dd, *J* = 17.1, 13.0 Hz, 1 H), 1.25 (d, *J* = 6.5 Hz, 3 H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 175.6, 148.4, 146.5, 129.7, 126.2, 113.5, 111.9, 56.1, 56.0, 53.7, 37.7, 35.3, 34.8, 17.6; IR ($CHCl_3$) ν 2930, 1647, 1524, 1256, 1107 cm^{-1}. Anal. Calcd. for $C_{14}H_{19}NO_3$: C, 67.45; H, 7.68; N, 5.62. Found: C, 67.24; H, 7.71; N, 5.66.

Other optically active compounds **3** were prepared in a similar manner.

(*R*)-7,8-Dimethoxy-2,4-dimethyl-4,5-dihydro-1*H*-benzo[c]-azepin-3(2*H*)-one (*R*-3a). White solid: mp 197.5−198.0 °C; $[\alpha]_D$ −122.2° (*c* = 1.07, $CHCl_3$); the enantiomeric purity was determined by HPLC analysis (230 nm, 40 °C) t_R 16.6 min (major); t_R 18.5 min (minor) [CHIRALPAK IC (2.1 mm × 250 mm) (from Daicel Chemical Ind., Ltd.) hexane/*i*-PrOH, 60/40, 1.00 mL/min] as 88% ee; ^{1}H NMR (500 MHz, $CDCl_3$) δ 6.60 (s, 1 H), 6.56 (s, 1 H), 5.17 (d, *J* = 16.3 Hz, 1 H), 3.87 (s, 3 H), 3.84 (s, 3 H), 3.72 (d, *J* = 16.4 Hz, 1 H), 3.38 (tt, *J* = 12.9, 6.4 Hz, 1 H), 3.05 (s, 3 H), 2.95 (dd, *J* = 17.0, 3.9 Hz, 1 H), 2.84 (dd, *J* = 17.1, 12.9 Hz, 1 H), 1.25 (d, *J* = 6.5 Hz, 3 H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 175.6, 148.4, 146.5, 129.7, 126.2, 113.5, 111.9, 56.1, 56.0, 53.7, 37.8, 35.3, 34.8, 17.6; IR ($CHCl_3$) ν 2930, 1647, 1524, 1256, 1211 cm^{-1}. Anal. Calcd. for $C_{14}H_{19}NO_3$: C, 67.45; H, 7.68; N, 5.62. Found: C, 67.27; H, 7.70; N, 5.63.

(*S*)-2-ethyl-7,8-Dimethoxy-4-methyl-4,5-dihydro-1*H*-benzo-[c]azepin-3(2*H*)-one (*S*-3g). White solid: mp 132.7−133.2 °C; $[\alpha]_D$ +103.7° (*c* = 1.15, $CHCl_3$); the enantiomeric purity was determined by HPLC analysis (230 nm, 40 °C) t_R 9.7 min (major); t_R 11.4 min (minor) [CHIRALPAK IC (2.1 mm × 250 mm) (from Daicel Chemical Ind., Ltd.) hexane/*i*-PrOH, 92/8, 1.00 mL/min] as 89% ee; ^{1}H NMR (500 MHz, $CDCl_3$) δ 6.59 (s, 1 H), 6.56 (s, 1 H), 5.10 (d, *J* = 16.3 Hz, 1 H), 3.87 (s, 3 H), 3.84 (s, 3 H), 3.79 (d, *J* = 16.5 Hz, 1 H), 3.54 (dd, *J* = 7.1, 2.0 Hz, 1 H), 3.51 (dd, *J* = 7.1, 1.9 Hz, 1 H), 3.35 (tt, *J* = 12.8, 6.5 Hz, 1 H), 2.93 (dd, *J* = 17.1, 4.2 Hz, 1 H), 2.86 (dd, *J* = 17.0, 12.7 Hz, 1 H), 1.25 (d, *J* = 6.5 Hz, 3 H), 1.07 (t, *J* = 7.2 Hz, 3 H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 175.1, 148.3, 146.6, 129.7, 126.9, 113.4, 111.6, 56.1, 56.0, 51.6, 42.7, 37.8, 34.8, 17.6, 13.7; IR ($CHCl_3$) ν 2972, 1643, 1520, 1462, 1252, 1202, 743 cm^{-1}; HRMS (ESI M + H) *m*/*z* 264.1598, calcd for $C_{15}H_{22}NO_3$ 264.1600.

(*R*)-2-Ethyl-7,8-dimethoxy-4-methyl-4,5-dihydro-1*H*-benzo-[c]azepin-3(2*H*)-one (*R*-3g). White solid: mp 132.7−133.2 °C; $[\alpha]_D$ −116.0° (*c* = 0.98, $CHCl_3$); the enantiomeric purity was determined by HPLC analysis (230 nm, 40 °C) t_R 11.6 min (major); t_R 9.8 min (minor) [CHIRALPAK IC (2.1 mm × 250 mm) (from Daicel Chemical Ind., Ltd.) hexane/*i*-PrOH, 92/8, 1.00 mL/min] as 89% ee; ^{1}H NMR (500 MHz, $CDCl_3$) δ 6.59 (s, 1 H), 6.56 (s, 1 H), 5.10 (d, *J* = 16.4 Hz, 1 H), 3.87 (s, 3 H), 3.84 (s, 3 H), 3.79 (d, *J* = 16.5 Hz, 1 H), 3.54 (dd, *J* = 7.2, 2.1 Hz, 1 H), 3.51 (dd, *J* = 7.1, 2.1 Hz, 1 H), 3.35 (tt, *J* = 13.0, 6.5 Hz, 1 H), 2.93 (dd, *J* = 17.1, 4.0 Hz, 1 H), 2.86 (dd, *J* = 17.1, 12.5 Hz, 1 H), 1.25 (d, *J* = 6.5 Hz, 3 H), 1.07 (t, *J* = 7.2 Hz, 3 H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 175.0, 148.3, 146.6, 129.7, 126.9, 113.3, 111.6, 56.1, 55.9, 51.6, 42.7, 37.8, 34.8, 17.6, 13.6; IR ($CHCl_3$) ν 2970, 1645, 1522, 1252 cm^{-1}. Anal. Calcd. for $C_{15}H_{21}NO_3$: C, 68.42; H, 8.04; N, 5.32. Found: C, 68.09; H, 8.05; N, 5.28.

(*S*)-7,8-Dimethoxy-4-methyl-2-propyl-4,5-dihydro-1*H*-benzo[c]azepin-3(2*H*)-one (*S*-3s). Pale yellow oil: $[\alpha]_D$ +91.4° (*c* = 0.98, $CHCl_3$); the enantiomeric purity was determined by HPLC analysis (230 nm, 40 °C) t_R 11.5 min (major); t_R 14.0 min (minor) [CHIRALPAK AD (2.1 mm × 250 mm) (from Daicel Chemical Ind., Ltd.) hexane/*i*-PrOH, 94/6, 1.00 mL/min] as 91% ee; ^{1}H NMR (500 MHz, $CDCl_3$) δ 6.59 (s, 1 H), 6.55 (s, 1 H), 5.11 (d, *J* = 16.3 Hz, 1 H), 3.86 (s, 3 H), 3.84 (s, 3H), 3.77 (d, *J* = 16.5 Hz, 1 H), 3.53−3.47 (m, 1 H), 3.41−3.31 (m, 2 H), 2.93 (dd, *J* = 16.9, 4.5 Hz, 1 H), 2.86 (dd, *J* = 17.1, 12.5 Hz, 1 H), 1.53−1.44 (m, 2 H), 1.25 (d, *J* = 6.5 Hz, 3 H), 0.81 (t, *J* = 7.4 Hz, 3 H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 174.8, 147.8, 146.1, 129.2, 126.5, 113.0, 111.4, 55.6, 55.4, 51.5, 49.1, 37.3, 34.3, 21.2, 17.1, 10.8; IR (neat) ν 2934, 1641, 1196, 907 cm^{-1}; HRMS (ESI M + H) *m*/*z* 278.1762, calcd for $C_{16}H_{24}NO_3$ 278.1756.

(*R*)-7,8-Dimethoxy-4-methyl-2-propyl-4,5-dihydro-1*H*-benzo[c]azepin-3(2*H*)-one (*R*-3s). Pale yellow oil: $[\alpha]_D$ −91.2° (*c* = 1.02, $CHCl_3$); the enantiomeric purity was determined by HPLC analysis (230 nm, 40 °C) t_R 13.6 min (major); t_R 11.0 min (minor) [CHIRALPAK AD (2.1 mm × 250 mm) (from Daicel Chemical Ind., Ltd.) hexane/*i*-PrOH, 94/6, 1.00 mL/min] as 89% ee; ^{1}H NMR (500 MHz, $CDCl_3$) δ 6.59 (s, 1 H), 6.55 (s, 1 H), 5.11 (d, *J* = 16.3 Hz, 1 H), 3.87 (s, 3 H), 3.84 (s, 3 H), 3.77 (d, *J* = 16.5 Hz, 1 H), 3.53−3.47 (m, 1 H), 3.41−3.32 (m, 2 H), 2.93 (dd, *J* = 17.0, 4.2 Hz, 1 H), 2.86 (dd, *J* = 17.1, 12.5 Hz, 1 H), 1.54−1.44 (m, 1 H), 1.25 (d, *J* = 6.5 Hz, 3 H), 0.81 (t, *J* = 7.4 Hz, 3 H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 175.2, 148.0, 146.3, 129.4, 126.6, 113.1, 111.5, 55.8, 55.7, 51.7, 49.4, 37.5, 34.5, 21.4, 17.3, 11.0; IR (neat) ν 2933, 1640, 1520, 1196 cm^{-1}; HRMS (ESI M + H) *m*/*z* 278.1758, calcd for $C_{16}H_{24}NO_3$ 278.1756.

(*S*)-4-Allyl-7,8-dimethoxy-2-methyl-4,5-dihydro-1*H*-benzo-[c]azepin-3(2*H*)-one (*S*-3t). White solid: mp 123.5−124.0 °C; $[\alpha]_D$ +93.9° (*c* = 1.09, $CHCl_3$); the enantiomeric purity was determined by HPLC analysis (230 nm, 40 °C) t_R 11.0 min (major); t_R 12.7 min (minor) [CHIRALPAK AD (2.1 mm × 250 mm) (from Daicel Chemical Ind., Ltd.) hexane/*i*-PrOH, 90/10, 1.00 mL/min] as 97% ee; ^{1}H NMR (500 MHz, $CDCl_3$) δ 6.61 (s, 1 H), 6.56 (s, 1 H), 5.95−5.85 (m, 1 H), 5.20−5.11 (m, 2 H), 5.07 (d, *J* = 10.2 Hz, 1 H), 3.87 (s, 3 H), 3.84 (s, 3 H), 3.73 (d, *J* = 16.4 Hz, 1 H), 3.29 (ddd, *J* = 12.9, 11.4, 6.7 Hz, 1 H), 3.05 (s, 3 H), 3.01 (dd, *J* = 17.0, 3.8 Hz, 1 H), 2.79 (dd, *J* = 17.0, 13.2 Hz, 1 H), 2.75−2.68 (m, 1 H), 2.22−2.15 (m, 1 H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 174.2, 148.1, 146.2, 136.4, 129.0, 125.8, 116.3, 113.3, 111.8, 55.7, 55.6, 53.2, 39.6, 36.0, 34.8, 34.7; IR ($CHCl_3$) ν 2936, 1643, 1252, 909 cm^{-1}. Anal. Calcd. for $C_{16}H_{21}NO_3$: C, 69.79; H, 7.69; N, 5.09. Found: C, 69.51; H, 7.82; N, 5.03.

(*R*)-4-Allyl-7,8-dimethoxy-2-methyl-4,5-dihydro-1*H*-benzo-[c]azepin-3(2*H*)-one (*R*-3t). White solid: mp 123.5−124.0 °C; $[\alpha]_D$ −92.5° (*c* = 2.81, $CHCl_3$); the enantiomeric purity was determined by HPLC analysis (230 nm, 40 °C) t_R 13.1 min (major); t_R 11.3 min (minor) [CHIRALPAK AD (2.1 mm × 250 mm) (from Daicel Chemical Ind., Ltd.) hexane/*i*-PrOH, 90/10, 1.00 mL/min] as 96% ee; ^{1}H NMR (500 MHz, $CDCl_3$) δ 6.61 (s, 1 H), 6.56 (s, 1 H), 5.90 (dddd, *J* = 17.2, 10.2, 8.2, 5.7 Hz, 1 H), 5.18 (d, *J* = 17.0 Hz, 1 H), 5.14 (d, *J* = 18.5 Hz, 1 H), 5.08 (d, *J* = 10.1 Hz, 1 H), 3.87 (s, 3 H), 3.84 (s, 3 H), 3.73 (d, *J* = 16.4 Hz, 1 H), 3.29 (ddd, *J* = 13.2, 11.2, 6.7 Hz, 1 H), 3.05 (s, 3 H), 3.01 (dd, *J* = 17.0, 4.1 Hz, 1 H), 2.79 (dd, *J* = 17.1, 13.2 Hz, 1 H), 2.75−2.68 (m, 1 H), 2.22−2.15 (m, 1 H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 174.5, 148.3, 146.4, 136.6, 129.3, 126.0, 116.6, 113.5, 111.9, 56.0, 55.8, 53.5, 39.9, 36.2, 35.1, 35.0; IR ($CHCl_3$) ν 2936, 1643, 1252, 1206 cm^{-1}; HRMS (ESI M + H) *m*/*z* 276.1605, calcd for $C_{16}H_{22}NO_3$ 276.1600.

(*S*)-4-Allyl-2-ethyl-7,8-dimethoxy-4,5-dihydro-1*H*-benzo[c]-azepin-3(2*H*)-one (*S*-3u). Colorless oil: $[\alpha]_D$ +89.1° (*c* = 1.08, $CHCl_3$); the enantiomeric purity was determined by HPLC analysis (230 nm, 40 °C) t_R 9.2 min (major); t_R 10.6 min (minor) [CHIRALPAK AD (2.1 mm × 250 mm) (from Daicel Chemical

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Ind., Ltd.) hexane/*i*-PrOH, 92/8, 1.00 mL/min] as 97% ee; ^{1}H NMR (500 MHz, $CDCl_3$) δ 6.60 (s, 1 H), 6.56 (s, 1 H), 5.90 (dddd, J = 16.0, 10.1, 8.2, 5.7 Hz, 1 H), 5.17−5.05 (m, 3 H), 3.86 (s, 3 H), 3.84 (s, 3 H), 3.80 (d, J = 16.5 Hz, 1 H), 3.52 (q, J = 7.1 Hz, 2 H), 3.25 (dt, J = 17.5, 6.7 Hz, 1 H), 3.01 (dd, J = 17.1, 3.3 Hz, 1 H), 2.80 (dd, J = 17.0, 13.3 Hz, 1 H), 2.75−2.67 (m, 1 H), 2.23−2.14 (m, 1 H), 1.07 (t, J = 7.2 Hz, 3 H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 173.9, 148.1, 146.4, 136.5, 129.2, 126.7, 116.4, 113.3, 111.5, 55.9, 55.7, 51.3, 42.4, 39.8, 36.0, 34.8, 13.4; IR (neat) ν 2934, 1640, 1120, 909 cm^{-1}; HRMS (ESI M + H) m/z 290.1774, calcd for $C_{17}H_{24}NO_3$ 290.1756.

(*R*)-4-Allyl-2-ethyl-7,8-dimethoxy-4,5-dihydro-1*H*-benzo[c]-azepin-3(2*H*)-one (*R*-3u). Colorless oil: $[\alpha]_D$ −87.7° (c = 3.09, $CHCl_3$); the enantiomeric purity was determined by HPLC analysis (230 nm, 40 °C) t_R 11.4 min (major); t_R 9.7 min (minor) [CHIRALPAK AD (2.1 mm × 250 mm) (from Daicel Chemical Ind., Ltd.) hexane/*i*-PrOH, 92/8, 1.00 mL/min] as 94% ee; ^{1}H NMR (500 MHz, $CDCl_3$) δ 6.60 (s, 1 H), 6.56 (s, 1 H), 5.90 (dddd, J = 17.1, 10.1, 8.2, 5.7 Hz, 1 H), 5.17−5.05 (m, 3 H), 3.86 (s, 3 H), 3.84 (s, 3 H), 3.80 (d, J = 16.5 Hz, 1 H), 3.53 (q, J = 7.2 Hz, 2 H), 3.25 (dtd, J = 11.0, 6.8, 4.1 Hz, 1 H), 3.02 (dd, J = 17.0, 3.3 Hz, 1 H), 2.80 (dd, J = 17.1, 13.2 Hz, 1 H), 2.71 (dtt, J = 14.6, 6.0, 1.5 Hz, 1 H), 2.19 (dt, J = 14.6, 7.8 Hz, 1 H), 1.07 (t, J = 7.2 Hz, 3 H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 174.0, 148.2, 146.5, 136.8, 129.4, 126.8, 116.6, 113.4, 111.6, 56.0, 55.8, 51.5, 42.6, 39.9, 36.2, 35.0, 13.5; IR (neat) ν 2934, 1640, 1200, 912 cm^{-1}; HRMS (ESI M + H) m/z 290.1755, calcd for $C_{17}H_{24}NO_3$ 290.1756.

(*S*)-4-Allyl-7,8-dimethoxy-2-propyl-4,5-dihydro-1*H*-benzo-[c]azepin-3(2*H*)-one (*S*-3v). Pale yellow oil: $[\alpha]_D$ +72.5° (c = 1.69, $CHCl_3$); the enantiomeric purity was determined by HPLC analysis (230 nm, 40 °C) t_R 10.7 min (major); t_R 12.6 min (minor) [CHIRALPAK AD (2.1 mm × 250 mm) (from Daicel Chemical Ind., Ltd.) hexane/*i*-PrOH, 94/6, 1.00 mL/min] as 96% ee; ^{1}H NMR (500 MHz, $CDCl_3$) δ 6.60 (s, 1 H), 6.55 (s, 1 H), 5.95−5.85 (m, 1 H), 5.13 (d, J = 18.3 Hz, 1 H), 5.11 (d, J = 16.4 Hz, 1 H), 5.07 (d, J = 10.1 Hz, 1 H), 3.86 (s, 3 H), 3.84 (s, 3 H), 3.78 (d, J = 16.5 Hz, 1 H), 3.54−3.46 (m, 1 H), 3.41−3.33 (m, 1 H), 3.26 (ddd, J = 13.0, 10.9, 6.6 Hz, 1 H), 3.01 (dd, J = 17.1, 3.2 Hz, 1 H), 2.81 (dd, J = 17.0, 13.3 Hz, 1 H), 2.76−2.67 (m, 1 H), 2.22−2.14 (m, 1 H), 1.53−1.44 (m, 2 H), 0.81 (t, J = 7.4 Hz, 3 H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 174.1, 148.0, 146.3, 136.4, 129.1, 126.5, 116.3, 113.2, 111.5, 55.7, 55.5, 51.6, 49.2, 39.7, 35.9, 34.7, 21.3, 10.9; IR (neat) ν 2936, 1643, 907, 725 cm^{-1}; HRMS (ESI M + H) m/z 304.1927, calcd for $C_{18}H_{26}NO_3$ 304.1913.

(*R*)-4-Allyl-7,8-dimethoxy-2-propyl-4,5-dihydro-1*H*-benzo-[c]azepin-3(2*H*)-one (*R*-3v). Pale yellow oil: $[\alpha]_D$ −75.2° (c = 1.04, $CHCl_3$); the enantiomeric purity was determined by HPLC analysis (230 nm, 40 °C) t_R 12.3 min (major); t_R 10.4 min (minor) [CHIRALPAK AD (2.1 mm × 250 mm) (from Daicel Chemical Ind., Ltd.) hexane/*i*-PrOH, 94/6, 1.00 mL/min] as 96% ee; ^{1}H NMR (500 MHz, $CDCl_3$) δ 6.60 (s, 1 H), 6.55 (s, 1 H), 5.94−5.85 (m, 1 H), 5.13 (dd, J = 17.1, 1.1 Hz, 1 H), 5.11 (d, J = 16.4 Hz, 1 H), 5.07 (d, J = 10.2 Hz, 1 H), 3.86 (s, 3 H), 3.84 (s, 3 H), 3.78 (d, J = 16.5 Hz, 1 H), 3.54−3.46 (m, 1 H), 3.41−3.34 (m, 1 H), 3.26 (ddd, J = 13.0, 10.9, 6.7 Hz, 1 H), 3.01 (dd, J = 17.1, 3.3 Hz, 1 H), 2.81 (dd, J = 17.0, 13.3 Hz, 1 H), 2.75−2.68 (m, 1 H), 2.22−2.14 (m, 1 H), 1.53−1.44 (m, 1 H), 0.81 (t, J = 7.4 Hz, 3 H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 174.2, 148.0, 146.3, 136.5, 129.1, 126.5, 116.3, 113.2, 111.5, 55.8, 55.6, 51.6, 49.3, 39.7, 35.9, 34.8, 21.3, 10.9; IR (neat) ν 2934, 1641, 1196, 910 cm^{-1}; HRMS (ESI M + H) m/z 304.1921, calcd for $C_{18}H_{26}NO_3$ 304.1913.

(*S*)-4-Benzyl-7,8-dimethoxy-2-methyl-4,5-dihydro-1*H*-benzo[c]azepin-3(2*H*)-one (*S*-3f). Colorless oil: $[\alpha]_D$ +140.1° (c = 1.01, $CHCl_3$); the enantiomeric purity was determined by HPLC analysis (230 nm, 40 °C) t_R 29.5 min (major); t_R 38.9 min (minor) [CHIRALPAK ID (2.1 mm × 250 mm) (from Daicel Chemical Ind., Ltd.) hexane/*i*-PrOH, 80/20, 1.00 mL/min] as 94% ee; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.34−7.26 (m, 4 H), 7.25−7.15 (m, 1 H), 6.54 (s, 1 H), 6.53 (s, 1 H), 5.16 (d, J = 16.3 Hz, 1 H), 3.85 (s, 3 H), 3.81 (s, 3 H), 3.70 (d, J = 16.4 Hz, 1 H), 3.54 (dq, J = 7.7, 5.5 Hz, 1 H), 3.35 (dd, J = 14.0, 5.8 Hz, 1 H), 3.05 (s, 3 H), 2.97 (dd, J = 17.0, 4.0 Hz, 1 H), 2.85 (dd, J = 16.8, 13.2 Hz, 1 H), 2.68 (dd, J = 14.0, 8.0 Hz, 1 H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 174.4, 148.2, 146.3, 140.1, 129.2, 129.1, 128.2, 126.0, 125.9, 113.5, 111.9, 55.9, 55.7, 53.4, 41.9, 37.8, 35.0, 34.8; IR (neat) ν 2936, 1645, 1252, 1207 cm^{-1}; HRMS (ESI M + H) m/z 326.1764, calcd for $C_{20}H_{24}NO_3$ 326.1756.

(*R*)-4-Benzyl-7,8-dimethoxy-2-methyl-4,5-dihydro-1*H*-benzo[c]azepin-3(2*H*)-one (*R*-3f). Colorless oil: $[\alpha]_D$ −138.4° (c = 0.99, $CHCl_3$); the enantiomeric purity was determined by HPLC analysis (230 nm, 40 °C) t_R 30.0 min (major); t_R 38.5 min (minor) [CHIRALPAK ID (2.1 mm × 250 mm) (from Daicel Chemical Ind., Ltd.) hexane/*i*-PrOH, 80/20, 1.00 mL/min] as 96% ee; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.33−7.26 (m, 4 H), 7.25−7.17 (m, 1 H), 6.54 (s, 1 H), 6.53 (s, 1 H), 5.16 (d, J = 16.3 Hz, 1 H), 3.85 (s, 3 H), 3.81 (s, 3 H), 3.70 (d, J = 16.4 Hz, 1 H), 3.61−3.47 (m, 1 H), 3.36 (dd, J = 14.0, 5.8 Hz, 1 H), 3.05 (s, 3 H), 2.97 (dd, J = 17.0, 4.1 Hz, 1 H), 2.85 (dd, J = 17.1, 13.1 Hz, 1 H), 2.69 (dd, J = 14.0, 8.0 Hz, 1 H); ^{13}C NMR (126 MHz,) δ 174.4, 148.2, 146.3, 140.1, 129.1, 129.1, 128.2, 126.0, 125.9, 113.5, 111.9, 55.9, 55.7, 53.4, 41.9, 37.8, 35.0, 34.8; IR (neat) ν 2936, 1643, 1252, 909 cm^{-1}; HRMS (ESI M + H) m/z 326.1754, calcd for $C_{20}H_{24}NO_3$ 326.1756.

(*S*)-4-Benzyl-2-ethyl-7,8-dimethoxy-4,5-dihydro-1*H*-benzo-[c]azepin-3(2*H*)-one (*S*-3l). Pale yellow oil: $[\alpha]_D$ +122.5° (c = 1.01, $CHCl_3$); the enantiomeric purity was determined by HPLC analysis (230 nm, 40 °C) t_R 32.8 min (major); t_R 29.0 min (minor) [CHIRALPAK IC (2.1 mm × 250 mm) (from Daicel Chemical Ind., Ltd.) hexane/*i*-PrOH, 80/20, 1.00 mL/min] as 98% ee; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.35−7.27 (m, 4 H), 7.24−7.15 (m, 1 H), 6.54 (s, 1 H), 6.53 (s, 1 H), 5.09 (d, J = 16.4 Hz, 1 H), 3.85 (s, 3 H), 3.80 (s, 3 H), 3.77 (d, J = 16.5 Hz, 1 H), 3.59−3.45 (m, 3 H), 3.36 (dd, J = 14.0, 5.5 Hz, 1 H), 2.95 (dd, J = 17.0, 3.8 Hz, 1 H), 2.85 (dd, J = 16.9, 13.0 Hz, 1 H), 2.69 (dd, J = 14.1, 8.3 Hz, 1 H), 1.07 (t, J = 7.2 Hz, 3 H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 174.0, 148.1, 146.4, 140.1, 129.2, 129.1, 128.2, 126.7, 126.0, 113.4, 111.5, 55.9, 55.7, 51.4, 42.6, 42.0, 37.8, 34.7, 13.4; IR (neat) ν 2934, 1643, 1200, 909 cm^{-1}; HRMS (ESI M + H) m/z 340.1912, calcd for $C_{21}H_{26}NO_3$ 340.1913.

(*R*)-4-Benzyl-2-ethyl-7,8-dimethoxy-4,5-dihydro-1*H*-benzo-[c]azepin-3(2*H*)-one (*R*-3l). Pale yellow oil: $[\alpha]_D$ −140.5° (c = 0.95, $CHCl_3$); the enantiomeric purity was determined by HPLC analysis (230 nm, 40 °C) t_R 29.0 min (major); t_R 33.0 min (minor) [CHIRALPAK IC (2.1 mm × 250 mm) (from Daicel Chemical Ind., Ltd.) hexane/*i*-PrOH, 80/20, 1.00 mL/min] as 98% ee; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.33−7.26 (m, 4 H), 7.24−7.17 (m, 1 H), 6.54 (s, 1 H), 6.53 (s, 1 H), 5.09 (d, J = 16.4 Hz, 1 H), 3.85 (s, 3 H), 3.81 (s, 3 H), 3.77 (d, J = 16.5 Hz, 1 H), 3.60−3.45 (m, 3 H), 3.36 (dd, J = 14.0, 5.6 Hz, 1 H), 2.95 (dd, J = 17.1, 3.4 Hz, 1 H), 2.85 (dd, J = 16.9, 12.9 Hz, 1 H), 2.69 (dd, J = 14.1, 8.3 Hz, 1 H), 1.07 (t, J = 7.2 Hz, 3 H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 173.9, 148.1, 146.4, 140.1, 129.2, 129.1, 128.2, 126.7, 126.0, 113.5, 111.6, 55.9, 55.7, 51.3, 42.6, 42.0, 37.8, 34.7, 13.4; IR (neat) ν 2934, 1641, 1200, 909 cm^{-1}; HRMS (ESI M + H) m/z 340.1911, calcd for $C_{21}H_{26}NO_3$ 340.1913.

(*S*)-4-Benzyl-7,8-dimethoxy-2-propyl-4,5-dihydro-1*H*-benzo-[c]azepin-3(2*H*)-one (*S*-3w). Pale yellow oil: $[\alpha]_D$ +122.1° (c = 1.03, $CHCl_3$); the enantiomeric purity was determined by HPLC analysis (230 nm, 40 °C) t_R 27.4 min (major); t_R 23.5 min (minor) [CHIRALPAK IC (2.1 mm × 250 mm) (from Daicel Chemical Ind., Ltd.) hexane/*i*-PrOH, 80/20, 1.00 mL/min] as 98% ee; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.32−7.27 (m, 4 H), 7.24−7.16 (m, 1 H), 6.53 (s, 2 H), 5.11 (d, J = 16.4 Hz, 1 H), 3.85 (s, 3 H), 3.81 (s, 3 H), 3.75 (d, J = 16.5 Hz, 1 H), 3.58−3.45 (m, 2 H), 3.39−3.30 (m, 2 H), 2.95 (dd, J = 17.0, 3.6 Hz, 1 H), 2.86 (dd, J = 16.7, 13.2 Hz, 1 H), 2.69 (dd, J = 14.0, 8.1 Hz, 1 H), 1.53−1.43 (m, 1 H), 0.80 (t, J = 7.4 Hz, 3 H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 174.0, 147.9, 146.2, 139.9, 128.9, 128.8, 128.0, 126.4, 125.7, 113.2, 111.4, 55.7, 55.4, 51.5, 49.2, 41.7, 37.6, 34.6, 21.3, 10.9; IR (neat) ν 2936, 1645, 907, 725 cm^{-1}; HRMS (ESI M + H) m/z 354.2043, calcd for $C_{22}H_{28}NO_3$ 354.2069.

(*R*)-4-Benzyl-7,8-dimethoxy-2-propyl-4,5-dihydro-1*H*-benzo[c]azepin-3(2*H*)-one (*R*-3w). Pale yellow oil: $[\alpha]_D$ −125.5° (c = 1.04, $CHCl_3$); the enantiomeric purity was determined by HPLC analysis (230 nm, 40 °C) t_R 23.5 min (major); t_R 27.8 min (minor) [CHIRALPAK IC (2.1 mm × 250 mm) (from Daicel Chemical Ind., Ltd.) hexane/*i*-PrOH, 80/20, 1.00 mL/min] as 99% ee; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.33−7.26 (m, 4 H), 7.24−7.16 (m, 1 H), 6.53 (s, 2

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H), 5.11 (d, J = 16.3 Hz, 1 H), 3.85 (s, 3 H), 3.81 (s, 3 H), 3.75 (d, J = 16.5 Hz, 1 H), 3.57−3.45 (m, 2 H), 3.39−3.31 (m, 1 H), 2.95 (dd, J = 17.1, 3.4 Hz, 1 H), 2.86 (dd, J = 17.0, 12.9 Hz, 1 H), 2.68 (dd, J = 14.1, 8.1 Hz, 1 H), 1.48 (h, J = 7.4 Hz, 2 H), 0.80 (t, J = 7.4 Hz, 3 H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 174.0, 147.9, 146.2, 140.0, 129.0, 128.9, 128.0, 126.5, 125.7, 113.2, 111.5, 55.7, 55.5, 51.5, 49.3, 41.8, 37.6, 34.6, 21.3, 10.9; IR (neat) ν 2936, 1643, 907, 725 cm^{-1}; HRMS (ESI M + H) m/z 354.2089, calcd for $C_{22}H_{28}NO_3$ 354.2069.

In Vitro Wound Healing Assay. HaCat cells (2.5×10^4 per well) were seeded in a 96-well plate and grown until they become confluent. Each monolayer was scratched with use of a 200-μL pipet tip to generate a cell-free zone (0.8−1 mm wide). After extensive washing with Dulbecco's modified Eagle's medium (DMEM), the cells were incubated for 24 h at 5% CO_2 and 37 °C with DMEM, containing various concentrations (0−30 μM) of compounds (final DMSO concentration of 0.1%). The cells were photographed immediately after wounding, the wounded area was marked on the base of the plate, and the same field was photographed again after incubation for 18 h. The migration of the cells into the wound area was then evaluated.

■ ASSOCIATED CONTENT

Ⓢ Supporting Information

Spectroscopic charts for compounds **2**−**9**. 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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