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Facile one-pot synthesis of (benzoxazol-2′-yl)bicyclo[2.2.2]octen-2-one derivatives

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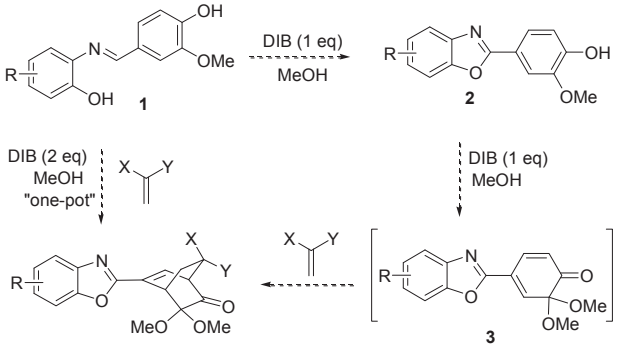
ABSTRACT

A simple and efficient one-pot synthesis of 5-(benzoxazol-2′-yl)bicyclo[2.2.2]octen-2-one derivatives from readily accessible starting materials has been demonstrated. The current protocol involves diacetoxyiodobenzene mediated domino oxidative cyclization–acetalization–Diels–Alder reaction.

1. Introduction

Organic compounds containing the benzoxazole scaffold belong to a significant class of heterocyclic compounds that are encountered in a number of natural products.[1] For example, benzoxazole core containing bicyclic systems calcimycin, cezomycin and routiennocin are isolated from the various strains of *Streptomyces*. and are found to act as good ionophore antibiotics.[2] Benzoxazole derivatives are found to have many applications in the field of medicinal chemistry. They act as estrogen receptor agonists,[3] melatonin receptor agonists,[4] anti tumor agents,[5] exhibit antimicrobial activities[6] and FAAH inhibitors.[7] These compounds are also used as herbicides like fenoxaprop and found to have applications in electronic devices,[8] photoluminescent dyes[9] and as sensors for metals,[10] due to their fluorescent properties. The wide spectrum of applications of benzoxazoles has fascinated the chemists to develop novel benzoxazole derivatives for various applications.[11,12]

Masked *o*-benzoquinones (MOBs), a class of 2,4-cyclohexadienones that can be transiently generated by the oxidative dearomatization of guaiacol derivatives[13,14] are useful synthons in organic synthesis. The bicyclic systems derived from the Diels–Alder reaction of these intermediates with various dienophiles are used as potential precursors in the synthesis of various complex natural products.[13,15,16] The MOB intermediates in the presence of Lewis acid are shown to be good acceptors in the reaction with electron-rich arenes to generate highly oxygenated unsymmetrical biaryls.[17] These cyclic dienones underwent conjugative addition with thiols under catalyst-free conditions to furnish unsymmetrical alkyl aryl/diaryl sulfides.[18] We have recently synthesized bicyclooctenone derivatives by the Diels–Alder reaction of relatively stable dienic 4-halo MOBs with various 2π-components.[19] In further investigation we envisaged the introduction of biologically significant benzoxazole core on the bicyclooctenone system by domino reaction. The strategy involves the sequential oxidative cyclization[20] of an aldimine **1** into the benzoxazol-2′-yl guaiacol **2**, oxidative dearomatization of **2** into MOB **3** and the Diels–Alder cycloaddition of **3** to provide the anticipated benzoxazolyl bicyclo



Scheme 1. Domino oxidative cyclization–acetalization–Diels–Alder strategy.

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[2.2.2]octenone derivatives (Scheme 1). Herein we report the one-pot synthesis of 5-(benzoxazol-2′-yl)bicyclo[2.2.2]octenone derivatives from easily accessible starting materials.

2. Results and discussions

Our studies began with the synthesis of aldimines from the readily available vanillin and *o*-aminophenol derivatives. Initially the aldimine **1a** was dissolved in methanol, and subjected to oxidation with 2.2 equiv of diacetoxyiodobenzene (DIB)[21] at room temperature. The in situ generated MOB has undergone self-dimerization in 4 h in the absence of external reactant to afford the corresponding Diels–Alder dimer **4a** in 79% yield. Of the eight possible isomers from the dimerization of substituted MOB **3a** provided single isomer **4a**. The assigned structure of this dimer is unambiguously confirmed by its single crystal X-ray analysis (Fig. 1).[22]

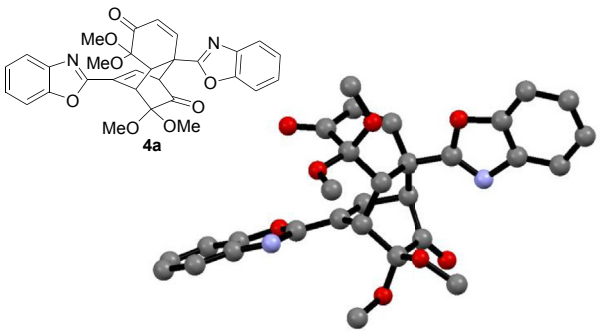


Fig. 1. Single crystal X-ray structure of **4a**.[22]

We were delighted with this event and proceeded further to carry out the reaction of aldimine **1a** with external dienophiles. Thus the reaction of **1a** with ethyl vinyl ether (5 equiv) in 5 mL of methanol in the presence of 2.2 equiv of DIB underwent smoothly to furnish the desired bicycloadduct **6a** in 82% yield via the Diels–Alder reaction of in situ generated MOB **3a** (R=H).

Though the result obtained was encouraging, we were curious to know whether the first step is oxidative cyclization or oxidative dearomatization. To understand the reaction sequence, we carried out the reaction with 1.1 equiv of oxidizing agent. The product formed in 10 min was isolated in 80% yield and its ^{1}H and ^{13}C NMR analysis revealed that the product was benzoxazole derivative **2a**. The product **2a** obtained in the initial step was oxidized further with DIB (1.1 equiv) in the presence of ethyl vinyl ether and methanol afforded the corresponding Diels–Alder adduct **6a** in 72% yield. As the overall chemical yield (58%) of **6a** obtained from the two individual steps is less than one-pot reaction (82%), we proceeded with one-pot synthesis of benzoxazolyl bicyclo[2.2.2]octenone derivatives. To further optimize the reaction conditions, several bases such as $NaHCO_3$, K_2CO_3, NEt_3 and $KHCO_3$ were tested. However, in all the cases only traces of benzoxazol-2′-yl guaiacol **2a** was observed from the ^{1}H NMR. At this juncture, we turned our focus on the quantity of dienophile. The reaction of **1a** was performed with 10 equiv of ethyl vinyl ether; and no appreciable change was noticed on the chemical yield. At higher amount (20 equiv) of styrene, the corresponding product **5a** was isolated in about 10% higher yield than that carried out with 10 equiv.

With the optimization conditions in hand, we advanced for uncovering the scope of this domino reaction. Several aldimines **1b**–**1e** bearing different substitutions on the aminophenol moiety were subjected to hypervalent iodine-mediated domino oxidative cyclization–acetalization–Diels–Alder protocol in methanol in the presence of dienophiles ethyl vinyl ether and styrene. The reaction proceeded smoothly to provide the bicyclic octenone adducts **5** and **6** (Table 1). We extended our investigations with electron-deficient dienophiles like methyl acrylate and methyl methacrylate. For this purpose, we performed the reaction of **1a** (0.5 mmol) with 2.2 equiv of DIB at rt in methanol in the presence of methyl acrylate (20 equiv). The reaction was found to be completed in 40 min and after purification by the silica gel column chromatography the corresponding bicycloadduct **7a** was obtained in 62% yield (Table 1). The generality of the cycloaddition of electron-deficient dienophiles in current strategy was also tested with MOBs derived from other aldimines. The bicyclic adducts **7** and **8** were obtained in relatively lower yields in comparison to the products derived from electron-rich ethyl vinyl ether (Table 1). Interestingly, the reaction of aldimine **1e** (R^1=Cl, R^2=H) derived from 2-amino-4-chlorophenol, with methyl acrylate and methyl methacrylate did not give any isolable products (Table 1). It appears that the MOB **3e** bearing chlorobenzoxazole moiety is not sufficiently electron-rich owing to the electron pulling nature of chlorine atom to drive the reaction with electron-deficient dienophiles used in this study.

The cyclic dienophiles—dihydrofuran and furan—were also used in the present protocol. The reaction of **1a** gave optimum results with 5 equiv of dihydrofuran and 20 equiv of furan. The reaction of aldimines **1a**–**e** with these dienophiles produced the corresponding adducts **9** and **10** in very high yields (Table 2).

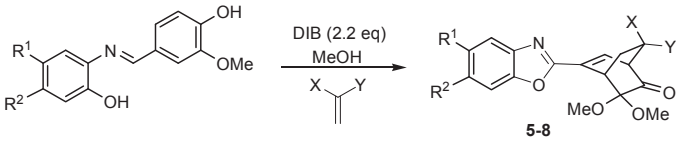
Each cycloadduct was obtained as racemic mixture of a single diastereomer. The structures of these Diels–Alder adducts were assigned based on the ^{1}H (500 MHz) and ^{13}C (125 MHz) NMR, DEPT and HRMS spectral analysis. In order to identify the chemical shifts of protons and carbon atoms, we have carried out ^{1}H–^{1}H decoupling experiments and 2D experiments such as ^{1}H–^{1}H COSY and HMQC. The protons H_a and H_d resonate in the range of δ 3.5–3.8 and 4.1–4.7 ppm, respectively. The coupling constants of H_d–H_e or H_d–H_f are observed predominantly in the range of J=2.5–3.5 Hz, which are in agreement with the assigned *ortho*-regiochemistry (Table 3).

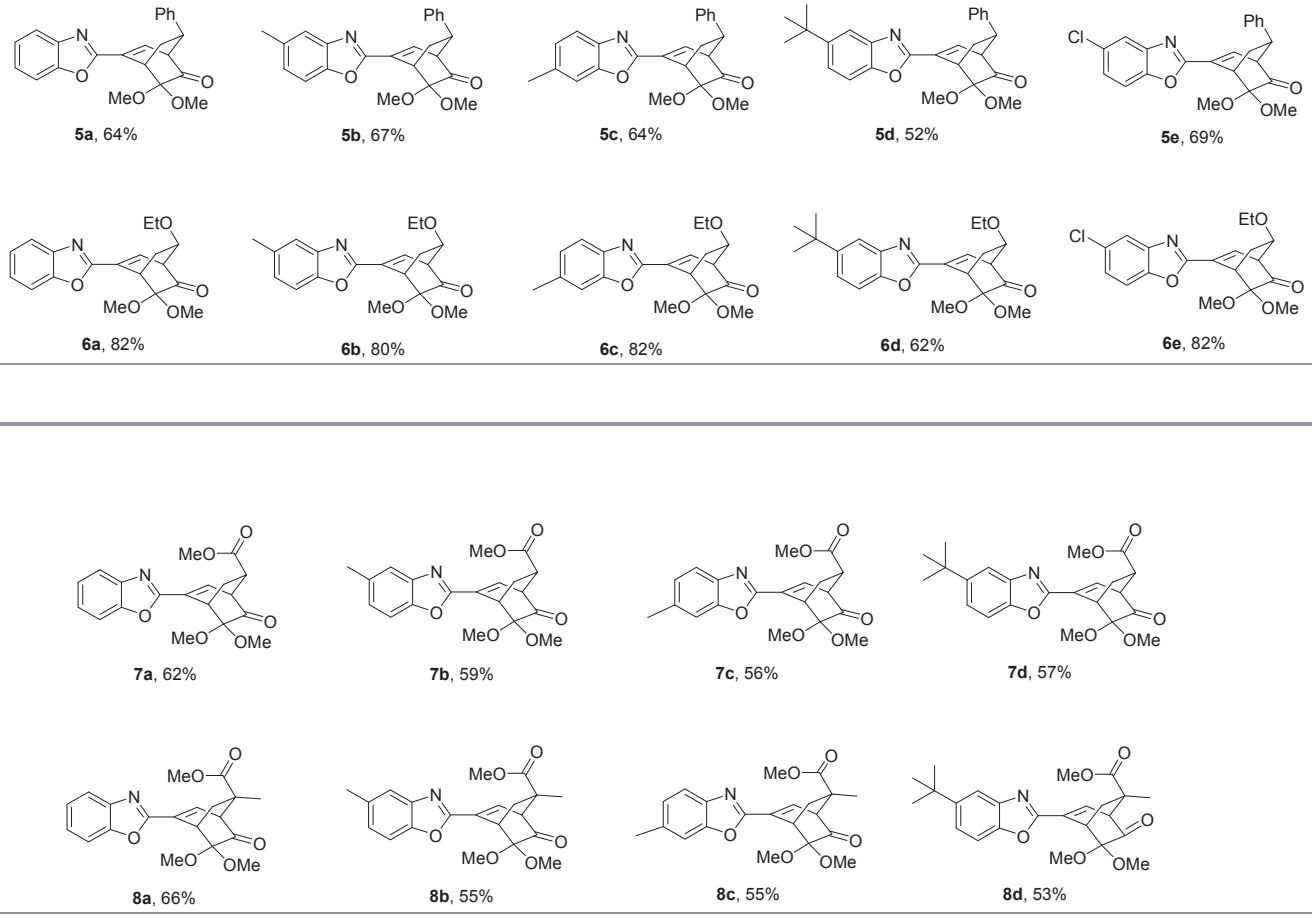
The proton H_f resonates in the range of δ 1.5–2.1 ppm and H_e resonate at downfield in the range of δ 2.4–2.7 ppm. The higher chemical shift of H_e may be attributed predominantly to the magnetic anisotropic effect of *exo*-methoxy group of ketal function, which is lying in its proximity. The coupling constants (J=6.0–7.0 Hz) between H_f–H_g, and those (J=8.5–10.5 Hz) between H_e–H_g reveals the *cis* relationship of the protons H_e and H_g, which confirms the assigned *endo*-stereochemistry.

In the ^{13}C NMR of the Diels–Alder adducts, the ring carbonyl carbon appears at around 200 ppm and the ketal quaternary carbon appears at around 93 ppm. Among the bridge-head carbons C_a (δ 55–57 ppm) and C_d (δ 39–40 ppm), the former, which is positioned next to the ring carbonyl resonates downfield. The cycloadducts exhibited IR absorptions at 1735–1745 cm^{-1}, a characteristic absorption of carbonyl function of bicyclo[2.2.2]octenones derived from MOBs. The selected ^{1}H and ^{13}C chemical shifts of some of the cycloadducts are shown in Fig. 2. The assigned regio- and stereoselectivities are further established by the single crystal X-ray analysis of the product **5e** (Fig. 3).[23] The regio-, stereo- and site-selectivity of the dimerization is in harmony with the literature precedents.[24]

In the initial step, the attack of lone pair of electrons of the imino nitrogen on the Lewis acidic trivalent iodine centre makes the adjacent carbon more electrophilic, making more susceptible for the attack of nucleophilic oxygen atom leading to the benzoxazoline intermediate **A** with concomitant elimination of acetic acid. The subsequent aromatization of dihydro oxazole ring takes place along with the elimination of acetic acid and iodobenzene to give benzoxazole derivative **2a**. Now, the attack of nucleophilic oxygen of methoxyphenol **2a** at the electrophilic iodine centre of DIB triggers acetalization by knocking acetic acid out and the addition of methanol either by associative pathway or by dissociative pathway leads to MOB **3a**. The nucleofugality of phenyliodanyl group helps the oxidation by two-electron reduction of iodine(III) centre to

Table 1
Scope of substrates[a]





[a]Reaction was carried out with aldimine **1** (0.5 mmol), a dienophile and 2.2 equiv. of DIB in 5 mL of methanol at rt for 20 min (40 min in case of electron-deficient dienophiles).

energetically preferable monovalent iodide i.e., iodobenzene. The dienone **3a** undergoes the [4+2] cycloaddition with the dienophile to deliver the desired cycloadduct (Scheme 2).

3. Conclusions

In summary, an efficient hypervalent iodine mediated domino oxidative cyclization–acetalization–Diels–Alder protocol for the title compounds bearing diverse functionalities obtained from this rapid synthesis shall be seen as overall yields of three steps. We are currently pursuing the application of domino reactions of benzoquinone monoketals in our laboratory.

4. Experimental section

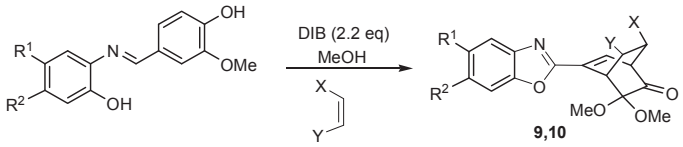
4.1. General information

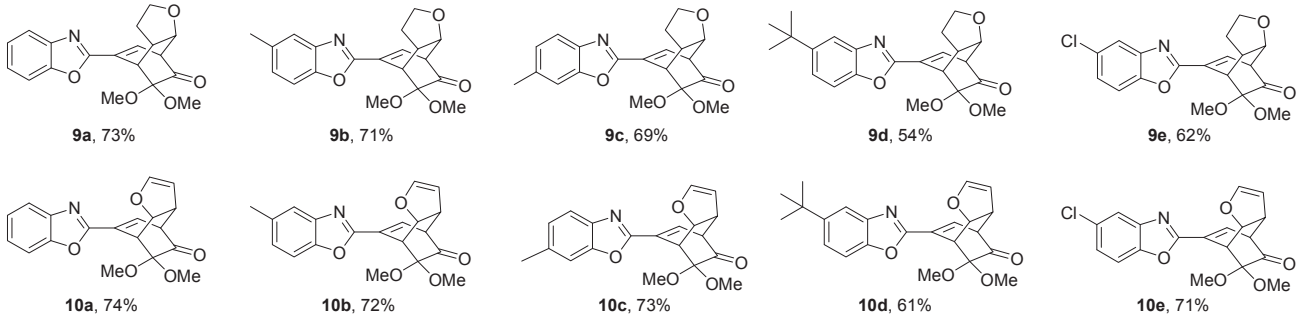
Unless otherwise noted, chemicals were purchased at the highest purity grade available and were used without further purification. IR spectra of the compounds are expressed as wavenumbers (cm^{-1}). NMR spectra were recorded in $CDCl_3$ using TMS as an internal standard. Chemical shifts of ^1H NMR spectra are given in parts per million with respect to TMS, and coupling constants (J) are reported in hertz. The signals from solvent $CDCl_3$ at 7.26 and 77.0 ppm were set as the reference peaks in ^1H NMR and ^{13}C NMR spectra, respectively. The following abbreviations are used to explain the multiplicities: s=singlet, d=doublet, dd=doublet of doublets, dt=doublet of triplets, t=triplet, q=quartet, m=multiplet, br=broad. HRMS was performed on a micrOTOF-Q II mass spectrometer.

4.2. General procedure

To a solution of aldimine **1** (0.5 mmol) and a dienophile [ethyl vinyl ether/dihydrofuran (5 equiv) or styrene/furan/methyl acrylate/methyl methacrylate (20 equiv)] in MeOH (5 mL), DIB (177 mg, 0.55 mmol) was added portion-wise at rt over a period of 5 min, then allowed to stir for 5 min. After complete disappearance of starting material as shown by TLC, another portion of DIB (177 mg, 0.55 mmol) was added over a period of 5 min and allowed to stir for

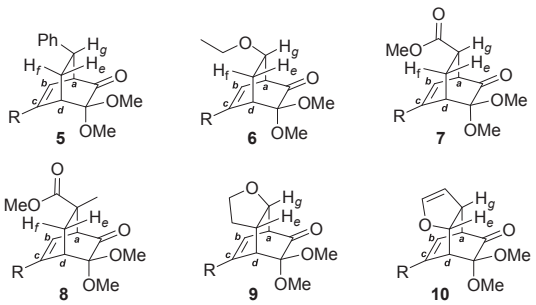
Table 2
Scope of substrates[a]





[a]Reaction was carried out with aldimine **1** (0.5 mmol), a dienophile (2.5 mmol of dihydrofuran or 10 mmol of furan) and 2.2 equiv. of DIB in 5 mL of methanol at rt for 20 min.

Table 3
Selected coupling constants (*J* in Hz) of the adducts **5**–**10**



S.No.	Adduct	*J* (Hz)			
		H_e–H_g	H_f–H_g	H_d–H_e	H_d–H_f
1	**5a**	8.5	6.5	3.0	2.5
2	**5b**	9.5	7.0	3.0	2.5
3	**5c**	9.5	7.0	3.0	3.0
4	**5d**	9.5	6.5	3.0	2.5
5	**5e**	10.0	7.0	3.0	3.0
6	**6a**	8.0	—	2.5	3.0
7	**6b**	8.5	—	3.0	3.5
8	**6c**	8.5	—	2.5	3.5
9	**6d**	8.0	—	2.5	3.5
10	**6e**	8.5	—	2.5	3.5
11	**7a**	10	6.0	3.0	3.0
12	**7b**	10	6.0	2.5	3.0
13	**7c**	—	6.0	—	2.5
14	**7d**	10.5	6.0	3.0	3.0
15	**8a**	—	—	3.5	2.0
16	**8b**	—	—	3.5	2.5
17	**8c**	—	—	3.5	2.5
18	**8d**	—	—	3.5	2.5
19	**9a**	8.0	—	3.0	—
20	**9b**	8.0	—	3.0	—
21	**9c**	8.0	—	3.0	—
22	**9d**	—	—	—	—
23	**9e**	—	—	—	—
24	**10a**	9.5	—	4.0	—
25	**10b**	9.5	—	4.0	—
26	**10c**	9.5	—	4.0	—
27	**10d**	9.5	—	4.0	—
28	**10e**	9.5	—	4.0	—

additional 5 min (or 25 min in case of an electron-deficient dienophile). After completion of the reaction as indicated by TLC, methanol was evaporated and the crude reaction mixture was purified by silica gel column chromatography with ethyl acetate/hexanes (20–30%) as eluting system.

*4.2.1. 4-(Benzo[d]oxazol-2′-yl)-2-methoxyphenol (**2a**).* Yield: 97 mg (80%) as white solid. Mp: 164–165 °C. IR (KBr): ν_{max} 2924, 1601, 1500, 1457, 1302, 1255, 1180 cm^{-1}. ^1H NMR (500 MHz, $CDCl_3$): δ 7.81 (dd, *J*=2.0, 8.5 Hz, 1H), 7.77 (d, *J*=2.0 Hz, 1H), 7.74–7.72 (m, 1H), 7.56–7.54 (m, 1H), 7.34–7.31 (m, 2H), 7.05 (d, *J*=8.0 Hz, 1H), 6.20 (br s, 1H), 4.01 (s, 3H) ppm. ^{13}C NMR (125 MHz, $CDCl_3$): δ 163.2, 150.7, 149.1, 146.9, 142.2, 124.7, 124.5, 121.9, 119.6, 119.3, 114.8, 110.4, 109.8, 56.2 ppm. HRMS (ES^+): *m*/*z* calcd for $[C_{14}H_{12}NO_3+1]^+$: 242.0817, found: 242.0811.

4.2.2. (1S,2S*,7R*,8R*)-7,11-(bis-Benzoxazol-2′-yl)-3,3,10,1-tetramethoxytricyclo[6.2.2.0^{2,7}]dodeca-5,11-diene-4,9-dione (**4a**).* Yield: 106 mg (79%) as yellow solid. Mp: 200–201 °C. IR (KBr): ν_{max} 2947, 2830, 1745, 1708, 1590, 1533, 1449, 1237, 1115 cm^{-1}. ^1H NMR (500 MHz, $CDCl_3$): δ 7.78–7.75 (m, 2H), 7.56–7.54 (m, 1H), 7.50–7.48 (m, 1H), 7.40–7.36 (m, 2H), 7.35–7.30 (m, 2H), 7.02 (dd, *J*=2.0, 7.0 Hz, 1H), 6.98 (d, *J*=10.0 Hz, 1H), 6.17 (d, *J*=10.0 Hz, 1H), 4.46 (s, 1H), 4.35 (t, *J*=2.0 Hz, 1H), 3.76 (d, *J*=7.0, Hz, 1H), 3.59 (s, 3H), 3.54 (s, 3H), 3.38 (s, 3H), 3.00 (s, 3H) ppm. ^{13}C NMR (125 MHz, $CDCl_3$): δ 197.8, 192.0, 164.9, 159.0, 150.8, 150.5, 143.8, 141.5, 140.6, 132.7, 130.7, 128.7, 125.7, 125.3, 124.6, 124.3, 120.8, 120.3, 110.5, 110.4, 97.5, 94.1, 58.9, 51.1, 50.0, 49.9, 49.5, 48.8, 43.5, 41.2 ppm. HRMS (ES^+): *m*/*z* calcd for $[C_{30}H_{26}N_2O_8+Na]^+$: 565.1581, found: 565.1587.

4.2.3. (1S,4R*,7S*)-5-(Benzoxazol-2′-yl)-3,3-dimethoxy-7-phenylbicyclo[2.2.2]oct-5-en-2-one (**5a**).* Yield: 121 mg (64%) as yellow solid. Mp: 99–100 °C. IR (KBr): ν_{max} 2949, 2830, 1737, 1633, 1529, 1447, 1132 cm^{-1}. ^1H NMR (500 MHz, $CDCl_3$): δ 7.77–7.75 (m, 1H), 7.52–7.49 (m, 1H), 7.34–7.30 (m, 2H), 7.25–7.22 (m, 2H), 7.20–7.16 (m, 2H), 7.14–7.12 (m, 2H), 4.28 (q, *J*=2.5 Hz, 1H), 3.60–3.55 (m, 1H), 3.54 (dd, *J*=1.5, 6.5 Hz, 1H), 3.49 (s, 3H), 3.41 (s, 3H), 2.74 (ddd, *J*=3.0, 8.5, 13.0 Hz, 1H), 1.78 (ddd, *J*=2.5, 6.5, 13.5 Hz,

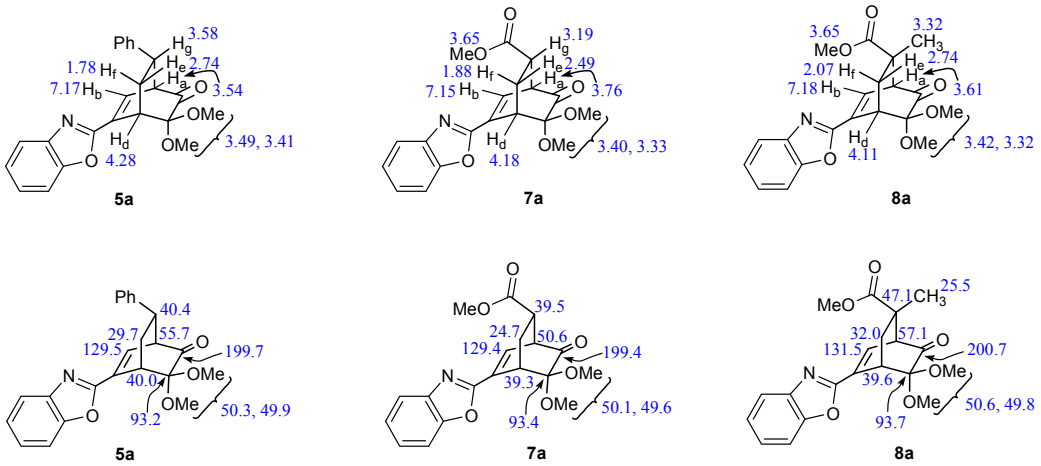


Fig. 2. Selected ^{1}H and ^{13}C chemical shifts (in ppm) of the cycloadducts **5a**, **7a**, and **8a**.

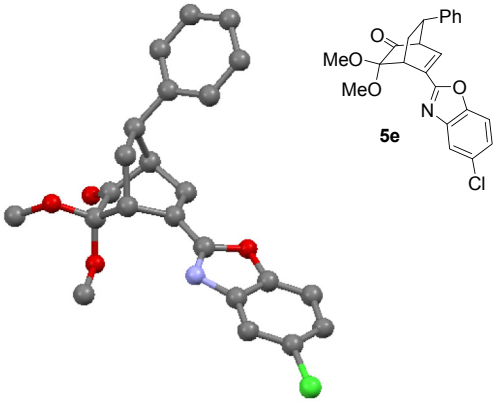
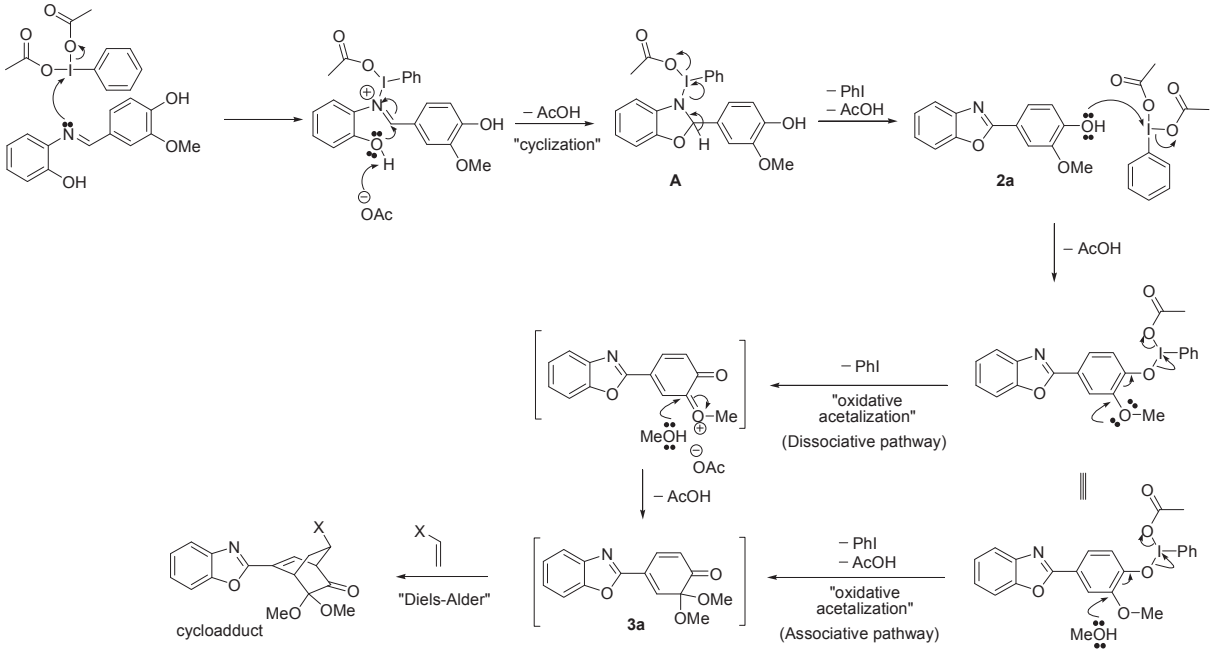


Fig. 3. Single crystal X-ray structure of **5e**.[23]

1H) ppm. ^{13}C NMR (125 MHz, $CDCl_3$): δ 199.7, 160.0, 150.5, 143.1, 141.5, 134.4, 129.5, 128.4, 127.1, 126.7, 125.4, 124.3, 120.0, 110.3, 93.2, 55.7, 50.3, 49.9, 40.4, 40.0, 29.7 ppm. HRMS (ES^{+}): m/z calcd for $[C_{23}H_{21}NO_4+Na]^{+}$: 398.1363, found: 398.1363.

4.2.4. (1S,4R*,7S*)-3,3-Dimethoxy-5-(5′-methylbenzoxazol-2′-yl)-7-phenylbicyclo[2.2.2]oct-5-en-2-one (**5b**).* Yield: 131 mg (67%) as yellow solid. Mp: 141–142 °C. IR (KBr): ν_{max} 2942, 2839, 1744, 1647, 1534, 1452, 1139 cm^{-1}. ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.52 (s, 1H), 7.39 (d, J=8.0 Hz, 1H), 7.24 (d, J=3.0 Hz, 1H), 7.23 (s, 1H), 7.20 (d, J=7.0 Hz, 1H), 7.16 (d, J=9.5 Hz, 1H), 7.14–7.11 (m, 3H), 4.23 (q, J=2.5 Hz, 1H), 3.56–3.53 (m, 1H), 3.51 (dd, J=1.5, 6.5 Hz, 1H), 3.47 (s, 3H), 3.37 (s, 3H), 2.70 (ddd, J=3.0, 9.5, 13.0 Hz, 1H), 2.46 (s, 3H), 1.76 (ddd, J=2.5, 7.0, 13.5 Hz, 1H) ppm. ^{13}C NMR (125 MHz, $CDCl_3$): δ 200.1, 160.3, 148.9, 143.3, 141.8, 134.7, 134.4, 129.2, 128.6, 127.3, 126.9, 126.8,



Scheme 2. Plausible mechanism.

120.1, 109.8, 93.4, 55.8, 50.5, 50.2, 40.6, 40.2, 30.0, 21.4 ppm. HRMS (ES^+): *m*/*z* calcd for $[C_{24}H_{23}NO_4+Na]^+$: 412.1525, found: 412.1522.

4.2.5. (1S,4R*,7S*)-3,3-Dimethoxy-5-(6′-methylbenzoxazol-2′-yl)-7-phenylbicyclo[2.2.2]oct-5-en-2-one (**5c**).* Yield: 123 mg (64%) as pale yellow solid. Mp: 99–100 °C. IR (KBr): ν_{max} 2937, 2834, 1742, 1631, 1530, 1449, 1245, 1128 cm^{-1}. ^1H NMR (500 MHz, $CDCl_3$): δ 7.62 (d, *J*=8.0, 1H), 7.32 (s, 1H), 7.26–7.22 (m, 2H), 7.20–7.11 (m, 5H), 4.25 (q, *J*=3.0 Hz, 1H), 3.58–3.54 (m, 1H), 3.52 (dd, *J*=1.5, 6.5 Hz, 1H), 3.49 (s, 3H), 3.40 (s, 3H), 2.72 (ddd, *J*=3.0, 9.5, 13.0 Hz, 1H), 2.48 (s, 3H), 1.77 (ddd, *J*=3.0, 7.0, 13.5 Hz, 1H) ppm. ^{13}C NMR (125 MHz, $CDCl_3$): δ 200.0, 159.7, 151.0, 143.3, 139.5, 136.2, 134.7, 128.9, 128.6, 127.3, 126.8, 125.8, 119.6, 110.6, 93.4, 55.8, 50.5, 50.1, 40.6, 40.2, 29.9, 21.7 ppm. HRMS (ES^+): *m*/*z* calcd for $[C_{24}H_{23}NO_4+Na]^+$: 412.1519, found: 412.1513.

4.2.6. (1S,4R*,7S*)-5-(5′-tert-Butylbenzoxazol-2′-yl)-3,3-dimethoxy-7-phenylbicyclo[2.2.2]oct-5-en-2-one (**5d**).* Yield: 113 mg (52%) as pale yellow liquid. IR (KBr): ν_{max} 2958, 2934, 1740, 1639, 1532, 1475, 1268, 1197 cm^{-1}. ^1H NMR (500 MHz, $CDCl_3$): δ 7.80–7.79 (m, 1H), 7.45–7.44 (m, 2H), 7.27–7.24 (m, 2H), 7.22–7.18 (m, 1H), 7.15–7.12 (m, 3H), 4.26 (q, *J*=2.5 Hz, 1H), 3.58–3.55 (m, 1H), 3.52 (dd, *J*=1.5, 6.5 Hz, 1H), 3.49 (s, 3H), 3.40 (s, 3H), 2.73 (ddd, *J*=3.0, 9.5, 13.0 Hz, 1H), 1.78 (ddd, *J*=2.5, 6.5, 13.5 Hz, 1H), 1.39 (s, 9H) ppm. ^{13}C NMR (125 MHz, $CDCl_3$): δ 200.3, 160.5, 148.8, 148.3, 143.4, 141.6, 134.8, 129.2, 128.7, 127.4, 127.0, 123.5, 116.8, 109.7, 93.5, 56.0, 50.6, 50.2, 40.8, 40.3, 34.9, 31.7, 30.0 ppm. HRMS (ES^+): *m*/*z* calcd for $[C_{27}H_{29}NO_4+Na]^+$: 454.1989, found: 454.1976.

4.2.7. (1S,4R*,7S*)-5-(5′-Chlorobenzoxazol-2′-yl)-3,3-dimethoxy-7-phenylbicyclo[2.2.2]oct-5-en-2-one (**5e**).* Yield: 142 mg (69%) as orange solid. Mp: 173–174 °C. IR (KBr): ν_{max} 2943, 2836, 1736, 1626, 1527, 1453, 1127 cm^{-1}. ^1H NMR (500 MHz, $CDCl_3$): δ 7.73 (d, *J*=2.0 Hz, 1H), 7.45 (d, *J*=8.5 Hz, 1H), 7.32 (dd, *J*=2.0, 8.5 Hz, 1H), 7.28–7.25 (m, 2H), 7.22–7.19 (m, 2H), 7.14–7.12 (m, 2H), 4.23 (q, *J*=3.0 Hz, 1H), 3.60–3.58 (m, 1H), 3.56 (dd, *J*=1.5, 6.5 Hz, 1H), 3.49 (s, 3H), 3.39 (s, 3H), 2.74 (ddd, *J*=3.0, 10.0, 13.5 Hz, 1H), 1.78 (ddd, *J*=3.0, 7.0, 13.5 Hz, 1H) ppm. ^{13}C NMR (125 MHz, $CDCl_3$): δ 199.9, 161.4, 149.3, 143.2, 142.8, 134.3, 130.7, 130.0, 128.7, 127.3, 127.0, 125.9, 120.2, 111.2, 93.3, 56.0, 50.6, 50.2, 40.6, 40.2, 29.9 ppm. HRMS (ES^+): *m*/*z* calcd for $[C_{23}H_{20}ClNO_4+Na]^+$: 432.0973, found: 432.0991.

4.2.8. (1S,4R*,7S*)-5-(Benzoxazol-2′-yl)-3,3-dimethoxy-7-ethoxybicyclo[2.2.2]oct-5-en-2-one (**6a**).* Yield: 142 mg (82%) as yellow solid. Mp: 101–102 °C. IR (KBr): ν_{max} 2939, 2842, 1738, 1643, 1531, 1447, 1191 cm^{-1}. ^1H NMR (500 MHz, $CDCl_3$): δ 7.68–7.67 (m, 1H), 7.46–7.43 (m, 1H), 7.29–7.24 (m, 2H), 7.04 (d, *J*=6.0 Hz, 1H), 4.07–4.06 (m, 2H), 3.78 (dd, *J*=2.0, 6.0 Hz, 1H), 3.52–3.45 (m, 1H), 3.41–3.35 (m, 1H), 3.34 (s, 3H), 3.28 (s, 3H), 2.55 (ddd, *J*=2.5, 8.0, 13.5 Hz, 1H), 1.46 (ddd, *J*=3.0, 3.0, 13.5 Hz, 1H), 1.10 (t, *J*=7.0 Hz, 3H) ppm. ^{13}C NMR (125 MHz, $CDCl_3$): δ 199.9, 160.2, 150.6, 141.6, 133.6, 128.8, 125.5, 124.4, 120.1, 110.4, 93.3, 74.9, 64.4, 54.7, 50.6, 49.8, 38.8, 30.0, 15.2 ppm. HRMS (ES^+): *m*/*z* calcd for $[C_{19}H_{21}NO_5+Na]^+$: 366.1312, found: 366.1329.

4.2.9. (1S,4R*,7S*)-3,3-Dimethoxy-7-ethoxy-5-(5′-methylbenzoxazol-2′-yl)bicyclo[2.2.2]oct-5-en-2-one (**6b**).* Yield: 142 mg (80%) as yellow solid. Mp: 109–110 °C. IR (KBr): ν_{max} 2972, 2843, 1738, 1643, 1534, 1447, 1128 cm^{-1}. ^1H NMR (500 MHz, $CDCl_3$): δ 7.50 (s, 1H), 7.37 (d, *J*=8.5 Hz, 1H), 7.15 (dd, *J*=1.5, 8.5 Hz, 1H), 7.06 (d, *J*=6.5 Hz, 1H), 4.14–4.09 (m, 2H), 3.82 (dd, *J*=2.5, 6.5 Hz, 1H), 3.57–3.51 (m, 1H), 3.46–3.41 (m, 1H), 3.38 (s, 3H), 3.32 (s, 3H), 2.59 (ddd, *J*=3.0, 8.5, 14.0 Hz, 1H), 2.46 (s, 3H), 1.50 (ddd, *J*=3.5, 3.5, 14.0 Hz, 1H), 1.15 (t, *J*=7.0 Hz, 3H) ppm. ^{13}C NMR (125 MHz, $CDCl_3$): δ 200.1, 160.3, 148.9, 141.8, 134.3, 133.8, 128.4, 126.8, 120.1, 109.8, 93.4, 75.0, 64.5, 54.6, 50.7, 49.9, 38.8, 30.1, 21.5, 15.2 ppm. HRMS (ES^+): *m*/*z* calcd for $[C_{20}H_{23}NO_5+Na]^+$: 380.1474, found 380.1462.

4.2.10. (1S,4R*,7S*)-3,3-Dimethoxy-7-methoxy-5-(6′-methylbenzoxazol-2′-yl)bicyclo[2.2.2]oct-5-en-2-one (**6c**).* Yield: 146 mg (82%) as thick brown liquid. IR (KBr): ν_{max} 2934, 2865, 1741, 1638, 1533, 1449, 1244, 1102 cm^{-1}. ^1H NMR (500 MHz, $CDCl_3$): δ 7.58 (d, *J*=8.0 Hz, 1H), 7.29 (s, 1H), 7.12 (d, *J*=8.0 Hz, 1H), 7.04 (d, *J*=6.0 Hz, 1H), 4.12–4.08 (m, 2H), 3.81 (dd, *J*=2.5, 6.0 Hz, 1H), 3.56–3.50 (m, 1H), 3.46–3.40 (m, 1H), 3.38 (s, 3H), 3.32 (s, 3H), 2.59 (ddd, *J*=2.5, 8.5, 14.0 Hz, 1H), 2.47 (s, 3H), 1.50 (ddd, *J*=3.5, 3.5, 14.0 Hz, 1H), 1.48 (t, *J*=6.5 Hz, 3H) ppm. ^{13}C NMR (125 MHz, $CDCl_3$): δ 200.0, 159.8, 151.0, 139.4, 136.2, 133.8, 128.1, 125.8, 119.5, 110.6, 93.4, 75.0, 64.4, 54.7, 50.7, 49.9, 38.9, 30.1, 21.8, 15.2 ppm. HRMS (ES^+): *m*/*z* calcd for $[C_{20}H_{23}NO_5+Na]^+$: 380.1474, found: 380.1465.

4.2.11. (1S,4R*,7S*)-5-(5′-tert-Butylbenzoxazol-2′-yl)-3,3-dimethoxy-7-ethoxybicyclo[2.2.2]oct-5-en-2-one (**6d**).* Yield: 124 mg (62%) as pale yellow liquid. IR (KBr): ν_{max} 2965, 2865, 1741, 1639, 1534, 1475, 1360, 1271, 1103 cm^{-1}. ^1H NMR (500 MHz, $CDCl_3$): δ 7.75 (s, 1H), 7.41–7.39 (m, 2H), 7.05 (dd, *J*=1.5, 6.5 Hz, 1H), 4.12–4.09 (m, 2H), 3.81 (dd, *J*=2.5, 6.5 Hz, 1H), 3.56–3.50 (m, 1H), 3.45–3.40 (m, 1H), 3.38 (s, 3H), 3.31 (s, 3H), 2.59 (ddd, *J*=2.5, 8.0, 13.5 Hz, 1H), 1.49 (ddd, *J*=3.5, 3.5, 14.0 Hz, 1H), 1.36 (s, 9H), 1.15 (t, *J*=5.5 Hz, 3H) ppm. ^{13}C NMR (125 MHz, $CDCl_3$): δ 200.0, 160.4, 148.7, 148.0, 141.5, 133.8, 128.3, 123.4, 116.7, 109.6, 93.4, 75.0, 64.4, 54.6, 50.7, 49.9, 38.9, 34.8, 31.7, 30.1, 15.2 ppm. HRMS (ES^+): *m*/*z* calcd for $[C_{23}H_{29}NO_5+Na]^+$: 422.1938, found: 422.1941.

4.2.12. (1S,4R*,7S*)-5-(5′-Chlorobenzoxazol-2′-yl)-3,3-dimethoxy-7-ethoxybicyclo[2.2.2]oct-5-en-2-one (**6e**).* Yield: 154 mg (82%) as orange solid. Mp: 80 °C. IR (KBr): ν_{max} 2978, 2839, 1740, 1637, 1529, 1448, 1126 cm^{-1}. ^1H NMR (500 MHz, $CDCl_3$): δ 7.70–7.69 (m, 1H), 7.42 (d, *J*=8.5 Hz, 1H), 7.33–7.30 (m, 1H), 7.11 (d, *J*=7.5 Hz, 1H), 4.14–4.11 (m, 1H), 4.09–4.07 (m, 1H), 3.84 (dd, *J*=2.5, 6.0 Hz, 1H), 3.57–3.51 (m, 1H), 3.46–3.40 (m, 1H), 3.38 (s, 3H), 3.31 (s, 3H), 2.60 (ddd, *J*=2.5, 8.5, 14.0 Hz, 1H), 1.50 (ddd, *J*=3.5, 3.5, 14.0 Hz, 1H), 1.15 (t, *J*=7.0 Hz, 3H) ppm. ^{13}C NMR (125 MHz, $CDCl_3$): δ 199.8, 161.4, 149.2, 142.7, 133.3, 129.9, 129.8, 125.8, 120.1, 111.2, 93.2, 74.9, 64.5, 54.7, 50.7, 49.8, 38.8, 30.0, 15.2 ppm. HRMS (ES^+): *m*/*z* calcd for $[C_{19}H_{20}ClNO_5+Na]^+$: 400.0928, found: 400.0917.

4.2.13. (1S,4R*,7S*)-5-(Benzoxazol-2′-yl)-3,3-dimethoxy-7-methoxycarbonylbicyclo[2.2.2]oct-5-en-2-one (**7a**).* Yield: 111 mg (62%) as thick yellow liquid. IR (KBr): ν_{max} 2952, 2839, 1737, 1636, 1525, 1443, 1332, 1165 cm^{-1}. ^1H NMR (500 MHz, $CDCl_3$): δ 7.73–7.69 (m, 1H), 7.49–7.46 (m, 1H), 7.34–7.29 (m, 2H), 7.15–7.13 (m, 1H), 4.18 (q, *J*=2.5 Hz, 1H), 3.76 (dd, *J*=2.0, 7.0 Hz, 1H), 3.66 (s, 3H), 3.40 (s, 3H), 3.33 (s, 3H), 3.19 (ddd, *J*=1.5, 6.0, 10.0 Hz, 1H), 2.49 (ddd, *J*=3.0, 10.0, 13.5 Hz, 1H), 1.88 (ddd, *J*=3.0, 6.0, 13.5 Hz, 1H) ppm. ^{13}C NMR (125 MHz, $CDCl_3$): δ 199.4, 172.8, 159.9, 150.6, 141.5, 134.4, 129.4, 125.7, 124.5, 120.2, 110.4, 93.4, 52.4, 50.6, 50.6, 50.1, 39.5, 39.3, 24.7 ppm. HRMS (ES^+): *m*/*z* calcd for $[C_{19}H_{19}NO_6+Na]^+$: 380.1105, found: 380.1102.

4.2.14. (1S,4R*,7S*)-3,3-Dimethoxy-7-methoxycarbonyl-5-(5′-methylbenzoxazol-2′-yl)bicyclo[2.2.2]oct-5-en-2-one (**7b**).* Yield: 109 mg (59%) as pale yellow solid. Mp: 118–119 °C. IR (KBr): ν_{max} 2946, 2838, 1738, 1633, 1527, 1440, 1323, 1143 cm^{-1}. ^1H NMR (500 MHz, $CDCl_3$): δ 7.49 (s, 1H), 7.34 (d, *J*=8.0 Hz, 1H), 7.12 (dt, *J*=1.5, 9.0 Hz, 2H), 4.17 (q, *J*=2.5 Hz, 1H), 3.75 (dd, *J*=2.0, 6.5 Hz, 1H), 3.66 (s, 3H), 3.40 (s, 3H), 3.34 (s, 3H), 3.19 (ddd, *J*=1.5, 6.0, 10.0 Hz, 1H), 2.49 (ddd, *J*=2.5, 10.0, 13.0 Hz, 1H), 2.44 (s, 3H), 1.88 (ddd, *J*=3.0, 6.0, 13.5 Hz, 1H) ppm. ^{13}C NMR (125 MHz, $CDCl_3$): δ 199.4, 172.8, 160.0,

148.9, 141.7, 134.6, 134.4, 129.0, 126.9, 120.1, 109.8, 93.4, 52.4, 50.6, 50.5, 50.1, 39.6, 39.4, 24.8, 21.4 ppm. HRMS (ES^+): *m*/*z* calcd for $[C_{20}H_{21}NO_6+Na]^+$: 394.1261, found: 394.1253.

4.2.15. (1S,4R*,7S*)-3,3-Dimethoxy-7-methoxycarbonyl-5-(6′-methylbenzoxazol-2′-yl)bicyclo[2.2.2]oct-5-en-2-one (**7c**).* Yield: 103 mg (56%) as pale yellow solid. Mp: 95–96 °C. IR (KBr): ν_{max} 2952, 2839, 1740, 1626, 1528, 1444, 1327, 1184, 1136 cm^{-1}. ^1H NMR (500 MHz, $CDCl_3$): δ 7.57 (d, *J*=8.0 Hz, 1H), 7.28 (s, 1H), 7.13–7.09 (m, 2H), 4.17–4.16 (m, 1H), 3.75 (d, *J*=6.5 Hz, 1H), 3.67 (s, 3H), 3.40 (s, 3H), 3.34 (s, 3H), 3.21–3.17 (m, 1H), 2.51–2.48 (m, 1H), 2.46 (s, 3H), 1.88 (ddd, *J*=2.5, 6.0, 13.0 Hz, 1H) ppm. ^{13}C NMR (125 MHz, $CDCl_3$): δ 199.5, 172.8, 159.5, 151.0, 139.4, 136.3, 134.6, 128.7, 125.8, 119.6, 110.6, 93.5, 52.4, 50.6, 50.1, 39.6, 39.4, 24.8, 21.8 ppm. HRMS (ES^+): *m*/*z* calcd for $[C_{20}H_{21}NO_6+Na]^+$: 394.1261, found: 394.1251.

4.2.16. (1S,4R*,7S*)-5-(5′-tert-Butylbenzoxazol-2′-yl)-3,3-dimethoxy-7-methoxycarbonylbicyclo[2.2.2]-oct-5-en-2-one (**7d**).* Yield: 118 mg (57%) as yellow solid. Mp: 94–95 °C. IR (KBr): ν_{max} 2952, 2839, 1740, 1626, 1526, 1444, 1327, 1184 cm^{-1}. ^1H NMR (500 MHz, $CDCl_3$): δ 7.74 (s, 1H), 7.40 (s, 2H), 7.11 (dd, *J*=2.0, 6.5 Hz, 1H), 4.18 (q, *J*=2.5 Hz, 1H), 3.76 (dd, *J*=2.0, 6.5 Hz, 1H), 3.66 (s, 3H), 3.40 (s, 3H), 3.34 (s, 3H), 3.20 (ddd, *J*=1.5, 6.0, 10.0 Hz, 1H), 2.49 (ddd, 3.0, 10.5, 13.5 Hz, 1H), 1.88 (ddd, 3.0, 6.0, 13.5, 1H), 1.35 (s, 9H) ppm. ^{13}C NMR (125 MHz, $CDCl_3$): δ 199.5, 172.8, 160.1, 148.7, 148.1, 141.4, 134.6, 128.9, 123.5, 116.7, 109.6, 93.5, 52.4, 50.6, 50.6, 50.1, 39.6, 39.4, 34.8, 31.6, 24.7 ppm. HRMS (ES^+): *m*/*z* calcd for $[C_{23}H_{27}NO_6+Na]^+$: 436.1736, found: 436.1736.

4.2.17. (1S,4R*,7S*)-5-(Benzoxazol-2′-yl)-3,3-dimethoxy-7-methoxycarbonyl-7-methylbicyclo[2.2.2]oct-5-en-2-one (**8a**).* Yield: 121 mg (66%) as yellow solid. Mp: 101–102 °C. IR (KBr): ν_{max} 2949, 2843, 1739, 1634, 1531, 1447, 1204, 1149 cm^{-1}. ^1H NMR (500 MHz, $CDCl_3$): δ 7.71 (d, *J*=7.5 Hz, 1H), 7.47 (d, *J*=7.5 Hz, 1H), 7.34–7.28 (m, 2H), 7.18 (d, *J*=6.5 Hz, 1H), 4.12–4.11 (m, 1H), 3.65 (s, 3H), 3.61 (d, *J*=6.5 Hz, 1H), 3.42 (s, 3H), 3.32 (s, 3H), 2.40 (dd, *J*=3.5, 14.0 Hz, 1H), 2.07 (dd, *J*=2.0, 14.0 Hz, 1H), 1.39 (s, 3H) ppm. ^{13}C NMR (125 MHz, $CDCl_3$): δ 200.7, 175.7, 160.1, 150.6, 141.6, 133.8, 131.5, 125.7, 124.5, 120.2, 110.5, 93.7, 57.1, 52.6, 50.6, 49.8, 47.1, 39.6, 32.0, 25.5 ppm. HRMS (ES^+): *m*/*z* calcd for $[C_{20}H_{21}NO_6+Na]^+$: 394.1261, found: 394.1247.

4.2.18. (1S,4R*,7S*)-3,3-Dimethoxy-7-methoxycarbonyl-7-methyl-5-(5′-methylbenzoxazol-2′-yl)bicyclo[2.2.2]oct-5-en-2-one (**8b**).* Yield: 106 mg (55%) as brown solid. Mp: 98 °C. IR (KBr): ν_{max} 2949, 2839, 1738, 1634, 1530, 1452, 1382, 1256, 1113 cm^{-1}. ^1H NMR (500 MHz, $CDCl_3$): δ 7.48 (s, 1H), 7.34 (d, *J*=8.5 Hz, 1H), 7.16–7.11 (m, 2H), 4.11–4.09 (m, 1H), 3.65 (s, 3H), 3.60 (d, *J*=6.5 Hz, 1H), 3.42 (s, 3H), 3.32 (s, 3H), 2.43 (s, 3H), 2.39 (dd, *J*=3.5, 14.0 Hz, 1H), 2.07 (dd, *J*=2.5, 14.0 Hz, 1H), 1.38 (s, 3H) ppm. ^{13}C NMR (125 MHz, $CDCl_3$): δ 200.7, 175.7, 160.2, 148.9, 141.7, 134.3, 133.9, 131.1, 126.8, 120.1, 109.8, 93.6, 57.1, 52.6, 50.5, 49.8, 47.1, 39.6, 32.0, 25.5, 21.4 ppm. HRMS (ES^+): *m*/*z* calcd for $[C_{21}H_{23}NO_6+Na]^+$: 408.1418, found: 408.1401.

4.2.19. (1S,4R*,7S*)-3,3-Dimethoxy-7-methoxycarbonyl-7-methyl-5-(6′-methylbenzoxazol-2′-yl)bicyclo[2.2.2]oct-5-en-2-one (**8c**).* Yield: 106 mg (55%) as white solid. Mp: 109–110 °C. IR (KBr): ν_{max} 2951, 2837, 1733, 1625, 1530, 1446, 1326, 1211, 1144 cm^{-1}. ^1H NMR (500 MHz, $CDCl_3$): δ 7.55 (d, *J*=8.5 Hz, 1H), 7.25 (s, 1H), 7.13–7.09 (m, 2H), 4.08–4.07 (m, 1H), 3.64 (s, 3H), 3.59 (d, *J*=6.0 Hz, 1H), 3.41 (s, 3H), 3.31 (s, 3H), 2.44 (s, 3H), 2.38 (dd, *J*=3.5, 14.0 Hz, 1H), 2.05 (dd, *J*=2.5, 14.0 Hz, 1H), 1.37 (s, 3H) ppm. ^{13}C NMR (125 MHz, $CDCl_3$): δ 200.6, 175.7, 159.7, 150.9, 139.3, 136.2, 133.9, 130.7, 125.7, 119.5, 110.5, 93.6, 57.0, 52.5, 50.5, 49.8, 47.1, 39.6, 31.9, 25.4, 21.7 ppm. HRMS (ES^+): *m*/*z* calcd for $[C_{21}H_{23}NO_6+Na]^+$: 408.1418, found: 408.1402.

4.2.20. (1S,4R*,7S*)-5-(5′-tert-Butylbenzoxazol-2′-yl)-3,3-dimethoxy-7-methoxycarbonyl-7-methylbicyclo[2.2.2]oct-5-en-2-one (**8d**).* Yield: 114 mg (53%) as yellow solid. Mp: 90 °C. IR (KBr): ν_{max} 2961, 2878, 1734, 1634, 1534, 1468, 1382, 1264, 1208, 1114 cm^{-1}. ^1H NMR (500 MHz, $CDCl_3$): δ 7.74 (s, 1H), 7.39 (s, 2H), 7.14 (dd, *J*=2.0, 6.5 Hz, 1H), 4.11–4.10 (m, 1H), 3.65 (s, 3H), 3.61 (d, *J*=6.5 Hz, 1H), 3.42 (s, 3H), 3.22 (s, 3H), 2.39 (dd, *J*=3.5, 14.0 Hz, 1H), 2.07 (dd, *J*=2.5, 14.0 Hz, 1H), 1.38 (s, 3H), 1.35 (s, 9H) ppm. ^{13}C NMR (125 MHz, $CDCl_3$): δ 200.7, 175.7, 160.3, 148.7, 148.1, 141.5, 133.9, 131.0, 123.5, 116.7, 109.6, 93.7, 57.1, 52.6, 50.5, 49.8, 47.2, 39.7, 34.8, 32.0, 31.7, 25.5 ppm. HRMS (ES^+): *m*/*z* calcd for $[C_{24}H_{29}NO_6+Na]^+$: 450.1893, found: 450.1893.

4.2.21. (1R,2R*,6R*,7S*)-11-(Benzoxazol-2′-yl)-8,8-dimethoxy-3-oxatricyclo[5.2.2.0^{2,6}]undec-10-en-9-one (**9a**).* Yield: 124 mg (73%) as green colour solid. Mp: 107–108 °C. IR (KBr): ν_{max} 2939, 2843, 1737, 1643, 1539, 1448, 1230, 1146 cm^{-1}. ^1H NMR (500 MHz, $CDCl_3$): δ 7.76–7.73 (m, 1H), 7.52–7.50 (m, 1H), 7.38–7.31 (m, 2H), 7.14–7.11 (m, 1H), 4.47 (dd, *J*=3.0, 8.0 Hz, 1H), 4.21 (t, *J*=2.5 Hz, 1H), 3.84 (dd, *J*=3.0, 6.0 Hz, 1H), 3.80–3.78 (m, 1H), 3.57–3.52 (m, 1H), 3.42 (s, 3H), 3.31 (s, 3H), 3.12 (ddd, *J*=3.0, 8.0, 17.5 Hz, 1H), 2.18–2.11 (m, 1H), 1.57–1.50 (m, 1H) ppm. ^{13}C NMR (125 MHz, $CDCl_3$): δ 199.7, 161.1, 150.7, 141.6, 131.8, 130.5, 125.8, 124.6, 120.3, 110.6, 93.1, 79.2, 69.1, 55.7, 50.7, 50.0, 43.3, 38.3, 30.2 ppm. HRMS (ES^+): *m*/*z* calcd for $[C_{19}H_{19}NO_5+Na]^+$: 364.1155, found: 364.1143.

4.2.22. (1R,2R*,6R*,7S*)-8,8-Dimethoxy-11-(5′-methylbenzoxazol-2′-yl)-3-oxatricyclo[5.2.2.0^{2,6}]undec-10-en-9-one (**9b**).* Yield: 126 mg (71%) as green solid. Mp: 144–145 °C. IR (KBr): ν_{max} 2939, 2878, 1737, 1636, 1526, 1451, 1262, 1146 cm^{-1}. ^1H NMR (500 MHz, $CDCl_3$): δ 7.51 (s, 1H), 7.37 (d, *J*=8.0 Hz, 1H), 7.15 (dd, *J*=1.0, 8.5 Hz, 1H), 7.08 (d, *J*=6.5 Hz, 1H), 4.45 (dd, *J*=3.0, 8.5 Hz, 1H), 4.19 (t, *J*=2.5 Hz, 1H), 3.82 (dd, *J*=3.0, 6.5 Hz, 1H), 3.79 (dd, *J*=3.0, 8.5 Hz, 1H), 3.56–3.50 (m, 1H), 3.40 (s, 3H), 3.30 (s, 3H), 3.11 (ddd, *J*=3.0, 8.0, 18.0 Hz, 1H), 2.45 (s, 3H), 2.16–2.10 (m, 1H), 1.55–1.47 (m, 1H) ppm. ^{13}C NMR (125 MHz, $CDCl_3$): δ 199.7, 161.2, 148.9, 141.8, 134.4, 131.9, 130.0, 126.8, 120.1, 109.9, 93.0, 79.1, 69.1, 55.6, 50.6, 50.0, 43.2, 38.2, 30.2, 21.4 ppm. HRMS (ES^+): *m*/*z* calcd for $[C_{20}H_{21}NO_5+Na]^+$: 378.1312, found: 378.1312.

4.2.23. (1R,2R*,6R*,7S*)-8,8-Dimethoxy-11-(6′-methylbenzoxazol-2′-yl)-3-oxatricyclo[5.2.2.0^{2,6}]undec-10-en-9-one (**9c**).* Yield: 121 mg (69%) as brown solid. Mp: 119–120 °C. IR (KBr): ν_{max} 2939, 2863, 1735, 1630, 1530, 1449, 1232, 1141 cm^{-1}. ^1H NMR (500 MHz, $CDCl_3$): δ 7.61 (d, *J*=8.0 Hz, 1H), 7.33 (s, 1H), 7.16 (d, *J*=8.5 Hz, 1H), 7.10–7.08 (m, 1H), 4.48 (dd, *J*=3.0, 8.5 Hz, 1H), 4.22–4.21 (m, 1H), 3.84 (dd, *J*=3.0, 6.5 Hz, 1H), 3.81 (dd, *J*=3.0, 8.5 Hz, 1H), 3.58–3.53 (m, 1H), 3.42 (s, 3H), 3.32 (s, 3H), 3.12 (ddd, *J*=3.0, 8.0, 17.5 Hz, 1H), 2.51 (s, 3H), 2.19–2.13 (m, 1H), 1.57–1.49 (m, 1H) ppm. ^{13}C NMR (125 MHz, $CDCl_3$): δ 199.7, 160.6, 150.8, 139.2, 136.3, 131.7, 129.7, 125.7, 119.5, 110.6, 93.0, 79.0, 69.0, 55.5, 50.6, 49.9, 43.1, 38.1, 30.1, 21.7 ppm. HRMS (ES^+): *m*/*z* calcd for $[C_{20}H_{21}NO_5+Na]^+$: 378.1312, found: 378.1320.

4.2.24. (1R,2R*,6R*,7S*)-11-(5′-tert-Butylbenzoxazol-2′-yl)-8,8-dimethoxy-3-oxatricyclo[5.2.2.0^{2,6}]undec-10-en-9-one (**9d**).* Yield: 106 mg (54%) as green colour solid. Mp: 158–159 °C. IR (KBr): ν_{max} 2952, 2894, 1743, 1639, 1532, 1269, 1141 cm^{-1}. ^1H NMR (500 MHz, $CDCl_3$): δ 7.80–7.77 (m, 1H), 7.43–7.42 (m, 2H), 7.10–7.08 (m, 1H), 4.46 (dd, *J*=3.0, 8.0 Hz, 1H), 4.21–4.20 (m, 1H), 3.82 (dd, *J*=3.0, 6.5 Hz, 1H), 3.79 (dt, *J*=3.0, 8.5 Hz, 1H), 3.56–3.51 (m, 1H), 3.41 (s, 3H), 3.31 (s, 3H), 3.14–3.08 (m, 1H), 2.17–2.11 (m, 1H), 1.57–1.48 (m, 1H), 1.37 (s, 9H) ppm. ^{13}C NMR (125 MHz, $CDCl_3$): δ 199.8, 161.3,

148.7, 148.2, 141.5, 131.9, 130.0, 123.6, 116.8, 109.7, 93.1, 79.2, 69.1, 55.7, 50.7, 50.0, 43.3, 38.2, 34.9, 31.7, 30.2 ppm. HRMS (ES^+): *m/z* calcd for $[C_{23}H_{27}NO_5+Na]^+$: 420.1781, found: 420.1781.

4.2.25. (1R,2R*,6R*,7S*)-11-(5′-Chlorobenzoxazol-2′-yl)-8,8-dimethoxy-3-oxatricyclo[5.2.2.0^{2,6}]undec-10-en-9-one (**9e**).* Yield: 116 mg (62%) as yellow solid. Mp: 127–128 °C. IR (KBr): ν_{max} 2940, 2882, 1740, 1589, 1499, 1450, 1275, 1218, 1130 cm^{-1}. ^1H NMR (500 MHz, $CDCl_3$): δ 7.71 (d, *J*=2.0 Hz, 1H), 7.44 (d, *J*=8.0 Hz, 1H), 7.33 (d, *J*=2.0, 9.0 Hz, 1H), 7.15–7.14 (m, 1H), 4.47 (dd, *J*=3.0, 8.0 Hz, 1H), 4.18–4.17 (m, 1H), 3.85 (dd, *J*=3.0, 6.5 Hz, 1H), 3.81 (dt, *J*=3.0, 13.0 Hz, 1H), 3.57–3.52 (m, 1H), 3.42 (s, 3H), 3.31 (s, 3H), 3.15–3.09 (m, 1H), 2.19–2.14 (m, 1H), 1.54–1.46 (m, 1H) ppm. ^{13}C NMR (125 MHz, $CDCl_3$): δ 199.6, 162.3, 149.3, 142.8, 131.6, 131.5, 130.1, 126.0, 120.3, 111.3, 93.0, 79.2, 69.1, 55.8, 50.8, 50.0, 43.3, 38.2, 30.3 ppm. HRMS (ES^+): *m/z* calcd for $[C_{19}H_{18}ClNO_5+Na]^+$: 398.0766, found: 398.0766.

4.2.26. (1R,2R*,6R*,7S*)-9-(Benzoxazol-2′-yl)-10,10-dimethoxy-3-oxatricyclo[5.2.2.0^{2,6}]undeca-4,8-dien-11-one (**10a**).* Yield: 126 mg (74%) as pale yellow solid. Mp: 129–130 °C. IR (KBr): ν_{max} 2953, 2839, 1743, 1621, 1534, 1456, 1135 cm^{-1}. ^1H NMR (500 MHz, $CDCl_3$): δ 7.75–7.73 (m, 1H), 7.50–7.48 (m, 1H), 7.36–7.31 (m, 2H), 7.16–7.13 (m, 1H), 6.17–6.16 (m, 1H), 5.28 (dd, *J*=4.0, 9.5 Hz, 1H), 4.78 (t, *J*=2.5 Hz, 1H), 4.72–4.70 (m, 1H), 3.58 (dd, *J*=1.5, 9.5 Hz, 1H), 3.47 (dd, *J*=2.5, 7.0 Hz, 1H), 3.44 (s, 3H), 3.39 (s, 3H) ppm. ^{13}C NMR (125 MHz, $CDCl_3$): δ 199.5, 160.7, 150.6, 148.4, 141.7, 130.9, 129.8, 125.6, 124.5, 120.5, 110.4, 100.0, 93.4, 79.2, 52.9, 50.5, 45.4, 44.4 ppm. HRMS (ES^+): *m/z* calcd for $[C_{19}H_{17}NO_5+Na]^+$: 362.0998, found: 362.0993.

4.2.27. (1R,2R*,6R*,7S*)-10,10-Dimethoxy-9-(5′-methylbenzoxazol-2′-yl)-3-oxatricyclo[5.2.2.0^{2,6}]undeca-4,8-dien-11-one (**10b**).* Yield: 127 mg (72%) as pale orange solid. Mp: 138–139 °C. IR (KBr): ν_{max} 2952, 2847, 1741, 1613, 1526, 1454, 1135 cm^{-1}. ^1H NMR (500 MHz, $CDCl_3$): δ 7.52 (s, 1H), 7.35 (d, *J*=8.5 Hz, 1H), 7.14 (d, *J*=8.0 Hz, 1H), 7.11 (dd, *J*=2.0, 7.0 Hz, 1H), 6.16 (t, *J*=2.5 Hz, 1H), 5.28 (dd, *J*=4.0, 9.5 Hz, 1H), 4.77 (t, *J*=2.5 Hz, 1H), 4.70 (dd, *J*=2.0, 4.0 Hz, 1H), 3,57 (dd, *J*=2.0, 9.5 Hz, 1H), 3.45 (dd, *J*=2.0, 7.0 Hz, 1H), 3.44 (s, 3H), 3.38 (s, 3H), 2.45 (s, 3H) ppm. ^{13}C NMR (125 MHz, $CDCl_3$): δ 199.5, 160.7, 148.8, 148.3, 141.9, 134.3, 130.5, 129.8, 126.7, 120.3, 109.7, 100.0, 93.4, 79.2, 52.8, 50.5, 50.4, 45.4, 44.3, 21.4 ppm. HRMS (ES^+): *m/z* calcd for $[C_{20}H_{19}NO_5+Na]^+$: 376.1155, found: 376.1153.

4.2.28. (1R,2R*,6R*,7S*)-10,10-Dimethoxy-9-(6′-methylbenzoxazol-2′-yl)-3-oxatricyclo[5.2.2.0^{2,6}]undeca-4,8-dien-11-one (**10c**).* Yield: 126 mg (73%) as white solid. Mp: 108–109 °C. IR (KBr): ν_{max} 2940, 2834, 1738, 1621, 1534, 1456, 1234, 1139 cm^{-1}. ^1H NMR (500 MHz, $CDCl_3$): δ 7.58 (d, *J*=11.5 Hz, 1H), 7.28 (s, 1H), 7.11 (dd, *J*=1.0, 8.0 Hz, 1H), 7.08 (dd, *J*=1.5, 5.5 Hz, 1H), 6.15 (dd, *J*=2.0, 2.5 Hz, 1H), 5.26 (dd, *J*=4.0, 9.5 Hz, 1H), 4.76 (t, *J*=2.5 Hz, 1H), 4.69 (dd, *J*=2.0, 3.5 Hz, 1H), 3.57–3.53 (m, 1H), 3.44 (dd, *J*=2.5, 5.0 Hz, 1H), 3.43 (s, 3H), 3.37 (s, 3H), 2.45 (s, 3H) ppm. ^{13}C NMR (125 MHz, $CDCl_3$): δ 199.4, 160.2, 150.8, 148.2, 139.4, 136.1, 130.2, 129.7, 125.6, 119.7, 110.5, 100.0, 93.4, 79.1, 52.8, 50.4, 45.3, 44.3, 21.7 ppm. HRMS (ES^+): *m/z* calcd for $[C_{20}H_{19}NO_5+Na]^+$: 376.1155, found: 376.1142.

4.2.29. (1R,2R*,6R*,7S*)-9-(5′-tert-Butylbenzoxazol-2′-yl)-10,10-dimethoxy-3-oxatricyclo[5.2.2.0^{2,6}]undeca-4,8-dien-11-one (**10d**).* Yield: 121 mg (61%) as yellow solid. Mp: 116–118 °C. IR (KBr): ν_{max} 2960, 2846, 1739, 1626, 1537, 1472, 1267, 1139 cm^{-1}. ^1H NMR (500 MHz, $CDCl_3$): δ 7.79–7.77 (m, 1H), 7.41–7.40 (m, 2H), 7.11 (ddd, *J*=1.0, 2.5, 7.0 Hz, 1H), 6.14 (dd, *J*=1.5, 2.5 Hz, 1H), 5.27 (dd, *J*=4.0, 9.5 Hz, 1H), 4.78–4.76 (m, 1H), 4.71 (dd, *J*=2.0, 3.5 Hz, 1H), 3.56 (dd, *J*=1.5, 9.5 Hz, 1H), 3.45 (dd, *J*=2.0, 6.5 Hz, 1H), 3.44 (s, 3H), 3.38 (s, 3H), 1.36 (s, 9H) ppm. ^{13}C NMR (125 MHz, $CDCl_3$): δ 199.5, 160.8, 148.5, 148.2, 148.0, 141.5, 130.4, 129.8, 123.3, 116.9, 109.5, 100.0, 93.4, 79.1, 52.8, 50.4, 45.4, 44.3, 34.8, 31.6, 28.5 ppm. HRMS (ES^+): *m/z* calcd for $[C_{23}H_{25}NO_5+Na]^+$: 418.1625, found: 418.1649.

4.2.30. (1R,2R*,6R*,7S*)-9-(5′-Chlorobenzoxazol-2′-yl)-10,10-dimethoxy-3-oxatricyclo[5.2.2.0^{2,6}]undeca-4,8-dien-11-one (**10e**).* Yield: 132 mg (71%) as yellow solid. Mp: 149–150 °C. IR (KBr): ν_{max} 2943, 2839, 1739, 1634, 1530, 1454, 1138 cm^{-1}. ^1H NMR (500 MHz, $CDCl_3$): δ 7.71 (d, *J*=2.0 Hz, 1H), 7.42 (d, *J*=9.0 Hz, 1H), 7.31 (dd, *J*=2.5, 9.0 Hz, 1H), 7.17 (dd, *J*=2.5, 7.0 Hz, 1H), 6.18–6.17 (m, 1H), 5.29 (dd, *J*=4.0, 9.5 Hz, 1H), 4.80 (t, *J*=2.5 Hz, 1H), 4.68 (dd, *J*=2.0, 3.5 Hz, 1H), 3.59 (dd, *J*=1.5, 9.5 Hz, 1H), 3.49 (dd, *J*=2.0, 6.5 Hz, 1H), 3.45 (s, 3H), 3.38 (s, 3H) ppm. ^{13}C NMR (125 MHz, $CDCl_3$): δ 199.3, 161.9, 149.2, 148.4, 142.9, 132.0, 130.0, 129.5, 125.9, 120.4, 111.2, 100.2, 93.4, 79.2, 53.0, 50.5, 45.5, 44.4 ppm. HRMS (ES^+): *m/z* calcd for $[C_{19}H_{16}ClNO_5+Na]^+$: 396.0615, found: 396.0610.

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