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**Author(s):** Vijayan, Ajesh; Baiju, T. V.; Jijy, E.; Prakash, Praveen; Shimi, M.; Joseph, Nayana; Pihko, Petri; Varughese, Sunil; Radhakrishnan, K. V.

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# Accepted Manuscript



An easy access to fused chromanones via rhodium catalyzed oxidative coupling of salicylaldehydes with heterobicyclic olefins

Ajesh Vijayan, T.V. Baiju, E. Jijy, Praveen Prakash, M. Shimi, Nayana Joseph, Petri M. Pihko, Sunil Varughese, K.V. Radhakrishnan

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## Graphical Abstract

**An easy access to fused chromanones via rhodium catalyzed oxidative coupling of salicylaldehydes with heterobicyclic olefins**

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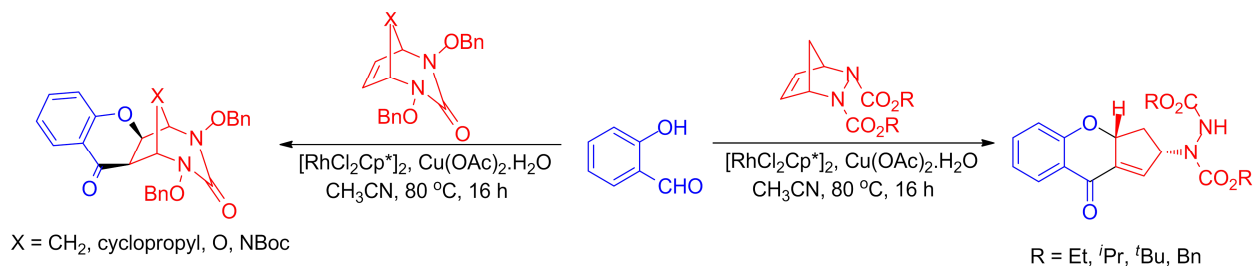
Ajesh Vijayan,<sup>a,b</sup> T. V. Baiju,<sup>a,b</sup> E. Jijy,<sup>a</sup> Praveen Prakash,<sup>a</sup> M. Shimi,<sup>a,b</sup> Nayana Joseph,<sup>a</sup> Petri M. Pihko,<sup>c</sup> Sunil Varughese<sup>d</sup> and K. V. Radhakrishnan<sup>\*a,b</sup>

<sup>a</sup>Organic Chemistry Section, Chemical Sciences and Technology Division, National Institute for Interdisciplinary Science and Technology (CSIR), Trivandrum 695 019, India. E-mail: radhu2005@gmail.com

<sup>b</sup>Academy of Scientific and Innovative Research (AcSIR), New Delhi 110001, India

<sup>c</sup>Department of Chemistry, University of Jyväskylä, Finland

<sup>d</sup>Inorganic Chemistry Section, Chemical Sciences and Technology Division, National Institute for Interdisciplinary Science and Technology (CSIR), Trivandrum, 695019, India





## An easy access to fused chromanones via rhodium catalyzed oxidative coupling of salicylaldehydes with heterobicyclic olefins

Ajesh Vijayan,<sup>a,b</sup> T. V. Baiju,<sup>a,b</sup> E. Jijy,<sup>a</sup> Praveen Prakash,<sup>a</sup> M. Shimi,<sup>a,b</sup> Nayana Joseph,<sup>a</sup> Petri M. Pihko,<sup>c</sup> Sunil Varughese<sup>d</sup> and K. V. Radhakrishnan<sup>\*a,b</sup>

<sup>a</sup> Organic Chemistry Section, Chemical Sciences and Technology Division, National Institute for Interdisciplinary Science and Technology (CSIR), Trivandrum 695 019, India. E-mail: [radhu2005@gmail.com](mailto:radhu2005@gmail.com)

<sup>b</sup> Academy of Scientific and Innovative Research (AcSIR), New Delhi 110001, India

<sup>c</sup> Department of Chemistry, University of Jyväskylä, Finland

<sup>d</sup> Inorganic Chemistry Section, Chemical Sciences and Technology Division, National Institute for Interdisciplinary Science and Technology (CSIR), Trivandrum, 695019, India

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### ABSTRACT

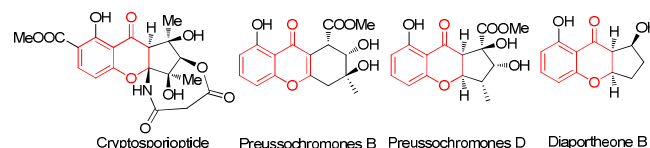
Herein we describe a detailed study on the rhodium catalyzed oxidative coupling of salicylaldehydes with heterobicyclic olefins such as diazabicyclic olefins and urea-derived bicyclic olefins. The developed method provides an ideal route to fused chromanone systems in a single synthetic step. Moreover, the scope of this methodology was extended to different oxa/aza-bridged bicyclic urea derivatives.

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### 1. Introduction

Transition metal catalyzed ring opening of strained heterobicyclic templates provides an efficient tool for the synthesis of diverse functionalized organic molecules with multiple stereocenters. Among the various heterobicyclic systems explored, majority of the investigations have been made on oxa/aza norbornadiene derivatives,<sup>1</sup> oxazabicycles,<sup>2</sup> Vince lactams<sup>3</sup> and diazabicyclic olefins.<sup>4</sup> Desymmetrization of diazabicyclic olefins opens a way to compounds of synthetic and biological interest and have been widely exploited. By utilizing these distinctive diazabicyclic olefins as synthons, our group has developed efficient methods for the synthesis of functionalized cyclopentenes<sup>5</sup> and various cyclopentene fused heterocycles.<sup>6</sup> Various other research groups; Micouin *et al.*,<sup>7</sup> Kaufmann *et al.*,<sup>8</sup> Pineschi *et al.*<sup>9</sup> and Lautens *et al.*<sup>10</sup> also utilized the reactivity of the diazabicyclic alkenes toward the synthesis of biologically relevant organic molecules. In addition to the diazabicyclic olefins derived from cyclopentadiene, we have explored the reactivity of modified diazabicyclic olefins such as spiro-tricyclic olefins bearing cyclopropyl<sup>11</sup> and vinylcyclopropyl group<sup>12</sup> and fulvene derived diazabicyclic olefins.<sup>13</sup> In search of new bicyclic systems having strained alkene moiety, we discerned that urea derived heterobicyclic adduct synthesized by Jeffrey *et al.* possess high synthetic potential.<sup>14</sup> Compounds containing urea

derivatives received substantial attention because of their potent biological activities.<sup>15</sup>



**Fig. 1** Natural Products Containing Fused Chromanones

Chromanones constitute an important class of heterocycles in view of their close resemblance with naturally occurring compounds like flavones, chromones and coumarins.<sup>16</sup> Due to their biological and pharmaceutical importance, more facile and convenient methods for their construction are still in the domain. Even though there exist many strategies for the synthesis of chromanones, attempts toward the synthesis of fused chromanone systems are limited. Fused ring chromanone skeletons are abundant in natural products like cryptosporioptide,<sup>17</sup> preusschchromones<sup>18</sup> and diaportheone<sup>19</sup> (Figure 1). Methods developed for the synthesis of fused chromanone derivatives include palladium catalyzed enantioselective intramolecular Conia-ene reaction of alkynes,<sup>20</sup> synthesis of antituberculosis agent diaportheone B,<sup>21</sup> stereoselective domino reactions toward 4-dehydroxydiversonol,<sup>22</sup> tandem reactions of 4-silyloxy-1-

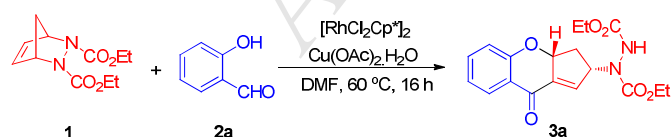
benzopyrylium salts<sup>23</sup> and tandem organocatalytic aldol/oxa-Michael reaction.<sup>24</sup> Recently, our group reported an efficient one pot strategy for the synthesis of cyclopentene fused chromanone derivatives through the direct oxidative coupling of salicylaldehydes with azabicyclic olefins in the presence of rhodium catalyst.<sup>25</sup>

Chelation-controlled hydroacylation reactions with salicylaldehydes have been developed as efficient and atom economic routes for the regioselective construction of ketones.<sup>26</sup> Among the various substrates, salicylaldehyde has been well utilized as a potent precursor for the hydroacylation of alkenes and alkynes under rhodium catalysis.<sup>27</sup> Miura *et al.* reported the seminal work on rhodium catalyzed oxidative coupling of salicylaldehydes with internal alkynes and the method provided a synthetic route to chromone derivatives.<sup>28</sup> Recently, Stanley and co-workers established a different path for synthesizing chromanone derivatives from salicylaldehydes by rhodium catalyzed hydroacylation with alkynes followed by intramolecular oxo-Michael addition.<sup>29</sup> The annulation reaction of salicylaldehydes with terminal alkynes,<sup>30</sup> alkenes<sup>31</sup> and allenes<sup>32</sup> under the rhodium catalyzed oxidative reaction conditions were investigated by different research groups. Terminal alkynes furnished coumarin derivatives while alkenes and allenes produced the benzofuranone motifs. The strained bicyclic olefins were also used as reactive coupling partners in transition metal catalyzed hydroacylation reactions with salicylaldehydes.<sup>33</sup> As already mentioned, our group also utilized the rhodium catalyzed oxidative coupling protocol for the synthesis of fused chromanones.<sup>25</sup> Our continued interest in the chemistry of transition metal catalyzed synthetic manipulation of strained bicyclic systems coupled with the aim of constructing biologically significant fused chromanones prompted us to investigate the reactivity of bicyclic urea adduct with salicylaldehyde under rhodium catalysis. In this paper, we report our entire effort on the rhodium catalyzed oxidative coupling of salicylaldehydes with bicyclic systems such as diazabicyclic olefins and bicyclic urea derivatives.

## 2. Results and discussion

Azabicyclic olefins required for our investigation were synthesized by the Diels-Alder cycloaddition of cyclopentadiene with various azadicarboxylates.<sup>34</sup> The urea derived bicyclic alkenes were prepared by the oxidative 1,4-diamination reaction of cyclic dienes such as cyclopentadiene, furan and N-protected pyrrole with N,N'-Dibenzoyloxurea.<sup>14b</sup>

Our preliminary experiments began with the reaction of azabicyclic olefin **1a** and salicylaldehyde **2a** in the presence of  $[\text{RhCl}_2\text{Cp}^*]_2$  as the catalyst and  $\text{Cu}(\text{OAc})_2 \cdot \text{H}_2\text{O}$  as an oxidant in DMF at 60 °C. To our delight, the reaction furnished cyclopentene fused chromanone **3a** in 46% yield.



**Scheme 1.** Desymmetrisation of Azabicyclic Olefins with Salicylaldehydes

The optimization studies indicated that Rh(III) catalyst,  $[\text{RhCl}_2\text{Cp}^*]_2$  exhibited superior catalytic activity compared to Rh(I) catalysts (Table 1, Entries 3-5). Our attempt to improve the yield by using different solvents proved that  $\text{CH}_3\text{CN}$  is the best medium for this reaction (Table 1, Entry 2), and the reaction is

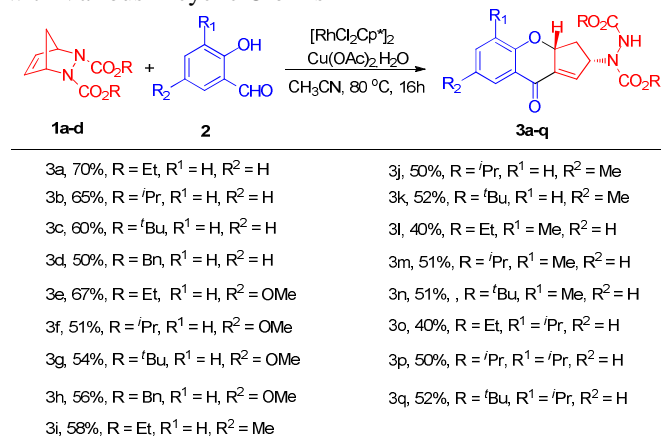
unsuccessful in solvents such as xylene, methanol, THF, toluene and dioxane (Table 1, Entry 8-12). In addition, the catalytic efficiencies of several oxidants were evaluated. The results showed that  $\text{Cu}(\text{OAc})_2 \cdot \text{H}_2\text{O}$  was a better oxidant compared to  $\text{Ag}_2\text{CO}_3$  and  $\text{AgOAc}$ . After a series of experiments, a maximum yield of 70% was obtained using 5 mol% of  $[\text{RhCl}_2\text{Cp}^*]_2$  as the catalyst with 2 equiv. of  $\text{Cu}(\text{OAc})_2 \cdot \text{H}_2\text{O}$  as an oxidant in acetonitrile at 80 °C (Entry 6).

**Table 1.** Reaction optimization studies

Entry	Catalyst	Oxidant	Ligand	Solvent	Yield %
1	$[\text{RhCl}_2\text{Cp}^*]_2$	$\text{Cu}(\text{OAc})_2 \cdot \text{H}_2\text{O}$	-	DMF	46
2	$[\text{RhCl}_2\text{Cp}^*]_2$	$\text{Cu}(\text{OAc})_2 \cdot \text{H}_2\text{O}$	-	$\text{CH}_3\text{CN}$	50
3	$[\text{RhCl}(\text{COD})]_2$	$\text{Cu}(\text{OAc})_2 \cdot \text{H}_2\text{O}$	-	$\text{CH}_3\text{CN}$	20
4	$[\text{RhOH}(\text{COD})]_2$	$\text{Cu}(\text{OAc})_2 \cdot \text{H}_2\text{O}$	-	$\text{CH}_3\text{CN}$	20
5	$[\text{Rh}(\text{acac})(\text{COD})]_2$	$\text{Cu}(\text{OAc})_2 \cdot \text{H}_2\text{O}$	-	$\text{CH}_3\text{CN}$	25
6 <sup>a</sup>	$[\text{RhCl}_2\text{Cp}^*]_2$	$\text{Cu}(\text{OAc})_2 \cdot \text{H}_2\text{O}$	-	$\text{CH}_3\text{CN}$	70
7 <sup>a</sup>	$[\text{RhCl}_2\text{Cp}^*]_2$	$\text{Cu}(\text{OAc})_2 \cdot \text{H}_2\text{O}$	$\text{C}_6\text{H}_5\text{Ph}_4$	$\text{CH}_3\text{CN}$	67
8	$[\text{RhCl}_2\text{Cp}^*]_2$	$\text{Cu}(\text{OAc})_2 \cdot \text{H}_2\text{O}$	-	THF	No reaction
9	$[\text{RhCl}_2\text{Cp}^*]_2$	$\text{Cu}(\text{OAc})_2 \cdot \text{H}_2\text{O}$	-	Xylene	No reaction
10	$[\text{RhCl}_2\text{Cp}^*]_2$	$\text{Cu}(\text{OAc})_2 \cdot \text{H}_2\text{O}$	-	MeOH	No reaction
11	$[\text{RhCl}_2\text{Cp}^*]_2$	$\text{Cu}(\text{OAc})_2 \cdot \text{H}_2\text{O}$	-	Toluene	No reaction
12	$[\text{RhCl}_2\text{Cp}^*]_2$	$\text{Cu}(\text{OAc})_2 \cdot \text{H}_2\text{O}$	-	Dioxane	No reaction
13	$[\text{RhCl}_2\text{Cp}^*]_2$	$\text{AgOAc}$	-	$\text{CH}_3\text{CN}$	Trace
14	$[\text{RhCl}_2\text{Cp}^*]_2$	$\text{Ag}_2\text{CO}_3$	-	$\text{CH}_3\text{CN}$	Trace

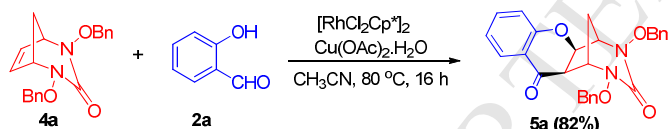
**Reaction Conditions:** diazabicyclic olefin (1 equiv.), salicylaldehyde (1 equiv.), catalyst (3 mol%), ligand (5 mol%), oxidant (2 equiv.), solvent (2 mL), 60 °C, <sup>a</sup>at 80 °C

The generality of the oxidative cyclization reaction was explored with different azabicyclic olefins and various substituted salicylaldehydes under the optimal reaction conditions. Salicylaldehyde **2a** underwent oxidative coupling with azabicyclic olefins derived from different dialkyl azodicarboxylates (**1a-d**) and yielded the fused chromanones (**3a-d**) in moderate to good yields (Table 2). Next, we evaluated the reactivity of various substituted salicylaldehydes under the aforementioned reaction conditions. Unsubstituted aldehydes showed better reactivity compared to substituted ones. The oxidative coupling reaction of methoxy and methyl substituted 2-hydroxybenzaldehydes (*para*-substituted related to -OH group) with different diazabicyclic olefins furnished the chromanone derivatives in comparable yields (Table 2, **3e-3k**). Further, we demonstrated that different *ortho*-substituted salicylaldehydes are also suitable substrates for the present reaction and provided the coupled products in moderate yields (Table 2, **3l-3q**).

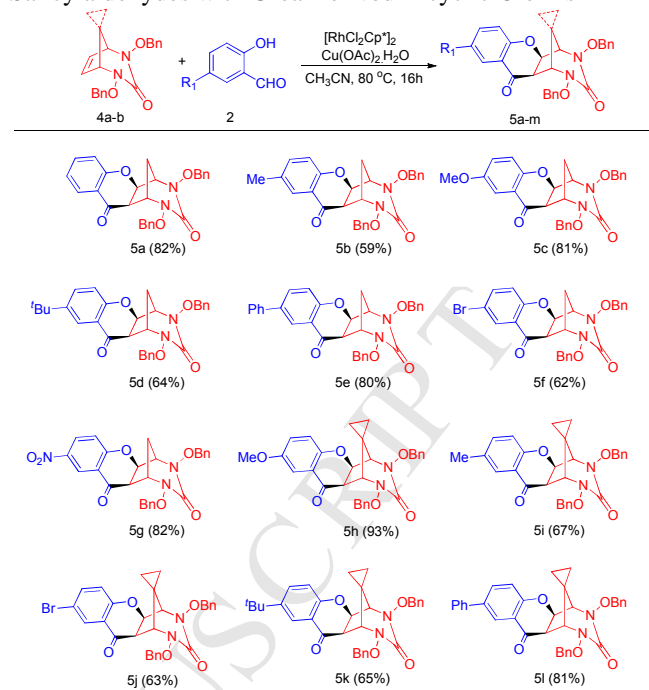
**Table 2.** Oxidative Coupling of Substituted Salicylaldehydes with Various Bicyclic Olefins

Reaction Conditions: diazabicyclic olefin (1 equiv.), salicylaldehyde (1 equiv.),  $[\text{RhCl}_2\text{Cp}^*]_2$  (3 mol%),  $\text{Cu}(\text{OAc})_2 \cdot \text{H}_2\text{O}$  (2 equiv.),  $\text{CH}_3\text{CN}$  (2 mL),  $80^\circ\text{C}$

Encouraged by the results that were obtained from the reaction of cyclopentadiene derived azabicyclic substrates with salicylaldehydes, we became interested in expanding the scope of this rhodium catalyzed oxidative coupling reaction to other heterobicyclic olefins such as urea-derived bicyclic alkenes. The synthesis of organic molecules bearing urea moiety has received considerable attention in the literature due to their biological properties. Inspired by this information, we envisioned that by incorporating urea moiety in chromanone skeleton, instead of hydrazine group, will exhibit improved biological properties. With this idea in mind, we have synthesized various urea derived heterobicyclic olefins. In an initial experiment, we carried out the reaction of urea derived bicyclic adduct **4a** with salicylaldehyde **2a** under the same optimized conditions. The reaction afforded highly functionalized fused chromanone derivative **5a** in 82% yield (Scheme 2). The structure of the product **5a** was assigned based on various spectroscopic techniques like  $^1\text{H}$  NMR,  $^{13}\text{C}$  NMR and HRMS (ESI) analysis.

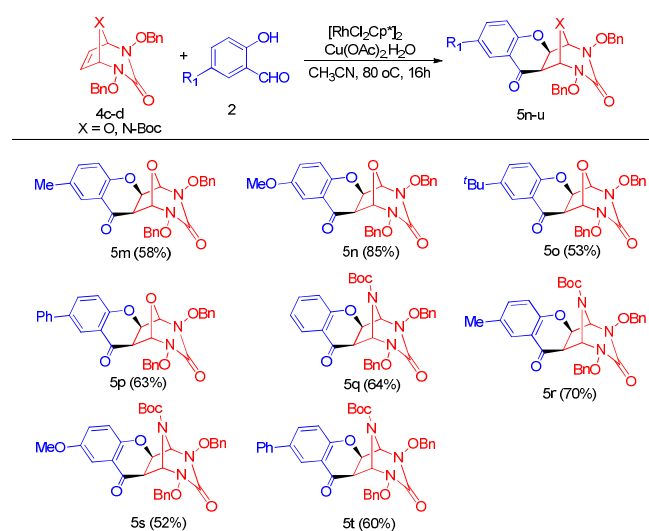
**Scheme 2.** Oxidative Coupling of Salicylaldehyde with Urea Derived Bicyclic Olefin

To illustrate the broad scope of the present method, we have examined the reactivity of various urea-derived bicyclic olefins and different salicylaldehydes under the optimized reaction conditions. The bicyclic urea adducts derived from cyclopentadiene and spiro[2.4]hepta-4,6-diene underwent annulation reaction with various salicylaldehydes and provided the corresponding fused chromanone derivatives in good yields. The results obtained are summarized in table 4. Also, the reaction was found to be compatible with different salicylaldehydes substituted with electron donating and electron withdrawing groups such as Me, OMe, *t*Bu, Ph, Br and  $\text{NO}_2$ .

**Table 3.** Oxidative Coupling of Substituted Salicylaldehydes with Urea Derived Bicyclic Olefins

Reaction Conditions: urea derived bicyclic alkene (1 equiv.), salicylaldehyde (1 equiv.),  $[\text{RhCl}_2\text{Cp}^*]_2$  (3 mol%),  $\text{Cu}(\text{OAc})_2 \cdot \text{H}_2\text{O}$  (2 equiv.),  $\text{CH}_3\text{CN}$  (2 mL),  $80^\circ\text{C}$

The importance of oxa/azabicyclic alkenes in the construction of synthetically versatile building blocks via the transition metal catalyzed ring opening or annulation reactions and hydro(hetero)arylation reactions, prompted us to expand the generality of this oxidative coupling reaction towards oxa/aza-bridged bicyclic urea derivatives.<sup>1</sup> These heterobicyclic urea adducts also underwent smooth oxidative coupling reactions with different substituted salicylaldehydes under the optimized condition and afforded the heteroatom enriched fused chromanone derivatives in good yields (Table 4). We were successful in obtaining the single crystal X-ray of compound **5q** from ethylacetate/hexane mixture (Figure 2).<sup>35</sup>

**Table 4.** Oxidative Coupling of Various Salicylaldehydes with Oxa/Aza Bridged Heterobicyclic Urea Derives

Reaction Conditions: urea derived bicyclic alkene (1 equiv.), salicylaldehyde (1 equiv.),  $[\text{RhCl}_2\text{Cp}^*]_2$  (3 mol%),  $\text{Cu}(\text{OAc})_2 \cdot \text{H}_2\text{O}$  (2 equiv.),  $\text{CH}_3\text{CN}$  (2 mL),  $80^\circ\text{C}$

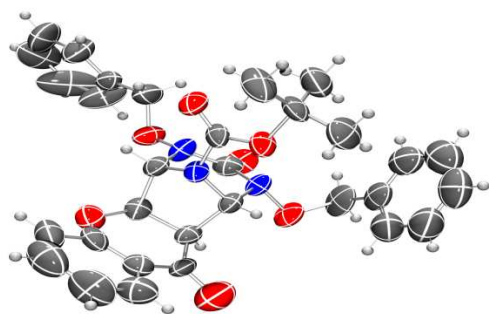
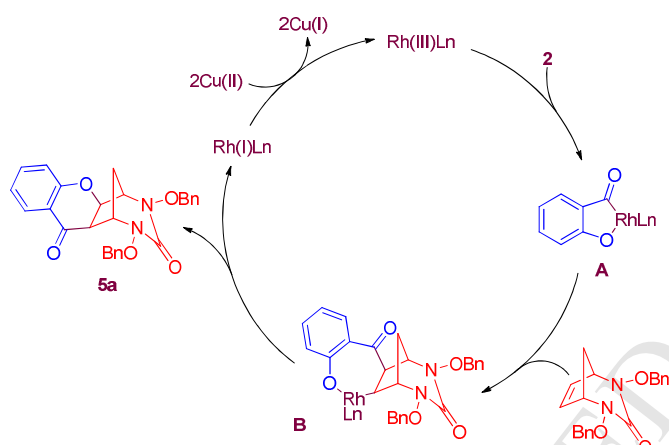


Fig 2. Single Crystal X-ray of Compound **5q**

In accordance with the previous studies, a reasonable reaction mechanism is proposed and is presented in scheme 3.<sup>28</sup> The coordination of hydroxyl group of salicylaldehyde to Rh<sup>III</sup>Ln species and the selective C-H bond cleavage generates a five-membered rhodacycle **A**. This is followed by alkene insertion to the rhodacycle furnishing the intermediate **B**, and successive reductive elimination provides the fused chromanone product. The active Rh<sup>III</sup>Ln catalyst is regenerated by the oxidation of Rh<sup>I</sup>Ln species in the presence of Cu(II) salt.



Scheme 3. Proposed reaction mechanism

### 3. Conclusions

In summary, we have developed an efficient one-pot strategy for the synthesis of fused chromanone derivatives through the rhodium catalyzed direct oxidative coupling of salicylaldehydes with heterobicyclic olefins. The diazabicyclic olefins underwent ring opening-ring closing processes in the presence of Rh/Cu catalyst system and provided cyclopentene fused chromanone derivatives. The developed method has also been applied to urea-derived bicyclic olefins and furnished fused chromanone derivatives. It is notable that the reaction performs well with different oxa/aza-bridged bicyclic urea derivatives. To the best of our knowledge, urea-derived bicyclic olefins have not been utilized for the synthesis of fused chromanone derivatives *via* Rh-catalyzed oxidative coupling reactions. Biological evaluation of synthesized fused chromanones and the detailed investigation on the reactivity of urea-derived bicyclic olefins with mono/bi-functional reagents under transition metal catalysis is currently underway in our laboratory.

### 4. Experimental section

#### 4.1. General

All chemicals were of the best grade commercially available and are used without further purification. All solvents were

purified according to standard procedure; dry solvents were obtained according to the literature methods and stored over molecular sieves. Analytical thin layer chromatography was performed on glass plates coated with silica gel containing calcium sulfate binder. Gravity column chromatography was performed using 60-120 or 100-200 mesh silica gel and mixtures of hexane-ethyl acetate were used for elution. Melting points were determined on a Buchi melting point apparatus and are uncorrected. Proton nuclear magnetic resonance spectra (<sup>1</sup>H NMR) were recorded on a Bruker Avance DPX 300 and Bruker AMX 500 spectrophotometer (CDCl<sub>3</sub> or CDCl<sub>3</sub>/CCl<sub>4</sub> (7:3 mixture) as solvent). Chemical shifts for <sup>1</sup>H NMR spectra are reported as δ in units of parts per million (ppm) downfield from SiMe<sub>4</sub> (δ 0.0) and relative to the signal of chloroform-d (δ 7.25, singlet). Multiplicities were given as: s (singlet); brs (broad singlet); d (doublet); t (triplet); q (quartet); dd (double doublet); m (multiplet). Coupling constants are reported as *J* value in Hz. Carbon nuclear magnetic resonance spectra (<sup>13</sup>C NMR) are reported as δ in units of parts per million (ppm) downfield from SiMe<sub>4</sub> (δ 0.0) and relative to the signal of chloroform-d (δ 77.03, triplet). Mass spectra were recorded under ESI/HRMS at 60,000 resolution using Thermo Scientific Exactive mass spectrometer. IR spectra were recorded on Bruker FT-IR spectrometer.

#### 4.1.1. General Procedure for the synthesis of urea derived bicyclic olefins

(diacetoxyiodo)benzene (DIB) (2.35 g, 0.0073 mol, 2.0 equiv.) and corresponding cyclic dienes (cyclopentadiene, 1.54 mL, 0.0184 mol, 5.0 equiv.) were added dropwise to a solution of CHF<sub>2</sub>CF<sub>2</sub>CH<sub>2</sub>OH (13 mL) and CHF<sub>2</sub>CF<sub>2</sub>CH<sub>2</sub>ONa (1.12 g, 0.0073 mol, 2.0 equiv.) at 0 °C. To this, a solution of 1,3-bis(benzyloxy)urea (1 g, 0.0037 mol, 1.0 equiv.) in anhydrous CH<sub>3</sub>CN (40 mL) was added dropwise slowly at 0 °C using a pressure equalizer. The reaction mixture was stirred till the complete consumption of urea, which was monitored by TLC (4-5 hours). The residue obtained after removing the volatiles under reduced pressure was dissolved in ethyl acetate, washed with water and separated the two layers. The organic phase was dried over anhydrous Na<sub>2</sub>SO<sub>4</sub> and concentrated under reduced pressure. The crude product was purified *via* silica gel (100-200 mesh) column chromatography using hexane/ethyl acetate mixture.

#### 4.1.2. General Procedure for the Rh-catalyzed oxidative coupling of salicylaldehydes with bicyclic olefins

A mixture of bicyclic olefin **1a** (80 mg, 0.3329 mmol, 1.0 equiv.), salicylaldehyde **2a** (41 mg, 0.3329 mmol, 1.0 equiv.), [RhCl<sub>2</sub>Cp\*]<sub>2</sub> (6 mg, 0.0099 mmol, 3 mol%) and Cu(OAc)<sub>2</sub>·H<sub>2</sub>O (133 mg, 0.6659 mmol, 2.0 equiv.) were weighed in a schlenk tube and degassed for 10 minutes. Dry acetonitrile was added and the reaction mixture was purged with argon and allowed to stir at 80 °C for 16 hours. The solvent was evaporated in vacuo and the residue on silica gel (100-200 mesh) column chromatography yielded fused chromanone derivatives.

#### 4.2. Characterization data of the compounds

**Compound 3a.** Yield: 84 mg; 70% as yellow viscous liquid; R<sub>f</sub>: 0.35(5:5 hexane/ethyl acetate). IR (neat) ν<sub>max</sub>: 3291, 2982, 2931, 1709, 1644, 1594, 1513, 1482, 1313, 1263, 1234, 1134, 1061, 1029, 865, 760 cm<sup>-1</sup>. <sup>1</sup>H NMR (300 MHz, CDCl<sub>3</sub>, TMS): δ 7.97 (d, *J* = 7.8 Hz, 1 H), 7.49 (t, *J* = 6.9 Hz, 1 H), 7.05 (t, *J* = 7.5 Hz, 1 H), 6.97 (d, *J* = 8.4 Hz, 1 H), 6.86 (brs, 1 H), 6.56 (brs, 1 H), 5.45 (brs, 1 H), 5.21-5.32 (m, 1 H), 4.24-4.18 (m, 4 H), 3.04-3.00 (m, 1 H), 2.33 (brs, 1 H), 1.31-1.24 (m, 6 H). <sup>13</sup>C NMR (125 MHz, CDCl<sub>3</sub>): δ 180.3, 160.9, 156.8, 155.5, 140.5, 138.8, 136.3, 127.7, 122.5, 118.4, 81.6, 63.0, 62.5, 62.4, 37.1, 14.5, 14.4.

HRMS (ESI): Calcd for  $C_{18}H_{20}N_2O_6$ , (M+Na): 383.12191; Found: 383.12125.

**Compound 3b.** Yield: 75 mg; 65% as yellow viscous liquid;  $R_f$ : 0.46 (5:5 hexane/ethyl acetate). IR (neat)  $\nu_{max}$ : 3299, 2982, 2935, 2879, 1715, 1645, 1608, 1464, 1303, 1235, 1108, 1049, 858, 760  $cm^{-1}$ .  $^1H$  NMR (300 MHz,  $CDCl_3$ , TMS):  $\delta$  7.95 (d,  $J = 7.5$  Hz, 1 H), 7.48 (t,  $J = 6.9$  Hz, 1 H), 7.04 (t,  $J = 7.5$  Hz, 1 H), 6.96 (d,  $J = 8.4$  Hz, 1 H), 6.84 (brs, 1 H), 5.47 (brs, 1 H), 6.35 (brs, 1 H), 5.29 (m, 1 H), 4.98-4.95 (m, 2 H), 2.98 (m, 1 H), 2.33-2.27 (brs, 1 H), 1.28-1.26 (m, 12 H).  $^{13}C$  NMR (125 MHz,  $CDCl_3$ ):  $\delta$  180.1, 161.0, 156.3, 155.0, 140.5, 138.6, 136.0, 127.7, 122.6, 121.8, 118.3, 81.7, 70.8, 70.3, 61.4, 37.0, 21.9, 21.8. HRMS (ESI): Calcd for  $C_{20}H_{24}N_2O_6$ , (M+Na): 411.15321; Found: 411.15286.

**Compound 3c.** Yield: 67 mg; 60% as white solid (m.p. = 140-143  $^{\circ}C$ );  $R_f$ : 0.53 (5:5 hexane/ethyl acetate). IR (neat)  $\nu_{max}$ : 3329, 2978, 2929, 1707, 1673, 1642, 1607, 1464, 1306, 1246, 1156, 1126, 1051, 1019, 856, 758  $cm^{-1}$ .  $^1H$  NMR (300 MHz,  $CDCl_3$ , TMS):  $\delta$  7.97 (d,  $J = 7.8$  Hz, 1 H), 7.49 (t,  $J = 6.9$  Hz, 1 H), 7.07-6.97 (m, 2 H), 6.88 (s, 1 H), 6.26 (brs, 1 H), 5.52-5.45 (m, 1 H), 5.29 (m, 1 H), 3.00-2.97 (m, 1 H), 2.29-2.14 (brs, 1 H), 1.52-1.43 (m, 18 H).  $^{13}C$  NMR (125 MHz,  $CDCl_3$ ):  $\delta$  180.4, 160.9, 155.6, 154.4, 139.4, 137.5, 136.7, 136.1, 127.7, 122.4, 121.8, 118.3, 82.0, 81.7, 60.2, 37.1, 28.2, 28.1, 27.8, 27.5. HRMS (ESI): Calcd for  $C_{22}H_{28}N_2O_6$ , (M+Na): 439.18451; Found: 439.18413.

**Compound 3d.** Yield: 53 mg; 50% as yellow viscous liquid;  $R_f$ : 0.43 (5:5 hexane/ethyl acetate). IR (neat)  $\nu_{max}$ : 3296, 2955, 2924, 2853, 1720, 1672, 1642, 1607, 1497, 1303, 1260, 1218, 1146, 1124, 1081, 1028, 857, 752  $cm^{-1}$ .  $^1H$  NMR (300 MHz,  $CDCl_3$ , TMS):  $\delta$  7.96 (d,  $J = 7.2$  Hz, 1 H), 7.48 (t,  $J = 7$  Hz, 1 H), 7.32-7.27 (m, 10 H), 7.04 (t,  $J = 7.5$  Hz, 1 H), 6.95 (d,  $J = 8.4$  Hz, 1 H), 6.84 (s, 1 H), 5.51 (s, 1 H), 5.26-5.17 (m, 5 H), 3.01 (s, 1 H), 2.31 (s, 1 H).  $^{13}C$  NMR (125 MHz,  $CDCl_3$ ):  $\delta$  179.9, 156.4, 155.1, 140.6, 138.3, 136.0, 135.3, 128.5, 128.4, 128.3, 128.2, 128.0, 127.7, 122.4, 121.7, 118.3, 112.9, 81.4, 68.4, 68.1, 62.1, 36.7. HRMS (ESI): Calcd for  $C_{28}H_{24}N_2O_6$ , (M+Na): 507.15321; Found: 507.15317.

**Compound 3e.** Yield: 87 mg; 67% as yellow viscous liquid;  $R_f$ : 0.33 (5:5 hexane/ethyl acetate). IR (neat)  $\nu_{max}$ : 3314, 2981, 2922, 2851, 1716, 1485, 1381, 1287, 1230, 1164, 1132, 1059, 1032, 870, 761  $cm^{-1}$ .  $^1H$  NMR (300 MHz,  $CDCl_3$ , TMS):  $\delta$  7.37 (s, 1 H), 7.10 (dd,  $J_1 = 3.3$  Hz,  $J_2 = 9$  Hz, 1 H), 6.92 (d,  $J = 9.0$  Hz, 1 H), 6.86 (s, 1 H), 6.59 (brs, 1 H), 5.49 (brs, 1 H), 5.26-5.24 (m, 1 H), 4.24-4.21 (m, 4 H), 3.84 (s, 3 H), 2.98 (m, 1 H), 2.30 (brs, 1 H), 1.31-1.28 (m, 6 H).  $^{13}C$  NMR (75 MHz,  $CDCl_3$ ):  $\delta$  179.9, 156.6, 155.6, 155.3, 154.4, 140.3, 138.5, 125.5, 122.3, 119.6, 107.7, 81.5, 62.9, 62.3, 60.8, 55.7, 36.9, 14.5, 14.4. HRMS (ESI): Calcd for  $C_{19}H_{22}N_2O_7$ , (M+Na): 413.13247; Found: 413.13229.

**Compound 3f.** Yield: 64 mg; 51% as yellow solid (m.p. = 101-103  $^{\circ}C$ );  $R_f$ : 0.41 (5:5 hexane/ethyl acetate). IR (neat)  $\nu_{max}$ : 3404, 2979, 2926, 2854, 1709, 1665, 1484, 1381, 1286, 1233, 1205, 1107, 1031, 865, 771  $cm^{-1}$ .  $^1H$  NMR (300 MHz,  $CDCl_3$ , TMS):  $\delta$  7.35-7.34 (m, 1 H), 7.07 (dd,  $J_1 = 3$  Hz,  $J_2 = 9$  Hz, 1 H), 6.90-6.87 (m, 1 H), 6.83 (s, 1 H), 6.35 (brs, 1 H), 5.46 (s, 1 H), 5.24 (m, 1 H), 4.97-4.95 (m, 2 H), 3.81 (s, 3 H), 2.95 (s, 1 H), 2.31 (brs, 1 H), 1.28-1.23 (m, 12 H).  $^{13}C$  NMR (125 MHz,  $CDCl_3$ ):  $\delta$  179.8, 155.5, 154.8, 154.3, 140.6, 138.6, 125.4, 122.4, 119.5, 107.7, 99.9, 81.5, 70.0, 62.1, 55.6, 37.3, 22.6, 22.0, 21.8. HRMS (ESI): Calcd for  $C_{21}H_{26}N_2O_7$ , (M+Na): 441.16377; Found: 441.16327.

**Compound 3g.** Yield: 65 mg; 54% as yellow solid (m.p. = 80-85  $^{\circ}C$ );  $R_f$ : 0.48 (5:5 hexane/ethyl acetate). IR (neat)  $\nu_{max}$ : 3318, 2978, 2932, 1707, 1673, 1641, 1618, 1485, 1393, 1337, 1287, 1251, 1159, 1082, 1035, 882, 778  $cm^{-1}$ .  $^1H$  NMR (300 MHz,  $CDCl_3$ , TMS):  $\delta$  7.35 (m, 1 H), 7.09-7.06 (m, 1 H), 6.90-6.88 (m, 2 H), 6.20 (s, 1 H), 5.42 (s, 1 H), 5.23 (m, 1 H), 3.81 (s, 3 H), 2.93 (brs, 1 H), 2.30 (brs, 1 H), 1.47-1.43 (m, 18 H).  $^{13}C$  NMR (125 MHz,  $CDCl_3$ ):  $\delta$  180.1, 155.7, 154.4, 140.1, 139.0, 124.7, 124.6, 122.6, 119.6, 108.6, 81.8, 61.1, 55.8, 37.0, 28.2, 28.1. HRMS (ESI): Calcd for  $C_{23}H_{30}N_2O_7$ , (M+Na): 469.19507; Found: 469.19505.

**Compound 3h.** Yield: 63 mg; 56% as yellow viscous liquid;  $R_f$ : 0.41 (5:5 hexane/ethyl acetate). IR (neat)  $\nu_{max}$ : 3336, 3034, 2924, 2853, 1715, 1666, 1590, 1485, 1356, 1287, 1227, 1124, 1039, 856, 754  $cm^{-1}$ .  $^1H$  NMR (300 MHz,  $CDCl_3$ , TMS):  $\delta$  7.36-7.33 (m, 11 H), 7.10 (dd,  $J_1 = 3$  Hz,  $J_2 = 9$  Hz, 1 H), 6.89 (d,  $J = 9$  Hz, 1 H), 6.80 (s, 1 H), 6.55 (s, 1 H), 5.52 (s, 1 H), 5.18 (m, 5 H), 3.83 (s, 3 H), 2.99 (s, 1 H), 2.26 (s, 1 H).  $^{13}C$  NMR (125 MHz,  $CDCl_3$ ):  $\delta$  180.0, 155.6, 155.3, 154.6, 140.8, 137.9, 135.5, 135.4, 130.9, 128.5, 128.4, 128.3, 128.0, 128.0, 125.3, 122.5, 119.6, 108.2, 81.6, 68.6, 68.1, 61.7, 55.8, 36.8. HRMS (ESI): Calcd for  $C_{29}H_{26}N_2O_7$ , (M+Na): 537.16377; Found: 537.16345.

**Compound 3i.** Yield: 72 mg; 58% as yellow viscous liquid;  $R_f$ : 0.33 (5:5 hexane/ethyl acetate). IR (neat)  $\nu_{max}$ : 3303, 2924, 2854, 1716, 1672, 1620, 1485, 1381, 1288, 1230, 1168, 1132, 1098, 1032, 828, 761  $cm^{-1}$ .  $^1H$  NMR (300 MHz,  $CDCl_3$ , TMS):  $\delta$  7.74 (s, 1 H), 7.31-7.27 (m, 1 H), 6.88-6.85 (m, 2 H), 6.47 (s, 1 H), 5.48 (s, 1 H), 5.26 (m, 1 H), 4.25-4.20 (m, 4 H), 2.98 (s, 1 H), 2.37-2.34 (m, 4 H), 1.32-1.26 (m, 6 H).  $^{13}C$  NMR (125 MHz,  $CDCl_3$ ):  $\delta$  180.2, 159.0, 155.4, 140.8, 137.1, 131.3, 127.2, 122.2, 118.1, 81.6, 62.9, 62.3, 62.2, 61.5, 37.0, 20.2, 14.3, 14.2. HRMS (ESI): Calcd for  $C_{19}H_{22}N_2O_6$ , (M+Na): 397.13756; Found: 397.13736.

**Compound 3j.** Yield: 60 mg; 50% as yellow viscous liquid;  $R_f$ : 0.43 (5:5 hexane/ethyl acetate). IR (neat)  $\nu_{max}$ : 3302, 2981, 2931, 2875, 1716, 1643, 1617, 1486, 1382, 1294, 1234, 1138, 1109, 1046, 826, 764  $cm^{-1}$ .  $^1H$  NMR (500 MHz,  $CDCl_3$ , TMS):  $\delta$  7.75 (s, 1 H), 7.31-7.27 (m, 1 H), 6.89-6.87 (m, 2 H), 6.38-6.32 (s, 1 H), 5.48 (s, 1 H), 5.30-5.26 (m, 1 H), 4.98-4.97 (m, 2 H), 2.98 (s, 1 H), 2.35-2.32 (m, 4 H), 1.27-1.23 (m, 12 H).  $^{13}C$  NMR (125 MHz,  $CDCl_3$ ):  $\delta$  179.9, 159.0, 156.1, 154.9, 140.6, 138.2, 136.9, 131.1, 127.3, 122.3, 118.1, 81.6, 70.6, 70.1, 61.4, 37.0, 22.6, 22.0, 21.9, 21.8, 20.3. HRMS (ESI): Calcd for  $C_{21}H_{26}N_2O_6$ , (M+Na): 425.16886; Found: 425.16834.

**Compound 3k.** Yield: 60 mg; 52% as yellow viscous liquid;  $R_f$ : 0.51 (5:5 hexane/ethyl acetate). IR (neat)  $\nu_{max}$ : 3325, 2978, 2927, 2856, 1709, 1644, 1619, 1485, 1394, 1295, 1249, 1158, 1083, 1052, 852, 761  $cm^{-1}$ .  $^1H$  NMR (500 MHz,  $CDCl_3$ , TMS):  $\delta$  7.75 (s, 1 H), 7.29 (m, 1 H), 6.87 (d,  $J = 8.5$  Hz, 2 H), 6.23 (s, 1 H), 5.44 (s, 1 H), 5.25 (m, 1 H), 2.96 (s, 1 H), 2.31 (m, 4 H), 1.48-1.42 (m, 18 H).  $^{13}C$  NMR (125 MHz,  $CDCl_3$ ):  $\delta$  180.4, 159.1, 155.6, 154.4, 140.3, 138.8, 137.0, 131.2, 127.2, 122.2, 118.2, 81.7, 61.2, 37.1, 28.2, 28.1, 20.2. HRMS (ESI): Calcd for  $C_{23}H_{30}N_2O_6$ , (M+Na): 453.20016; Found: 453.20033.

**Compound 3l.** Yield: 50 mg; 40% as yellow viscous liquid;  $R_f$ : 0.48 (5:5 hexane/ethyl acetate). IR (neat)  $\nu_{max}$ : 3297, 2982, 2926, 2856, 1717, 1673, 1642, 1617, 1573, 1485, 1383, 1293, 1229, 1134, 1095, 1060, 879, 762  $cm^{-1}$ .  $^1H$  NMR (500 MHz,  $CDCl_3$ , TMS):  $\delta$  7.82 (d,  $J = 7.5$  Hz, 1 H), 7.35 (d,  $J = 7$  Hz, 1 H), 6.94 (t,  $J = 8$  Hz, 1 H), 6.84 (s, 1 H), 6.53 (s, 1 H), 5.51 (s, 1 H), 5.28 (t,  $J = 7$  Hz, 1 H), 4.23-4.18 (m, 4 H), 3.04 (t,  $J = 6$  Hz, 1 H), 2.36 (s, 1 H), 2.24 (s, 3 H), 1.29-1.24 (m, 6 H).  $^{13}C$  NMR (125 MHz,  $CDCl_3$ ):  $\delta$  180.5, 159.1, 156.7, 155.4, 140.7, 137.8,



137.0, 127.6, 125.3, 122.2, 121.2, 81.5, 62.9, 62.3, 61.5, 37.1, 15.7, 14.3, 14.2. HRMS (ESI): Calcd for  $C_{19}H_{22}N_2O_6$ , (M+Na): 397.13756; Found: 397.13746.

**Compound 3m.** Yield: 61 mg; 51% as yellow viscous liquid;  $R_f$ : 0.58 (5:5 hexane/ethyl acetate). IR (neat)  $\nu_{max}$ : 3319, 2981, 2927, 2856, 1714, 1668, 1643, 1598, 1470, 1299, 1237, 1109, 1039, 829, 759  $cm^{-1}$ .  $^1H$  NMR (500 MHz,  $CDCl_3$ , TMS):  $\delta$  7.82 (d,  $J = 7.5$  Hz, 1 H), 7.36 (d,  $J = 7$  Hz, 1 H), 6.95 (t,  $J = 7.5$  Hz, 1 H), 6.85-6.84 (m, 1 H), 6.35 (s, 1 H), 5.50 (s, 1 H), 5.28 (t,  $J = 7$  Hz, 1 H), 5.00-4.93 (m, 2 H), 3.04 (t,  $J = 6.5$  Hz, 1 H), 2.24 (m, 4 H), 1.27-1.23 (m, 12 H).  $^{13}C$  NMR (125 MHz,  $CDCl_3$ ):  $\delta$  180.2, 159.0, 156.4, 154.8, 140.2, 138.2, 136.9, 127.4, 125.4, 122.1, 121.1, 81.3, 70.0, 69.9, 60.7, 37.1, 22.0, 15.9. HRMS (ESI): Calcd for  $C_{21}H_{26}N_2O_6$ , (M+Na): 425.16886; Found: 425.16841.

**Compound 3n.** Yield: 59 mg; 51% as yellow solid (m.p. = 103-107 °C);  $R_f$ : 0.68 (5:5 hexane/ethyl acetate). IR (neat)  $\nu_{max}$ : 3315, 2978, 2929, 1710, 1670, 1599, 1477, 1368, 1344, 1301, 1251, 1157, 1053, 1019, 852, 757  $cm^{-1}$ .  $^1H$  NMR (500 MHz,  $CDCl_3$ , TMS):  $\delta$  7.82 (d,  $J = 8$  Hz, 1 H), 7.35 (d,  $J = 7$  Hz, 1 H), 6.94 (t,  $J = 7.5$  Hz, 1 H), 6.85 (s, 1 H), 6.23 (s, 1 H), 5.45 (s, 1 H), 5.27 (t,  $J = 6.5$  Hz, 1 H), 3.02 (s, 1 H), 2.25-2.24 (m, 4 H), 1.52-1.43 (m, 18 H).  $^{13}C$  NMR (125 MHz,  $CDCl_3$ ):  $\delta$  180.6, 159.2, 155.6, 154.4, 140.2, 138.5, 136.8, 127.5, 125.3, 122.3, 121.1, 82.0, 81.6, 61.0, 37.2, 28.2, 28.1, 15.6. HRMS (ESI): Calcd for  $C_{23}H_{30}N_2O_6$ , (M+Na): 453.20016; Found: 453.20013.

**Compound 3o.** Yield: 54 mg; 40% as yellow viscous liquid;  $R_f$ : 0.41 (5:5 hexane/ethyl acetate). IR (neat)  $\nu_{max}$ : 3299, 2967, 2928, 2870, 1717, 1670, 1646, 1595, 1472, 1383, 1292, 1230, 1123, 1060, 858, 760  $cm^{-1}$ .  $^1H$  NMR (500 MHz,  $CDCl_3$ , TMS):  $\delta$  7.84-7.82 (m, 1 H), 7.43 (d,  $J = 7.5$  Hz, 1 H), 7.01 (t,  $J = 7.5$  Hz, 1 H), 6.85-6.83 (m, 1 H), 6.51 (s, 1 H), 5.50 (s, 1 H), 5.26 (t,  $J = 7$  Hz, 1 H), 4.23-4.17 (m, 4 H), 3.35-3.30 (m, 1 H), 3.04 (t,  $J = 6.5$  Hz, 1 H), 2.38-2.30 (m, 1 H), 1.29-1.20 (m, 12 H).  $^{13}C$  NMR (125 MHz,  $CDCl_3$ ):  $\delta$  180.4, 158.2, 156.6, 155.4, 140.8, 138.1, 138.0, 132.6, 122.6, 121.5, 120.8, 81.5, 62.8, 62.2, 61.6, 37.0, 26.9, 22.5, 22.3, 14.4, 14.2. HRMS (ESI): Calcd for  $C_{21}H_{26}N_2O_6$ , (M+Na): 425.16886; Found: 425.16791.

**Compound 3p.** Yield: 64 mg; 50% as yellow viscous liquid;  $R_f$ : 0.53 (5:5 hexane/ethyl acetate). IR (neat)  $\nu_{max}$ : 3300, 2979, 2933, 2872, 1716, 1673, 1646, 1596, 1472, 1383, 1303, 1235, 1146, 1108, 1051, 855, 760  $cm^{-1}$ .  $^1H$  NMR (500 MHz,  $CDCl_3$ , TMS):  $\delta$  7.83 (d,  $J = 7.5$  Hz, 1 H), 7.43 (d,  $J = 7.5$  Hz, 1 H), 7.01 (t,  $J = 7.5$  Hz, 1 H), 6.85-6.83 (m, 1 H), 6.34 (s, 1 H), 5.49 (s, 1 H), 5.26 (t,  $J = 7$  Hz, 1 H), 4.99-4.93 (m, 2 H), 3.35-3.30 (m, 1 H), 3.04-3.02 (m, 1 H), 2.38-2.30 (m, 1 H), 1.28-1.20 (m, 18 H).  $^{13}C$  NMR (125 MHz,  $CDCl_3$ ):  $\delta$  180.5, 158.2, 156.3, 155.0, 140.7, 138.0, 132.6, 125.2, 122.6, 121.5, 81.6, 70.7, 70.2, 61.7, 37.0, 26.9, 22.5, 22.3, 21.9, 21.8. HRMS (ESI): Calcd for  $C_{23}H_{30}N_2O_6$ , (M+Na): 453.20016; Found: 453.19932.

**Compound 3q.** Yield: 64 mg; 52% as yellow viscous liquid;  $R_f$ : 0.61 (5:5 hexane/ethyl acetate). IR (neat)  $\nu_{max}$ : 3327, 2972, 2928, 2871, 1707, 1670, 1594, 1473, 1369, 1253, 1157, 1048, 857, 757  $cm^{-1}$ .  $^1H$  NMR (500 MHz,  $CDCl_3$ , TMS):  $\delta$  7.83 (d,  $J = 7$  Hz, 1 H), 7.43 (d,  $J = 6$  Hz, 1 H), 7.02-6.99 (m, 1 H), 6.86 (s, 1 H), 6.24 (s, 1 H), 5.46 (s, 1 H), 5.26-5.24 (m, 1 H), 3.36-3.30 (m, 1 H), 3.02-3.01 (m, 1 H), 2.41-2.37 (m, 1 H), 1.48-1.42 (m, 18 H), 1.26-1.20 (m, 6 H).  $^{13}C$  NMR (125 MHz,  $CDCl_3$ ):  $\delta$  180.5, 158.3, 155.6, 154.3, 140.3, 138.4, 137.9, 132.5, 125.2, 122.6, 121.4, 81.9, 81.6, 61.2, 37.1, 28.2, 28.1, 27.1, 27.0, 22.5, 22.4. HRMS (ESI): Calcd for  $C_{25}H_{34}N_2O_6$ , (M+Na): 489.23146; Found: 489.23146.

**Compound 4a.** Yield: 1.02 g; 82% as pale brown viscous liquid;  $R_f$ : 0.38 (7:3 hexane/ethyl acetate).  $^1H$  NMR (500 MHz,

$CDCl_3$ , TMS):  $\delta$  7.45-7.44 (m, 4 H), 7.37-7.32 (m, 6 H), 6.32 (s, 2 H), 5.00 (d,  $J = 11.0$  Hz, 2 H), 4.86 (d,  $J = 11.0$  Hz, 2 H), 3.93 (d,  $J = 4.0$  Hz, 2 H), 1.96 (d,  $J = 11.0$  Hz, 1 H), 1.77-1.73 (m, 1 H).  $^{13}C$  NMR (125 MHz,  $CDCl_3$ ):  $\delta$  161.2, 136.4, 136.3, 129.5, 128.4, 128.4, 78.1, 65.0, 38.8. HRMS (ESI): Calcd for  $C_{20}H_{20}N_2NaO_3$ , (M+Na): 359.13716; Found: 359.13597.

**Compound 4b.** Yield: 979 mg; 73% as off-white solid (m.p. = 133.6-134.8 °C);  $R_f$ : 0.39 (7:3 hexane/ethyl acetate).  $^1H$  NMR (500 MHz,  $CDCl_3$ , TMS):  $\delta$  7.44-7.42 (m, 4 H), 7.35-7.31 (m, 6 H), 6.44 (d,  $J = 1.5$  Hz, 2 H), 4.99 (d,  $J = 11.0$  Hz, 2 H), 4.84 (d,  $J = 11.0$  Hz, 2 H), 3.05 (s, 2 H), 0.53-0.50 (m, 2 H), 0.42-0.39 (m, 2 H).  $^{13}C$  NMR (125 MHz,  $CDCl_3$ ):  $\delta$  161.5, 138.1, 136.3, 129.8, 128.4, 128.2, 78.0, 70.4, 32.5, 10.5, 8.2. HRMS (ESI): Calcd for  $C_{22}H_{22}N_2NaO_3$ , (M+Na): 385.15281; Found: 385.15207.

**Compound 4c.** Yield: 1 g; 80% as white solid (m.p. = 94.3-94.9 °C);  $R_f$ : 0.36 (7:3 hexane/ethyl acetate).  $^1H$  NMR (500 MHz,  $CDCl_3$ , TMS):  $\delta$  7.44-7.42 (m, 4 H), 7.37-7.33 (m, 6 H), 6.32 (s, 2 H), 5.22 (s, 2 H), 5.00 (d,  $J = 11.0$  Hz, 2 H), 4.91 (d,  $J = 11.5$  Hz, 2 H).  $^{13}C$  NMR (125 MHz,  $CDCl_3$ ):  $\delta$  160.2, 135.8, 133.7, 129.7, 128.8, 128.7, 128.5, 92.5, 78.8. HRMS (ESI): Calcd for  $C_{19}H_{18}N_2NaO_4$ , (M+Na): 361.11643; Found: 361.11619.

**Compound 4d.** Yield: 1.39 g; 86% as pale yellow viscous liquid;  $R_f$ : 0.44 (7:3 hexane/ethyl acetate).  $^1H$  NMR (500 MHz,  $CDCl_3$ , TMS):  $\delta$  7.44 (s, 4 H), 7.37-7.32 (m, 6 H), 6.54 (s, 2 H), 5.47-5.42 (m, 2 H), 5.04-5.02 (m, 2 H), 4.91-4.87 (m, 2 H), 1.47 (s, 9 H).  $^{13}C$  NMR (125 MHz,  $CDCl_3$ ):  $\delta$  161.3, 151.1, 134.8, 129.6, 128.9, 128.5, 128.4, 81.9, 78.4, 75.2, 74.6, 28.2. HRMS (ESI): Calcd for  $C_{24}H_{27}N_3NaO_5$ , (M+Na): 460.18484; Found: 460.18344.

**Compound 5a.** Yield: 89 mg; 82% as white solid (m.p. = 156-158 °C);  $R_f$ : 0.54 (hexane/ethyl acetate = 7:3). IR (neat)  $\nu_{max}$ : 3063, 3032, 2925, 2874, 2391, 2353, 1717, 1677, 1605, 1582, 1498, 1463, 1374, 1312, 1275, 1219, 1155, 1114, 1082, 1029, 919, 883, 752, 698, 675  $cm^{-1}$ .  $^1H$  NMR (500 MHz,  $CDCl_3$ ):  $\delta$  7.67 (dd,  $J_1 = 8$  Hz,  $J_2 = 2$  Hz, 1 H), 7.50-7.46 (m, 4 H), 7.42-7.31 (m, 7 H), 6.97-6.94 (m, 1 H), 6.82-6.80 (m, 1 H), 5.13 (d,  $J = 7.5$  Hz, 1 H), 5.06-5.03 (m, 2 H), 4.93-4.90 (m, 2 H), 4.04-4.03 (m, 1 H), 3.8 (d,  $J = 2.5$  Hz, 1 H), 3.6 (dd,  $J_1 = 8$  Hz,  $J_2 = 1$  Hz, 1 H), 2.04 (d,  $J = 13$  Hz, 1 H), 1.86-1.84 (m, 1 H).  $^{13}C$  NMR (125 MHz,  $CDCl_3$ ):  $\delta$  188.6, 159.7, 159.2, 136.3, 135.9, 135.5, 129.7, 129.5, 128.8, 128.5, 128.4, 126.9, 122.1, 120.4, 117.9, 79.7, 78.0, 77.9, 68.0, 66.4, 54.0, 30.8. HRMS (ESI):  $m/z$  calcd for  $C_{27}H_{25}N_2O_5$ : 457.17635; Found: 457.17712.

**Compound 5b.** Yield: 66 mg; 59% as pale yellow viscous liquid;  $R_f$ : 0.67 (hexane/ethyl acetate = 7:3). IR (neat)  $\nu_{max}$ : 3033, 2923, 2348, 1717, 1673, 1618, 1584, 1542, 1492, 1454, 1421, 1373, 1300, 1220, 1156, 1081, 1018, 915, 832, 750, 699, 677  $cm^{-1}$ .  $^1H$  NMR (500 MHz,  $CDCl_3$ ):  $\delta$  7.52-7.46 (m, 5 H), 7.41-7.33 (m, 6 H), 7.23 (dd,  $J_1 = 8$  Hz,  $J_2 = 2$  Hz, 1 H), 6.73 (d,  $J = 8.5$  Hz, 1 H), 5.11 (d,  $J = 7.5$  Hz, 1 H), 5.08-5.05 (m, 2 H), 4.95-4.92 (m, 2 H), 4.05-4.04 (m, 1 H), 3.81 (d,  $J = 3$  Hz, 1 H), 3.57 (dd,  $J_1 = 8$  Hz,  $J_2 = 1$  Hz, 1 H), 2.27 (s, 3 H), 2.05 (d,  $J = 13$  Hz, 1 H), 1.89-1.84 (m, 1 H).  $^{13}C$  NMR (125 MHz,  $CDCl_3$ ):  $\delta$  189.0, 159.2, 157.7, 137.4, 135.9, 135.5, 131.6, 129.7, 129.5, 128.8, 128.5, 128.4, 126.5, 120.1, 117.7, 115.3, 79.6, 78.0, 78.0, 67.9, 66.3, 54.1, 30.8, 20.4. HRMS (ESI):  $m/z$  calcd for  $C_{28}H_{27}N_2O_5$ : 471.19200; Found: 471.19293.

**Compound 5c.** Yield: 94 mg; 81% as yellow viscous liquid;  $R_f$ : 0.56 (hexane/ethyl acetate = 7:3). IR (neat)  $\nu_{max}$ : 3063, 3031, 2939, 2878, 2837, 1716, 1675, 1616, 1588, 1489, 1454, 1432, 1372, 1290, 1207, 1174, 1157, 1121, 1083, 1059, 1032, 915, 885,

862, 831, 750, 698, 675, 621, 582  $\text{cm}^{-1}$ .  $^1\text{H}$  NMR (500 MHz,  $\text{CDCl}_3$ ):  $\delta$  7.53-7.48 (m, 4 H), 7.40-7.33 (m, 6 H), 7.10 (d,  $J = 3.5$  Hz, 1 H), 7.03 (dd,  $J_1 = 9$  Hz,  $J_2 = 3$  Hz, 1 H), 6.77 (d,  $J = 9$  Hz, 1 H), 5.11-5.05 (m, 3 H), 4.96-4.92 (m, 2 H), 4.06 (dd,  $J_1 = 4.5$  Hz,  $J_2 = 1.5$  Hz, 1 H), 3.83 (d,  $J = 3$  Hz, 1 H), 3.74 (s, 3 H), 3.56 (dd,  $J_1 = 7.5$  Hz,  $J_2 = 1$  Hz, 1 H), 2.06 (d,  $J = 13$  Hz, 1 H), 1.90-1.86 (m, 1 H).  $^{13}\text{C}$  NMR (125 MHz,  $\text{CDCl}_3$ ):  $\delta$  189.1, 159.2, 154.5, 154.3, 135.9, 135.4, 129.7, 129.5, 128.8, 128.6, 128.5, 128.5, 125.4, 120.3, 119.3, 107.4, 79.6, 78.1, 78.0, 67.8, 66.3, 55.8, 54.1, 30.9. HRMS (ESI):  $m/z$  calcd for  $\text{C}_{28}\text{H}_{27}\text{N}_2\text{O}_6$ : 487.18691; Found: 487.18811.

**Compound 5d.** Yield: 78 mg; 64% as pale yellow viscous liquid;  $R_f$ : 0.66 (hexane/ethyl acetate = 7:3). IR (neat)  $\nu_{\text{max}}$ : 3063, 3032, 2960, 2872, 1958, 1717, 1677, 1612, 1492, 1455, 1422, 1367, 1300, 1255, 1218, 1142, 1107, 1082, 1013, 911, 832, 748, 698, 676  $\text{cm}^{-1}$ .  $^1\text{H}$  NMR (500 MHz,  $\text{CDCl}_3$ ):  $\delta$  7.69 (d,  $J = 2.5$  Hz, 1 H), 7.53-7.48 (m, 5 H), 7.42-7.33 (m, 6 H), 6.78 (d,  $J = 8.5$  Hz, 1 H), 5.13-5.11 (m, 1 H), 5.11-5.05 (m, 2 H), 4.96-4.92 (m, 2 H), 4.06-4.05 (m, 1 H), 3.83 (d,  $J = 3$  Hz, 1 H), 3.59 (dd,  $J_1 = 8$  Hz,  $J_2 = 1.5$  Hz, 1 H), 2.06 (d,  $J = 12.5$  Hz, 1 H), 1.89-1.86 (m, 1 H), 1.26 (s, 9 H).  $^{13}\text{C}$  NMR (125 MHz,  $\text{CDCl}_3$ ):  $\delta$  189.3, 159.2, 157.7, 145.2, 135.9, 135.4, 134.3, 129.7, 129.5, 128.8, 128.6, 128.5, 128.5, 127.6, 127.0, 122.8, 119.5, 117.6, 79.7, 78.1, 78.0, 68.0, 66.5, 54.1, 34.3, 31.2. HRMS (ESI):  $m/z$  calcd for  $\text{C}_{31}\text{H}_{33}\text{N}_2\text{O}_5$ : 513.23895; Found: 513.23906.

**Compound 5e.** Yield: 101 mg; 80% as pale brown viscous liquid;  $R_f$ : 0.53 (hexane/ethyl acetate = 7:3). IR (neat)  $\nu_{\text{max}}$ : 3061, 3032, 2924, 2876, 1955, 1716, 1678, 1612, 1540, 1506, 1478, 1453, 1416, 1373, 1299, 1275, 1258, 1211, 1157, 1137, 1082, 1026, 1008, 914, 833, 749, 698  $\text{cm}^{-1}$ .  $^1\text{H}$  NMR (500 MHz,  $\text{CDCl}_3$ ):  $\delta$  7.92 (d,  $J = 2.5$  Hz, 1 H), 7.67 (dd,  $J_1 = 9$  Hz,  $J_2 = 2.5$  Hz, 1 H), 7.53-7.49 (m, 6 H), 7.42-7.32 (m, 9 H), 6.91 (d,  $J = 9.0$  Hz, 1 H), 5.18-5.17 (m, 1 H), 5.10-5.06 (m, 2 H), 4.97-4.94 (m, 2 H), 4.09-4.08 (m, 1 H), 3.87 (d,  $J = 2.5$  Hz, 1 H), 3.63 (dd,  $J_1 = 8$  Hz,  $J_2 = 1.0$  Hz, 1 H), 2.09 (d,  $J = 13.0$  Hz, 1 H), 1.91-1.87 (m, 1 H).  $^{13}\text{C}$  NMR (125 MHz,  $\text{CDCl}_3$ ):  $\delta$  189.0, 159.2, 159.1, 139.2, 135.9, 135.5, 135.3, 135.2, 129.8, 129.5, 129.0, 128.9, 128.6, 128.6, 128.5, 127.6, 126.7, 124.8, 120.2, 118.5, 80.0, 78.1, 78.0, 68.0, 66.5, 54.1, 30.9. HRMS (ESI):  $m/z$  calcd for  $\text{C}_{33}\text{H}_{29}\text{N}_2\text{O}_5$ : 533.20765; Found: 533.20819.

**Compound 5f.** Yield: 79 mg; 62% as pale yellow viscous liquid;  $R_f$ : 0.70 (hexane/ethyl acetate = 7:3). IR (neat)  $\nu_{\text{max}}$ : 3063, 3031, 2932, 2876, 1717, 1680, 1598, 1494, 1467, 1417, 1373, 1286, 1215, 1158, 1131, 1082, 1010, 916, 858, 819, 749, 699, 655  $\text{cm}^{-1}$ .  $^1\text{H}$  NMR (500 MHz,  $\text{CDCl}_3$ ):  $\delta$  7.79 (d,  $J = 2.5$  Hz, 1 H), 7.52-7.47 (m, 5 H), 7.41-7.34 (m, 6 H), 6.74 (d,  $J = 9.0$  Hz, 1 H), 5.14-5.13 (m, 1 H), 5.08-5.05 (m, 2 H), 4.95-4.92 (m, 2 H), 4.03-4.02 (m, 1 H), 3.83 (d,  $J = 2.5$  Hz, 1 H), 3.59 (dd,  $J_1 = 9$  Hz,  $J_2 = 1.0$  Hz, 1 H), 2.08 (d,  $J = 12.5$  Hz, 1 H), 1.86-1.81 (m, 1 H).  $^{13}\text{C}$  NMR (125 MHz,  $\text{CDCl}_3$ ):  $\delta$  187.8, 159.1, 158.6, 139.1, 135.7, 135.4, 129.7, 129.5, 129.3, 128.9, 128.6, 128.5, 121.3, 120.1, 114.7, 80.0, 78.1, 78.1, 67.9, 66.4, 53.8, 30.9. HRMS (ESI):  $m/z$  calcd for  $\text{C}_{27}\text{H}_{24}\text{BrN}_2\text{O}_5$ : 535.08686; Found: 535.08771.

**Compound 5g.** Yield: 98 mg; 82% as pale yellow solid (m. p. = 101-103  $^\circ\text{C}$ );  $R_f$ : 0.40 (hexane/ethyl acetate = 7:3). IR (neat)  $\nu_{\text{max}}$ : 3090, 3033, 2930, 2876, 1685, 1617, 1587, 1523, 1475, 1440, 1343, 1290, 1222, 1158, 1107, 1080, 1008, 917, 876, 835, 747, 699  $\text{cm}^{-1}$ .  $^1\text{H}$  NMR (500 MHz,  $\text{CDCl}_3$ ):  $\delta$  8.59 (s, 1H), 8.27 (dd,  $J_1 = 9$  Hz,  $J_2 = 3.0$  Hz, 1 H), 7.51-7.47 (m, 4 H), 7.41-7.34 (m, 6 H), 6.97 (d,  $J = 9.0$  Hz, 1 H), 5.27-5.26 (m, 1 H), 5.09-5.06 (m, 2 H), 4.95-4.92 (m, 2 H), 4.03-4.02 (m, 1 H), 3.85 (d,  $J = 2.5$  Hz, 1 H), 3.70 (dd,  $J_1 = 8$  Hz,  $J_2 = 1.0$  Hz, 1 H), 2.13-2.11 (m, 1 H), 1.82-1.77 (m, 1 H).  $^{13}\text{C}$  NMR (125 MHz,  $\text{CDCl}_3$ ):  $\delta$  186.8,

163.5, 158.9, 142.5, 135.6, 135.3, 130.7, 129.7, 129.5, 128.9, 128.7, 128.6, 128.5, 123.4, 119.3, 118.8, 81.0, 78.2, 78.1, 68.0, 66.8, 53.4, 30.9. HRMS (ESI):  $m/z$  calcd for  $\text{C}_{27}\text{H}_{23}\text{N}_3\text{O}_7\text{Na}$ : 524.14337; Found: 524.14337.

**Compound 5h.** Yield: 105 mg; 93% as brown viscous liquid;  $R_f$ : 0.58 (hexane/ethyl acetate = 7:3). IR (neat)  $\nu_{\text{max}}$ : 3065, 3032, 2925, 1716, 1672, 1618, 1541, 1490, 1456, 1432, 1368, 1292, 1227, 1202, 1177, 1121, 1057, 1029, 919, 828, 752, 700  $\text{cm}^{-1}$ .  $^1\text{H}$  NMR (500 MHz,  $\text{CDCl}_3$ ):  $\delta$  7.49-7.45 (m, 4 H), 7.38-7.31 (m, 6 H), 7.09 (d,  $J = 3.0$  Hz, 1 H), 7.02 (dd,  $J_1 = 9$  Hz,  $J_2 = 3.0$  Hz, 1 H), 6.74 (d,  $J = 9.0$  Hz, 1 H), 5.21 (d,  $J = 8.0$  Hz, 1 H), 5.07-5.04 (m, 2 H), 4.92-4.90 (m, 2 H), 3.75 (s, 3 H), 3.69 (d,  $J = 8.5$  Hz, 1 H), 3.25 (d,  $J = 2.5$  Hz, 1 H), 2.96 (d,  $J = 2.0$  Hz, 1 H), 0.52-0.49 (m, 2 H), 0.47-0.44 (m, 1 H), 0.31-0.28 (m, 1 H).  $^{13}\text{C}$  NMR (125 MHz,  $\text{CDCl}_3$ ):  $\delta$  189.1, 159.7, 154.2, 135.8, 135.6, 129.9, 129.8, 128.7, 128.5, 128.4, 128.3, 128.2, 125.4, 119.7, 119.1, 107.2, 80.3, 78.0, 78.0, 73.6, 72.2, 55.6, 54.6, 26.2, 10.3, 4.5. HRMS (ESI):  $m/z$  calcd for  $\text{C}_{30}\text{H}_{29}\text{N}_2\text{O}_6$ : 513.20256; Found: 513.20319.

**Compound 5i.** Yield: 74 mg; 67% as pale yellow viscous liquid;  $R_f$ : 0.42 (hexane/ethyl acetate = 7:3). IR (neat)  $\nu_{\text{max}}$ : 3031, 3005, 2932, 2875, 1955, 1717, 1676, 1617, 1583, 1492, 1454, 1422, 1369, 1299, 1225, 1185, 1161, 1136, 1057, 1009, 952, 916, 823, 750, 699  $\text{cm}^{-1}$ .  $^1\text{H}$  NMR (500 MHz,  $\text{CDCl}_3$ ):  $\delta$  7.49-7.46 (m, 5 H), 7.38-7.31 (m, 6 H), 7.22 (dd,  $J_1 = 8.5$  Hz,  $J_2 = 2.5$  Hz, 1 H), 6.71 (d,  $J = 8.5$  Hz, 1 H), 5.22 (d,  $J = 8.5$  Hz, 1 H), 5.07-5.04 (m, 2 H), 4.92-4.90 (m, 2 H), 3.69 (d,  $J = 8.5$  Hz, 1 H), 3.25 (d,  $J = 2.0$  Hz, 1 H), 2.97 (d,  $J = 2.0$  Hz, 1 H), 2.26 (s, 3 H), 0.52-0.42 (m, 3 H), 0.30-0.26 (m, 1 H).  $^{13}\text{C}$  NMR (125 MHz,  $\text{CDCl}_3$ ):  $\delta$  189.2, 159.7, 157.7, 137.4, 135.8, 135.6, 131.1, 129.9, 129.8, 128.7, 128.5, 128.4, 128.4, 128.3, 128.2, 126.4, 119.5, 117.6, 80.3, 78.0, 77.9, 73.7, 72.2, 54.7, 26.2, 20.4, 10.3, 4.5. HRMS (ESI):  $m/z$  calcd for  $\text{C}_{30}\text{H}_{29}\text{N}_2\text{O}_5$ : 497.20765; Found: 497.20840.

**Compound 5j.** Yield: 78 mg; 63% as pale brown viscous liquid;  $R_f$ : 0.64 (hexane/ethyl acetate = 7:3). IR (neat)  $\nu_{\text{max}}$ : 3065, 3033, 2931, 2877, 1673, 1599, 1469, 1419, 1370, 1288, 1231, 1204, 1163, 1132, 1056, 1023, 952, 897, 856, 824, 748, 699  $\text{cm}^{-1}$ .  $^1\text{H}$  NMR (500 MHz,  $\text{CDCl}_3$ ):  $\delta$  7.78 (d,  $J = 2.5$  Hz, 1 H), 7.49-7.45 (m, 5 H), 7.38-7.32 (m, 6 H), 6.72 (d,  $J = 9.0$  Hz, 1 H), 5.25 (d,  $J = 8.5$  Hz, 1 H), 5.06-5.04 (m, 2 H), 4.92-4.89 (m, 2 H), 3.71 (d,  $J = 8.0$  Hz, 1 H), 3.20 (d,  $J = 2.0$  Hz, 1 H), 2.94 (d,  $J = 2.5$  Hz, 1 H), 0.52-0.49 (m, 2 H), 0.43-0.39 (m, 1 H), 0.28-0.24 (m, 1 H).  $^{13}\text{C}$  NMR (125 MHz,  $\text{CDCl}_3$ ):  $\delta$  187.6, 159.5, 158.5, 138.9, 135.7, 135.6, 129.9, 129.8, 129.2, 128.8, 128.6, 128.4, 128.3, 120.7, 119.8, 114.3, 80.7, 78.0, 78.0, 73.6, 72.3, 54.3, 26.2, 10.3, 4.6. HRMS (ESI):  $m/z$  calcd for  $\text{C}_{29}\text{H}_{26}\text{BrN}_2\text{O}_5$ : 561.10251; Found: 561.10284.

**Compound 5k.** Yield: 77 mg; 65% as white solid (m. p. = 170-172  $^\circ\text{C}$ );  $R_f$ : 0.61 (hexane/ethyl acetate = 7:3). IR (neat)  $\nu_{\text{max}}$ : 3063, 3032, 3005, 2961, 2872, 1956, 1715, 1676, 1613, 1581, 1492, 1455, 1423, 1366, 1301, 1258, 1227, 1196, 1164, 1143, 1106, 1077, 1056, 1005, 952, 913, 831, 776, 748, 700, 622, 597, 528  $\text{cm}^{-1}$ .  $^1\text{H}$  NMR (500 MHz,  $\text{CDCl}_3$ ):  $\delta$  7.67 (d,  $J = 3.0$  Hz, 1 H), 7.50-7.47 (m, 5 H), 7.39-7.32 (m, 6 H), 6.76 (d,  $J = 8.5$  Hz, 1 H), 5.23 (d,  $J = 8.0$  Hz, 1 H), 5.08-5.05 (m, 2 H), 4.94-4.91 (m, 2 H), 3.71 (d,  $J = 8.5$  Hz, 1 H), 3.27 (d,  $J = 2.0$  Hz, 1 H), 2.99 (d,  $J = 2.5$  Hz, 1 H), 1.27 (s, 9 H), 0.53-0.47 (m, 3 H), 0.33-0.29 (m, 1 H).  $^{13}\text{C}$  NMR (125 MHz,  $\text{CDCl}_3$ ):  $\delta$  189.4, 159.8, 157.7, 144.7, 135.8, 135.6, 134.1, 129.9, 129.8, 128.7, 128.5, 128.4, 128.3, 122.7, 119.2, 117.4, 80.4, 78.0, 78.0, 73.6, 72.2, 54.8, 34.3, 31.2, 26.2, 10.3, 4.4. HRMS (ESI):  $m/z$  calcd for  $\text{C}_{33}\text{H}_{35}\text{N}_2\text{O}_5$ : 539.25460; Found: 539.25555.

**Compound 5l.** Yield: 100 mg; 81% as yellow viscous liquid;  $R_f$ : 0.54 (hexane/ethyl acetate = 7:3). IR (neat)  $\nu_{\text{max}}$ : 3063, 3033,

2934, 2877, 1957, 1885, 1674, 1613, 1506, 1478, 1454, 1417, 1369, 1310, 1266, 1203, 1161, 1137, 1058, 1005, 900, 833, 805, 746, 699, 622  $\text{cm}^{-1}$ .  $^1\text{H}$  NMR (500 MHz,  $\text{CDCl}_3$ ):  $\delta$  7.90 (d,  $J = 2.5$  Hz, 1 H), 7.66 (dd,  $J_1 = 8.5$  Hz,  $J_2 = 2.0$  Hz, 1 H), 7.50-7.47 (m, 5 H), 7.41-7.30 (m, 10 H), 6.88 (d,  $J = 9.0$  Hz, 1 H), 5.29 (d,  $J = 8.5$  Hz, 1 H), 5.08-5.05 (m, 2 H), 4.94-4.91 (m, 2 H), 3.75 (d,  $J = 8.5$  Hz, 1 H), 3.27 (d,  $J = 2.0$  Hz, 1 H), 2.99 (d,  $J = 2.0$  Hz, 1 H), 0.53-0.46 (m, 3 H), 0.33-0.29 (m, 1 H).  $^{13}\text{C}$  NMR (125 MHz,  $\text{CDCl}_3$ ):  $\delta$  188.8, 159.7, 159.0, 139.3, 135.8, 135.6, 135.0, 134.9, 130.0, 129.8, 128.9, 128.7, 128.5, 128.4, 128.3, 127.4, 126.6, 124.8, 119.7, 118.3, 80.6, 78.0, 78.0, 73.7, 72.3, 54.6, 26.2, 10.3, 4.6. HRMS (ESI):  $m/z$  calcd for  $\text{C}_{35}\text{H}_{31}\text{N}_2\text{O}_5$ : 559.22330; Found: 559.22375.

**Compound 5m.** Yield: 65 mg; 58% as pale yellow solid (m. p. = 120-122  $^\circ\text{C}$ );  $R_f$ : 0.57 (hexane/ethyl acetate = 7:3). IR (neat)  $\nu_{\text{max}}$ : 3033, 2936, 1720, 1679, 1619, 1586, 1492, 1455, 1422, 1374, 1304, 1217, 1133, 1076, 1005, 918, 855, 825, 749, 699  $\text{cm}^{-1}$ .  $^1\text{H}$  NMR (500 MHz,  $\text{CDCl}_3$ ):  $\delta$  7.50-7.46 (m, 5 H), 7.42-7.35 (m, 6 H), 7.25 (dd,  $J_1 = 8.5$  Hz,  $J_2 = 2.5$  Hz, 1 H), 6.72 (d,  $J = 8.5$  Hz, 1 H), 5.31 (s, 1 H), 5.16 (s, 1 H), 5.10-5.07 (m, 2 H), 5.03-4.99 (m, 2 H), 4.92 (d,  $J = 8.0$  Hz, 1 H), 3.43 (d,  $J = 8.0$  Hz, 1 H), 2.26 (s, 3 H).  $^{13}\text{C}$  NMR (125 MHz,  $\text{CDCl}_3$ ):  $\delta$  186.5, 157.4, 156.6, 137.9, 135.3, 135.2, 131.7, 129.9, 129.8, 129.6, 129.1, 128.8, 128.7, 128.6, 126.7, 126.4, 119.0, 117.7, 96.3, 95.3, 79.7, 78.9, 78.7, 53.6, 20.4. HRMS (ESI):  $m/z$  calcd for  $\text{C}_{27}\text{H}_{24}\text{N}_2\text{O}_6\text{Na}$ : 495.15321; Found: 495.15332.

**Compound 5n.** Yield: 98 mg; 85% as brown solid (m. p. = 98-100  $^\circ\text{C}$ );  $R_f$ : 0.63 (hexane/ethyl acetate = 7:3). IR (neat)  $\nu_{\text{max}}$ : 3032, 2937, 1730, 1680, 1617, 1590, 1541, 1489, 1456, 1433, 1372, 1297, 1206, 1124, 1071, 1031, 918, 856, 749, 699, 625, 584  $\text{cm}^{-1}$ .  $^1\text{H}$  NMR (500 MHz,  $\text{CDCl}_3$ ):  $\delta$  7.5-7.46 (m, 4 H), 7.41-7.33 (m, 7 H), 7.09-7.08 (m, 1 H), 6.75 (d,  $J = 9$  Hz, 1 H), 5.29 (s, 1 H), 5.13 (s, 1 H), 5.09-5.06 (m, 2 H), 5.02-4.01 (m, 2 H), 4.91 (d,  $J = 8$  Hz, 1 H), 3.75 (s, 3 H), 3.41 (d,  $J = 10$  Hz, 1 H).  $^{13}\text{C}$  NMR (125 MHz,  $\text{CDCl}_3$ ):  $\delta$  186.5, 156.7, 154.6, 153.9, 135.3, 135.1, 129.8, 129.6, 129.1, 128.8, 128.7, 128.6, 126.1, 119.2, 107.1, 96.3, 95.3, 79.7, 78.9, 78.7, 55.7, 53.5. HRMS (ESI):  $m/z$  calcd for  $\text{C}_{27}\text{H}_{24}\text{N}_2\text{O}_7\text{Na}$ : 511.14812; Found: 511.14883.

**Compound 5o.** Yield: 65 mg; 53% as reddish brown viscous liquid;  $R_f$ : 0.63 (hexane/ethyl acetate = 7:3). IR (neat)  $\nu_{\text{max}}$ : 3063, 3032, 2961, 2872, 2031, 1728, 1679, 1639, 1613, 1583, 1492, 1456, 1424, 1367, 1304, 1259, 1211, 1143, 1111, 1075, 1000, 914, 855, 747, 699, 622, 586, 556  $\text{cm}^{-1}$ .  $^1\text{H}$  NMR (500 MHz,  $\text{CDCl}_3$ ):  $\delta$  7.69 (d,  $J = 2.5$  Hz, 1 H), 7.52-7.47 (m, 5 H), 7.43-7.36 (m, 6 H), 6.77 (d,  $J = 9.0$  Hz, 1 H), 5.33 (s, 1 H), 5.18 (s, 1 H), 5.11-5.07 (m, 2 H), 5.04-5.00 (m, 2 H), 4.92 (d,  $J = 8.0$  Hz, 1 H), 3.44 (d,  $J = 8.0$  Hz, 1 H), 1.26 (s, 9 H).  $^{13}\text{C}$  NMR (125 MHz,  $\text{CDCl}_3$ ):  $\delta$  186.7, 157.4, 156.7, 145.2, 135.3, 134.7, 129.8, 129.6, 129.1, 128.9, 128.7, 128.6, 127.0, 122.8, 118.5, 117.5, 96.4, 95.4, 79.7, 78.9, 78.7, 53.6, 34.3, 31.2. HRMS (ESI):  $m/z$  calcd for  $\text{C}_{30}\text{H}_{31}\text{N}_2\text{O}_6$ : 515.21821; Found: 515.21906.

**Compound 5p.** Yield: 79 mg; 63% as yellow viscous liquid;  $R_f$ : 0.64 (hexane/ethyl acetate = 7:3). IR (neat)  $\nu_{\text{max}}$ : 3062, 3033, 2940, 2881, 1731, 1681, 1614, 1541, 1505, 1478, 1454, 1417, 1354, 1313, 1212, 1138, 1075, 1000, 915, 855, 781, 748, 698, 620, 587, 565  $\text{cm}^{-1}$ .  $^1\text{H}$  NMR (500 MHz,  $\text{CDCl}_3$ ):  $\delta$  7.93 (d,  $J = 2.0$  Hz, 1 H), 7.69 (dd,  $J_1 = 9.0$  Hz,  $J_2 = 2.5$  Hz, 1 H), 7.52-7.48 (m, 6 H), 7.43-7.33 (m, 9 H), 6.91 (d,  $J = 9.0$  Hz, 1 H), 5.34 (s, 1 H), 5.20 (s, 1 H), 5.12-5.09 (m, 2 H), 5.05-5.01 (m, 2 H), 4.97 (d,  $J = 8.0$  Hz, 1 H), 3.49 (d,  $J = 8.0$  Hz, 1 H).  $^{13}\text{C}$  NMR (125 MHz,  $\text{CDCl}_3$ ):  $\delta$  186.3, 158.7, 156.6, 153.3, 139.1, 135.5, 135.5, 129.9, 129.8, 129.7, 129.6, 129.2, 129.1, 128.9, 128.9, 128.8, 128.6, 126.7, 124.8, 119.2, 118.3, 96.4, 95.4, 79.9, 78.9, 78.7, 53.6.

HRMS (ESI):  $m/z$  calcd for  $\text{C}_{32}\text{H}_{27}\text{N}_2\text{O}_6$ : 535.18691; Found: 535.18799.

**Compound 5q.** Yield: 65 mg; 64% as reddish brown solid (m. p. = 112-114  $^\circ\text{C}$ );  $R_f$ : 0.67 (hexane/ethyl acetate = 7:3). IR (neat)  $\nu_{\text{max}}$ : 3064, 3033, 2977, 2934, 2880, 1960, 1727, 1682, 1607, 1583, 1496, 1464, 1370, 1325, 1222, 1157, 1116, 1073, 1001, 942, 915, 890, 834, 750, 699, 592  $\text{cm}^{-1}$ .  $^1\text{H}$  NMR (500 MHz,  $\text{CDCl}_3$ ):  $\delta$  7.74 (dd,  $J_1 = 8.0$  Hz,  $J_2 = 2.0$  Hz, 1 H), 7.51-7.45 (m, 5 H), 7.40-7.33 (m, 6 H), 7.03-6.99 (m, 1 H), 6.89 (d,  $J = 8.0$  Hz, 1 H), 5.49 (brs, 1 H), 5.40 (brs, 1 H), 5.25 (d,  $J = 8.0$  Hz, 1 H), 5.09-5.05 (m, 2 H), 4.97-4.93 (m, 2 H), 3.72 (d,  $J = 8.0$  Hz, 1 H), 1.42 (s, 9 H).  $^{13}\text{C}$  NMR (125 MHz,  $\text{CDCl}_3$ ):  $\delta$  187.0, 159.5, 159.2, 152.2, 136.9, 135.3, 134.9, 129.5, 129.2, 128.8, 128.6, 128.5, 127.6, 127.0, 127.0, 122.3, 119.6, 118.0, 83.1, 78.4, 78.2, 65.3, 53.2, 28.0. HRMS (ESI):  $m/z$  calcd for  $\text{C}_{31}\text{H}_{32}\text{N}_3\text{O}_7$ : 558.22403; Found: 558.22534.

**Compound 5r.** Yield: 74 mg; 70% as pale yellow solid (m. p. = 126-128  $^\circ\text{C}$ );  $R_f$ : 0.60 (hexane/ethyl acetate = 7:3). IR (neat)  $\nu_{\text{max}}$ : 3064, 3033, 2977, 2931, 2880, 1726, 1680, 1618, 1587, 1492, 1455, 1422, 1370, 1333, 1302, 1223, 1158, 1075, 1002, 944, 832, 748, 699  $\text{cm}^{-1}$ .  $^1\text{H}$  NMR (500 MHz,  $\text{CDCl}_3$ ):  $\delta$  7.52-7.47 (m, 5 H), 7.39-7.33 (m, 6 H), 7.27 (dd,  $J_1 = 8.5$  Hz,  $J_2 = 2.0$  Hz, 1 H), 6.79 (d,  $J = 8.5$  Hz, 1 H), 5.46 (brs, 1 H), 5.36 (brs, 1 H), 5.20 (d,  $J = 8.0$  Hz, 1 H), 5.07-5.04 (m, 2 H), 4.96-4.92 (m, 2 H), 3.68 (d,  $J = 8.0$  Hz, 1 H), 2.28 (s, 3 H), 1.42 (s, 9 H).  $^{13}\text{C}$  NMR (125 MHz,  $\text{CDCl}_3$ ):  $\delta$  187.0, 159.2, 157.6, 152.2, 137.9, 135.4, 134.9, 131.7, 129.9, 129.5, 129.2, 128.8, 128.6, 128.5, 128.5, 126.9, 126.5, 119.3, 117.8, 82.9, 78.3, 78.1, 65.2, 53.3, 28.0, 20.4. HRMS (ESI):  $m/z$  calcd for  $\text{C}_{32}\text{H}_{34}\text{N}_3\text{O}_7$ : 572.23968; Found: 572.23860.

**Compound 5s.** Yield: 56 mg; 52% as yellow viscous liquid;  $R_f$ : 0.62 (hexane/ethyl acetate = 7:3). IR (neat)  $\nu_{\text{max}}$ : 3064, 3033, 2977, 2936, 2881, 2838, 1722, 1677, 1618, 1490, 1455, 1433, 1370, 1332, 1293, 1231, 1204, 1158, 1123, 1061, 1033, 943, 832, 786, 749, 699  $\text{cm}^{-1}$ .  $^1\text{H}$  NMR (500 MHz,  $\text{CDCl}_3$ ):  $\delta$  7.52-7.47 (m, 4 H), 7.41-7.34 (m, 6 H), 7.15 (d,  $J = 3.5$  Hz, 1 H), 7.07 (dd,  $J_1 = 9.0$  Hz,  $J_2 = 3.5$  Hz, 1 H), 6.83 (d,  $J = 9.0$  Hz, 1 H), 5.48 (brs, 1 H), 5.38-5.37 (m, 1 H), 5.20 (d,  $J = 3.0$  Hz, 1 H), 5.08-5.05 (m, 2 H), 4.97-4.93 (m, 2 H), 3.77 (s, 3 H), 3.69 (d,  $J = 8.0$  Hz, 1 H), 1.43 (s, 9 H).  $^{13}\text{C}$  NMR (125 MHz,  $\text{CDCl}_3$ ):  $\delta$  186.8, 159.2, 154.6, 154.1, 152.2, 135.3, 134.9, 129.5, 129.1, 128.8, 128.6, 128.5, 128.5, 127.0, 125.9, 119.5, 119.4, 107.3, 83.0, 78.3, 78.2, 65.2, 55.8, 53.2, 28.0. HRMS (ESI):  $m/z$  calcd for  $\text{C}_{32}\text{H}_{34}\text{N}_3\text{O}_8$ : 588.23459; Found: 588.23566.

**Compound 5t.** Yield: 70 mg; 60% as yellow viscous liquid;  $R_f$ : 0.58 (hexane/ethyl acetate = 7:3). IR (neat)  $\nu_{\text{max}}$ : 3063, 3033, 2977, 2933, 2879, 1953, 1726, 1683, 1614, 1541, 1506, 1479, 1454, 1417, 1370, 1332, 1259, 1236, 1207, 1157, 1075, 1002, 943, 909, 872, 836, 786, 748, 698, 620, 598, 569  $\text{cm}^{-1}$ .  $^1\text{H}$  NMR (500 MHz,  $\text{CDCl}_3$ ):  $\delta$  7.96 (d,  $J = 2.5$  Hz, 1 H), 7.71 (dd,  $J_1 = 9.0$  Hz,  $J_2 = 1.0$  Hz, 1 H), 7.52-7.49 (m, 6 H), 7.42-7.31 (m, 9 H), 6.97 (d,  $J = 9.0$  Hz, 1 H), 5.51 (brs, 1 H), 5.42 (brs, 1 H), 5.27 (d,  $J = 8.5$  Hz, 1 H), 5.10-5.06 (m, 2 H), 4.98-4.95 (m, 2 H), 3.75 (d,  $J = 8.0$  Hz, 1 H), 1.43 (s, 9 H).  $^{13}\text{C}$  NMR (125 MHz,  $\text{CDCl}_3$ ):  $\delta$  186.8, 159.2, 158.9, 152.2, 139.2, 135.6, 135.5, 134.9, 129.6, 129.2, 129.0, 129.0, 128.9, 128.6, 128.6, 128.5, 128.2, 127.6, 126.7, 124.9, 119.5, 118.6, 83.1, 78.4, 78.2, 53.3, 28.0. HRMS (ESI):  $m/z$  calcd for  $\text{C}_{37}\text{H}_{36}\text{N}_3\text{O}_7$ : 634.25533; Found: 634.25580.

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## Supplementary Material

Experimental details and characterization data are available.