

Recyclable Polymer Supported DMAP Catalyzed One-Pot Cascade Synthesis of Di-/Trisubstituted α -Pyrone

3.1 INTRODUCTION

Nature is a unique source of heterocyclic compounds that participate in a variety of metabolic processes and exhibit valuable biological functions.²¹⁶ As a result, the vast majority of medications marketed in recent decades have been derived from natural sources, either directly containing natural ingredients or being inspired by them.²¹⁷ Among them, oxygen rich α -pyrones are widely distributed in a variety of natural products that have been isolated from animals, plants, bacteria, fungi, insects, and marine organisms.²¹⁸ Many compounds containing 2-pyrone exhibit a diverse range of bioactivity, such as antibiotic, antifungal, neurotoxic, phytotoxic, and cytotoxic (Figure 3.1).²¹⁹ 2-Pyrone play essential roles in these structures as signaling molecules, metabolic intermediates, or end products.²²⁰ Natural 2-pyrone also display a wide range of biological activities with enormous therapeutic significance, including effects on telomerase, antifungal, anti-inflammatory, anti-influenza, antiviral, antibacterial, neurotoxic, HIV protease, and cardiotoxic processes.²²¹ Besides their bioactivity, they can serve as versatile synthetic building blocks for constructing complex molecules due to the presence of multiple reactive sites.⁷⁶ A number of approaches have been established to build and manipulate such a complex framework while considering the synthetic potential and biological significance of α -pyrones. The majority of the metal-catalyzed reactions leading to 2-pyrone are annulations, ring expansion, C-H activations, cycloadditions, and coupling reactions.²²² Traditional approaches²²³ over organocatalytic pathways primarily rely on α -halocarbonyl reactions mediated by ammonium/sulfur ylides and NHC catalysis.

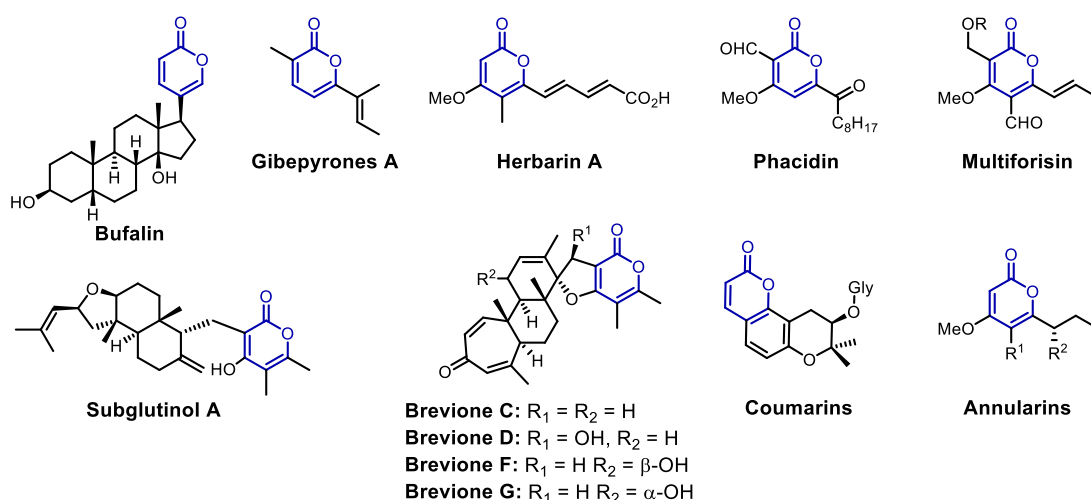


Figure 3.1: Selected examples of biologically active α -pyrone core containing natural products

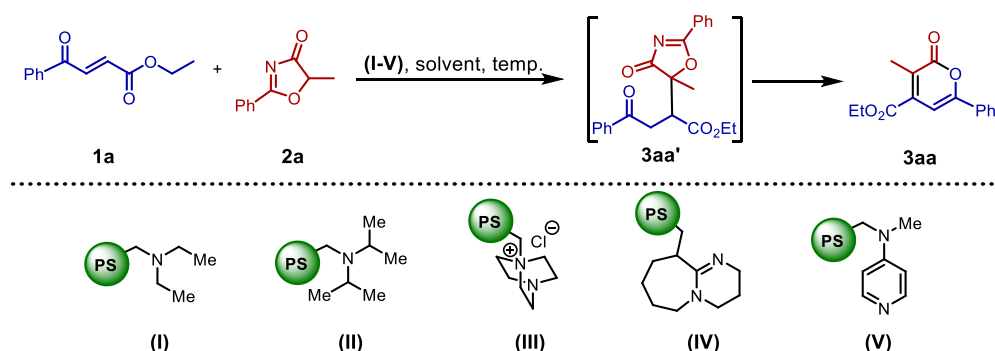
On the other hand, azalactam (5H-oxazol-4-one) is one of the strategic pronucleophiles having an active methylene group at C-5 and serves as a potential surrogate of α -hydroxy carboxylic acid.²²⁴ Oxazolones have been widely employed in numerous asymmetric transformations, producing scaffolds with a variety of structural properties.²²⁴ However, the potential for even more varied oxazolone reactions in cyclization/annulation processes has not been investigated. We envisioned that base-promoted Michael addition of oxazolone C-5 center

to an activated α,β -unsaturated ketone in a conjugate fashion, followed by ring-opening/cyclization, could result in the formation of a highly functionalized 2-pyrone. The utilization of heterogeneous bases as catalysts/mediators makes the processes more sustainable and greener. Therefore, we envisioned to use supported-amines as a catalyst for our proposed strategies. Heterogeneous organic bases, primarily amines, have been utilized as catalysts/mediators and ligands for several metal-catalyzed reactions.^{18,215} Herein, we present the first polystyrene-supported DMAP-catalyzed cascade synthesis of highly substituted 2-pyrones via conjugate-addition of 5H-oxazol-4-one to α,β -unsaturated- β -keto esters followed by lactonization-elimination.

3.2 RESULT AND DISCUSSION

We began our research by employing the model substrates α,β -unsaturated- β -ketoester **1a** and 5H-oxazol-4-one **2a** in toluene at room temperature in the presence of diethylaminomethyl-polystyrene **I** as a catalyst. Even after 4 days, the reaction was not completed, resulting in a low yield of the Michael addition product **3aa'** (Table 3.1, entry 1).

Table 3.1: Optimization of reaction conditions^a



entry	PS-Cat. (mole %)	solvent	temp. (° C)	time (d)	yield (%) ^b
1	I (30)	toluene	rt	4	(30)
2	I (30)	toluene	50	4	(47)
3	I (30)	toluene	80	4	(87)
4	I (30)	toluene	80	8	15
5	II (30)	toluene	80	8	12
6	III (30)	toluene	80	8	39
7	IV (30)	toluene	80	8	61
8	V (30)	toluene	80	8	68
9	V (30)	toluene	80	4	45
10	V (50)	toluene	80	4	62
11 ^c	V (50)	toluene	80	4	70
12 ^c	V (50)	CH ₃ CN	80	4	32
13 ^c	V (50)	EtOAc	80	4	35
14 ^c	V (50)	(CH ₂ Cl) ₂	80	4	trace
15 ^c	V (50)	dioxane	80	4	49
16 ^c	V (50)	benzene	80	4	51
17 ^c	V (50)	o-xylene	80	4	65
18 ^c	V (50)	m-xylene	80	4	62
19 ^c	V (50)	p-xylene	80	4	68
20 ^c	V (50)	mesitylene	80	4	59

^aReaction conditions: **1a** (81.6 mg, 0.4 mmol, 1 equiv.), **2a** (84.0 mg, 0.48 mmol, 1.2 equiv.), PS-Cat. **I-V**, toluene (2 mL) unless specified. ^bIsolated yield; ^c50 mg of MgSO₄ was added. Yields in the parenthesis are for Michael adduct **3aa'** only.

Increasing the temperature to 50 °C and 80 °C, the yield of **3aa'** increased significantly. However, no additional ring-opening or cyclization occurred (Table 3.1, entries 2-3). Notably, when the reaction was prolonged for 8 days, only 15% yield of the desired 2-pyrone **3aa** was obtained (Table 3.1, entry 4). These preliminary findings have encouraged us to continue optimizing the reaction parameters. First, we alter the supported amines to begin the investigation. Comparable results were obtained with diisopropylaminomethyl-polystyrene **II** (Table 3.1, entry 5). In the presence of polymer-supported-DABCO **III**, a slightly higher yield of product **3aa** was noted (Table 3.1, entry 6). PS-DBU and PS-DMAP provided a moderate yield (Table 3.1, entries 7 and 8). PS-DMAP was selected for further studies. Importantly, the cascade reaction produced 62% isolated yield in just 4 days when the catalyst loading was increased to 50% (Table 3.1, entry 10). Pleasingly, the isolated yield was further improved to 70% by adding anhydrous magnesium sulphate (Table 3.1, entry 11).

Table 3.2: Reaction with various substituted 5H-oxazolone^a

Reaction scheme: **1a** + **2** $\xrightarrow[\text{MgSO}_4 (50 \text{ mg}), \text{toluene}]{\text{V (50 mol \%)}}$ **3aa**

entry	Ar ¹	temp (° C)	time (h)	yield (%) ^b
1	C ₆ H ₅	80	96	70
2	<i>o</i> -CH ₃ C ₆ H ₄	80	96	trace
3	<i>m</i> -CH ₃ C ₆ H ₄	80	96	58
4	<i>p</i> -CH ₃ C ₆ H ₄	80	96	39
5	<i>o</i> -ClC ₆ H ₄	80	96	39
6	<i>o</i> -BrC ₆ H ₄	80	96	22
7	C ₆ H ₅	reflux	48	85
8 ^c	C ₆ H ₅	reflux	36	92

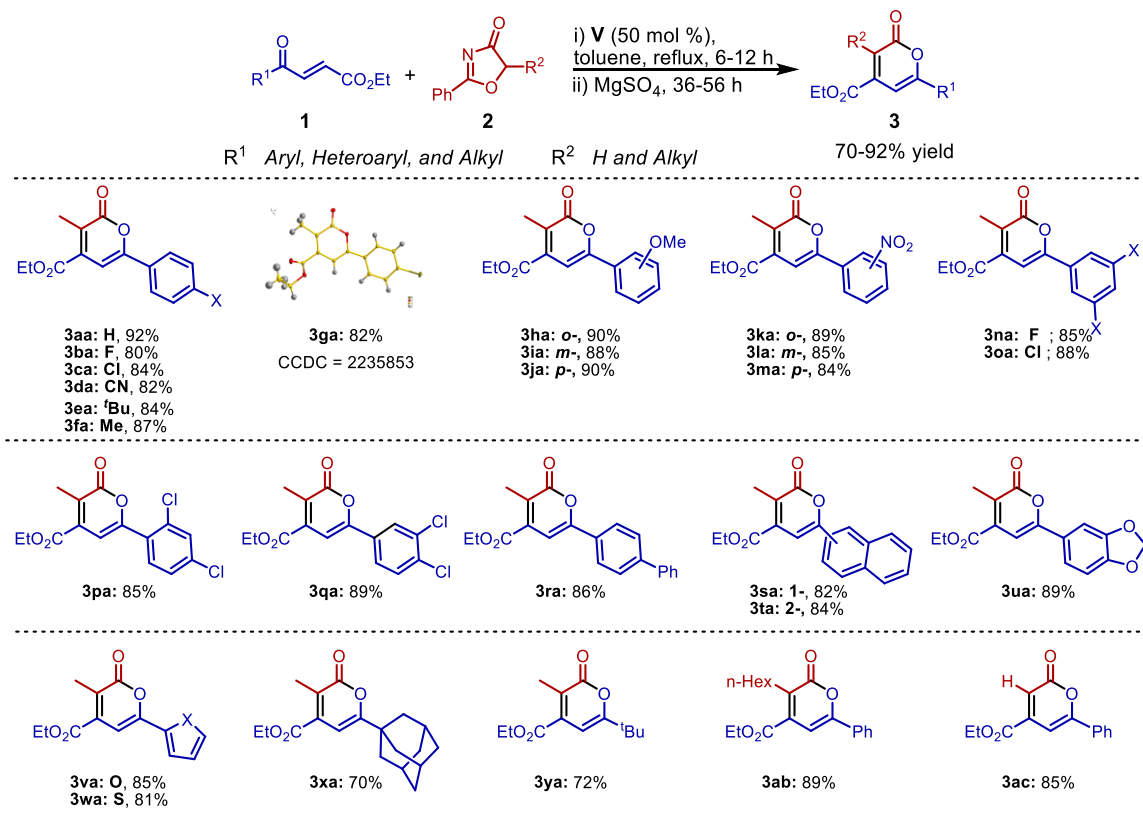
^aReaction conditions: **1a** (0.0816 g, 0.4 mmol, 1 equiv.), **2** (0.48 mmol, 1.2 equiv.), PS-DMAP **V** (0.2 mmol, 66.7 mg; 0.5 equiv., 3 mmol/g DMAP-content), toluene (2 mL) unless specified; ^bIsolated yield; ^cMgSO₄ was added after complete consumption of **1a** (6 h).

Next, we have carried out more investigation using different solvents in the reaction medium (Table 3.1, entries 12-20). A negative effect on the yield was observed with polar solvent. A trace amount of product was obtained with dichloroethane as a solvent (Table 3.1, entry 14). The optimal solvent for this cascade Michael addition/cyclization process was eventually found to be toluene. Furthermore, the pattern of substitution of the aryl ring at the 2-position was examined to determine the optimum 5H-oxazolones. With *ortho*-methyl phenyl substituted oxazolone, a very small amount of product was seen (Table 3.2, entry 2). A moderate yield was provided by *meta*- and *para*-methyl phenyl-substituted oxazolone (Table 3.2, entries 3-4). *ortho*-Chloro and *ortho*-bromo substitution showed comparable results (Table 3.2, entries 5-6). Fortunately, refluxing the reaction in toluene, further enhancement in the yield was observed (Table 3.2, entry 7). Further, it was found that the addition of MgSO₄ after the consumption of the Michael acceptor, namely α,β -unsaturated- β -ketoester **1a**, had a significant impact on lowering the overall reaction time and improving yield (Table 3.2, entry 8).

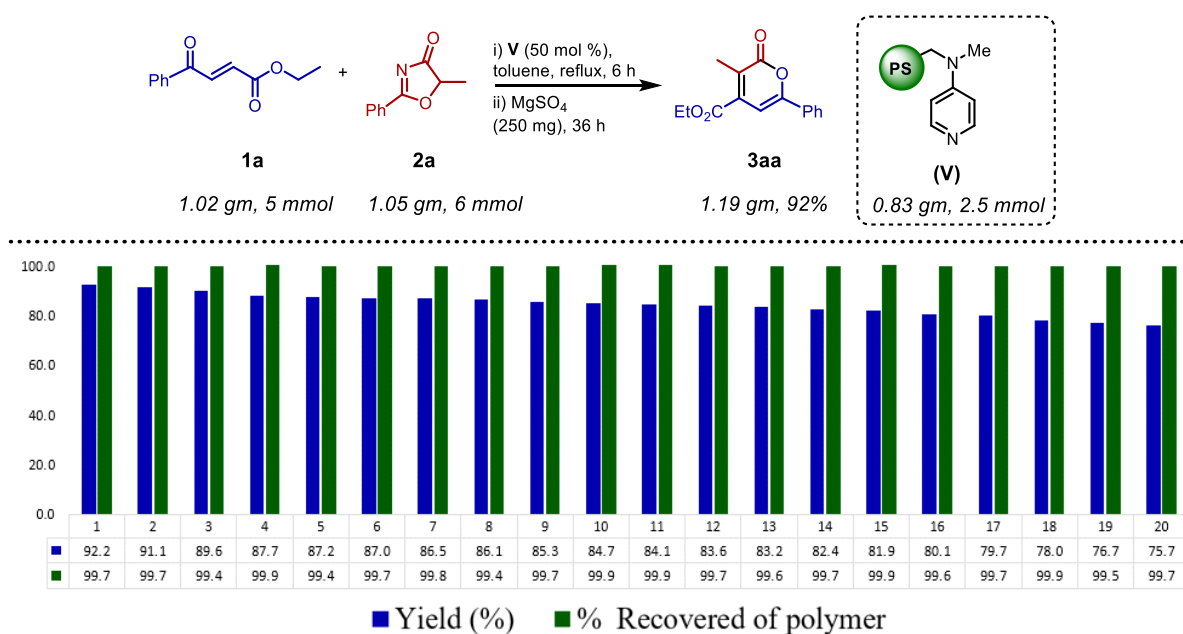
With the optimized conditions in hand, the substrate generality of this cascade reaction was investigated (Table 3.3). We have examined the electronic and steric effects of substituents on various positions of α,β -unsaturated- β -ketoesters **1**. *p*-Halo-substituted (fluoro-, chloro-, and bromo-) ketoesters **1b-1d** were well tolerated. Both electron-donating and withdrawing groups on phenyl ring (**1e-1g**) also provided admirable results. It was observed that the *o*-, *m*-, and *p*-nitro substituted α,β -unsaturated- β -ketoesters **1k-1m** took less time as compared to *o*-, *m*-, and *p*-methoxy substituted α,β -unsaturated- β -ketoesters **1h-1j**. Importantly, 2-pyrones (**3na-qa**)

bearing dihalo- on the phenyl were synthesized in high yields under an optimized cascade strategy. Tri-substituted pyrones, structurally fascinating groups such as biphenyl (**1r**), 1- and 2-naphthyls (**1s** and **1t**), and benzo[d][1,3]dioxol (**1u**) containing keto-esters could be successfully prepared.

Table 3.3: Substrate scope of cascade approach^a



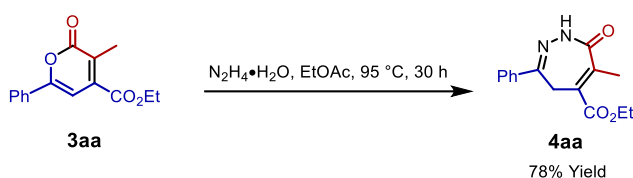
^aReaction conditions: **1** (0.4 mmol, 1 equiv.), **2** (0.48 mmol, 1.2 equiv.), PS-DMAP **V** (0.2 mmol, 0.5 equiv., 66.7 mg; 3 mmol/g DMAP-content), toluene (2 mL) unless specified; ^bIsolated yield.



Scheme 3.1: Scale-up synthesis and recycling of PS-DMAP

Heteroaryls like 2-furyl (**3va**) and 2-thienyl (**3wa**) enriched α -Pyrones were also synthesized efficiently. The cascade reactions for the β -alkyl β -ketoesters (adamantyl **1x** and *tert*-butyl **1y**) were relatively slow. However, the excellent yield of products was observed. Next, instead of methyl-substituted, *n*-hexyl (**2b**) substituted oxazolone at 5-position was used under optimized reaction conditions. Gratifyingly, the corresponding 2-pyrone (**3ab**) was formed in excellent yield. The developed approaches might be employed as well to construct disubstituted α -pyrones (**3ac**: $R^1 = H$) in practical yields. The structure of α -pyrone was further confirmed by X-ray single crystal diffraction analysis of product **3ga**.

To demonstrate the reaction scalability of the established approach, a gram-scale reaction was carried out. α -pyrone was isolated in a 92% yield (Scheme 3.1). Further, PS-DMAP was recovered and utilized for the subsequent cycle under the optimized conditions. We were delighted to see that the recovered PS-DMAP was found to be efficient after 20 cycles (Scheme 3.1). In addition, the product **3aa** was transformed into a seven-membered 1,2-diazepine derivative **4aa** by treating it with hydrazine hydrate (Scheme 3.2).



Scheme 3.2: Synthetic transformation of α -pyrone

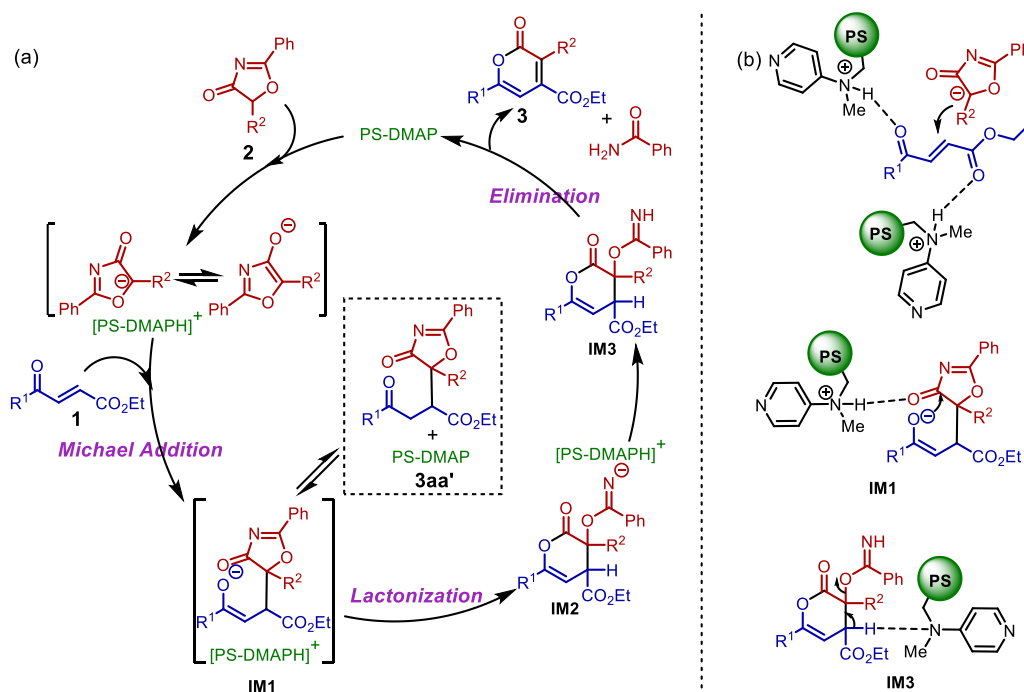
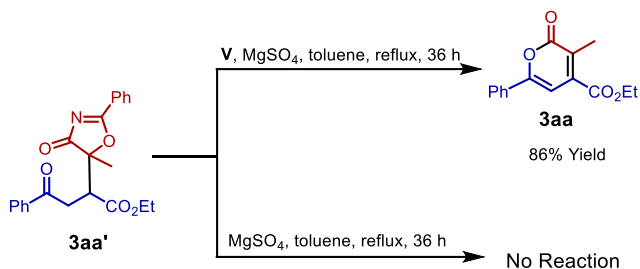


Figure 3.2: a) Plausible catalytic cycle for one-pot cascade synthesis of α -pyrones b) Plausible modes of activation of intermediates by PS-DMAP in lactonization and elimination steps

The plausible mechanism of this cascade reaction was illustrated in Figure 3.2. Our preliminary investigation of the reaction conditions revealed that the reaction proceeded via Michael addition of pronucleophile oxazolone **2a** to activated olefine **1a** to generate intermediate Michael adduct **3aa'**. Following this, the oxazolone ring of Michael adduct opens up via lactonization to produce intermediate **IM2**. The **IM2** then undergoes an elimination step assisted by PS-DMAP to afford product **3aa**. Benzamide was detected by the HRMS data analysis of the crude reaction mixture which supports the elimination pathway. Control studies were also conducted to further validate the reaction pathways (Scheme 3.3). Two separate sets of reaction

conditions were applied to the isolated intermediate Michael adduct **3aa'**. (i) refluxed with PS-DMAP in toluene, (ii) refluxed without any base in toluene. According to the findings, the PS-DMAP is necessary for the cyclization and elimination stages that produce α -pyrone. We believe that the protonated PS-DMAP activates the azalactam ring of **IM1** to facilitate the attack of enolate oxygen on imide carbonyl. Additionally, DMAP may assist in removing benzamide from **IM3** to produce the final product.



Scheme 3.3: Control experiment

3.3 EXPERIMENTAL

3.3.1 General Information

Unless otherwise noted, all reactions were carried out in closed vial. ¹H NMR spectra was recorded on a 500 MHz spectrometer (125 MHz for ¹³C NMR). The following abbreviations were used to designate chemical shift multiplicities: s = singlet, d = doublet, t = triplet, q = quartet, m = multiplet. Oil bath on the top of hot plate is used for heating wherever required. TLC was performed with silica gel GF₂₅₄ precoated on aluminium plates and spots were visualized with UV. Flash column chromatography was performed on silica gel. IR spectra were recorded on a FT-IR spectrometer and only major peaks were reported in cm⁻¹. High-resolution mass spectra (HRMS) were obtained by the ESI-TOF method. Melting points were recorded on a digital melting point apparatus and are uncorrected. Ethyl-(*E*)-4-oxo-4-alkyl/arylbut-2-enoate **1** derivatives¹ and 5-alkyl-2-alkyl/aryloxazol-(5*H*)-4-one derivatives **2** were prepared according to the reported methods. All the other reagents were purchased from commercial sources and used as received, unless specified. 4-(Dimethylamino)pyridine, polymer-bound extent of labelling: ~3.0 mmol/g DMAP loading, matrix crosslinked with 2% DVB purchased from Sigma Aldrich. Diisopropylamine, polymer-bound - 100-200 mesh, extent of labelling: 2.0-3.5 mmol/g loading, 1% cross-linked with divinylbenzene purchased from Sigma Aldrich. Diethylaminomethyl-polystyrene extent of labelling: ~3.2 mmol/g loading, 200 - 400 MESH purchased from Sigma Aldrich. 1,8-Diazabicyclo[5.4.0]undec-7-ene, polymer-bound, 100-200 mesh, extent of labelling: 1.5-2.5 mmol/g loading, 1% cross-linked with divinylbenzene purchased from Sigma Aldrich. Chloromethyl Polystyrene Resin cross-linked with 1% DVB (100-200 mesh) (2.0-3.0 mmol/g) purchased from TCI chemicals.

3.3.2 Synthetic procedure for the Synthesis of α -pyrones and Their Characterization

3.3.2.1 Synthetic Procedure

(a) Synthesis of polymer-supported DABCO (PS-DABCO) catalyst

Merrifield resin (2.5 mmol, 1 equiv., 1 g; 2.5 mmol/g Cl-content) was added slowly to the solution of DABCO (1.35 g, 12.5 mmol, 5 equiv.) in dry THF under an inert atmosphere. The progress of the reaction was monitored by TLC. After the complete consumption of DABCO, the solid was filtered and washed with acetone to afford the PS-DABCO catalyst. [Elemental Anal. for PS-DABCO **III** Found: C 73.69, H 8.41, N 4.67; DABCO content = 1.67 mmol/g]

(b) General procedure for PS-DMAP catalyzed cascade synthesis of α -pyrones

PS-DMAP (66.7 mg, 0.2 mmol, 0.5 equiv., 3 mmol/g *N*-content) **V** was added to the mixture of α , β -unsaturated- β -ketoester derivatives (0.4 mmol, 1 equiv.) **1** and substituted 5*H*-oxazole-4-ones (0.48 mmol, 1.2) **2** in toluene (2 mL) and the mixture was stirred at 120 °C. After complete consumption of **1**, anhydrous magnesium sulphate (50 mg) was added to the reaction mixture and the stirring was continued. The progress of the reaction was monitored by TLC. The mixture was cooled to room temperature and the solid residue was filtered. The filtrate was concentrated under a vacuum to get the crude product. Product **3** was purified by flash column chromatography on silica support (hexane/ethyl acetate = 20:1).

(c) Scale-up condition for the synthesis of α -pyrone and recycling study

PS-DMAP (0.83 g, 2.5 mmol, 0.5 equiv., 3 mmol/g *N*-content) **V** was added to the mixture of ethyl (*E*)-4-oxo-4-phenylbut-2-enoate (1.02 g, 5 mmol, 1 equiv.) **1a** and 5-methyl-2-phenyloxazol-(5*H*)-4-one (1.05 g, 6 mmol, 1.2 equiv.) **2a** in toluene (25 mL) and the mixture was stirred at 120 °C. After complete consumption of **1a**, anhydrous magnesium sulphate (250 mg) was added into the reaction mixture and the stirring was continued. The progress of the reaction was monitored by TLC. The mixture was cooled to room temperature and the solid residue was filtered. The filtrate was concentrated under a vacuum to get the crude product. Product **3** was purified by flash column chromatography on silica support (hexane/ethyl acetate = 20:1).

(d) Recovery procedure of supported catalyst

The filtered residue (PS-DMAP) was washed with CH₂Cl₂ (3 x 30 ml), acetone (3 x 30 ml) respectively and dried under vacuum to give reddish brown beads and the recovered polymer was used for the next cycle.

Table 3.4: Recycling of PS-DMAP **V**

Cycle	weight (3aa)	yield 3aa (%)	polymer weight (mg)	polymer loss (mg)	% of recovered polymer
1	1.191	92.2	830.00	2.52	99.7
2	1.177	91.1	827.48	2.52	99.7
3	1.157	89.6	824.97	5.03	99.4
4	1.132	87.7	819.94	1.01	99.9
5	1.126	87.2	818.93	5.03	99.4
6	1.123	87.0	813.90	2.52	99.7
7	1.117	86.5	811.39	2.01	99.8
8	1.112	86.1	809.38	5.03	99.4
9	1.102	85.3	804.35	2.52	99.7
10	1.094	84.7	801.83	1.01	99.9
11	1.087	84.1	800.82	1.01	99.9
12	1.079	83.6	799.82	2.52	99.7
13	1.075	83.2	797.30	3.02	99.6
14	1.064	82.4	794.28	2.01	99.7
15	1.058	81.9	792.27	1.01	99.9
16	1.035	80.1	791.27	3.52	99.6
17	1.029	79.7	787.75	2.52	99.7
18	1.007	78.0	785.23	1.01	99.9
19	0.991	76.7	784.22	4.02	99.5
20	0.977	75.7	780.20	2.52	99.7

^a% of recovered polymer = (Polymer Weight – Polymer loss) / Polymer Weight*100

(e) Synthesis of ethyl 6-methyl-7-oxo-3-phenyl-4,7-dihydro-1*H*-1,2-diazepine-5-carboxylate (**4aa**)

Solution of α -pyrone **3aa** (103.3 mg, 0.4 mmol, 1 equiv.) in ethyl acetate (1 ml) was added to the 24% aq. solution of hydrazine hydrate (19.2 mg, 0.6 mmol, 1.2 equiv.). The biphasic solution was vigorously stirred at 95 °C for 30 h. The reaction was monitored by TLC. After the complete consumption of reactant **3aa** add ethyl acetate and the organic phase was separated and dried

over Na₂SO₄. The organic phase was evaporated under reduced pressure and the crude product was purified by column chromatography. The product **4aa** was obtained as an off-white solid (85.0 mg, 78%).

3.3.2.2 Characterization

(a) Characterization of Intermediates

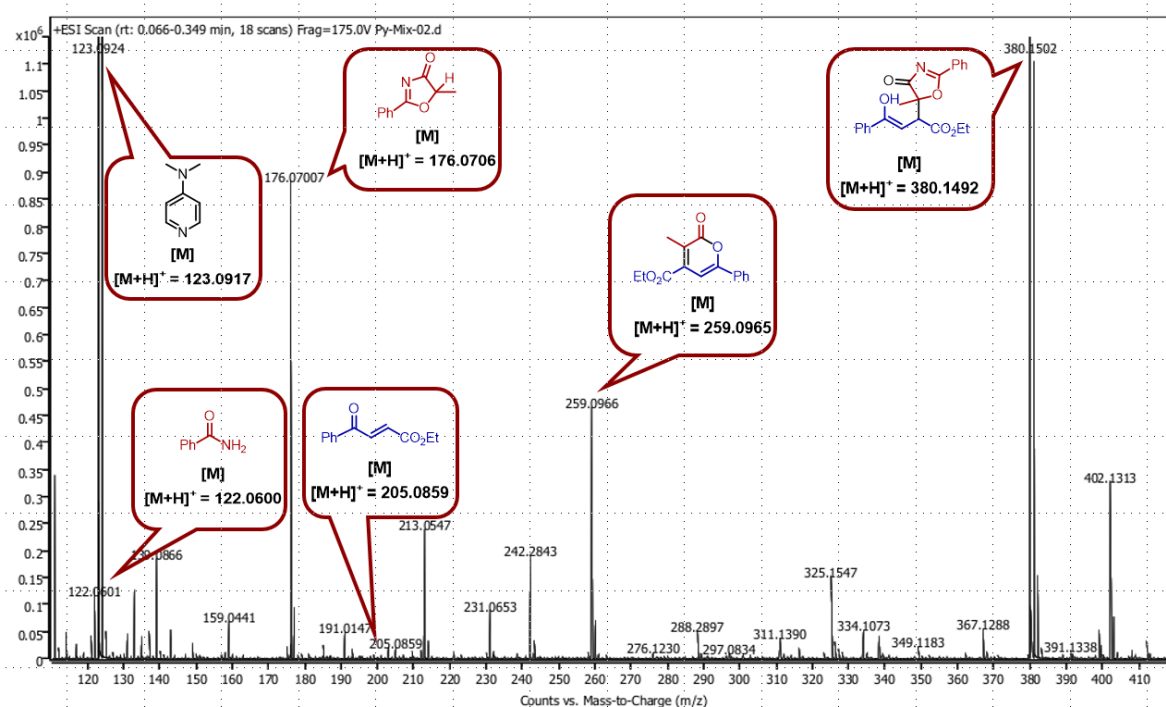


Figure 3.3: HRMS analysis of reaction mixture

Intermediate Michael Adduct 3aa': Ethyl-4-hydroxy-2-(5-methyl-4-oxo-2-phenyl-4,5-dihydrooxazol-5-yl)-4-phenylbut-3-enoate: Yellow solid, ¹H NMR (500 MHz, CDCl₃) δ 8.28 – 8.26 (m, 2H), 8.23 – 8.21 (m, 0.88H), 8.00 – 7.98 (m, 0.88H), 7.89 – 7.87 (m, 2H), 7.75 – 7.71 (m, 1.48H), 7.58 – 7.53 (m, 4.35H), 7.49 – 7.46 (m, 0.92H), 7.43 – 7.40 (m, 2H), 4.21 – 4.12 (m, 2.89H), 3.65 – 3.58 (m, 3.32H), 3.15 (dd, *J* = 17.3, 2.9 Hz, 1H), 1.69 (s, 3H), 1.67 (s, 1.32H), 1.24 – 1.21 (dd, *J* = 10.2, 4.1 Hz, 4.36H); HRMS (ESI) *m/z*: [M+H]⁺ calcd for C₂₂H₂₂NO₅ 380.1492; found: 380.1502.

(b) Characterization of compounds

Ethyl 3-methyl-2-oxo-6-phenyl-2H-pyran-4-carboxylate 3aa: Yellow solid, Yield = 92% (95.1 mg), *t*₁ = 6 h & *t*₂ = 36 h; ¹H NMR (500 MHz, CDCl₃) δ 7.85 – 7.81 (m, 2H), 7.47 – 7.43 (m, 3H), 6.91 (s, 1H), 4.42 (q, *J* = 7.1 Hz, 2H), 2.38 (s, 3H), 1.42 (t, *J* = 7.1 Hz, 3H); ¹³C NMR (125 MHz, CDCl₃) δ 165.5, 163.8, 157.3, 140.5, 131.3, 130.8, 129.1, 126.2, 125.5, 100.5, 62.4, 14.3, 14.3; IR (ATR): ν 3161, 3102, 3067, 3002, 2992, 1868, 1792, 1772, 173, 1717, 1684, 1670, 1653, 1636, 1559, 1541, 1507, 1489, 1457, 1276, 1257 cm⁻¹; IR (ATR): ν 3161, 3102, 3067, 3002, 2992, 1868, 1792, 1772, 173, 1717, 1684, 1670, 1653, 1636, 1559, 1541, 1507, 1489, 1457, 1276, 1257 cm⁻¹; HRMS (ESI) *m/z*: [M+H]⁺ calcd for C₁₅H₁₅O₄ 259.0965; found: 259.0949; M. P. 73-75 °C.

Ethyl 6-(4-fluorophenyl)-3-methyl-2-oxo-2H-pyran-4-carboxylate 3ba: Yellow solid, Yield = 80% (88.4 mg), *t*₁ = 6 h & *t*₂ = 42 h; ¹H NMR (500 MHz, CDCl₃) δ 7.86 – 7.74 (m, 2H), 7.22 – 7.07 (m, 2H), 6.84 (s, 1H), 4.41 (q, *J* = 7.1 Hz, 2H), 2.36 (s, 3H), 1.42 (t, *J* = 7.1 Hz, 3H); ¹³C NMR (125 MHz, CDCl₃) δ 165.3 (*J*_{C-F} = 13.75 Hz), 163.6, 163.2, 156.3, 140.4, 127.6, 127.5 (*J*_{C-F} = 5 Hz), 126.1, (*J*_{C-F} = 1.25 Hz), 116.3 (*J*_{C-F} = 21.3 Hz), 100.3 (*J*_{C-F} = 1 Hz), 62.4, 14.3, 14.3; IR (ATR): ν 3161, 3102, 3067,

3002, 2992, 1868, 1792, 1772, 173, 1717, 1684, 1670, 1653, 1636, 1559, 1541, 1507, 1489, 1457, 1276, 1257 cm⁻¹; HRMS (ESI) m/z: [M+H]⁺ calcd for C₁₅H₁₅O₄ 259.0965; found: 259.0949; M. P. 73-75 °C.

Ethyl 6-(4-chlorophenyl)-3-methyl-2-oxo-2H-pyran-4-carboxylate 3ca: Yellow solid, Yield = 84% (98.4 mg), t₁ = 7 h & t₂ = 43 h; ¹H NMR (500 MHz, CDCl₃) δ 7.81 – 7.69 (m, 2H), 7.46 – 7.38 (m, 2H), 6.89 (s, 1H), 4.42 (q, J = 7.1 Hz, 2H), 2.38 (s, 3H), 1.42 (t, J = 7.1 Hz, 3H); ¹³C NMR (125 MHz, CDCl₃) δ 165.3, 163.5, 156.1, 140.3, 136.9, 129.7, 129.4, 126.7, 126.7, 100.7, 62.5, 14.4, 14.3; IR (ATR): ν 3101, 3066, 3006, 2989, 1829, 1792, 1772, 1717, 1685, 1653, 1636, 1595, 1558, 1491, 1457, 1409, 1339, 1259 cm⁻¹; HRMS (ESI) m/z: [M+H]⁺ calcd for C₁₅H₁₄ClO₄ 293.0575; found: 293.0565; M. P. 81-83 °C.

Ethyl 6-(4-cyanophenyl)-3-methyl-2-oxo-2H-pyran-4-carboxylate 3da: Yellow solid, Yield = 82% (92.9 mg), t₁ = 8 h & t₂ = 39 h; ¹H NMR (500 MHz, CDCl₃) δ 7.93 (d, J = 8.5 Hz, 2H), 7.75 (d, J = 8.6 Hz, 2H), 7.02 (s, 1H), 4.42 (q, J = 7.1 Hz, 2H), 2.40 (s, 3H), 1.42 (t, J = 7.1 Hz, 3H); ¹³C NMR (125 MHz, CDCl₃) δ 164.9, 162.9, 154.6, 139.8, 135.1, 132.9, 128.6, 125.8, 118.3, 114.0, 102.6, 62.6, 14.5, 14.3; IR (ATR): ν 3101, 3080, 3006, 3065, 2990, 1844, 1829, 1792, 1770, 1730, 1717, 1700, 1684, 1617, 1576, 1541, 1510, 1489, 1437, 1374, 1276 cm⁻¹; HRMS (ESI) m/z: [M+H]⁺ calcd for C₁₆H₁₄NO₄ 284.0917; found: 284.0939; M. P. 133-135 °C.

Ethyl 6-(4-(tert-butyl)phenyl)-3-methyl-2-oxo-2H-pyran-4-carboxylate 3ea: Yellow solid, Yield = 84% (105.6 mg), t₁ = 7 h & t₂ = 42 h; ¹H NMR (500 MHz, CDCl₃) δ 7.75 (d, J = 8.6 Hz, 2H), 7.46 (d, J = 8.7 Hz, 2H), 6.87 (s, 1H), 4.41 (q, J = 7.1 Hz, 2H), 2.36 (s, 3H), 1.42 (t, J = 7.1 Hz, 3H), 1.34 (s, 9H); ¹³C NMR (125 MHz, CDCl₃) δ 165.6, 163.9, 157.5, 154.4, 140.7, 128.5, 126.0, 125.5, 125.3, 100.0, 62.3, 35.1, 31.3, 14.3, 14.3; IR (ATR): ν 3134, 3101, 3066, 3005, 2966, 2907, 2870, 1869, 1844, 1792, 1772, 1717, 1684, 1653, 1636, 1541, 1489, 1363, 1226 cm⁻¹; HRMS (ESI) m/z: [M+H]⁺ calcd for C₁₉H₂₃O₄ 315.1591; found: 315.1580; M. P. 86-88 °C.

Ethyl 3-methyl-2-oxo-6-(p-tolyl)-2H-pyran-4-carboxylate 3fa: Yellow solid, Yield = 87% (94.8 mg), t₁ = 8 h & t₂ = 45 h; ¹H NMR (500 MHz, CDCl₃) δ 7.71 (d, J = 8.3 Hz, 2H), 7.25 (d, J = 8.1 Hz, 2H), 6.85 (s, 1H), 4.41 (q, J = 7.1 Hz, 2H), 2.39 (s, 3H), 2.36 (s, 3H), 1.42 (t, J = 7.1 Hz, 3H); ¹³C NMR (125 MHz, CDCl₃) δ 165.6, 163.9, 157.5, 141.3, 140.7, 129.8, 128.5, 125.4, 125.4, 99.9, 62.3, 21.6, 14.3, 14.2; IR (ATR): ν 3135, 3102, 3080, 3066, 3005, 2990, 1850, 1830, 1790, 1772, 1734, 1717, 1670, 1617, 1507, 1457, 1276 cm⁻¹; HRMS (ESI) m/z: [M+H]⁺ calcd for C₁₆H₁₇O₄ 273.1121; found: 273.1131; M. P. 81-83 °C.

Ethyl 6-(4-bromophenyl)-3-methyl-2-oxo-2H-pyran-4-carboxylate 3ga: Yellow solid, Yield = 82% (110.6 mg), t₁ = 7 h & t₂ = 43 h; ¹H NMR (500 MHz, CDCl₃) δ 7.71 – 7.64 (m, 2H), 7.62 – 7.54 (m, 2H), 6.89 (s, 1H), 4.41 (q, J = 7.1 Hz, 2H), 2.36 (s, 3H), 1.42 (t, J = 7.1 Hz, 3H); ¹³C NMR (125 MHz, CDCl₃) δ 165.3, 163.4, 156.1, 140.3, 132.3, 130.1, 126.9, 126.7, 125.3, 100.7, 62.4, 14.4, 14.3; IR (ATR): ν 3117, 3101, 3080, 3004, 2992, 1844, 1792, 1774, 1740, 1720, 1700, 1684, 1668, 1636, 1576, 1507, 1473, 1437, 1374, 1260 cm⁻¹; HRMS (ESI) m/z: [M+H]⁺ calcd for C₁₅H₁₄BrO₄ 337.0070 & 339.0050; found: 337.0075 & 339.0065; M. P. 93-95 °C.

Ethyl 6-(2-methoxyphenyl)-3-methyl-2-oxo-2H-pyran-4-carboxylate 3ha: Yellow solid, Yield = 90% (103.8 mg), t₁ = 6 h & t₂ = 45 h; ¹H NMR (500 MHz, CDCl₃) δ 7.44 – 7.27 (m, 3H), 6.97 (d, J = 7.3 Hz, 1H), 6.88 (s, 1H), 4.40 (q, J = 7.1 Hz, 2H), 3.85 (s, 3H), 2.36 (s, 3H), 1.41 (t, J = 7.0 Hz, 3H); ¹³C NMR (125 MHz, CDCl₃) δ 165.4, 163.7, 160.1, 157.0, 140.4, 132.6, 130.1, 126.2, 117.9, 116.8, 110.5, 100.8, 62.3, 55.6, 14.3, 14.3; IR (ATR): ν 3134, 3068, 3003, 2951, 2926, 2846, 1869, 1844, 1825, 1788, 1718, 1653, 1596, 1576, 1507, 1437, 1363, 1224 cm⁻¹; HRMS (ESI) m/z: [M+H]⁺ calcd for C₁₆H₁₇O₅ 289.1071; found: 289.1082; M. P. 103-105 °C.

Ethyl 6-(3-methoxyphenyl)-3-methyl-2-oxo-2H-pyran-4-carboxylate 3ia: Yellow solid, Yield = 88% (101.5 mg), t₁ = 7 h & t₂ = 42 h; ¹H NMR (500 MHz, CDCl₃) δ 7.89 (dd, J = 7.9, 1.7 Hz, 1H), 7.40 – 7.35 (m, 1H), 7.30 (s, 1H), 7.06 – 7.01 (m, 1H), 6.97 (d, J = 8.3 Hz, 1H), 4.39 (q, J = 7.1 Hz, 2H), 3.92 (s, 3H), 2.33 (s, 3H), 1.40 (t, J = 7.1 Hz, 3H); ¹³C NMR (125 MHz, CDCl₃) δ 165.8, 164.0, 157.4,

154.3, 141.1, 131.6, 128.7, 125.3, 121.0, 119.9, 111.5, 105.5, 62.1, 55.7, 14.3, 14.1; IR (ATR): ν 3134, 3102, 3080, 3066, 3006, 2990, 1829, 1792, 1772, 1733, 1717, 1670, 1653, 1617, 1551, 1521, 1473, 1436, 1276 cm^{-1} ; HRMS (ESI) m/z : $[M+H]^+$ calcd for $\text{C}_{16}\text{H}_{17}\text{O}_5$ 289.1071; found: 289.1082; M. P. 83-85 $^{\circ}\text{C}$.

Ethyl 6-(4-methoxyphenyl)-3-methyl-2-oxo-2H-pyran-4-carboxylate 3ja: Yellow solid, Yield = 90% (103.8 mg), t_1 = 6 h & t_2 = 44 h; ^1H NMR (500 MHz, CDCl_3) δ 7.77 (d, J = 8.9 Hz, 2H), 6.95 (d, J = 8.9 Hz, 2H), 6.78 (s, 1H), 4.40 (q, J = 7.1 Hz, 2H), 3.86 (s, 3H), 2.34 (s, 3H), 1.41 (t, J = 7.1 Hz, 3H); ^{13}C NMR (125 MHz, CDCl_3) δ 165.7, 163.9, 161.7, 157.5, 140.9, 127.1, 124.5, 123.8, 114.5, 99.1, 62.3, 55.6, 14.3, 14.2; IR (ATR): ν 3166, 3079, 3065, 2989, 1829, 1792, 1772, 1733, 1684, 1671, 1653, 1541, 1473, 1419, 1374, 1259 cm^{-1} ; HRMS (ESI) m/z : $[M+H]^+$ calcd for $\text{C}_{16}\text{H}_{17}\text{O}_5$ 289.1071; found: 289.1059; M. P. 73-75 $^{\circ}\text{C}$.

Ethyl 3-methyl-6-(2-nitrophenyl)-2-oxo-2H-pyran-4-carboxylate 3ka: Yellow solid, Yield = 89% (108.0 mg), t_1 = 8 h & t_2 = 36 h; ^1H NMR (500 MHz, CDCl_3) δ 8.04 (dd, J = 8.1, 1.1 Hz, 1H), 7.73 – 7.70 (m, 1H), 7.66 – 7.63 (m, 1H), 7.61 (dd, J = 7.5, 1.4 Hz, 1H), 6.67 (s, 1H), 4.40 (q, J = 7.1 Hz, 2H), 2.41 (s, 3H), 1.40 (t, J = 7.1 Hz, 3H); ^{13}C NMR (125 MHz, CDCl_3) δ 164.9, 162.9, 154.8, 148.0, 139.6, 133.4, 131.4, 131.1, 128.4, 127.4, 125.2, 104.3, 62.5, 14.5, 14.3; IR (ATR): ν 3121, 3102, 3080, 3065, 3006, 2989, 1850, 1829, 1793, 1775, 1734, 1700, 1671, 1653, 1617, 1534, 1489, 1457, 1437, 1419, 1351, 1259 cm^{-1} ; HRMS (ESI) m/z : $[M+H]^+$ calcd for $\text{C}_{15}\text{H}_{14}\text{NO}_6$ 304.0816; found: 304.0796; M. P. 81-83 $^{\circ}\text{C}$.

Ethyl 3-methyl-6-(3-nitrophenyl)-2-oxo-2H-pyran-4-carboxylate 3la: Yellow solid, Yield = 85% (103.1 mg), t_1 = 7 h & t_2 = 37 h; ^1H NMR (500 MHz, CDCl_3) δ 8.64 (t, J = 1.9 Hz, 1H), 8.34 – 8.24 (m, 1H), 8.22 – 8.11 (m, 1H), 7.67 (t, J = 8.1 Hz, 1H), 7.04 (s, 1H), 4.44 (q, J = 7.1 Hz, 2H), 2.41 (s, 3H), 1.44 (t, J = 7.1 Hz, 3H); ^{13}C NMR (125 MHz, CDCl_3) δ 164.9, 162.9, 154.3, 148.8, 139.9, 132.9, 130.9, 130.3, 128.4, 125.1, 120.3, 102.1, 62.7, 14.5, 14.3; IR (ATR): ν 3189, 3105, 3006, 2990, 1829, 1790, 1772, 1733, 1684, 1636, 1559, 1489, 1473, 1457, 1437, 1387, 1350, 1211 cm^{-1} ; HRMS (ESI) m/z : $[M+H]^+$ calcd for $\text{C}_{15}\text{H}_{14}\text{NO}_6$ 304.0816; found: 304.0821; M. P. 140-142 $^{\circ}\text{C}$.

Ethyl 3-methyl-6-(4-nitrophenyl)-2-oxo-2H-pyran-4-carboxylate 3ma: Yellow solid, Yield = 84% (101.9 mg), t_1 = 8 h & t_2 = 36 h; ^1H NMR (500 MHz, CDCl_3) δ 8.41 – 8.26 (m, 2H), 8.05 – 7.92 (m, 2H), 7.07 (s, 1H), 4.44 (q, J = 7.1 Hz, 2H), 2.42 (s, 3H), 1.43 (t, J = 7.1 Hz, 3H); ^{13}C NMR (125 MHz, CDCl_3) δ 164.9, 162.9, 154.3, 148.8, 139.8, 136.8, 129.0, 126.2, 124.4, 103.1, 62.7, 14.6, 14.3; IR (ATR): ν 3144, 3101, 3080, 3065, 2990, 1850, 1830, 1792, 1772, 1717, 1684, 1636, 1616, 1541, 1489, 1419, 1362, 1261 cm^{-1} ; HRMS (ESI) m/z : $[M+H]^+$ calcd for $\text{C}_{15}\text{H}_{14}\text{NO}_6$ 342.0374; found: 304.0796; M. P. 114-116 $^{\circ}\text{C}$.

Ethyl 6-(3,5-difluorophenyl)-3-methyl-2-oxo-2H-pyran-4-carboxylate 3na: Yellow solid, Yield = 85% (100.1 mg), t_1 = 8 h & t_2 = 42 h; ^1H NMR (500 MHz, CDCl_3) δ 7.96 – 7.91 (m, 1H), 7.05 (s, 1H), 7.00 (dd, J = 11.8, 4.6 Hz, 1H), 6.95 – 6.91 (m, 1H), 4.40 (q, J = 7.1 Hz, 2H), 2.37 (s, 3H), 1.41 (t, J = 7.1 Hz, 3H); ^{13}C NMR (125 MHz, CDCl_3) δ 165.2, 165.0, 164.9, 163.2, 163.0, 162.9, 161.6, 161.5, 159.5, 159.5, 151.1, 151.1, 140.6, 129.9, 129.9, 129.8, 129.8, 126.9, 116.2, 116.1, 116.1, 116.1, 112.5, 112.5, 112.3, 112.3, 105.4, 105.2, 105.2, 105.2, 105.0, 62.4, 14.3, 14.3; IR (ATR): ν 3101, 3080, 3003, 2990, 1870, 1845, 1830, 1794, 1770, 1700, 1670, 1617, 1541, 1436, 1374, 1230 cm^{-1} ; HRMS (ESI) m/z : $[M+H]^+$ calcd for $\text{C}_{15}\text{H}_{13}\text{F}_2\text{O}_4$ 295.0776; found: 295.0768; M. P. 108-110 $^{\circ}\text{C}$.

Ethyl 6-(3,5-dichlorophenyl)-3-methyl-2-oxo-2H-pyran-4-carboxylate 3oa: Yellow solid, Yield = 88% (115.2 mg), t_1 = 8 h & t_2 = 44 h; ^1H NMR (500 MHz, CDCl_3) δ 7.91 (d, J = 2.1 Hz, 1H), 7.64 (dd, J = 8.5, 2.1 Hz, 1H), 7.52 (d, J = 8.5 Hz, 1H), 6.90 (s, 1H), 4.42 (q, J = 7.1 Hz, 2H), 2.38 (s, 3H), 1.43 (t, J = 7.1 Hz, 3H); ^{13}C NMR (125 MHz, CDCl_3) δ 165.1, 163.1, 154.6, 140.0, 135.0, 133.7, 131.1, 131.1, 127.5, 127.2, 124.4, 101.4, 77.4, 77.2, 76.9, 62.6, 14.4, 14.3; IR (ATR): ν 3133, 3101, 3080, 3066, 2990, 1869, 1844, 1829, 1772, 1734, 1700, 1670, 1636, 1617, 1541, 1489, 1396, 1276 cm^{-1} ; HRMS (ESI) m/z : $[M+H]^+$ calcd for $\text{C}_{15}\text{H}_{13}\text{Cl}_2\text{O}_4$ 327.0185; found: 327.0178; M. P. 100-102 $^{\circ}\text{C}$.

Ethyl 6-(2,4-dichlorophenyl)-3-methyl-2-oxo-2H-pyran-4-carboxylate 3pa: Yellow solid, Yield = 85% (111.2 mg), $t_1 = 9$ h & $t_2 = 44$ h; ^1H NMR (500 MHz, CDCl_3) δ 7.61 (d, $J = 8.5$ Hz, 1H), 7.50 (d, $J = 2.1$ Hz, 1H), 7.35 (dd, $J = 8.5, 2.1$ Hz, 1H), 6.98 (s, 1H), 4.40 (q, $J = 7.1$ Hz, 2H), 2.39 (s, 3H), 1.40 (t, $J = 7.1$ Hz, 3H); ^{13}C NMR (125 MHz, CDCl_3) δ 165.1, 163.4, 153.8, 139.8, 136.8, 133.1, 131.3, 130.8, 129.3, 127.8, 127.7, 106.3, 62.4, 14.3, 14.3; IR (ATR): ν 3124, 3080, 3006, 2990, 1869, 1844, 1829, 1792, 1772, 1733, 1684, 1670, 1636, 1541, 1507, 1474, 1457, 1276, 1257 cm^{-1} ; HRMS (ESI) m/z : $[\text{M}+\text{H}]^+$ calcd for $\text{C}_{15}\text{H}_{13}\text{Cl}_2\text{O}_4$ 327.0185; found: 327.0160; M. P. 87-89 °C.

Ethyl 6-(3,4-dichlorophenyl)-3-methyl-2-oxo-2H-pyran-4-carboxylate 3qa: Yellow solid, Yield = 89% (116.5 mg), $t_1 = 8$ h & $t_2 = 42$ h; ^1H NMR (500 MHz, CDCl_3) δ 7.90 (d, $J = 2.1$ Hz, 1H), 7.62 (dd, $J = 8.5, 2.1$ Hz, 1H), 7.51 (d, $J = 8.5$ Hz, 1H), 6.89 (s, 1H), 4.41 (q, $J = 7.1$ Hz, 2H), 2.37 (s, 3H), 1.42 (t, $J = 7.1$ Hz, 3H); ^{13}C NMR (125 MHz, CDCl_3) δ 165.0, 163.1, 154.6, 140.0, 134.9, 133.7, 131.1, 131.1, 127.5, 127.2, 124.4, 101.4, 62.5, 14.4, 14.3; IR (ATR): ν 3151, 3097, 3067, 3005, 2989, 1869, 1844, 1792, 1772, 1717, 1685, 1636, 1559, 1521, 1489, 1455, 1397, 1338, 1259, 1236 cm^{-1} ; HRMS (ESI) m/z : $[\text{M}+\text{H}]^+$ calcd for $\text{C}_{15}\text{H}_{13}\text{Cl}_2\text{O}_4$ 327.0185; found: 327.0178; M. P. 108-110 °C.

Ethyl 6-([1,1'-biphenyl]-4-yl)-3-methyl-2-oxo-2H-pyran-4-carboxylate 3ra: Yellow solid, Yield = 86% (115.0 mg), $t_1 = 6$ h & $t_2 = 42$ h; ^1H NMR (500 MHz, CDCl_3) δ 7.95 – 7.86 (m, 2H), 7.72 – 7.66 (m, 2H), 7.64 – 7.62 (m, 2H), 7.49 – 7.46 (m, 2H), 7.42 – 7.36 (m, 1H), 6.95 (s, 1H), 4.43 (q, $J = 7.1$ Hz, 2H), 2.39 (s, 3H), 1.44 (t, $J = 7.1$ Hz, 3H); ^{13}C NMR (125 MHz, CDCl_3) δ 165.5, 163.8, 157.0, 143.5, 140.6, 140.0, 130.0, 129.1, 128.2, 127.7, 127.2, 126.0, 125.9, 100.5, 62.4, 14.4, 14.3; IR (ATR): ν 3166, 3115, 3094, 3004, 2986, 1874, 1844, 1792, 1732, 1653, 1636, 1541, 1507, 1473, 1437, 1397, 1372, 1260 cm^{-1} ; HRMS (ESI) m/z : $[\text{M}+\text{H}]^+$ calcd for $\text{C}_{21}\text{H}_{19}\text{O}_4$ 335.1278; found: 335.1265; M. P. 101-103 °C.

Ethyl 3-methyl-6-(naphthalen-1-yl)-2-oxo-2H-pyran-4-carboxylate 3sa: Yellow solid, Yield = 82% (101.1 mg), $t_1 = 8$ h & $t_2 = 44$ h; ^1H NMR (500 MHz, CDCl_3) δ 8.18 (d, $J = 8.1$ Hz, 1H), 7.97 – 7.88 (m, 2H), 7.69 (d, $J = 7.1$ Hz, 1H), 7.58 – 7.50 (m, 3H), 6.79 (s, 1H), 4.41 (q, $J = 7.1$ Hz, 2H), 2.44 (s, 3H), 1.40 (t, $J = 7.1$ Hz, 3H); ^{13}C NMR (125 MHz, CDCl_3) δ 165.3, 164.1, 158.5, 140.4, 133.8, 131.2, 130.4, 130.0, 128.8, 127.9, 127.5, 126.5, 126.4, 125.1, 124.9, 105.6, 62.3, 14.3, 14.3; IR (ATR): ν 3144, 3112, 3095, 3047, 2984, 2927, 1869, 1829, 1792, 1772, 1685, 1636, 1508, 1473, 1437, 1369, 1275 cm^{-1} ; HRMS (ESI) m/z : $[\text{M}+\text{H}]^+$ calcd for $\text{C}_{19}\text{H}_{17}\text{O}_4$ 309.1121; found: 309.1133; M. P. 77-79 °C.

Ethyl 3-methyl-6-(naphthalen-2-yl)-2-oxo-2H-pyran-4-carboxylate 3ta: Yellow solid, Yield = 84% (103.6 mg), $t_1 = 7$ h & $t_2 = 40$ h; ^1H NMR (500 MHz, CDCl_3) δ 8.39 (d, $J = 0.9$ Hz, 1H), 7.96 – 7.77 (m, 4H), 7.62 – 7.49 (m, 2H), 7.02 (s, 1H), 4.43 (q, $J = 7.1$ Hz, 2H), 2.39 (s, 3H), 1.44 (t, $J = 7.1$ Hz, 3H); ^{13}C NMR (125 MHz, CDCl_3) δ 165.5, 163.8, 157.1, 140.5, 134.3, 133.2, 129.1, 128.9, 128.2, 127.8, 127.7, 127.1, 126.2, 125.8, 121.9, 100.9, 62.4, 14.4, 14.3; IR (ATR): ν 3164, 3116, 3064, 2989, 1869, 1829, 1792, 1772, 1684, 1636, 1541, 1507, 1489, 1473, 1437, 1397, 1340, 1260 cm^{-1} ; HRMS (ESI) m/z : $[\text{M}+\text{H}]^+$ calcd for $\text{C}_{19}\text{H}_{17}\text{O}_4$ 309.1121; found: 309.1125; M. P. 97-99 °C.

Ethyl 6-(benzo[d][1,3]dioxol-5-yl)-3-methyl-2-oxo-2H-pyran-4-carboxylate 3ua: Yellow solid, Yield = 89% (107.6 mg), $t_1 = 8$ h & $t_2 = 40$ h; ^1H NMR (500 MHz, CDCl_3) δ 7.38 (dd, $J = 8.2, 1.8$ Hz, 1H), 7.26 (s, 1H), 6.86 (d, $J = 8.2$ Hz, 1H), 6.75 (s, 1H), 6.03 (s, 2H), 4.40 (q, $J = 7.1$ Hz, 2H), 2.34 (s, 3H), 1.41 (t, $J = 7.1$ Hz, 3H); ^{13}C NMR (125 MHz, CDCl_3) δ 165.5, 163.7, 157.1, 150.0, 148.6, 140.7, 125.5, 125.0, 120.4, 108.8, 105.7, 101.9, 99.5, 62.3, 14.3, 14.2; IR (ATR): ν 3102, 3066, 3006, 2990, 1829, 1795, 1772, 1717, 1684, 1653, 1617, 1540, 1489, 1457, 1419, 1258, 1206 cm^{-1} ; HRMS (ESI) m/z : $[\text{M}+\text{H}]^+$ calcd for $\text{C}_{16}\text{H}_{15}\text{O}_6$ 303.0863; found: 303.0836; M. P. 117-119 °C.

Ethyl 6-(furan-2-yl)-3-methyl-2-oxo-2H-pyran-4-carboxylate 3va: Yellow solid, Yield = 85% (84.4 mg), $t_1 = 7$ h & $t_2 = 42$ h; ^1H NMR (500 MHz, CDCl_3) δ 7.51 (d, $J = 1.4$ Hz, 1H), 6.96 (d, $J = 3.5$ Hz, 1H), 6.80 (s, 1H), 6.53 (dd, $J = 3.5, 1.8$ Hz, 1H), 4.39 (q, $J = 7.1$ Hz, 2H), 2.34 (s, 3H), 1.41 (t, $J = 7.1$ Hz, 3H); ^{13}C NMR (125 MHz, CDCl_3) δ 165.2, 162.9, 149.4, 146.4, 144.8, 140.5, 125.7, 112.5, 111.4, 99.0, 62.3, 14.3, 14.3; IR (ATR): ν 3115, 3006, 2990, 1869, 1845, 1790, 1772, 1760, 1718, 1684, 1670,

1647, 1541, 1507, 1489, 1457, 1276, 1234 cm⁻¹; HRMS (ESI) m/z: [M+H]⁺ calcd for C₁₃H₁₃O₅ 249.0757; found: 249.0762; M. P. 102–104 °C.

Ethyl 3-methyl-2-oxo-6-(thiophen-2-yl)-2H-pyran-4-carboxylate 3wa: Yellow solid, Yield = 81% (85.6 mg), t₁ = 8 h & t₂ = 44 h; ¹H NMR (500 MHz, CDCl₃) δ 7.58 (d, J = 3.7 Hz, 1H), 7.46 – 7.39 (m, 1H), 7.10 (dd, J = 4.9, 3.8 Hz, 1H), 6.72 (s, 1H), 4.40 (q, J = 7.1 Hz, 2H), 2.35 (s, 3H), 1.42 (t, J = 7.1 Hz, 3H); ¹³C NMR (125 MHz, CDCl₃) δ 165.3, 163.1, 153.1, 140.6, 135.0, 128.7, 128.4, 127.1, 125.4, 99.7, 62.4, 14.4, 14.3; IR (ATR): ν 3133, 3101, 3006, 2989, 1869, 1844, 1829, 1790, 1770, 1733, 1717, 1684, 1670, 1686, 1576, 1541, 1507, 1497, 1473, 1396, 1339, 1270 cm⁻¹; HRMS (ESI) m/z: [M+H]⁺ calcd for C₁₃H₁₃O₄S 265.0529; found: 265.0515; M. P. 95–97 °C.

Ethyl 6-((1s,3s)-adamantan-1-yl)-3-methyl-2-oxo-2H-pyran-4-carboxylate 3xa: Yellow solid, Yield = 70% (88.6 mg), t₁ = 12 h & t₂ = 54 h; ¹H NMR (500 MHz, CDCl₃) δ 6.13 (s, 1H), 4.35 (q, J = 7.1 Hz, 2H), 2.25 (s, 3H), 2.06 (s, 3H), 1.88 – 1.87 (m, 6H), 1.76 – 1.68 (m, 3H), 1.71 – 1.68 (m, 3H), 1.37 (t, J = 7.1 Hz, 3H); ¹³C NMR (125 MHz, CDCl₃) δ 169.3, 165.9, 164.5, 140.6, 124.5, 98.6, 62.1, 39.6, 37.7, 36.5, 28.0, 14.3, 14.0; IR (ATR): ν 3109, 3066, 3006, 2990, 2908, 1869, 1845, 1830, 1795, 1733, 1718, 1684, 1653, 1617, 1559, 1541, 1489, 1473, 1457, 1437, 1276, 1259, 1229 cm⁻¹; HRMS (ESI) m/z: [M+H]⁺ calcd for C₁₉H₂₅O₄ 317.1747; found: 317.1737; M. P. 135–137 °C.

Ethyl 6-(tert-butyl)-3-methyl-2-oxo-2H-pyran-4-carboxylate 3ya: Yellow solid, Yield = 72% (68.6 mg), t₁ = 11 h & t₂ = 56 h; ¹H NMR (500 MHz, CDCl₃) δ 6.21 (s, 1H), 4.36 (q, J = 7.1 Hz, 2H), 2.26 (s, 3H), 1.38 (t, J = 7.1 Hz, 3H), 1.26 (s, 9H); ¹³C NMR (125 MHz, CDCl₃) δ 169.3, 165.8, 164.4, 140.5, 124.5, 98.6, 62.2, 36.0, 28.0, 14.3, 14.0; IR (ATR): ν 3117, 3080, 3006, 2995, 1869, 1844, 1827, 1792, 1773, 1734, 1717, 1699, 1684, 1670, 1636, 1559, 1541, 1489, 1457, 1280 cm⁻¹; HRMS (ESI) m/z: [M+H]⁺ calcd for C₁₃H₁₉O₄ 239.1278; found: 239.1276; M. P. 77–79 °C.

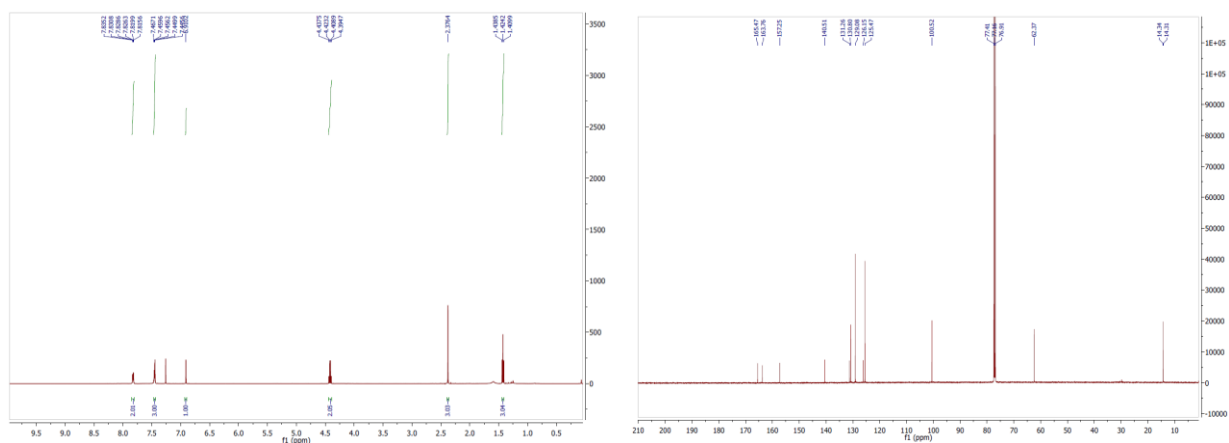
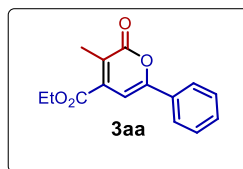
Ethyl 3-hexyl-2-oxo-6-phenyl-2H-pyran-4-carboxylate 3ab: Yellow solid, Yield = 89% (116.9 mg), t₁ = 6 h & t₂ = 38 h; ¹H NMR (500 MHz, CDCl₃) δ 7.84 – 7.80 (m, 2H), 7.46 – 7.43 (m, 3H), 6.86 (s, 1H), 4.41 (q, J = 7.1 Hz, 2H), 2.80 – 2.73 (m, 2H), 1.60 – 1.54 (m, 2H), 1.42 (t, J = 7.1 Hz, 3H), 1.39 – 1.25 (m, 6H), 0.90 – 0.87 (m, 3H); ¹³C NMR (125 MHz, CDCl₃) δ 165.6, 163.3, 157.4, 140.6, 131.3, 130.8, 130.1, 129.1, 125.5, 100.6, 77.4, 62.3, 31.8, 29.7, 29.1, 28.4, 22.7, 14.3, 14.2; IR (ATR): ν 3067, 3006, 2360, 2341, 1868, 1792, 1772, 1733, 1717, 1669, 1684, 1670, 1636, 1559, 1473, 1457, 1276, 1257 cm⁻¹; IR (ATR): ν 3067, 3006, 2360, 2341, 1868, 1792, 1772, 1733, 1717, 1669, 1684, 1670, 1636, 1559, 1473, 1457, 1276, 1257 cm⁻¹; HRMS (ESI) m/z: [M+H]⁺ calcd for C₂₀H₂₅O₄ 329.1747; found: 329.1762; M. P. 71–73 °C.

Ethyl 2-oxo-6-phenyl-2H-pyran-4-carboxylate 3ac: Yellow solid, Yield = 85% (83.0 mg), t₁ = 6 h & t₂ = 42 h; ¹H NMR (400 MHz, CDCl₃) δ 7.94 – 7.82 (m, 2H), 7.53 – 7.41 (m, 3H), 7.12 (d, J = 1.1 Hz, 1H), 6.89 (d, J = 1.2 Hz, 1H), 4.41 (q, J = 7.1 Hz, 2H), 1.41 (t, J = 7.1 Hz, 3H); ¹³C NMR (100 MHz, CDCl₃) δ 163.6, 162.0, 161.4, 144.8, 131.4, 131.2, 129.2, 125.9, 115.7, 99.5, 62.7, 14.2; IR (ATR): ν 3145, 3115, 3095, 2984, 2927, 1869, 1829, 1792, 1772, 1685, 1636, 1508, 1473, 1369, 1280 cm⁻¹; HRMS (ESI) m/z: [M+H]⁺ calcd for C₁₉H₁₇O₄ 246.0842; found: 246.0843; M. P. 81–83 °C.

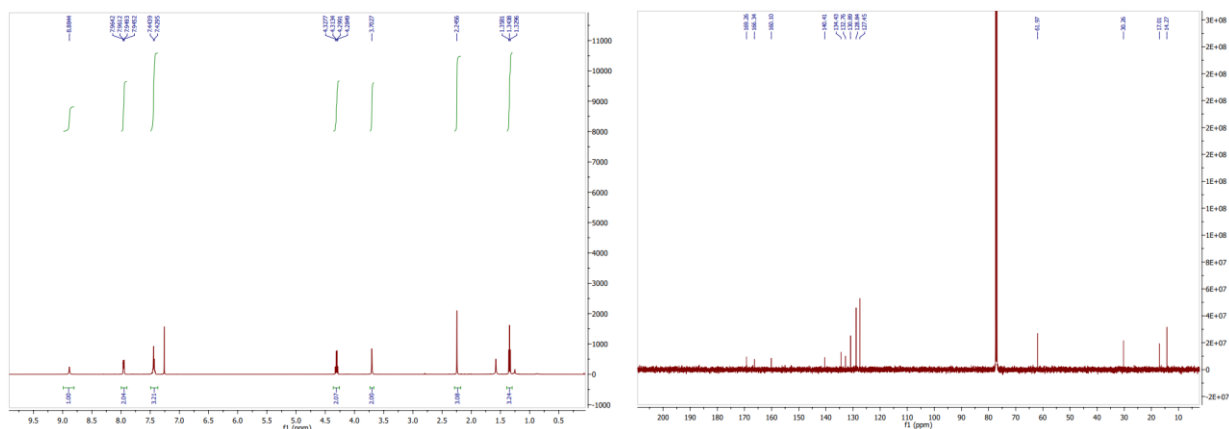
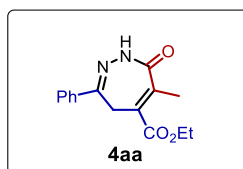
Ethyl 6-methyl-7-oxo-3-phenyl-4,7-dihydro-1H-1,2-diazepine-5-carboxylate 4aa: Off-white solid, Yield = 78% (85.0 mg), ¹H NMR (500 MHz, CDCl₃) δ 8.88 (s, 1H), 7.96 – 7.95 (m, 2H), 7.44 – 7.43 (m, 3H), 4.31 (q, J = 7.1 Hz, 2H), 3.70 (s, 2H), 2.25 (s, 3H), 1.34 (t, J = 7.1 Hz, 3H); ¹³C NMR (125 MHz, CDCl₃) δ 169.3, 166.3, 160.1, 140.4, 134.4, 132.8, 130.9, 128.8, 127.5, 62.0, 30.3, 17.0, 14.3; IR (ATR): ν 3285, 3095, 2984, 2927, 1869, 1829, 1792, 1772, 1685, 1636, 1570, 1508, 1473, 1369, 1280 cm⁻¹; HRMS (ESI) m/z: [M+H]⁺ calcd for C₁₅H₁₇N₂O₃ 273.1234; found: 273.1249; M. P. 89–91 °C.

3.4 SPECTRAL DATA

3.4.1 ^1H and ^{13}C NMR spectra



500 MHz ^1H NMR and 125 MHz ^{13}C NMR Spectra of **3aa**



500 MHz ^1H NMR and 125 MHz ^{13}C NMR Spectra of **4aa**

