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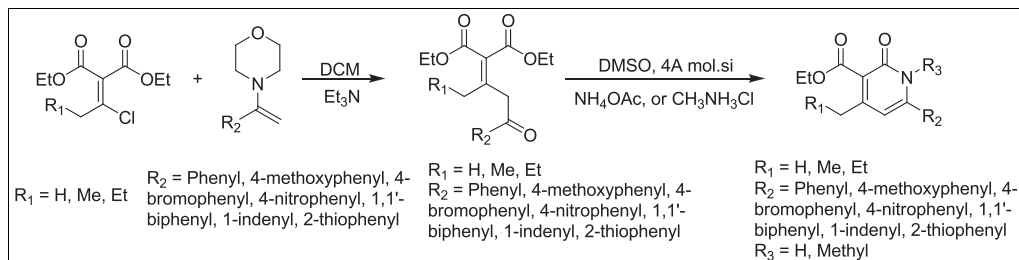
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A novel approach has been developed for the synthesis of β -arylacyl/ β -heteroarylacyl- β -alkylidene malonates in moderate to good yields by the reaction of Stork aryl and heteroaryl enamine with β -chloroalkylidene malonates. The reaction involves conjugate (Michael) addition of Stork enamine on β -chloroalkylidene malonates and elimination of chloride ion. These Michael adducts were utilized as intermediates for the synthesis of highly substituted 1,4-dialkyl-2-oxo-6-aryl/heteroaryl-1,2-dihydro-pyridine-3-carboxylic acid ethyl esters *via* 5 + 1 ring annulation protocol.

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INTRODUCTION

Enols and enolate equivalents are important intermediates in organic synthesis and many exceptionally useful reactions rely on their utilization. A particularly useful strategy for the generation of enolate equivalents are *via* Stork enamine intermediates [1]. Use of enamine for electrophilic α -substitution of aldehydes [2] and ketones [3] has resulted in formidable collection of literature. Enamines are well utilized in the total syntheses of several natural products [4] and also for the commercial manufacture of active pharmaceutical ingredients [5]. Conjugate addition (Michael) reaction of enamine on highly activated Michael acceptors are also well reported [6]. Although β -chloroalkylidene malonates **1** [7] and its derivatives such as β -aryl alkylidene malonates **2** [8, 9] are functionally enriched organic synthons, the literature precedence for these class of compounds are rather very limited, whereas β -arylacyl/ β -heteroarylacyl- β -alkylidene malonates **3** are totally unreported (Fig. 1). Herein, we report a highly regioselective, mild, and practical approach for the synthesis of hitherto unreported β -arylacyl/heteroarylacyl- β -alkylidene malonates **3** by reaction of Stork aryl and heteroaryl enamine **5** to β -chloroalkylidene malonates **1** and further their application in synthesis of 1,4,6-trisubstituted pyridine-3-carboxylates **9** *via* 5 + 1 heterocycloannulation protocol.

RESULTS AND DISCUSSION

β -chloroalkylidene malonates (**1a–c**) required for the study were prepared as per the literature procedure involving initial treatment of diethyl malonate with acid chloride and subsequent chlorination with phosphorous oxychloride [10]. The Stork aryl and heteroaryl enamines (**5a–g**) were synthesized by the reaction of appropriate ketones with morpholine in presence of titanium tetrachloride (Scheme 1) [11].

The reaction of enamine **5** with highly activated Michael acceptors such as α , β -unsaturated ketones, esters, amides, and nitrostyrenes are known to give 1,4-addition products in varying yields [12]. However, in the product, the carbon atoms of the newly formed carbon–carbon bond will be of different oxidation state. The presence of a highly labile leaving group at β -position of Michael acceptors will help to retain the oxidation (hybridization) state of reactive carbon atoms *via* elimination during the course of Michael addition reaction. Having considered these assumptions, we have studied the reactivity of enamine **5a** with β -chloroalkylidene malonate **1a** under various reaction conditions. Thus, under an optimized reaction condition, a solution of **1a** in dichloromethane was added to a freshly prepared solution of 1-(2-phenyl vinyl) morpholine **5a** in dichloromethane at room temperature. Reaction mixture was stirred for nearly 14–18 h at room temperature (monitored by

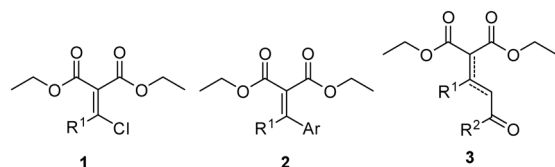
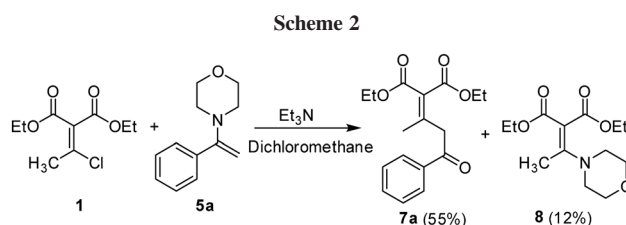


Figure 1. Structure of β -chloroalkylidene, β -aryl alkylidene and β -arylacyl/ β -alkylidene malonates.

TLC), quenched in water, and extracted with dichloromethane. After work up and column chromatographic purification, product 1-(2-methyl-3-oxo-3-phenyl-propylidene) malonic acid diethyl ester (**7a**) was isolated as brown viscous liquid in 55% of yield (Scheme 2). The reaction also resulted in the formation of β -morpholinoalkylidene malonate (**8**) as byproduct around 12–14% of yield.

Encouraged by the finding that Stork enamine **5a** underwent the sequential conjugate addition–elimination reaction with β -chloroethylidene malonate **1a**, broader applicability of reaction sequence for the synthesis of variety of β -arylacyl/heteroaryl β -acyl alkylidene malonates was investigated further. Thus, several β -chloroalkylidene malonates with β -methyl (**1a**), β -ethyl (**1b**), and β -propyl (**1c**) substituents were synthesized. Vinyl amine derived from acetophenone **5a**, 4-methoxy acetophenone **5b**, 4-bromoacetophenone **5c**, 4-nitroacetophenone **5d**, 4-acetyl-biphenyl **5e**, 1-indanone **5f**, and 2-acetyl thiophene **5g**, respectively, were then reacted with β -chloroalkylidene malonates (**1a–c**) under the above reaction conditions and the products 1-(2-alkyl-3-oxo-3-phenyl-propylidene) malonic acid diethyl esters (**7a–l**) were isolated in satisfactory yields (Table 1). The vinyl amine derived from 1-indanone **5f** also underwent smooth Michael addition–elimination reaction, and the product **7j** was isolated in 48% of yield. All the reactions were completed within 18 h, and the products were isolated by column chromatographic purification. The electron-withdrawing substituent on the aryl ring of enamine 1-{1-(4-nitrophenyl) vinyl} morpholine (**5d**) has much influence on reactivity, as the product diethyl-2-(5-(4-nitrophenyl)-5-oxopent-2-ene-3-yl) malonate (**7h**) was isolated in considerably lower yield.

NMR spectral data of these Michael adducts indicate that when the alkyl chain length in 1-(2-alkyl-3-oxo-3-aryl-alkylidene)malonic acid diethyl ester increases,



products tend to exist as α,γ -unsaturated esters, rather than α,β -unsaturated esters (Fig. 2).

The interesting feature of the transformation reported herein is the very high chemo and regio selectivity of the Michael addition–elimination sequences in presence of other reactive functional groups in β -chloroalkylidene malonates (**1a–c**). Unlike other transition metal-catalyzed Michael-addition elimination reaction sequences, no multiple addition products were observed in these reaction conditions.

The β -arylacyl/heteroarylacyl- β -alkylidene malonates synthesized by Michael addition–elimination of Stork aryl and heteroarylenamine to β -chloroalkylidene malonates provides an interesting 5-carbon synthon. To demonstrate the utility of conjugate adducts (**7a–i**), we further investigated its application in the synthesis of 4,6-disubstituted-1,2-dihydro-2-oxo-3-pyridine carboxylic acid esters. Functionalized 2(1*H*)-pyridones have been of long interest in pharmaceutical and agrochemical research, and their biological activities have been attracted much attention [13]. β -Chloroalkylidene malonates (**7a–i**) obtained by conjugate addition reaction were used as intermediates for the synthesis of substituted pyridones *via* 5 + 1 heteroannulation [14]. In a typical experiment, to a solution of conjugate adduct **7a** in dimethyl sulphoxide, ammonium acetate and molecular sieves were added, and reaction mixture was stirred at 75–80°C for 4 h. The product was isolated as a yellow crystalline solid after usual workup procedure and column chromatographic purification and characterized as 4-ethyl-2-oxo-6-phenyl-1,2-dihydro-pyridine-3-carboxylic acid ethyl ester (**9b**) based on the spectral and analytical data (Scheme 3). Similarly, heterocyclization of **7b** was also attempted with methyl amine, and 1-*N*-methyl-4-ethyl-2-oxo-6-phenyl-1,2-dihydro-pyridine-3-carboxylic acid ethyl ester (**9b**) was isolated in 70% of yield as yellow crystalline solid after column chromatographic purification.

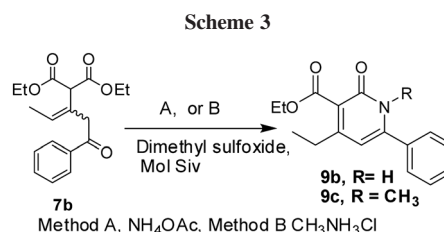
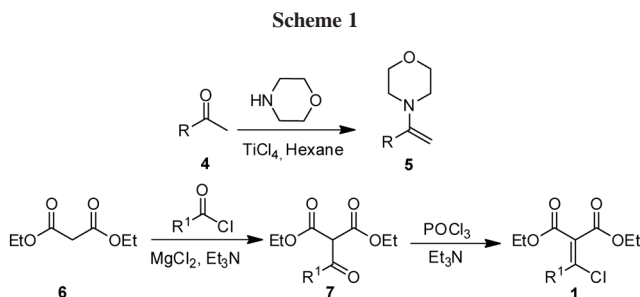
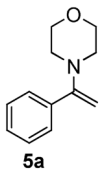
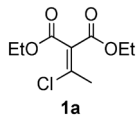
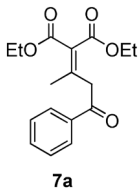
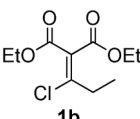
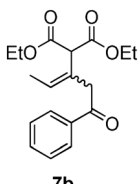
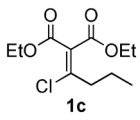
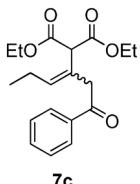
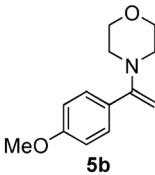
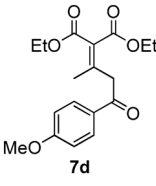
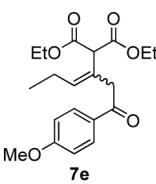
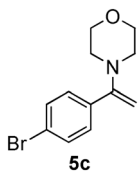
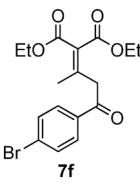
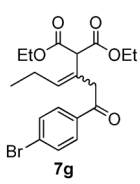


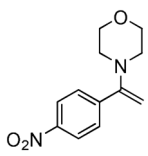
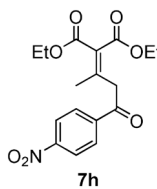
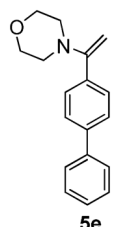
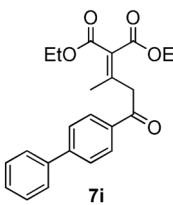
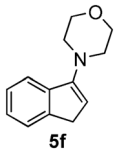
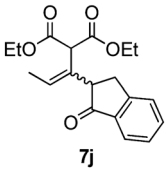
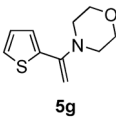
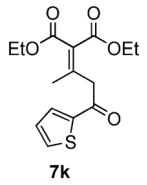
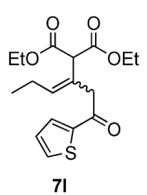
Table 1Synthesis of β -arylacryl alkylidene malonates.

Sl No	Enamine	Vinyl Ester	Product	Yield (%)
1				55
2	5a			45
3	5a			42
4		1a		48
5	5b	1c		43
6		1a		50
7	5c	1c		45

(Continued)

Table 1

(Continued)

Sl No	Enamine	Vinyl Ester	Product	Yield (%)
8		1a		30
9		1a		56
10		1b		48
11		1a		45
12	5g	1c		45

To establish the generality of the above methodology in pyridone synthesis, several 4-alkyl-2-oxo-6-aryl/heteroaryl-1,2-dihydro-pyridine-3-carboxylic acid ethyl esters (**9c–j**) were synthesized *via* 5 + 1 heteroannulation protocols with Michael addition–elimination adducts (**7a–k**) and

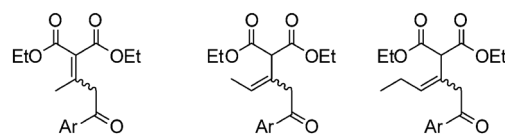
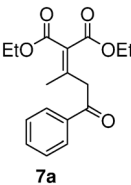
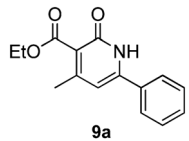
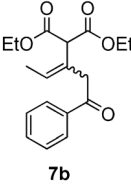
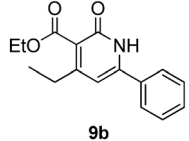
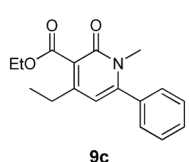
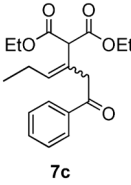
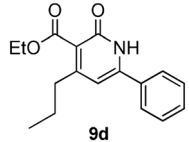
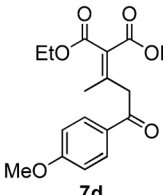
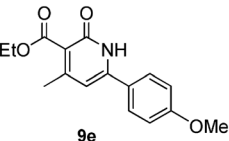
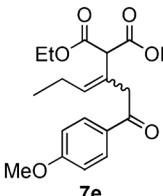
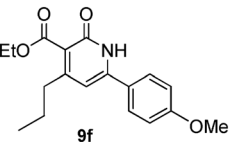
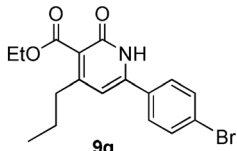


Figure 2. Structure of α , β and α , γ 1-(2-alkyl-3-oxo-3-aryl-alkylidene) malonic acid diethyl ester.

Table 2

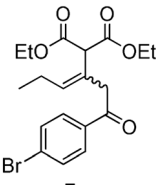
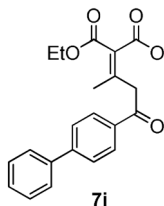
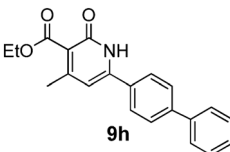
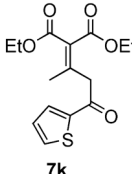
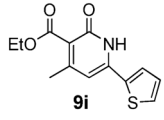
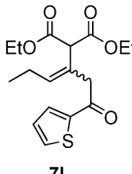
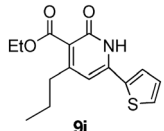
Synthesis of 4-alkyl-2-oxo-6-aryl/heteroaryl-1,2-dihydro-pyridine-3-carboxylic acid ethyl esters.

Sl No	Reactant	Product	Yield (%)	MP (°C)
1			83	151
2			83	125
3			70	112
4			75	149
5			80	157
6			82	132
7			80	167

(Continued)

Table 2

(Continued)

Sl No	Reactant	Product	Yield (%)	MP (°C)
				
8			85	202
9			78	133
10			70	Viscous liquid

ammonium acetate in dimethyl sulfoxide at elevated temperature (70–80°C). The products 1,4,6-trisubstituted pyridine-3-carboxylates (**9a–j**) were isolated in good yields (Table 2) and well characterized by means of spectral and other analytical data.

CONCLUSION

In summary, an efficient protocol for the Michael addition–elimination strategy of Stork enamine to β -chloroalkylidene malonates was developed for the first time in the literature. Also, the synthetic utility of these Michael adducts were demonstrated with an efficient synthesis of diverse array of highly substituted pyridones in good yield *via* 5 + 1 heterocycloannulation protocols with high functional flexibility. The application of this methodology for the synthesis of few alkaloids such as camptothecin and luotonin is under progress.

EXPERIMENTAL

Experimental section. Solvents and reagents are obtained from commercial sources and are not purified unless specified. $^1\text{H-NMR}$ data was obtained on a Varian Gemini 400-MHz FT-NMR spectrometer. Infrared spectra (IR) were recorded on a Perkin-Elmer 1650 FTIR spectrometer. Mass spectra were recorded on an HP-5989A quadrupole mass spectrometer. Melting points were taken in open capillaries and are uncorrected.

General procedure for synthesis of β -chloroalkylidene malonates. To a stirred solution of enamine **5a** (2.5 gm, 0.013 mol, 1 equiv) in dichloromethane (25 mL, 10 volume), triethyl amine (2.7 g, 0.026 mol, 2 equiv) was added at room temperature (28–35°C). To this reaction mixture, β -chloroalkylidene malonate **1** (3.2 g, 0.014, mol, 1.1 equiv) in dichloromethane (12.5 mL, five volumes) was added drop wise over a period of 45–50 min at room temperature. The reaction mixture was then stirred at that temperature for 10–12 h (monitored by TLC). It was then quenched in water (25 mL), washed with 10% HCl solution (38 mL, 15 volumes) followed by bicarbonate solution (10% solution, 20 mL), and water (25 mL $\times$ 3). The organic layer was then separated, dried over sodium sulphate, and concentrated under vacuum. The crude product was then purified by column chromatography over silica gel (230–400 mesh) using hexane: ethyl acetate (10 : 1) as eluent. The product **7a** was isolated as a viscous liquid in 55% of yield.

Diethyl 2-(4-oxo-4-phenylbutan-2-ylidene)malonate (7a). Yield: 55%; viscous liquid, IR (neat): 1063, 1252, 1690, 1726, 1735, 2982; $^1\text{H-NMR}$ (CDCl_3 , 400 MHz) δ : 1.05–1.30 (m, 6H), 2.07 (s, 3H), 3.91 (s, 2H), 3.93–4.05 (m, 4H), 7.52 (m, 2H), 7.61 (m, 1H), 7.96 (m, 2H). $^{13}\text{C-NMR}$ (CDCl_3 , 50 MHz) δ : 13.6, 23.0, 43.8, 57.3, 120.1, 125.6, 133.1, 135.3, 136.2, 163.6, 167.1, 195.3. MS: m/z (%) 305 [M+H] $^+$, 273, 259, 213. Anal. Calcd for $\text{C}_{17}\text{H}_{20}\text{O}_5$ (304.1): C, 67.09; H, 6.62; Found: C, 67.04; H, 6.60.

Diethyl 2-(5-oxo-5-phenylpent-2-en-3-yl)malonate (7b). Yield: 45%; viscous liquid, IR (neat): 757, 847, 1047, 1243, 1736, 2984 cm^{-1} ; $^1\text{H-NMR}$ (CDCl_3 , 400 MHz) δ : 1.23 (t, 6H, $J = 7.2$ Hz), 1.75 (d, 3H, $J = 6.8$ Hz), 3.91 (s, 2H), 4.15 (q, 4H, $J = 14$ Hz), 4.58 (s, 1H), 5.63 (q, 1H, $J = 13.6$ Hz), 7.45 (m, 2H), 7.55 (m, 1H), 7.98 (m, 2H); $^{13}\text{C-NMR}$ (CDCl_3 , 50 MHz) δ : 13.9, 43.9, 52.6, 61.6, 125.9, 128.0, 128.2, 128.4, 130.7, 132.8, 136.8, 167.8, 198.0. MS: m/z (%) 319 [M+H] $^+$, 273, 227. Anal. Calcd for $\text{C}_{18}\text{H}_{22}\text{O}_5$ (318.15): C, 67.91; H, 6.97; Found: C, 67.90; H, 6.91.

Diethyl 2-(1-oxo-1-phenylhex-3-en-3-yl)malonate (7c). Yield: 42%, viscous liquid, IR (neat): 754, 1216, 1267, 1684, 1731, 2982, 3020 cm^{-1} ; $^1\text{H-NMR}$ (CDCl_3 , 400 MHz) δ : 0.98 (t, 3H, $J = 3.6$ Hz), 1.23 (t, 6H, $J = 7.2$ Hz), 2.15 (m, 2H), 3.9 (s, 2H), 4.15 (q, 4H, $J = 14$ Hz), 4.56 (s, 1H), 5.53 (t, 1H, $J = 7.2$ Hz), 7.48 (m, 3H), 7.99 (dd, 2H). $^{13}\text{C-NMR}$ (CDCl_3 , 50 MHz) δ : 13.7, 13.9, 21.7, 43.8, 52.8, 61.6, 124.4, 128.3, 128.4, 132.8, 136.9, 138.2, 167.9, 198.1. MS: m/z (%) 333 [M+H] $^+$, 287, 241, 161. Anal. Calcd for $\text{C}_{19}\text{H}_{24}\text{O}_5$ (332.16): C, 68.66; H, 7.28; Found: C, 68.60; H, 7.21.

Diethyl 2-(4-(4-methoxyphenyl)-4-oxobutan-2-ylidene)malonate (7d). Yield: 48%, viscous liquid, IR (neat): 630, 1027, 1258, 1509, 1602, 1676, 2841 cm^{-1} ; $^1\text{H-NMR}$ (CDCl_3 , 400 MHz) δ : 1.23–1.38 (m, 6H), 2.1 (s, 3H), 3.9 (s, 2H), 4.2 (m, 7H), 6.98 (d, 2H, $J = 6$ Hz), 7.9 (m, 2H). $^{13}\text{C-NMR}$ (CDCl_3 , 50 MHz) δ : 13.7, 22.9, 44.9, 55.4, 61.7, 113.8, 123.5, 129.6, 130.4, 151.9, 165.9, 167.5, 190.1. MS: m/z (%) 335 [M+H] $^+$, 289, 243, 135. Anal. Calcd for $\text{C}_{18}\text{H}_{22}\text{O}_6$ (334.3): C, 64.60; H, 6.63; Found: C, 64.59; H, 6.61.

Diethyl 2-(1-(4-methoxyphenyl)-1-oxohex-3-en-3-yl) malonate (7e). Yield: 43%, viscous liquid, IR (neat): 758, 1215, 1731, 2982, 3020 cm^{-1} ; $^1\text{H-NMR}$ (CDCl_3 , 400 MHz) δ : 0.97 (t, 3H, $J = 7.2$ Hz), 1.23 (t, 6H, $J = 7.2$), 2.13 (m, 2H), 3.84 (s, 2H), 3.85 (s, 3H), 4.15 (q, 4H), 4.55 (s, 1H), 5.51 (t, 1H, $J = 6.8$ Hz), 6.90 (m, 2H), 7.99 (d, 2H, $J = 8.8$ Hz). MS: m/z (%) 363.17 [M+H] $^+$. Anal. Calcd for $\text{C}_{20}\text{H}_{26}\text{O}_6$ (362.17): C, 66.28; H, 7.23; Found: C, 66.21; H, 7.21.

Diethyl 2-(4-(4-bromophenyl)-4-oxobutan-2-ylidene) (7f). Yield: 50%, viscous liquid, IR (neat): 757, 1047, 1241, 1373, 1741, 2985 cm^{-1} . $^1\text{H-NMR}$ (CDCl_3 , 400 MHz) δ : 1.21–1.32 (m, 6H), 2.07 (s, 3H), 4.15 (s, 2H), 4.21–4.3 (m, 4H), 7.62 (m, 2H), 7.85 (m, 2H). MS: m/z (%) 383 [M+H] $^+$, 339, 291, 183. Anal. Calcd for $\text{C}_{17}\text{H}_{19}\text{BrO}_5$ (382.04): C, 53.28; H, 5.00; Found: C, 53.20; H, 5.01.

Diethyl 2-(4-(4-nitrophenyl)-4-oxobutan-2-ylidene) malonate (7h). Yield: 30%, viscous liquid, IR (neat): 1047, 1240, 1374, 1742, 2984 cm^{-1} . $^1\text{H-NMR}$ (CDCl_3 , 400 MHz) δ : 1.21–1.32 (m, 6H), 2.10 (s, 3H), 4.2 (m, 4H), 4.23 (s, 2H), 8.10 (m, 2H), 8.40 (m, 2H). MS: m/z (%) 364 [M+H] $^+$, 323, 258. Anal. Calcd for $\text{C}_{18}\text{H}_{21}\text{NO}_7$ (382.04): C, 59.7; H, 5.83, N, 3.85; Found: C, 53.20; H, 5.01.

Diethyl 2-[4-(biphenyl-4-yl)-4-oxobutan-2-ylidene] malonate (7i). Yield: 56%, off white solid, MP: 202°C, IR (KBr): 650, 733, 908, 1686, 1719, 1793, 2253, 2984 cm^{-1} . $^1\text{H-NMR}$ (CDCl_3 , 400 MHz) δ : 1.2 (t, 3H, $J = 7.2$ Hz), 1.3 (t, 3H, $J = 3.2$ Hz), 2.13 (s, 3H), 4.16 (q, 2H, $J = 7.2$ Hz), 4.31 (s, 2H), 4.32 (m, 2H), 7.45 (m, 1H), 7.5 (m, 2H), 7.62 (m, 2H), 7.65 (m, 2H), 8.15 (d, 2H, $J = 8.2$ Hz). $^{13}\text{C-NMR}$ (CDCl_3 , 50 MHz) δ : 14.0, 14.1, 23.1, 45.2, 60.9, 61.1, 127.2, 127.3, 128.2, 128.7, 128.9, 129.0, 135.2, 139.7, 145.9, 151.6, 164.3, 165.9, 194.9, 195. MS: m/z (%) 381 [M+H] $^+$, 380.5, 289, 181. Mass Calcd. for $\text{C}_{23}\text{H}_{24}\text{O}_5$ C, 72.61; H, 6.36 found: C, 72.60; H, 6.34.

Diethyl 2-[1-(1-oxo-2,3-dihydro-1H-inden-2-yl)prop-1-enyl]malonate (7j). Yield: 48%, viscous liquid, IR (neat): 634, 1049, 1238, 1374, 1459, 1749, 2874, 2959 cm^{-1} . $^1\text{H-NMR}$ (CDCl_3 , 400 MHz) δ : 1.26 (t, 3H, $J = 6.8$ Hz), 1.31 (t, 3H, $J = 7.2$ Hz), 1.73 (d, 3H, $J = 6.8$ Hz), 3.11 (dd, 1H, $J = 4.4$ Hz, 17 Hz), 3.52 (m, 1H), 3.6 (dd, 1H, $J = 4.4$, 24 Hz), 4.2 (m, 2H), 4.35 (m, 2H), 4.46 (s, 1H), 5.59 (q, 1H, $J = 14$ Hz), 7.35 (m, 1H), 7.42 (m, 1H), 7.62 (m, 1H), 7.75 (m, 1H). $^{13}\text{C-NMR}$ (CDCl_3 , 50 MHz) δ : 13.9, 14.0, 29.6, 35.5, 52.6, 52.9, 61.5, 61.7, 123.9, 126.3, 127.3, 129.1, 131.5, 134.5, 136.5, 153.4, 167.7, 168.1, 205. MS: m/z (%) 331 [M+H] $^+$, 285, 239. Anal. Calcd for $\text{C}_{19}\text{H}_{22}\text{O}_5$ (330.37): C, 69.06; H, 6.71; Found: C, 69.04; H, 6.70.

Diethyl 2-[1-oxo-1-(thiophen-2-yl)butan-2-ylidene] malonate (7k). Yield: 45%, viscous liquid, IR (neat): 727, 1064, 1251, 1415, 1666, 1721, 2982 cm^{-1} . $^1\text{H-NMR}$ (CDCl_3 , 400 MHz): 1.22 (t, 3H, $J = 6.7$ Hz), 1.30 (t, 3H, $J = 6.7$ Hz), 2.14 (s, 3H), 4.15 (m, 2H), 4.21 (s, 2H), 4.31 (q, 2H, $J = 11.8$ Hz), 7.18 (m, 1H), 7.60 (m, 1H), 7.80 (m, 1H). MS: m/z (%) 311 [M+H] $^+$, 265, 219, 149. Anal. Calcd for $\text{C}_{15}\text{H}_{18}\text{O}_5$ (310.3): C, 58.05; H, 5.85; Found: C, 58.01; H, 5.80.

Diethyl 2-[1-oxo-1-(thiophen-2-yl)hex-3-en-3-yl] malonate (7l). Yield: 45%, viscous liquid, IR (neat): 754, 1215, 1275, 1663, 1731, 3020 cm^{-1} ; $^1\text{H-NMR}$ (CDCl_3 , 400 MHz) δ : 1.00 (t, 3H, $J = 7.6$ Hz), 1.21 (t, 6H, $J = 7.3$ Hz), 2.14 (q, 2H, $J = 7.6$ Hz), 3.83 (s, 2H), 4.16 (m, 4H), 4.55 (s, 1H), 5.61 (t, 1H, $J = 7.2$ Hz), 7.11 (m, 1H), 7.61 (m, 1H), 7.81 (m, 1H). $^{13}\text{C-NMR}$ (CDCl_3 , 50 MHz) δ : 13.6, 13.9, 21.7, 44.3, 52.8, 61.6, 123.9, 128.0, 132.3, 133.4, 138.3, 144.1, 167.9, 190.7. MS: m/z (%) 339 [M+H] $^+$, 293, 247. Anal. Calcd for $\text{C}_{17}\text{H}_{22}\text{O}_5\text{S}$ (338.42): C, 60.33; H, 6.55; Found: C, 60.31; H, 6.54.

General procedure for synthesis of pyridones. To a stirred solution of β -arylacyl alkylidene malonates **7a** (1 g, 0.0032 mol, 1 equiv) in dimethyl sulfoxide (10 mL, 10 volume), molecular sieves (1 g) and ammonium acetate (0.76 g, 0.0096 mol, 3 equiv) were added at room temperature. The reaction mixture was then stirred at 45–50°C for 3 h (monitored by TLC). The molecular sieves were filtered-off, and the reaction mass was then diluted with water (25 mL), extracted with dichloromethane (3 $\times$ 15 mL), and washed with water (2 $\times$ 10 mL). The combined organic layers were dried over sodium sulphate and concentrated under vacuum. The crude product was then purified by column chromatography over silica gel (230–400 mesh) using hexane: ethyl acetate (10 : 2.5) as eluent. The product **9a** was isolated as yellow solid in 83% of yield.

Ethyl-4-methyl-2-oxo-6-phenyl-1,2-dihydropyridine-3-carboxylate (9a). Yield: 83%; MP: 151°C, yellow solid, IR (KBr): 1123, 1259, 1637, 1728, 2925 cm⁻¹. ¹H-NMR (CDCl₃, 400 MHz) δ : 1.26 (t, 3H, J = 7.6 Hz), 2.19 (s, 3H), 4.26 (q, 2H, J = 7.6 Hz), 6.56 (s, 1H), 7.48 (m, 3H), 7.7 (m, 2H), 11.96 (brs, 1H); ¹³C-NMR (CDCl₃, 50 MHz) δ : 14.0, 19.1, 60.5, 107.0, 121.3, 126.8, 128.6, 129.9, 133.1, 147.2, 149.1, 160.1, 166. MS: m/z (%) 258 [M+H]⁺, 234, 212 Anal. Calcd for C₁₅H₁₅NO₃ (257.3): C, 70.02; H, 5.88; N, 5.44; Found: C, 70.00; H, 5.87; N, 5.4.

Ethyl-4-ethyl-2-oxo-6-phenyl-1,2-dihydropyridine-3-carboxylate (9b). Yield: 83%; MP: 125°C; IR (KBr): 769, 921, 1095, 1240, 1622, 1730, 2934 cm⁻¹; ¹H-NMR (CDCl₃, 400 MHz) δ : 1.26 (t, 3H J = 7.6 Hz), 1.35 (t, 3H, J = 7.2 Hz), 2.62 (q, 2H, J = 15 Hz), 4.38 (m, 2H), 6.65 (s, 1H), 7.46 (m, 3H), 7.80 (m, 2H), 12.21 (brs, 1H). ¹³C-NMR (CDCl₃, 50 MHz) δ : 14.2, 14.5, 27.3, 61.2, 106.2, 121.0, 126.3, 128.9, 130.1, 133.1, 147.9, 156.7, 162.5, 166.7; MS: m/z (%) 272 [M+H]⁺, 226; C₁₆H₁₇NO₃ (271.3): C, 70.83; H, 6.32; N, 5.16; Found: C, 70.82; H, 6.30; N, 5.17.

Ethyl-4-ethyl-1-methyl-2-oxo-6-phenyl-1,2-dihydropyridine-3-carboxylate (9c). Yield: 70%; yellow solid, MP 112 °C IR (KBr): 734, 908, 1138, 1642, 1725, 2252, 2979, 3608 cm⁻¹. ¹H-NMR (CDCl₃, 400 MHz) δ : 1.21 (t, 3H, J = 7.6 Hz), 1.40 (t, 3H, J = 7.2 Hz), 2.52 (q, 2H, J = 14.8 Hz), 3.35 (s, 3H), 4.4 (q, 2H, J = 14.4 Hz), 6.02 (s, 1H), 7.32 (m, 2H), 7.47 (m, 3H) ¹³C-NMR (CDCl₃, 50 MHz) δ : 14.0, 14.2, 26.0, 34.2, 61.3, 108.5, 122.0, 128.2, 128.7, 129.4, 135.1, 150.3, 153.2, 160.6, 166.7; MS: m/z (%) 286 [M+H]⁺, 242.3, 174; C₁₇H₁₉NO₃ (285.34): C, 71.56; H, 6.71; N, 4.91; Found: C, 71.55; H, 6.72; N, 4.83.

Ethyl-2-oxo-6-phenyl-4-propyl-1,2-dihydropyridine-3-carboxylate (9d). Yield: 75%; MP: 149 °C; yellow solid; IR (KBr): 847, 1047, 1243, 1374, 1740, 2985 cm⁻¹; ¹H-NMR (CDCl₃, 400 MHz) δ : 1.09 (t, 3H, J = 7.2 Hz), 1.35 (t, 3H, J = 7.2 Hz), 1.7 (m, 2H), 2.59 (m, 2H), 4.38 (q, 2H, J = 14 Hz), 6.44 (s, 1H), 7.46 (m, 3H), 7.74 (m, 2H) 11.8 (s, 1H). ¹³C-NMR (CDCl₃, 100 MHz) δ : 14.0, 14.2, 23.3, 36.1, 61.3, 107.1, 120.7, 126.7, 129.0, 130.3, 133.3, 147.8, 155.5, 162.3, 166.8 MS: m/z (%) 286.2 [M+H]⁺, 240; Anal. Calcd for C₁₇H₁₉NO₃ (285.34): C, 71.56; H, 6.71; N, 4.91; Found: C, 71.55; H, 6.72; N, 4.83.

Ethyl-6-(4-methoxyphenyl)-4-methyl-2-oxo-1,2-dihydropyridine-3-carboxylate (9e). Yield: 80%; MP: 157; yellow solid; IR (KBr): 1258, 1517, 1606, 1630, 1734, 2933, 2976 cm⁻¹. ¹H-NMR (CDCl₃, 400 MHz) δ : 1.37 (t, 3H, J = 7.2 Hz), 2.35 (s, 3H), 3.85 (s, 3H), 4.39 (q, 2H, 6.8 Hz), 6.42 (s, 1H), 6.97 (t, 2H, J = 8.3 Hz), 7.7 (t, 2H, J = 8.3 Hz), 12.09 (brs, 1H); ¹³C-NMR (CDCl₃, 50 MHz) δ : 14.3, 20.8, 55.4, 61.2, 107.8,

114.4, 125.7, 128.0, 128.3, 148.5, 151.9, 161.4, 162.6, 167.2 MS: m/z (%) 288 [M+H]⁺, 219, 201, 162, 148. Anal. Calcd for C₁₆H₁₇NO₄ (287.0): C, 66.89; H, 5.96; N, 4.88, Found: C, 66.80; H, 5.94; N, 4.87.

Ethyl-6-(4-methoxyphenyl)-2-oxo-4-propyl-1,2-dihydropyridine-3-carboxylate (9f). Yield: 82%; MP: 132°C; yellow solid, IR (KBr): 787, 1047, 1241, 1373, 1742, 2985 cm⁻¹. ¹H-NMR (CDCl₃, 400 MHz) δ : 1.00 (t, 3H, J = 7.6 Hz), 1.36 (t, 3H, J = 7.2 Hz), 1.63 (m, 2H), 2.59 (m, 2H), 3.89 (s, 3H), 4.36 (q, 2H, J = 14.4 Hz), 6.38 (s, 1H), 6.99 (d, 2H, J = 4.8 Hz), 7.74 (dd, 2H, J = 2, 6.8 Hz) 11.9 (brs, 1H). ¹³C-NMR (CDCl₃, 50 MHz) δ : 14.0, 14.2, 23.3, 36.2, 55.4, 61.9, 106.1, 114.4, 120.0, 125.6, 128.3, 147.6, 155.6, 161.3, 162.5, 167.0 MS: m/z (%) 316 [M+H]⁺, 270; Anal. Calcd for C₁₈H₂₁NO₄ (315.36): C, 68.55; H, 6.71; N, 4.44; Found: C, 68.51; H, 6.73; N, 4.48.

Ethyl-6-(4-bromophenyl)-2-oxo-4-propyl-1,2-dihydropyridine-3-carboxylate (9g). Yield: 80%; MP: 167°C; yellow solid IR (KBr): 847, 1047, 1240, 1374, 1742, 2985 cm⁻¹. ¹H-NMR (CDCl₃, 400 MHz) δ : 0.97 (t, 3H, J = 7.2 Hz), 1.37 (t, 3H, J = 7.2 Hz), 1.63 (q, 2H, J = 14.8 Hz), 2.63 (m, 2H), 4.4 (q, 2H, J = 14.4 Hz), 6.52 (s, 1H), 7.52–7.67 (m, 4H), 12.2 (brs, 1H). ¹³C-NMR (CDCl₃, 50 MHz) δ : 14.0, 14.2, 23.3, 36.1, 61.4, 107.5, 120.7, 124.8, 128.6, 132.1, 132.3, 147.3, 155.5, 162.9, 166.8; MS: m/z (%) 365.1 [M+H]⁺, 318.0; C₁₇H₁₈BrNO₃ (364.23): C, 56.06; H, 4.98; N, 3.85; Found: C, 56.01; H, 4.91; N, 3.81.

Ethyl-6-(biphenyl-4-yl)-4-methyl-2-oxo-1,2-dihydropyridine-3-carboxylate (9h). Yield: 85%; MP: 202°C; White solid IR (KBr): 650, 908, 1091, 1632, 2253, 2983, 3387 cm⁻¹. ¹H-NMR (CDCl₃, 400 MHz) δ : 1.37 (t, 3H, J = 7.2 Hz), 2.41 (s, 3H), 4.41 (q, 2H, J = 14.4 Hz), 6.6 (s, 1H), 7.37–7.72 (m, 7H), 7.86 (d, 2H, J = 8.4 Hz), 11.58 (brs, 1H). ¹³C-NMR (CDCl₃, 50 MHz) δ : 14.2, 20.9, 61.4, 108.9, 118.0, 127.0, 127.3, 127.6, 127.8, 128.8, 132.3, 139.9, 143.1, 148.5, 151.9, 162.7, 167.2; MS: m/z (%) 334 [M+H]⁺, 288; Anal. Calcd for C₂₁H₁₉NO₃ (333.38): C, 75.66; H, 5.74; N, 4.20; Found: C, 75.69; H, 5.76; N, 4.17.

Ethyl 4-methyl-2-oxo-6-(thiophen-yl)-1,2-dihydropyridine-3-carboxylate (9i). Yield: 78%; MP: 133°C; yellow solid; IR (KBr): 1090, 1270, 1545, 1609, 1638, 1715, 2932, 2978 cm⁻¹. ¹H-NMR (CDCl₃, 400 MHz) δ : 1.42 (t, 3H, J = 7.8 Hz), 2.43 (s, 3H), 4.43 (q, 2H, J = 6.8 Hz), 6.65 (s, 1H), 7.11 (dd, 1H, J = 4, 4.8 Hz), 7.43 (m, 1H), 7.92 (d, 1H, J = 4 Hz), 12.6 (brs, 1H); ¹³C-NMR (CDCl₃, 50 MHz) δ : 14.3, 21.5, 61.5, 109.6, 127.8, 128.5, 128.6, 137.9, 146.2, 152.4, 156.0, 163.6, 167.9; MS: m/z (%) 264 [M+H]⁺, 218, 192, 168, 110; Anal. Calcd for C₁₃H₁₃NO₃S (263.3): C, 59.37; H, 4.98; N, 5.32; Found: C, 59.37; H, 4.99; N, 4.97.

Ethyl-2-oxo-4-propyl-6-(thiophen-2-yl)-1,2-dihydropyridine-3-carboxylate (9j). Yield: 70%; yellow solid; IR (KBr): 847, 1047, 1243, 1374, 1740, 2985 cm⁻¹. ¹H-NMR (CDCl₃, 400 MHz) δ : 1.02 (t, 3H J = 7.3 Hz), 1.41 (t, 3H, J = 7.2 Hz), 1.64 (q, 2H, J = 14.8 Hz), 2.64 (m, 2H), 4.43 (m, 2H), 6.6 (s, 1H), 7.26 (m, 1H), 7.4 (m, 1H), 7.9 (m, 1H), 12.27 (brs, 1H); ¹³C-NMR (CDCl₃, 50 MHz) δ : 14.0, 14.2, 23.5, 36.4, 61.4, 107.7, 124.5, 127.7, 128.3, 128.5, 137.2, 144.5, 156.1, 163.2, 167.5; Mass: m/z ratio (%) 292.1 [M+H]⁺, 246.1.; Anal. Calcd for C₁₅H₁₇NO₃S (291.37): C, 61.83; H, 5.88; N, 4.81. found: C, 61.83; H 5.89; N, 4.79.

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