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# Synthesis of ester functionalized 2-pyridone derivatives using KF/Alumina as a catalyst

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**Abstract:** A simple and efficient method for synthesis of ester functionalized 2-pyridone derivatives (**4a-m**) via tri component reaction of primary amine, mono ester acetylene and diester acetylene using KF/alumina as catalyst under microwave irradiation is reported.

**Keywords**: KF/alumina; ester functionalized 2-pyridones; primary amine; acetylenic ester; microwave irradiation. 

## 1. Introduction

The chemistry of pyridones has been studied for over a century due to their diverse biological activities and resemblance with the nucleosides[1]. It is reported that many of the pyridone derivatives are playing an essential role in several biological processes[2]. Specifically, 2-pyridones represent a unique class of pharmacophores which are present in various therapeutic agents [3] and antibiotics[4] such as HIV-1 non-nucleoside reverse transcriptase inhibitors (NNRTIs)[5], antibacterial[6], antifungal[7] sedative[8] and cardiotonic agents[9]. Apart from the medicinal and pharmaceutical utilities they are also used as good ligands for 3d-metals and are in persistence of their applications in co-ordination chemistry[10]. They are also useful as versatile precursors for the construction of complex natural products[11], pyridines[12] and larger pyridone systems such as those found in the nitro guanidine insecticide Imidacloprid[13]. Consequently, many new methodologies have been reported for the synthesis of 2-pyridones[14-16].

The synthesis of ester substituted 2-pyridones from amine, monoester acetylene and diester acetylene involves Michael addition catalyzed by various basic and acidic catalysts,[17-19] but the reports are very scare[20,21]. In such, Issa Yavari *et. al.*[20], have successfully synthesized triester substituted 2-pyridones using *N*-Methylimidazole as a catalyst, but they failed to obtain diester substituted 2-pyridones. Similarly, Qinglei[21] *et.al*., also successfully synthesized both di and triester substituted 2-pyridones in catalyst free condition, but the methodology is not that much worthwhile due to the long reaction times. Though these are some successful contributions to these compounds, many of these methods are associated with various drawbacks such as harsh reaction conditions, tedious experimental procedures, unsatisfactory yields, long reaction times and usage of expensive and moisture sensitive catalysts.

In such search of the effective catalyst, we have focused our vision on the solid supported catalysts, which are attracting widespread interest within the synthetic chemistry researchers. Finally, we identified potassium fluoride impregnated over alumina as a useful system to afford the target products. The merit of the KF/alumina system is that, its basic sites of the alumina is associated to a

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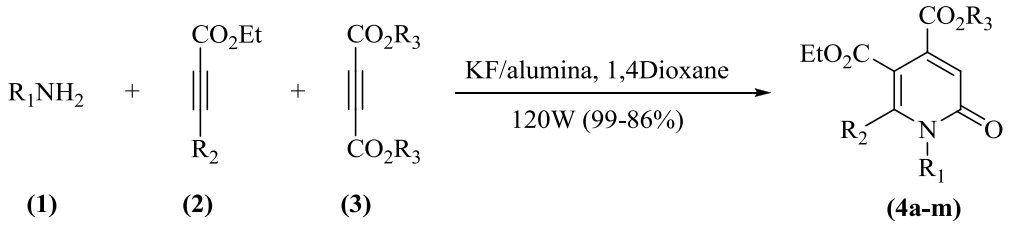
very hard anion ($F^-$ ion), which possibly augments the surface to be act as a potential base and differentiate from other alkaline earth metal oxide base catalysts in affording the target molecules[22].

## 2. Results and discussion

We report KF/alumina catalyzed three component reaction of primary amine, monoester acetylene and diester acetylene for the synthesis of ester functionalized 2-pyridone derivatives **4a-m** (Figure 1).




**$R_1$**= alkyl, aryl; **$R_2$**=H, COOEt; **$R_3$**= Me, Et

**Figure 1.** Synthesis of ester functionalized 2-pyridone derivatives (**4a-m**).

**Table 1.** Optimization of the model reaction with various catalysts and solvent condition[a]

| Entry | Catalyst | Solvent | MW (Watt) | Time (Min) | Yield (%)[b] |
|---|---|---|---|---|---|
| 1 | No Catalyst | Solvent-Free | 120 | 16 | 32 |
| 2 | KF-$Al_2O_3$ (5 mol%) | Solvent-Free | 120 | 10 | 49 |
| 3 | KF-$Al_2O_3$ (5 mol%) | THF | 120 | 12 | 55 |
| 4 | KF-$Al_2O_3$ (5 mol%) | $CH_3CN$ | 120 | 12 | 59 |
| 5 | KF-$Al_2O_3$ (5 mol%) | 1,4-Dioxane | 120 | 12 | 67 |
| 6 | KF-$Al_2O_3$ (10 mol%) | 1,4-Dioxane | 120 | 10 | 75 |
| 7 | KF-$Al_2O_3$ (15 mol%) | 1,4-Dioxane | 120 | 10 | 69 |
| 8 | KF-$Al_2O_3$ (20 mol%) | 1,4-Dioxane | 120 | 10 | 61 |
| 9 | Neutral Alumina (10 mol%) | 1,4-Dioxane | 120 | 12 | 61 |
| 10 | $K_2CO_3$ (10 mol%) | 1,4-Dioxane | 120 | 12 | 63 |
| 11 | Amberlyst-15 (10 mol%) | 1,4-Dioxane | 120 | 12 | 58 |
| 12 | Celite-545 (10 mol%) | 1,4-Dioxane | 120 | 12 | 60 |
| 13 | Silica Gel-60 (10 mol%) | 1,4-Dioxane | 120 | 12 | 66 |
| 14 | KF-$Al_2O_3$ (10 mol%) | 1,4-Dioxane | 120 | 12 | 69 |
| 15 | KF-$Al_2O_3$ (10 mol%) | 1,4-Dioxane | 120 | 12 | 65 |

[a]Reaction conditions: benzyl amine (1 mmol), ethyl propiolate (1 mmol) and di ethyl-2-butynediate (1 mmol);
[b]Isolated yield

To establish the optimal experimental condition for the synthesis of target compound (**4a-m**), the reaction of benzyl amine, ethyl propiolate and di ethyl-2-butynediate were studied for synthesis of **4a** as a model reaction. Thus, the reaction was performed using various catalysts with microwave irradiation (Table 1). When the reaction was performed under catalyst free condition low product yield was obtained (Table 1**,** entry 1). Various catalysts such as silicagel 60, celite 545, amberlyst 15, $K_2CO_3$, neutral alumina, KF/alumina were screened for the synthesis **4a**, among them KF/alumina functioned well over others (Table 1**,** entry 2-15). Our further study on the required concentration of catalyst KF/alumina showed that 10 mol% offers best yield (Table 1, entry 6). However, on further decreasing or increasing the concentration of catalyst to 5, 15 and 20 mol% respectively no improvement in the yield was observed (Table 1, entry 5, 7 and 8). Study on the diversity of solvent systems shown that 1,4 Dioxane acts as a good solvent (Table 1, entry 2, 3, 4 and 5). Finally, we

performed the model reaction under various microwave power ranges but, better yields are obtained when the reaction carried out at 120 W (Table 1, entry 6). Further increasing microwave power to 180 W and 210 W showed decrease in the product yield (Table 1, entry 14 and 15). Perhaps this may be due to formation of complex reaction mixture at high microwave power.

The practicality of this transformation was demonstrated by taking various primary amines and acetylenic esters. Under optimized condition results were shown in Table 2. Both aliphatic and aromatic primary amines were smoothly involved in these transformations. Yields of triester substituted 2-pyridones are slightly higher than yields of diester substituted 2-pyridones at the same optimized condition (Table 2, entry 4b and 4o) which may be due to presence of additional electron withdrawing group (ester) on **4m**.

**Table 2.** Scope for KF/alumina catalyzed synthesis of ester functionalized 2-pyridones (**4a-m**)

| Entry | $R^1$ | $R^2$ | $R^3$ | Time (Min) | Yield (%)[b] |
|---|---|---|---|---|---|
| 4a | $C_6H_5CH_2$- | H | Et | 10 | 75 |
| 4b | 4-$FC_6H_4$ $CH_2$- | H | Et | 10 | 73 |
| 4c | Cyclohexyl | H | Et | 10 | 70 |
| 4d | $C_6H_5CH_2$- | H | Me | 10 | 72 |
| 4e | 4-$FC_6H_4$ $CH_2$- | H | Me | 10 | 70 |
| 4f | Cyclohexyl | H | Me | 10 | 69 |
| 4g | $C_6H_5$- | $EtCO_2$- | Et | 10 | 86 |
| 4h | $4CH_3C_6H_4$- | $EtCO_2$- | Et | 10 | 77 |
| 4i | $4OMeC_6H_4$- | $EtCO_2$- | Et | 10 | 74 |
| 4j | $C_6H_5CH_2$- | $EtCO_2$- | Et | 10 | 81 |
| 4k | $4CH_3C_6H_4CH_2$- | $EtCO_2$- | Et | 10 | 69 |
| 4l | $4OMeC_6H_4CH_2$- | $EtCO_2$- | Et | 10 | 76 |
| 4m | 4-$FC_6H_4$ $CH_2$- | $EtCO_2$- | Et | 10 | 81 |

[b]Isolated yield

All the synthesized compounds were fully characterized on the basis of their physical and spectral (infrared (IR), NMR, mass spectrographic (MS)) data. They showed strong IR absorption bands at 1738-1711, 1610-1590 and 2940-2800 $cm^{-1}$for the carbonyl, aromatic -C=C-, -$CH_2$- and –$CH_3$ groups respectively. Their $^1$H NMR spectra showed characteristic signals of ester group at 3.50-3.90 (q, 2H) and 1.30-1.45 (t, 3H) with the same coupling constants. The signals at 8.35-8.49 correspond to pyridone C-H. The $^{13}$C NMR data confirm the presence of carbonyl group as its chemical shift appeared at 161.0-166.9 ppm.

A plausible mechanism for the synthesis of ester functionalized 2-pyridones is presented in (Figure 2). Initially a Michael addition occurred between primary amine (**1**) and acetylenic ester (**2**) which are promoted by $F^-$ (catalyst). The formed intermediate (**I**) subsequently undergo one more Michael addition with acetylenic ester (**3**). Finally, intermediate (**IV**) undergo cyclyzation to form the desired product (**4**).

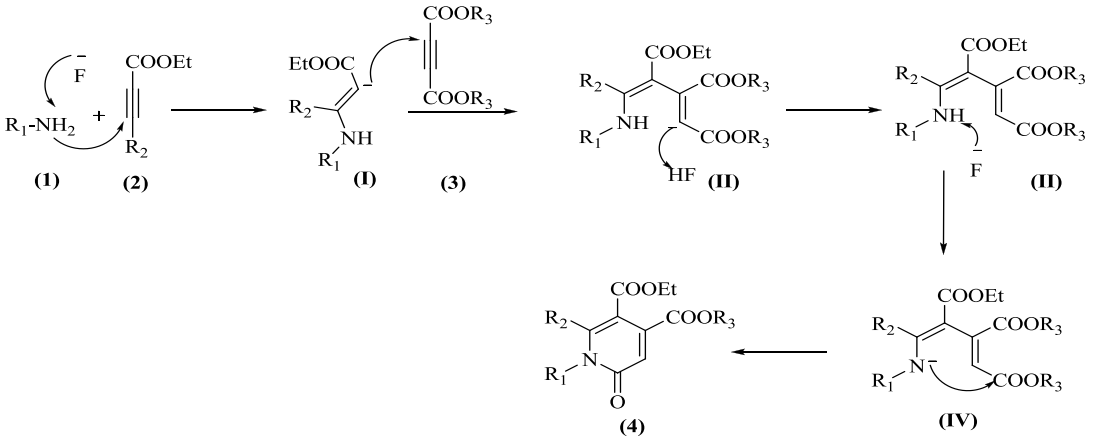


**Figure 2.** Plausible mechanism for the synthesis of ester functionalized 2-pyridones (**4a-m**).

## 3. Experimental

Solvents and reagents were procured from Sigma-Aldrich & Merck and are used as such without further purification. The reactions were carried out on Microwave Oven, CATALYST-4R, Research Model, Made in India. Melting points were determined using a calibrated thermometer by Guna Digital Melting Point apparatus. IR spectra were recorded on FT-IR spectrometer. $^{1}H$ and $^{13}C$ NMR spectra were recorded as solutions in $CDCl_3$ on a Bruker AMX 500 MHz spectrometer operating at 300 MHz for $^{1}H$ and 75.4 MHz for $^{13}C$. For $^{1}H$ and $^{13}C$ chemical shifts tetramethylsilane (TMS) was used as an internal standard. ESI mass spectra were recorded on a Micromass Quattro LC instrument. Elemental analysis was performed on Thermo Finnegen Instrument.

### 3.*1. General procedure for the synthesis of 4a-f*:

Terminal alkyne (1 mmol %), primary amine (1 mmol %), dioxane (2 mL) and $KF/Al_2O_3$ (10 mol%) were taken in a 10 mL pressure tube and were subjected to microwave heating (CEM Discover, 120 W, 250 psi, 100 °C) for 2 min. Subsequently internal alkyne (1mol%) was added and subjected to microwave heating under similar conditions for 8 min. After completion of the reaction (as monitored by TLC), the solvent was removed under reduced pressure and the resulting residue was subjected to silica gel chromatography to give the desired product.

*3.1.1. Diethyl1-benzyl-6-oxo-1,6-dihydropyridine-3,4-dicarboxylate (4a):* Yield 75%, m.p. 113-115 °C; IR (Neat): *v* 2980 (-$CH_3$), 1736 (-C=O of ester), 1659 (-C=O of lactam) 1141 (C-O-C) $cm^{-1}$; $^{1}H$ NMR ($CDCl_3$): $\delta$ 1.09 (t, *J* = 7.3 Hz, 3H, $CH_3$), 1.30 (t, *J* = 7.1 Hz, 3H, $CH_3$), 3.91 (q, *J* = 7.3 Hz, 2H, $OCH_2$), 4.30 (q, *J* = 7.1 Hz, 2H, $OCH_2$), 5.16 (s, 2H, benzylic $CH_2$), 6.90 (s, 1H, Pyridone C-H), 7.80 (s, 1H, Ar C-H), 7.25 (d, *J* = 7.8 Hz, 2H, Ar C-H), 7.53 (d, *J* = 7.9 Hz, 2H, Ar C-H), 8.31 (s, 1H, Pyridone C-H); $^{13}C$ NMR ($CDCl_3$) $\delta$ 13.2 ($CH_3$), 13.9 ($CH_3$), 52.1 (benzylic $CH_2$), 62.1 ($OCH_2$), 62.6 ($OCH_2$), 106.9 (Ar-C), 121.1 (Ar-C), 128.3 (Ar-C), 129.3 (Ar-C), 129.9 (Ar-C), 136.4 (Ar-C), 143.3 (Ar-C), 145.1 (Ar-C), 160.2 (C=O), 163.2 (C=O), 165.4 (C=O); MS (ESI): *m/z* 330.14 $[M + H]^+$; Anal.Calcd for $C_{18}H_{19}NO_5$: C, 65.64; H, 5.81; N, 4.25; O, 24.29. Found: C, 65.64; H, 5.65; N, 4.10; O, 24.11.

*3.1.2. Diethyl 1-(4-fluorobenzyl)-6-oxo-1,6-dihydropyridine-3,4-dicarboxylate (4b):* Yield 73%, m.p. 122-124 °C; IR (Neat): *v* 2980 (-$CH_3$), 1734 (-C=O of ester), 1661 (-C=O of lactam) 1142 (C-O-C) $cm^{-1}$; $^{1}H$ NMR ($CDCl_3$): $\delta$ 1.23 (t, *J* = 7.1 Hz, 3H, $CH_3$), 1.33 (t, *J* = 7.2 Hz, 3H, $CH_3$), 4.26 (q, *J* = 7.1 Hz, 2H, $OCH_2$), 4.39 (q, *J* = 7.2 Hz, 2H, $OCH_2$), 5.13 (s, 2H, benzylic $CH_2$), 6.61 (s, 1H, Pyridone C-H), 7.06 (t, *J* = 8.1Hz, 2H, Ar C-H), 7.35 (t, *J* = 8.1Hz, 2H, Ar C-H), 8.15 (s, 1H, Pyridone C-H); $^{13}C$ NMR ($CDCl_3$) $\delta$ 13.8 ($CH_3$), 19.5 ($CH_3$), 52.1 (benzylic $CH_2$), 61.4 ($OCH_2$), 62.1 ($OCH_2$), 107.9 (Ar-C), 118.7 (Ar-C), 130.1 (Ar-C), 143.0 (Ar-C), 144.4 (Ar-C), Please add $\delta$ of C-F 162.9 (C=O), 164.2

(C=O), 165.9 (C=O); MS (ESI): *m/z* 348.23 $[M + H]^+$; Anal.Calcd for $C_{18}H_{18}FNO_5$: C, 62.24; H, 5.22; F, 5.47; N, 4.03; O, 23.03. Found: C, 62.24; H, 5.10; F, 5.14; N, 4.23; O, 23.21.

*3.1.3. Diethyl1-cyclohexyl-6-oxo-1,6-dihydropyridine-3,4-dicarboxylate (4c):* Yield 70%, oil; IR (Neat): *ν* 2989 (-$CH_3$), 1750 (-C=O of ester), 1675 (-C=O of lactam) 1141 (C-O-C) $cm^{-1}$; $^1$H NMR ($CDCl_3$): *δ* 1.10-1.45 (m, 10H, Cyclohexyl H), 1.50 (t, *J* = 7.4 Hz, 3H, $CH_3$), 1.91 (d, *J* = 7.0 Hz, 3H, $CH_3$), 4.39 (q, *J* = 7.4 Hz, 2H, $OCH_2$), 4.46 (q, *J* = 7.0 Hz, 2H, $OCH_2$), 4.86 (m, 1H, Cyclohexyl C-H), 6.58 (s, 1H, Pyridone C-H), 8.19 (s, 1H, Pyridone C-H); $^{13}$C NMR ($CDCl_3$) *δ* 13.7 ($CH_3$), 13.9 ($CH_3$), 24.8 (Cyclohexyl C), 25.3 (Cyclohexyl C), 32.1 Cyclohexyl C), 54.8 (Cyclohexyl C), 61.1 ($OCH_2$), 61.8 ($OCH_2$), 107.3 (Ar-C), 117.9 (Ar-C), 139.6 (Ar-C), 143.1 (Ar-C), 161.1 (C=O), 163.1 (C=O), 166.1 (C=O); MS (ESI): *m/z* 322.13 $[M + H]^+$; Anal.Calcd for $C_{17}H_{23}NO_5$: C, 63.54; H, 7.21; N, 4.36; O, 24.89. Found: C, 63.50; H, 7.11; N, 4.25; O, 24.57.

*3.1.4. 3-Ethyl 4-methyl 1-benzyl-6-oxo-1,6-dihydropyridine-3,4-dicarboxylate (4d):* Yield 72%, m.p. 128-130 °C; IR (Neat): *ν* 2988 (-$CH_3$), 1733 (-C=O of ester), 1658 (-C=O of lactam) 1139 (C-O-C) $cm^{-1}$; $^1$H NMR ($CDCl_3$): *δ* 1.30 (t, *J* = 7.4 Hz, 3H, $CH_3$), 3.96 (q, *J* = 7.4 Hz, 2H, $OCH_2$), 4.03 (s, 3H, $OCH_3$), 5.16 (s, 2H, benzylic $CH_2$), 6.90 (s, 1H, Pyridone C-H), 7.80 (s, 1H, Ar C-H), 7.25 (d, *J* = 7.9 Hz, 2H, Ar C-H), 7.52 (d, *J* = 7.9 Hz, 2H, Ar C-H), 8.31 (s, 1H, Pyridone C-H); $^{13}$C NMR ($CDCl_3$) *δ* 14.5 ($CH_3$), 52.1 (benzylic $CH_2$), 62.1 ($OCH_3$), 62.6 ($OCH_2$), 106.9 (Ar-C), 121.1 (Ar-C), 128.3 (Ar-C), 129.3 (Ar-C), 129.9 (Ar-C), 136.4 (Ar-C), 143.3 (Ar-C), 145.5 (Ar-C), 160.4 (C=O), 163.2 (C=O), 165.3 (C=O); MS (ESI): *m/z* 316.11 $[M + H]^+$; Anal.Calcd for $C_{17}H_{17}NO_5$: C, 64.75; H, 5.43; N, 4.44; O, 25.37. Found: C, 64.69; H, 5.38; N, 4.29; O, 25.31.

*3.1.5. 3-Ethyl 4-methyl 1-(4-fluorobenzyl)-6-oxo-1,6-dihydropyridine-3,4-dicarboxylate (4e):* Yield 70%, m.p. 138-139 °C; IR (Neat): *ν* 2985 (-$CH_3$), 1739 (-C=O of ester), 1666 (-C=O of lactam) 1150 (C-O-C) $cm^{-1}$; $^1$H NMR ($CDCl_3$): *δ* 1.32 (t, *J* = 7.1 Hz, 3H, $CH_3$), 4.21 (s, 3H, $OCH_3$), 4.40 (q, *J* = 7.1 Hz, 2H, $OCH_2$), 5.13 (s, 2H, benzylic $CH_2$), 6.62 (s, 1H, Pyridone C-H), 7.09 (t, *J* = 7.0 Hz, 2H, Ar C-H), 7.35 (t, *J* = 7.0 Hz, 2H, Ar C-H), 8.14 (s, 1H, Pyridone C-H); $^{13}$C NMR ($CDCl_3$) *δ* 13.9 ($CH_3$), 52.9 (benzylic $CH_2$), 61.9 ($OCH_3$), 62.5 ($OCH_2$), 107.9 (Ar-C), 118.6 (Ar-C), 129.5 (Ar-C), 143.2 (Ar-C), 144.1 (Ar-C), 160.6 (Ar-C), 162.5 (C=O), 164.1 (C=O), 165.8 (C=O); MS (ESI): *m/z* 333.13 $[M + H]^+$; Anal.Calcd for $C_{17}H_{16}FNO_5$: C, 61.26; H, 4.84; F, 5.70; N, 4.20; O, 24.00. Found: C, 61.20; H, 4.79; F, 5.60; N, 4.12; O, 24.14.

*3.1.6. 3-Ethyl 4-methyl 1-cyclohexyl-6-oxo-1,6-dihydropyridine-3,4-dicarboxylate (4f):* Yield 69%, m.p. 77-79 °C; IR (Neat): *ν* 2981 (-$CH_3$), 1733 (-C=O of ester), 1660 (-C=O of lactam) 1141 (C-O-C) $cm^{-1}$; $^1$H NMR ($CDCl_3$): *δ* 1.11-1.48 (m, 10H, Cyclohexyl H), 1.86 (t, *J* = 7.3 Hz, 3H, $CH_3$), 3.84 (s, 3H, $OCH_3$), 4.24 (q, *J* = 7.3 Hz, 2H, $OCH_2$), 4.67-4.70 (m, 1H, Cyclohexyl C-H), 6.43 (s, 1H, Pyridone C-H); 8.31 (s, 1H, Pyridone C-H); $^{13}$C NMR ($CDCl_3$) *δ* 14.4 ($CH_3$), 25.7 (Cyclohexyl C), 26.4 (Cyclohexyl C), 32.4 (Cyclohexyl C), 52.2 Cyclohexyl C), 56.9 ($OCH_3$), 61.7 ($OCH_2$), 107.3(Ar-C), 118.4 (Ar-C), 141.5(Ar-C), 143.9 (Ar-C), 161.1 (C=O), 164.4 (C=O), 167.4 (C=O); MS (ESI): *m/z* 308.23 $[M + H]^+$; Anal.Calcd for $C_{16}H_{21}NO_5$: C, 62.53; H, 6.89; N, 4.56; O, 26.03. Found: C, 62.44; H, 6.71; N, 4.44; O, 26.24.

### *3.2. General procedure for the synthesis of 4g-m*:

Acetylenic alkyne (2 mmol %), primary amine (1 mmol %), dioxane (2 mL) and $KF/Al_2O_3$ (10 mol%) were taken in a 10mL pressure tube and were subjected to microwave heating (CEM Discover, 120 W, 250 psi, 100 °C) for 10 Min. After completion of the reaction (as monitored by TLC), the solvent was removed under reduced pressure and the resulting residue was subjected to silica gel chromatography to give the desired product.

*3.2.1. Triethyl6-oxo-1-phenyl-1,6-dihydropyridine-2,3,4-tricarboxylate (4g):* Yield 86%, yellow oil; IR (Neat): *ν* 2981 (-$CH_3$), 1732 (-C=O of ester), 1682 (-C=O of lactam) 1141 (C-O-C) $cm^{-1}$; $^1$H NMR ($CDCl_3$): *δ* 0.90 (t, *J* = 7.1 Hz,3H, $CH_3$), 1.29 (t, *J* = 7.1 Hz, 3H, $CH_3$), 1.31 (t, *J* = 6.9 Hz, 3H, ), 3.91 (q, *J* = 7.1 Hz, 2H, $OCH_2$), 4.26 (q, *J* = 6.9 Hz, 2H, $OCH_2$), 4.39 (q, *J* = 7.1 Hz, 2H, $OCH_2$), 6.91 (s,

1H, Pyridone C-H), 7.81 (s, 1H, Ar C-H), 7.25 (d, *J* = 7.9 Hz, 2H, Ar C-H), 7.50 (d, *J* = 7.9 Hz, 2H, Ar C-H); $^{13}$C NMR ($CDCl_3$) $\delta$ 13.2 ($CH_3$), 13.7 ($CH_3$), 13.9 ($CH_3$), 62.0 ($OCH_2$), 62.3 ($OCH_2$), 62.6 ($OCH_2$), 106.9 (Ar-C), 121.1 (Ar-C), 128.2 (Ar-C), 129.2 (Ar-C), 129.8 (Ar-C), 136.3 (Ar-C), 143.5 (Ar-C), 145.4 (Ar-C), 160.6 (C=O), 163.1 (C=O), 165.1 (C=O); MS (ESI): *m/z* 388.11 $[M + H]^+$; Anal.Calcd for $C_{20}H_{21}NO_7$: C, 62.01; H, 5.46; N, 3.62; O, 28.91. Found: C, 62.01; H, 5.36; N, 3.54; O, 28.88.

*3.2.2. Triethyl6-oxo-1-(p-tolyl)-1,6-dihydropyridine-2,3,4-tricarboxylate (4h):* Yield 77%, m.p. 77-79 °C; IR (Neat): $\nu$ 2979 (-$CH_3$), 1743 (-C=O of ester), 1665 (-C=O of lactam) 1151 (C-O-C) cm$^{-1}$; $^1$H NMR ($CDCl_3$): $\delta$ 0.91 (t, *J* = 7.1 Hz, 3H, $CH_3$), 1.20 (t, *J* = 7.1 Hz, 3H, $CH_3$), 1.39 (t, *J* = 7.0 Hz, 3H, $CH_3$), 2.21 (s, 3H, Ph-$CH_3$), 3.91 (q, *J* = 7.1 Hz, 2H, $OCH_2$), 4.24 (q, *J* = 7.0 Hz, 2H, $OCH_2$), 4.31 (q, *J* = 7.0 Hz, 2H, $OCH_2$), 6.91 (s, 1H, Pyridone C-H), 7.10-7.25 (d, 4H, Ar C-H); $^{13}$C NMR ($CDCl_3$) $\delta$ 13.2 ($CH_3$), 13.7 ($CH_3$), 13.9 ($CH_3$), 21.1 (Ph-$CH_3$), 62.0 ($OCH_2$), 62.2 ($OCH_2$), 62.5 ($OCH_2$), 129.8 (Ar-C), 133.6 (Ar-C), 140.0 (Ar-C), 143.4 (Ar-C), 145.6 (Ar-C), 160.7 (C=O), 160.8 (C=O), 163.1 (C=O), 121.0 (Ar-C), 127.9 (Ar-C), 165.1 (C=O); MS (ESI): *m/z* 402.24 $[M + H]^+$; Anal.Calcd for $C_{21}H_{23}NO_7$: C, 62.83; H, 5.78; N, 3.49; O, 27.90. Found: C, 62.78; H, 5.73; N, 3.41; O, 27.88.

*3.2.3. Triethyl1-(4-methoxyphenyl)-6-oxo-1,6-dihydropyridine-2,3,4-tricarboxylate (4i):* Yield 74%, Yellow oil; IR (Neat): $\nu$ 2982 (-$CH_3$), 1733 (-C=O of ester), 1681 (-C=O of lactam) 1141 (C-O-C) cm$^{-1}$; $^1$H NMR ($CDCl_3$): $\delta$ 1.11 (t, *J* = 7.1 Hz, 3H, $CH_3$), 1.29 (t, *J* = 7.2 Hz, 3H, $CH_3$), 1.38 (t, *J* = 7.1 Hz, 3H, $CH_3$), 3.83 (s, 3H, $OCH_3$), 3.97 (q, *J* = 7.1 Hz, 2H, $OCH_2$), 4.26 (q, *J* = 7.2 Hz, 2H, $OCH_2$), 4.38 (q, *J* = 7.1 Hz, 2H, $OCH_2$), 6.35 (s, 1H, Pyridone C-H), 6.98 (t, *J* = 8.9 Hz, 2H, Ar C-H), 7.19 (t, *J* = 8.9 Hz, 2H, Ar C-H); $^{13}$C NMR ($CDCl_3$) $\delta$ 13.2 ($CH_3$), 13.6 ($CH_3$), 13.8 ($CH_3$), 52.1 ($OCH_3$), 61.2 ($OCH_2$), 62.3 ($OCH_2$), 62.6 ($OCH_2$), 121.0 (Ar-C), 127.8 (Ar-C), 129.9 (Ar-C), 133.7 (Ar-C), 140.1 (Ar-C), 143.4 (Ar-C), 145.5 (Ar-C), 169.3 (C=O), 160.7 (C=O), 163.2 (C=O), 165.2 (C=O); MS (ESI): *m/z* 418.13 $[M + H]^+$; Anal.Calcd for $C_{21}H_{23}NO_8$: C, 60.43; H, 5.55; N, 3.36; O, 30.66. Found: C, 60.39; H, 5.51; N, 3.37; O, 30.45.

*3.2.4. Triethyl1-benzyl-6-oxo-1,6-dihydropyridine-2,3,4-tricarboxylate (4j):* Yield 81%, Yellow oil; IR (Neat): $\nu$ 2982 (-$CH_3$), 1733 (-C=O of ester), 1662 (-C=O of lactam) 1142 (C-O-C) cm$^{-1}$; $^1$H NMR ($CDCl_3$): $\delta$ 0.90 (t, *J* = 7.2 Hz, 3H, $CH_3$), 1.29 (t, *J* = 7.2 Hz, 3H, $CH_3$), 1.31 (t, *J* = 7.3 Hz, 3H, $CH_3$), 3.91 (q, *J* = 7.2 Hz, 2H, $OCH_2$), 4.30 (q, *J* = 7.2 Hz, 2H, $OCH_2$), 4.51 (q, *J* = 7.3 Hz, 2H, $OCH_2$), 5.16 (s, 2H, benzylic $CH_2$), 6.80 (s, 1H, Ar C-H), 7.25 (d, *J* = 7.9 Hz, 2H, Ar C-H), 7.53 (d, *J* = 7.9 Hz, 2H, Ar C-H), 7.25-7.52 (m, 5H, Ar C-H); $^{13}$C NMR ($CDCl_3$) $\delta$ 13.3 ($CH_3$), 13.5 ($CH_3$), 13.9 ($CH_3$), 52.1 (benzylic $CH_2$), 62.1 ($OCH_2$), 62.4 ($OCH_2$), 62.6 ($OCH_2$), 106.9 (Ar-C), 121.1 (Ar-C), 128.2 (Ar-C), 129.2 (Ar-C), 129.8 (Ar-C), 136.3 (Ar-C), 143.4 (Ar-C), 145.2 (Ar-C), 160.3 (C=O), 163.1 (C=O), 165.3 (C=O); MS (ESI): *m/z* 402.15 $[M + H]^+$; Anal.Calcd for $C_{21}H_{23}NO_7$: C, 62.83; H, 5.78; N, 3.49; O, 27.90. Found: C, 62.81; H, 5.77; N, 3.50; O, 27.89.

*3.2.5. Triethyl1-(4-methylbenzyl)-6-oxo-1,6-dihydropyridine-2,3,4-tricarboxylate (4k):* Yield 69%, oil; IR (Neat): $\nu$ 2988 (-$CH_3$), 1734 (-C=O of ester), 1661 (-C=O of lactam) 1143 (C-O-C) cm$^{-1}$; $^1$H NMR ($CDCl_3$): $\delta$ 1.09 (t, *J* = 7.4 Hz, 3H, $CH_3$), 1.20 (t, *J* = 6.9 Hz, 3H, $CH_3$), 1.39 (t, *J* = 7.1 Hz, 3H, $CH_3$), 2.20 (s, 3H, Ph-$CH_3$), 3.92 (q, *J* = 7.4 Hz, 2H, $OCH_2$), 4.25 (q, *J* = 6.9 Hz, 2H, $OCH_2$), 4.31 (q, *J* = 7.1 Hz, 2H, $OCH_2$), 5.14 (s, 2H, benzylic $CH_2$), 6.92 (s, 1H, Pyridone C-H), 7.25 (d, *J* = 8.9 Hz, 4H, Ar C-H); $^{13}$C NMR ($CDCl_3$) $\delta$ 13.3 ($CH_3$), 13.7 ($CH_3$), 13.9 ($CH_3$), 21.1 (Ph-$CH_3$), 51.6 (benzylic $CH_2$), 62.0 ($OCH_2$), 62.2 ($OCH_2$), 62.6 ($OCH_2$), 121.0 (Ar-C), 127.9 (Ar-C), 129.8 (Ar-C), 133.6 (Ar-C), 140.1 (Ar-C), 143.4 (Ar-C), 145.5 (Ar-C), 160.2 (C=O), 163.2 (C=O), 165.5 (C=O); MS (ESI): *m/z* 416.18 $[M + H]^+$; Anal.Calcd for $C_{22}H_{26}NO_7$. MS (ESI): *m/z* 416.18 $[M + H]^+$; Anal.Calcd for $C_{22}H_{25}NO_7$: C, 63.60; H, 6.07; N, 3.37; O, 26.96. Found: C, 63.59; H, 6.01; N, 3.36; O, 26.88.

*3.2.6. Triethyl1-(4-methoxybenzyl)-6-oxo-1,6-dihydropyridine-2,3,4-tricarboxylate (4l):* Yield 74%, Yellow oil; IR (Neat): $\nu$ 2981 (-$CH_3$), 1735 (-C=O of ester), 1670(-C=O of lactam) 1144 (C-O-C) cm$^{-1}$; $^1$H NMR ($CDCl_3$): $\delta$ 1.15 (t, *J* = 7.1 Hz, 3H, $CH_3$), 1.27 (t, *J* = 6.9 Hz, 3H, $CH_3$), 1.39 (t, *J* = 7.3 Hz, 3H, $CH_3$), 3.84 (s, 3H, $OCH_3$), 3.96 (q, *J* = 7.1 Hz, 2H, $OCH_2$), 4.25 (q, *J* = 6.9 Hz, 2H, $OCH_2$), 4.37 (q, *J* = 7.3 Hz, 2H, $OCH_2$), 5.12 (s, 2H, benzylic $CH_2$), 6.34 (s, 1H, Pyridone C-H), 6.97 (t, 2H, Ar C-

H), 7.18 (t, 2H, Ar C-H); $^{13}$C NMR ($CDCl_3$) $\delta$ 13.1 ($CH_3$), 13.7 ($CH_3$), 13.7 ($CH_3$), 59.0 ($OCH_3$), 61.2 ($OCH_2$), 62.2 ($OCH_2$), 62.5 ($OCH_2$), 121.5 (Ar-C), 127.1 (Ar-C), 129.6 (Ar-C), 133.6 (Ar-C), 140.1 (Ar-C), 143.0 (Ar-C), 145.9 (Ar-C), 159.5 (C=O), 160.6 (C=O), 163.1 (C=O), 165.1 (C=O); MS (ESI): *m/z* 432.19 $[M + H]^+$; Anal.Calcd for $C_{22}H_{25}NO_8$: C, 61.25; H, 5.84; N, 3.25; O, 29.67. Found: C, 61.21; H, 5.80; N, 3.21; O, 29.55.

*3.2.7. Triethyl1-(4-fluorobenzyl)-6-oxo-1,6-dihydropyridine-2,3,4-tricarboxylate (4m):* Yield 81%, oil; IR (Neat): *v* 2981 (-$CH_3$), 1742 (-C=O of ester), 1673 (-C=O of lactam) 1140 (C-O-C) cm$^{-1}$; $^1$H NMR ($CDCl_3$): $\delta$ 0.99 (t, *J* = 7.1 Hz, 3H, $CH_3$), 1.31 (t, *J* = 7.3 Hz, 3H, $CH_3$), 1.43 (t, *J* = 7.1 Hz, 3H, $CH_3$), 3.98 (q, *J* = 7.1 Hz, 2H, $OCH_2$), 4.29 (q, *J* = 7.3 Hz, 2H, $OCH_2$), 4.38 (q, *J* = 7.1 Hz, 2H, $OCH_2$), 5.13 (s, 2H, benzylic $CH_2$), 6.59 (s, 1H, Pyridone C-H), 7.06 (t, *J* = 8.3 Hz, 2H, Ar C-H), 7.36 (t, *J* = 8.3 Hz, 2H, Ar C-H); $^{13}$C NMR ($CDCl_3$) $\delta$ 12.9 ($CH_3$), 13.1 ($CH_3$), 29.5 ($CH_3$), 52.1 (benzylic $CH_2$), 60.6 ($OCH_2$), 61.4 ($OCH_2$), 62.1 ($OCH_2$), 107.9 (Ar-C), 118.7 (Ar-C), 130.1 (Ar-C), 143.0 (Ar-C), 144.1 (Ar-C), 161.3 (C=O), 162.9 (C=O), 164.2 (C=O), 165.9 (C=O); MS (ESI): *m/z* 420.15 $[M + H]^+$; Anal.Calcd for $C_{21}H_{22}FNO_7$: C, 60.14; H, 5.29; F, 4.53; N, 3.34; O, 26.70. Found: C, 60.10; H, 5.21; F, 4.44; N, 3.31; O, 26.66.

## 4. Conclusion

In conclusion, we have developed a facile and efficient method for the synthesis of ester functionalized both di and triester 2-pyridones in dioxane in the presence of $KF/Al_2O_3$. The mild reaction conditions, less expensiveness, operational simplicity and high product yields are the practical advantages of the present catalyst over the reported protocols. To the best of our knowledge, this is the first report to synthesize di and tri ester 2-pyridones by using $KF/Al_2O_3$ as a potential catalyst.

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