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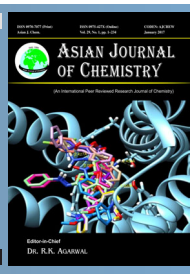

Multicomponent One Pot Synthesis and Characterization of Novel 4-Furyl-1,4-dihydropyridines

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A series of dihydropyridines were prepared from the multi-component reaction of 5-arylfuran-2-carbaldehydes, ethylacetoacetate and ammonium acetate. These compounds were characterized through elemental analysis and various spectroscopic techniques (FTIR, ^{1}H NMR, ^{13}C NMR and mass).

Keywords: Dihydropyridines, 5-Arylfuran-2-carbaldehydes, Multicomponent reaction, Meerwein Arylation reaction.

INTRODUCTION

Dihydropyridines are important class of compounds showing interesting pharmacological properties. Most important of these are their actions as calcium channel blockers. Acaricidal, insecticidal, bactericidal, herbicidal, antiaggregatory, cerebral antiischemic and properties such as chemo sensitizers have also been reported [1]. Some of these amlopidine, nifedipine and nicardipine are calcium channel blockers and are in common clinical use for the prevention of hypertension [1,2]. There are others which are acetylchlonestrase inhibitors and neuroprotectants [2-8].

Most of these are available through Hantzsch dihydropyridine synthesis in a multicomponent (MCR) strategy of cyclocondensation between an aldehyde and active methylene compound and ammonium acetate in an alcohol solvent [2,9-13]. In continuation of our work on multicomponent reactions for the synthesis of heterocyclic compounds of potential biological interest, we have prepared a number of novel 1,4-dihydropyridines by employing arylfurfurals as the aldehydic component of the reaction. This we would like to report in the present communication. Although various aryl aldehydes have been employed for this synthesis and some 1,4-dihydropyridines containing a 4-furyl substituent are reported but *hitherto* arylfurfurals have not been used for such syntheses.

EXPERIMENTAL

The reagents and chemicals used were commercially available from Merck or Fluka and were used as such. However when needed, were purified using normal techniques. The solvents used were distilled and dried. Melting points were taken on a GallenKamp melting point apparatus and are uncorrected. FTIR spectra were recorded on a Bruker Tensor 27. ^{1}H NMR and ^{13}C NMR spectra were taken on Bruker DPX instrument at 300 and 400 MHz. High resolution mass spectra were recorded on a Fisons VG Platform II spectrometer.

Synthesis of 5-arylfuran-2-carbaldehydes (1-9): The compounds 5-arylfuran-2-carbaldehydes (**1-9**) were synthesized and characterized according to the reported method [3,13].

5-(2'-Nitrophenyl)furan-2-carbaldehyde (1): Yield: 67 %; m.p.: 80-81 °C (lit. m.p. 90-92 °C) [1].

5-(4'-Nitrophenyl)furan-2-carbaldehyde (2): Yield: 64 %; m.p.: 196 °C (lit. m.p. 192 °C) [3].

5-(2',3'-Dichlorophenyl)furan-2-carbaldehyde (3): Yield: 59 %; m.p.: 90-92 °C [4].

5-(2',4'-Dichlorophenyl)furan-2-carbaldehyde (4): Yield: 53 %; m.p.: 63 °C.

5-(5'-Chloro-2'-nitrophenyl)furan-2-carbaldehyde (5): Yield: 52 %; m.p.: 76 °C.

5-(3',4'-Dichlorophenyl)furan-2-carbaldehyde (6): Yield: 61 %; m.p.: 105 °C.

5-(3'-Nitrophenyl)furan-2-carbaldehyde (7): Yield: 61 %; m.p.: 148 °C (lit. m.p 150 °C) [2].

5-(4'-Chlorophenyl)furan-2-carbaldehyde (8): Yield: 62 %; m.p.: 118 °C [4].

5-(2'-Chloro-4'-nitrophenyl)furan-2-carbaldehyde (9): Yield: 61 %; m.p.: 114 °C.

Synthesis of dihydropyridines (10-20): An arylfuran-2-carbaldehyde (1 mmol), ethyl acetoacetate (2 mmol) and ammonium acetate (1mmol) was refluxed in ethanol for 3 h (reaction monitored through TLC). After cooling the reaction mixture was poured into ice cold water. Precipitates were filtered, washed with water and cold ethanol, dried and recrystallized from ethanol to give dihydropyridines (**10-20**).

Diethyl 2,6-dimethyl-4-[5'-(4''-nitro phenyl)furan-2'-yl]-1,4-dihydropyridine-3,5-dicarboxylate (10): Yield: 95 %; m.p.: 145-150 °C; IR (KBr, ν_{max}, cm^{-1}): 3834.9 (N-H stretching), 3107.0 (Ar-H), 2984.0 (C-H stretching of CH_3), 1714.3 (C=O ester), 1512.3, 1330.4 (NO_2); ^{1}H NMR ($CDCl_3$), δ: 2.379 (s, 6H, $2CH_3$), 1.319 (t, 6H, $2\underline{CH_3}CH_2$, *J* = 10.68 Hz), 4.234 (q, 4H, $2CH_3\underline{CH_2}$, *J* = 12.63 Hz), 7.74 (H-2", 6"), 8.25 (H-3", 5"); ^{13}C NMR ($CDCl_3$), δ: 14.08 ($\underline{C}H_3$), 61.70 (CH_3-$\underline{C}H_2$), 167.20 ($\underline{C}$=O), 107.70 ($\underline{C}$=C), 149.98 ($\underline{C}$-NH), 14.39 ($\underline{C}H_3$), 33.83 ($\underline{C}$H-C), 150.21 (CH=$\underline{C}$-O), 100.37 ($\underline{C}$H-CH), 107.70 (CH-$\underline{C}$H), 154.79 ($\underline{C}$H-aromatic ring), 136.91, 130.83, 123.2, 124.80, 125.59, 149.81 (aromatic carbons); Mass: *m/z*: 440.2 (M) 96.7 %, 411.2 (M-$2CH_3$) 100 %, 395.2 (M-NO_2) 30.1 %, 383.1 (M-$2C_2H_5$) 23.3 %, 367.2 (M-$COOC_2H_5$) 100 %, 337.2 (M-$COOC_2H_5$-$2CH_3$) 26.7 %, 321.1 (M-$COOC_2H_5$-C_2H_5O) 30.4 %, 293.1 (M-$2COOC_2H_5$) 11.7 %, 252.1 (M-$C_{10}H_6NO_3$) 14.9 %, 196.1 (M-$C_{10}H_6NO_3$-$2C_2H_5$) 13.8 %, 179.1 (M-$C_{10}H_6NO_3$-$2C_2H_5$-CH_3) 10.7 %, 150.1 (M-$C_{10}H_6NO_3$-C_2H_5O-CH_3) 15.4 %, 120.1 (M-$C_{17}H_{20}NO_5$) 13.0 %, 55.1 (C_4H_5) 6.5 %, 43.0 (C_2H_4O) 9.9 %.

Diethyl-2,6-dimethyl 4-[5'-(2'',3''-dichlorophenyl)furan-2'-yl]-1,4-dihydropyridine-3-carboxylate (11): Yield :43 %; m.p.: 110-112 °C; IR (KBr, ν_{max}, cm^{-1}): 3902.4 (N-H stretching), 3327.9 (Ar-H), 2982.2 (C-H stretching of CH_3), 1651.7 (C=O ester); Mass: 465.1 (M+2) 13.9 %, 463.1 (M) 24.1 %, 434.1 (M-$2CH_3$) 21.2 %, 390.1 (M-$COOC_2H_5$) 47.4 %, 364.0 (M-$COOC_2H_5$-$2CH_3$), 344.0 (M-$COOC_2H_5$-C_2H_5O), 252.1 (M-$C_{10}H_5Cl_2O$) 8.9 %, 196.1 (M-$C_{10}H_5Cl_2O$-$2CH_3$-C_2H_5) 5.1 %, 173.0 (M-$2COOC_2H_5$-$C_6H_3Cl_2$) 7.1 %, 149.0 (M-$C_{10}H_5Cl_2O$-$2C_2H_5O$-CH_3) 7.9 %. ^{1}H NMR ($CDCl_3$), δ: 2.358 (s, 6H, $2CH_3$), 1.261 (t, 6H, $2\underline{CH_3}$-CH_2, *J* = 10.71 Hz), 4.197 (q, 4H, 2CH3-$\underline{CH_2}$, *J* = 10.86 Hz), 5.265 (s, 1H, CH), 7.027 (d, 1H, H-4", *J* = 2.55), 7.179 (t, 1H, H-5"), 7.265 (d, 1H, H-6"); ^{13}C NMR ($CDCl_3$), δ: 14.40 ($\underline{C}H_3CH_2$), 59.93 ($CH_3\underline{C}H_2$), 167.29 ($\underline{C}$=O), 100.62 ($\underline{C}$C), 145.20 ($\underline{C}$C), 19.62 ($\underline{C}H_3$C), 33.60 ($\underline{C}$H-furan part), 100.62 ($\underline{C}$H-furan), 145.20 ($\underline{C}$-furan), 106.84 ($\underline{C}$H-furan), 125.69, 127.04, 128.04, 131.76, 134.07, 145.20 (aromatic ring). Anal. calcd. (%): ($C_{23}H_{23}Cl_2NO_5$): C, 59.64; H, 4.96; N, 3.02; Found (%): C, 59.71; H, 4.88, N, 2.84 %

Diethyl-2,6-dimethyl-4-[5'-(2''-chloro-4''-nitrophenyl)-furan-2'-yl]1,4-dihydropyridine-3-carboxylate (12): Yield: 59 %, m.p.: 220 °C, IR (KBr, ν_{max}, cm^{-1}): 3311.9 (N-H stretching), 3087.5 (Ar-H), 2983.5 (C-H stretching of CH_3), 1652.7 (C=O ester), 1487.3, 1332.7 (NO_2).Mass: 476.0 (M+2)14.4 %, 473.9 (M) 49.6 %, 444.9 (M-$2CH_3$) 54.4 %, 401.0 (M-$COOC_2H_5$) 100 %, 371.0 (M-$COOC_2H_5$-$2CH_3$) 6.55 %, 328.0 (M-$2COOC_2H_5$) 6.9 %, 252.1 (M-$C_{10}H_5ClNO_3$) 14.4 %, 223.0 (M-$C_{13}H_{18}NO_4$) 5.3 %, 183.9 (M-$C_{10}H_5ClNO_3$-$COOC_2H_5$) 10.2 %, 150.0 (M-$C_{10}H_5ClNO_3$-$COOC_2H_5$-$2CH_3$) 7.3 %. ^{1}H NMR ($CDCl_3$), δ: 2.374 (s, 6H, $2CH_3$), 1.302 (t, 6H, $2\underline{CH_3}CH_2$, *J* = 10.62 Hz), 4.184 (q, 4H, $2CH_3\underline{CH_2}$, *J* = 10.41 Hz), 5.303 (s, 1H, CH), 7.28 (d, 4H, H-6", *J* = 6.00 Hz), 8.275 (s, 1H, H-3"); ^{13}C NMR ($CDCl_3$), δ: 14.40 ($\underline{C}H_3CH_2$), 60.02 ($CH_3\underline{C}H_2$), 167.13 ($\underline{C}$=O), 100.33 ($\underline{C}$C), 145.42 (C$\underline{C}$NH), 19.62 ($\underline{C}H_3$CNH), 33.81 ($\underline{C}$H-furan), 145.42, 100.33, 107.92, 146.61 (furan ring), 145.27, 129.19, 116.01, 135.42, 126.24, 134.90 (phenyl ring).

Diethyl 2,6-dimethyl-4-[5'-(2''-nitrophenyl)furan-2-yl]-1,4-dihydropyridine-3-carboxylate (13): Yield: 50 %; m.p.: 120-122 °C; IR (KBr, ν_{max}, cm^{-1}): 3732.1 (N-H stretching), 3347.7 (Ar-H), 2984.9 (C-H stretching of CH_3), 1648.2 (C=O ester), 1478.8, 1336.2 (NO_2). Mass: 440.2 (M) 27.4 %, 423.1 (M-CH_3) 22.3 %, 395.1 (M-NO_2) 15.8 %, 367.1 (M-$COOC_2H_5$) 100 %, 337.1 (M-$COOC_2H_5$-$2CH_3$) 5.3 %, 293.1 (M-$2COOC_2H_5$) 5.0 %, 252.1 (M-$C_{10}H_6No_3$)18.5 %, 224.1 (M-$C_{10}H_6No_3$-$2CH_3$) 6.3 %, 150.0 (M-$C_{10}H_6No_3$-$2CH_3$-$COOC_2H_5$) 7.8 %, 77.0 (M-$C_{17}H_{20}NO_5$-NO_2) 3.4 %.^{1}H NMR ($CDCl_3$), δ: 2.361 (s, 6H, $2CH_3$), 1.288 (t, 6H, $2\underline{CH_3}CH_2$, *J* = 10.62 Hz), 4.181 (q, 4H, $2CH_3\underline{CH_2}$, *J* = 10.04 Hz), 5.138 (s, 1H, CH), 6.120, 6.127 (2H of furan ring, H-3', H-4'), 6.593 (d, 1H, H-6", *J* = 3.57 Hz), 7.958 and 7.82 (H-2" and H-3" respectively). ^{13}C NMR ($CDCl_3$), δ: 14.36 ($\underline{C}H_3CH_2$), 59.82 ($CH_3\underline{C}H_2$), 167.21 ($\underline{C}$=O), 99.82 (2C), 146.129 (2C), 19.567 ($2CH_3$), 33.378 (CH), 99.699 (CH-furan), 146.494 (C-furan), 106.453 (CH-furan), 147.037 (C-furan), 127.561 (C-aromatic), 127.228 (CH-aromatic), 127.561 (C-NO_2-aromatic).

Diethyl-2,6-dimethyl 4-[5'-(2'',4''-dichlorophenyl)furan-2-yl]-1,4-dihydropyridine-3-carboxylate (14): Yield: 83 %; m.p.: 180 °C; IR (KBr, ν_{max}, cm^{-1}): 3941.6 (N-H stretching), 3319.5 (Ar-H), 2986.0 (C-H stretching of CH_3), 1652.7 (C=O ester); Mass: 465.0 (M+2) 43.0 %, 463.0 (M) 76.0 %, 434.1 (M-$2CH_3$) 70.3 %, 390.1 (M-$COOC_2H_5$) 100 %, 362.0 (M-$COOC_2H_5$-$2CH_3$) 15.9 %, 344.0 (M-$COOC_2H_5$-$2CH_3$–Cl) 11.4 %, 317.0 (M-$2COOC_2H_5$) 7.9 %, 252.1 (M-$C_{10}H_5Cl_2O$) 16.1 %, 212.0 (M-$C_{13}H_{18}NO_4$) 6.0 %, 196.1 (M-$C_{10}H_5Cl_2O$-$2CH_3$-C_2H_5) 14.9 %, 150.1 (M-$C_{10}H_5Cl_2O$-$COOC_2H_5$-$2CH_3$) 9.2 %. ^{1}H NMR ($CDCl_3$), δ: 2.283 (s, 6H, $2CH_3$), 1.207 (t, 6H, $2\underline{CH_3}CH_2$, *J* = 10.62 Hz), 4.122 (q, 4H, $2CH_3\underline{CH_2}$, *J* = 12.09 Hz), 5.112 (s, 1H, CH), 6.034 (d, 1H, H-3', *J* = 2.55 Hz), 7.622, 7.522, 7.412 (H-6", H-5", H-3" respectively), 9.052 (s, 1H, NH of dihydropyridine); ^{13}C NMR ($CDCl_3$), δ: 14.40 ($\underline{C}H_3CH_2$), 59.95 ($CH_3\underline{C}H_2$), 167.35 ($\underline{C}$=O), 106.89 ($\underline{C}$C), 147.43 ($\underline{C}$NH), 19.58 ($\underline{C}H_3$CNH), 33.53 ($\underline{C}$H-furan), 145.32, 100.51, 106.89, 112.19, 158.88 (furan ring), 132.06, 130.28, 129.91, 128.17, 127.97, 127.05 (phenyl ring).

Diethyl-2,6-dimethyl-4-[5'-(5''-chloro-2''-nitrophenyl)-furan-2-yl]-1,4-dihydropyridine-3-carboxylate (15): Yield: 59 % m.p.: 135 °C; IR (KBr, ν_{max}, cm^{-1}): 3745.5 (N-H stretching), 3353.1 (Ar-H), 2985.4 (C-H stretching of CH_3), 1651.4 (C=O ester), 1476.3, 1363.8 (NO_2). Mass: 476.1 (M+2) 16.9 %, 474.1 (M) 57.5 %, 457.1 (M-CH_3) 48.0 %, 444.1 (M-$2CH_3$) 8.2 %, 429.1 (M-NO_2) 26.6 %, 401.1 (M-$COOC_2H_5$) 100 %, 373.1 (M-$COOC_2H_5$-$2CH_3$) 11.2 %, 355.1 (M-$COOC_2H5$-NO_2) 26.1 %, 327.1 (M-$2COOC_2H_5$) 9.7 %, 283.1 (M-$2COOC_2H_5$-NO_2)

16.2 %, 252.1 (M-$C_{10}H_5ClNO_3$) 48.9 %, 224.1 (M-$C_{13}H_{18}NO_4$) 12.0 %, 150.1 (M-$C_{10}H_5ClNO_3$-$COOC_2H_5$-$2CH_3$) 19.0 %. ^{1}H NMR ($CDCl_3$), δ: 2.355 (s, 6H, $2CH_3$), 1.267 (t, 6H, $2\underline{CH_3}CH_2$, *J* = 10.68 Hz), 4.179 (q, 4H, $2CH_3\underline{CH_2}$, *J* = 9.66 Hz), 5.140 (s,1H,CH), 6.127 (d, 1H, H-3', *J* = 2.45 Hz), 6.576 (s, 1H, H-4'), 7.502 (s, 1H, H-6"); ^{13}C NMR ($CDCl_3$), δ: 14.34 ($\underline{C}H_3CH_2$), 59.83 ($CH_3\underline{C}H_2$), 167.216 (2C=O), 99.672 (2C), 146.958 (2C), 19.611 ($2CH_3$), 33.499 (2CH), 99.672 (CH-furan), 145.481 (C-furan), 106.675 (CH-furan), 132.567 (C-aromatic), 131.537 (CH-aromatic), 128.529 (CH-aromatic), 123.779 (CH-aromatic), 146.107 (C-NO_2-aromatic).

Diethyl 2,6-dimethyl-4-[5'-(2''-chloro-5''-nitro phenyl)-furan-2'-yl]-1,4-dihydropyridine-3,5-dicarboxylate (16): Yield: 25 %; m.p.: 160 °C; IR (KBr, ν_{max}, cm^{-1}): 3730.0 (N-H stretching), 3104.6 (Ar-H), 2985.3 (C-H stretching of CH_3), 1656.3 (C=O ester), 1520.5, 1383.4 (NO_2).Mass: 476.1 (M+2) 18.2 %, 474.1 (M) 58.5 %, 457.1 (M-CH_3) 64.5 %, 445 (M-$2CH_3$) 85.9 %, 401.1 (M-$COOC_2H_5$) 100 %, 373 (M-$2CH_3$-$COOC_2H_5$) 27.2 %, 328 (M-$2COOC_2H_5$)13.3 %, 252.1 (M-$C_{10}H_5ClNO_3$) 24.6 %, 224.1 (M-$C_{10}H_5ClNO_3$-$2CH_3$)8.9 %, 150.1 (M-$C_{10}H_5ClNO_3$-$2CH_3$-$COOC_2H_5$) 14.4 %, (M-$C_{10}H_5ClNO_3$-$2CH_3$-$COOC_2H_5$-NH) 6.3 %. ^{1}H NMR ($CDCl_3$) δ: 2.178 (s, 6H, $2CH_3$), 1.323 (t, 6H, $2\underline{CH_3}CH_2$, *J* = 10.65 Hz), 4.241 (q, 4H, $2CH_3\underline{CH_2}$, *J* = 8.31 Hz), 5.290 (s, 1H, CH), 7.270 (1H, H-3"), 7.542 (1H, H-4"), 8.613 (1H, H-6"); ^{13}C NMR ($CDCl_3$), δ: 14.111 ($2CH_3$), 60.026 ($2CH_2$), 167.267 (2C=O), 100.205 (2C), 151.318 (2C-N), 14.379 ($2CH_3$), 30.902 (CH), 149.232 (C), (furan), 100.205 (CH), 107.172 (CH), 160.092 (C), 136.787 (C-aromatic), 123.231 (CH), 146.106 (C-N), 122.920 (CH), 130.642 (CH), 135.168 (C-Cl); Anal. calcd. (%): $C_{23}H_{23}N_2O_7Cl$: C, 58.26; H, 4.85: N, 5.90; Found (%): C, 58.04; H, 4.70; N, 5.46.

Diethyl 2,6-dimethyl-4-[5'-(2'',5''-dichlorophenyl furan-2'-yl]-1,4-dihydropyridine-3,5-dicarboxylate (17) : Yield, 90 %; m.p.: 150 °C; IR (KBr, ν_{max}, cm^{-1}): 3334.5 (Ar-H), 2982.1 (C-H stretching of CH_3), 1648.3 (C=O ester); Mass: 467.0 (M+4) 7.6 %, 465.0 (M+2) 9.4 %, 463.0 (M) 64.6 %, 434.0 (M-$2CH_3$) 65.6 %, 390.0 (M-$COOC_2H_5$) 100 %, 362.0 (M-$COOC_2H_5$-$2CH_3$)16.9 %, 317.0 (M-$2COOC_2H_5$) 7.6 %, 252.1 (M-$C_{10}H_5Cl_2O$) 17.0 %, 224.1 (M-$C_{10}H_5Cl_2O$-$2CH_3$) 5.3 %. ^{1}H NMR ($CDCl_3$), δ: 2.368 (s, 6H, $2CH_3$), 1.305 (t, 6H, $2\underline{CH_3}CH_2$, *J* = 10.65 Hz), 4.231 (q, 4H, $2CH_3\underline{CH_2}$, *J* = 10.37 Hz), 5.273 (s, 1H, CH), 7.284 (d, 1H, H-3", *J* = 6.60 Hz), 7.047 (d, 1H, H-4", *J* = 2.52 Hz), 7.711 (1H, H-6"); ^{13}C NMR ($CDCl_3$), δ: 14.442 ($2CH_3$), 19.572 ($2CH_3$), 60.044 ($2CH_2$), 167.381 (2C=O), 100.400 (2C), 147.048 (2C), 33.495 (CH), 159.144 (C), 100.400 (CH-furan), 106.942 (CH), 159.144 (C), 126.878 (CH), 132.643 (C-Cl), 130.720 (CH) and 131.720 (C-Cl).

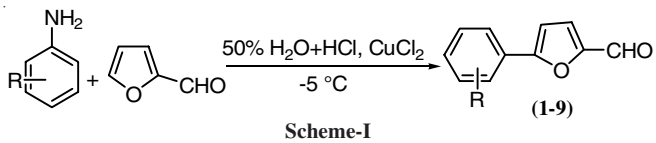
Diethyl 2,6-dimethyl-4-[5'-(3'',4''-dichlorophenyl)-furan-2'-yl]-1,4-dihydropyridine-3,5-dicarboxylate (18): Yield: 83 %; m.p.: 145 °C; IR (KBr, ν_{max}, cm^{-1}): 3654.0 (N-H stretching), 3330.0 (Ar-H), 2981.2 (C-H stretching of CH_3), 1650.9 (C=O ester); ^{1}H NMR ($CDCl_3$), δ: 2.368 (s, 6H, $2CH_3$), 1.305 (t, 6H, $2\underline{CH_3}CH_2$, *J* = 10.65 Hz), 4.231 (q, 4H, $2CH_3\underline{CH_2}$, *J* = 10.37 Hz), 7.43, 7.27, 7.30 (H-2", 5", 6"); ^{13}C NMR ($CDCl_3$), δ: 19.58 ($2CH_3$), 14.39 ($2CH_3CH_2$), 59.92 ($2CH_3CH_2$), 167.29 (2C=O), 100.64 (2C), 149.69 (2C, C-2), 33.66 (CH), 106.96, 107.30, 159.60 (4C of furan ring), 122.41, 124.94, 130.07, 130.48, 131.28, 132.69 (6C of 3, 4-dichloro phenyl ring); Mass: 467.0 (M+4) 7.4 %, 465.0 (M+2) 35.5 %, 463.0 (M) 53.2 %, 434.0 (M-$2CH_3$) 65.7 %, 390.0 (M-$COOC_2H_5$) 100 %, 357.9 (M-$COOC_2H_5$-Cl) 27.0 %, 344.0 (M-$COOC_2H_5$-Cl-CH_3) 14.1 %, 317.0 (M-$COOC_2H_5$-$COOC_2H_5$) 8.7 %, 290.0 (M-$COOC_2H_5$-$COOC_2H_5$-$2CH_3$) 5.5 %, 252.1 (M-$C_{10}H_5Cl_2O$) 25.8 %, 223.0 (M-$C_{10}H_5Cl_2O$-$2CH_3$) 9.6 %, 179.1 (M-$C_{10}H_5Cl_2O$-$COOC_2H_5$) 20.8 %. Anal. calcd. (%):$C_{23}H_{23}Cl_2NO_5$ C, 59.64; H, 4.96; N, 3.02; Found (%): C, 60.45; H, 5.21; N, 3.03 %.

Diethyl 2,6-dimethyl-4-[5'-(3''-nitrophenyl)furan-2'-yl]-1,4-dihydropyridine-3,5-dicarboxylate (19): Yield: 61 %; m.p.: 178 °C; IR (KBr, ν_{max}, cm^{-1}): 3334.70 (Ar-H), 1684.46 (C=O ester), 1345.92, 1537.60 (NO_2). Mass: 440.0 (M) 49.5 %, 411.0 (M-$2CH_3$) 71.1 %, 367.0 (M-$COOC_2H_5$) 100 %, 339.0 (M-$COOC_2H_5$-CH_3) 13.2 %, 321.0 (M-$COOC_2H_5$-NO_2) 13.5 %, 294.0 (M-$COOC_2H_5$-NO_2-$2CH_3$) 10.1 %, 252.1 (M-$C_{13}H_{18}NO_4$) 15.3 %, 196.0 (M-$C_{13}H_{18}NO_4$-$2C_2H_5$) 13.2 %, 179.0 (M-$C_{13}H_{18}NO_4$-$COOC_2H_5$)9.1 %, 150.0 (M-$C_{13}H_{18}NO_4$-$2CH_3$) 17.3 %; ^{1}H NMR, ($CDCl_3$) δ: 2.379 (s, 6H, $2CH_3$), 1.319 (t, 6H, $2\underline{CH_3}CH_2$, *J* = 10.68 Hz), 4.234 (q, 4H, $2CH_3\underline{CH_2}$, *J* = 12.63 Hz), 5.273 (s, 1H, CH), 7.266 (1H, H-5"), 8.41 (1H, H-2"), 8.15 (1H, H-4"), 7.87 (1H, H-6"); ^{13}C NMR ($CDCl_3$), δ: 14.36 ($\underline{C}H_3CH_2$), 59.82 ($CH_3\underline{C}H_2$), 167.21 ($\underline{C}$=O), 99.82 (2C), 146.129 (2C), 19.567 ($2CH_3$), 33.378 (CH), 99.699 (CH-furan), 146.494 (C-furan), 106.453 (CH-furan), 147.037 (C-furan), 129.571 (C-aromatic), 135.82 (CH-aromatic), 146.961 (C-NO_2-aromatic); Anal. calcd. (%): $C_{23}H_{24}N_2O_7$: C, 62.57; H, 5.45; N, 6.36; Found (%): C, 63.49; H, 5.68; N, 6.48 %.

Diethyl 2,5-dimethyl-4-[5'-(4''-chlorophenyl)furan-2'-yl]-1,4-dihydropyridine-3,5-dicarboxylate (20): Yield: 24 %; m.p.: 150-152 °C; Mass: 431 (M+2)15.8 %, 429.1 (M) 48.9 %, 400.0 (M-$2CH_3$) 55.4 %, 356.0 (M-$COOC_2H_5$) 100 %, 328.0 (M-$COOC_2H_5$-$2CH_3$) 10.7 %, 283.0 (M-$COOC_2H_5$) 7.4 %, 252.1 (M-$C_{13}H_{18}NO_4$) 9.9 %, 178.0 (M-$C_{13}H_{18}NO_4$-$COOC_2H_5$) 13.9 %. ^{1}H NMR ($CDCl_3$), δ: 2.355 (s, 6H, $2CH_3$), 1.295 (t, 6H, $2\underline{CH_3}CH_2$, *J* = 10.62 Hz), 4.207 (q, 4H, $2CH_3\underline{CH_2}$, *J* = 12.21 Hz), 5.232 (s, 1H, CH), 6.484 (d, 1H, H-4', *J* = 2.49 Hz), 7.288 (d, 2H, H-3", H-5", *J* = 6.54 Hz), 7.469 (d, 2H, H-2", H-6", *J* = 6.48 Hz); ^{13}C NMR ($CDCl_3$), δ: 14.40 ($2CH_3$), 59.92 ($2CH_2$), 167.43 (2C=O), 100.595 (2C), 30.985 (CH), 145.305 (2C), 19.581 ($2CH_3$), 158.98 (C), 106.260 (CH), 106.763 (CH), 150.946 (C), 128.680 (2CH), 129.837 (2CH), 132.120 (C) and 124.466 (CH).

RESULTS AND DISCUSSION

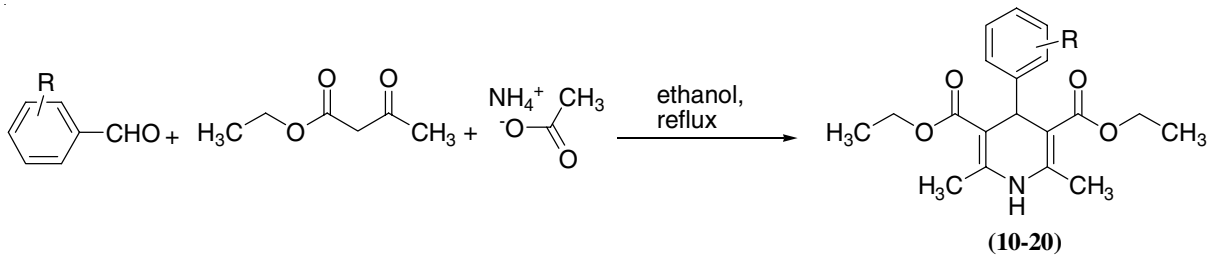
Although furyl containing 1,4-dihydropyridines have been reported but there does not seem to be mention of 4-aryl-furfuryl-1,4-dihydropyridines which are reported in this communication. 5-Arylfuran-2-carbaldehydes (**1-9**) used for this synthesis were obtained from Meerwein arylation of furan-2-carbaldehyde [3] (**Scheme-I**).



Scheme-I

When 5-arylfuran-2-carbaldehydes (**1-9**) were reacted with ethyl acetoacetate and ammonium acetate in refluxing ethanol, the desired arylated products (**10-20**) were obtained in good yields (**Scheme-II**). The structure of different aldehydes and final products along with reaction time are given in Table-1.

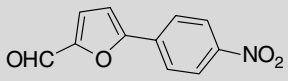
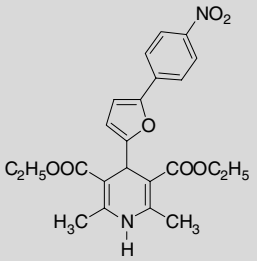
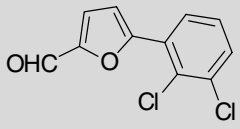
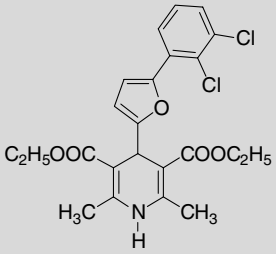
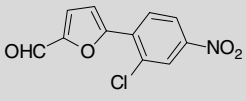
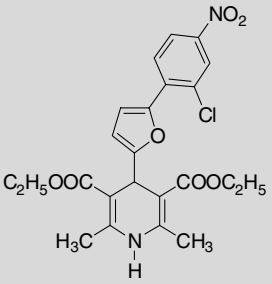
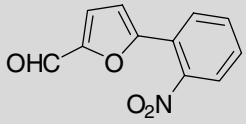
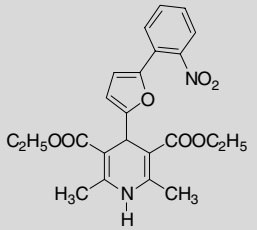
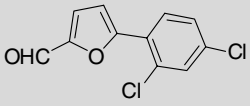
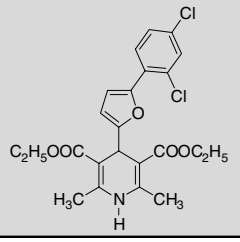
All 5-arylfuran-2-carbaldehydes smoothly underwent this multicomponent Hanztsch condensation with ethyl acetoacetate

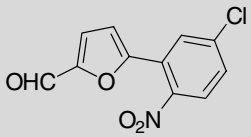
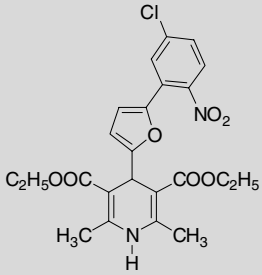
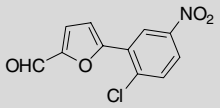
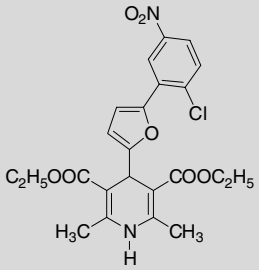
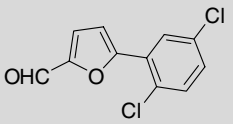
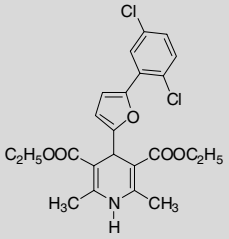
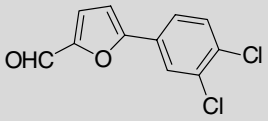
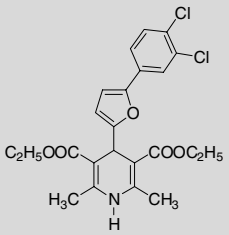
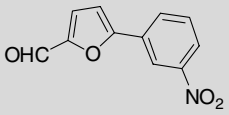
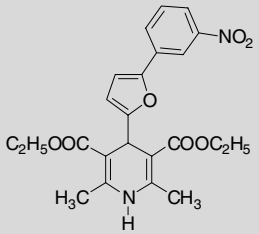
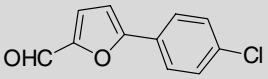
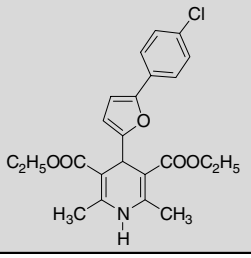


(10-20)

Scheme-II

TABLE-1
DIETHYL 4-(5'-ARYLFURAN-2'-YL)-2,6-DIMETHYL-1,4-DIHYDROPYRIDINES

Compound No.	Aldehyde	Time (h)	Final product	TLC
10		6.0		EtOAc:*n*-Hexane 1:4
11		6.0		EtOAc:*n*-Hexane 1:4
12		6.0		EtOAc:*n*-Hexane 1:4
13		6.0		EtOAc:*n*-Hexane 1:4
14		6.5		EtOAc:*n*-Hexane 1:4

Compound No.	Aldehyde	Time (h)	Final product	TLC
15		6.0		EtOAc:*n*-Hexane 1:4
16		6.0		EtOAc:*n*-Hexane 1:4
17		6.0		EtOAc:*n*-Hexane 1:4
18		6.0		EtOAc:*n*-Hexane 1:4
19		6.0		EtOAc:*n*-Hexane 1:4
20		6.0		EtOAc:*n*-Hexane 1:4

and relatively less toxic ammonium acetate. The analytical data of the compounds i**s** given in experimental part. The brief discussion however follows:

The IR spectra of compounds **10-20** show the absorbtion peaks due to C=O of ester group at 1648-1714 cm^{-1}; the aromatic ring at 3080-3350 cm^{-1} and the N-H stretching at 3310-3945 cm^{-1}. The ^1H NMR spectra of these dihydropyridines show the signals of six protons of two methyl groups at C-2 and C-6 in the range of δ 2.17 to 2.37, six protons of the ester at C-3, C-5 in the range of δ 1.203-1.323 and the *J* values show a narrow range of 10.62-10.70 Hz**.** The methylene signal of the ester is shown in the range of δ 4.075-4.241 and the *J*-values are in a wide range of 8.31-12.63 Hz, the protons of aromatic rings are in the expected positions.

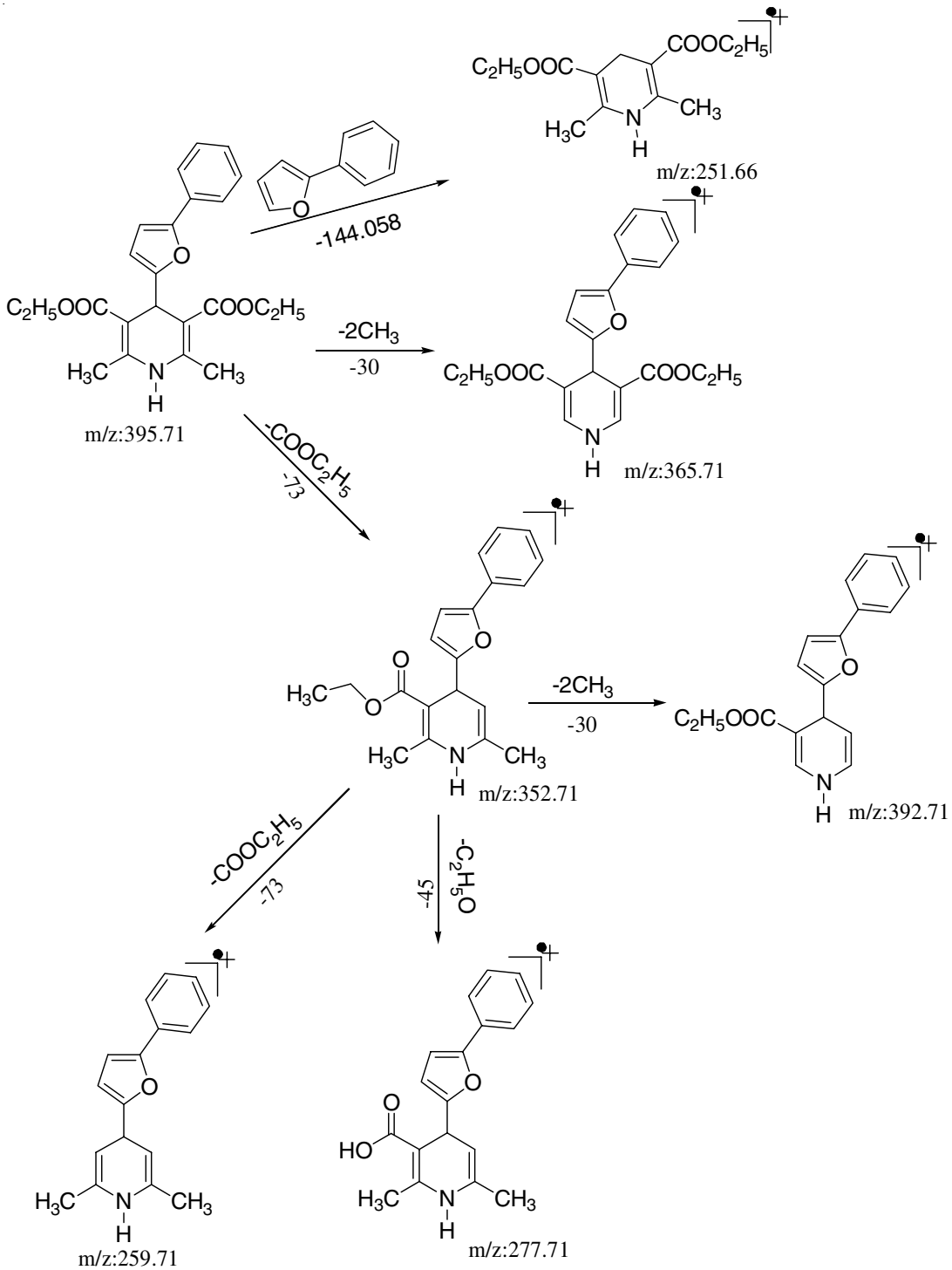
The ^{13}C NMR spectra displayed the signals for the carbons of esters in the range of δ 14.08-14.44, 59.82-60.70 and

167.07-167.43 (CH_3, CH_2 and C=O respectively), the signals for the carbons of the furan ring are in the range of δ 145.26-146.49, 99.69-101.89, 106.84-112-19 and 147.03-149.23 (C-2', C-3', C-4' and C-5' respectively) and the carbons of the phenyl group are found in the corresponding ranges with some variations due to their different substituents.

As far as the mass spectra are concerned, there are M^+ peaks corresponding to the expected masses as well as M^++2 and M^++4 peaks for the expected halogen compounds. As in compound **1** (*m/z* 301.2) and as well as in others, a peak is observed at M^+-73 (100 %) which denotes a M^+ minus an ester group. The general pattern observed for the mass fragmentation is observed as follows **(Scheme-III**).

ACKNOWLEDGEMENTS

A.M. Zafar and S. Aslam like to thank Higher Education Commission, Government of Pakistan for Indigenous scholarships. M.A. Khan is grateful to HEC for their analytical support program.



Expected mass fragmentation pattern

Scheme-III

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