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# CATALYST-FREE ONE-POT FOUR-COMPONENT SYNTHESIS OF SOME NEW 2,4,6-TRIARYL PYRIDINE DERIVATIVES

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**Abstract**
In the present work, a new series of 2,4,6-triaryl pyridines derivatives *via* one-pot four-component condensation reaction of dibenzobarallene, 4-amino acetophenone, various aromatic aldehydes and ammonium acetate in acetic acid as solvent were synthesized. The structures of synthesized products were confirmed by FT-IR, $^{1}$H-NMR, $^{13}$C-NMR spectra and analytical data.

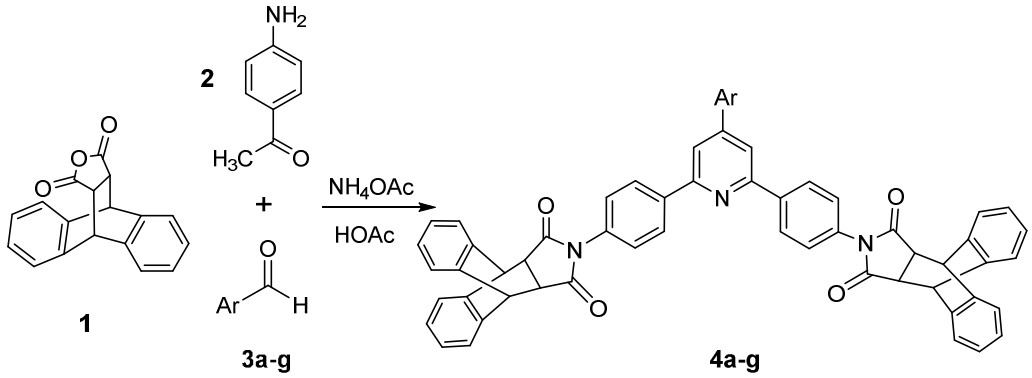
**Keywords:** Dibenzobarallen; Catalyst-free; 2,4,6-Triaryl pyridines derivatives; multi-component reaction.

## Introduction

The obtained products, in this synthesis, are important in two respects, one based on creating a new molecular tweezer[i], and the other due to forming three functional pyridine derivatives, that each one these cases can be used in the chemistry related sciences[ii].
Molecular tweezers bearing dibenzobarallene pincers can interact with, guest molecules via, hydrogen bonding, π-π interactions, vander waals forces, metal coordination, and electrostatic effects[iii],and can be utilized in, characterization and material measure, to avoid aggregate, and the formation of amyloid proteins, that they cause to create the diseases, such as Alzheimer, Parkinson, Diabetes type 2, and etc.[iv].
Pyridine ring system, particularly 2,4,6-triarylpyridine is of immense interest because of its unique position in medicinal chemistry[v,vi]. Moreover, they are prominent synthons in supramolecular chemistry, with their π-stacking ability along with directional H-bonding capacity[vii-ix]. In addition, the excellent thermal stabilities of these pyridines have instigated a growing interest for their use as monomeric building blocks in thin films and organometallic polymers[x-xii]. Recent studies have highlighted the biological activity of triarylpyridines, providing impetus for further studies in utilizing this scaffold in new therapeutic drug classes[xiii]. These molecules have been found to be useful for the synthesis of DNA binding ligands, in particular targeting G-quadruplex DNA which has recently received much attention as a possible target in cancer therapy[xiv-xvii].

Consequently, the synthesis of these materials remains interesting topic in modern synthetic chemistry[xviii]. In recent years, various methods have been developed for their synthesis, including classical heating condition, microwave irradiation, and sonication in the presence of bismuth triflate, copper triflate, and mesoporous nanocrystalline $MgAl_2O_4$ catalysts[xix-xxii]. Nevertheless, the development of new methods for the synthesis of new 2,4,6-trisubstituted pyridines is in high demand.

Thus in this study, a new series of 2,4,6-triaryl pyridines derivatives *via* one-pot four-component condensation reaction of dibenzobarallene, 4-amino acetophenone, various aromatic aldehydes and ammonium acetate in acetic acid as solvent were synthesized (Scheme1).



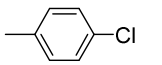
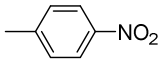
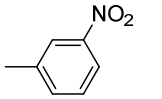
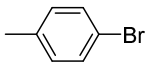

**Scheme1.**One-pot four components synthesis of 2,4,6-triaryl pyridines derivatives (**4a-g**)

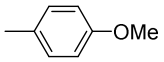
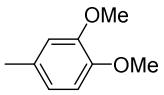
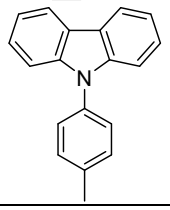
**Results and Discussion**

At first to find the optimum reaction conditions, the reaction of reaction dibenzobarallene (**1**), 4-amino acetophenone (**2**), 4-chlorobenzaldehyde (**3a**) and ammonium acetate in acetic acid was selected as a model reaction and this reaction was performed in different temperatures.The best result was the reflux conditions.

In order to evaluate the generality of above optimized reaction conditions, a range of 2,4,6-triaryl pyridines derivatives has been synthesized (Table 1). In all cases, aromatic aldehydes with substituents carrying either electron donating or electron-withdrawing groups reacted successfully and gave the expected products in good to excellent yields in relatively short reaction times. The kind of aldehyde has no significant effect on the reaction.

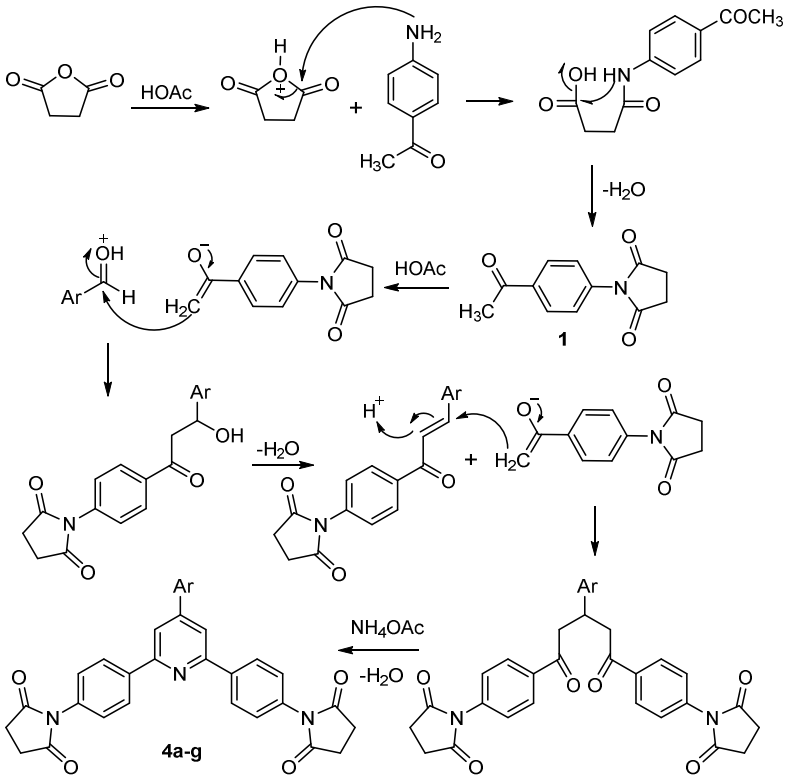
**Table 1.** Synthesis of 2,4,6-triaryl pyridines derivatives (**4a-g**) in acetic acid as a solvent

| Entry | Ar | Product | Yield (%)[a] | Time (h) | m.p ($^oC$) |
|---|---|---|---|---|---|
| 1 |  | **4a** | 65 | 6 | 256-258 |
| 2 |  | **4b** | 74 | 6 | 266-268 |
| 3 |  | **4c** | 70 | 6 | 231-234 |
| 4 |  | **4d** | 75 | 6 | 246-248 |

| | | | | | |
|---|---|---|---|---|---|
| 5 |  | **4e** | 64 | 6 | 266-268 |
| 6 |  | **4f** | 65 | 6 | 251-253 |
| 7 |  | **4g** | 75 | 6 | 275-277 |

[a]Dibenzobarallene**1**(2.5 mmol), 4-amino acetophenone**2**(2.5 mmol), aromatic aldehydes **3a-g** (1.0 mmol) and ammonium acetate (1.5 mmol) in acetic acid (15 ml) at 120 $^{o}$C.

Based on the proposed mechanism in the literature[xxiii,xxiv], it is reasonable to assume that, in the first stage, the nitrogen of 4-amino acetophenone could attack to activated carbonyl group of dibenzobarallene, and after remove water, intermediate of **1** was formed. In the second stage, acetophenone group of compound **1** in the presence of acetic acid is converted into its enol form, which gives nucleophilic additionon the aldehyde to afford aldol condensation. Then second molecule of acetophenone undergoes Michael addition reaction with previous intermediate to form the 1,5-diketone intermediate. This1,5-diketone on reaction with ammonium acetate followed by cyclization and dehydration gives compounds **4a-g** (Scheme 2).




**Scheme 2.** Plausible mechanism of synthesis of 2,4,6-triaryl pyridines derivatives (**4a-g**)

## Experimental

### Synthesis of 2,4,6-triaryl pyridines derivatives (4a-g)

In a round bottomed flask (50ml), dibenzobarallene**1** (25 mmol),4-amino acetophenone**2** (25 mmol), aromatic aldehydes **3a-g** (10 mmol), ammonium acetate **3** (15 mmol) and acetic acid (15ml) was refluxed at 120℃ for 6h. Progress of the reaction was monitored by TLC. After completion the reaction, the reaction was allowed to cool to room temperature and filtered. The precipitate was completely washed with hot ethanol and dried at oven at 80 ℃ for 1h to give the products **4a-g**.

### Spectral data

*(3as, 3a′s, 4R, 4′R, 9R,9aR, 9′R, 9a′R)-2,2′-((4-(4-chlorophenyl)-pyridine-2,6-diyl)-bis-(3,1-phenylene)) bis (4-methyl-9-phenyl-3a,4,9,9a-tetrahydro-1H-benzo[f]isoindole-1,3(2H)-dione)*(**4a**)

FT-IR; $v$($cm^{-1}$): 3042 (=CH), 2962 (-CH), 1775 (C=O), 1709 (C=O), 1681(C=O), 1590 (C=C), 1487 (C=C), 1386, 1265, 1187 (C-N), 766 (OOP-HAr); $^1$HNMR; (300MHz, DMSO-$d_6$) $\delta$(ppm): 3.49 (4H, s), 4.92 (4H, s), 6.67 (1H, d, *J*= 8.7 Hz), 6.72 (3H, d, *J*= 8.4 Hz), 7.21-7.26 (8H, m), 7.32-7.37 (4H, m), 7.53(4H, t, *J*= 2.4 Hz), 7.56 (2H, d, *J* = 2.4 Hz), 7.78 (1H, s), 7.93 (3H, d, *J*= 3.9 Hz),7.96 (2H, t, *J* = 3 Hz), 8.15 (3H, d, *J* = 8.4 Hz).$^{13}$CNMR; (75MHz, DMSO-$d_6$) $\delta$(ppm): 45.4, 47.2, 123.1, 124.8, 125.3, 126.9,127.0, 127.1, 129.2, 129.4, 129.7, 131.1, 134.1, 135.7, 136.2, 137.6, 139.8,142.0, 143.4, 176.1.

*(3as, 3a′s, 4R, 4′R, 9R, 9aR, 9′R, 9a′R)-2,2′-((4-(4-nithrophenyl)-pyridine-2,6-diyl)-bis-(3,1-phenylene))-bis-(4-methyl-9-phenyl-3a,4,9,9a-tetrahydro-1H-benzo[f]isoindole-1,3(2H)-dione)* (**4b**)

FT-IR; $v$($cm^{-1}$): 3070 (=CH), 2963 (-CH), 1777 (C=O), 1711 (C=O), 1605(C=C), 1517, 1343 ($NO_2$), 1191, 1112 (C-N), 832, 761 (OOP-HAr); $^1$HNMR; (300 MHz, DMSO-$d_6$) $\delta$(ppm): 3.50 (4H, s), 4.94 (4H, s), 6.68 (2H, d, *J*= 8.4 Hz), 6.76 (2H, d, *J*= 8.4 Hz), 7.20-7.27 (8H, m), 7.34-7.39 (4H, m), 7.53-7.55 (4H, m), 7.87 (1H, s), 7.94 (2H, d, *J*= 8.4 Hz), 8.14-8.20 (5H, m), 8.30 (2H, d, *J* = 8.4 Hz).

*(3as, 3a′s, 4R, 4′R, 9R,9aR, 9′R, 9a′R)-2,2′-((4-(3-nithrophenyl)-pyridine-2,6-diyl)-bis-(3,1-phenylene))-bis-(4-methyl-9-phenyl-3a,4,9,9a-tetrahydro-1H-benzo[f]isoindole-1,3(2H)-dione)* (**4c**).

FT-IR;$v$($cm^{-1}$): 3033(=CH),2956(CH),1770(C=O),1706(C=O),1593(C=C),1487(C=C),1548, 1343($NO_2$)761(OOP-HAr); $^1$HNMR; (300MHz, DMSO-$d_6$) $\delta$(ppm): 3.49 (4H, s), 4.93 (4H, s), 6.69 (2H, d, *J*= 6.6 Hz), 6.76 (2H, d, *J*= 6.6 Hz), 7.19-7.27 (8H, m), 7.34-7.39 (4H, m), 7.52-7.56 (4H, m), 7.74 (1H, t, *J*= 7.8 Hz), 7.86-7.96 (3H, m), 8.12-8.33 (5H, m), 8.85 (1H, s); $^{13}$CNMR; (75MHz, DMSO-$d_6$) $\delta$(ppm): 45.4, 47.3, 123.5, 124.9, 125.0, 125.2, 125.3, 126.9, 127.0, 129.3, 129.9, 130.8, 135.7, 136.9, 137.4, 139.7, 139.8, 142.0, 142.3, 176.1.

*(3as, 3a′s, 4R, 4′R, 9R,9aR, 9′R, 9a′R)-2,2′-((4-(4-bromophenyl)-pyridine-2,6-diyl)-bis-(3,1-phenylene))-bis-(4-methyl-9-phenyl-3a,4,9,9a-tetrahydro-1H-benzo[f]isoindole-1,3(2H)-dione)* (**4d**)

FT-IR; $v$($cm^{-1}$): 3071 (=CH), 2964 (-CH), 1776 (C=O), 1707 (C=O), 1605(C=C), 1486 (C=C), 809, 770 (OOP-HAr); $^1$HNMR; (300MHz, DMSO-$d_6$) $\delta$(ppm): 3.48 (4H, s), 4.92 (4H, s), 6.66 (1H, d, *J*= 8.4 Hz), 6.71 (3H, d, *J* = 8.4 Hz), 7.21-7.29 (8H, m), 7.32-7.37 (4H, dt, *J* = 5.4, 3.3 Hz), 7.52-7.56 (4H, dt, *J* = 5.4, 3.3 Hz), 7.69 (1H, d, *J* = 8.4 Hz), 7.70 (2H,s), 7.76 (1H, s), 7.88 (2H, d, *J* = 8.4 Hz), 7.92 (1H, d, *J* = 2.7 Hz), 7.96 (1H, d, *J*= 10.2 Hz), 8.14 (2H, d, *J* = 8.4 Hz); $^{13}$CNMR; (75MHz, DMSO-$d_6$) $\delta$(ppm): 45.4, 47.3, 123.2, 124.6, 124.9,

125.3,126.9, 126.9, 127.0, 129.2, 129.3, 131.3, 132.4, 134.4, 136.2, 137.6, 139.7,139.8, 142.0, 143.5, 176.1.

*(3as, 3a′s, 4R, 4′R, 9R,9aR, 9′R, 9a′R)-2,2′-((4-(4-methophenyl)-pyridine-2,6-diyl)-bis-(3,1-phenylene))-bis-(4-methyl-9-phenyl-3a,4,9,9a-tetrahydro-1H-benzo[f]isoindole-1,3(2H)-dione)* (**4e**)

FT-IR; $\upsilon$($cm^{-1}$): 3021 (=CH), 2959 (-CH), 1776 (C=O), 1710 (C=O), 1605(C=C), 1464 (C=C), 827, 762 (OOP-HAr); $^{1}$HNMR; (300MHz, DMSO-$d_6$) $\delta$(ppm): 3.49 (4H, s), 3.84 (3H, s, O-CH3), 4.93 (4H, s), 6.68 (1H, d, *J* = 8.7 Hz), 6.72 (3H, d, *J* = 8.7 Hz), 7.06 (2H, d, *J* = 9 Hz), 7.20-7.26 (8H, m), 7.33-7.38 (4H, m), 7.52 (4H, dt, *J* = 5.4, 3.3 Hz), 7.75 (2H, s), 7.88 (3H, d, *J* = 8.7 Hz), 7.94 (1H, d, *J* = 8.7 Hz), 8.13 (2H, d, *J* = 8.4Hz); $^{13}$CNMR; (75MHz, DMSO-$d_6$) $\delta$(ppm): 45.4, 47.3, 55.9, 114.9, 119.9, 124.9, 125.2, 125.3, 126.9, 126.9, 127.0, 127.1, 127.2, 127.7, 129.3, 129.5, 131.4, 138.1, 139.7, 139.8, 142.0, 145.0, 176.1.

*(3as, 3a′s, 4R, 4′R, 9R,9aR, 9′R, 9a′R)-2,2′-((4-(3.4-methophenyl)-pyridine-2,6-diyl)-bis-(3,1-phenylene))-bis-(4-methyl-9-phenyl-3a,4,9,9a-tetrahydro-1H-benzo[f]isoindole-1,3(2H)-dione)* (**4f**)

FT−IR:$\upsilon$($cm^{1}$):3021(=CH),2959(−CH),1776(C=O),1710(C=O),1605 (C=C),1464(C=C),827,762(OOP-HAr); $^{1}$HNMR; (300MHz, DMSO-$d_6$) $\delta$(ppm):3.49(4H,s),3.84(3H,s,O-c$H_3$),4.93(4H,s),6.68(1H,d,*J*=8.7Hz), 6.72(3H,d,*J*=8.7 Hz),7.06(2H,d,*J*=9Hz), 7.20-7.26(8H,m),7.33-7.38(4H,m),7.52(4H,dt,*J*=5.4,3.3Hz)7.75(2H,s),7.88(3H,d,*J*=8.7 Hz),7.94(1H,d,J=8.7 Hz), 8.13(2H,d,J=8.4 Hz);$^{13}$CNMR; (75MHz, DMSO-$d_6$) $\delta$(ppm): 45.4, 47.3, 56.1, 56.2, 111.2, 112.0, 119.9, 124.7, 124.9, 125.3, 126.9, 127.0, 127.1, 127.2, 129.3, 129.5, 136.2, 139.9, 142.1, 145.5, 149.5, 151.9, 176.1.

*(3as, 3a′s, 4R, 4′R, 9R,9aR, 9′R, 9a′R)-2,2′-((4-(4-carbazolphenyl)-pyridine-2,6-diyl)-bis-(3,1-phenylene))-bis-(4-methyl-9-phenyl-3a,4,9,9a-tetrahydro-1H-benzo[f]isoindole-1,3(2H)-dione)*(**4g**)

FT-IR;$\nu$($cm^{-1}$):3066(=CH),2960(-CH),1776(C=O),1711(C=O),1607(C=C),1544(C=C),1260,1193(C-O),762(OOP-HAr); $^{1}$HNMR; (300MHz, DMSO-$d_6$) $\delta$(ppm): 3.47 (4H, s), 4.92 (4H, s), 6.59 (2H, d, *J*= 8.1 Hz), 7.20-7.38 (18H, m), 7.47 (8H, d, *J* = 4.2 Hz), 7.53 (2H, d, *J* = 5.4 Hz), 7.55 (2H, d, *J* = 5.4 Hz), 8.28 (4H, d, *J* = 7.8 Hz); $^{13}$CNMR; (75MHz, DMSO-$d_6$) $\delta$(ppm): 45.4, 47.2, 110.2, 120.6, 121.0, 123.3, 124.8, 125.3, 126.8, 126.9, 127.1, 127.3, 127.5, 139.8, 140.5, 142.1, 176.4.

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