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Novel solid-supported dimerization–heteroannulation of chalcones: simple and efficient synthesis of 2,4,6-triaryl-3-methylarylpyridines

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Abstract—2,4,6-Triaryl-3-methylarylpyridines were obtained, in 60–70% yield, by a novel one-pot solventless solid-supported dimerization–heteroannulation reaction of chalcones and compounds possessing terminal $-CONH_2$ functionality, at 125–135 °C, using immobilized Bi(III) nitrate and Zn(II) chloride as co-catalyst. Initially, chalcones were prepared, in nearly quantitative yield, by a modified aldol condensation, in neutral aqueous medium, in the presence of *p*-toluenesodium sulfonate.

1. Introduction

The preparation of polyarylpyridines constitutes an important and attractive subject in organic synthesis. Indeed, these products find wide application in the preparative organic chemistry,[1] as therapeutic agents[2] and as substrates for the preparation of supramolecules.[3] The synthesis[4] of the compounds possessing the 2,4,6-triarylpyridine nucleus is of special interest because of their close structural resemblance with the recommended photodynamic cell-specific symmetrical triaryl-telluropyrylium, -selenopyrylium and thiopyrylium cancer therapeutic agents.[5] In our earlier communication,[6] we reported the synthesis of 2,4,6-triarylpyridines from chalcones and urea (2:1 mole ratio), using immobilized non-toxic[7] bismuth nitrate as catalyst, and proposed that in the course of this one-pot cascade sequence of reactions the loss of a benzylidene moiety probably occurred via *retro-aldol* disproportionation of tetrasubstituted 1,4-dihydropyridinium ion intermediate. Now, it seemed to us that it may be possible to restrict this disproportionation by the catalyst manipulation and secure direct access to a new group of tetrasubstituted pyridines, without altering the requisite structural features for their photodynamic activity.

Traditionally, chalcones are prepared by the base catalyzed Claisen–Schmidt condensation[8] of arylaldehydes and acetophenones, though acid catalyzed,[9] solid[10] and resin supported,[11] and microwave assisted[12] versions of the condensation reaction are also known. Since, these methodologies are fraught with one or the other drawbacks like poor yields, long reaction times, the involvement of expensive reagents and catalysts, sometimes in stoichiometric amounts, we also considered the preparation of chalcones from appropriate arylaldehyde and acetophenone, in neutral aqueous medium.

In this paper, we describe the quantitative preparation of chalcones **1a**–**1m**, in neutral aqueous medium, using *para*-toluenesodium sulfonate as catalyst, and their subsequent one-pot solid-supported dimerization–heteroannulation reaction with compounds possessing NH_2–C═X (X═O, S) functionality, to yield new 2,4,6-triaryl-3-methylarylpyridines, using heterocatalyst mixture of immobilized Bi(III) nitrate in the presence of co-catalyst Zn(II) chloride.

2. Results and discussion

The dimerization–heteroannulation of chalcones **1a**–**1m** and urea (2:1 mole ratio) to afford 2,4,6-triaryl-3-methylarylpyridines was achieved by one-pot solid-supported thermal reaction of the substrates at a temperature of 125–135 °C, using a Bi(III) nitrate catalyst, immobilized on neutral alumina, in the presence of co-catalyst Zn(II) chloride. Initially, chalcones **1a**–**1m** were obtained, in nearly quantitative yield (98–100%, Table 1), by stirring a heterogeneous mixture of appropriate aldehyde, acetophenone (1:1 mole), and catalyst

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Table 1. Yield of chalcones **1a–1m** in aqueous medium

Compound	Yield (%)	Time (h)
1a	99	0.5
1b	99	0.5
1c	94	2.5
1d	97	2.0
1e	98	2.0
1f	97	2.0
1g	97	0.5
1h	96	3.5
1i	96	2.5
1j	98	3.0
1k	98	0.5
1l	98	1.5
1m	96	1.0

para-toluenesodium sulfonate (20 mol %) (Scheme 1), in aqueous medium, for 0.5–3 h.

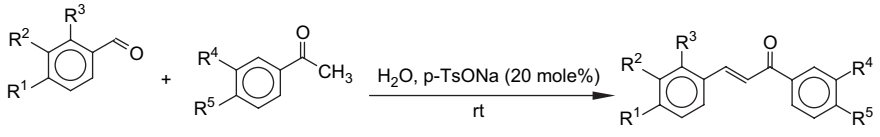
Chalcones **1a–1m** were found to be sufficiently pure to permit further reaction. However, for ascertaining the identity by mp and mixed mp with authentic samples,[6] **1a–1m** were further purified by crystallization from hot methanol. The isolated chalcones were primarily of trans stereochemistry. Interestingly, this procedure worked well even with aldehydes containing an acidic proton. The dimerization–heteroannulation reaction of **1a–1m** and urea was attempted under solventless conditions, using the catalyst Bi(III) nitrate (5% w/w), immobilized on neutral alumina,[6] and another metal salt as co-catalyst. After several failed attempts with the chloride, bromide, and nitrate salts of sodium, potassium, magnesium, and iron, Zn(II) chloride was found to be an effective co-catalyst for the reaction. The heterocatalyst mixture was prepared by stirring, overnight, a solution of 2.5% (w/w) Zn(II) chloride in dry acetone, with activated Bi(III) nitrate (5% w/w)–Al_2O_3 catalyst, which was initially prepared by the previously described adsorption process.[6] After removing the solvent in vacuum, the heterocatalyst mixture (coded BALZ) was again activated, at 105–115 °C, in a thermostatically controlled hot-air oven. The catalyst mixture was reactivated for 0.5 h, each time before use.

A mixture of chalcones **1a–1m**, urea (2:1 mole), and catalyst BALZ, in proportion by the mass of chalcone (equivalent to $\approx 2.5\times10^{-3}$ mol % of Bi(III) nitrate and 1.25×10^{-3} mol % of Zn(II) chloride) was heated, at 130±5 °C, in a thermostatically controlled hot-air oven. On completion of the reactions (3–3.5 h) binary mixture of products was obtained (Scheme 2).

These mixtures were separated by column chromatography on silica gel, to afford **3a–3m** (60–70%), as the major product, and **4a–4m** (30–35%), as the minor product (Table 2). The compounds **4a–4m** were identified as 2,4,6-triarylpyridines by their spectral data, TLC, mp, and mixed mp, with authentic samples.[6] The compounds **3a–3m** were characterized as 2,4,6-triaryl-3-methylarylpyridines by spectral methods: HRMS, IR, ^{1}H NMR, ^{13}C NMR, ^{1}H–^{1}H COSY, DEPT-135, and HMQC. The structure **3g** was confirmed by crystal structure analysis (Fig. 1, CCDC no. 631138), and based upon that **3a–3m** were further confirmed using spectral methods.

Encouraged by these observations, we attempted to generalize this reaction by reacting chalcones **1a–1d** with thiourea **2b**, acetamide **2c**, benzamide **2d**, and biuret **2e**, at 125–135 °C, using the BALZ catalyst. Except for the reactions with **2e**, the yield of the products **3a–3d** as well as **4a–4d** was comparable with the yield obtained by the reaction of the chalcones and urea (Table 3). The reactions involving benzamide **2d**, as the source of nitrogen, also afforded benzoic acid.

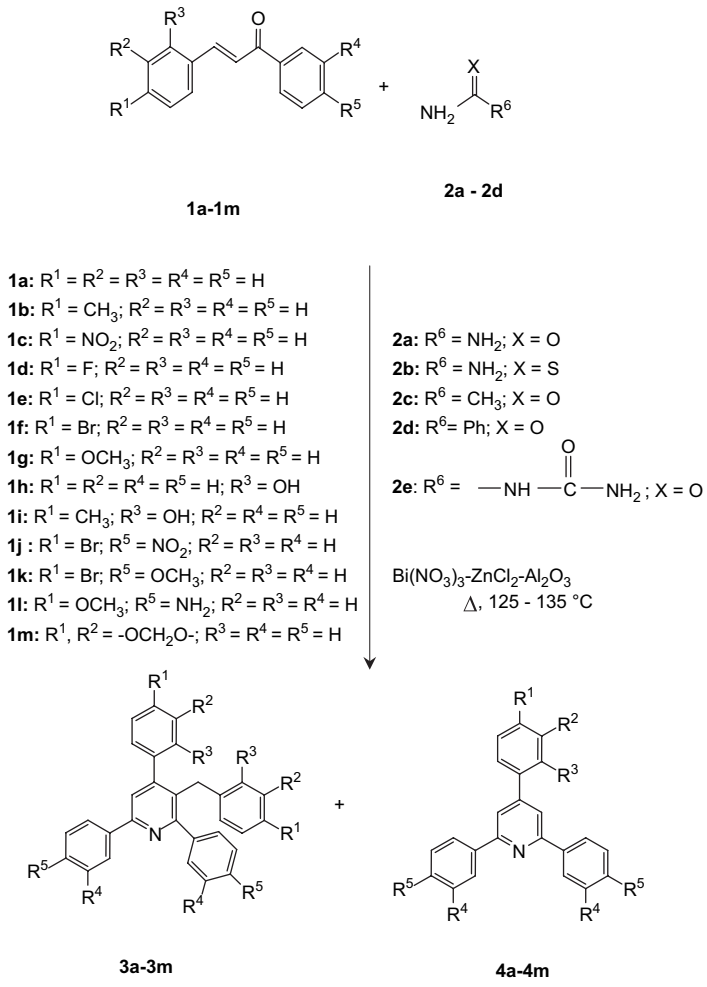
Although, the exact mode of action of co-catalyst $ZnCl_2$ is not quite clear, it seems that the reaction of chalcones and compounds carrying NH_2–C=X (X=O, S) functionality initially follows the same mechanistic pathway as a



1a-1m

1a: R^1= R^2 = R^3 = R^4 = R^5= H
1b: R^1= CH_3; R^2= R^3 = R^4= R^5= H
1c: R^1= NO_2; R^2= R^3= R^4= R^5 = H
1d: R^1= F; R^2= R^3= R^4= R^5= H
1e: R^1= Cl; R^2= R^3= R^4= R^5= H
1f: R^1= Br; R^2= R^3= R^4= R^5= H
1g: R^1= OCH_3; R^2= R^3= R^4= R^5= H
1h: R^1= R^2= R^4 = R^5= H; R^3= OH
1i: R^1= CH_3; R^3 = OH; R^2= R^4= R^5= H
1j: R^1= Br; R^5= NO_2; R^2= R^3= R^4= H
1k: R^1= Br; R^5= OCH_3; R^2= R^3= R^4= H
1l: R^1= OCH_3; R^5= NH_2; R^2= R^3= R^4= H
1m: R^1, R^2= OCH_2O; R^3= R^4= R^5= H

Scheme 1. Chalcones from appropriate aldehydes and acetophenone.



Scheme 2. Triarylmethylarylpyridines from chalcones and urea derivatives.

homomolecular Michael addition of enolized chalcones to form 1,5-diketoenol followed by heteroannulation, via imine formation, to form dihydropyridinium ion intermediate **a** (Scheme 3), as in the synthesis of 2,4,6-triarylpyridines.[6]

The dihydropyridinium ion intermediate **a**, probably by the involvement of Zn(II) ions, instead of undergoing *retro-aldol* disproportionation, may undergo rearrangement of π-bonds via dehydration to give 2,4,6-triaryl-3-methylaryl-pyridinium ion **b** (Scheme 3). Subsequent hydrolysis of this ion may lead to the formation of 2,4,6-triaryl-3-methyl-arylpyridines.

Since the use of microwave irradiation in organic synthesis has been shown to be beneficial, we repeated the reactions

Table 2. Percent yield of the products **3a**–**3m** and **4a**–**4m**

Compound	Yield (%)		Compound	Yield (%)		MW time (min)
	Oven	MW		Oven	MW	
3a	65	66	**4a**	30	31	20
3b	67	69	**4b**	31	33	22
3c	70	71	**4c**	25	28	20
3d	66	67	**4d**	28	29	23
3e	69	70	**4e**	29	30	19
3f	64	66	**4f**	27	29	18
3g	65	67	**4g**	29	30	20
3h	66	68	**4h**	30	32	21
3i	67	68	**4i**	32	33	22
3j	63	65	**4j**	24	26	24
3k	62	64	**4k**	32	34	23
3l	60	61	**4l**	34	35	25
3m	61	63	**4m**	33	36	24

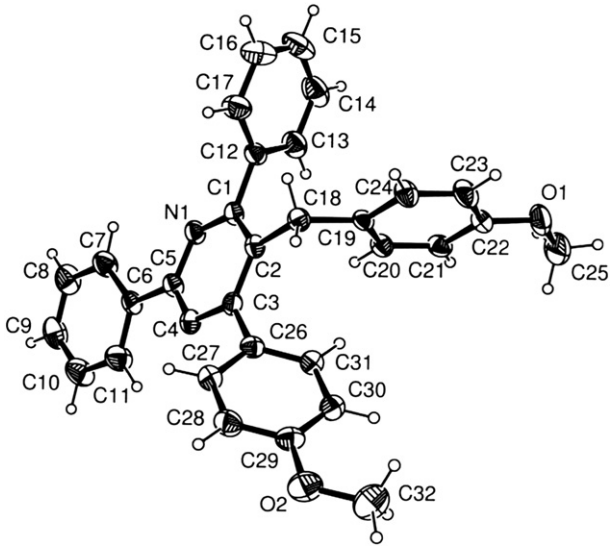


Figure 1. The ORTEP drawing and the labeling scheme used in the structural analysis.

Table 3. Percent yield of products **3a–3d** and **4a–4d** using different amino derivatives (**2b–2e**)

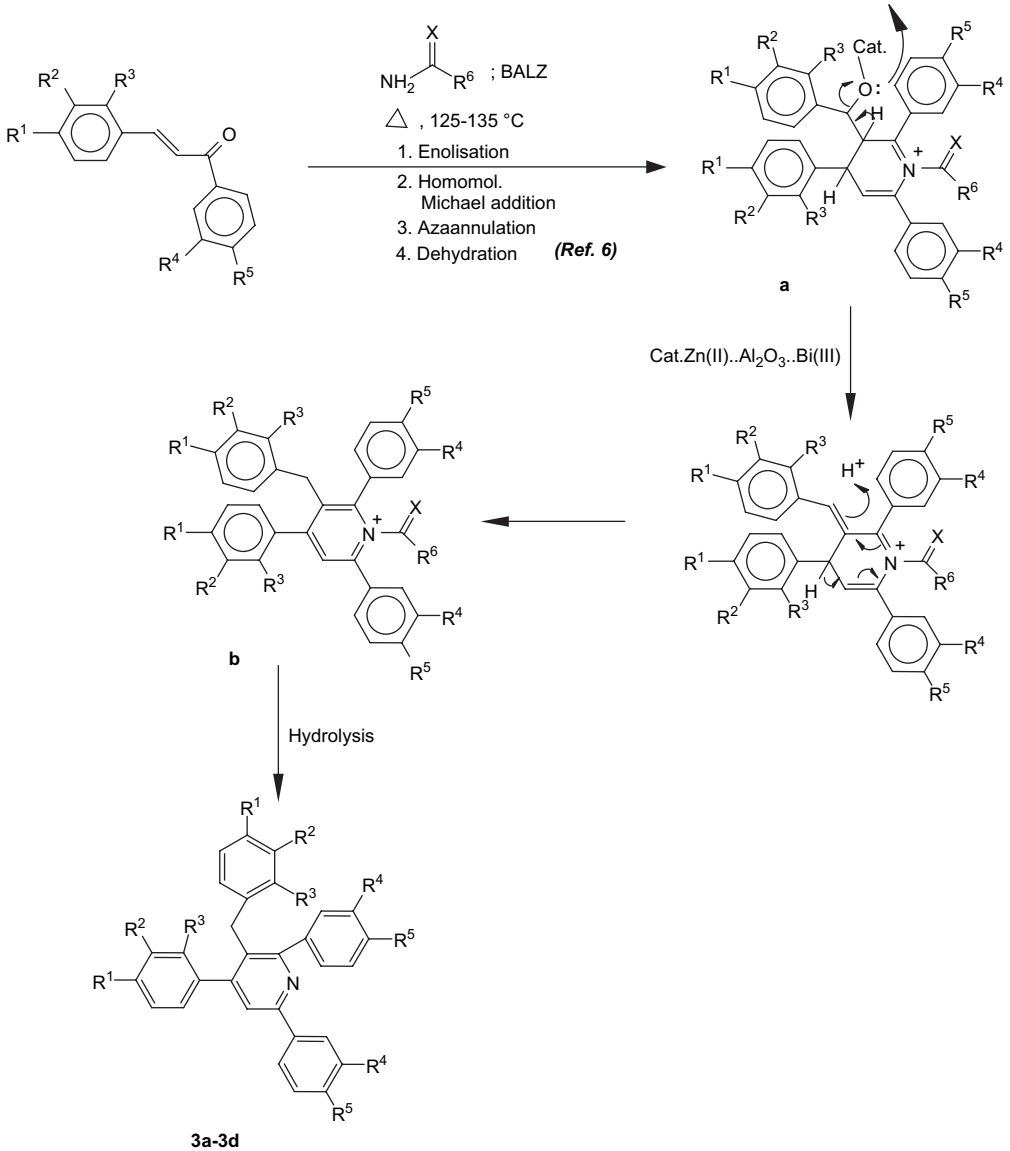
Amino derivative	**3a/4a** (%)	**3b/4b** (%)	**3c/4c** (%)	**3d/4d** (%)
2b	63/28	64/30	68/27	65/25
2c	62/25	61/29	65/30	64/29
2d	60/26	58/25	61/23	57/24
2e	27/61	26/62	28/65	29/60

of chalcones **1a–1m** with urea in a domestic microwave oven (2450 MHz), using 60% power, and followed the procedure of Mukhopadhyay et al.,[13] which allows the temperature to remain at ca. 130 °C. The reactions were completed in 18–25 min without any substantial improvement in the yield of **3a–3m** or **4a–4m** (Table 2).

We also carried out the reactions of chalcones **1a–1d** and urea with Zn(II) chloride, immobilized on neutral alumina, in the absence of Bi(III) nitrate. The reactions did not proceed satisfactorily indicating that the presence of Bi(III) nitrate was necessary for the formation of **3a–3m**. On carrying out the reaction of **1a–1d**, urea (2:1 mole ratio), and catalyst BALZ in solution, using solvents like CH_2Cl_2, toluene, acetonitrile, and ethanol the reactions failed to give **3a–3d**, even on refluxing for 72 h. On optimizing the reaction conditions for the preparation of **3a–3m** from chalcones, amines, and catalyst BALZ, the reaction was found to be temperature dependent; optimum temperature being 125–135 °C.

3. Conclusions

In summary, we have developed a simple one-pot procedure for the preparation of 2,4,6-triaryl-3-methylarylpyridines from chalcones and urea derivatives, using a heterocatalyst mixture of Bi(III) nitrate and Zn(II) chloride, immobilized on neutral alumina, under solventless conditions, and have demonstrated the efficacy of immobilized mixed salt heterocatalyst mixture of Bi(III) nitrate and Zn(II) chloride in



Scheme 3. Probable mechanism for the dimerization–heteroannulation reaction of chalcones.

diverting the reaction pathway, via preferential elimination, in an one-pot cascade sequence of reactions. The added advantage of this methodology is the non-toxic nature of the catalyst mixture.

4. Experimental section

4.1. General

Melting points are uncorrected and were determined on Perfit melting point apparatus. IR spectra, in KBr discs, were recorded on a Brucker 4800 IR spectrometer. ^{1}H NMR (300 MHz) and ^{13}C NMR (50.3 MHz) spectra were recorded in $CDCl_3$ solution using a Brucker Ac DPX-200 spectrometer; some spectra were recorded on Varian Gemini 300 MHz instrument using TMS as standard. HREIMS were recorded at 70 eV on a JEOL D-300 mass spectrometer; CHN analysis was done on CHNS-Leco-932 instrument. TLC was performed on 0.5 mm thick plates using BDH silica gel-G adsorbent. Column chromatography was performed on silica gel (BDH, mesh size 60–120) using graded solvent system of petroleum ether (40–60 °C), petroleum ether–$CHCl_3$, and $CHCl_3$–EtOAc. Microwave irradiations were carried out in a domestic microwave oven (LG model no. MS-255R, no. 4140W1A 347A) with frequency of 2450 MHz and output of 900 W. The calculated mass values are based on the values obtained by Chem 4-D Draw (Cheminnovation) Software.

4.2. Preparation of catalyst (BALZ)

Bi(III) nitrate–5H_2O (2.5 g) was dissolved in 1:1 MeOH–H_2O (150 mL) and the solution was added to neutral alumina (50 g) and stirred for 12 h at room temperature. The mixture was air dried and then heated at 110±5 °C in a thermostatic hot-air oven for 6 h. A solution of anhydrous Zn(II) chloride (1.25 g), in dry CH_3CN (100 mL), was added to the activated Bi(III) nitrate–Al_2O_3 catalyst mixture. The mixture was again stirred overnight, at room temperature. The solvent was removed under vacuum and the dry solid catalyst mixture was again activated, at 110±5 °C, for 6 h, cooled in a desiccator, and stored. The catalyst was reactivated, at 110±5 °C, for 1 h, each time before use.

4.3. General method for the preparation of chalcones 1a–1m

Chalcones **1a**–**1m** were prepared from the appropriate aldehyde and acetophenone (1:1 mole) by stirring, at room temperature, the substrate mixture suspended in water (150–200 mL) containing 2.5 mol % of *p*-toluenesodium sulfonate. The mixture was stirred for 0.5–3 h until the chalcones precipitated. The stirring was continued for another 0.5 h, and the precipitates were filtered and washed with water (4×50 mL). The residue was then dried under vacuum. TLC on silica gel, using petroleum ether (bp 40–60 °C)–CH_2Cl_2 (19:1 v/v) showed the formation of single products of sufficient purity for further use. Chalcones **1a**–**1m** were crystallized from hot methanol for spectral analysis and for the determination of mp, mixed mp, and co-TLC with authentic samples.[6,9]

4.4. General procedure for the preparation of 3a–3m

Chalcones **1a**–**1m** (2 mmol) and compounds **2a**–**2e** possessing NH_2–C═X functionality (1 mmol) were dissolved in 2–3 mL of $CHCl_3$ and added to the catalyst mixture, taken in proportion by weight of the chalcones (approx. concn of Bi(III) nitrate=0.5 mol %; Zn(II) chloride>0.025 mol %). The reaction mixture was dried in air and heated at 130±5 °C, in a thermostatically controlled hot-air oven. Simultaneously, separate experiments were conducted to monitor the reaction by comparative TLC of the ethyl acetate extract of the aliquots drawn out from the reaction flask at 0.5 h intervals, using petroleum ether–CH_2Cl_2 (9:1, 7:3, and 3:7 v/v), as solvent systems. The plates were developed by spraying with Ce(IV) ions and heating at 110±5 °C for 10 min when dark blue spots of Ce(IV) complexes of 2,4,6-triarylpyridines **4a**–**4m** and light bluish yellow spots of the 2,4,6-triphenyl-3-methylarylpyridines **3a**–**3m** were observed against a white background. On completion of the reaction (3.5 h), the product mixtures were extracted with hot $CHCl_3$ (100–150 mL), in a Soxhlet extractor, freed from the solvent, and separated by column chromatography, using petroleum ether (40–60 °C)–CH_2Cl_2 graded solvent systems. The solvent was distilled and the residue was purified by crystallization from $CHCl_3$–petroleum ether (40–60 °C) and $CHCl_3$–MeOH. This gave **3a**–**3m**, as major product, and **4a**–**4m**, as the minor product (Table 2). In addition to these compounds, minor quantities of aldehydes from which **1a**–**1m** were also obtained.

4.5. General procedure for microwave irradiation

Chalcones **1a**–**1m** and compounds possessing NH_2–C═X functionality (2:1 mmol) were dissolved in $CHCl_3$ (2–3 mL) and added to the catalyst BALZ, taken in proportion by mass of chalcone. The reaction mixture was dried in vacuum and heated in a domestic microwave (2450 MHz), using 60% power (540 W) and the procedure of Mukhopadhyay et al.,[13] which permits the control of temperature at ca. 130 °C. The reactions were monitored by TLC and on completion of the reaction (18–25 min) the products were extracted with hot $CHCl_3$ (75–100 mL) and purified as before. The products were identified by TLC, mp, and mixed mp with **3a**–**3m** and **4a**–**4m**.

4.5.1. 2,4,6-Triphenyl-3-methylphenylpyridine, 3a. Colorless needles, mp 97–98 °C. IR: ν_{max} 3036, 3010, 1610, 1490, 1476, 1450, 1371, 1245, 1050, 965 cm^{-1}. ^{1}H NMR (300 MHz, $CDCl_3$): δ 3.98 (2H, s,), 7.12–7.23 (4H, m), 7.20 (1H, s), 7.41–7.45 (3H, m), 7.50–7.56 (4H, m), 7.73–7.76 (2H, m). ^{13}C NMR: δ_C 36.2, 120.6, 125.5, 127.2, 129.3, 130.1, 132.4, 141.2, 152.1, 154.3, 157.1. HREIMS: *m*/*z* (rel int.) 397.1842 (M^+) (32) (calcd for $C_{30}H_{23}N$, 397.1830), 320 (100%), 294 (23), 218 (20), 192 (44), 115 (50), 102 (25), 91 (50), 77 (78). Anal. CHN (%), found: C, 89.96; H, 6.6, N, 3.47. Calcd: C, 90.64; H, 5.83; N, 3.52.

4.5.2. 4-(4-Methylphenyl)-3-[(4-methylphenyl)methyl]-2,6-diphenylpyridine, 3b. Colorless needles, mp 121–122 °C. IR: ν_{max} 3035, 3010, 1618, 1500, 1475, 1456, 1430, 1375, 1290, 1050, 965 cm^{-1}. ^{1}H NMR (300 MHz, $CDCl_3$): δ 2.36 (3H, s), 2.39 (3H, s), 4.03 (2H, s), 7.20 (2H, d, *J* 8.5 Hz), 7.26 (2H, d, *J* 8.5 Hz), 7.30–7.36 (4H,

m), 7.38–7.50 (4H, m), 7.53 (2H, d, *J* 8.5 Hz), 7.60 (1H, s), 7.63 (2H, d, *J* 8.5 Hz), 8.01 (2H, ddd, *J* 8.6, 3.3, 1.0 Hz). ^{13}C NMR ($CDCl_3$): δ_C 34.10, 120.6, 125.4, 126.9, 127.6, 128.1, 128.2, 128.5, 130.1, 131.2, 132.4, 133.2, 139.5, 152.9, 154.4, 157.1. HREIMS: *m/z* (rel int.) 425.2185 (M^+) (42) (calcd for $C_{32}H_{27}N$, 425.2143), 348 (100%), 334 (45), 322 (20), 232 (25), 220 (45), 129 (55), 116 (25), 105 (47), 91 (70). Anal. CHN (%), found: C, 89.89; H, 6.51; N, 3.57. Calcd: C, 90.31; H, 6.39; N, 3.29.

4.5.3. 4-(4-Nitrophenyl)-3-[(4-nitrophenyl)methyl]-2,6-diphenylpyridine, 3c. Colorless cubes, mp 128–129 °C. IR: ν_{max} 3038, 3012, 1615, 1495, 1478, 1452, 1373, 1247, 1052, 967 cm^{-1}. ^{1}H NMR (300 MHz, $CDCl_3$): δ 4.36 (2H, s), 7.33–7.46 (8H, m), 7.50 (2H, d, *J* 8.7 Hz), 7.55 (2H, d, *J* 8.7 Hz), 7.63 (1H, s), 8.01 (2H, ddd, *J* 8.6, 3.2, 1.0 Hz), 8.19 (2H, d, *J* 8.7 Hz), 8.25 (2H, d, *J* 8.7 Hz). ^{13}C NMR ($CDCl_3$): δ_C 40.5, 120.1, 126.5, 126.9, 127.9, 128.6, 128.7, 137.0, 138.0, 140.4, 140.7, 142.6, 143.4, 146.4, 148.1, 154.4, 157.3, 158.5. HREIMS: *m/z* (rel int.) 487.1548 (M^+) (38) (calcd for $C_{30}H_{21}N_3O_4$, 487.1533), 410 (100%), 384 (30), 365 (24), 288 (38), 263 (30), 160 (58), 147 (56), 136 (38), 122 (87). Anal. CHN (%), found: C, 74.31; H, 4.49, N, 8.70. Calcd: C, 73.91; H, 4.34; N, 8.62.

4.5.4. 4-(4-Fluorophenyl)-3-[(4-fluorophenyl)methyl]-2,6-diphenylpyridine, 3d. Colorless cubes, mp 113–114 °C. IR: ν_{max} 3004, 1618, 1500, 1470, 1455, 1430, 1398, 1371, 1294, 1253, 1030, 967 cm^{-1}. ^{1}H NMR (300 MHz, $CDCl_3$): δ 4.80 (2H, s), 7.12 (2H, dd, *J* 8.8, 8.7 Hz), 7.26 (2H, dd, *J* 8.8, 8.7 Hz), 7.73 (2H, dd, *J* 8.8, 5.4 Hz), 7.76 (2H, dd, *J* 8.8, 5.4 Hz). ^{13}C NMR ($CDCl_3$): δ_C 39.4, 116.4 (d, *J* 8.2 Hz), 117.2 (d, *J* 8.2 Hz), 117.4 (d, *J* 8.2 Hz), 118.3 (d, *J* 8.2 Hz), 112.6, 126.8, 126.9, 127.6, 128.6, 128.7, 129.1 (d, *J* 8.2 Hz), 130.0 (d, *J* 8.2 Hz), 151.9, 155.3, 157.6, 163.9, 164.7. HREIMS: *m/z* (rel int.) 433.1666 (M^+) (42) (calcd for $C_{30}H_{21}F_2N$, 433.1642) 356 (100%), 338 (29), 330 (50), 236 (66), 228 (46), 133 (23), 109 (37), 95 (73). Anal. CHN (%), found: C, 83.42; H, 5.09; N, 3.36. Calcd: C, 83.12; H, 4.88; N, 3.23.

4.5.5. 4-(4-Chlorophenyl)-3-[(4-chlorophenyl)methyl]-2,6-diphenylpyridine, 3e. Colorless prisms, mp 120–121 °C. IR: ν_{max} 3025, 1610, 1495, 1475, 1385, 1350, 1140, 1090, 1072, 1050, 926 cm^{-1}. ^{1}H NMR (300 MHz, $CDCl_3$): δ 4.52 (2H, s), 7.35–7.49 (4H, m), 7.40 (2H, d, *J* 8.4 Hz), 7.49 (2H, d, *J* 8.4 Hz), 7.50–7.67 (4H, m), 7.61 (1H, s), 7.61 (1H, s), 7.65 (2H, dd, *J* 8.4, 3.8 Hz), 7.72 (2H, dd, *J* 8.6, 3.8 Hz), 8.01 (2H, ddd, *J* 8.6, 3.3, 1.0 Hz). ^{13}C NMR ($CDCl_3$): δ_C 34.30, 120.5, 127.0, 127.7, 128.2, 128.3, 128.4, 128.5, 129.5, 130.2, 130.4, 132.1, 132.2, 136.9, 137.1, 139.6, 141.3, 152.1, 154.3, 157.9. HREIMS: *m/z* (rel int.) 465.1023, 469.0989 (M^+) (49, 37) (calcd for $C_{30}H_{21}Cl_2N$, 465.1051, 469.0996), 388 (100%), 363 (22), 354.5 (56), 261 (33), 252 (13), 149 (45), 136 (39), 125 (14), 111 (67). Anal. CHN (%), found: C, 77.76; H, 4.38; N, 3.29. Calcd:. C, 77.36; H, 4.54; N, 3.10.

4.5.6. 4-(4-Bromophenyl)-3-[(4-bromophenyl)methyl]-2,6-diphenylpyridine, 3f. Colorless needles, mp 123–125 °C. IR: ν_{max} 3026, 1612, 1497, 1477, 1386, 1351, 1142, 1090, 1073, 1050, 928 cm^{-1}. ^{1}H NMR (300 MHz, $CDCl_3$): δ 4.20 (2H, s), 7.30–7.46 (4H, m), 7.47–7.52 (4H, m), 7.54 (2H, d, *J* 8.7 Hz), 7.56 (2H, d, *J* 8.7 Hz), 7.61 (1H, s), 7.62 (2H, d, *J* 8.7 Hz), 7.68 (2H, d, *J* 8.7 Hz), 8.01 (2H, ddd, *J* 8.6, 3.2, 1.0 Hz). ^{13}C NMR ($CDCl_3$): δ_C 36.7, 121.3, 125.4, 125.6, 127.5, 127.8, 128.4, 128.6, 128.7, 129.5, 130.3, 131.4, 131.5, 131.9, 132.1, 139.9, 141.6, 145.2, 154.4, 154.8. HREIMS: *m/z* (rel int.) 553.0104, 557.0100 (M^+) (22, 32) (calcd for $C_{30}H_{21}Br_2N$, 553.0041, 557.0001), 476 (100%), 452 (31), 399 (21), 350 (63), 297 (53), 194 (59), 181 (41), 170 (44), 156 (72). Anal. CHN (%), found: C, 65.09; H, 3.69; N, 2.69. Calcd: C, 64.89; H, 3.81; N, 2.52.

4.5.7. 4-(4-Methoxyphenyl)-3-[(4-methoxyphenyl)-methyl]-2,6-diphenylpyridine, 3g. Colorless cubes, mp 123–125 °C. IR: ν_{max} 3035, 3004, 1618, 1500, 1470, 1455, 1430, 1371, 1294, 1050, 967 cm^{-1}. ^{1}H NMR (300 MHz, $CDCl_3$): δ 3.56 (3H, s), 3.58 (3H, s), 4.01 (2H, s), 6.84 (2H, d, *J* 8.4 Hz), 6.85 (2H, d, *J* 8.4 Hz), 7.23–7.36 (4H, m), 7.25 (2H, dd, *J* 8.7, 2.7 Hz), 7.37–7.49 (4H, m), 7.60 (1H, s), 8.07 (2H, dd, *J* 9.6, 2.3, 1.0 Hz). ^{13}C NMR ($CDCl_3$): δ_C 34.13, 55.1, 55.3, 113.3, 113.6, 120.9, 126.9, 127.7, 127.9, 128.6, 128.7, 129.1, 132.4, 133.2, 139.5, 141.4, 151.2, 151.9, 154.4, 157.4, 159.2. HREIMS: *m/z* (rel int.) 457.2068 (M^+) (21) (calcd for $C_{32}H_{27}NO_2$, 457.2042), 380 (100), 354 (41), 350 (66), 252 (25), 248 (42), 145 (55), 132 (28), 121 (54), 107 (67). Anal. CHN (%), found: C, 84.50; H, 6.19; N, 3.31. Calcd: C, 84.00; H, 5.95; N, 3.15.

4.5.8. 2-{3-[(2-Hydroxyphenyl)methyl]-2,6-diphenyl-4-pyridyl}phenol, 3h. Colorless plates, mp 172–173 °C. IR: ν_{max} 3460, 3430, 3050, 1605, 1550, 1485, 1380, 1345, 1280, 1140, 1096, 1050, 920, 750 cm^{-1}. ^{1}H NMR (300 MHz, $CDCl_3$): δ 4.15 (2H, s), 7.01 (1H, dd, *J* 7.3, 7.7 Hz), 7.10 (2H, dd, *J* 7.3, 7.7 Hz), 7.19 (1H, d, *J* 8.7 Hz), 7.23 (1H, d, *J* 8.7 Hz), 7.30–7.51 (4H, m), 7.35 (2H, dd, *J* 8.7, 2.3 Hz), 7.38 (2H, dd, *J* 7.8, 2.3 Hz), 7.42 (1H, dd, *J* 7.8, 2.3 Hz), 7.53–7.67 (4H, m), 7.59 (1H, s), 8.10 (2H, ddd, *J* 8.6, 3.0, 1.0 Hz), 10.16 (1H, s, exch. D_2O), 10.90 (1H, s, exch. D_2O). ^{13}C NMR ($CDCl_3$): δ_C 34.20, 118.3, 118.7, 119.1, 119.9, 120.4, 120.8, 126.9, 127.1, 127.6, 128.3, 128.6, 129.5, 130.2, 130.4, 133.7, 145.7, 145.9, 154.6, 157.8, 158.5. HREIMS: *m/z* (rel int.) 429.1768 (M^+) (13) (calcd for $C_{30}H_{23}NO_2$, 429.1729), 352 (100), 36 (42), 326 (46), 234 (54), 224 (25), 131 (75), 118 (25), 107 (35), 93 (78). Anal.: not done.

4.5.9. 2-{3-[(2-Hydroxy-4-methylphenyl)methyl]-2,6-diphenyl(4-pyridyl)}-5-methylphenol, 3i. Colorless plates, mp 165–166 °C. IR: ν_{max} 3478, 3466, 3050, 1610, 1555, 1480, 1385, 1340, 1270, 1145, 1096, 1050, 920, 730 cm^{-1}. ^{1}H NMR (300 MHz, $CDCl_3$): δ 2.36 (3H, s), 2.39 (3H, s), 3.95 (2H, s), 6.85 (1H, dd, *J* 8.0, 0.91 Hz), 6.88 (1H, d, *J* 8.0 Hz), 6.92 (1H, br s), 7.20 (1H, d, *J* 8.0 Hz), 7.25 (1H, d, *J* 8.0 Hz), 7.50–7.53 (4H, m), 7.53–7.68 (4H, m), 7.67 (1H, s), 8.01 (2H, ddd, *J* 8.6, 2.2, 1.0 Hz), 10.18 (2H, s, exch. D_2O). ^{13}C NMR ($CDCl_3$): δ_C 114.6, 117.6, 120.7, 121.0, 127.1, 127.3, 127.5, 128.5, 130.1, 130.4, 145.1, 147.9, 154.6, 157.1. HREIMS: *m/z* (rel int.) 457.2091 (M^+) (24) (calcd for $C_{32}H_{27}NO_2$, 457.2042), 380 (100), 354 (39), 350 (56), 252 (23), 248 (34), 145 (35), 132 (15), 121 (79). Anal.: not done.

4.5.10. 2,6-Bis(4-nitrophenyl)-4-(4-bromophenyl)-3-[(4-bromophenyl)methyl]pyridine, 3j. Colorless prisms, mp

165–166 °C. IR: ν_{max} 3045, 1605, 1585, 1496, 1410, 1385, 1370, 1346, 1150, 1050, 920, 760 cm^{-1}. ^1H NMR (300 MHz, $CDCl_3$): δ 4.73 (2H, s), 7.54 (4H, d, *J* 8.7 Hz), 7.60 (2H, d, *J* 8.7 Hz), 7.65 (2H, d, *J* 8.7 Hz), 7.73 (2H, d, *J* 8.7 Hz), 7.76 (2H, d, *J* 8.7 Hz), 7.96 (1H, s), 8.26 (4H, d, *J* 8.7 Hz). ^{13}C NMR ($CDCl_3$): δ_C 36.4, 122.3, 129.1, 130.9, 131.2, 137.5, 140.1, 142.7, 146.3, 154.2, 159.5, 159.7. HREIMS: *m*/*z* (rel int.) 643.0968, 647.0030 (M^+) (21, 12) (calcd for $C_{30}H_{19}Br_2^-N_3O_4$, 642.9742, 646.9703), 520 (10), 497 (48), 489 (45), 485 (100), 350 (43), 350 (32), 342 (13), 194 (59), 181 (19), 170 (69), 156 (87). Anal. CHN (%), found: C, 55.79; H, 3.08; N, 6.59. Calcd: C, 55.84; H, 2.97; N, 6.51.

4.5.11. 1-{4-(4-Bromophenyl)-3-[(4-bromophenyl)-methyl]-6-(4-methoxyphenyl)(2-pyridyl)}-4-methoxybenzene, 3k. Colorless cubes, mp 123–125 °C. IR: ν_{max} 3050, 1605, 1545, 1490, 1410, 1387, 1350, 1150, 1050, 920, 700 cm^{-1}. ^1H NMR (300 MHz, $CDCl_3$): δ 3.56 (3H, s), 3.58 (3H, s), 4.12 (2H, s), 6.85 (4H, d, *J* 8.6 Hz), 7.27 (2H, d, *J* 8.6 Hz), 7.51 (2H, d, *J* 8.7 Hz), 7.54 (2H, d, *J* 8.7 Hz), 7.62 (2H, d, *J* 8.7 Hz), 7.60 (1H, s), 8.01 (2H, ddd, *J* 8.0, 3.2, 1.0 Hz). ^{13}C NMR ($CDCl_3$): δ_C 36.2, 55.3, 55.4, 113.9, 114.3, 120.8, 125.3, 125.8, 128.1, 128.4, 128.7, 131.4, 131.6, 131.8, 131.9, 146.4, 147.3, 157.2, 158.2. HREIMS: *m*/*z* (rel int.) 613.0271, 617.0292 (M^+) (19, 25) (calcd for $C_{32}H_{25}Br_2NO_2$, 613.0252, 617.0212), 508 (100), 482 (33), 459 (26), 350 (24), 327 (39), 194 (65), 181 (11), 170 (66), 156 (87). Anal.: not done.

4.5.12. 4-{6-(4-Aminophenyl)-4-(4-methoxyphenyl)-5-[(4-methoxyphenyl)methyl]-2-pyridyl}phenylamine, 3l. Colorless plates, mp 220–221 °C (dec). IR: ν_{max} 3430, 3036, 3012, 1610, 1500, 1470, 1455, 1435, 1399, 1370, 1295, 1250, 1050, 1030, 967, 730 cm^{-1}. ^1H NMR (300 MHz, $CDCl_3$): δ 3.50 (2H, br s), 3.55 (2H, br s), 3.70 (3H, s), 3.72 (3H, s), 4.10 (2H, s), 6.80 (2H, d, *J* 8.6 Hz), 6.85 (2H, d, *J* 8.6 Hz), 6.93 (4H, d, *J* 8.3 Hz), 7.37 (2H, d, *J* 8.6 Hz), 7.43 (2H, d, *J* 8.6 Hz), 7.50 (1H, s), 8.20 (4H, d, *J* 8.3 Hz). ^{13}C NMR ($CDCl_3$): δ_C 35.30, 55.2, 55.4, 110.5, 110.6, 112.1, 113.3, 113.8, 115.2, 126.3, 127.7, 128.2, 128.5, 128.6, 129.5, 154.0, 154.5, 156.5, 157.3, 158.2, 160.5. HREIMS: *m*/*z* (rel int.) 487.2299 (M^+) (11) (calcd for $C_{32}H_{29}N_3O_2$, 487.2260), 395 (100), 380 (34), 369 (25), 263 (44), 252 (23), 145 (67), 132 (26), 121 (42), 107 (65). Anal.: not done.

4.5.13. 5-[3-(2*H*-Benzo[*d*]1,3-dioxolen-5-ylmethyl)-2,6-diphenyl-4-pyridyl]-2*H*-benzo[*d*]-1,3-dioxolane, 3m. Colorless plates, mp 165–166 °C. IR: ν_{max} 3195, 3052, 1590, 1494, 1390, 1350, 1260, 1050, 920, 760 cm^{-1}. ^1H NMR (300 MHz, $CDCl_3$): δ 4.00 (2H, s), 6.01 (2H, s), 6.04 (2H, s), 6.76 (1H, dd, *J* 8.0, 0.9 Hz), 6.80 (1H, dd, *J* 8.0, 0.9 Hz), 6.96 (1H, s), 6.99 (1H, s), 7.26 (1H, d, *J* 8.0 Hz), 7.30 (1H, d, *J* 8.0 Hz), 7.43–7.50 (4H, m), 7.50–7.56 (4H, m), 8.01 (2H, ddd, *J* 8.6, 3.3, 1.0 Hz). ^{13}C NMR ($CDCl_3$): δ_C 34.4, 100.9, 101.1, 118.4, 119.4, 119.6, 120.2, 120.4, 126.9, 127.7, 128.6, 128.7, 129.5, 130.7, 145.4, 147.5, 148.2, 154.1, 154.3, 155.6, 157.5, 158.2, 159.5. HREIMS: *m*/*z* (rel int.) 485.1678 (M^+) (34) (calcd for $C_{32}H_{23}NO_4$, 485.1628), 408 (100), 382 (45), 364 (67), 280 (22), 248 (42), 159 (64), 146 (24), 135 (65), 121 (71). Anal.: not done.

4.5.14. X-ray data collection, structural determination, and refinement. Data were collected on a Siemens P4 four-circle diffractometer using graphite-monochromatized Mo Kα (λ=0.71073 Å) radiations. The data were corrected for Lorentz and polarization effects. The structure was refined by full-matrix least-squares refinement methods based on F^2, using SHELXTL/PC.[14] Complex neutral atom scattering factors were used for calculations. An anisotropic refinement of non-hydrogen atoms was done. All the hydrogens were attached geometrically. None of these hydrogens were refined, and they were made to ride on their respective atoms. The hydrogens bonded to secondary and tertiary carbons were assigned an isotropic thermal parameter, which was 1.2 times the U_{iso} value of their carrier atom, whereas hydrogens of primary carbons were given a U_{iso} value of 1.5 times that of their carrier. The dihedral angles, least-squares planes, hydrogen bonding, and torsion angles were measured using computer program PARST.[15]

The other refinement details are given in Table 4. The crystallographic data have been deposited at Cambridge Crystallographic Data Centre (CCDC no. 631138).

Table 4. Crystal data and structural refinement for **3g**

Identification code	**3g**
Empirical formula	$C_{32}H_{26}NO_2$
Formula weight	456.57
Temperature	293(2) K
Wavelength	0.71069 Å
Crystal system, space group	Triclinic, *P*-1
Unit cell dimensions	a=9.801(5) Å, b=10.929(5) Å, c=12.488(5) Å, α=103.630(5)°, β=100.620(5)°, γ=95.390(5)°
Volume	1264.4(10) $Å^3$
Z, calculated density	2, 1.199 Mg/m^3
Absorption coefficient	0.074 mm^{-1}
F(000)	482
Crystal size	0.2×0.3×0.2 mm
θ Range for data collection	1.72–25.50°
Limiting indices	$0\leq h\leq 7$, $-12\leq k\leq 12$, $-15\leq l\leq 14$
Reflections collected/unique	4010/3717 [*R*(int)=0.0275]
Completeness to θ=25.50	79.0%
Absorption correction	None
Refinement method	Full-matrix least-squares on F^2
Data/restraints/parameters	3717/0/316
Goodness-of-fit on F^2	1.015
Final *R* indices [$I>2\sigma(I)$]	R_1=0.0544, wR_2=0.1445
R indices (all data)	R_1=0.1095, wR_2=0.1933
Largest diff. peak and hole	0.473 and −0.198 e $Å^{-3}$
CCDC no.	631138

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Supplementary data

^1H NMR, ^{13}C NMR, DEPT-130, ^1H–^1H COSY, and ^1H–^{13}C COSY spectra of representative compound **3g**, as model compound. Supplementary data associated with this article

can be found in the online version, at doi:10.1016/j.tet.2007.06.049.

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