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Convenient one-pot synthesis of *N*-acyl-1,3-diaryl-2-azaphenalene derivatives via solvent-free five-component condensation reactions

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Abstract *N*-Acyl-1,3-diaryl-2-azaphenalene derivatives have been synthesized by one-pot condensation reaction of aromatic aldehydes, 2,7-naphthalenediol, carboxylic acids, and aqueous ammonia (25 %). Different aromatic aldehydes and carboxylic acids have been used in the reaction and the products were always obtained in good to high yields. The method is simple, solvent free, and involves a short reaction time. These relatively rapid reactions possibly proceed via a Betti reaction mechanism.

Keywords 2-Azaphenalene · 2,7-Naphthalenediol · One-pot · Multi-component · Solvent-free

Introduction

Multicomponent reactions (MCRs) are important in modern organic synthesis because they can introduce additional diversity into a molecule in a one pot reaction [1–4]. Some major advantages of MCRs are atom-economy, convergent character, operational simplicity, structural diversity, and complexity of the molecules. These reactions are also increasingly important in combinatorial chemistry and drug discovery [5, 6]. In the history of multicomponent one-pot reactions, the Strecker synthesis, which led to α-aminonitriles, was the first to be studied [7]. Subsequently, there has been substantial development of this MCR procedure. Mention may be made of the Biginelli [8], Passerini [9], Ugi [10], and Mannich [11] reactions. The Mannich reaction, aminoalkylation of aldehydes in which C–N and C–C single

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bonds replace the C=O double bond, is one of the most important MCRs in organic synthesis [12].

The Betti reaction [13] is a Mannich-type reaction for synthesis of α-aminobenzylnaphthol derivatives in which an aromatic aldehyde, ammonia, and 2-naphthol are combined in one pot procedure [14]. This reaction has been developed by using different *N* sources, substituted benzaldehydes or formaldehyde [15, 16], and 1-naphthol [17]. The order and nature of these compounds substantially determine the reaction conditions and the method of isolation of the Mannich product [18]. Because of the potential utility of Mannich-type phenolic bases, particular attention has been devoted to aminoalkylation of naphthol derivatives [19–21], which can be used as intermediates for synthesis of derivatives with substantial antibacterial, hypotensive, and bradycardiac activity [22]. Their phenolic hydroxyl groups and amino groups can be used to develop several synthetic building blocks [23]. Furthermore, optically active Betti bases can be used as chiral catalysts in enantioselective transformations [14].

Azaphenalenyl, a heteroatomic modification of the phenalenyl system, is an important building block in the synthesis of organic multifunctional electronic and magnetic materials [24–26]. Azaphenalene derivatives have very low oxidation potentials and very low negative reduction potentials and are, thus, extremely promising antioxidants in biological systems [27]. Several alkaloid-based compounds with a tricyclic azaphenalene core have been isolated from a variety of ladybird species; the most prominent of these are precoccinelline, myrrhine, and hippodamine [28]. Because of their high biological activity, scarce natural supply, and difficult, only small-scale, isolation from natural sources, synthesis of this heterocyclic nucleus is currently of major importance.

We have developed a facile, rapid, and efficient method for synthesis of *N*-acyl-1,3-diaryl-2-azaphenalene derivatives in good to high yield via a catalyst-free five-component condensation reaction under solvent-free classical heating conditions.

Experimental

General

All chemicals were purchased from Merck or Fluka and used without further purification. Melting points were measured in capillary tubes on an electro thermal digital apparatus and are uncorrected. Known products were identified by comparison of their melting points and spectral data with those reported in the literature. FTIR spectra were recorded on a Unicom Galaxy Series FT-IR 5000 spectrophotometer in the region 4,000–400 cm^{-1}, using pressed KBr discs. NMR spectra were recorded on Bruker Avance spectrophotometer (300 MHz), in DMSO-d_6, using TMS as internal standard. Elemental analysis was performed with a Vario EL III elemental analyzer.

General procedure for preparation of *N*-acyl-1,3-diaryl-2-azaphenalene derivatives (**5a**–**5p**)

A mixture of 2,7-naphthalenediol (1 mmol), aldehyde (2 mmol), carboxylic acid (1.2 mmol), and aqueous ammonia (0.2 mL, 25 %) was stirred under solvent-free conditions at 120 °C for an appropriate time (indicated in Table 2). The progress of the reaction was monitored by TLC. After completion of the reactions, saturated aqueous NaCl (20 mL) was added, the suspension was stirred for 30 min, and the precipitate was isolated by filtration, washed with water, and air-dried. The crude products were washed with ethyl acetate–*n*-hexane, (20 mL, 1:4) to afford the pure products.

Characterization data for new compounds

*Compound **5b** (Table 2, entry 2)*

IR (KBr): ν_{max} = 3371, 3076, 2864, 1626, 1526, 1512, 1424, 1346, 1321, 1275, 1156, 1024, 832, 699 cm^{-1}; ^1H NMR (300 MHz, DMSO-d_6): δ = 5.30 (s, 2H), 6.91 (d, J = 8.8 Hz, 2H), 7.67–7.48 (m, 9H), 7.94 (s, 4H), 8.08 (d, J = 7.6 Hz, 2H), 9.45 (s, 2H, disappeared on D_2O exchange); ^{13}C NMR(75 MHz, DMSO-d_6): δ = 53.5, 114.9, 115.4, 122.0, 122.8, 123.0, 128.5, 129.0, 129.7, 131.3, 131.7, 133.2, 135.4, 147.2, 148.1, 150.9, 167.9; Anal calcd. for $C_{31}H_{21}N_3O_7$: C, 68.00; H, 3.87; N, 7.67. Found: C, 67.85; H, 3.98; N, 7.53.

*Compound **5f** (Table 2, entry 6)*

IR (KBr): ν_{max} = 3319, 3211, 3015, 2823, 2696, 1632, 1604, 1543, 1516, 1429, 1309, 1248, 1174, 1130, 831, 773, 657 cm^{-1}; ^1H NMR (300 MHz, DMSO-d_6): δ = 1.90 (s, 3H), 5.32 (s, 2H), 6.60–6.50 (m, 4H), 6.95–6.84 (m, 6H), 7.53 (d, J = 7.4 Hz, 2H), 8.92 (br, 4H, disappeared on D_2O exchange); ^{13}C NMR(75 MHz, DMSO-d_6): δ = 22.1, 53.3, 115.0, 115.3, 116.0, 122.6, 127.7, 129.4, 132.0, 134.2, 150.7, 156.4, 173.0; Anal calcd. for $C_{26}H_{21}NO_5$: C, 73.06; H, 4.95; N,3.28. Found: C, 72.86; H, 4.81; N, 3.16.

*Compound **5g** (Table 2, entry 7)*

IR (KBr): ν_{max} = 3250–2420, 2362, 1626, 1512, 1433, 1330, 1273, 1080, 881, 765, 700, 634 cm^{-1}; ^1H NMR (300 MHz, DMSO-d_6): δ = 0.99 (t, J = 7.5 Hz, 3H), 2.21 (q, J = 7.5 Hz, 2H), 5.18 (s, 2H), 6.85 (d, J = 8.7 Hz, 2H), 7.08 (d, J = 7.5 Hz, 4H), 7.13–7.7.24 (m, 6H), 7.57 (d, J = 8.7 Hz, 2H), 9.18 (br, 2H, disappeared on D_2O exchange); ^{13}C NMR (75 MHz, DMSO-d_6): δ = 9.6, 27.4, 53.9, 115.2, 116.3, 122.8, 126.6, 127.7, 128.2, 128.3, 132.2, 145.0, 150.5, 175.8; Anal calcd. for $C_{27}H_{23}NO_3$: C, 79.20; H, 5.66; N, 3.42. Found: C, 79.35; H, 5.53; N, 3.51.

*Compound **5h** (Table 2, entry 8)*

IR (KBr): ν_{max} = 3086, 2974, 2883, 2702, 2621, 1626, 1604, 1512, 1438, 1332, 1232, 1161, 1080, 833, 781, 626 cm^{-1}; ^1H NMR (300 MHz, DMSO-d_6): δ = 0.98 (t, J = 7.5 Hz, 3H), 2.18 (q, J = 7.5 Hz, 2H), 5.15 (s, 2H), 6.85 (d, J = 8.7 Hz, 2H), 7.00–7.10 (m, 8H), 7.57 (d, J = 8.7 Hz, 2H), 9.21(br, 2H, disappeared on D_2O exchange); ^{13}C NMR (75 MHz, DMSO-d_6): δ = 9.6, 27.4, 53.2, 114.9, 115.3, 116.1, 122.8, 127.9, 130.2, 132.0, 141.1, 150.6, 162.9, 175.7; Anal calcd. for $C_{27}H_{21}F_2NO_3$: C, 72.80; H, 4.75; N, 3.14. Found: C, 72.91; H, 4.81; N, 3.06.

*Compound **5i** (Table 2, Entry 9)*

IR (KBr): ν_{max} = 3350–2840, 2706, 1631, 1595, 1514, 1460, 1282, 1240, 1051, 831, 744 cm^{-1}; ^1H NMR (300 MHz, DMSO-d_6): δ = 0.99 (t, J = 7.5 Hz, 3H), 2.21 (q, J = 7.5 Hz, 2H), 5.69 (s, 2H), 5.92–6.03 (m, 4H), 6.34 (d, J = 7.9 Hz, 2H), 6.59 (t, J = 7.5 Hz, 2H), 6.99 (d, J = 8.7 Hz, 2H), 7.69 (d, J = 8.7 Hz, 2H), 9.44 (br, 4H, disappeared on D_2O exchange); ^{13}C NMR (75 MHz, DMSO-d_6): δ = 10.2, 28.7, 49.6, 111.3, 114.9, 115.0, 117.6, 122.5, 124.8, 127.9, 128.7, 128.9, 130.7, 151.8, 157.1, 177.3; Anal calcd. for $C_{27}H_{23}NO_5$: C, 73.46; H, 5.25; N, 3.17. Found: C, 73.32; H, 5.15; N, 3.26.

*Compound **5j** (Table 2, entry 10)*

IR (KBr): ν_{max} = 3063, 2980, 2885, 2822, 2650, 1626, 1595, 1512, 1421, 1323, 1269, 1238, 1132, 1074, 881, 835, 787, 690, 632 cm^{-1}; ^1H NMR (300 MHz, DMSO-d_6): δ = 0.98 (t, J = 7.5 Hz, 3H), 2.21 (q, J = 7.5 Hz, 2H), 5.15 (s, 2H), 6.88 (d, J = 8.8 Hz, 2H), 7.11 (d, J = 7.2 Hz, 2H), 7.18–7.24 (m, 4H), 7.37 (d, J = 7.8 Hz, 2H), 7.61 (d, J = 8.8 Hz, 2H), 9.33 (s, 2H, disappeared on D_2O exchange); ^{13}C NMR (75 MHz, DMSO-d_6): δ = 9.6, 27.4, 53.6, 115.3, 115.5, 121.6, 122.7, 127.5, 128.1, 129.5, 130.5, 130.9, 131.8, 147.9, 150.7, 175.7; Anal calcd. for $C_{27}H_{21}Br_2NO_3$: C, 57.17; H, 3.73; N, 2.47. Found: C, 57.23; H, 3.87; N, 2.55.

*Compound **5k** (Table 2, entry 11)*

IR (KBr): ν_{max} = 3065, 2966, 2877, 2793, 2715, 2642, 1624, 1514, 1411, 1329, 1257, 1085, 833, 765, 698 cm^{-1}; ^1H NMR (300 MHz, DMSO-d_6): δ = 0.85 (t, J = 7.4 Hz, 3H), 1.04 (d, J = 7.0 Hz, 3H), 1.34–1.43 (m, 1H), 1.51–1.58 (m, 1H), 2.22–2.28 (m, 1H), 5.18 (s, 2H), 6.86 (d, J = 8.7 Hz, 2H), 7.09 (d, J = 7.4 Hz, 4H), 7.13–7.24 (m, 6H), 7.57 (d, J = 8.7 Hz, 2H), 9.18 (br, 2H, disappeared on D_2O exchange); ^{13}C NMR (75 MHz, DMSO-d_6): δ = 11.9, 17.0, 26.7, 40.6, 53.9, 115.2, 116.3, 122.8, 126.6, 127.7, 128.2, 128.3, 132.2, 145.1, 150.6, 177.9; Anal calcd. for $C_{29}H_{27}NO_3$: C, 79.61; H, 6.22; N, 3.20. Found: C, 79.50; H, 6.35; N, 3.15.

*Compound **5l** (Table 2, entry 12)*

IR (KBr): ν_{max} = 3265–2500, 1626, 1593, 1516, 1410, 1329, 1049, 883, 831, 686 cm^{-1}; ^1H NMR (300 MHz, DMSO-d_6): δ = 0.85 (t, J = 7.4 Hz, 3H), 1.05 (d, J = 7.0 Hz, 3H), 1.34–1.45 (m, 1H), 1.48–1.61 (m, 1H), 2.20–2.26 (m, 7H), 5.14 (s, 2H), 6.84 (d, J = 8.5 Hz, 2H), 6.94–7.03 (m, 8H), 7.55 (d, J = 8.5 Hz, 2H), 9.16 (br, 2H, disappeared on D_2O exchange); ^{13}C NMR (75 MHz, DMSO-d_6): δ = 11.9, 17.0, 21.1, 26.7, 40.71, 53.6, 115.2, 116.5, 122.8, 127.6, 128.3, 128.8, 132.2, 135.5, 142.0, 150.5, 177.9; Anal calcd. for $C_{31}H_{31}NO_3$: C, 79.97; H, 6.71; N, 3.01. Found: C, 80.11; H, 6.59; N, 2.95.

*Compound **5m** (Table 2, entry 13)*

IR (KBr): ν_{max} = 3464–2885, 2681, 1631, 1589, 1512, 1454, 1388, 1313, 1089, 1012, 829, 775, 694 cm^{-1}; ^1H NMR (300 MHz, DMSO-d_6): δ = 5.50 (s, 2H), 6.68–6.75 (m, 10H), 7.00 (d, J = 8.7 Hz, 2H), 7.53 (d, J = 8.1 Hz, 2H), 7.69 (d, J = 8.7 Hz, 2H), 7.93 (d, J = 8.1 Hz, 2H), 9.43 (br, 2H, disappeared on D_2O exchange); ^{13}C NMR (75 MHz, DMSO-d_6): δ = 52.8, 113.7, 114.8, 122.7, 125.7, 126.9, 128.3, 128.8, 128.9, 131.0, 131.5, 131.9, 137.4, 141.9, 151.3, 167.5; Anal calcd. for $C_{31}H_{22}ClNO_3$: C, 75.68; H, 4.51; N, 2.85. Found: C, 75.77; H, 4.58; N, 2.78.

*Compound **5n** (Table 2, entry 14)*

IR (KBr): ν_{max} = 3530–2837, 2714, 2584, 1633, 1591, 1516, 1460, 1394, 1278, 1095, 885, 831, 748 cm^{-1}; ^1H NMR (300 MHz, DMSO-d_6): δ = 5.84 (s, 2H), 5.93 (d, J = 7.5 Hz, 2H), 6.06 (t, J = 7.3 Hz, 2H), 6.43 (d, J = 7.9 Hz, 2H), 6.63 (t, J = 7.5 Hz, 2H), 7.05 (d, J = 8.8 Hz, 2H), 7.50 (d, J = 8.2 Hz, 2H), 7.77 (d, J = 8.8 Hz, 2H), 8.00 (d, J = 8.2 Hz, 2H), 10.00 (br, 4H, disappeared on D_2O exchange); ^{13}C NMR (75 MHz, DMSO-d_6): δ = 49.9, 109.6, 115.0, 115.1, 117.9, 122.4, 123.3, 128.4, 128.5, 128.9, 129.4, 130.3, 131.6, 135.8, 135.9, 152.3, 156.7, 169.9; Anal calcd. for $C_{31}H_{22}ClNO_5$: C, 71.06; H, 4.23; N, 2.67. Found: C, 69.90; H, 4.32; N, 2.75.

*Compound **5o** (Table 2, entry 15)*

IR (KBr): ν_{max} = 3460–2818, 2671, 2521, 1620, 1591, 1539, 1516, 1433, 1388, 1319, 1273, 835, 761, 700 cm^{-1}; 1H NMR (300 MHz, DMSO-d_6): δ = 2.36 (s, 3H), 5.19 (s, 2H), 6.87 (d, J = 8.7 Hz, 2H), 7.09 (d, J = 7.2 Hz, 4H), 7.14–724 (m, 6H), 7.34–7.43 (m, 2H), 7.58 (d, J = 8.7 Hz, 2H), 7.75 (d, J = 8.7 Hz, 2H), 9.20 (br, 2H, disappeared on D_2O exchange); ^{13}C NMR (75 MHz, DMSO-d_6): δ = 21.4, 54.1, 115.3, 122.7, 127.0, 128.1, 128.3, 128.7, 128.8, 129.7, 130.3, 132.1, 132.6, 132.9, 133.4, 138.1, 143.9, 151.0, 168.4; Anal calcd. for $C_{32}H_{25}NO_3$: C, 81.51; H, 5.34; N, 2.97. Found: C, 81.36; H, 5.21; N, 2.90.

*Compound **5p** (Table 2, entry 16)*

IR (KBr): ν_{max} = 3489–2816, 2677, 1626, 1602, 1512, 1379, 1319, 1226, 1163, 835, 761 cm^{-1}; ^1H NMR (300 MHz, DMSO-d_6): δ = 2.36 (s, 3H), 5.18 (s, 2H), 6.88 (d, J = 8.7 Hz, 2H), 7.01–7.11 (m, 8H), 7.34–7.43 (m, 2H), 7.59 (d, J = 8.7 Hz, 2H), 7.76 (d, J = 8.6 Hz, 2H), 9.20 (br, 2H, disappeared on D_2O exchange); ^{13}C NMR (75 MHz, DMSO-d_6): δ = 21.3, 53.2, 114.7, 115.3, 115.8, 122.7, 126.9, 127.9, 128.8, 130.1, 130.2, 131.7, 131.9, 133.7, 138.2, 140.7, 150.7, 162.9, 168.1; Anal calcd. for $C_{32}H_{23}F_2NO_3$: C, 75.73; H, 4.57; N, 2.76. Found: C, 75.52; H, 4.63; N, 2.70.

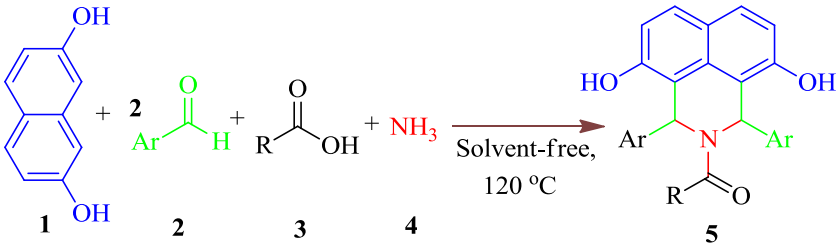
*N-((2,7-Dihydroxynaphthalen-1-yl)(phenyl)methyl)benzamide (Compound **6**)*

IR (KBr): ν_{max} = 3425, 3225–2550, 1629, 1580, 1518, 1323, 1219, 1060, 837, 727, 638 cm^{-1}; ^1H NMR (300 MHz, DMSO-d_6): δ = 6.90 (s, 1H), 7.02 (d, J = 8.6 Hz, 1H), 7.15–7.21 (m, 2H), 7.26–7.38 (m, 4H), 7.47–7.56 (m, 4H), 7.68 (t, J = 8.6 Hz, 2H), 7.87 (d, J = 7.0 Hz, 2H), 9.01 (s, 1H), 9.76 (s, 1H), 10.33 (s, 1H); ^{13}C NMR (75 MHz, DMSO-d_6): δ = 49.9, 104.7, 115.7, 117.7, 123.5, 126.9, 127.0, 127.4, 127.9, 128.7, 129.1, 129.7, 130.8, 131.9, 134.6, 134.8, 142.7, 153.9, 156.9, 166.0; Anal calcd. for $C_{24}H_{19}NO_3$: C, 78.03; H, 5.18; N, 3.79. Found: C, 77.90; H, 5.25; N, 3.68.

Results and discussion

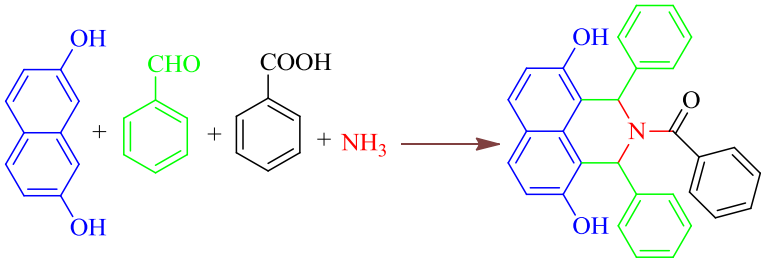
We recently reported a simple and efficient method of synthesis of 1,3-diphenyl-2-azaphenalene [29] and *N*-acyl-1,3-diphenyl-2-azaphenalene derivatives [30] via a Betti-type reaction in which 2-naphthol was replaced by 2,7-naphthalenediol. These good results prompted us to further investigate the reaction of aldehydes, 2,7-naphthalenediol, and ammonia. In continuation of our efforts to develop synthetic methods for important transformations [31–34], we now report a simple and efficient procedure for synthesis of new *N*-acyl-1,3-diaryl-2-azaphenalene derivatives by condensation of 2,7-naphthalenediol, aromatic aldehydes, carboxylic acids, and aqueous ammonia (25 %) under solvent-free conditions (Scheme 1).

To optimize the reaction conditions, reaction of benzaldehyde **2a** (1 mmol), 2,7-naphthalenediol **1**, benzoic acid **3a**, and aqueous ammonia (25 %) was used as a model, and was conducted under different reaction conditions, for example solvent and temperature. Initially, the model reaction was conducted in several solvents (ethanol, chloroform, 1,4-dioxane, tetrahydrofuran, dimethylformamide, and toluene) and under solvent-free conditions to investigate the effect of solvents. As shown in Table 1, it was found that conventional heating (at 120 °C) under solvent-free conditions is more efficient than use of organic solvents in respect of reaction time and yield of the desired azaphenalene **5a** (Table 1, entry 9). When the same reaction was conducted at room temperature or at 70 °C, yields were low. Increasing the reaction temperature to 140 °C did not increase yield of the product (Table 1).



Scheme 1 Synthesis of *N*-acyl-1,3-diphenyl-2-azaphenalene derivatives

Table 1 Optimization of the conditions for synthesis of *N*-benzoyl-1,3-diphenyl-4,9-dihydroxy-2,3-dihydro-2-azaphenalene (Table 2, entry 1)



Entry	Solvent	Conditions	Time (h)	Yield (%)[a]
1	EtOH	Reflux	10	86
2	$CHCl_3$	Reflux	10	<10
3	1,4-Dioxane	Reflux	10	35
4	THF	Reflux	10	15
5	DMF	Reflux	10	0
6	Toluene	Reflux	10	<10
7	Solvent-free	RT	5	0
8	Solvent-free	70 °C	1	23
9	Solvent-free	120 °C	0.25	89
10	Solvent-free	140 °C	0.25	85

Benzaldehyde (2 mmol), 2,7-naphthalenediol (1 mmol), benzoic acid (1.2 mmol), and aqueous ammonia (0.2 mL, 25 %)

[a] Isolated yields

Reaction of 2,7-naphthalenediol with a variety of aromatic aldehydes, benzoic acid, and ammonia was performed under solvent-free conditions at 120 °C and afforded the corresponding *N*-acyl-1,3-diaryl-2-azaphenalene derivatives in good to high yields (Table 2). The scope of the reaction with regard to aromatic aldehydes was examined, and it was found that substituents, for example electron-withdrawing groups and electron-donating groups, could tolerate the reaction conditions. However, when aliphatic aldehydes, for example propionaldehyde and isobutyraldehyde, were used in

Table 2 Synthesis of *N*-acyl-1,3-diaryl-2-azaphenalene derivatives under solvent-free conditions

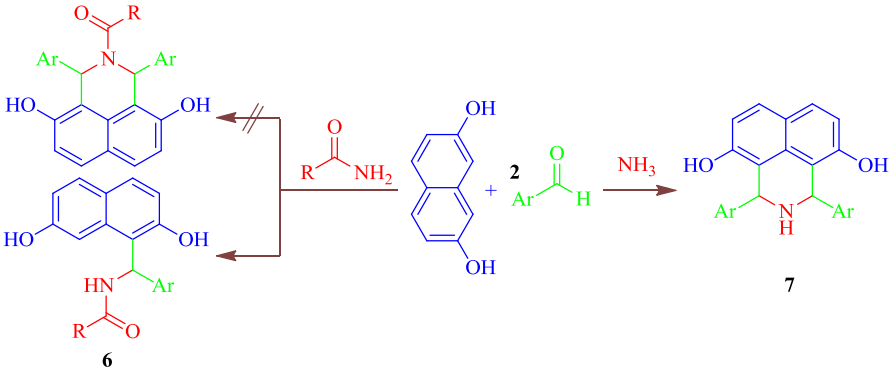
Entry	Ar (2)	R (3)	Product	Time (min)	Yield (%)[a]	M.p. (°C)	
						Found	Reported [Ref.]
1	C_6H_5	C_6H_5	**5a**	15	89	215–217	214–215 [30]
2	3-$NO_2C_6H_4$	C_6H_5	**5b**	20	80	198–199	–
3	4-ClC_6H_4	C_6H_5	**5c**	15	87	218–220	219–221 [30]
4	C_6H_5	CH_3	**5d**	10	88	208–209	207–208 [30]
5	3-BrC_6H_4	CH_3	**5e**	10	90	217–219	219–220 [30]
6	4-OHC_6H_4	CH_3	**5f**	15	82	216–217	–
7	C_6H_5	CH_3CH_2	**5g**	10	85	212–214	–
8	4-FC_6H_4	CH_3CH_2	**5h**	15	79	200–201	–
9	2-OHC_6H_4	CH_3CH_2	**5i**	15	83	248–250	–
10	3-BrC_6H_4	CH_3CH_2	**5j**	10	80	180–181	–
11	C_6H_5	$CH_3CH_2CH(CH_3)$	**5k**	10	87	200–202	–
12	4-MeC_6H_4	$CH_3CH_2CH(CH_3)$	**5l**	15	74	190–191	–
13	C_6H_5	4-ClC_6H_4	**5m**	15	80	231–232	–
14	2-OHC_6H_4	4-ClC_6H_4	**5n**	15	81	262–263	–
15	C_6H_5	3-MeC_6H_4	**5o**	10	74	203–205	–
16	4-FC_6H_4	3-MeC_6H_4	**5p**	10	72	218–220	–

[a] Isolated yields

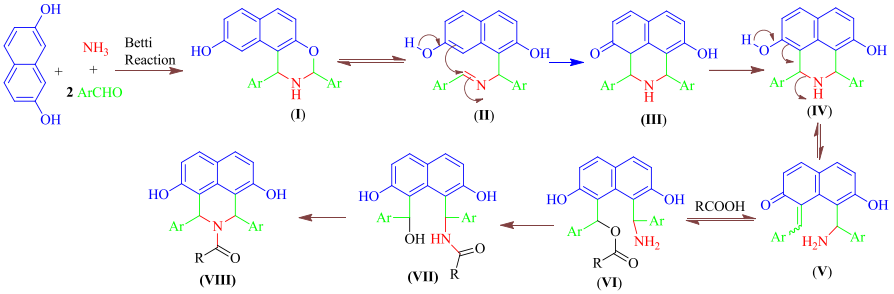
this procedure under the above optimized conditions, only trace amounts of product were detected.

To investigate the generality of the reaction, different aldehydes with either electron-donating or electron-withdrawing groups were reacted with structurally and electronically diverse carboxylic acids, 2,7-naphthalenediol, and aqueous ammonia (25 %) under the optimized reaction conditions; the results are summarized in Table 2. All reactions proceeded efficiently at 120 °C and the desired products were obtained in good to high yields (72–90 %) in relatively short reaction times, without formation of any side products. As is apparent from Table 2, the procedure was highly effective and the nature of substituents on the aromatic ring of aldehydes did not have obvious effects in terms of yields and times under the reaction conditions.

To study mechanistic aspects of this multi-component reaction, reaction of benzaldehyde with 2,7-naphthalenediol, benzoic acid, and ammonia was used as model reaction. First, we attempted to explain the reaction on the basis of formation of benzamide from ammonia and benzoic acid at 120 °C. Therefore, reaction of 2,7-naphthalenediol with benzaldehyde, and benzamide was performed under solvent-free conditions at 120 °C, similar to use of 2-naphthol in the synthesis of amidoalkyl naphthols [35–37], but the reaction was unsuccessful and only the corresponding amidoalkyl naphthol **6** was obtained (Scheme 2). When reaction of 2,7-naphthalenediol, benzaldehyde, and ammonia under solvent-free conditions at 120 °C was investigated 1,3-diaryl-2-azaphenalene derivatives **7** were obtained as isolable intermediates [29] (Scheme 2).



Scheme 2 Condensation of 2,7-naphthalenediol and aldehyde with amide or ammonia



Scheme 3 A plausible mechanism for synthesis of *N*-acyl-1,3-diaryl-2-azaphenalene derivatives

These results suggest formation of the desired products can be explained on the basis of the Betti reaction [13]. 2,7-Naphthalenediol may produce naphthoxazine **I** or isomeric Schiff base **II**, similar to 2-naphthol in the Betti reaction. Because of the tautomerism of these condensation products [15, 16], the Schiff base intermediate furnished the 1,3-diaryl-2-azaphenalene derivatives on intermolecular cyclization and keto–enol tautomerization (Scheme 3). This intermediate **IV** can be converted to intermediate **V** and reacted with benzoic acid to produce intermediate **VI** (an explanation of this behavior might be that the aromatic Mannich reaction is a reversible reaction [38]). Finally the expected products **VIII** were afforded by intermolecular acylation of **VI** and intermolecular ring-closure reaction of intermediate **VII**.

Conclusion

In conclusion, we have described a new, efficient, one-pot method for synthesis of *N*-acyl-1,3-diaryl-2-azaphenalene derivatives by five-component cyclo-condensation reaction of 2,7-naphthalenediol, aromatic aldehydes, carboxylic acids, and

aqueous ammonia (25 %) under solvent-free conditions at 120 °C. In addition to the efficiency and simplicity of this catalyst-free procedure, advantages include ease of workup, good to high yields of products, and environmental friendliness.

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