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Eco-friendly Synthesis of 2-(3*H*-Imidazo[4,5-*b*]pyridin-2-yl)-*N*-phenylbenzamides

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Eco-friendly synthesis of 2-(3*H*-imidazo[4,5-*b*]pyridin-2-yl)-*N*-phenylbenzamide derivatives from diethylphthalate, anilines and pyridine-2,3-diamine was described by one-pot three component method *via* green approaches. Phosphoric acid has been used as an effective catalyst for this kind of one-pot three component reaction. This reaction takes short time, easy workup and gives excellent yields in glycerol medium.

Keywords: Glycerol, Diethylphthalate, Anilines, Pyridine-2,3-diamine, Green approaches.

INTRODUCTION

Green chemistry forced deep change to meet the chemical reactions environmentally begin [1]. It shows that degradable, non-toxic and environmentally safe solvent [2] like glycerol and water [3-5]. Glycerol is a green, biodegradable and low toxic solvent [6]. It has a high boiling point, thus chemical reactions performed at high temperature for creating acceleration of reaction in the synthesis of biologically active compounds. Due to these unique properties, we used glycerol as solvent in the synthesis of 2-(3*H*-imidazo[4,5-*b*]pyridin-2-yl)-*N*-phenylbenzamidederivatives.

Pyridomidazole derivatives have significant biological activities, such as anticancer [7], tuberculostatic [8], antiviral [9] and antimitotic [10] activities. Due to these results, herein we are reporting the synthesis of 2-(3*H*-imidazo[4,5-*b*]pyridin-2-yl)-*N*-phenylbenzamidederivatives form diethyl phthalate with anilines and pyridine-2,3-diamine as new chemical entities in glycerol.

EXPERIMENTAL

Melting points were uncorrected and found in H_2SO_4 bath in open capillary tubes. TLC was run on silica gel-G and visualizations were found using UV light. Infrared spectra were done by instrument Perkin 1000 in KBr pellets. ^{1}H NMR spectra were recorded using TMS as standard in DMSO-d_6 with 400 MHz. Mass spectra were recorded by Agilent insrument. Starting materials were received from commercial sources and treated as such for reactions.

Procedure for synthesis of 2-(3*H*-imidazo[4,5-b]pyridin-2-yl)-N-phenylbenzamide (4) from diethyl phthalate (1), aniline (2) and pyridine 2,3-diamine (3) by one-pot reaction: Charged **1** (5 mmol), **2** (5 mmol) and **3** (5 mmol) in glycerol (20 mL) and heated at 100 ºC for 120-150 min in the presence of H_3PO_4 (5 mmol). Reaction progress was monitored by TLC. After completion of the reaction added water (50 mL) and stirred for 10-15 min to separate out colourless solid from the reaction mixture which was collected by filtration. The isolated solid was washed with water (10 mL) twice and dried at 50 ºC under above 650 mmHg vaccum for 10-12 h. The crude compound was purified by recrystallization method using methanol as a solvent to get desired compound **4** (**Scheme-I**).

Synthesis of ethyl 2-(phenylcarbamoyl)benzoate (5): Charged compounds **1** (5 mmol) and **2a** (5 mmol) in glycerol (20 mL) and heated at 100 ºC for 20 min in the presence of H_3PO_4 (5 mmol). Reaction progress was monitered by TLC. After completion of the reaction added water (50 mL) and stirred for 10-15 min to separate out colourless solid from the reaction mixture, which was collected by filtration. The isolated solid was washed with water (10 mL) twice and dried at 50 ºC under above 650 mmHg vaccum for 10-12 h. The crude compound was purified by recrystallization method using methanol as a solvent to get desired compound **5**.

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Procedure for synthesis of compound 4a by step-wise synthesis: Charged compounds **5** (5 mmol) and **3** (5 mmol) in glycerol (20 mL) and heated at 100 ºC for 120 min in the presence of H_3PO_4 (5 mmol). Reaction progress was monitered by TLC. After completion of the reaction added water (50 mL) and stirred for 10-15 min to separate out colourless solid from the reaction mixture, which was collected by filtration. The isolated solid was washed with water (10 mL) twice and dried at 50 ºC under above 650 mmHg vaccum for 10-12 h. The crude compound was purified by recrystallization using methanol as a solvent to get desired compound **4a**.

Synthesis of compound 6: Charged compounds **1** (5 mmol) and **3** (5 mmol) in glycerol (20 mL) and heated at 100 ºC for 20 min in the presence of H_3PO_4 (5 mmol). Reaction progress was monitered by TLC. After completion of the reaction added water (50 mL) and stirred for 10-15 min to separate out colourless solid from the reaction mixture which was collected by filtration. The isolated solid was washed with water (10 mL) twice and dried at 50 ºC under above 650 mmHg vaccum for 10-12 h. The crude compound was purified by recrystallisation method using methanol as a solvent to get desired compound **6**.

Procedure for synthesis of compound 4a by step-wise synthesis: Charged compounds **6** (5 mmol) and compound **2a** (5 mmol) in glycerol (20 mL) heated at 100 ºC for 120 min in the presence of H_3PO_4 (5 mmol). Reaction progress was monitered by TLC. After completion of the reaction added water (50 mL) and stirred for 10-15 min to separate out colourless solid from the reaction mixture which was collected by filtration. The isolated solid was washed with water (10 mL) twice and dried at 50 ºC under above 650 mmHg vaccum for 10-12 h. The crude compound was purified by recrystallization method using methanol as a solvent to get desired compound **4a**.

Spectral data

2-(3*H*-Imidazo[4,5-*b*]pyridin-2-yl)-*N*-phenylbenzamide (4a): Yield: 89 %, m.p. > 220 ºC; IR (KBr, ν_{max}, cm^{-1}): 3051-3434 (br, medium, -NH-), 1655 (s, strong, -CO-NH-). ^{1}H NMR (400 MHz, DMSO-d_6, TMS): δ 7.0-7.9 (m, 12H, arom.-H), 10.4 (s, 1H, -NH-), 12.6 (s, 1H, -NH-). ^{13}C NMR (100 MHz, DMSO-d_6): δ 115.3, 120.2, 121.8, 123.2, 127.3, 128.5, 128.9, 129.0, 129.0, 130.5, 130.7, 133.2, 135.6, 137.6, 138.7, 150.9, 151.0, 167.6; M^+.1 = 315. Anal. calcd. (found) (%) for $C_{19}H_{14}N_4O$ (314.34): C, 72.60 (72.63); H, 4.49 (4.45); N, 17.82 (17.87.

2-(3*H*-Imidazo[4,5-*b*]pyridin-2-yl)-*N*-(4-chlorophenyl)-benzamide (4b): Yield: 80 %, m.p. > 220 ºC; IR (KBr, ν_{max}, cm^{-1}): 3032-3357 (br, medium, -NH-), 1691 (s, strong, -CO-NH-). ^{1}H NMR (400 MHz, DMSO-d_6, TMS): δ 7.0-7.9 (m, 11H, arom.-H), 10.4 (s, 1H, -NH-), 12.6 (s, 1H, -NH-). ^{13}C NMR (100 MHz, DMSO-d_6): 114.3, 121.6, 121.8, 123.4, 127.5, 128.3, 128.7, 130.2, 131.6, 131.9, 134.1, 134.2,136.7,139.7, 151.3, 169.3; M^+.1 = 349. Anal. calcd. (found) (%) for $C_{19}H_{13}N_4OCl$ (348.79): C, 65.43 (65.49); H, 3.76 (3.79); N, 16.06 (16.02).

2-(3*H*-Imidazo[4,5-*b*]pyridin-2-yl)-*N*-(4-methylphenyl)-benzamide (4c): Yield: 80 %, m.p. > 220 ºC; IR (KBr, ν_{max}, cm^{-1}): 3035-3358 (br, medium, -NH-), 1699 (s, strong, -CO-NH-). ^{1}H NMR (400 MHz, DMSO-d_6, TMS): δ 2.2 (s, 3H, -CH_3), 7.0-7.9 (m, 11H, arom.-H), 10.4 (s, 1H, -NH-), 12.6 (s, 1H, -NH-). ^{13}C NMR (100 MHz, DMSO-d_6): 23.3, 114.7, 121.6, 121.9, 123.8, 127.4, 128.6, 128.9, 130.1, 131.4, 131.6, 134.3, 134.8, 136.8, 139.7, 151.4, 169.2; M^+.1 = 329. Anal. calcd. (found) (%) for $C_{20}H_{16}N_4O$ (328.37): C, 73.15 (73.10); H, 4.91 (4.96); N, 17.06 (17.09).

2-(3*H*-Imidazo[4,5-*b*]pyridin-2-yl)-*N*-(2-methylphenyl)-benzamide (4d): Yield: 83 %, m.p. > 220 ºC; IR (KBr, ν_{max}, cm^{-1}): 3045-3450 (br, medium, -NH-), 1658 (s, strong, -CO-NH-). ^{1}H NMR (400 MHz, DMSO-d_6, TMS): δ 2.3 (s, 3H, -CH_3), 7.0-7.9 (m, 11H, arom.-H), 10.4 (s, 1H, -NH-), 12.6 (s, 1H, -NH-); ^{13}C NMR (100 MHz, DMSO-d_6): 22.3, 116.5, 119.5, 123.5, 127.6, 128.9, 128.9, 130.1, 131.2, 131.3, 134.3, 134.4, 136.8, 139.7, 151.2, 169.4; M^+.1 = 329. Anal. calcd. (found) (%) for $C_{20}H_{16}N_4O$ (328.37): C, 73.15 (73.11); H, 4.91 (4.90); N, 17.06 (17.03).

2-(3*H*-Imidazo[4,5-*b*]pyridin-2-yl)-*N*-(4-bromophenyl)-benzamide (4e): Yield: 84 %, m.p. > 220 ºC; IR (KBr, ν_{max}, cm^{-1}): 3045-3459 (br, medium, -NH-), 1690 (s, strong, -CO-NH-). ^{1}H NMR (400 MHz, DMSO-d_6, TMS): δ 7.0-7.9 (m, 11H, arom.-H), 10.4 (s, 1H, -NH-), 12.6 (s, 1H, -NH-). ^{13}C NMR (100 MHz, DMSO-d_6): 114.2, 121.3, 121.8, 123.2, 127.4, 128.6, 128.9, 129.0, 129.2, 130.5, 130.6, 133.2, 135.7, 137.3, 138.6, 150.8, 151.0, 168.6; M^+.1 = 393. Anal. calcd. (found) (%) $C_{19}H_{13}BrN_4O$ (393.24): C, 58.03 (58.08); H, 3.33 (3.30); N, 14.25 (14.29).

2-(3*H*-Imidazo[4,5-*b*]pyridin-2-yl)-*N*-(4-iodophenyl)-benzamide (4f): Yield: 80 %, m.p. > 220 ºC; IR (KBr, ν_{max}, cm^{-1}): 3038-3429 (br, medium, -NH-), 1690 (s, strong, -CO-NH-); ^{1}H NMR (400 MHz, DMSO-d_6, TMS): δ 7.0-7.9 (m, 11H, arom.-H), 10.4 (s, 1H, -NH-), 12.6 (s, 1H, -NH-). ^{13}C NMR (100 MHz, DMSO-d_6): 114.2, 121.6, 121.9, 123.3, 127.3, 128.3, 128.5, 129.0, 129.1, 130.5, 130.8, 133.2, 135.7, 137.5, 138.7, 150.8, 151.1, 169.5; M^+.1 = 441. Anal. calcd. (found) (%) for $C_{19}H_{13}N_4OI$ (440.24): C, 51.84 (51.89); H, 2.98 (2.91); N, 12.73 (12.79).

2-(3*H*-Imidazo[4,5-*b*]pyridin-2-yl)-*N*-(4-methoxyphenyl)benzamide (4g): Yield: 82 %, m.p. > 220 ºC; IR (KBr, ν_{max}, cm^{-1}): 3040-3463 (br, medium, -NH-), 1655 (s, strong, -CO-NH-). ^{1}H NMR (400 MHz, DMSO-d_6, TMS): δ 3.7 (s, 3H, -OCH_3), 7.0-7.9 (m, 11H, arom.-H), 10.4 (s, 1H, -NH-), 12.6 (s, 1H, -NH-). ^{13}C NMR (100 MHz, DMSO-d_6): 55.8, 118.3, 120.2, 121.4, 123.6, 127.5, 128.4, 128.9, 129.0, 129.1, 130.6, 130.8, 133.1, 136.5, 137.1, 138.8, 150.9, 151.2, 167.7; M^+.1 = 345. Anal. calcd. (found) (%) for $C_{20}H_{16}N_4O_2$ (344.37): C, 69.76 (69.79); H, 4.68 (4.61); N, 16.27 (16.20).

2-(3*H*-Imidazo[4,5-*b*]pyridin-2-yl)-*N*-(2-hydroxyphenyl)benzamide (4h): Yield: 82 %, m.p. > 220 ºC; IR (KBr, ν_{max}, cm^{-1}): 3048-3458 (br, medium, -NH-), 1695 (s, strong, -CO-NH-). ^{1}H NMR (400 MHz, DMSO-d_6, TMS): δ 7.0-7.9 (m, 11H, arom.-H), 8.30 (s, 1H, -OH), 10.4 (s,1H, -NH-), 12.6 (s, 1H, -NH-); ^{13}C NMR (100 MHz, DMSO-d_6): 115.1, 120.2, 121.7, 123.3, 127.5, 128.5, 128.9, 129.0, 129.0, 130.6, 130.6, 133.1, 135.6, 137.4, 138.9, 150.9, 151.0, 167.4; M^+.1 = 331. Anal. calcd. (found) (%) for $C_{19}H_{14}N_4O_2$ (330.34): C, 69.08 (69.02); H, 4.27 (4.21); N, 16.96 (16.92).

2-(3*H*-Imidazo[4,5-*b*]pyridin-2-yl)-*N*-(4-nitrophenyl)-benzamide (4i): Yield: 82 %, m.p. > 220 ºC; IR (KBr, ν_{max}, cm^{-1}): 3045-3455 (br, medium, -NH-), 1694 (s, strong, -CO-NH-). ^{1}H NMR (400 MHz, DMSO-d_6, TMS): δ 7.0-7.9 (m, 11H, arom.-H), 10.4 (s, 1H, -NH-), 12.6 (s, 1H, -NH-). ^{13}C NMR (100 MHz, DMSO-d_6): 114.8, 120.1, 121.7, 122.3, 127.5, 128.5, 128.8, 129.5, 129.8, 130.2, 130.5, 132.5, 136.7, 137.9, 138.9, 150.6, 151.2, 168.4; M^+.1 = 360. Anal. calcd. (found) (%) for $C_{19}H_{13}N_5O_3$ (359.34): C, 63.51 (63.56); H, 3.65 (3.69); N, 19.49 (19.42).

2-(3*H*-Imidazo[4,5-*b*]pyridin-2-yl)-*N*-(2-nitrophenyl)-benzamide (4j): Yield: 82 %, m.p. > 220 ºC; IR (KBr, ν_{max}, cm^{-1}): 3043-3478 (br, medium, -NH-), 1695 (s, strong, -CO-NH-). ^{1}H NMR (400 MHz, DMSO-d_6, TMS): δ 7.0-7.9 (m, 11H, arom.-H), 10.4 (s, 1H, -NH-), 12.6 (s, 1H, -NH-). ^{13}C NMR (100 MHz, DMSO-d_6): 115.1, 120.1, 121.4, 123.8, 127.4, 128.8, 128.9, 129.2, 129.8, 130.3, 130.5, 132.2, 136.4, 137.1, 138.2, 139.2, 139.3, 151.8, 168.8; M^+.1 = 360. Anal. calcd. (found) (%) for $C_{19}H_{13}N_5O_3$ (359.34): C, 63.51 (63.58); H, 3.65 (3.68); N, 19.49 (19.40).

2-(3*H*-Imidazo[4,5-*b*]pyridin-2-yl)-*N*-(2-chlorophenyl)-benzamide (4k): Yield: 82 %, m.p. > 220 ºC; IR (KBr, ν_{max}, cm^{-1}): 3041-3459 (br, medium, -NH-), 1699 (s, strong, -CO-NH-). ^{1}H NMR (400 MHz, DMSO-d_6, TMS): δ 7.0-7.9 (m, 11H, arom.-H), 10.4 (s, 1H, -NH-), 12.6 (s, 1H, -NH-). ^{13}C NMR (100 MHz, DMSO-d_6): 115.2, 120.3, 121.7, 123.6, 127.5, 128.6, 128.9, 129.21, 129.3, 130.3, 130.8, 132.2, 136.4, 137.2, 138.4, 139.0, 139.6, 151.9, 168.6; M^+.1 = 350. Anal. calcd. (found) (%) for $C_{19}H_{13}N_4OCl$ (348.79): C, 65.43 (65.47); H, 3.76 (3.71); N, 16.06 (16.01).

2-(3*H*-Imidazo[4,5-*b*]pyridin-2-yl)-*N*-(4-fluorophenyl)-benzamide (4l): Yield: 82 %, m.p. > 220 ºC; IR (KBr, ν_{max}, cm^{-1}): 3044-3455 (br, medium, -NH-), 1693 (s, strong, -CO-NH-). ^{1}H NMR (400 MHz, DMSO-d_6, TMS): δ 7.0-7.9 (m, 11H, arom.-H), 10.32 (s, 1H, -CO-NH-), 12.29 (s, 1H, -NH-). ^{13}C NMR (100 MHz, DMSO-d_6): 115.3, 120.2, 121.5, 123.4, 127.4, 128.6, 128.8, 129.2, 129.3, 130.3, 130.9, 132.2, 136.4, 137.2, 138.4, 139.2, 139.6, 151.8, 168.2; M^+.1 = 333. Anal. calcd. (found) (%) for $C_{19}H_{13}N_4OF$ (332.33): C, 68.67 (68.62); H, 3.94 (3.99); N, 16.86 (16.81).

RESULTS AND DISCUSSION

Initially, using one-pot three component reaction of diethyl phthalate (**1**) with aniline (**2a**) and pyridine-2,3-diamine (**3**) as a model for synthesis of 2-(3*H*-imidazo[4,5-*b*]pyridin-2-yl)-*N*-phenylbenzamide derivative (**4a**), we examined the suitable solvents like glycerol, polyethylene glycol-600, ethylene glycol, DMSO and DMF at different temperature in the presence of 1eq. H_3PO_4 as catalyst. Results were summarised in Table-1. Lower and higher temperature gave low yield in formation of compound **4a** (Table-1, entry No. 1 & 3). However, formation of compound **4a** by one-pot three component reaction in glycerol at 100 ºC for 120 min gave excellent yield 89% compare to other conditions (Table-1, entry No. 2). The structure of compound **4a** was confirmed by NMR, IR and mass spectra.

Further studies carried out that changing catalyst like H_2SO_4 and CH_3COOH for formation of compound **4a** by using compounds **1**, **2a** and **3**. By using H_2SO_4 and CH_3COOH as catalyst for this reaction, low yield was obtained and results are summarized in Table-1, entry No. 12 and 13.

In the continuous efforts for the optimization of this one-pot three component reaction, different catalyst amount was used like 0.5 eq. ,1 eq. and 2 eq. of H_3PO_4 and optimized as 1 eq. of H_3PO_4. However, formation of compound **4a** in glycerol as solvent at 100 ºC in the presence of 1 eq. of H_3PO_4 gave excellent yield. The results are summarized in Table-1.

Having the optimized one-pot three component reaction conditions in hand, we explored the scope and limitations with series of substituted anilines **2a-l**. It was found that both electron-deficient and electron-rich anilines were applicable for this optimized conditions affording the corresponding benzothiazole derivatives yields 85-89 %. Results are summarized in Table-1.

Encouraged by these results, synthesis of compounds **4a-l** were carried out in one-pot three component reaction by using compounds **1**, **2a-l** and **3** in glycerol at 100 ºC in the presence of 1 eq. H_3PO_4 for 120 min (**Scheme-I**) with excellent yields 85-89%. Structures of compounds were confirmed by NMR, IR and mass spectra.

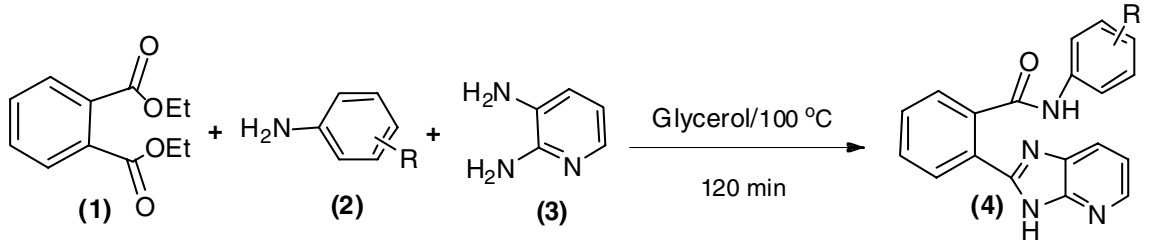
Mechanisms: Plausible mechanisms for formation of compound **4** from compounds **1**, **2** and **3** by one-pot three component reactions have been designed in Mechanism-1 and Mechanism-2.

In mechanism-1 (**Scheme-II**), diethyl phthalte (**1**) was reacted with aniline (**2**) in the presence of 1 eq. of H_3PO_4 in glycerol gave intermediate 2-phenylisoindoline-1,3-dione (**5**). Then, compound **5** was converted as desired product **4** by reacting with pyridine-2,3-diamine (**3**). Confirmation for the above stated mechanism gives from the fact that intermediate **5** was obtained separately by reaction of compounds **1** and **2**. After that reacted with compound **3** in glycerol to give compound **4**.

In second plausible mechanism-2 (**Scheme-III**), diethyl phthalate (**1**) reacted with pyridine-2,3-diamine (**3**) to form

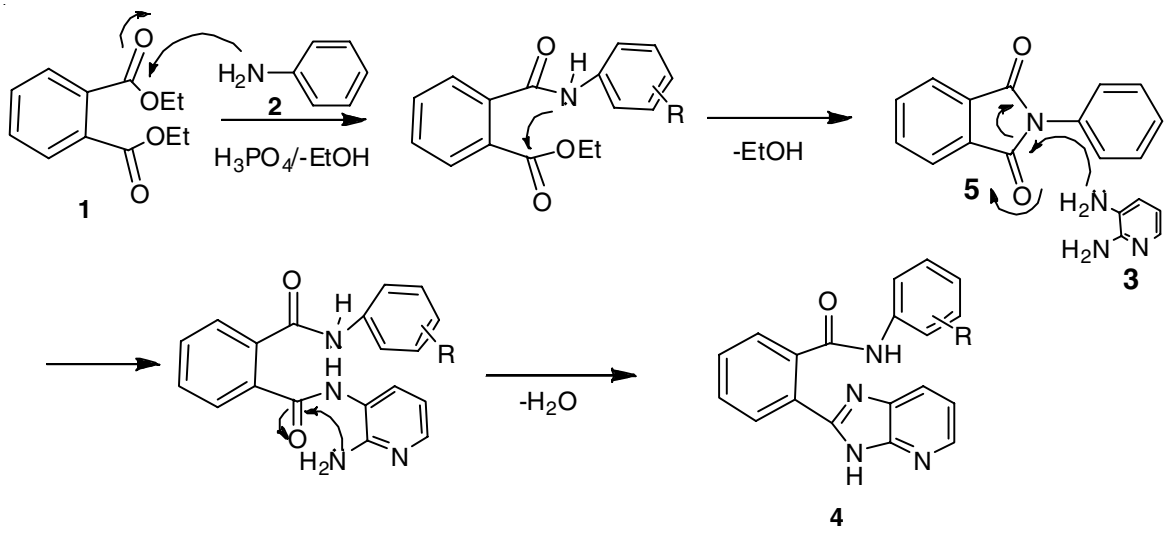
TABLE-1
OPTIMIZATION OF REACTION CONDITION

S. No.	Solvent	Temp. (°C)	Catalyst	Time (h)	Yield (%)
1	Glycerol	Room temp.	1 eq. of H_3PO_4	5.0	–
2	Glycerol	100	1 eq. of H_3PO_4	2.0	89
3	Glycerol	150	1 eq. of H_3PO_4	2.0	78
4	PEG-600	Room temp.	1 eq. of H_3PO_4	5.0	–
5	PEG-600	100	1 eq. of H_3PO_4	2.5	75
6	Ethylene glycol	Room temp.	1 eq. of H_3PO_4	5.0	–
7	Ethylene glycol	100	1 eq. of H_3PO_4	2.5	78
8	DMF	Room temp.	1 eq. of H_3PO_4	5.0	15
9	DMF	100	1 eq. of H_3PO_4	1.5	60
10	DMSO	Room temp.	1 eq. of H_3PO_4	5.0	–
11	DMSO	100	1 eq. of H_3PO_4	2.0	60
12	Glycerol	100	1 eq. of H_2SO_4	2.0	78
13	Glycerol	100	1 eq. of CH_3COOH	3.0	80
14	Glycerol	100	0.5 eq. of H_3PO_4	3.0	78
15	Glycerol	100	2 eq. of H_3PO_4	1.5	75



R = -H, -Cl(*p*), -CH_3(*p*), - CH_3(*o*), -Br(*p*), -I (*p*), -OCH_3(*p*), - OH(*p*), -NO_2(*p*), -NO_2(*m*), -Cl(*o*), -F(*p*).
(2) (2a) (2b) (2c) (2d) (2e) (2f) (2g) (2h) (2i) (2j) (2K) (2l)

Scheme-I: Synthesis of **4a-4l** by one-pot synthesis in glycerol

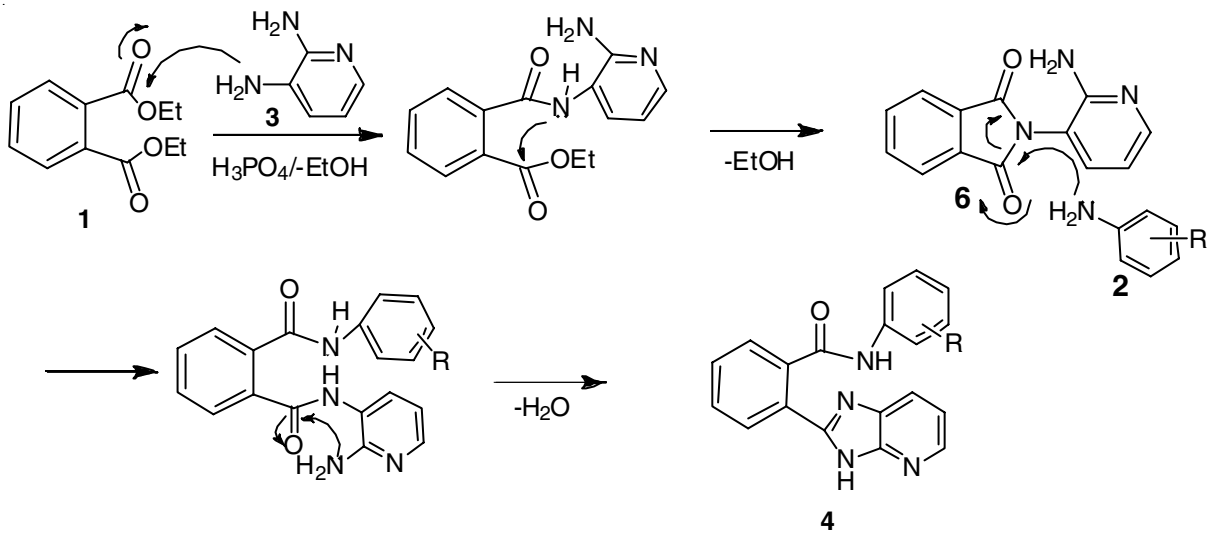


Scheme-II: Mechanism-1

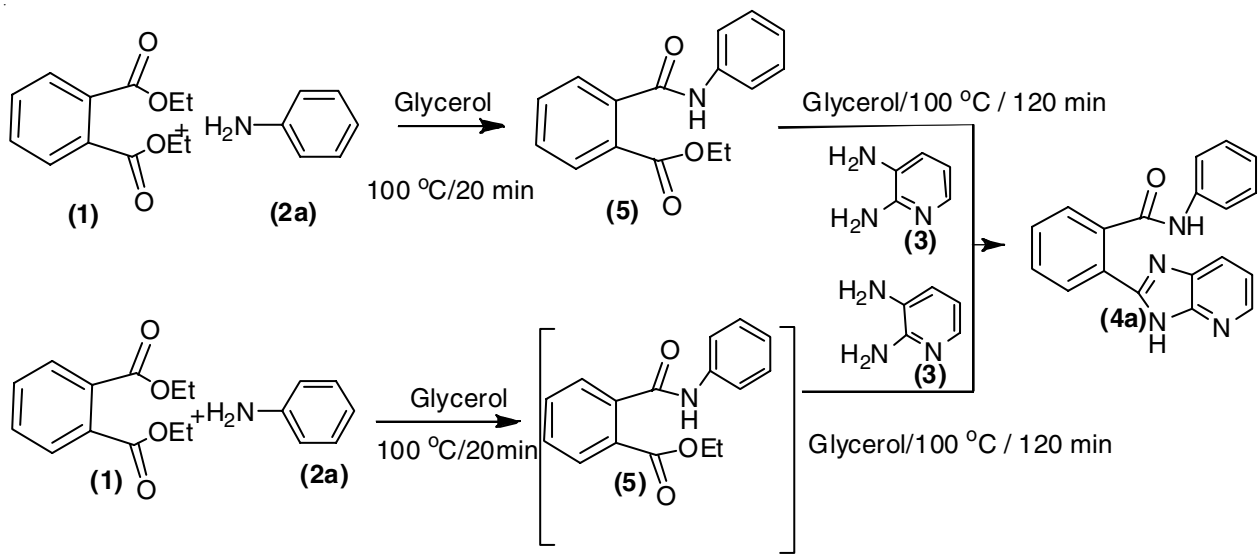
an intermediate 2-(2-aminopyridin-3-yl)isoindoline-1,3-dione (**6**). Then, this intermediate **6** was reacted with aniline (**2**) to form desired product **4**. Confirmation for the above mechanism stated that intermediate **6** was obtained separately by reaction of compounds **1** and **3**. Then reacted with compound **2** in glycerol to give compound **4**.

The difference between above two plausible mechanisms for formation of compound **4** stated that mechanism-1 involves a prior reaction of compounds **1** and **2** followed by condensation with compound **3** whereas mechanism-2 involves reaction of compound **1** with compound **3** followed by condensation of compound **2**.

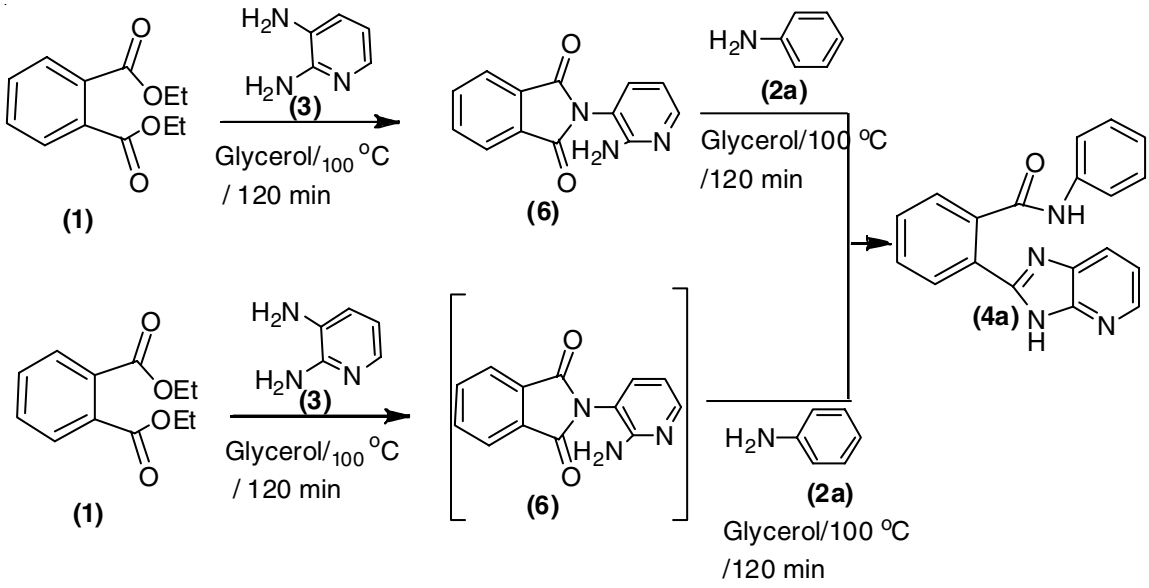
Alternative synthesis of compound 4 (Route-1): By using optimized condition, compound **4a** has been synthesized *via* step-wise and Tadam synthesis also with condensation of diethyl-phthalate (**1**) and anilines (**2a**) in glycerol to form 2-(arylcarbamoyl)benzoic acids (**5a**) as intermediates in the presence of H_3PO_4 at 100 ºC for 20 min [11-14]. Then, com-



Scheme-III: Mechanism-2



Scheme-IV: Synthesis of **4** by step-wise and by Tandem reaction



Scheme-V: Alternative synthesis 2 of 4 by step-wise and by Tandem reaction

pound **5a** was condensed with compound **3** at 100 ºC for 120 min in glycerol in the presence of H_3PO_4 at 100 ºC with good yield (80 %) (**Scheme-IV**) for 120 min.

Alternative synthesis of compound 4 (Route-2): Diethyl-phthalate (**1**) was condensed with pyridine-2,3-diamine (**3**) in glycerol at 100 ºC for 120 min to gave compound **6** in the presence of H_3PO_4. The compound was confirmed by spectral data and physical data of reported same compound [11-14]. Then, compound **6** was condensed with compound **2a** in glycerol for 120 min at 100 ºC to give desired compound **4a** in the presence of H_3PO_4. Compound **4a** should also prepared by tandem synthesis, diethyl-phthalate (**1**) was condensed with compound **3** in glycerol to form intermediate compound **6** at 100 ºC until the compound **1** disappeared on TLC in the presence of H_3PO_4. Then, intermediate **6** was condensed with compound **3** at 100 ºC for 120 min in glycerol to give compound **4a** with good yield (80 %) (**Scheme-V**) in the presence of H_3PO_4.

CONFLICT OF INTEREST

The authors declare that there is no conflict of interests regarding the publication of this article.

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