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# PEG-400: An efficient and recyclable reaction medium for the synthesis of pyrazolo[1,5-a]pyrimidines

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ABSTRACT

An efficient and convenient route is described for the synthesis of new pyrazolo [1,5-a] pyrimidine derivatives by the reaction of 4-(4'-chloro-phenylazo)-5-amino pyrazole with α,β-unsaturated carbonyl compounds (chalcones) using polyethylene glycol (PEG-400) as benign reaction medium. The advantage of this protocol includes the excellent yields, operational simplicity, short reaction times and avoidance of volatile organic solvents and expensive catalysts.

## 1. Introduction

In the past few years, there has been a growing interest in the chemistry of pyrazolo [1,5-a] pyrimidines, which is due to the extent of their applications in pharmacological science. Indeed they are known for their antitrypanosomal [1] and antichistosomal [2] activities, their sedative and anxiolitic–like properties [3,4] and they are potential as HMG-CoA reductase inhibitors [5], COX-2-selective inhibitors [6], AMP phoshodiestarase inhibitors [7], KDR kinase inhibitors [8] and selective peripheral benzodiazepine receptor ligands [9,10]. These interesting biological properties have been prompt us to the development of new procedures for the synthesis of pyrazolo [1,5-a] pyrimidines [11,12]. Classical conditions for the synthesis of pyrazolo [1,5-a] pyrimidines involve refluxing a 5-amino-4-aryl-pyrazole with a commercially available 2-aryl malondialdehyde in ethanol with catalytic acetic acid for 24 h to deliver pyrazolo [1,5-a] pyrimidines in 40-60% yields [13].

Recently, liquid polymers or low melting polymers have emerged as alternative green reaction media with unique properties such as thermal stability, commercial availability, non-volatility, immiscibility with a number of organic solvents and recyclability. PEGs are preferred over other polymers because they are inexpensive, completely non-halogenated, easily degradable and of low toxicity [14]. Many organic reactions have been carried out using PEGs as solvent or co-solvent such as Heck reaction [15], asymmetric dihydroxylation [16,17], Suzuki cross-coupling reaction [18], oxy-dehydrogenation of alcohols and cyclic dienes, oxidation of sulfides, Wacker reaction [19], deallylation [20] and partial reduction reaction of alkynes [21]. The use of PEG as a recyclable solvent system for the metal mediated radical polymerization of methyl methacrylate and styrene has also been reported [22]. A number of recent literatures have also covered PEG as a green reaction solvent [23-26].

Continuing our studies on the development of new, selective, and environmentally friendly methodologies using PEG-400 as a solvent for the preparation of biologically active compounds [27-30], herein I report the expeditious synthesis of novel pyrazolo [1,5-a] pyrimidine derivatives by the reaction of amino pyrazole with novel α,β-unsaturated carbonyl compounds in PEG-400 as green reaction solvent under mild temperature.

## 2. Experimental

Melting points were uncorrected and determined in an open capillary tube. IR spectra were recorded on FTIR-Shimadzu spectrometer. $^1$H NMR spectra were recorded in DMSO-$d_6$ on Avance-300 MHz spectrometer using TMS as an internal standard. The mass spectra were recorded on EI-Shimadzu-GC-MS spectrometer.


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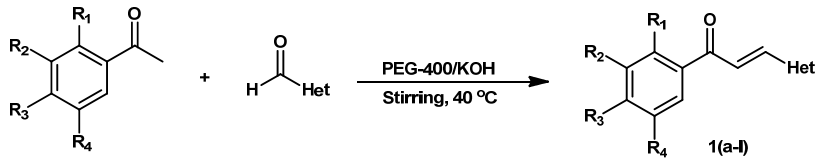
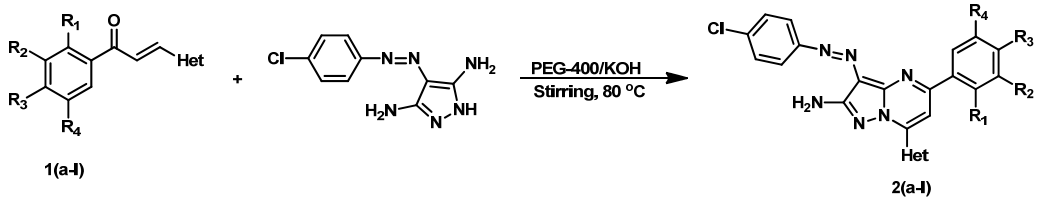



**Scheme 1**




**Scheme 2**

Elemental analyses were performed on a Carlo Erba 106 Perkin-Elmer model 240 analyzer.

### *2.1. General procedure for the synthesis of chalcones 1(a-l) [31]*

An equimolar mixture of substituted acetophenone (1 mmol), hetero aromatic aldehyde (1 mmol) and KOH (2 mmol) was stirred in PEG-400 (15 mL) at 40 °C for 1 hour. After completion of the reaction (monitored by TLC), the crude mixture was worked up in ice cold water (100 mL). Product separated out was filtered and processed out. The PEG was recycled and reused to synthesize further chalcones (Scheme 1).

### *2.2. Typical procedure for the synthesis of pyrazolo [1, 5-a] pyrimidines (2a-l)*

A mixture of **1b** (0.322 g, 1 mmol) and 4-(4'-chloro-phenylazo)-5-amino pyrazole (0.236 g, 1 mmol) was stirred in PEG-400 (10 mL) at 80 °C for 2 hours. The progress of the reaction was monitored by TLC. After completion, the reaction mixture was extracted with ethyl acetate (2×20 mL). The combined organic layers were dried over anhydrous $Na_2SO_4$, and the solvent was evaporated under reduced pressure. The crude product was recrystallized from aqueous DMF to afford to the pure product **2b**. The remaining mother liquor was recovered and recycled in subsequent reactions (Scheme 2).

*2-((3E)-3-(2-(4-chlorophenyl)diazenyl)-2-amino-7-(2-butyl-4-chloro-1H-imidazol-5-yl)pyrazolo[1, 5-a]pyrimidin-5-yl)-4-chlorophenol* (**2a**): Color: Reddish brown. Yield: 90%. M.p.: 112-114 °C. FT-IR (KBr, ν, $cm^{-1}$): 1618 (-C=N), 3096 (-OH), 3329 (-$NH_2$). $^1$H NMR (300 MHz, DMSO-$d_6$, δ, ppm): 0.93 (t, *J* = 7.5 Hz, 3H, $CH_3$), 1.31-136 (m, 2H, -$CH_2$-), 1.66-1.69 (m, 2H, -$CH_2$-), 2.76 (t, *J* = 7.2 Hz, 2H, $CH_2$), 4.01 (bs, 2H, $NH_2$), 7.02-7.96 (m, 7H, Ar-H), 8.11(s, 1H, NH), 8.51 (s, 1H, 6H-pyrimidine), 12.36 (s, 1H, -OH, $D_2O$ exchangeable). $^{13}$C NMR (75 MHz, DMSO-$d_6$, δ, ppm): 14, 22, 29, 30, 93, 115, 119, 120, 121, 122, 123, 125, 126, 127, 128, 129 (2 x C), 130 (2 x C), 132, 146, 152, 155, 161, 163. MS (EI, *m/z* (%)): 554 ($M^+$), 127 (100%). Anal. calcd. for $C_{25}H_{21}N_8OCl_3$: C, 54.02; H, 3.81; N, 20.16. Found: C, 54.11; H, 3.88; N, 20.12%.

*(3E)-3-(2-(4-chlorophenyl)diazenyl)-7-(2-butyl-4-chloro-1H-imidazol-5-yl)-5-(4-chlorophenyl)pyrazolo[1, 5-a]pyrimidin-2-amine* (**2b**): Color: Reddish brown. Yield: 92%. M.p.: 125-127 °C. FT-IR (KBr, ν, $cm^{-1}$): 1619 (-C=N), 3359 (-$NH_2$). $^1$H NMR (300 MHz, DMSO-$d_6$, δ, ppm): 0.93 (t, *J* = 7.2 Hz, 3H, $CH_3$), 1.32-1.36 (m, 2H, -$CH_2$-), 1.68-1.72 (m, 2H, -$CH_2$-), 2.74 (t, *J* = 7.2 Hz, 2H, $CH_2$), 4.16 (bs, 2H, $NH_2$), 7.05-7.99 (m, 8H, Ar-H), 8.16 (s, 1H, NH), 8.49 (s, 1H, 6H-pyrimidine). $^{13}$C NMR (75 MHz, DMSO-$d_6$, δ, ppm): 14, 22, 29, 30, 93, 119, 120, 122, 123, 125, 126, 127 (2 x C), 128 (2 x C), 129 (2 x C), 130 (2 x C), 132, 134, 135, 152, 161, 163. MS (EI, *m/z* (%)): 538 ($M^+$), 127 (100%). Anal. calcd. for $C_{25}H_{21}N_8Cl_3$: C, 55.64; H, 3.91; N, 20.76. Found: C, 55.51; H, 3.99; N, 20.61%.

*2-((3E)-3-(2-(4-chlorophenyl)diazenyl)-2-amino-7-(2-butyl-4-chloro-1H-imidazol-5-yl)pyrazolo[1, 5-a]pyrimidin-5-yl)-4-chloro-6-iodophenol* (**2c**): Color: Dark Brown. Yield: 86%. M.p.: 134-136 °C. FT-IR (KBr, ν, $cm^{-1}$): 1616 (-C=N), 3142 (-OH), 3325 (-$NH_2$). $^1$H NMR (300 MHz, DMSO-$d_6$, δ, ppm): 0.91 (t, *J* = 7.2 Hz, 3H, $CH_3$), 1.35-1.39 (m, 2H, -$CH_2$-), 1.66-1.71 (m, 2H, -$CH_2$-), 2.78 (t, *J* = 7.5 Hz, 2H, $CH_2$), 4.05 (bs, 2H, $NH_2$), 7.11-7.95 (m, 6H, Ar-H), 8.18 (s, 1H, NH), 8.48 (s, 1H, 6H-pyrimidine), 12.48 (s, 1H, -OH, $D_2O$ exchangeable). MS (EI, *m/z* (%)): 682 ($M^+$), 127 (100%). Anal. calcd. for $C_{25}H_{20}N_8OCl_3I$: C, 44.04; H, 2.96; N, 16.44. Found: C, 44.11; H, 2.91; N, 16.53%.

*2-((3E)-3-(2-(4-chlorophenyl)diazenyl)-2-amino-7-(2-butyl-4-chloro-1H-imidazol-5-yl)pyrazolo[1, 5-a]pyrimidin-5-yl)-6-bromo-4-chlorophenol* (**2d**): Color: Brown. Yield: 89%. M.p.: 121-123 °C. FT-IR (KBr, ν, $cm^{-1}$): 1620 (-C=N), 3126 (-OH), 3338 (-$NH_2$). $^1$H NMR (300 MHz, DMSO-$d_6$, δ, ppm): 0.91 (t, *J* =7 .5 Hz, 3H, $CH_3$), 1.33-1.38 (m, 2H, -$CH_2$-), 1.65-1.69 (m, 2H, -$CH_2$-), 2.71 (t, *J* = 7.2 Hz, 2H, $CH_2$), 4.12 (bs, 2H, $NH_2$), 7.11-7.88 (m, 6H, Ar-H), 8.18 (s, 1H, NH), 8.46 (s, 1H, 6H-pyrimidine), 12.51 (s, 1H, -OH, $D_2O$ exchangeable). MS (EI, *m/z* (%)): 634 ($M^+$), 79 (100). Anal. calcd. for $C_{25}H_{20}N_8OCl_3Br$: C, 47.31; H, 3.18; N, 17.65. Found: C, 47.38; H, 3.15; N, 17.73%.

*2-((3E)-3-(2-(4-chlorophenyl)diazenyl)-2-amino-7-(2-butyl-4-chloro-1H-imidazol-5-yl)pyrazolo[1, 5-a]pyrimidin-5-yl)-4-chloro-5-methylphenol* (**2e**): Color: Reddish brown. Yield: 86%. M.p.: 138-140 °C. FT-IR (KBr, ν, $cm^{-1}$): 1620 (-C=N), 3068 (-OH), 3315 (-$NH_2$). $^1$H NMR (300 MHz, DMSO-$d_6$, δ, ppm): 0.91 (t, *J* = 7.2 Hz, 3H, $CH_3$), 1.35-1.38 (m, 2H, -$CH_2$-), 1.66-1.72 (m, 2H, -$CH_2$-), 2.21 (s, 3H, $CH_3$), 2.65 (t, *J* = 7.2 Hz, 2H, $CH_2$), 4.11 (bs, 2H, $NH_2$), 7.05-7.98 (m, 6H, Ar-H), 8.21 (s, 1H, NH), 8.46 (s, 1H, 6H-pyrimidine), 12.28 (s, 1H, -OH, $D_2O$ exchangeable). MS (EI, *m/z* (%)): 570 ($M^+$), 43 (100). Anal. calcd. for $C_{26}H_{23}N_8OCl_3$: C, 54.80; H, 4.07; N, 19.656. Found: C, 54.72; H, 4.13; N, 19.76%.

*6-((3E)-3-(2-(4-chlorophenyl)diazenyl)-2-amino-7-(2-butyl-4-chloro-1H-imidazol-5-yl)pyrazolo[1, 5-a]pyrimidin-5-yl)-4-chloro-6-iodo-5-methylphenol* (**2f**): Color: Reddish brown. Yield: 86%. M.p.: 152-154 °C. FT-IR (KBr, ν, $cm^{-1}$): 1622 (-C=N), 3088 (-OH), 3328 (-$NH_2$). $^1$H NMR (300 MHz, DMSO-$d_6$, δ, ppm): 0.91 (t, *J* = 7.5 Hz, 3H, $CH_3$), 1.33-1.38 (m, 2H, -$CH_2$-), 1.68-1.72 (m, 2H, -$CH_2$-), 2.24 (s, 3H, $CH_3$), 2.68 (t, *J* = 7.2 Hz, 2H, $CH_2$), 4.18 (bs, 2H, $NH_2$), 7.05-7.95 (m, 5H, Ar-H), 8.22 (s, 1H, NH),

8.51 (s, 1H, 6H-pyrimidine), 12.42 (s, 1H, -OH, $D_2O$ exchangeable). MS (EI, *m/z* (%)): 695 ($M^+$), 127 (100). Anal. calcd. for $C_{26}H_{22}N_8OCl_3I$: C, 44.88; H, 3.19; N, 16.10. Found: C, 44.76; H, 3.28; N, 16.18%.

*6-((3E)-3-(2-(4-chlorophenyl)diazenyl)-2-amino-7-(2-butyl-4-chloro-1H-imidazol-5-yl)pyrazolo[1, 5-a]pyrimidin-5-yl)-6-bromo-4-chloro-5-methylphenol* (**2g**): Color: Brown. Yield: 88%. M.p.: 105-107 °C. FT-IR (KBr, ν, $cm^{-1}$): 1618 (-C=N), 3095 (-OH), 3335 (-$NH_2$). $^1H$ NMR (300 MHz, DMSO-$d_6$, δ, ppm): 0.93 (t, J=7.2 Hz, 3H, $CH_3$), 1.33-1.39 (m, 2H, -$CH_2$-), 1.68-1.71 (m, 2H, -$CH_2$-), 2.28 (s, 3H, $CH_3$), 2.71 (t, J=7.5 Hz, 2H, $CH_2$), 3.98 (bs, 2H, $NH_2$), 7.12-8.05 (m, 5H, Ar-H), 8.24 (s, 1H, NH), 8.49 (s, 1H, 6H-pyrimidine), 12.35 (s, 1H, -OH, $D_2O$ exchangeable). MS (EI, *m/z* (%)): 648 ($M^+$), 77 (100). Anal. calcd. for $C_{26}H_{22}N_8OCl_3Br$: C, 48.13; H, 3.42; N, 17.27. Found: C, 48.21; H, 3.51; N, 17.38%.

*2-((3E)-3-(2-(4-chlorophenyl)diazenyl)-2-amino-7-(2-amino-4-(4-chlorophenyl)thiazol-5-yl)pyrazolo[1, 5-a]pyrimidin-5-yl)-4-chlorophenol* (**2h**): Color: Brick red. Yield: 86%. M.p.: 158-160 °C. FT-IR (KBr, ν, $cm^{-1}$): 1616 (-C=N), 3092 (-OH), 3325 (-$NH_2$). $^1H$ NMR (300 MHz, DMSO-$d_6$, δ, ppm): 4.26 (bs, 2H, $NH_2$, $D_2O$ exchangeable), 7.15-8.21 (m, 11H, Ar-H), 8.32 (s, 2H, $NH_2$-thiazole, $D_2O$ exchangeable), 8.58 (s, 1H, 6H-pyrimidine), 11.91 (s,1H, OH, $D_2O$ exchangeable). Anal. calcd. for $C_{27}H_{17}N_8OSCl_3$: C, 53.35; H, 2.82; N, 18.43. Found: C, 53.22; H, 2.92; N, 18.38%.

*(3E)-3-(2-(4-chlorophenyl)diazenyl)-7-(2-amino-4-(4-chlorophenyl)thiazol-5-yl)-5-(4-chlorophenyl)pyrazolo[1,5-a]pyrimidin-2-amine* (**2i**): Color: Brick red. Yield: 90%. M.p.: 165-167 °C. FT-IR (KBr, ν, $cm^{-1}$): 1619 (-C=N), 3096 (-OH), 3338 (-$NH_2$). $^1H$ NMR (300 MHz, DMSO-$d_6$, δ, ppm): 4.21 (bs, 2H, $NH_2$, $D_2O$ exchangeable), 7.11-8.16 (m, 12H, Ar-H), 8.33 (s, 2H, $NH_2$-thiazole, $D_2O$ exchangeable), 8.51 (s, 1H, 6H-pyrimidine). MS (EI, *m/z* (%)): 592 ($M^+$), 43 (100). Anal. calcd. for $C_{27}H_{17}N_8SCl_3$: C, 54.79; H, 2.89; N, 18.93. Found: C, 53.86; H, 2.94; N, 18.86%.

*2-((3E)-3-(2-(4-chlorophenyl)diazenyl)-2-amino-7-(2-amino-4-(4-chlorophenyl)thiazol-5-yl)pyrazolo[1, 5-a]pyrimidin-5-yl)-4-chloro-6-iodophenol* (**2j**): Color: Brick red. Yield: 88%. M.p.: 131-133 °C. FT-IR (KBr, ν, $cm^{-1}$): 1618 (-C=N), 3111 (-OH), 3335 (-$NH_2$). $^1H$ NMR (300 MHz, DMSO-$d_6$, δ, ppm): 4.11 (bs, 2H, $NH_2$, $D_2O$ exchangeable), 7.15-8.15 (m, 10H, Ar-H), 8.33 (s, 2H, $NH_2$-thiazole, $D_2O$ exchangeable), 8.46 (s, 1H, 6H-pyrimidine), 12.25 (s, 1H, OH, $D_2O$ exchangeable). Anal. calcd. for $C_{27}H_{16}N_8OSCl_3$: C, 44.19; H, 2.20; N, 15.27. Found: C, 44.11; H, 2.29; N, 15.34%.

*2-((3E)-3-(2-(4-chlorophenyl)diazenyl)-2-amino-7-(2-amino-4-(4-chlorophenyl)thiazol-5-yl)pyrazolo[1, 5-a]pyrimidin-5-yl)-6-bromo-4-chlorophenol* (**2k**): Color: Brick red. Yield: 90%. M.p.: 142-144 °C. FT-IR (KBr, ν, $cm^{-1}$): 1618 (-C=N), 3118 (-OH), 3338 (-$NH_2$). $^1H$ NMR (300 MHz, DMSO-$d_6$, δ, ppm): 4.21 (bs, 2H, $NH_2$, $D_2O$ exchangeable), 7.11-8.05 (m, 10H, Ar-H), 8.34 (s, 2H, $NH_2$-thiazole, $D_2O$ exchangeable), 8.51 (s, 1H, 6H-pyrimidine), 12.26 (s, 1H, OH, $D_2O$ exchangeable). MS (EI, *m/z* (%)): 686 ($M^+$), 79 (100). Anal. calcd. for $C_{27}H_{16}N_8OSCl_3Br$: C, 47.22; H, 2.35; N, 16.32. Found: C, 47.28; H, 2.31; N, 16.41%.

*6-((3E)-3-(2-(4-chlorophenyl)diazenyl)-2-amino-7-(2-amino-4-(4-chlorophenyl)thiazol-5-yl)pyrazolo[1, 5-a]pyrimidin-5-yl)-4-chloro-5-methylphenol* (**2l**): Color: Brick red. Yield: 88%. M.p.: 174-176 °C. FT-IR (KBr, ν, $cm^{-1}$): 1622 (-C=N), 3098 (-OH), 3335 (-$NH_2$). $^1H$ NMR (300 MHz, DMSO-$d_6$, δ, ppm): 2.24 (s, 3H, $CH_3$), 4.18 (bs, 2H, $NH_2$, $D_2O$ exchangeable), 7.05-8.14 (m, 9H, Ar-H), 8.32 (s, 2H, $NH_2$-thiazole, $D_2O$ exchangeable), 8.46 (s, 1H, 6H-pyrimidine), 12.38 (s, 1H, OH, $D_2O$ exchangeable). Anal. calcd. for $C_{28}H_{18}N_8OSCl_3I$: C, 44.97; H, 2.43; N, 14.98. Found: C, 44.91; H, 2.49; N, 14.89%.

## 3. Results and discussion

The newly synthesized α,β-unsaturated carbonyl compounds **1a-l** were prepared by Claisen-Schmidt condensation method [31] from substituted acetophenones and different hetero aldehydes in polyethylene glycol (PEG-400) under alkaline medium at 40 °C for 1 hour (Scheme 1), while the 4-(4'-chloro-phenylazo)-5-amino pyrazole was prepared in two steps from the corresponding *p*-chloroamine by diazotization and then treatment with malononitrile followed by reaction with hydrazine hydrate [32,33].

The initial investigation was concerned with the condensation of 1-(4-chlorophenyl)-3-(2-butyl-4-chloro-1*H*-imidazol-5-yl)-2-propen-1-one with 4-(4'-chloro-phenylazo)-5-amino pyrazole in polyethylene glycol (PEG-400) as reaction solvent at 80 °C for 2 hours to formed the corresponding product (**2b**) (Scheme 2). We choose this system as model reaction. In order to optimize the reaction conditions, we carried out the above reaction in different solvents such as ethanol, dichloromethane, acetonitrile, acetic acid and PEG-400 (Table 1). We found that PEG-400 as an efficient reaction medium in terms of reaction time as well as yield (92%). Encouraged by these results, we next turned our attention to different chalcones and 5-amino pyrazole in PEG-400 at 80 °C to afford the corresponding products in excellent yields (Scheme 2, Table 2).

**Table 1.** Solvent effect on the reaction of 1-(4-chlorophenyl)-3-(2-butyl-4-chloro-1*H*-imidazol-5-yl)-2-propen-1-one with 4-(4'-chloro-phenylazo)-5-amino pyrazole at 80 °C.

| Entry | Solvent | Time (h) | Yield (%) |
|---|---|---|---|
| 1 | EtOH | 12 | 58 |
| 2 | DCM | 8 | 62 |
| 3 | $CH_3CN$ | 9 | 65 |
| 4 | Acetic acid | 10 | 68 |
| 5 | PEG-400 | 2 | 92 |

In addition, it is noticed that the PEG-400 was recovered and reused for four runs without loss of its activity. To determine the reusability of the solvent, the reaction mixture was extracted with ethyl acetate and the PEG was isolated and subjected for second run by charging the same substrates. The obtained results are shown in graphical representation (Figure 1).

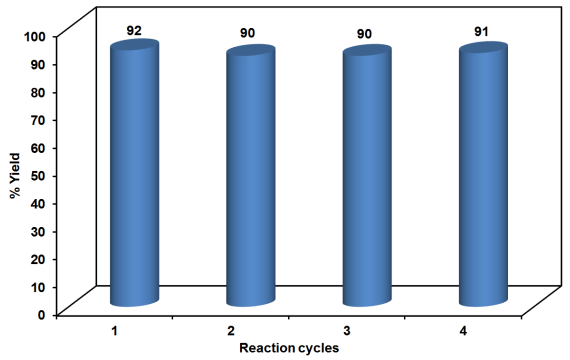
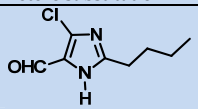
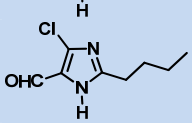
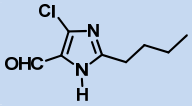
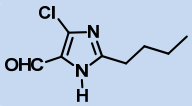
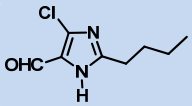
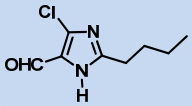
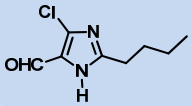
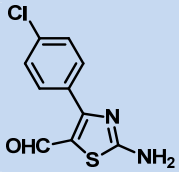
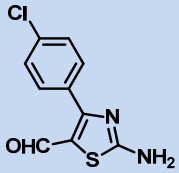
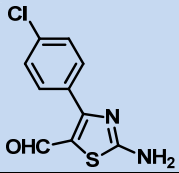



**Figure 1.** Recyclability of PEG-400.

The formation of products **2a-l** were assumed to proceed through the Micheal type addition of the ring nitrogen in 5-amino pyrazole (which is more active) to the activated double bond followed by intra-molecular cyclisation [34,35] with elimination of water and dehydrogenation. The structure of compounds **2a-l** was appropriately established by spectroscopic and analytical methods. The IR spectra of compound **2a** revealed the presence of $NH_2$ at 3329 $cm^{-1}$ while the $^1H$ NMR data were consistent with structure **2a** and exhibits a singlet at δ 12.36 ppm ($D_2O$ exchangeable, phenolic -OH), multiplate at δ 7.02-7.96 ppm (aromatic protons) and a broad signal at δ 3.98 ppm ($D_2O$ exchangeable, -$NH_2$ protons). Also, mass spectrum of compound **2a** exhibited a molecular ion peak *m/z* = 554 [$M^+$].

**Table 2.** Physical and analytical data of pyrazolo [1,5-a] pyrimidines (**2a-l**).

| Product | $R_1$ | $R_2$ | $R_3$ | $R_4$ | Hetero substitution | Yield [a, b] (%) | M.p. (°C) |
|---|---|---|---|---|---|---|---|
| 2a | OH | H | H | Cl |  | 90 | 112-114 |
| 2b | H | H | Cl | H |  | 92 | 125-127 |
| 2c | OH | I | H | Cl |  | 86 | 134-136 |
| 2d | OH | Br | H | Cl |  | 89 | 121-123 |
| 2e | OH | H | $CH_3$ | Cl |  | 86 | 138-140 |
| 2f | OH | I | $CH_3$ | Cl |  | 86 | 152-154 |
| 2g | OH | Br | $CH_3$ | Cl |  | 88 | 105-107 |
| 2h | OH | H | H | Cl |  | 86 | 158-160 |
| 2i | H | H | Cl | H |  | 90 | 165-167 |
| 2j | OH | I | H | Cl |  | 88 | 131-133 |
| 2k | OH | Br | H | Cl |  | 90 | 142-144 |
| 2l | OH | I | $CH_3$ | Cl |  | 88 | 174-176 |

[a] Isolated yield.
[b] Products are characterized by IR, $^1$H NMR and Mass spectroscopy.

It is noteworthy to mention that the pyrazolo [1,5-a] pyrimidines **2a-l** having variety of substituents such as hydroxy, chloro, bromo, iodo, methyl were prepared in high yields. In addition, the remarkable feature of the present methodology include the introduction of novel heterocyclic moiety in pyrazolo[1,5-a]pyrimidines.

## 4. Conclusion

In summary, we report a novel, efficient and environmentally benign methodology for the synthesis of pyrazolo [1,5-a] pyrimidines by the reaction of 5-amino pyrazoles with α,β-unsaturated carbonyl compounds in PEG-400 is described. The introduction of novel heterocyclic moiety in pyrazolo [1,5-a] pyrimidines, it may enhance biological activity as well as scope and applications. The advantages of the present protocol are the simplicity of operation; the high yields of products, the recyclability of PEG-400 and preclusion of the usage of volatile organic solvents.

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