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An efficient synthesis of pyrazolo[1,5-*a*]pyrimidines and evaluation of their antimicrobial activity

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Abstract. A series of new pyrazolo[1,5-*a*]pyrimidine derivatives has been synthesized by using 7-hydrazinyl-5-methylpyrazolo[1,5-*a*]pyrimidine-3-carbonitrile **1** and 7-amino-5-methylpyrazolo[1,5-*a*]pyrimidine-3-carbonitrile **2** as precursors. The pyrazolo[3,4-*d*] pyrimidines **3a–b** have been synthesized by a three-step reaction starting with **1**. Compound **1** was utilized for the synthesis of dioxopyrrolidindolinylamio-pyrazolo-pyrimidines **4a–b**, and dioxoisoindolin-pyrazolo-pyrimidines **4c–d**. Also, compounds **4a-d** were synthesized using deep eutectic solvents (DES). This method using DES provides several advantages such as benign environment, high yield, scalable and simple work-up procedure. Similarly, the cyclocondensation of **2** with α-acetyl-γ-butyrolactone afforded pyrazolo-pyrido-pyrimidine **5** and dihydrofuro-pyrido-pyrazolo-pyrimidine **6.** All synthesized compounds were screened for antimicrobial activity.

Keywords. Pyrazolo-pyrimidine; pyrazolyl-pyrazolo-pyrimidine; deep eutectic solvents; DES; α-acetyl-γ-butyrolactone.

1. Introduction

As analogues of purine, pyrazolo[1,5-*a*]pyrimidines have attracted chemists owing to their biological and pharmacological importance such as hypnotic,[1] anti-inflammatory,[2] anti-tumor,[3–7] antimycobacterial,[8] anti-viral,[9–11] antitrypanosomal,[12] antischistosomal,[13] and most importantly anti-tumor activity.[14–17] Literature survey revealed that Zaleplon is an ideal hypnotic drug which was structural mimic to the pyrazolo[1,5-*a*]pyrimidine and has generated a lot of interest in the pyrazolo[1,5-*a*]pyrimidine derivatives.[18]

In the literature, it was also found that not only the core moieties showed biological activity but also the additional ring annulated system, namely, hydrazine annulated pyrazolo[3,4-*d*] pyrimidines,[19] dioxo dihydroisoindols, dioxo dihydropyrrols,[20] pyrazoles,[21] also exhibited diverse spectrum of biological activities. However, the synthesis and bioactivity of amino and hydrazone derivative of pyrazolo[1,5-*a*]pyrimidine is limited.[22,23]

Synthesis of the above stated target compounds suffer from limitations that include use of toxic reagents, volatile solvents or expensive catalysts. The reaction conditions were harsh in most of the protocols and tedious work-up procedures in a few cases. Therefore, efficient protocol for the synthesis of hydrazine-annulated dioxo pyrrolidones and pyrazolones under milder conditions and in an environmentally benign manner is needed.

Deep eutectic mixtures belong to an interesting set of eutectics which have been recently explored in important organic reactions.[24,25] Deep eutectic solvents (DESs) are the special type of ionic solvents composed of quaternary salt like choline chloride (ChCl) and neutral molecules like urea, glycerol, etc. The melting point of such mixtures is much lower when compared with either of the individual components.[26] Although they are somewhat similar in features to conventional ionic liquids, their advantages are due to the major differences between them. The eutectics are cost effective, non-toxic and easy to store than most ionic liquids owing to the fact that choline is a naturally occurring bio-compatible compound and choline chloride is also commercially produced on a large scale as a chicken feed additive. For this reason, DESs gain increasing attention in synthetic organic chemistry and industry. This also offers several benefits, including negligible vapour pressure, non-flammability, chemical/thermal stability, and non-reactivity towards water.

To address this problem and as a continuation of our work towards the synthesis of nitrogen containing

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heterocycles,[27,28] we intended to develop a convenient synthetic approach for the synthesis of new pyrazolo [1,5-*a*]pyrimidine annulated heterocycles.

2. Experimental

2.1 *Reagents*

Reactions were monitored by thin layer chromatography (TLC), carried out on 0.2 mm silica gel 60 F_{254} precoated (Merck) plates using UV light (254 and 366 nm) for detection. Compounds were purified by column chromatography using silica gel of 5–20 μm (Merck, 60–120 mesh). Column dimension was 39 × 2 cm and elution volume used was about 200–400 mL for each product. Common reagent grade chemicals were either commercially purchased and used without further purification or were prepared by standard literature procedures.

2.2 *Characterization*

Melting points were determined on a Gallenkamp melting point apparatus. The ^{1}H NMR (300 MHz) and ^{13}C NMR (75 MHz) spectra were recorded on a Varian XL-300 spectrometer. Chemical shifts are reported in ppm relative to tetramethylsilane (TMS), and multiplicities are given as s (singlet), bs (broad singlet), d (doublet), t (triplet), q (quartet), and m (multiplet). Infrared spectra were recorded as KBr pellets on a Shimadzu FTIR-408 spectrophotometer. Mass spectra were recorded on a Shimadzu LC-MS: EI QP 2010A mass spectrometer with ionization potential 70 eV. Elemental analyses were performed on Thermo Quest Flash 1112 Series EA analyzer.

2.3 *Preparation of deep eutectic mixture (DES) from choline chloride and urea*

In this study, deep eutectic solvent (DES) was synthesized according to the procedures reported the literature (Figure 1).[30] The preparation involved reaction of choline chloride **1** (1 mol) with urea **2** (2 mol) at 74°C till a clear solution was obtained which was used for reactions without any purification. This method gave deep eutectic solvent with 100% atom economy since it completely forms a eutectic mixture without by-product formation. Also, other eutectic mixtures were synthesized in a similar manner. The recovery and recycling of deep eutectic solvent is given in Table 1.

2.4 *Synthesis and characterization of compounds*

2.4a *Synthesis of compound 7-Hydrazinyl-5-methylpyrazolo[1,5-a]pyrimidine-3-carbonitrile* ***2***: A solution of 7-chloro-5-methylpyrazolo[1, 5-*a*]pyrimidine-3-carbonitrile (**1**) (0.192 g, 0.001 mol) and hydrazine hydrate (0.100 g, 0.002 mol) in ethanol (10 mL) was stirred at room temperature for 10 min. After completion of the reaction (Monitored by TLC using dichloromethane: methanol 9:1), reaction mixture was poured in ice cold water (10 mL) and further stirred for one hour. The solid obtained was suction filtered, washed with water, dried and purified by column chromatography (eluted with 1% methanol in dichloromethane) to obtain **2**. Colorless solid; yield -0.172 g, 92%; M.p. 259–261°C; IR (KBr): 3591, 3321, 3267, 3037, 2981, 2219, 1600 cm^{-1}; ^{1}H NMR data (DMSO-d_6): δ 2.45 (s, 3H, Ar-CH_3), 4.82 (bs, 2H, -NH_2), 6.55 (s, 1H, Ar-H), 8.55 (s, 1H, Ar-H), 9.56 (bs, 1H, -NH); ^{13}C NMR data (DMSO-d_6): δ 24.4, 77.2, 88.5, 114.4, 146.3, 149.2, 150.5, 162.3; MS (*m*/*z*): 189 (M+1, 100%); Anal. Calcd. (%) For $C_8H_8N_6$ (188.19): C, 51.06; H, 4.28; N, 44.66; Found (%) C, 51.25; H, 4.46; N, 44.48.

2.4b *Synthesis of 7-Azido-5-methylpyrazolo[1,5-a]pyrimidine-3-carbonitrile (**3**)*: To a solution of compound **1** (0.192 g, 0.001 mol) in dimethyl formamide (5 mL), sodium azide (0.065 g, 0.001 mol) was added portionwise at 0–5°C and stirred for 30 min. After completion of the reaction (TLC check with dichloromethane/

Table 1. The yield and recycling of deep eutectic solvent.

Entry	Yield[b]
Fresh	92
I	91
II	90
III	92

[a]Reaction carried at 50-60°C; [b]Isolated Yields.

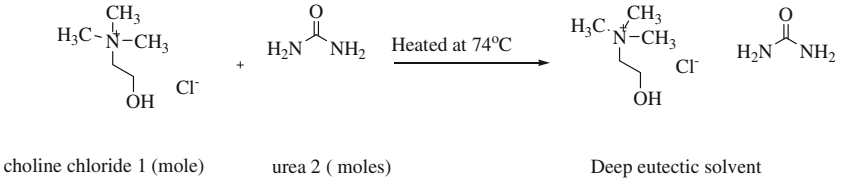


Figure 1. Preparation of deep eutectic mixture (DES).

methanol 9:1), the reaction mixture was poured in ice cold water (10 mL) and stirred for two hours. The solid obtained was suction filtered, washed with water, dried and purified by column chromatography (eluting with 1% methanol in dichloromethane) to furnish compound **3**. Brown solid; yield-0.163 g, 82%; M.p. 149–151°C; IR (KBr): 3039, 2225, 2150, 1623, 1544 cm^{-1}; ^1H NMR data ($CDCl_3$): δ 2.69 (s, 3H, Ar-CH_3), 6.59 (s, 1H, Ar-H), 8.34 (s, 1H, Ar-H); MS (*m/z*): 199 (M^+, 100%); Anal. Calcd. (%) For $C_8H_5N_7$ (199.17): C, 48.24; H, 2.53; N, 49.23; Found (%) C, 48.31; H, 2.61; N, 49.26.

2.4c *Synthesis of 7-Amino-5-methylpyrazolo[1, 5-a]pyrimidine-3-carbonitrile (**4**)*: A solution of compound **3** (0.199 g, 0.001 mol) and sodium dithionite (0.174 g, 0.001 mol) in dry methanol (10 mL) was heated under reflux at 70°C for 90 min. After completion of the reaction (TLC check with dichloromethane/methanol 9:1) the reaction mixture was poured in ice cold water (10 mL) and further stirred for one hour. The solid obtained was suction filtered, washed with water, dried and purified by column chromatography (eluting with 1% methanol in dichloromethane) to furnish compound **4**. Yellow solid; yield-0.140 g, 81%; M.p. 276–278°C; IR (KBr): 3337, 3332, 2904, 2227, 1600 cm^{-1}; ^1H NMR data (DMSO-d_6): δ 2.40 (s, 3H, Ar-CH_3), 6.18 (s, 1H, Ar-H), 8.14 (bs, 2H, -NH_2), 8.55 (s, 1H, Ar-H); ^{13}C NMR (DMSO-d_6): δ 24.1, 77.3, 90.6, 114.5, 146.4, 148.3, 150.7, 162.0; MS (*m/z*): 173 (M^+, 100%); Anal. Calcd. (%) For $C_8H_7N_5$ (173.17): C, 55.48; H, 4.07; N, 40.44; Found (%) C, 55.74; H, 4.22; N, 40.68.

2.4d *Synthesis of ethyl 5-amino-1-(3-cyano-5-methylpyrazolo[1,5-a]pyrimidin-7-yl)-1H-pyrazole-4-carboxylate (**6**)*: To a solution of compound **2** (0.188 g, 0.001 mol) in ethanol (10 mL), ethoxymethylenecyanoacetate solution (0.169 g, 0.001 mol) in ethanol (10 mL) was added dropwise over the period of 10 minutes. Then the reaction mixture was refluxed for three hours. After completion of the reaction (TLC check with dichloromethane/methanol 9:1) the reaction mixture was poured in ice cold water (10 mL). The solid obtained was suction filtered, washed with water, dried and recrystallized from acetonitrile to afford compound **6** as colorless solid. Colorless solid; yield-0.295 g, 95%; M.p. 302–304°C; IR (KBr): 3325, 3299, 2904, 2221, 1709, 1610 cm^{-1}; ^1H NMR data ($CDCl_3$): δ 1.35 (t, J = 7.5 Hz, 3H, CH_3), 2.77 (s, 3H, Ar-CH_3), 4.32 (q, J = 7.8 Hz, 2H, CH_2), 6.66 (s, 2H, -NH_2), 7.29 (s, 1H, Ar-H), 7.99 (s, 1H, Ar-H), 8.44 (s, 1H, Ar-H); ^{13}C NMR data (DMSO-d_6): δ 14.4, 24.4, 59.0, 81.2, 93.3, 110.3, 113.1, 139.4, 143.1, 147.2, 151.1, 152.2, 162.8, 165.1; MS (*m/z*): 312 (M+1, 100%); Anal. Calcd. (%) For $C_{14}H_{13}N_7$ (311.3): C, 54.02; H, 4.21; N, 31.50; Found (%) C, 53.75; H, 4.29; N, 31.81.

2.4e *Synthesis of 7-(5-Amino-4-cyano-1H-pyrazol-1-yl)-5-methylpyrazolo[1,5-a]pyrimidine-3-carbonitrile (**8**)*: To a solution of compound **2** (0.188 g, 0.001 mol) in ethanol, (10 mL) ethoxymethylenmalonitrile (0.122 g, 0.001 mol) in ethanol (10 mL) was added dropwise over the period of 10 min. Then the reaction mixture was refluxed for six hours. After completion of the reaction (TLC check with dichloromethane/methanol 9:1) the reaction mixture was poured in ice cold water (10 mL). The solid obtained was suction filtered, washed with water, dried and recrystallized from acetonitrile afforded compound **8**. Yellow solid; yield-0.248 g, 94%; M.p. 333–335°C; IR (KBr): 3406, 3336, 2914, 2237, 2219, 1600 cm^{-1}; ^1H NMR data (DMSO-d_6): δ 2.72 (s, 3H, Ar-CH_3), 7.24 (s, 2H, -NH_2), 7.61 (s, 1H, Ar-H), 8.01 (s, 1H, Ar-H) 8.77 (s, 1H, Ar-H); ^{13}C NMR data (DMSO-d_6): δ 24.4, 72.1, 81.4, 110.7, 113.1, 114.0, 138.8, 144.5, 147.3, 151.1, 153.9, 165.2; MS (*m/z*): 265 (M+1, 100%); Anal. Calcd. (%) For $C_{12}H_8N_8$ (264.25): C, 54.54; H, 3.05; N, 42.41; Found (%) C, 54.32; H, 3.26; N, 42.19.

2.4f *Synthesis of compounds **4** and ethyl 5-amino-1H-pyrazole-4-carboxylate (**10**)*: A solution of ethyl 5-amino-1-(3-cyano-5-methylpyrazolo[1,5-*a*]pyrimidin-7-yl)-1*H*−pyrazole-4-carboxylate (**6**) (0.311 g, 0.001 mol) and ammonia (0.100 g, 0.002 mol) in tetrahydrofuron (10 mL) was stirred at 50–55°C for 5 min. After completion of the reaction (TLC check with dichloromethane: methanol 9:1) obtained solid was suction filtered, washed with hexane, dried and it was a mixture of two compounds (TLC check). The mixture was separated by column eluting with 0.5% methanol in dichloromethane and was characterized by spectral and analytical data. Compound **4** is already in hand and its structure was confirmed by comparison of physical data. Compound **10**: yield-0.33 g, 12%; M.p. 102–103°C, (Sigma-Aldrich CAS No. 103259-35-4). M.p. 101–104°C., IR (KBr): 3588, 3320, 3260, 3031, 2983, 2219, 1709, 1610 cm^{-1}; ^1H NMR data (DMSO-d_6): δ 1.20 (t, J = 7.2 Hz, 3H, CH_3), 4.11 (q, J = 7.2 Hz, 2H, CH_2), 5.81 (s, 2H, -NH_2), 7.51 (s, 1H, Ar-H), 11.86 (bs, 1H, -NH).

2.4g *Synthesis of compounds **2** and **10***: A solution of ethyl 5-amino-1-(3-cyano-5-methylpyrazolo[1,5-*a*]pyrimidin-7-yl)-1*H*−pyrazole-4-carboxylate (**6**) (0.311 g, 0.001 mol) and hydrazine hydrate (0.100 g, 0.002 mol) in ethanol (10 mL) was stirred at 50–55°C for 5 min. After completion of the reaction (TLC check with dichloromethane: methanol 9:1) obtained solid was suction

filtered, washed with hexane, dried and it was a mixture of two compounds (as observed from TLC). The mixture was separated by column eluting with 0.5% methanol in dichloromethane and characterized by spectral and analytical data. The characterization data for **2** and **10** are given above.

2.4h *Synthesis of (E)-Ethyl 1-(3-cyano-5-methylpyrazolo[1,5-a]pyrimidin-7-yl)-5(ethoxymethylene)amino)-1H-pyrazole-4-carboxylate (**12**)*: To a solution of (**6**) (0.311 g, 0.001 mol), triethyl orthoformate (0.296 g, 0.002 mol) in acetic anhydride (10 mL) was added and the reaction mixture was stirred at 110–115°C for 15 min. After completion of the reaction (TLC check with dichloromethane/methanol 9:1), the excess of solvent was removed under reduced pressure, the solid obtained was suction filtered, washed with water, dried and recrystallized from ethanol to afford compound **12**. Colorless solid, yield-0.348 g, 95%; M.p. 310–312°C., IR (KBr): 2950, 2227, 1704, 1629 cm^{-1}; ^{1}H NMR data (DMSO-d_6): δ 1.00 (t, J = 7.2 Hz, 3H, CH_3), 1.25 (t, J = 7.2 Hz, 3H, CH_3), 2.72 (s, 3H, Ar-CH_3), 3.95 (q, J = 7.8 Hz, 2H, CH_2), 4.20 (q, J = 7.8 Hz, 2H, CH_2), 7.6 (s, 1H, Ar-H), 8.12 (s, 1H, Ar-H), 8.47 (s, 1H, -N=CH) 8.72 (s, 1H, Ar-H); ^{13}C NMR data (DMSO-d_6): δ 13.4, 13.9, 24.5, 59.9, 63.3, 81.4, 102.7, 110.1, 112.9, 139.2, 144.3, 147.3, 150.7, 151.6, 161.8, 164.1, 165.3; MS (*m*/*z*:) 368 (M+1, 100%); Anal.Calcd. (%) For $C_{17}H_{17}N_7$ (367.36): C, 55.58; H, 4.66; N, 26.69; Found (%) C, 55.35; H, 4.39; N, 26.41.

2.4i *Synthesis of compounds (**13 a–b**) and (**6**)*: A mixture of compound **12** (0.367 g, 0.001 mol) and primary amine (0.002 mol) in anhydrous acetonitrile (10 mL) was stirred at 40°C for 8–24 h. After completion of the reaction (TLC check with dichloromethane/methanol 9:1), the solvent was removed under reduced pressure to obtain solid. It was suction filtered, washed with cold acetonitrile, dried and purified by column chromatography (eluting with 1% methanol in dichloromethane) to afford compound **13 a–b** and **6**.

*7-(4,5-Dihydro-4-oxo-5-phenylpyrazolo[3,4-d]pyrimidin-1-yl)-5-methylpyrazolo[1,5-a] pyrimidine-3-carbonitrile (**13a**)*: IR (KBr): 3008, 2904, 2227, 1665, 1600 cm^{-1}; Colorless solid, yield 0.184 g, 50%; M.p. 339–341°C; ^{1}H NMR data (DMSO-d_6): δ 2.65 (s, 3H, Ar-CH_3), 6.52 (s, 1H, Ar-H), 7.42-7.62 (m, 6H, Ar-H), 8.72 (s, 1H, Ar-H), 10.44 (s, 1H, Ar-H); ^{13}C NMR data (DMSO-d_6): δ 24.6, 81.7, 102.9, 111.1, 113.2, 122.4, 122.4, 125.2, 131.1, 131.1, 133.4, 139.5, 144.8, 147.9, 151.1, 162.3, 163.8, 165.7, 166.2; MS (*m*/z): 369 (M+1, 100%); Anal. Calcd. (%) For $C_{19}H_{12}N_8O$ (368.35): C, 61.95; H, 3.28; N, 30.42; Found (%) C, 61.68; H, 2.98.; N, 30.68.

*7-(5-(4-Chlorophenyl)-4,5-dihydro-4-oxopyrazolo[3,4-d]pyrimidin-1-yl)-5-methylpyrazolo [1,5-a]pyrimidine-3-carbonitrile (**13b**)*: IR (KBr): 3012, 2907, 2233, 1663, 1600 cm^{-1}; Colorless solid, yield 0.201 g, 50%; M.p. 351–353°C; ^{1}H NMR data (DMSO-d_6): δ 2.69 (s, 3H, Ar-CH_3), 6.53 (s, 1H, Ar-H), 7.52–7.73 (m, 5H, Ar-H), 8.73 (s, 1H, Ar-H), 10.49 (s, 1H, Ar-H); ^{13}C NMR data (DMSO-d_6): δ 25.0, 81.5, 103.0, 111.4, 113.3, 123.0, 123.0, 132.0, 132.0, 133.1, 133.6, 140.1, 145.2, 148.1, 151.7, 162.6, 164.0, 165.6, 166.3; MS (*m*/*z*): 402 (M^+, 100%), 404 (M+2, 33%); Anal. Calcd. (%) For $C_{19}H_{11}ClN_8O$ (402.8): C, 56.65; H, 2.75; N, 27.82; Found (%) C, 56.41; H, 2.98.; N, 28.02.

2.4j *Synthesis of compounds (**14 a–d**)*: A mixture of compound **2** (0.188 g, 0.001 mol) and the corresponding anhydrides (0.001 mol) in DES (Choline chloride: urea) (1 gm) and catalytic amount of glacial acetic acid (2 drops) was stirred at 50°C for 5–8 h. After completion of the reaction (TLC check with dichloromethane/methanol 9:1) the viscous mass was cooled and extracted with a mixture of hexane/ethyl acetate (1:4) four times (4 × 10 mL). The organic layer was then washed with brine solution, water and dried over anhydrous sodium sulfate. Then, solvent was removed under reduced pressure to obtain solid which was purified by column chromatography (eluting with 5% methanol in dichloromethane) to furnish **14a–d**.

*7-(2,5-Dioxopyrrolidin-1-ylamino)-5-methylpyrazolo[1,5-a]pyrimidine-3-carbonitrile (**14a**)*: IR (KBr): 3205, 3030, 2229, 1670, 1612, 1571 cm^{-1}; ^{1}H NMR data ($CDCl_3$): δ 2.08 (s, 3H, Ar-CH_3), 2.62 (s, 4H, pyrrolidone), 6.76 (s, 1H, Ar-H), 8.20 (s, 1H, Ar-H), 8.84 (bs, 1H, -NH); ^{13}C NMRdata (DMSO-d_6): δ 24.2, 31.0 (2C's), 77.3, 88.6, 114.5, 146.5, 149.5, 150.7, 162.3, 167.3 (2C's); MS (*m*/*z*): 271 (M+1, 100%); Anal. Calcd. (%) For $C_{12}H_{10}N_6O_2$ (270.25): C, 53.33; H, 3.73; N, 31.10. Found (%) C, 53.10; H, 3.45; N, 30.82.

*7-(2,5-Dioxo-2H-pyrrol-1(5H)-ylamino)-5-methylpyrazolo[1,5-a]pyrimidine-3-carbonitrile (**14b**)*: IR (KBr): 3231, 3065, 2221, 1680, 1625, cm^{-1}; ^{1}H NMR data ($CDCl_3$): δ 2.10 (s, 3H, Ar-CH_3), 4.32 (s, 2H, pyrrolidone), 6.79 (s, 1H, Ar-H), 8.25 (s, 1H, Ar-H), 8.87 (bs, 1H, -NH); MS (*m*/*z*): 269 (M+1, 100%); Anal. Calcd. (%) For $C_{12}H_8N_6O_2$ (268.23): C, 53.73; H, 3.01; N, 31.33. Found (%) C, 53.46; H, 3.18; N, 31.49.

*7-(1,3-Dioxoisoindolin-2-ylamino)-5-methylpyrazolo[1,5-a]pyrimidine-3-carbonitrile **14c***: Colorless solid;

yield-0.270 g, 85%; M.p. 296–297°C; IR (KBr): 3225, 2915, 2227, 1693, 1618 cm^{-1}; ^1H NMR data (DMSO-d_6): δ 2.12 (s, 3H, Ar-CH_3), 6.71 (s, 1H, Ar-H), 7.5–7.9 (m, 4H, Ar-H), 8.69 (s, 1H, Ar-H), 10.89 (bs, 1H, -NH); ^{13}C NMR data (DMSO-d_6): δ 24.5, 78.1, 88.5, 114.7, 128.4 (2C's), 133.4 (2C's), 134.0 (2C's), 147.1, 149.2, 151.9, 162.5, 166.5 (2C's); MS (*m/z*): 319 (M+1, 100%); Anal.Calcd. (%) For $C_{16}H_{10}N_6O_2$ (318.29): C, 60.38; H, 3.17; N, 26.40. Found (%): C, 60.75; H, 3.49; N, 26.73.

*7-(Hexahydro-1, 3-dioxo-1H-isoindol-2(3H)-ylamino)-5-methylpyrazolo[1, 5-a] pyrimidine-3-carbonitrile (**14d**)*: IR (KBr): 3230, 2923, 2221, 1710, 1627, 1560, 1537 cm^{-1}; ^1H NMR data (DMSO-d_6): δ 1.77 (s, 4H, -CH_2), 2.37 (s, 4H, -CH_2), 2.20 (s, 3H, Ar-CH_3), 2.52 (s, 2 × CH), 6.69 (s, 1H, Ar-H), 8.78 (s, 1H, Ar-H), 10.79 (bs, 1H, -NH); ^{13}C NMR data (DMSO-d_6): δ 24.3, 25.5 (2C's), 27.1 (2C's), 42.1 (2C's), 78.8, 88.8, 115.7, 147.1, 150.1, 152.1, 163.2, 170.1 (2C's); MS (*m/z*): 324 (M^+, 100%); Anal. Calcd. (%) For $C_{16}H_{16}N_6O_2$ (324.34): C, 59.25; H, 4.97; N, 25.91. Found (%) C, 58.98; H, 4.81; N, 25.70.

2.4k *Synthesis of compound **16** and **17***: General procedure for the synthesis of compounds **16** and **17**: A mixture of compound **3** (0.173 g, 0.001 mol) and α-acetyl-γ-butyrolactone **15** (0.128 g, 0.001 mol) in dry toluene: phosphorous oxychloride (3:7) was heated under reflux for 12 h. After completion of reaction (TLC check with dichloromethane/methanol 9:1), excess of solvent was removed under reduced pressure and poured in ice cold water (20 mL), stirred, suction filtered to afford mixture of two compounds, which were separated by column chromatography (eluting with 0.5% ethyl acetate in hexane) to furnish **16** and **17**.

*6-Chloro-7-(2-chloroethyl)-5,8-dimethylpyrazolo[1,5-a]pyrido[3,2-e]pyrimidine-3-carbonitrile (**16**)*: Colorless solid; yield-0.153 g, 48%; M.p. 251–253°C, IR (KBr): 3050, 2938, 2227, 1615 cm^1; ^1H NMR data ($CDCl_3$): δ 2.45 (s, 3H, Ar-CH_3), 2.71 (s, 3H, Ar-CH_3), 3.07 (t, 3H, J = 6.8 Hz, $\underline{CH_2}CH_2Cl$), 3.70 (t, 3H, J = 6.8 Hz, $CH_2\underline{CH_2}Cl$), 8.27 (s, 1H, Ar-H); ^{13}C NMR data (DMSO-d_6): δ 22.1, 24.1, 32.2, 38.2, 77.3, 90.6 ,114.5, 142.8, 146.4, 148.3, 152.7, 159.9, 162.0, 168; MS (*m/z*): 319 (M^+, 100%) 321 (M+2, 65.2%) 323 (M+4, 10.5%); Anal. Calcd. (%) For $C_{14}H_{11}Cl_2N_5$ (320.18): C, 52.52; H, 3.46; N, 21.87. Found (%): C, 52.67; H, 3.80; N, 21.62.

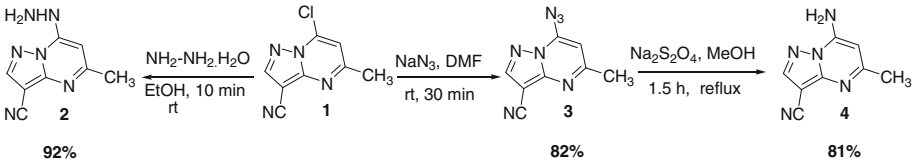
*6,10-Dimethyl-7,8-dihydrofuro[2′,3′:4,5]pyrido[3,2-e]pyrazolo[1,5-a]pyrimidine-1-carbonitrile (**17**)*: Colorless solid; yield-0.153 g, 48%; M.p. 250–253°C, IR (KBr): 3043, 2910, 2232, 1617, 1205 cm^{-1}; ^1H NMR data ($CDCl_3$): δ 2.45 (s, 3H, Ar-CH_3), 2.71 (s, 3H, Ar-CH_3), 2.94 (t, 3H, J = 6.3 Hz, CH_2CH_2O), 3.81 (t, 3H, J = 6.3 Hz, CH_2CH_2O), 8.27 (s, 1H, Ar-H); ^{13}C NMR (DMSO-d_6): δ 22.5, 24.2, 26.5, 76.4, 77.3, 90.4, 114.5, 146.2, 146.3, 148.5, 152.4, 162.1, 166.8, 168.4; MS (*m/z*): 265 (M^+, 100%); Anal. Calcd. (%) For $C_{14}H_{11}N_5O$ (265.27): C, 63.39; H, 4.18; N, 26.40. Found (%): C, 63.67; H, 3.89; N, 26.82.

3. Results and discussion

3.1 *Chemistry*

As part of our ongoing investigations, herein we directed our attention towards the development of new and efficient methods for synthesis of pyrazolo[1,5-*a*]pyrimidine derivatives using 7-chloro-5-methylpyrazolo[1,5-*a*]pyrimidine-3-carbonitrile **1** as a substrate.[29] Compound **1** was synthesized by the known literature procedure.[23] The reaction sequence employed for synthesis of two key scaffolds, 7-hydrazinyl-5-methylpyrazolo[1,5-*a*] pyrimidine-3-carbonitrile **2** and 7-amino-5-methylpyrazolo[1,5-*a*] pyrimidine-3-carbonitrile **4** is given in Scheme 1.

The reaction of compound **1** with hydrazine hydrate in ethanol at room temperature underwent S_NAr displacement to give hydrazine derivative **2** in 92% yield. It was characterised by spectroscopic and analytical data. For instance, the ^1H NMR showed broad singlet at δ 4.82 and 9.56 which verified -NH_2 and -NH protons, respectively. While the IR spectrum showed strong absorption bands at 3591, 3321, 3267 and 2219 cm^{-1} which indicated presence of -NH_2, -NH and –CN, respectively. The MS showed a molecular ion peak at *m/z* = 189 [M+1] corresponding to the molecular

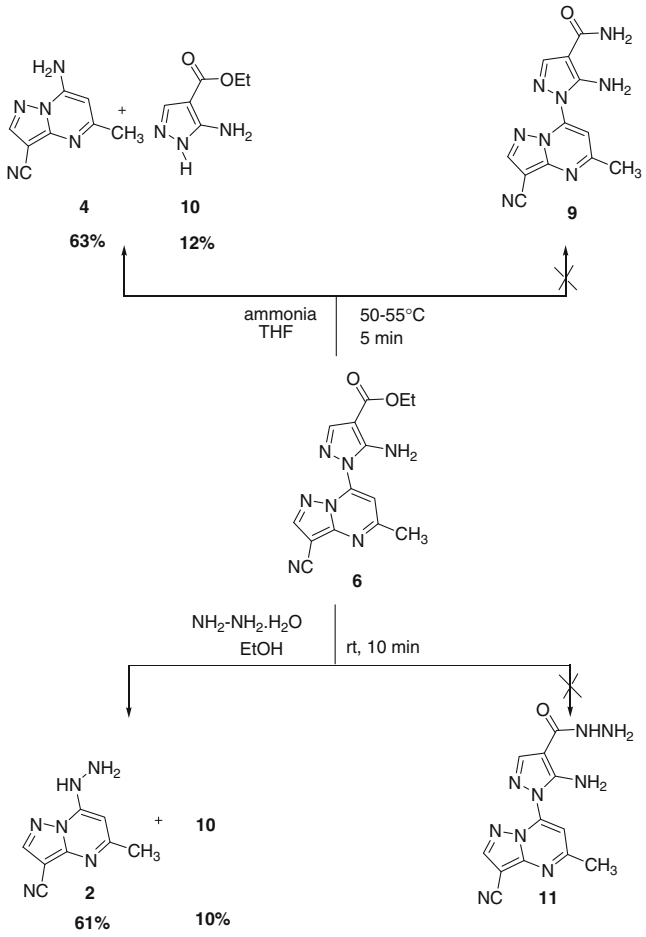


Scheme 1. Synthesis of 7-hydrazinyl-5-methylpyrazolo[1,5-*a*]pyrimidine-3-carbonitrile **2** and 7-amino-5-methylpyrazolo[1,5-*a*] pyrimidine-3-carbonitrile **4**.

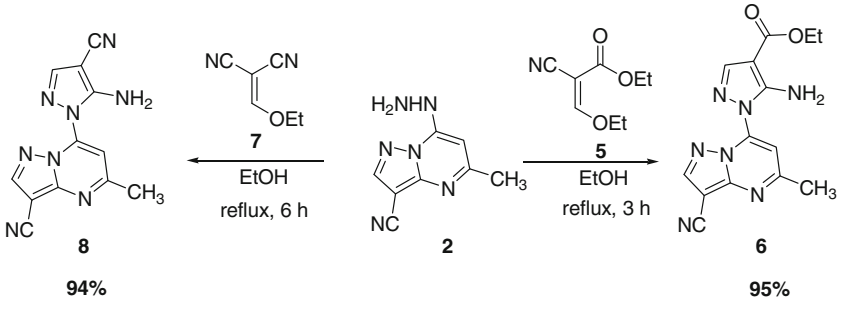
formula $C_8H_8N_6$. The azidation of **1** was successfully achieved by the S_NAr displacement of chloro by azide using sodium azide in dimethyl formamide to obtained compound **3** in 82% yield. The structure of **3** was confirmed by spectral and analytical data. The characteristic stretching frequency was observed at 2150 cm^{-1} due to azide group in IR spectrum of **3**. It is worth to note that addition of sodium azide in one lot into reaction mixture at 0°C or at higher temperature turned the reaction mixture to green color and that might lead to decomposition of product; hence, sodium azide was added portion wise at 0–5°C under stirring. The reduction of azido group was successfully achieved by using sodium dithionite in methanol at 65°C to obtain the desired compound **4** in 81% yield. The structure of compound **4** was confirmed by spectroscopic and analytical data. The ^1H NMR showed four broad singlets at δ 2.40, 6.18, 8.14 and 8.55 corresponding to -CH_3, pyrimidine ring protons, -NH_2 and pyrazole ring protons, respectively. In IR spectrum bands at 3337 and 3332 cm^{-1} correspond to –NH_2 group (Scheme 2).

Further the treatment of compound **2** with ethoxymethylenecyanoacetate **5** in presence of ethanol underwent annulation of pyrazole ring to afford ethyl 5-amino-1-(3-cyano-5-methylpyrazolo[1,5-*a*]pyrimidin-7-yl)-1*H*-pyrazole-4-carboxylate **6**, which was characterized by spectroscopic methods. For instance, the ^1H NMR spectrum of compound **6** showed triplet-quartet pattern at δ 1.35 and 4.32 representing the protons of ethoxy group, while -NH_2 protons appeared as broad singlet at δ 6.66 and the MS showed a molecular ion peak at m/z = 312 [M+1] corresponding to the molecular formula $C_{14}H_{13}N_7$. Similarly, condensation of compound **2** with ethoxymethylenmalononitrile **7** afforded compound **8** in 94% yield. Compound **8** was characterized by spectroscopic and analytical data. The presence of two nitrile functionalities were confirmed by appearance of bands at 2237 and 2219 cm^{-1} in its IR spectrum, which were in corroboration with the signals at δ 72.1 and 81.4 in its ^{13}C NMR.

An attempt to convert the ester functionality **6** into amide with ammonia was unsuccessful. Thus, compound **6** on treatment with ammonia in THF at 50–55°C yielded a mixture of two compounds **A** and **B** with 63% and 12%, respectively (Scheme 3). This mixture was separated by column chromatography eluting with 0.5% methanol in dichloromethane. Compound **A** was assigned to structure **4** while compound **B** was



Scheme 3. Reaction on ethyl 5-amino-1-(3-cyano-5-methylpyrazolo[1,5−*a*] pyrimidin-7-yl)-1*H*-pyrazole-4-carboxylate.



Scheme 2. Synthesis of Ethyl 5-amino-1-(3-cyano-5-methylpyrazolo[1,5-*a*] pyrimidin-7-yl)-1*H*-pyrazole-4-carboxylate **6** and 7-(5-Amino-4-cyano-1H-pyrazol-1-yl)-5-methylpyrazolo[1,5-a]pyrimidine-3-carbonitrile **8.**

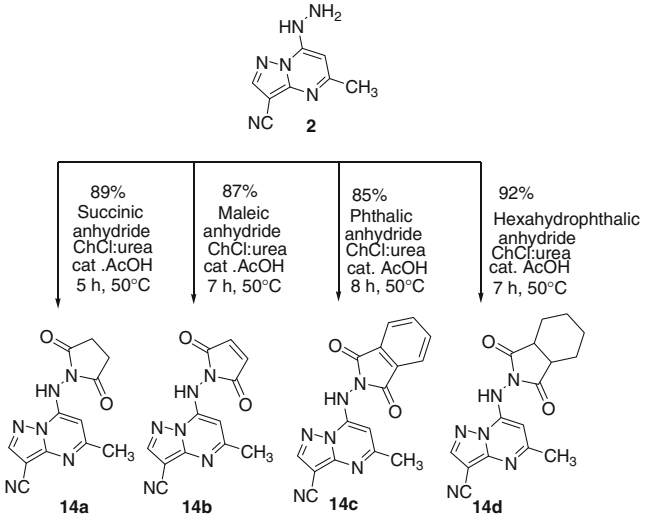
assigned to structure **10** on the basis of spectroscopic and analytical data. In this reaction, expected amide **9** was not formed, however, the heterocyclic nitrogen bond between pyrazolo pyrimidine and pyrazole ring was broken which could be due to basic medium. Similarly, we intended to convert ester group in **6** into acid hydrazide **11** which was also unsuccessful in an analogous manner; the carbon-nitrogen bond fission was observed and mixture of compounds **2** and **10** was obtained in 61% and 10% yield, respectively, which were separated by column chromatography and characterized by spectroscopic and analytical data.

The amino functionality in compound **6** could be utilized for the annulations of pyrimidine on pyrazole nucleus. Thus, **6** was treated with triethyl orthoformate using acetic anhydride as a catalyst which yielded synthon **12** in 90% yield (Scheme 4).

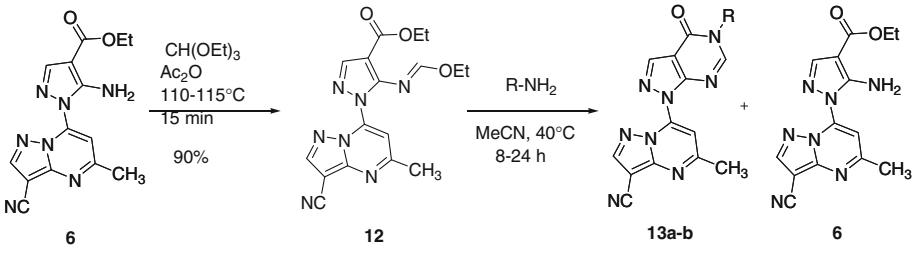
Further compound **12** reacted with aniline and substituted anilines yielded a mixture of two compounds **A** and **B**. The mixture was separated by column chromatography eluting with 1% methanol in dichloromethane. On the basis of spectroscopic and analytical data, compound **13a** was assigned to **A** and compound **6** was assigned to **B**. Analogously, compound **12** with *p*-chloro aniline yielded a mixture of two compounds, **13b** and **6**, which were characterised by spectral and analytical data.

The reactive hydrazine functionality in **2** was readily converted to their dioxopyrrolidinyl (**14a–b**) and dioxoisoindolyl (**14c–d**) derivatives with anhydrides (Scheme 5). Herein, we studied the different catalyst, reaction condition and solvent on model reaction (Table 2). The result revealed that when the reaction was carried out at 100°C in presence of acetic acid, products in good yield were obtained even after prolonged reaction time. However, analogous reaction in DES (ChCl:glycerol) and catalytic amount of acetic acid at 50°C furnished desired compounds with increased yield and reduced reaction time. Other eutectic mixtures (cholin chloride:urea and cholin chloride:malonic acid) were also tried to improve the yields. The DES of (cholin chloride:urea) in presence of catalytic amount of acetic acid was found to be most effective amongst the tested ones. It was also noted that, analogous reaction in the absence of acetic acid did not give satisfactory results. The structural assignments **14a–d** is based upon spectroscopic and analytical data (given in Experimental section).

Compound **4** having amino functionality was further employed for the annulation of tricyclic and tetracyclic heterocycles by condensation reaction with α-acetyl-γ-butyrolactone **15**. Thus, the condensation reaction of compound **4** with α-acetyl-γ-butyrolactone in phosphorous oxychloride/toluene (7:3) underwent cyclocondensation reaction to afford a mixture of



Scheme 5. Synthesis of dioxo pyrrolidones and dioxoisoindol **14 a-d**.



13	R
a	-C_6H_5
b	*p*-$CH_3C_6H_4$

Scheme 4. Synthesis of pyrazolo[3,4-*d*]pyrimidines- pyrazolo[1,5-*a*]pyrimidine **13a-b**.

Table 2. Optimization of solvent and catalysts for the synthesis of dioxo pyrrolidones and dioxoisoindol **14 a–d**.

Entry	Comp. No	Solvent, catalyst	Time(h)	Temp (°C)	Yield[a] (%)
1	**14a**	AcOH	12	100	58
		DES(ChCl:glycerol), AcOH	6	50	60
		DES(ChCl:urea), AcOH	5	50	89
		DES(ChCl:malonic acid), AcOH	5.5	50	97
2	**14b**	AcOH	15	100	55
		DES(ChCl:glycerol), AcOH	8	50	62
		DES(ChCl:urea), AcOH	7	50	87
		DES(ChCl:malonic acid), AcOH	7	50	86
3	**14c**	AcOH	13	100	54
		DES(ChCl:glycerol), AcOH	9	50	70
		DES(ChCl:urea), AcOH	8	50	85
		DES(ChCl:malonic acid), AcOH	8.5	50	82
4	**14d**	AcOH	13	100	57
		DES(ChCl:glycerol), AcOH	8	50	68
		DES(ChCl:urea), AcOH	7	50	92
		DES(ChCl:malonic acid), AcOH	8	50	91

6-chloro-7-(2-chloroethyl)-5,8-dimethylpyrazolo[1,5-*a*] pyrido[3,2-*e*]pyrimidine-3-carbonitrile **16** and 6,10-dimethyl-7,8-dihydrofuro[2′, 3′:4,5]pyrido[3,2-*e*]pyrazolo [1,5-*a*]pyrimidine-1-carbonitrile **17** in 48% and 15% yield, respectively. The mixture was separated by column eluting with 0.5% methanol in chloroform. The structures of compounds **16** and **17** were confirmed by spectroscopic and analytical data.

3.2 *Biological activity*

The antimicrobial activities of the synthesized compounds were evaluated by the agar cup plate method. The antibacterial and antifungal assays were performed in Muller-Hinton broth and Czapek Dox broth, respectively. Evaluation was performed using the bacteria reseeded in broth for 24 h at 37°C, and the fungi were reseeded in broth for 48 h at 25°C. The antibacterial activity of tested samples was studied against one Gram positive *Bacillus subtilis* NCIM 2250 and Gram negative *Escherichia Coli* ATCC 25922 bacteria while *Candida albicans* MTCC 277, *Candida tropicalis* MTCC 184, *Aspergillus niger* MCIM 545 and *Aspergillus clavatus* MTCC 1323 were used as standard fungal strains. The compounds were diluted in DMF with required concentration for bioassay. DMF was also loaded as control. Streptomycin and griseofluvin were used as standards to evaluate the potency of the tested compounds under same conditions. The zone of inhibition was determined from the diameter of the zone of inhibition using caliper. Each inhibition zone was measured three times to get average value. The minimum inhibitory concentration (MIC) values were determined on MH agar plates by pouring the molten agar in Petri dishes according to National Committee for Clinical Laboratory Standards (NCCLS, M7-A5 January 2000), containing the following concentrations (mg/mL): 0 (control), 5, 10, 15, 20, 30, 40. The MIC was defined as the lowest concentration of tested samples showing no visible bacterial growth after 24 h incubation period at 37°C.

Table 3. Antibacterial activity of compounds **6**, **8**, **13a–c**, **14a–d**, **16** and **17**.

Entry	*Bacillus subtilis* NCIM 2250	*Escherichia Coli* ATCC 25922
	ZI[a] (MIC)[b]	ZI (MIC)
6	17.1(25)	15.4(20)
8	16.1(20)	14.2(25)
13a	14.3 (15)	13.1(20)
13b	**14.0(15)**	**12.2(10)**
13c	14.2 (20)	16.3(25)
14a	**15.2(10)**	**14.8(10)**
14b	17.0(20)	16.4(20)
14c	15.1(25)	16.2(25)
14d	**16.4(10)**	13.2(25)
16	15.1 (20)	15.3(25)
17	14.1(25)	**16.4(10)**
Strept.	16.2(05)	16.4(05)

Bold values indicate better results. [a]Zone of inhibition in mm.
[b]Minimum inhibitory concentration in μg/mL.
[c]n.t. not tested.

The antibacterial and antifungal assay of compounds **6**, **8**, **13a–c**, **14a–d**, **16** and **17** are given in Tables 3 and 4, respectively. The results depicted revealed that most of the tested compounds displayed variable inhibitory effects on the growth of the tested Gram positive and Gram negative bacterial strains, and also against antifungal strains in micromolar concentration.

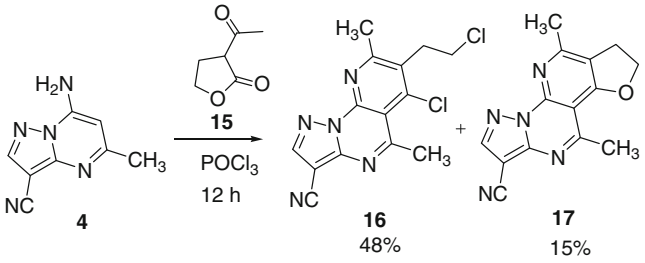
Table 4. Antifungal activity of compounds **6**, **8**, **13a–c**, **14a–d**, **16** and **17**.

Entry	*Candida albicans* MTCC 277	*Candida tropicalis* MTCC 184	*Aspergillus niger* MCIM 545	*Aspergillus clavatus* MTCC 1323
	ZI (MIC)	ZI (MIC)	ZI (MIC)	ZI (MIC)
6	–	15.4(20)	–	14.4(20)
8	17.1(25)	–	–	–
13a	15.3(20)	16.8(20)	14.4(20)	12.4(20)
13b	**13.4(15)**	13.7(20)	**15.2(15)**	**13.1(15)**
13c	17.4(20)	13.8(20)	16.6(20)	11.4(20)
14a	13.5(20)	16.2(20)	16.3(25)	15.3(20)
14b	–	16.4(20)	–	14.4(25)
14c	–	17.4(20)	–	13.4(20)
14d	19.1(25)	**15.8(10)**	**14.6(10)**	**17.6(15)**
16	15.4(20)	16.8(20)	17.2(20)	13.4(20)
17	–	16.4(20)	–	17.7(20)
Gris.	16.8(05)	17.3(05)	16.9(05)	17.6(05)

Bold values indicates better results. [a]Zone of inhibition in mm.
[b]Minimum inhibitory concentration in μg/mL.
[c]n.t. not tested.

Compound **14a** exhibited excellent antibacterial activity against gram-positive *B. subtilis* and gram-negative *E. coli* when compared with reference drug Streptomycin. While **17** showed comparable activity against only gram-negative *E. coli* in comparison with reference drug Streptomycin. On the other hand, compounds **13a** and **14b** showed good activity against gram-positive *B. subtilis* and gram-negative *E. coli* bacteria, respectively. However, compounds **6**, **8**, **13b**, **14c** and **16** showed comparatively weak activity against gram-positive *B. subtilis* and gram-negative *E. coli* bacteria. Compound **14d** was proven to be comparable antifungal agent against *C. tropicalis, A. niger and A. clavatus* and compounds **13a**, **13b** and **14a** illustrate good activity against *C. albicans, C. tropicalis, A. clavatus* and *A. niger*. The remaining compounds were found to have moderate activity against the tested organisms and some of the compounds were found to be inactive (indicated by – sign).

The variation in biological efficacy of tested compounds **6**, **8**, **13a–b**, **14a–d**, **16** and**17** might be due to their structural variations. In particular, compounds **14a** and **14d** containing dioxopyrrolidine, dioxo-isoindol alicyclic moieties and **17** with dihydrofuro-pyrido moiety might be the reason for excellent activity (Scheme 6). Thus, presence of these functional groups could be useful for synthesis of new derivatives with better potency.



Scheme 6. Synthesis of pyrazolo-pyrido-pyrimidine **16** and dihydrofuro-pyridopyrazolo-pyrimidine **17**.

4. Conclusions

Suitably functionalized pyrazolo[1,5-*a*]pyrimidines were successfully utilized for the synthesis of new pyrazolo[1,5-*a*]pyrimidine annulated heterocycles. The recyclable, nonvolatile deep eutectic solvents have been adopted for the synthesis of dioxopyrrolidinylamino-pyrazolo-pyrimidines (**14a–b**) dioxoisoindolinylamino-pyrazolo-pyrimidines (**14c–d)**, replacing less attractive solvents (for example acetic acid), with increased yields and reduced reaction times. The synthesized heterocycles were obtained by operationally simple, inexpensive and efficient methods in moderate to excellent yields. This method is currently being extended with the goal of generating a small library of fused pyrazolo[1,5-*a*] pyrimidines. Synthesized compounds were evaluated for antimicrobial activity. It was found that compound **14a** is a good antibacterial agent and **14d** is an excellent antifungal agent.

Supplementary Information (SI)

All additional information pertaining to characterization of the compounds using synthesis of pyrazolo[1,5-*a*]pyrimidine derivatives (Schemes S1–6), 1H-NMR spectra (Figures S1, 3, 4, 7, 9, 11, 13, 15, 17, 19, 20, 22,

24, 26), Mass spectrum (Figure S6), 13C-NMR spectra (Figures S2, 5, 8, 10, 12, 14, 16, 18, 21, 23, 25, 27) are given in Supplementary Information. The recovery and recycling of deep eutectic solvent (Table S1), Optimization of solvent and catalysts for the synthesis of dioxo pyrrolidones and dioxoisoindol (Table S2), antibacterial activity of compounds (Table S3) and antifungal activity of compounds (Table S4) are also given in the Supporting Information, available at www.ias.ac.in/chemsci.

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References

1. George C F P 2001 *Lancet.* **357** 1623
2. Stefano A, Anna A, Maurizio B, Alessandra T, Francisco O, Silvia S, Chiara B and Matilde Y 2010 *Chem. Med. Chem.* **5** 1242
3. Curran K J, Verheijen J C, Kaplan J, Richard D J, Toral-Barza L, Hollander I, Lucas J, Ayral-Kaloustian S, Yu K and Zask A 2010 *Bioorg. Med. Chem. Lett.* **20** 1440
4. Zask A, Verheijen J C, Curran K, Kaplan J, Richard D J, Nowak P, Malwitz D J, Brooijmans N, Bard J and Svenson K 2009 *J. Med. Chem.* **52** 5013
5. Manetti F, Santucci A, Locatelli G A, Maga G, Spreafico A, Serchi T, Orlandini M, Bernardini G, Caradonna N P and Spallarossa A 2007 *J. Med. Chem.* **50** 5579
6. Schenone S, Bruno O, Ranise A, Bondavalli F, Brullo C, Fossa P, Mosti L, Menozzi G, Carraro F and Naldini A 2004 *Bioorg. Med. Chem. Lett.* **14** 2511
7. Traxler P, Bold G, Frei J, Lang M, Lydon N, Mett H, Buchdunger E, Meyer T, Mueller M and Furet P 1997 *J. Med. Chem.* **40** 3601
8. Ballell L, Field R A, Chungc G A C and Youngc R J 2007 *Bioorg. Med. Chem. Lett.* **17** 1736
9. Gudmundsson K S, Johns B A and Weatherhead J 2009 *Bioorg. Med. Chem. Lett.* **19** 5689
10. Rashad A E, Hegab M I, Abdel-Megeid R E, Micky J A and Abdel-Megeid F M E 2008 *Bioorg. Med. Chem.* **16** 7102
11. Frizzo C P, Scapin E, Campos P T, Moreira D N and Martins M A P 2009 *J. Mol. Struct.* **933** 142
12. Novinson T, Bhooshan B, Okabe T, Revankar G R, Wilson H R, Robins R K and Senga K 1976 *J. Med. Chem.* **19** 512
13. Senga K, Novinson T, Wilson H R and Robins R K 1981 *J. Med. Chem.* **24** 610
14. Di Grandi M J, Berger D M, Hopper D W, Zhang C, Dutia M, Dunnick A L, Torres N, Levin J I, Diamantidis G and Zapf C W 2009 *Bioorg. Med. Chem. Lett.* **19** 6957
15. Ahmed O M, Mohamed M A, Ahmed R R and Ahmed S A 2009 *Eur. J. Med. Chem.* **44** 3519
16. Heathcote D A, Patel H, Kroll S H B, Hazel P, Periyasamy M, Alikian M, Kanneganti S K, Jogalekar A S, Scheiper B and Barbazanges M 2010 *J. Med. Chem.* **53** 8508
17. Fraley M E, Rubino R S, Hoffman W F, Hambaugh S R, Arrington K L, Hungate R W, Bilodeau M T, Tebben A J, Rutledge R Z and Kendall R L 2002 *Bioorg. Med. Chem. Lett.* **12** 3537
18. Petroski R E, Pomeroy J E, Das R, Bowman H, Yang W, Chen A P and Foster A C 2006 *J. Pharmacol. Exp. Ther.* **317** 369
19. Bantwal S and Manjathuru M 2006 *Bioorg. Med. Chem. Lett.* **14** 2040
20. Sherif A F 2010 *Bioorg. Med. Chem.* **18** 2767
21. Agarwal R, Sumran G and Garg N 2011 *Eur. J. Med. Chem.* **46** 3038
22. Jorda R, Havlícek L, McNae I W, Walkinshaw M D, Voller J, Sturc A, Navrátilová J, Kuzma M, Mistrík M, Bártek J, Strnad M and Krystof V 2011 *J. Med. Chem.* **54** 2980
23. Wang S Q, Fang L, Liu X and Zaho K 2004 *Chin. Chem. Lett.* **15** 885
24. Singh B and Lobo H 2011 *Catal. Lett.* **141** 178
25. Pawar P M and Jarag K J 2011 *Green Chem.* **13** 2130
26. Abott A and Capper G 2003 *Chem. Commun.* 70
27. Chikhalikar S, Bhawe V, Ghotekar B, Jachak M and Ghagare M 2011 *J. Org. Chem.* **76** 3829
28. Chiklikar S, Bhawe V, Jachak M and Ghagare M 2011 *Eur. J. Org. Chem.* **42** 6085
29. Rote R, Shelar D, Patil S and Jachak M 2011 *Org. Prep. Proced. Int.* **43** 457
30. Balwant S and Ganpati S 2011 *Catal. Lett.* **141** 178