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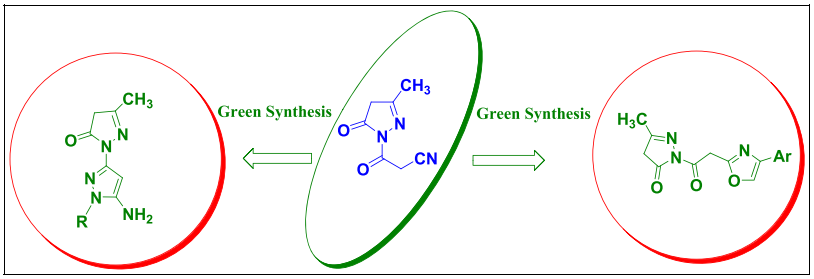
Received May 29, 2018
DOI 10.1002/jhet.3360
Published online 19 November 2018 in Wiley Online Library (wileyonlinelibrary.com).



New intermediate 3-methyl-5-oxopyrazol propanenitrile was synthesized by one pot three component reactions using ethyl cyanoacetate, hydrazine hydrate, and ethyl acetoacetate and was used for the synthesis of new oxazole and pyrazole derivatives. All reactions were carried out using eco-friendly solvents and without catalyst.

J. Heterocyclic Chem., **56**, 38 (2019).

INTRODUCTION

Green chemistry provide alternative synthetic pathway for prevention of pollution in the utilization of set of principal that reduces or eliminates the use or generation of hazardous substances in the design, manufacture, and application of chemical products or processes [1]. Organic solvents are used in preparative chemistry for years as they offer many advantages such as the ability to dissolve reagents, substrates, and catalysts. The most commonly used aprotic solvents include *N*,*N*-dimethylformamide, dimethylacetamide, and *N*-methyl-2-pyrrolidone. On the downside, however, over 80% of the waste produced was organic solvents employed for synthesis, workup, and purification. Recently, much of the efforts have been directed towards developing alternative reaction media, thereby providing an important contribution to green chemistry. Therefore, it is required to develop chemical procedures based on greener organic solvents.

Dimethyl carbonate (DMC) is a nonpolar, aprotic solvent with good miscibility with water, biodegrades readily in the atmosphere, and is non-toxic. DMC is classified under the greenest "recommended" bracket according to the solvent selection guide [2,3] that include other green solvents such as water and ethanol. DMC can be a potential replacement for methyl ethyl ketone, ethyl acetate, and most other ketones [4]. Glycerol as solvents, whose properties can be tailored, tuned, and adjusted according to the requirement of each reaction and separation [5]. Ionic liquid is a liquid entirely composed of ions that are fluid at relatively low temperature, from ambient temperature to 100°C. Ionic liquids have been investigated as a viable substitute for conventional volatile organic solvents. Ionic liquids impart low volatility/flammability and high chemical or electrochemical stability [6]. Water can be considered as the greenest solvent as it is non-toxic to health and the environment. Moreover, it is the safest and least expensive solvent. Considerable attention has been directed towards the use of water as a medium in organic synthesis for sustainability, non-toxicity, and safety reasons [7]. Switching from organic solvents to water at an industrial scale has been discussed [8]. The aqueous-ethanol mixture could be used as the reaction medium in many reactions [9–15]. Bentley *et al.* used aqueous alcohol for the solvolysis study of *p*-methoxybenzoyl chloride in and found the rate of reactions are not much affected in water and in aqueous alcohol medium [16]. A synthesis of benzopinacol from benzophenone is carried out by Geeta Verma using ethanol as a solvent [17]. Mirgane *et al.* utilized aqueous ethanol as suitable medium for diastereoslective Diels–Alder reaction of anthrone and (*R*)-(+)-*N*-α-methylbenzylmaleimide using chiral bases [18]. Bioethanol could be the green alternative for sustainable future [19].

The development of green solvents in biomass processing and for biorefinery applications has been presented [20]. Further, the importance of green chemistry in pharmaceutical industry [21] and textile

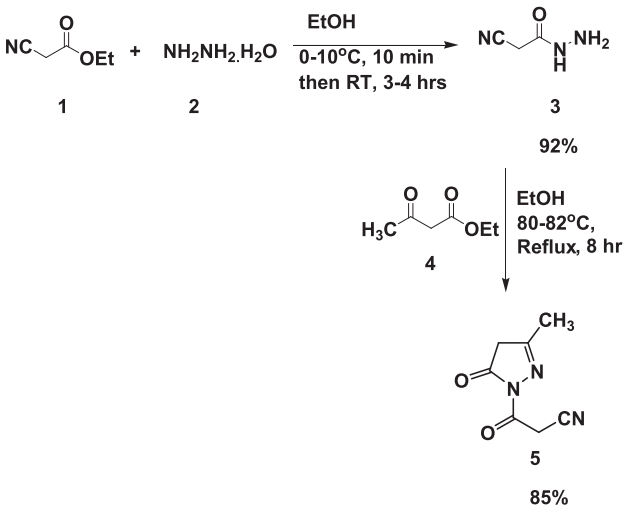
industry [22] has been described. Development of sustainable synthetic strategy is the great challenge for the organic chemist. The development of green synthetic pathway needs multifunctional reaction intermediate. Such intermediate should also need to have higher oxidation potential to reduce the reactants. The driving force for new C—C bond formation is the high oxidation potential of the intermediate that avoid the drastic reaction conditions or hazardous catalyst. Syntheses of substituted oxazole derivatives are important because of their diverse range of biological activities in pharmaceutical areas [23]. Oxazoles are continued to be of interest for both their biological activities and synthetic utility [24–26]. The synthesis of aryl-oxazole is the subject of ongoing improvements [27]. It is worth to mention that the combination of heterocyclic moiety fused with pyrazole ring may increase their biological activities or create new medicinal properties due to different electronic distribution [28,29]. Solvent and catalyst free method was reported for substituted oxazole using 2-bromo-1-phenylethanone, urea and easily recoverable and reusable polyethylene glycol as a non-ionic liquid [30]. Fused oxazole could be synthesized by microwave method using mixture of 4-phenyl-pyridine-4,6-dione, bromoacetothiophenone, K_2CO_3, and *N*,*N*-dimethylformamide [31]. Copper (I) and zinc (II) catalyzed routes for synthesis of oxazoles via secondary propargylamides in one pot multicomponent reaction from aldehydes, LiN $(TMS)_2$, alkynes, and acid chlorides were reported [32]. Oxazole derivatives were synthesized by reacting with ketone and aldehyde to form keto enol intermediate that was reacted with a base hydroxylamine hydrochloride to obtained oxazole derivative [33]. Synthesis of 2,4,5-trisubstituted oxazoles via copper catalyzed oxidative cyclization of arylamides and β-diketones was also reported [34]. Tomi *et al*. reported the synthesis of some oxazole derivatives from hippuric acid and demonstrated their biological activities [35].

These literature reports and broad spectrum of oxazole and pyrazole derivatives inspired us to design new derivatives and their synthesis without harming the environment. In this paper, we have reported green and efficient synthesis of pyrazole and oxazole derivatives from 3-(4,5-dihydro-3-methyl-5-oxopyrazol-1-yl)-3-oxopropanenitrile **5**. Anintermediate compound 3-(4,5-dihydro-3-methyl-5-oxopyrazol-1-yl)-3-oxopropanenitrile **5** was used for the synthesis of verity of pyrazole and oxazole derivatives.

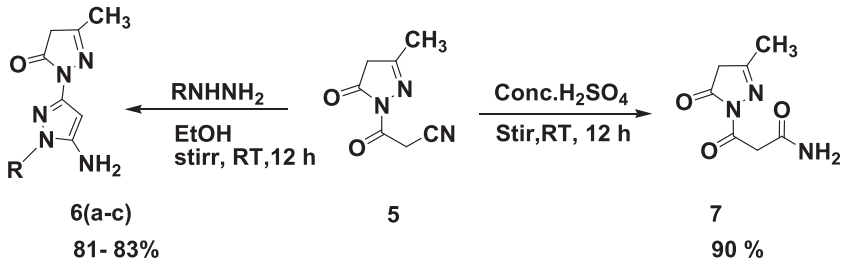
RESULTS AND DISCUSSION

2-Cyano acetohydrazide **3** was obtained by the reaction of ethyl cyanoacetate **1** and hydrazine hydrate **2** in ethanol at room temperature according to literature method [34]. This compound **3** was condensed with ethylacetoacetate **4** yielded intermediate 3-(4,5-dihydro-3-methyl-5-oxopyrazol-1-yl)-3-oxopropanenitrile **5** in 85% yields (Scheme 1). The structure of compound **5** was established by spectral and analytical techniques. The IR spectra of 3-(4,5-dihydro-3-methyl-5-oxopyrazol-1-yl)-3-oxopropanenitrile **5** showed the characteristics carbonyl (C═O) stretching frequency at 1695–1700 cm^{-1}, (CN) stretching at 2200 cm^{-1} and (H—C═O) at 3200 cm^{-1}. The ^1H NMR showed singlet at 1.31 δ for three protons of methyl (CH_3) group. The singlet appeared at 3.54 δ corresponded to two protons of CH_2 group attached to CN and the singlet at 2.44 δ for two protons of another CH_2 group of pyrazolone ring. The mass spectrum of **5** showed characteristic M^+ peak at 165 (exact mass is 165.15) and corresponded to the molecular formula $C_7H_7N_3O_2$. On the basis of spectral and analytical data, structure was assigned as 3-(4,5-dihydro-3-methyl-5-oxopyrazol-1-yl)-3-oxopropanennitrile **5**. The reaction of oxopropanenitrile **5** and substituted hydrazines in ethanol at room temperature yielded 1-(5-amino-1-phenyl-1*H*-pyrazol-3-yl)-3-methyl-1*H*-pyrazol-5(4*H*)-one **6** in 81–83% yield (Scheme 2). The compound **6a** was characterized by spectral and analytical techniques. The IR spectra of the compound **6** showed the characteristics carbonyl (C═O) stretching frequency at 1705 cm^{-1}, (C═N) stretching at 2235 cm^{-1}, (H—C) stretching frequency at 2850 cm^{-1}, and (H—N) stretching frequency at 3350 cm^{-1} (Scheme 2).The ^1H NMR (DMSO-d_6) spectrum of compound **6** showed singlet at 1.32 δ for three protons of methyl (CH_3) group. The singlet appeared at 2.45 δ corresponded to two protons of CH_2 group pyrazolone. The compound **6a** also showed broad singlet at 4.30 δ for two protons of NH_2 group. The singlet appeared at 6.55 δ corresponded to one

Scheme 1. Synthesis of 3-(4,5-dihydro-3-methyl-5-oxopyrazol-1-yl)-3-oxopropanenitrile **5**.



Scheme 2. Synthesis of pyrazole derivatives.



6	R	% Yield
a	H	81
b	Phenyl	87
c	2,4-DNP	83

proton of =CH group of pyrazole ring and broad singlet appeared at 12.06 δ corresponded to NH proton of pyrazole ring. The mass spectrum of the compound **6a** showed characteristic M^+ peak at 179 (exact mass is 179.18) corresponded to molecular formula $C_7H_9N_5O$. The confirmation of compound **6a** as 1-(5-amino-1-phenyl-1*H*-pyrazol-3-yl)-3-methyl-1*H*-pyrazol-5(4*H*)-one was based on the aforementioned spectral and analytical data.

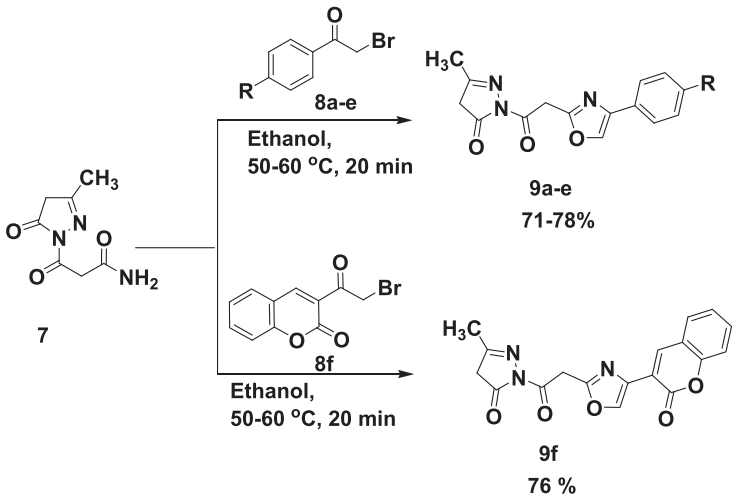
The reaction of 3-(4,5-dihydro-3-methyl-5-oxopyrazol-1-yl)-3-oxopropanenitrile **5** with concentration H_2SO_4 at room temperature for 12 h furnished 3-(4,5-dihydro-3-methyl-5-oxopyrazol-1-yl)-3-oxopropanamide **7** in excellent yield (Scheme 2). It was characterized by spectral and analytical techniques. The IR spectra of **7** showed the characteristics carbonyl (C=O) stretching frequency at 1705 cm^{-1}, (C=N) stretching at 1695 cm^{-1}, amide (H_2N—C=O) stretching frequency at 1685 $cm^{-1}$and (H—C) stretching frequency at 2855 cm^{-1}. The ^1H NMR spectrum (DMSO-d_6) of 3-(4,5-dihydro-3-methyl-5-oxopyrazol-1-yl)-3-oxopropanamide **7** showed singlet at 1.33 δ for three proton of methyl CH_3 group. The singlets appeared at 2.54 and 3.64 δ corresponded proton of two CH_2 groups of pyrazolone and methylene CH_2 attached amide. The broad singlet at 10.67 δ was for two protons of NH_2 group. The mass spectrum of compound **7** showed characteristic M^+ peak at 183 (exact mass is 183.16) corresponded to the molecular formula $C_7H_9N_3O_3$. On the basis of these analysis structure **7**, that is, 3-(4,5-dihydro-3-methyl-5-oxopyrazol-1-yl)-3-oxopropanamide **7** was assigned to this compound. The reaction of 3-(4,5-dihydro-3-methyl-5-oxopyrazol-1-yl)-3-oxopropanamide **7** with substituted phenacyl bromide **8a–e** in ethanol under heating for 20 min yielded oxazole derivatives of 3-methyl-5-oxopyrazol propanenitrile **9a–e** in 68–78% yield (Scheme 3).

It was characterized by spectral and analytical techniques. The IR spectra of **9a** showed the characteristics carbonyl (C=O) stretching frequency at 1696–1705 cm^{-1}, (C=N) stretching at 1690 cm^{-1} and (H—C) stretching frequency at 2855 cm^{-1}. The ^1H NMR spectrum (DMSO) of this solid showed singlet at 1.28 δ for three protons of methyl CH_3 group. The singlet appeared at 2.39 δ corresponded to two protons of CH_2 group near to C=O in pyrazolone ring. The broad singlet at 3.49 δ was for two protons of CH_2 group attached to oxazole ring. The doublets appeared at 7.30 and 7.50 δ corresponded to aromatic proton of benzene ring. The ^{13}C NMR spectrum (DMSO) of this solid showed peak at 24.3 δ assigned to carbon of the methyl groups. ^{13}C NMR showed the aromatic carbon appears at their respective position. The peaks at 162.8 and 163.2 δ corresponded to two carbonyl carbons. The mass spectrum of solid showed characteristic M + 1 and M + 2 peaks at 317 and 319, respectively, (exact mass is 317.73) corresponded to the molecular formula $C_{15}H_{12}ClN_3O_3$. On the basis of these analysis structures, 1-(2-(4-(4-chlorophenyl) oxazol-2-yl) acetyl)-3-methyl-1*H*-pyrazol-5(4*H*)-one **9a** was assigned to this compound.

MATERIALS AND METHODS

All the chemicals and solvents had been purified by standard literature procedures, and moisture was removed from the glass apparatus using $CaCl_2$ drying tubes. The melting points determined in open capillary tubes with Gallenkamp melting point apparatus and are uncorrected. FT-IR spectra recorded on Bruker FTIR-TENSOR II spectrophotometer using Platinum ATR discs. ^1H NMR spectra of synthesized compounds recorded on Bruker Ascend 500 NMR spectrophotometer at 500 MHz frequency in $CDCl_3$ or dimethyl sulfoxide (DMSO-d_6) using tetramethylsilane as internal standard. Chemical shifts recorded in δ ppm and multiplicities are given as s (singlet), bs (broad singlet), d (doublet), t (triplet), q (quartet), or m (multiplet). Mass spectra were recorded on

Scheme 3. Synthesis of oxazole derivatives.



9	R	% Yield
a	Cl	**78**
b	Br	**73**
c	NO_2	**71**
d	CH_3	**68**
e	OCH_3	**77**

a Shimadzu LC–MS QP 2010A mass spectrometer with an ionization potential of 70 eV. Elemental analyses were performed on Thermo Quest Flash 1112 Series EA analyzer. Reactions monitored by thin layer chromatography using 0.2 mm silica gel 60 F_{254} (Merck, Delhi, India) plates using UV light (254 and 366 nm) for detection. Common reagent grade available chemicals were utilized without further purification or prepared by standard literature procedures. All the compounds have been synthesized by conventional methods.

EXPERIMENTAL

The mixture of ethyl cyanoacetate **1** (10.63 mL, 0.1 mol) and hydrazine hydrate **2** (4.85 mL, 0.1 mol) in 20 mL ethanol was stirred at 0–10°C for 10 min and further stirred at room temperature for 3 h. The white crystalline product formed was filtered, washed with ethanol (20 mL), and dried in a hot air oven at 60°C; mp: 109–110°C, lit. [35], mp: 108°C; yield: 92%.

Synthesis of 3-(4,5-dihydro-3-methyl-5-oxopyrazol-1-yl)-3-oxopropanenitrile (5). 3-(4,5-dihydro-3-methyl-5-oxopyrazol-1-yl)-3-oxopropanenitrile **5** was prepared by cyclization reaction of 2-cyanoacetichydrazide **3** (0.99 g, 0.01 mol) and ethylacetoacetate **4** (1.27 mL, 0.01 mol) at reflux temperature (82°C) in ethanol (30 mL) for 7–8 h (TLC check). The white solid separated was filtered, washed with ethanol, and recrystallized from ethanol afforded white crystalline solid **5** in good yield.

White crystalline solid, mp: 211–212°C, yield: 85%; IR (KBr) (νcm^{-1}): 3380, 2980, 1640, 1542; ^{1}H NMR (DMSO-d_6) δ: 1.31 (s, 3H, CH_3), 2.44 (s, 2H, CH_2), 3.54 (s, 2H, CH_2CN) ppm; ^{13}C NMR (DMSO-d_6) δ: 24.6, 42.1, 76.3, 151.8, 153.7, 160.3, 172.8 ppm; MS (70 eV) m/z (%): 165 [M^+]. *Anal*. Calcd. for $C_7H_7N_3O_2$ (mol. wt. 165.13): C(50.91), H(4.27), N(25.44); found: C(50.78), H(4.52), N(25.68).

Synthesis of substituted 1-(5-amino-1*H*-pyrazol-3-yl)-3-methyl-1*H*-pyrazol-5(4*H*)-one (6a–c). The solution of 3-methyl-5-oxopyrazol propanenitrile **5** (1.651 g, 0.01 mol) in ethanol (20 mL) was added drop wise to the hydrazine hydrate (0.49 mL, 0.01 mol), phenyl hydrazine (0.98 mL, 0.01 mol), or 2,4-dinitro phenyl hydrazine (1.981 g, 0.01 mol) respectively with constant stirring for 12 h. The precipitate was filtered and washed with water and recrystallized from ethanol afforded compounds **6a**.

1-(5-Amino-1*H*-pyrazol-3-yl)-3-methyl-1*H*-pyrazol-5(4*H*)-one (6a). mp: 188–189°C, yield: 81%; pale yellow solid; IR (KBr) (ν): 3360, 2840, 2230, 1710 cm^{-1}; ^{1}H NMR (DMSO-d_6) δ: 1.32 (s, 3H, CH_3), 2.45 (s, 2H, CH_2), 4.30 (s, 2H, NH_2), 6.55 (s, 1H, pyrazole ═CH), 12.06 (bs, 1H, NH) ppm; ^{13}C NMR (DMSO-d_6) δ: 27.6, 48.8, 58.6, 85.4, 156.7, 160.8, 173.5 ppm; MS (70 eV) m/z (%): 179 [M^{+1}]. *Anal*. Calcd. for $C_7H_9N_5O$: C(46.92), H(5.06), N(39.09); found: C(46.79), H(5.32), N(39.36).

1-(5-Amino-1-phenyl-1*H*-pyrazol-3-yl)-3-methyl-1*H*-pyrazol-5(4*H*)-one (6b). mp: 196–197°C, yield: 87%; yellow solid; IR (KBr) (ν): 3350, 2850, 2235, 1705 cm^{-1}; ^1H NMR (DMSO-d_6) δ: 1.31 (s, 3H, CH_3), 2.45 (s, 2H, CH_2), 3.64 (bs, 2H, NH_2), 6.57 (s, 1H, pyrazole ═CH), 7.52–7.54 (m, 5H, Ar─H) ppm; ^{13}C NMR (DMSO-d_6) δ: 24.8, 42.3, 80.5, 120.4 (2C) 126.3, 129.6 (2C), 140.1, 146.2, 160.2, 161.6, 172.4 ppm; MS (70 eV) m/z (%): 255 [M^+]. *Anal*. Calcd. for $C_{13}H_{13}N_5O$ (mol. wt. 255.18): C(61.17), H(5.13), N(27.43); found: C(60.94), H(5.33), N(27.73).

1-(5-Amino-1-(2,4-dinitrophenyl)-1*H*-pyrazol-3-yl)-3-methyl-1*H*-pyrazol-5(4*H*)-one (6c). mp: 203–204°C, yield: 83%; orange solid; IR (KBr) (ν): 3380, 2980, 2240, 1730 cm^{-1}; ^1H NMR (DMSO-d_6) δ: 1.33 (s, 3H, CH_3), 2.60 (s, 2H, CH_2), 4.85 (bs, 2H, NH_2), 6.8 (s, 1H, pyrazole ═CH), 8.1 (d, 1H, J = 8.3 Hz, Ar─H), 8.8 (d, 1H, J = 8.3 Hz, Ar─H), 9.4 (q, 1H, Ar─H) ppm; ^{13}C NMR (DMSO-d_6) δ: 24.3, 42.6, 80.5, 122.8, 123.4, 127.8, 129.6, 139.5 141.3, 146.8, 147.9, 161.5, 173.7 ppm; MS (70 eV) m/z (%): 345 [M^+]. *Anal*. Calcd. for $C_{13}H_{11}N_7O_5$ (mol. wt. 345.27): C(45.22), H(3.21), N(28.40); found: C(44.98), H(3.44), N(28.63).

3-(4,5-Dihydro-3-methyl-5-oxopyrazol-1-yl)-3-oxopropanamide (7). In 3-methyl-5-oxopyrazol propanenitrile **5** (1.651 g, 0.01 mol) concentration H_2SO_4 was added drop wise with constant stirring for 12 h (TLC checked, Toluene : Acetone; 8:2). After completion of reaction, the reaction mixture was poured in ice cold water, stirred continuously to remove excess of impurities formed during the reaction. The solid obtained was collected by filtration, washed with water, dried, and recrystallized from ethanol.

mp: 183–184°C, yield: 90%; yellow solid; IR (KBr) (ν): 2855, 1705, 1695, 1685 cm^{-1}; ^1H NMR (DMSO-d_6): 1.33 (s, 3H, CH_3), 2.54 (s, 2H, CH_2), 3.64 (s, 2H, CH_2), 10.67 (bs, 2H, NH_2) ppm; ^{13}C NMR (DMSO-d_6) δ: 24.8, 42.5, 44.6, 160.1, 163.3, 170.8, 171.5 ppm; MS (70 eV) m/z (%): 183 [M^+]. *Anal*. Calcd. for $C_7H_9N_3O_3$ (mol. wt. 183.16): Calcd: C(45.90), H(4.95), N(22.94); found: C(45.74), H(5.15), N(23.13).

Synthesis of oxazole derivatives of 3-methyl-5-oxopyrazol propanenitrile (9a–e). 3-(4,5-Dihydro-3-methyl-5-oxopyrazol-1-yl)-3-oxopropanamide **7** (1.831 g, 0.01 mol) in ethanol (10 mL), the reaction mixture was stirred for 10 min in ethanol. To this solution, appropriate phenacyl bromide **9a–f** (0.01 mol) was added, and the reaction mixture was heated at 50–60°C for 20 min (TLC check Hexane : Ethyl acetate 2:1 mixture). The brown solid separated was filtered, dried, and recrystallized from ethanol.

Synthesis of 1-(2-(4-(4-chlorophenyl)oxazol-2-yl)acetyl)-3-methyl-1*H*-pyrazol-5(4*H*)-one (9a). mp: 252–253°C, yield: 78%; pale yellow solid; IR (KBr) (ν): 3385, 2960, 2245, 1710, 1685 cm^{-1}; ^1H NMR (DMSO-d_6) δ: 1.28 (s, 3H, CH_3), 2.39 (s, 2H, CH_2), 3.49 (s, 2H, CH_2), 7.30 (d, 2H, J = 8.3 Hz, Ar─H), 7.50 (d, 2H, J = 8.3 Hz, Ar─H), 7.85 (s, 1H, oxazole ═CH) ppm; ^{13}C (DMSO-d_6) δ: 24.3, 33.8, 42.5, 128.9 (2C), 129.5 (2C), 131.3, 134.5,140.1, 140.3, 150.7, 159.5,162.8, 163.2 ppm; MS (70 eV) m/z (%): 317 [M^+], 319 [M^{+2}]. *Anal*. Calcd. For $C_{15}H_{12}ClN_3O_3$ (mol. wt. 317.73): C(56.70), H(3.81), N(13.23); found: C(56.48), H(4.08), N(13.51).

Synthesis of 1-(2-(4-(4-bromophenyl)oxazol-2-yl)acetyl)-3-methyl-1*H*-pyrazol-5(4*H*)-one (9b). mp: 260–261°C, yield: 73%; pale yellow solid; IR (KBr) (ν): 3373, 2940, 2230, 1705, 1682 cm^{-1}; ^1H NMR (DMSO-d_6) δ: 1.31 (s, 3H, CH_3), 2.50 (s, 2H, CH_2), 3.45 (s, 2H, CH_2), 7.45 (d, 2H, J = 8.2 Hz, Ar─H), 7.68 (d, 2H, J = 8.2 Hz, Ar─H), 7.92 (s, 1H, oxazole ═CH) ppm. *Anal*. Calcd. for $C_{15}H_{12}BrN_3O_3$ (mol. wt. 362.18): C(49.74), H(3.34), N(11.60); found: C(49.51), H(3.55), N(11.83).

Synthesis of 3-methyl-1-(2-(4-(4-nitrophenyl)oxazol-2-yl) acetyl)-1*H*-pyrazol-5(4*H*)-one (9c). mp: 277–278°C, yield: 71%; yellow solid; IR (KBr) (ν): 3378, 2940, 2285, 1704, 1680, 1545, 1355 cm^{-1}; ^1H NMR (DMSO-d_6) δ: 1.38 (s, 3H, CH_3), 2.35 (s, 2H, CH_2), 3.73 (s, 2H, CH_2), 7.93 (d, 2H, J = 8.5 Hz, Ar─H), 7.97 (s, 1H, oxazole ═CH), 8.09 (d, 2H, J = 8.5 Hz, Ar─H) ppm. *Anal*. Calcd. for $C_{15}H_{12}N_4O_5$ (mol. wt. 328.28): C(54.88), H(3.68), N(17.07); found: C(54.60), H(3.91), N(17.31).

Synthesis of 3-methyl-1-(2-(4-*p*-tolyloxazol-2-yl)acetyl)-1*H*-pyrazol-5(4*H*)-one (9d). mp: 234–235°C, yield: 68%, color: light orange solid; IR (KBr) (ν): 3370, 2930, 2280, 1705, 1680 cm^{-1}; ^1H NMR (DMSO-d_6) δ: 1.20 (s, 3H, CH_3), 2.34 (s, 2H, CH_2), 2.48 (s, 3H, CH_3), 3.83 (s, 2H, CH_2), 7.21 (d, 2H, J = 8.0 Hz, Ar─H), 7.46 (d, 2H, J = 8.0 Hz, Ar─H), 7.90 (s, 1H, oxazole ═CH) ppm. *Anal*. Calcd. for $C_{16}H_{15}N_3O_3$ (mol. wt. 297.31): C(64.64), H(5.09), N(14.13); found: C(64.42), H(5.34), N(14.38).

Synthesis of 1-(2-(4-(4-methoxyphenyl)oxazol-2-yl)acetyl)-3-methyl-1*H*-pyrazol-5(4*H*)-one (9e). mp: 217–218°C, yield: 77%; orange solid; IR (KBr) (ν): 3364, 2915, 2273, 1704, 1683 cm^{-1}; ^1H NMR (DMSO-d_6) δ: 1.34 (s, 3H, CH_3), 2.51 (s, 2H, CH_2), 3.46 (s, 2H, CH_2), 3.89 (s, 3H, OCH_3), 7.11 (d, 2H, J = 8.0 Hz, Ar─H), 7.33 (d, 2H, J = 8.0 Hz, Ar─H), 7.85 (s, 1H, oxazole ═CH) ppm. *Anal*. Calcd. for $C_{16}H_{15}N_3O_4$ (mol. wt. 313.31): C(61.34), H(4.83), N(13.41); found: C(61.04), H(5.03), N(13.68).

Synthesis of 3-methyl-1-(2-(4-(2-oxo-2*H*-chromen-3-yl) oxazol-2-yl)acetyl)-1*H*-pyrazol-5(4*H*)-one (9f). mp: 281–282°C, yield: 76%; light brown solid; IR (KBr) (ν): 3380, 2943, 2281, 1704, 1695, 1682 cm^{-1}; ^1H NMR (DMSO-d_6) δ: 1.38 (s, 3H, CH_3), 2.58 (s, 2H, CH_2), 3.81 (s, 2H, CH_2), 7.28 (d, 2H, J = 1.2, 8.5 Hz, Ar─H), 7.33 (d, 1H, J = 2.2, 8.5 Hz, Ar─H), 7.41 (m, 1H, J = 1.2, 2.2, 8.5 Hz, Ar─H), 7.73 (s, 1H, oxazole ═CH), 7.82 (s, 1H,

chromrne =CH) ppm; ^{13}C NMR (DMSO-d_6) δ: 24.8, 33.9, 42.7, 121.7, 122.1, 125.5 (2C), 126.9, 128.52, 129.65, 141.8, 146.1, 150.5, 159.7, 162, 163.1, 163.3 ppm; MS (70 eV) m/z (%): 351 [M^+]. *Anal*. Calcd. for $C_{18}H_{13}N_3O_5$ (mol. wt. 351.31): C(61.54), H(3.73), N(11.96); found: C(61.16), H(3.98), N(12.24).

CONCLUSION

We have reported green synthesis of pyrazole and oxazole derivatives using eco-friendly solvent without using any catalyst. Valuable features of the present method include broad substrate scope, short reaction time, straightforward procedure, and easy aqueous work up that facilitated 80–85% recovery of pure product and use of inexpensive chemicals and reagents.

Acknowledgments. Authors thanks Sophisticated Analytical Instrumentation Facility centre, Panjab University, Chandigad, Savitribai Phule Pune University for providing analytical service to scan 1H NMR, 13C NMR etc. and KTHM College, Nashik for other facilities.

REFERENCES AND NOTES

[1] Anastas, P. T.; Warner, J. C. Green Chemistry: Theory and practice; Oxford University Press: Oxford, 1998.
[2] Jessop, P. G. Green Chem 2011, 13, 1391.
[3] Prat, D.; Wells, A.; Hayler, J.; Sneddon, H.; McElroy, C. R.; Abou-Shehada, S.; Dunn, P. Green Chem 2016, 18, 288.
[4] Pyo, S.; Park, J. H.; Chang, T.; Hatti-Kaul Curr Opin Green Sustainable Chem 2017, 5, 61.
[5] Wolfson, A.; Snezhko, A.; Meyouhas, T.; Tavor, D. Green Chem Lett Rev 2012, 5, 7.
[6] Yoo, C. G.; Pu, Y.; Ragauskas, A. J Curr Opin Green Sustainable Chem 2017, 5, 5.
[7] Sheldon, R. A. Green Chem 2017, 19, 18.
[8] Parmentier, M.; Gabriel, C. M.; Guo, P.; Isley, N. A.; Zhou, J.; Gallou, F. Curr. Opin. Green Sustainable Chem. 2017, 7, 13.
[9] Prat, D.; Hayler, J.; Wells, A. Green Chem 2014, 16, 4546.
[10] Reinhardt, D.; Ilgen, F.; Kralisch, D.; König, B.; Kreisel, G. Green Chem 2008, 10, 1170.
[11] Alaimo, P. J Org Lett 2008, 10, 5111.
[12] Laitinen, A.; Takebayashi, Y.; Kylänlahti, I.; Yli-Kauhaluoma, J.; Sugeta, T.; Otake, K. Green Chem 2004, 6, 49.
[13] Pai, C. K.; Smith, M. B. J Org Chem 1995, 60, 3731.
[14] Li, C. J.; Chen, L. Chem Soc Rev 2006, 35, 68.
[15] Kobayashi, S.; Hamada, T.; Nagayama, S.; Manabe, K. Org Lett 2001, 3, 165.
[16] Bentley, W. T.; Ebdon, D. N.; Kim, E. J.; Koo, I. S. J Org Chem 2005, 70, 1647.
[17] Geeta Verma Chem Sci J 2017, 8, 3.
[18] Mirgane Nitin, A.; Karnik Anil, V. Green Chem Lett Rev 2011, 4, 269.
[19] Clark, J. H.; Farmer, T. J.; Hunt, A. J.; Sherwood, J. Int J Mol Sci 2015, 16, 17101.
[20] Soh, L.; Eckelman, M. J. ACS Sustainable Chem Eng 2016, 4, 5821.
[21] Koenig, S. G.; Dillon, B. Curr. Opin. Green Sust Chem. 2017, 7, 56.
[22] Islam, S.; Sun, G. ACS Sust Chem Eng 2017, 5, 7451.
[23] Dabholkar, V. V.; Ahmed, S. S. Indian J Het Chem 2010, 20, 171.
[24] Trogu, E.; Cecchi, D. L.; Sarlo, F.; Guideri, L.; Ponticelli, F.; Machetti, F. Eur J Org Chem 2009, 5, 5971.
[25] Bode, J. W.; Hachisu, Y.; Matsuura, T.; Suzuki, K. Org Lett 2003, 5, 391.
[26] Han, X.; Li, C.; Mosher, M. D.; Rider, K. C.; Zhou, P.; Crawford, R. L.; Fusco, W.; Paszczynski, A.; Natale, N. R. Bioorg Med Chem 2009, 17, 1671.
[27] Smeltzer, C.; Cannon, M. J.; Pinson, P.; Munger, J. S.; West, F. G.; Grissom, C. B. Org Lett 2001, 3, 799.
[28] Pinho, T.; Melo, E. Curr Org Chem 2005, 9, 925.
[29] Yeh, V. S. C. Tetrahedron 2004, 60, 11995.
[30] Gokhale, K. M.; Wagal, O. A.; Kanitkar, A. S. IntJPharmPhytopharmacolRes 2012, 1, 156.
[31] Dabholkar, V. V.; Mustaqeem, M. A.; Shinde, N. B.; Yadav, O. G Res J Chem Sci 2014, 4, 42.
[32] Wang, Q.; Ganem, B. Tetrahedron Lett 2003, 44, 6829.
[33] Black, D. A.; Arndtsen, B. A Tetrahedron 2005, 61, 11317.
[34] Bai, Y.; Chen, W.; Chen, Y.; Huang, H.; Xiao, F.; Deng, G.-J. RSC Adv 2015, 5, 8002.
[35] Tomi, I. H. R.; Jumbad, H.; Tomma, A.; Al-Daraji, H. R.; Al-Dujaili, A. H. J Saudi Chem. Soc 2015, 19, 392.