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SYNTHESIS OF 3-(1-SUBSTITUTED-5-PHENYL-4,5-DIHYDRO-1*H*-PYRAZOL-3-YL)-4-SUBSTITUTED BENZO[4,5]IMIDAZO[2,1-C][1,2,4]TRIAZINES AS INSECTICIDAL AGENTS

Kanti Sharma* [a], Lokesh Kumar Sharma[a] and Renuka Jain[b]

[a]*Department of Chemistry, R.L. Saharia Govt. P.G. College, Kaladera, Jaipur-303 801, India*
[b]*Department of Chemistry, University of Rajasthan, Jaipur-302 004, India*
* E-mail: drkanti@gmail.com

Abstract
An efficient, one pot, three component (1-(4-substituted benzo[4,5]imidazo[2,1-c] [1,2,4] triazin-3-yl) ethanones **4**, benzaldehyde and hydrazino derivative), more sustainable and catalyst free reaction has been developed for the synthesis of 3-(1-substituted-5-phenyl-4,5-dihydro-1*H*-pyrazol-3-yl)-4-substitutedbenzo[4,5]imidazo[2,1-c] 1,2,4]triazines **5-7** in glycerol in good yields that were comparable to or better than in conventional media or alternative green solvent. It is noteworthy that the reaction was exclusively carried out in glycerol- water system, rendering the methodology highly valuable from both environmental and economic points of view. 1-(4-Substituted benzo[4,5]imidazo [2,1-c][1,2,4]triazin-3-yl) ethanones **4** have also been prepared by the cyclization of 2-(1*H*-benzimidazol-2-yl) hydrazono-1,3-disubstituted-1,3-diketones **3** in glycerol. The synthesized compounds have been characterized by analytical and spectral (IR, ^{1}H NMR, ^{13}C NMR and mass) data and screened for insecticidal activity against *Periplaneta americana* and exhibited excellent results.

Keywords: 3-(1-Substituted-5-phenyl-4,5-dihydro-1*H*-pyrazol-3-yl)-4-substituted benzo[4,5] imidazo[2,1-c][1,2,4]triazines, glycerol-water mediated syntheses, insecticidal agents.

Introduction:

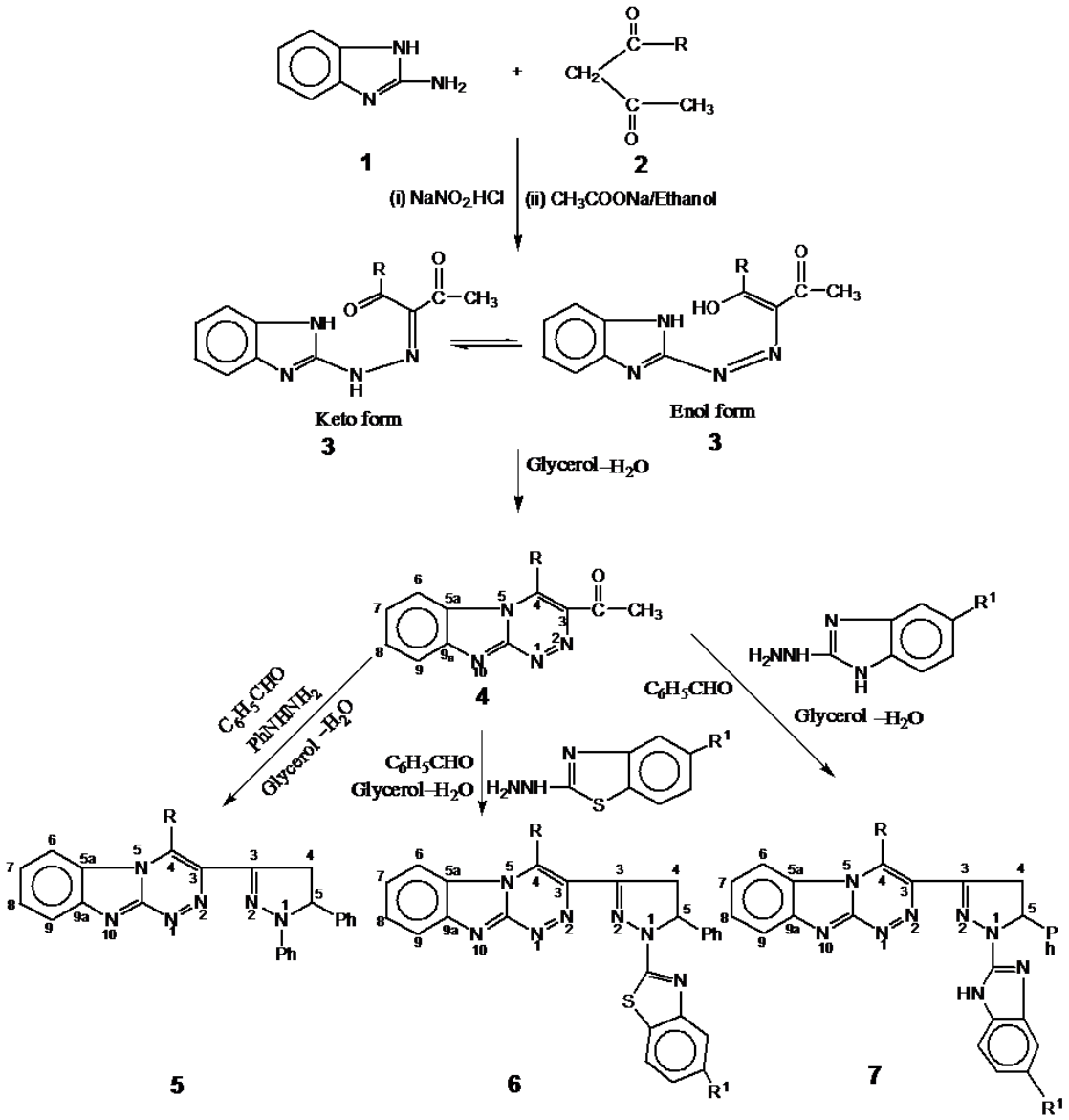
The chemists are increasingly using safer solvents *i.e*. green solvents instead of the hazardous organic solvents in the reaction during the past decades. The pathways for syntheses are selected so as to avoid the generation of toxic materials and enable the recyclability of the materials if possible. This reduces the impact of the process on the environment in terms of pollution or consumption.

The simplest and most easily available solvent, water is of ecological and economical concern because of its specific physical and chemical properties *i.e*. network of H-bonding, high heat specific capacity and low viscosity. In recent decades, glycerol, a trihydric alcohol which is a colorless, viscous, polar liquid and easily miscible with water is used as a green solvent in many organic reactions. A combination of these two is a still better option due to the high boiling point and increased solubility of organic compounds.

Benzimidazoles show wide range of biological activities like antimicrobial,[i] antifungal,[ii] anticancer,[iii] analgesic and anti-inflammatory.[iv] Pyrazoles are found to be associated with

analgesic,[v] antipyretic,[vi] antioxidative,[vii] anti-inflammatory,[viii] antitubercular, [ix] etc. activities. Triazines show antimicrobial, [x] antifungal, [xi] etc. activities. In the course of syntheses of bioactive benzimidazoles[xii-xv] through greener route some novel benzo[4,5]imidazo[1,2-c] [1,2,4] triazines (**Scheme 1**) have been synthesized using glycerol as an alternative green solvent with a hope that the additive effect of three nuclei would enhance the biological activity.

2-Aminobenzimidazole (**1**) was diazotized with $NaNO_2$ and HCl at 0 °C and reacted with acetyl ketones **(2)** *i.e.* acetylacetone / benzoyl acetone in the presence of sodium acetate in ethanol to give 2-(1*H*-benzimidazol-2-yl) hydrazono-1, 3-disubstituted-1, 3-diketones (**3**). [xv] The compounds **3** were cyclized in glycerol–H_2O resulting in the formation of 1-(4-substituted benzo[4,5]imidazo[2,1-c] [1,2,4] triazin-3-yl) ethanones **4**.



Scheme 1: Synthesis of compounds **4-7**

Compound	R	R^1	Compound	R	R^1	Compound	R	R^1
4a	CH_3	-	**6a**	CH_3	H	**7a**	CH_3	H
4b	C_6H_5	-	**6b**	CH_3	Cl	**7b**	CH_3	CH_3
5a	CH_3	-	**6c**	C_6H_5	H	**7c**	C_6H_5	H
5b	C_6H_5	-	**6d**	C_6H_5	Cl			

Cyclization in this medium is being reported for the first time. Similar cyclization reaction with other nucleus has been reported in PPA.[xvi] Triazine fused tetrazolone derivatives were prepared by 1,3-dipolar cycloaddition.[xvii] Polat et al[xviii] synthesized triazine-thiones by reacting pyridoin with thiosemicarbazides in ethanol in presence of *p*-toluene sulfonic acid and also studied equilibrium and stability constant using ethanol - water mixtures.

Due to low cost, lesser time for reaction and simple workup process one pot multi-component synthesis was carried out. Benzaldehyde, phenyl hydrazine/ 2-hydrazinobenzothiazole/ 2-hydrazinobenzimidazole and **4** were reacted in glycerol-H_2O as green solvent, yielding 3-(1-substituted-5-phenyl-4,5-dihydro-(1*H*-pyrazol-3-yl)-4-substituted benzo[4,5]imidazo[2,1-c][1,2,4]triazines (**5-7**) in 92-98 % yields. Syntheses of **4** and **5** were also investigated in various solvent systems, but best results were obtained in glycerol-water system.

All the synthesized compounds were evaluated for insecticidal activity and excellent results were obtained.

Experimental:

Melting points are uncorrected and were taken in open glass capillaries using Gallenkamp melting point apparatus. The IR spectra were recorded on an 8400S SHIMADZU IR spectrometer in KBr pellets and band positions are recorded in wave numbers (cm^{-1}). ^1H NMR and ^{13}C NMR spectra were recorded on a JEOL 300 MHz instrument using $CDCl_3$ at 300 and 75 MHz, respectively and chemical shifts (δ) are given in ppm. TMS was used as internal reference. The mass spectra were recorded on Xevo-Q-TOF (ASAP) mass spectrometer. Elemental analyses were performed at Central Drug Research Institute, Lucknow, India. Chemicals were purchased from Acros organics. Hydrazono compounds **3**,[xv] 2-hydrazino benzothiazoles[xix] and 2-hydrazinobenzimidazoles[xix] were synthesized according to the literature methods.

*General procedure for preparation of 1-(4-substituted benzo[4,5]imidazo[2,1-c] [1,2,4]triazin-3-yl-ethanone (**4**)*

The hydrazono compound **3** (5 mmol) was added to glycerol (5 mL) and water (2 mL) mixture and heated further to 90 °C with stirring. The progress of reaction was monitored by TLC using EtOAc-n hexane (1:4). After completion of reaction, warm water (5 mL) was added and the insoluble crude products were isolated by simple filtration. This was dissolved in warm EtOH and allowed to stand at room temperature for 5-6 h. The crystalline solid was collected and dried to give **4**.The filtrate containing glycerol was extracted with methyl *tert*-butyl ether (2×5mL) to remove any organic compounds dissolved in aqueous phase. The aqueous layer was separated and water was evaporated under reduced pressure at 100 ^oC to give pure glycerol which was used for next run under similar conditions.

1-(4-Methylbenzo[4,5] imidazo[2,1-c][1,2,4]triazin-3-yl)-ethanone (4a): Yield: 95 %; m.p. 204-206 °C; Anal. Calcd. for $C_{12}H_{10}N_4O$: C, 63.70; H, 4.45; N, 24.76 %. Found: C, 63.73,

H, 4.42, N, 24.80 %; IR (KBr, cm^{-1}): 1680 (**C**OCH_3), 1535 (N=N), 1280, 1195; ^{1}H NMR (300 MHz, $CDCl_3$, δ/ppm): 7.82-6.58 (m,4H,Ar-H), 3.56 (s, 3H, $COCH_3$), 1.82 (s, 3H, CH_3); ^{13}C NMR (75 MHz, $CDCl_3$, δ/ppm): 175.3 (**C**OCH_3), 141.5 (C=N), 138.6 (C-N), 138.5 (C-N), 137.8 (C-N), 137.7 (C-N), 122.9 (CH=), 122.8 (CH=), 116.5 (CH=), 116.4 (CH=), 74.1 (CO**C**H_3), 28.4 (CH_3); HRMS (m/z): 227.2470 $(M+H)^+$.

1-(4-Phenylbenzo[4,5] imidazo[2,1-c][1,2,4]triazin-3-yl)-ethanone (4b): Yield: 93 %; m.p. 230-232 °C; Anal. Calcd. for $C_{17}H_{12}N_4O$: C, 70.82; H, 4.19, N, 19.43 %. Found: C, 70.85, H, 4.18, N, 19.46 %; IR (KBr, cm^{-1}): 1685(**C**OCH_3), 1530 (N=N), 1285, 1200; ^{1}H NMR (300 MHz, $CDCl_3$, δ/ppm): 7.86-6.42 (m,9H,Ar-H), 3.58 (s, 3H, $COCH_3$); ^{13}C NMR (75 MHz, $CDCl_3$, δ/ppm): 176.4 (**C**OCH_3), 141.5 (C=N), 138.8 (C-N), 138.7 (C-N), 137.7 (C-N), 137.6 (C-N), 136.5 (C), 129.2 (CH=), 129.1 (CH=), 128.5 (CH=), 127.1 (CH=), 127.0 (CH=), 122.9 (CH=), 122.8 (CH=), 115.3 (CH=), 115.2 (CH=), 74.4 (CO**C**H_3); HRMS (m/z): 289.3197 $(M+H)^+$.

*General procedure for the preparation of 3-(1-substituted-5-phenyl-4,5-dihydro-1H-pyrazol-3-yl)-4-substituted benzo[4,5]imidazo[2,1-c][1,2,4]triazines (**5-7**)*

To a stirred solution of **4** (1 mmol) in water (2 mL) and glycerol (5 mL) benzaldehyde (1 mmol) was added and the reaction mixture was heated to 90 °C. After 30 min hydrazino derivative (1.2 mmol) was added to the mixture. The reaction mixture was stirred vigorously at 90 °C for further 60-90 min and the progress of reaction was monitored by TLC using EtOAc-n hexane (1:4). After completion of reaction, warm water (5 mL) was added .Glycerol dissolved in water and insoluble crude products were isolated by simple filtration. The solid obtained was crystallized from EtOH to afford the pure compounds **5-7**.The filtrate containing glycerol was extracted with methyl *tert*-butyl ether (2×5mL) to remove any organic compounds dissolved in aqueous phase. The aqueous layer was separated and water was evaporated under reduced pressure at 100 ^oC to give pure glycerol which was used for next run under similar conditions.

3-(1,5-Diphenyl-4,5-dihydro-1H-pyrazol-3-yl)4-methylbenzo[4,5]imidazo[2,1-c][1,2,4]triazine (5a): Yield: 93 %; m.p. 220-221 °C; Anal. Calcd. for $C_{25}H_{20}N_6$: C, 74.25; H, 4.95; N, 20.79 %. Found: C, 74.21, H, 4.92, N, 20.81 %; IR (KBr, cm^{-1}) : 1620 (C=N, pyrazoline); ^{1}H NMR (300 MHz, $CDCl_3$, δ/ppm) : 7.89-6.65 (m, 14H, Ar-H), 5.51 (t, J = 7.7Hz,1H, C**H**Ph), 3.15 (d, J = 7.9Hz, 2H, CH_2), 1.78 (s, 3H, CH_3); ^{13}C NMR (75 MHz, $CDCl_3$, δ/ppm) : 163.8 (C=N), 143.5(N-N-C), 142.4 (C), 141.6 (C=N), 138.8 (C-N), 138.7 (C-N), 137.8 (C-N), 137.7 (C-N), 129.3 (CH=), 129.2 (CH=), 128.3 (CH=), 128.2 (CH=), 127.1 (CH=), 127.0 (CH=), 126.5 (CH=), 126.4 (CH=), 122.9 (CH=), 122.8 (CH=), 121.8 (CH=), 121.6 (CH=), 115.3 (CH=), 115.2 (CH=) , 78.8 (**C**HPh), 44.9 (CH_2), 30.2 (CH_3); HRMS (m/z): 401.4863 $(M+H)^+$.

3-(1,5-Diphenyl-4,5-dihydro-1H-pyrazol-3-yl)4-phenylbenzo[4,5]imidazo[2,1-c][1,2,4]triazine (5b) : Yield: 94 %; m.p. 231-233 °C; Anal. Calcd. for $C_{30}H_{22}N_6$: C, 77.23; H, 4.75, N, 18.01 %. Found: C, 77.21, H, 4.76, N, 18.03 %; IR (KBr, cm^{-1}): 1625 (C=N , pyrazoline); ^{1}H NMR (300 MHz, $CDCl_3$, δ/ppm) : 7.85-6.75 (m, 19H, Ar-H), 5.54 (t, J = 7.7Hz,1H, C**H**-Ph), 3.18 (d, J = 7.9Hz, 2H, CH_2); ^{13}C NMR (75 MHz, $CDCl_3$, δ/ppm) : 164.2 (C=N), 143.5 (N-N-C), 142.4 (C), 141.5 (C=N), 138.7 (C-N), 138.5 (C-N), 137.6 (C-N), 137.5 (C-N), 136.5 (C), 129.4 (CH=), 129.3 (CH=), 129.2 (CH=), 129.1 (CH=), 128.6 (CH=), 128.5 (CH=), 128.2 (CH=), 127.3 (CH=),127.2 (CH=), 127.1 (CH=), 127.0 (CH=), 122.8 (CH=), 122.7 (CH=), 121.7 (CH=), 121.5 (CH=), 116.2 (CH=), 116.1 (CH=), 115.5 (CH=), 115.4 (CH=), 79.2 (**C**H-Ph), 44.7 (CH_2); HRMS (m/z): 467.5580 $(M+H)^+$.

3-[1-(Benzothiazol-2-yl)-5-phenyl-4,5-dihydro-1H-pyrazol-3yl]-4-methylbenzo[4,5]imidazo[2,1-c][1,2,4]triazine (6a): Yield: 92 %; m.p. 275-277 °C; Anal. Calcd. for $C_{26}H_{19}N_7S$: C, 67.64; H, 4.15;N, 21.25;S,6.94 %. Found: C, 67.67, H, 4.18, N, 21.28; S, 6.92 %; IR (KBr, cm^{-1}): 1625 (C=N, pyrazoline); ^{1}H NMR (300 MHz, $CDCl_3$,

δ/ppm) : 7.88-6.78 (m,13H, Ar-H), 5.56 (t, J = 7.7Hz, 1H, C**H**Ph), 3.20 (d, J = 7.9Hz, 2H, CH_2), 1.68 (s, 3H, CH_3); ^{13}C NMR (75 MHz, $CDCl_3$, δ/ppm) : 174.5(N–C=N), 163.8 (C=N), 148.1(C-N), 141.5(C=N), 142.4(C), 138.7(C-N), 138.6(C-N), 137.8(C-N), 137.7(C-N), 128.3(CH=), 128.2(CH=), 127.1(CH=), 127.0(CH=), 126.5(CH=), 125.8(CH=), 125.1(CH=), 122.9(CH=), 122.8(CH=), 122.7(CH=), 122.6(C-S), 122.1(CH=), 115.5(CH=), 115.4(CH=), 78.8 (**C**H-Ph), 44.8 (CH_2), 29.5 (CH_3); HRMS (m/z) : 462.5602 $(M+H)^+$.

3-[1-(5-Chlorobenzothiazol-2-yl)-5-phenyl-4,5-dihydro-1H-pyrazol-3-yl]-4-methylbenzo [4,5] imidazo [2,1-c] [1,2,4] triazine (6b): Yield: 95 %; m.p. 280-282 °C; Anal. Calcd. for $C_{26}H_{18}N_7SCl$: C, 62.96; H, 3.65; N, 19.76; S, 6.46 %. Found: C, 63.00, H, 3.62, N, 19.79, S, 6.48 %; IR (KBr, cm^{-1}): 1620 (C=N, pyrazoline), 765 (C-Cl); ^1H NMR (300 MHz, $CDCl_3$, δ/ppm): 7.86-6.75 (m,12H,Ar-H), 5.51 (t, J = 7.7Hz,1H, C**H**Ph), 3.22 (d, J = 7.9Hz, 2H, CH_2), 1.72 (s, 3H, CH_3); ^{13}C NMR (75 MHz, $CDCl_3$, δ/ppm): 174.5(N–C=N), 164.4 (C=N), 149.5(C-N), 142.4(C), 141.5(C=N), 138.8(C-N), 138.7(C-N), 137.8(C-N), 137.7(C-N), 130.4(C-Cl), 128.3(CH=), 128.2(CH=), 127.2(CH=), 127.1(CH=), 126.5(CH=), 126.2(CH=), 124.1(CH=), 122.9(CH=), 122.8(CH=), 122.5(CH=), 120.7(C-S), 115.5(CH=), 115.4(CH=), 74.2 (**C**H-Ph), 44.5 (CH_2), 29.8 (CH_3) ; HRMS (m/z) : 497.0052 $(M+H)^+$.

3-[1-(Benzothiazol-2-yl)-5-phenyl-4,5-dihydro-1H-pyrazol-3yl]-4-phenylbenzo[4,5] imidazo [2,1-c] [1,2,4]triazine (6c) **:**Yield: 94 %; m.p. 286-287 °C; Anal. Calcd. for $C_{31}H_{21}N_7S$: C, 71.12; H, 4.01; N, 18.73; S, 6.11 %. Found: C, 71.11, H, 4.04, N, 18.70; S, 6.15 %; IR (KBr, cm^{-1}) : 1610 (C=N, pyrazoline); ^1H NMR (300 MHz, $CDCl_3$, δ/ppm) : 7.75-6.68 (m,18H,Ar-H), 5.52 (t, J = 7.7Hz, 1H, C**H**Ph), 3.16 (d, J = 7.9Hz, 2H, CH_2); ^{13}C NMR (75MHz,$CDCl_3$,δ/ppm) : 174.5(N-C=N), 164.4(C=N), 148.1(C-N), 142.4(C), 141.5(C=N), 138.9(C-N), 138.8(C-N), 137.8(C-N), 137.7(C-N), 136.5(C), 129.1(CH=), 129.0(CH=), 128.5(CH=), 128.3(CH=), 128.1(CH=), 127.3(CH=), 127.2(CH=), 127.1(CH=), 127.0(CH=), 126.5(CH=), 125.8(CH=), 125.1(CH=), 122.9(CH=), 122.8(CH=), 122.7(CH=), 122.6(C-S), 122.1(CH=), 115.5(CH=), 115.4 (CH=), 78.5 (**C**H-Ph), 45.2 (CH_2); HRMS (m/z) : 524.6318 $(M+H)^+$.

3-[1-(5-Chloro-benzothiazol-2-yl)-4,5-dihydro-1H-pyrazol-3yl]-4-phenylbenzo[4,5] imidazo[2,1-c][1,2,4]triazine (6d): Yield: 98 %; m.p. 294-295 °C; Anal. Calcd. for $C_{31}H_{20}N_7SCl$: C, 66.72; H, 3.61; N, 17.57; S, 5.74 %. Found: C, 66.75, H, 3.60, N, 17.60, S, 5.75 %; IR (KBr, cm^{-1}) : 1625 (C=N, pyrazoline), 7.60 (-C-Cl); ^1H NMR (300 MHz, $CDCl_3$, δ/ppm) : 7.78 -6.65 (m,17H,Ar-H), 5.52 (t, J = 7.7Hz, 1H, C**H**Ph), 3.18 (d, J = 7.9Hz, 2H, CH_2); ^{13}C NMR (75 MHz, $CDCl_3$, δ/ppm) : 174.5(N-C=N), 164.4 (C=N), 149.5(C-N), 142.4(C), 141.5(C=N), 138.7(C-N), 138.6(C-N), 137.8(C-N), 137.7(C-N), 136.5(C), 130.4(C-Cl), 129.1(CH=), 129.0(CH=), 128.5(CH=), 128.3(CH=), 128.1(CH=), 127.3(CH=), 127.2(CH=), 127.1(CH=), 127.0(CH=), 126.5(CH=), 126.2(CH=), 124.1(CH=), 122.9(CH=), 122.8(CH=), 122.5(CH=), 120.7(C-S), 115.9(CH=), 115.8(CH=) , 78.5 (**C**H-Ph), 45.8 (CH_2) ; HRMS (m/z) : 559.0769 $(M+H)^+$.

3-[1-(Benzimidazol-2-yl)-5-phenyl-4,5-dihydro-1H-pyrazol-3yl]-4-methylbenzo[4,5] imidazo[2,1-c][1,2,4]triazine (7a): Yield: 96 %; m.p. 245-247 °C; Anal. Calcd. for $C_{26}H_{20}N_8$:C, 70.25; H, 4.53; N, 25.20 %. Found:C, 70.28, H, 4.54, N, 25.23 %; IR (KBr, cm^{-1}): 3310 (NH benz.), 1620 (C=N, pyrazoline); ^1H NMR (300 MHz, $CDCl_3$, δ/ppm) : 9.24(s,1H,NH), 7.86-6.75 (m, 13H, Ar-H), 5.55 (t, J = 7.7Hz, 1H, C**H**Ph), 3.22 (d, J = 7.9Hz, 2H, CH_2), 1.65 (s, 3H, CH_3); ^{13}C NMR (75 MHz, $CDCl_3$, δ/ppm): 163.6 (C=N), 142.4 (C), 141.8 (N-C=N), 141.5 (C=N), 138.9 (C-N), 138.8 (C-N), 137.9 (C-N), 137.8 (C-N), 137.7 (C-N), 137.6 (C-N), 128.3 (CH=), 128.2 (CH=), 127.1 (CH=), 127.0 (CH=), 126.5 (CH=), 122.9 (CH=), 122.8 (CH=), 122.7 (CH=), 122.6 (CH=), 115.9 (CH=), 115.8 (CH=), 115.5 (CH=), 115.4 (CH=), 78.6 (**C**H-Ph), 44.8 (CH_2), 30.4 (CH_3); HRMS (m/z) : 445.5108 $(M+H)^+$.

3-[1-(5-Methylbenzimidazol-2-yl)-5-phenyl-4,5-dihydro-1H-pyrazol-3yl]-4-methylbenzo[4,5]imidazo[2,1-c][1,2,4]triazine (7b): Yield: 95 %; m.p. 251-252 °C; Anal. Calcd. for $C_{27}H_{22}N_8$; C, 70.72; H, 4.83; N, 24.43 %. Found: C, 70.76, H, 4.82, N, 24.43 %; IR (KBr, cm^{-1}) : 3320 (NH benz.), 1630 (C=N, pyrazoline); ^{1}H NMR (300 MHz, $CDCl_3$, δ/ppm) : 9.23 (s, 1H, NH), 7.84-6.78 (m, 12H, Ar-H), 5.52 (t, J = 7.7Hz, 1H, C**H**Ph), 3.19 (d, J = 7.9Hz, 2H, CH_2), 1.82 (s, 3H, CH_3), 1.68 (s, 3H, CH_3); ^{13}C NMR (75 MHz, $CDCl_3$, δ/ppm) : 164.2 (C=N), 142.4 (C), 141.7 (N-C=N), 141.5 (C=N), 138.8 (C-N), 138.7 (C-N), 137.9 (C-N), 137.8 (C-N), 137.7 (C-N), 134.9 (C-NH), 132.1 (C), 128.3 (CH=), 128.2 (CH=), 127.1(CH=), 127.0 (CH=), 126.5 (CH=), 123.6 (CH=), 122.9 (CH=), 122.8 (CH=), 115.9 (CH=), 115.8 (CH=), 115.3 (CH=), 115.2 (CH=), 78.5 (**C**H-Ph), 45.2 (CH_2), 30.8 (CH_3), 28.4 (CH_3) ;HRMS (m/z) :459.5379 $(M+H)^+$.

3-[1-(Benzimidazol-2-yl)-5-phenyl-4,5-dihydro-1H-pyrazol-3yl]-4-phenylbenzo[4,5]imidazo[2,1-c][1,2,4]triazine (7c): Yield: 92 %; m.p. 263-265 °C; Anal. Calcd. for $C_{31}H_{22}N_8$: C, 75.60; H, 4.47; N, 19.91 %. Found: C, 75.63, H, 4.43, N, 19.95 %; IR (KBr, cm^{-1}) : 3320 (NH benz.), 1615 (C=N, pyrazoline); ^{1}H NMR (300 MHz, $CDCl_3$, δ/ppm) : 9.22 (s, 1H, NH), 7.85-6.75 (m, 18H,Ar-H), 5.57 (t, J = 7.7Hz, 1H, C**H**Ph), 3.26(d, J = 7.9Hz, 2H, CH_2), ; ^{13}C NMR (75 MHz, $CDCl_3$, δ/ppm) : 163.9 (C=N), 142.4 (C), 141.7 (N-C=N), 141.5 (C=N), 138.8 (C-N), 138.7 (C-N), 137.9 (C-N), 137.8 (C-N), 137.7 (C-N), 137.6 (C-NH), 136.5 (C), 129.2 (CH=), 129.1 (CH=), 128.6 (CH=), 128.5 (CH=), 128.3 (CH=), 127.3 (CH=), 127.2 (CH=), 127.1 (CH=), 127.0 (CH=), 122.9 (CH=), 122.8 (CH=), 122.7 (CH=), 122.6 (CH=), 115.9 (CH=), 115.8 (CH=), 115.5 (CH=), 115.4 (CH=), 78.2 (**C**HPh), 44.8 (CH_2), 30.2 (CH_3); HRMS (m/z): 493.5758 $(M+H)^+$.

Insecticidal Activity:

For insecticidal activity, [xx, xxi] *Periplaneta americana* was taken and 1% and 2% solutions in DMF of prepared compounds were injected in the abdominal region of the cockroach with the help of microsyringe. At the time of death the antennae become motionless, the appendages shrunk and folded towards central side and the cockroach lay dorsally which was noted as KD (knock down) value. The KD values of synthesized heterocyclic derivatives were compared with control drug (cypermethrin) where the compounds (4**- 7)** exhibited good results. Some of the compounds **4a**, **6a**, **6b**, **6c**, **6d** and **7a** showed better activity (KD value 3-6 min) than cypermethrin (KD value 5-7 min) indicating their possible use as insecticides after further studies. The results are recorded in **Table 1**.

Table1: Results of Insecticidal activity against *Periplaneta americana* (KD values in min) of compounds **4-7**

Compound	Time (min)	
	1% (Conc.)	2% (Conc.)
4a	6	4
4b	7	5
5a	9	7
5b	10	8
6a	4	3
6b	5	3
6c	6	4
6d	4	3
7a	6	3
7b	7	4
7c	8	6
Cypermethrin	7	5

Results and Discussion:

Initially, the cyclization reaction of **3** to give **4** was carried out in various solvent systems such as ethanol, ethanol–CH_3COOH, CH_3COOH, PPA, glycerol and glycerol–H_2O and observed that highest yield was observed in glycerol–H_2O system without using any catalyst.

We have also investigated the one pot, three component reactions of **4**, C_6H_5CHO and hydrazino derivative as model reaction to obtain compound **5a** in different solvents such as ethanol, ethanol–CH_3COOH, CH_3COOH, DMF, ionic liquid [bmim] PF_6, H_2O, glycerol, glycerol–H_2O and best results are obtained in glycerol-water as green solvent. The purpose of this study is to explore the scope and limitations of glycerol as alternative green reaction medium. For our initial condensation reaction in aqueous glycerol with stirring at room temperature, it was observed that the starting materials were consumed after long reaction time as indicated by TLC analysis. To optimize the reaction conditions to afford the desired compound in good yields, some reactions were conducted at different reaction temperature and it was observed that as temperature increases, rate of reaction increases and good yield (92-98 %) was obtained at 90 °C within 1h (**Table 2**). Again the advantage to this protocol is, after the workup procedure, glycerol is successfully recovered and reused for another reaction without affecting the yields. In order to study the effect of solvent on the rate of reaction, we executed the same reaction in absence of water, but the yield of the product decreased drastically. It was observed that in ethanol, ethanol –CH_3COOH and DMF, the reaction did not reach completion even after heating for long time (5 h) as indicated by TLC and in water reactants are not soluble. The reaction completed in [bmim] PF_6, glycerol and glycerol–H_2O only. However the yield in ionic liquid and glycerol was low. The ionic liquid is costly therefore; this one pot reaction was carried out in glycerol–H_2O mixture from the economic and environmental point of view.

Then, we investigated the possibility of recycling of glycerol. After first cycle for the model reaction the product was poured into water and extracted with methyl *tert*-butyl ether to remove any organic compounds dissolved in aqueous phase. The aqueous layer was separated and water was evaporated under reduced pressure at 100 ^oC to give pure glycerol which was used for next run under similar conditions.[xxii]

The formation of compounds is assumed to proceed through two step domino sequence. The first step is believed to be formation of chalcone after reaction of the benzaldehyde and benzo-imidazo-triazin-3-yl ethanones **4**. The next step is the reaction of chalcones to the hydrazino derivatives to give pyrazolyl-benzo-imidazo-triazines **5-7**.

The structures of the synthesized compounds were confirmed by IR, ^1H NMR, ^{13}C NMR and mass spectroscopic data.

Cyclization of **3a-b** to **4a-b** were confirmed by IR spectra which shows disappearance of band due to hydrazono group and -NH of benzimidazole moiety and appearance of band at 1535 (N=N), 1280 (-C-N=N) and 1195 (-N=N-C) cm^{-1}.^1H NMR also confirms the disappearance of both of -NH. ^{13}C NMR show peaks at δ 74 and 175 ppm due to CO**C**H_3 and **C**OCH_3 respectively (**4a**).

In the formation of compound **4b**, the phenyl group is at C-4 since the direction of enolization is towards the phenyl and not the methyl group.

Formation of pyrazoline derivatives (**5-7**) were confirmed by IR spectra, which show disappearance of peak due to C=O of –$COCH_3$ and appearance of peak at 1620, C=N of pyrazoline ring, ^1H NMR shows peak at δ 5.51 ppm (t, J = 7.7Hz,1H, 5H) due to –C**H**-Ph present at C-5 carbon of pyrazoline ring and at δ 3.15 ppm (d, J = 7.9Hz, 2H, CH_2) due to proton at C-4 position. ^{13}C NMR shows peak at δ 78.8 (C-5 of pyrazoline) and δ 44.9 ppm (C-4 of pyrazoline).

Further, high resolution mass spectra the $(M+H)^+$ values of all the compounds (**4-7**) were recorded, which corresponded well to their molecular formula.

Table2: Optimization of reaction condition for model reaction generating **5a**

Compound	Solvent	Time (h)	Temp. (°C)	Yield (%)
5a	Ethanol	5	Reflux	Nil
5a	Ethanol-AcOH	5	Reflux	Nil
5a	AcOH	5	Reflux	Nil
5a	DMF	5	180	Nil
5a	H_2O	5	100	Nil
5a	[bmim] PF_6	5	85 ± 2	25
5a	Glycerol	5	50 ± 2	57
5a	Glycerol	3	90 ± 2	63
5a	Glycerol-H_2O (2.5:1)	10	Room temp.	12
5a	Glycerol-H_2O (2.5:1)	2	50 ± 2	75
5a	Glycerol-H_2O (2.5:1)	1	90 ± 2	96

Conclusion

In conclusion, the present study reports the syntheses of novel 1-(4-substituted)benzo[4,5]imidazol[2,1-c][1,2,4]triazin-3-yl)ethanone (**4**) and 3-(1-substituted-5-phenyl[4,5]imidazo[2,1-c][1,2,4]triazines (**5-7**) using glycerol-water as a solvent. The advantage of present method lies in using economic and environmentally benign glycerol as solvent, no need of catalyst, mild reaction conditions, good yields and glycerol is recycled for further use. Insecticidal activity against *Periplanata americana* exhibited excellent results.

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