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Efficient, environment friendly and regioselective synthetic strategy for 2/3-substituted-8,8-dimethyl-8,9-dihydropyrazolo[1,5-a]quinazolin-6(7*H*)-ones and their structure elucidation

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ABSTRACT

An efficient and regioselective synthetic reaction friendly to the environment has been described to synthesize various derivatives of pyrazolo[1,5-a]quinozolinone. Condensation of aminopyrazole (**4a-m**) with formylated dimedone (**3**) in the presence of $KHSO_4$, under ultrasonic irradiation furnished 2/3-substituted 8,8-dimethyl-8,9-dihydropyrazolo[1,5-*a*]quinazolin-6(7*H*)-one (**6a-m**). This is a clean reaction, giving excellent yields with short reaction time. The structures were elucidated with the help of spectral and analytical data. X-ray crystallographic studies of a model compound **6a** ascertained its structural configuration, crystal data for $C_{12}H_{12}BrN_3O$ (M =294.152 g/mol): Triclinic, space group P-1 (no. 2), a = 5.872(4) Å, b = 10.870(8) Å, c = 19.523(15) Å, α = 90.013(10)°, β = 90.009(11)°, γ = 93.838(11)°, V = 1243.3(16) Å^3, Z = 4, T = 296.15 K, μ(Mo Kα) = 3.293 mm^{-1}, *Dcalc* = 1.571 g/cm^3, 37271 reflections measured (4.18° ≤ 2Θ ≤ 52.7°), 5073 unique (R_{int} = 0.2404, R_{sigma} = 0.2366) which were used in all calculations. The final R_1 was 0.0596 (I≥2σ(I)) and wR_2 was 0.1759 (all data).

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1. Introduction

In view of the biological properties of pyrazolo[1,5-*a*]pyrimidine derivatives, we have recently published the synthesis and biological properties of a variety of molecules of this class for example 3, 7-diarylpyrazolo[1,5-*a*]pyrimidines (A) [1], 3, 6-diarylpyrazolo[1, 5-*a*]pyrimidin-7-amines (B) [1], 7-aryl-3-(4-chlorophenyl)-*N*-phenylpyrazolo[1, 5-*a*]pyrimidin-2-amines (C) [2], 6/7-substituted *N*-phenylpyrazolo[1,5-*a*]pyrimidine-3-carboxamides (D) [3], 6,7-substituted 2-(4-methoxyphenyl) pyrazolo[1,5-*a*]pyrimidines (E) [4], 6/7-substituted *N*-(1,5-dimethyl-3-oxo-2-phenyl-2, 3-dihydro-1*H*-pyrazol-4-yl)pyrazolo[1, 5-*a*]pyrimidine-3-carboxamides (F) [5], ethyl 7-(p-halide / nitro / aryl)pyrazolo[1, 5-*a*]pyrimidine-3-carboxylates (G) [6], ethyl 7-(naphthalen-2-yl)pyrazolo[1,5-*a*]pyrimidine-3-carboxylates (H) [6], 2-methyl-3,6-diphenylpyrazolo[1,5-*a*] pyrimidin-7-amines (I) [7], *etc.* (Figure 1).

Recently, synthesis and studies of pyrazoloquinazoline derivatives are becoming popular among researchers, as they are reported to exhibit a wide spectrum of bioactivities such as antibacterial [8], anticancer [9], antioxidant [10], anti-inflammatory [11], anti-diabetic [12], antiviral [13] and therapeutic applications in neurodegenerative disorders [14], adenosine receptor antagonist [15], $GABA_A$ subtype receptor [16], *etc.* In continuation with these studies and in view of the importance of pyrazoloquinozolines, we herein report the synthesis and X-ray crystallographic studies of pyrazolo[1,5-*a*]quinozolin-6(7*H*)-one derivatives.

2. Experimental

2.1. Instrumentation

The melting points of each of the synthesized compounds **6a-m** were recorded by the open capillary method and are uncorrected. The ^{1}H NMR and ^{13}C NMR spectra were recorded using DELTA JNM-ESC 400 MHz using $(Me)_4Si$ as the internal standard in chloroform-*d*. Chemical shift (δ ppm) and coupling constants (Hz) are reported in the standard manner. The abbreviations s, d, dd, t, and m stand for singlet, doublet, double-doublet, triplet, and multiplet, respectively. Chemical shift (δ, ppm) and coupling constants (Hz) are reported in a standard fashion. The electrospray mass spectrum was recorded on a Thermo Finnigan LCQ Advantage max ion trap mass spectrometer. The FT-IR spectra were recorded using Perkin Elmer Spectrum Two spectrometer.

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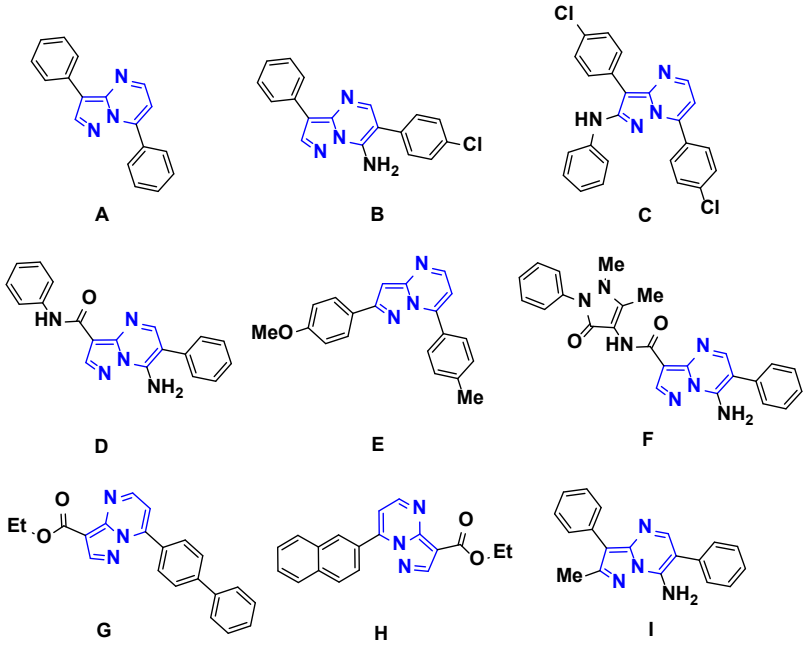


Figure 1. Some of our reported pyrazolo[1,5-*a*]pyrimidine derivatives.

The X-ray diffraction data were collected at 293 K with MoKα radiation (λ = 0.71073 Å) using a Bruker APEX-II CCD (Charge Coupled Device) [17] diffractometer which is equipped with a graphite monochromator. The structures were refined by using Olex2-1.3 [18,19] *via* full-matrix least-squares based on F-square. All non-H-atoms were refined in anisotropic approximation, and H-atoms were located at calculated positions. US irradiation was carried out in an Equitron Digital Ultrasonic cleaner 2.5 L, model number 8425.025.424 at 170 Watts and 50 Hz. 3-Aminopyrazoles (**4a-d**) and (**4f-j**) were obtained from commercial sources and compounds **4e** and **4k-m** were prepared by a reported procedure [4].

2.2. Synthesis of substituted 8,9-dihydropyrazolo[1,5-a]quinazolin-6(7H)-ones (6a-m)

To a solution of 2-((dimethylamino)methylene)-5,5-dimethylcyclohexane-1,3-dione (**3**) (0.5 mmol) (prepared by a reported procedure [6]) and 3-aminopyrazole (**4**) (0.5 mmol) in 1.5 mL of ethanol in a round bottom flask, a solution of $KHSO_4$ (1 mmol) in 1.5 mL of water was added and the resulting mixture was irradiated in an ultrasound cleaner bath maintained at 60 °C for 5-12 minutes monitoring the progress of the reaction by thin layer chromatography. At the end of the reaction, the flask was cooled to room temperature and the precipitate formed was collected by filtration, washed repeatedly with water ensuring complete removal of the acid, and finally dried to give practically pure compound **6** in 70-95% overall yields. Analytically pure products were obtained by column chromatography (silica gel, 10% ethyl acetate:hexane). The characterization data of the unreported compounds are presented below and the known compounds were compared with the reported data.

3-Bromo-8, 8-dimethyl-8, 9-dihydropyrazolo[1, 5-a]quinazolin-6(7H)-one (**6a**): Color: Light brown solid. Yield: 86%. M.p.: 130-131 °C. FT-IR (KBr, ν, cm^{-1}): 1682 (C=O), 1606 (C=N), 1531 (C=C). ^{1}H NMR (400 MHz, $CDCl_3$, δ, ppm): 1.19 (s, 6H, 2(CH_3)), 2.56 (s, 2H, C_7-H), 3.30 (s, 2H, C_9-H), 8.22 (s, 1H, C_2-H), 8.99 (s, 1H, C_5-H). ^{13}C NMR (100 MHz, $CDCl_3$, δ, ppm): 28.6 (2C, CH_3), 32.9 (1C, C_8), 36.9 (1C, C_9), 50.9 (1C, C_7), 87.2 (1C, C_3), 113.9 (1C, C_5-*C*-C_6), 146.0 (1C, C_2), 147.5 (1C, C_3-*C*-N), 148.0 (1C, C_5), 152.9 (1C, N-*C*-C_9), 194.5 (1C, C=O). MS (ESI, *m/z*): 295.2 (MH^+).

8, 8-Dimethyl-2-phenyl-8, 9-dihydropyrazolo[1, 5-a]quinazolin-6(7H)-one (**6b**): Color: White solid. Yield: 70%. M.p.: 241-242 °C (244-245 °C [20]). MS (ESI, *m/z*): 292.0 (MH^+).

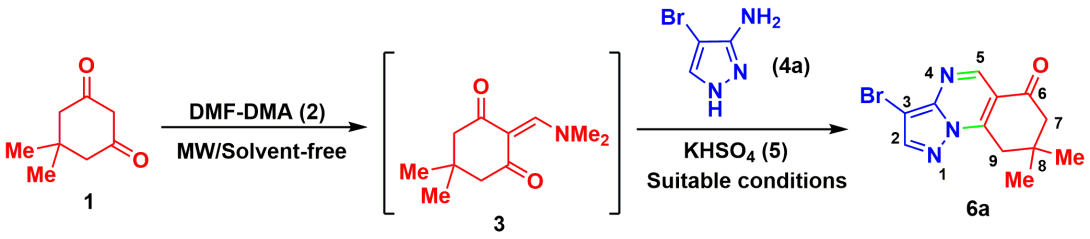
8, 8-Dimethyl-8, 9-dihydropyrazolo[1, 5-a]quinazolin-6(7H)-one (**6c**): Color: Pale yellow solid. Yield: 85 %. M.p.: 140-141 °C (142 °C [21]). FT-IR (KBr, ν, cm^{-1}): 1680 (C=O), 1608 (C=N), 1532 (C=C). ^{1}H NMR (400 MHz, $CDCl_3$, δ, ppm): 1.19 (s, 6H, 2(CH_3)), 2.55 (s, 2H, C_7-H), 3.33 (s, 2H, C_9-H), 6.75 (s, 1H, C_3-H), 8.22 (s, 1H, C_2-H), 8.94 (s, 1H, C_5-H). ^{13}C NMR (100 MHz, $CDCl_3$, δ, ppm): 28.7 (2C, CH_3), 32.9 (1C, C_8), 37.3 (1C, C_9), 51.0 (1C, C_7), 99.2 (1C, C_3), 113.4 (1C, C_5-*C*-C_6), 147.1 (1C, C_2), 147.6 (1C, C_3-*C*-N), 149.4 (1C, C_5), 152.4 (1C, C_9-*C*-N), 194.8 (1C, C=O). MS (ESI, *m/z*): 216.0 (MH^+).

2-(Tert-butyl)-8, 8-dimethyl-8, 9-dihydropyrazolo[1, 5-a]quinazolin-6(7H)-one (**6d**): Color: Light brown solid. Yield: 84 %. M.p.: 203-204 °C. FT-IR (KBr, ν, cm^{-1}): 1690 (C=O), 1607 (C=N), 1533 (C=C). ^{1}H NMR (400 MHz, $CDCl_3$, δ, ppm): 1.20 (s, 6H, 2(CH_3)), 1.39 (s, 9H, C(CH_3)$_3$), 2.53 (s, 2H, C_7-H), 3.35 (s, 2H, C_9-H), 6.61 (s, 1H, C_3-H), 8.88 (s, 1H, C_5-H). ^{13}C NMR (100 MHz, $CDCl_3$, δ, ppm): 28.7 (2C, CH_3), 30.3 (3C, C(*C*H_3)), 32.8 (1C, *C*(CH_3)), 33.3 (1C, C_8), 37.3 (1C, C_9), 51.1 (1C, C_7), 95.7 (1C, C_3), 112.7 (1C, C_5-*C*-C_6), 146.6 (1C, C_3-*C*-N), 149.7 (1C, C_2), 152.2 (1C, C_5), 171.0 (1C, C_9-C-N), 195.0 (1C, C=O). MS (ESI, *m/z*): 272.3 (MH^+).

2, 8, 8-Trimethyl-3-phenyl-8, 9-dihydropyrazolo[1, 5-a]quinazolin-6(7H)-one (**6e**): Color: Brown solid. Yield: 95 %. M.p.: 196-197 °C (195-197 °C [4,20,22,23]).

8, 8-Dimethyl-6-oxo-6, 7, 8,9-tetrahydropyrazolo[1,5-a]quinazoline-3-carbonitrile (**6f**): Color: Pale yellow solid. Yield: 93 %. M.p.: 165-166 °C (162-163 °C [24]).

8,8-Dimethyl-8,9-dihydropyrazolo[1,5-a]quinazoline-2,6(1H, 7H)-dione (**6g**): Color: Cream colored solid. Yield: 82 %. M.p.: 202-203 °C. FT-IR (KBr, ν, cm^{-1}): 1686 (C=O), 1614 (C=N), 1540 (C=C). ^{1}H NMR (400 MHz, $CDCl_3$, δ, ppm): 0.95 (s, 6H, 2(CH_3)), 2.29 (s, 2H, C_7-H), 2.98 (s, 2H, C_9-H), 5.84 (s, 1H, C_3-H), 8.57 (s, 1H, C_5-H), 10.77 (s, 1H, NH). ^{13}C NMR (100 MHz, $CDCl_3$, δ, ppm): 28.5 (2C, CH_3), 32.5 (1C, C_8), 37.2 (1C, C_9), 39.9 (1C, C_7), 84.2 (1C, C_3), 111.9 (1C, C_5-*C*-C_6), 146.7 (1C, C_9-*C*-N), 149.9 (1C, C_3-*C*-N), 151.1 (1C, C_5), 168.7 (1C, NH-*C*=O), 194.4 (1C, C=O).,



Scheme 1. Optimization of the reaction conditions.

Table 1. Results of the optimization of the reaction.

Entry	Mode	Temperature (°C)	Solvent	Reaction time (min)	Yield (%)
1	Silent	Room temperature	Water	300	28
2	Silent	Room temperature	Water-ethanol (1:1, v:v)	270	32
3	Silent	60	Water	300	32
4	Silent	60	Water-ethanol (1:1, v:v)	270	35
5	Sonication	Room temperature	Water	36	57
6	Sonication	Room temperature	Water-ethanol (1:1, v:v)	30	62
7	Sonication	60	Water	5	78
8	Sonication	60	Water-ethanol (1:1, v:v)	5	86

2-(4-Methoxyphenyl)-8, 8-dimethyl-8,9-dihydropyrazolo[1,5-a]quinazolin-6(7H)-one (**6h**): Color: Pale yellow solid. Yield: 86 %. M.p.: 210-212 °C (214 °C [4]).

2, 8, 8-Trimethyl-8, 9-dihydropyrazolo[1, 5-a]quinazolin-6(7H)-one (**6i**): Color: Pale yellow solid. Yield: 81 %. M.p.: 132-133 °C (134-135 °C [25]).

3-Bromo-8, 8-dimethyl-2-phenyl-8,9-dihydropyrazolo[1, 5-a]quinazolin-6(7H)-one (**6j**): Color: Brown solid. Yield: 86 %. M.p.: 81-83 °C. FT-IR (KBr, ν, cm^{-1}): 1672 (C=O), 1602 (C-N), 1514 (C=C). ^{1}H NMR (400 MHz, $CDCl_3$, δ, ppm): 1.23 (s, 6H, 2(CH_3)), 2.39 (s, 2H, C_7-H), 2.46(s, 2H, C_9-H), 7.40-7.45 (m, 3H, ArH), 7.67-7.74 (m, 2H, ArH), 9.04 (s, 1H, C_5-H). ^{13}C NMR (100 MHz, $CDCl_3$, δ, ppm): 28.4 (2C, CH_3), 28.7 (1C, C_8), 31.0 (1C, C_9), 51.4 (1C, C_7), 94.2 (1C, C_3), 120.4 (1C, C_5-*C*-C_6), 126.9 (2C, $C_{2'}$, $C_{6'}$), 128.5 (1C, $C_{4'}$), 128.7 (2C, $C_{3'}$,$C_{5'}$), 135.1 (1C, $C_{1'}$), 136.3 (1C, C_3-*C*-N), 144.5 (1C, C_2), 156.6 (1C, C_5), 172.4 (1C, C_9-*C*-N), 191.8 (1C, C=O).

8, 8-Dimethyl-3-(naphthalen-2-yl)-8, 9-dihydropyrazolo[1, 5-a]quinazolin-6(7H)-one (**6k**): Color: Light brown solid. Yield: 84 %. M.p.: 212-214 °C. FT-IR (KBr, ν, cm^{-1}): 1683 (C=O). ^{1}H NMR (400 MHz, $CDCl_3$, δ, ppm): 1.15 (s, 6H, 2(CH_3)), 2.84 (s, 2H, C_7-H), 2.90 (s, 2H, C_9-H), 7.42-7.46 (m, 2H, ArH), 7.79-7.81 (m, 3H, ArH), 8.10-8.13 (m, 1H, ArH), 8.44 (s, 1H, ArH), 8.62 (s, 1H, C_2-H), 9.01 (s, 1H, C_5-H). ^{13}C NMR (100 MHz, $CDCl_3$, δ, ppm): 28.6 (2C, CH_3), 32.7 (1C, C_8), 37.2 (1C, C_9), 50.8 (1C, C_7), 112.7 (1C, C_3), 113.6 (1C, C_5-*C*-C_6), 124.8 (1C, $C_{10'}$), 127.7 (2C, $C_{6'}$, $C_{7'}$), 128.2 (1C, $C_{2'}$, $C_{3'}$), 128.4 (2C, $C_{5'}$, $C_{8'}$), 128.6 (1C, C_3-*C*-N), 132.4 (1C, C_2), 145.7 (1C, $C_{1'}$), 146.9 (1C, $C_{4'}$), 152.6 (1C, C_5), 162.6 (1C, C_9-*C*-N), 194.7 (1C, C=O). MS (ESI, *m*/*z*): 342.2 (MH^+).

3-Benzoyl-8, 8-dimethyl-8, 9-dihydropyrazolo[1, 5-a]quinazolin-6(7H)-one (**6l**): Color: Light yellow solid. Yield: 83 %. M.p.: 113-115 °C. FT-IR (KBr, ν, cm^{-1}): 1738 (C=O), 1679 (C-N), 1608 (C=C). ^{1}H NMR (400 MHz, $CDCl_3$, δ, ppm): 1.23 (s, 6H, 2(CH_3)), 2.16 (s, 2H, C_7-H), 2.58 (s, 2H, C_9-H), 6.98-7.01 (m, 3H, ArH), 7.75-7.78 (m, 2H, ArH), 7.93 (s, 1H, C_2-H), 8.94 (s, 1H, C_5-H). ^{13}C NMR (100 MHz, $CDCl_3$, δ, ppm): 26.4 (2C, CH_3), 36.5 (1C, C_8), 42.0 (1C, C_9), 46.6 (1C, C_7), 114.6 (1C, C_3), 120.4 (1C, C_5-*C*-C_6), 128.1 (1C, $C_{3'}$), 128.2 (1C, $C_{5'}$), 132.5 (1C, $C_{2'}$, $C_{6'}$), 132.6 (1C, $C_{4'}$), 140.6 (1C, $C_{1'}$), 150.1 (2C, C_2, C_3-*C*-N), 161.2 (1C, C_5), 176.6 (1C, C_9-*C*-N), 198.5 (2C, C=O).

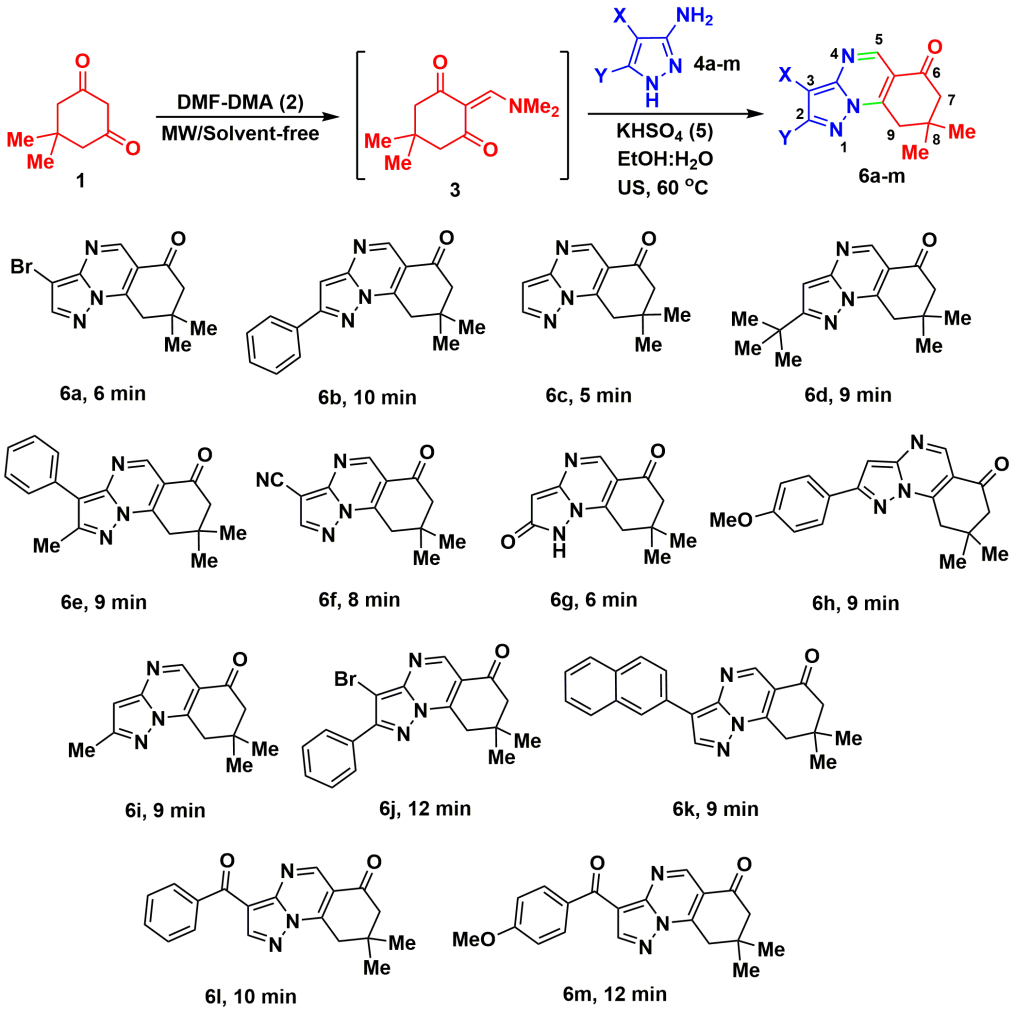
3-(4-Methoxybenzoyl)-8, 8-dimethyl-8, 9-dihydropyrazolo[1, 5-a]quinazolin-6(7H)-one (**6m**): Color: Light yellow solid. Yield: 71 %. M.p.: 133-134 °C. FT-IR (KBr, ν, cm^{-1}): 1672 (C=O), 1616 (C=O), 1518 (C=C). ^{1}H NMR (400 MHz, $CDCl_3$, δ, ppm): 1.23 (s, 6H, 2(CH_3)), 2.16 (s, 2H, C_7-H), 2.58 (s, 2H, C_9-H), 3.86 (s, 3H, OCH_3), 6.99 (d, 2H, *J* = 9.2 Hz, ArH), 7.25 (s, 1H, C_2-H), 7.76 (d, 2H, *J* = 9.2 Hz, ArH), 7.93 (s, 1H, C_5-H). ^{13}C NMR (100 MHz, $CDCl_3$, δ, ppm): 26.4 (2C, CH_3), 31.0 (1C, C_8), 36.5 (1C, C_9), 42.0 (1C, C_7), 46.6 (1C, OCH_3), 89.2 (1C, C_3), 114.6 (2C, $C_{3'}$, $C_{5'}$), 114.7 (1C, C_5-*C*-C_6), 120.3 (1C, $C_{1'}$), 128.2 (2C, $C_{2'}$, $C_{6'}$), 132.5 (1C, C_2), 140.6 (1C, C_3-*C*-N), 150.1 (1C, C_5), 161.1 (1C, $C_{4'}$-*C*-OCH_3), 176.6 (1C, C_9-*C*-N), 207.6 (2C, C=O). MS (ESI, *m*/*z*): 350.0 (MH^+).

3. Results and discussion

3.1. Chemistry

In this paper, we have reported the synthesis of various pyrazolo[1,5-*a*]quinazolin-6(7*H*)-one derivatives by reacting enaminone derived from dimedone with 2/3-substituted 3-amino-1*H*-pyrazole by an eco-friendly and simple protocol. To standardize the synthetic protocol, dimedone **1** (0.5 mmol) was formylated by reacting with dimethylformamide-dimethylacetal (DMF-DMA) to produce enaminone **3** according to a reported protocol [6]. To crude enaminone **3** was added 4-bromo-3-amino-1*H*-pyrazole (0.5 mmol) **4a** and the resulting mixture was taken in selected solvents. Subsequently, $KHSO_4$ **5** (1 mmol) in the selected solvent was added and the resulting mixture was subjected to reaction under various conditions of solvent, temperature, and silent/ultrasonication conditions (Scheme 1, Table 1). At the end of each reaction (as monitored by TLC) the precipitated product was collected by filtration with repeated washing with cold water to remove traces of acid present, and then dried. For its analytical studies, the product was purified further *via* column chromatography (silica gel, 10% ethyl acetate:hexane). The structure of the product was assigned to be 3-bromo-8,8-dimethyl-8,9-dihydropyrazolo[1,5-*a*]quinazolin-6(7*H*)-one (**6a**). The data presented in Table 1 clearly shows that the most suitable condition (yield 86 %) for the reaction was ultrasonication at 60 °C in a solvent system of water-ethanol (1:1). Hence, this condition was further adopted to generalize the synthetic strategy.

For further reactions, we selected thirteen aminopyrazoles of which compounds **4a-j** of which were commercially available and compounds **4k-m** were synthesized by our reported procedure [4]. Enaminone **3** derived from dimedone was prepared using our previous reported method [6]. Thus, enaminone **3** was synthesized by reacting dimedone with DMF-DMA under microwave irradiation. Enaminone **3** was then reacted with an equimolar amount of animopyrazole **4** in the presence of 2 equivalents of $KHSO_4$ in a water-ethanol mixture (1:1) under ultrasonication when a solid product precipitated in good to excellent yield (70-95%). The product thus formed was practically pure. However, for analytical studies, the products were purified by column chromatography.



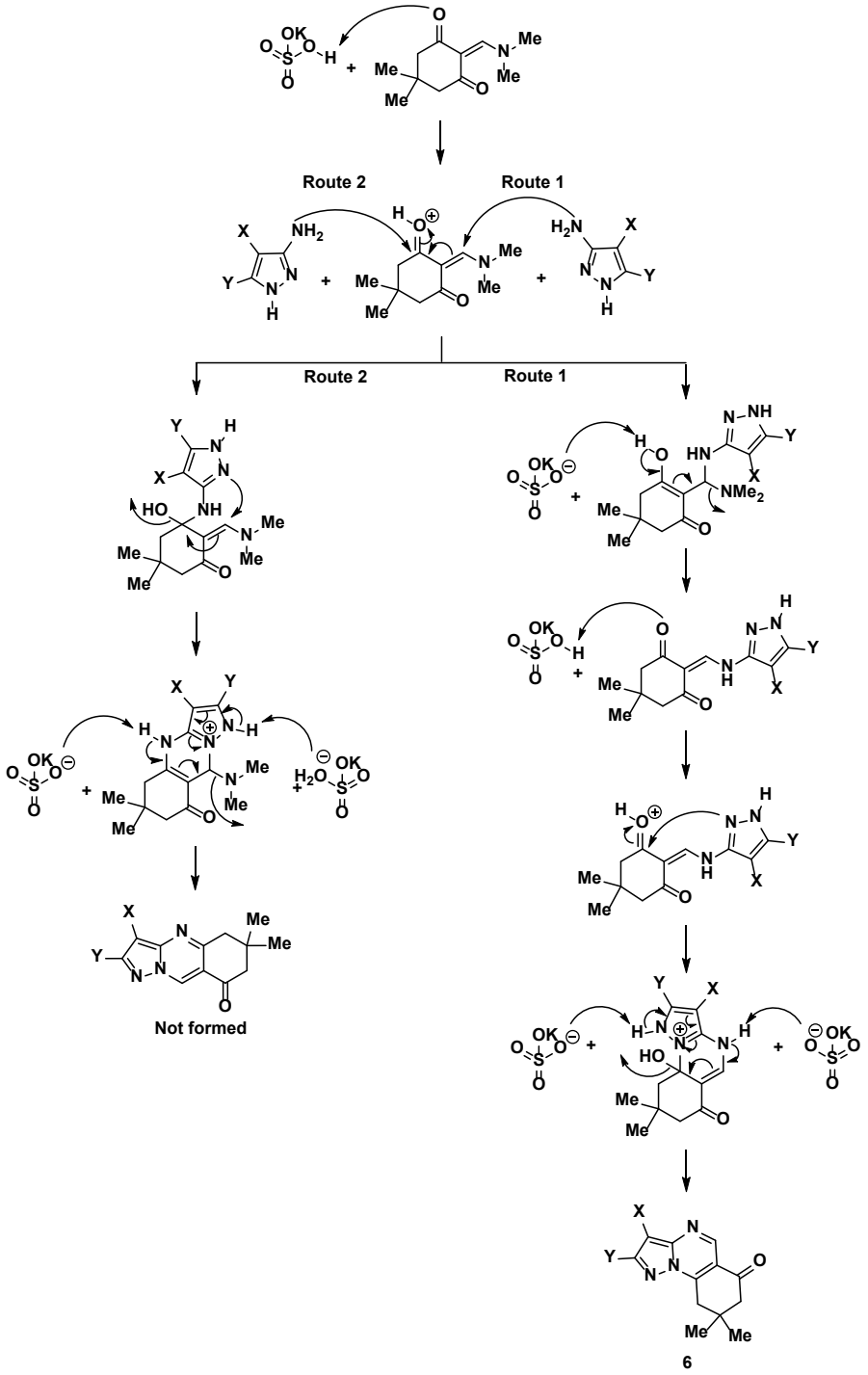
Scheme 2. Synthesis of 2,3-substituted 8,8-dimethyl-8,9-dihydropyrazolo[1,5-*a*]quinazolin-6(7*H*)-one derivatives.

The structures of the products **6a**-**m** were well established to be 2/3-substituted 8,8-dimethyl-8, 9-dihydropyrazolo[1, 5-*a*]quinazolin-6(7*H*)-one with the help of analytical and spectral data such as ^{1}H NMR, ^{13}C NMR, FT-IR, and mass spectrometry and also by comparison with reported data of the known products. Thus, following this strategy, we have successfully synthesized thirteen molecules (Scheme 2).

In the ^{1}H NMR spectra, singlets were found resonating for six protons (two methyl groups) at δ 1.19 ppm for compounds **6a** and **6c**, at δ 1.20 ppm for compound **6d**, at δ 0.95 ppm for compound **6g**, at δ 1.23 ppm for compounds **6j**, **6l**-**m** and at δ 1.15 ppm for compound **6k**. The two CH_2 protons at C_7 and C_9 at two distinct singlets at δ 2.57 and 3.31 ppm for compound **6a**, at δ 2.55 and 3.33 ppm for compound **6c**, while at δ 2.53 and 3.35 ppm for compound **6d**, at δ 2.29 and 2.98 ppm for compound **6g**, at δ 2.34 and 2.46 ppm for compound **6j**, at δ 2.84 and 2.91 ppm for compound **6k**, in δ 2.16 and 2.58 ppm for compounds **6l** and **6m**. In the NMR spectra of compound **6a**, the C_2-H and C_5-H protons resonated as singlets at δ 8.21 and 8.99 ppm, respectively. In compound **6c**, C_3-H, C_2-H and C_5-H appeared as clear singlet at δ 6.75, 8.22 and 8.95 ppm, respectively. Furthermore, in compound **6d**, the C3-H and C_5-H protons gave singlets at δ 6.61 and 8.88 ppm, respectively, and the nine protons of the substituent $C(CH_3)_3$ gave a singlet at δ 1.40 ppm. The NMR spectra of compound **6g** exhibited singlets for C_3-H and C_5-H of pyrazolo[1,5-*a*]quinozoline ring at δ 5.84 and 8.57 ppm, respectively, and at δ 10.77 ppm for NH proton. In compound **6j**, C_5-H was found to resonate at δ 9.04 ppm as a singlet. In compound **6k,** C_5-H and C_2-H were resonating as singlets at δ 8.62 and 9.01 ppm, respectively, whereas, the seven protons of naphthyl group appeared as multiplet in the range δ 7.43-7.46 ppm for two protons, as multiplet in the range δ 7.79-7.89 ppm for three protons, as singlets at δ 8.45 and 8.13 ppm for one proton each. In compound **6l**, C_2-H and C_5-H resonated as singlets at δ 7.93 and 8.94 ppm respectively, whereas the phenyl group protons gave signals at expected chemical shifts. The spectral data for compound **6m** exhibited singlets for C_2-H and C_5-H at δ 7.25 and 7.93 ppm, respectively, and the three protons of OCH_3resonatedas singlet at δ 3.86 ppm, whereas the protons of the phenyl group gave two doublets at δ 6.99 and 7.76 ppm with coupling constant J = 9.2 Hz.

The ^{13}C spectra of the new derivatives of 8,8-dimethyl-8,9-dihydroxypyrazolo[1,5-*a*]quinozolin-6-(7*H*)-one showed signals at expected chemical shifts. In the FT-IR spectra of the products, neither signals for NH_2 group (3400-3600 cm^{-1}) nor for carbonyl of enaminones (1600-1750 cm^{-1}) were observed, thus conforming participation of the two groups leading to cyclization. The mass spectra of the molecules were also in support of the proposed structures.

A plausible mechanism for the formation of target molecules is rationalized as follows (Scheme 3). Thus, assisted by $KHSO_4$, Aza-Michael addition elimination occurs resulting in the formation of an adduct which further, in the presence of $KHSO_4$, undergoes cyclodehydration to yield the target molecule **6**.



Scheme 3. A representative plausible mechanism for the formation of pyrazolo[1,5-a]quinozoline.

3.2. Crystallographic details of molecule 6a

To ascertain the structural configuration of the synthesized compounds, a model molecule **6a** was selected and its detailed single-crystal X-ray was studied. Pale yellow crystals of compound **6a** were obtained by slow recrystallization from a mixture of dichloromethane and hexane (9:1). The X-ray diffraction data of the crystal **6a** was collected at 296.2 K with MoKα radiation using a Bruker APEX-II CCD diffractometer equipped with a graphite monochromator. Compound **6a** crystallized in a triclinic crystal system with space group *P*-1. It was also found that the molecule exists as a dimer (Figure 2). The summary of various refinement factors and parameters is tabulated in Table 3. The three fused rings in pyrazolo[1,5-*a*]quinozolione were found to be in the same plane, which could be easily understood from its geometrical parameters, such as the length of the bond, the angles of the bond and the angles of torsion of some selected atoms obtained from the crystal structure mentioned in Tables 4 and 5 (Figure 3).

The C-C bond lengths in the three fused rings of pyrazolo[1,5-*a*]quinozolinone ranged from 1.311 to 1.536 Å, while the torsion angles between C_{13}-C_{24}-N_5-C_{15}, C_{21}-C_{22}-C_{23}-N_6, C_{21}-C_{22}-C_{15}-N_5, C_{16}-C_{15}-C_{22}-C_{21}, N_4-N_5-C_{15}-C_{22}, N_3-C_{11}-C_{10}-C_3, C_4-C_3-C_{10}-C_9, N_3-C_{12}-N_2-N_1, N_2-C_3-C_4-C_5 were obtained at 176.96°,

Table 3. Crystal data and structure refinement for compound **6a**.

Empirical formula	$C_{12}H_{12}BrN_3O$
Formula weight	294.152
Temperature (K)	296.15
Crystal system	Triclinic
Space group	*P*-1
a, (Å)	5.872(4)
b, (Å)	10.870(8)
c, (Å)	19.523(15)
α (°)	90.013(10)
β (°)	90.009(11)
γ (°)	93.838(11)
Volume (Å^3)	1243.3(16)
Z	4
ρ_{calc} (g/cm^3)	1.571
μ (mm^{-1})	3.293
F(000)	591.4
Radiation	Mo Kα (λ = 0.71073)
2Θ range for data collection (°)	4.18 to 52.7
Index ranges	$-7 \le h \le 7$, $-14 \le k \le 14$, $-26 \le l \le 26$
Reflections collected	37271
Independent reflections	5073 [R_{int} = 0.2404, R_{sigma} = 0.2366]
Data/restraints/parameters	5073/0/312
Goodness-of-fit on F^2	1.023
Final R indexes [I≥2σ (I)]	R_1 = 0.0596, wR_2 = 0.1160
Final R indexes [all data]	R_1 = 0.2104, wR_2 = 0.1759
Largest diff. peak/hole (e.Å^{-3})	1.32/-0.96
CCDC No	2064851

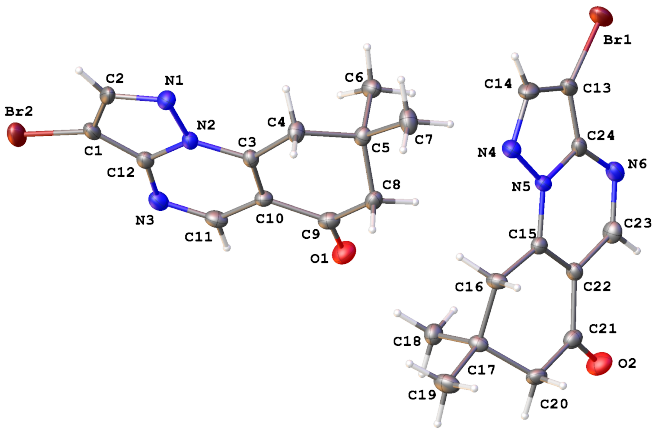


Figure 2. Molecular structure of compound **6a**.

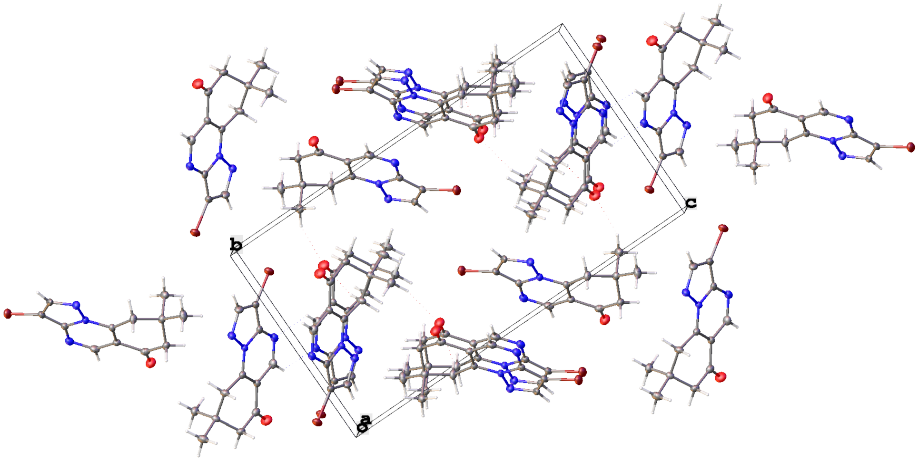


Figure 3. Packing of compound **6a**.

178.48°, 179.69°, -1.66°, 179.63°, 2.30°, 2.65°, -179.04-157.48°, respectively. The single bond lengths between C_{13}-C_{14}, C_{24}-N_5, C_{24}-N_6, C_{22}-C_{23}, N_5-C_{15}, or C_1-C_2, C_{12}-N_2, N_1-N_2, N_3-C_{12}, C_3-N_2, C_{11}-C_{10}, N_2-C_3 are mostly equal to those of double bonds between C_{13}-C_{24}, C_{14}-N_4, N_6-C_{23}, C_{22}-C_{15} or C_1-C_{12}, C_2-N_1, N_3-C_{11}, C_{10}-C_3 which could be explained due to the 10π electron delocalization. However, the bond lengths between C_{16}-C_{17}, C_{17}-C_{20}, C_{20}-C_{21}, C_{21}-C_{22}, C_{22}-C_{15} or C_{21}-C_{20}, C_{22}-C_{21}, C_{17}-C_{20}, C_{17}-C_{16}, C_{15}-C_{16} are equivalent to C-C single bonds.

Table 4. Bond lengths for compound **6a**.

Atom	Atom	Length (Å)	Atom	Atom	Length (Å)	Atom	Atom	Length (Å)
Br1	C13	1.875(7)	Br2	C1	1.859(7)	C1	C12	1.356(9)
O2	C21	1.229(8)	O1	C9	1.235(8)	C3	C4	1.482(8)
N4	N5	1.367(7)	N1	N2	1.376(7)	C3	C10	1.359(8)
N4	C14	1.342(8)	N1	C2	1.329(8)	C4	C5	1.532(8)
N5	C15	1.354(7)	N2	C3	1.371(7)	C5	C6	1.543(8)
N5	C24	1.396(8)	N2	C12	1.383(8)	C5	C7	1.529(9)
N6	C23	1.311(8)	N3	C11	1.306(8)	C5	C8	1.510(8)
N6	C24	1.357(8)	N3	C12	1.356(8)	C8	C9	1.482(9)
C13	C14	1.374(10)	C1	C2	1.393(10)	C9	C10	1.498(9)
C13	C24	1.372(10)	C20	C21	1.513(9)	C10	C11	1.416(9)
C15	C16	1.489(8)	C21	C22	1.470(9)	C17	C19	1.539(9)
C15	C22	1.376(8)	C22	C23	1.432(9)	C17	C20	1.526(8)
C16	C17	1.526(8)	C17	C18	1.539(8)			

Table 5. Bond angles for compound **6a**.

Atom	Atom	Atom	Angle (°)	Atom	Atom	Atom	Angle (°)	Atom	Atom	Atom	Angle (°)
C14	N4	N5	102.4(6)	C2	N1	N2	102.7(6)	C10	C3	N2	114.3(6)
C15	N5	N4	124.7(6)	C3	N2	N1	124.5(6)	C10	C3	C4	125.8(6)
C24	N5	N4	112.9(6)	C12	N2	N1	111.9(6)	C5	C4	C3	112.0(6)
C24	N5	C15	122.4(7)	C12	N2	C3	123.5(6)	C6	C5	C4	109.4(5)
C24	N6	C23	115.3(6)	C12	N3	C11	115.3(7)	C7	C5	C4	109.9(5)
C14	C13	Br1	128.7(7)	C2	C1	Br2	127.8(6)	C7	C5	C6	108.3(6)
C24	C13	Br1	124.8(7)	C12	C1	Br2	126.8(7)	C8	C5	C4	109.1(6)
C24	C13	C14	106.3(7)	C12	C1	C2	105.2(7)	C8	C5	C6	109.2(5)
C13	C14	N4	113.7(7)	C1	C2	N1	113.8(7)	C8	C5	C7	110.8(6)
C16	C15	N5	119.6(6)	C4	C3	N2	119.8(6)	C9	C8	C5	114.7(6)
C22	C15	N5	116.1(6)	C21	C20	C17	113.0(5)	C8	C9	O1	123.0(7)
C22	C15	C16	124.3(6)	C20	C21	O2	121.4(7)	C10	C9	O1	120.1(7)
C17	C16	C15	112.4(6)	C22	C21	O2	121.9(7)	C10	C9	C8	116.9(7)
C18	C17	C16	110.3(5)	C22	C21	C20	116.7(7)	C9	C10	C3	118.1(7)
C19	C17	C16	109.8(5)	C21	C22	C15	119.6(6)	C11	C10	C3	120.3(6)
C19	C17	C18	109.2(6)	C23	C22	C15	119.0(6)	C11	C10	C9	121.6(7)
C20	C17	C16	109.0(5)	C23	C22	C21	121.4(7)	C10	C11	N3	124.9(7)
C20	C17	C18	109.5(5)	C22	C23	N6	124.8(7)	N3	C12	N2	121.6(7)
C20	C17	C19	109.2(5)	N6	C24	N5	122.4(7)	C1	C12	N2	106.4(7)
C13	C24	N5	104.6(7)	C13	C24	N6	132.9(8)	C1	C12	N3	132.0(8)

4. Conclusions

In this article, we have reported a facile, regioselective, environment-friendly, effective, and high-yielding synthetic protocol for substituted pyrazolo[1,5-*a*]quinozolinone derivatives by the reaction of formylated dimedone with various substituted 3-amino-1*H*-pyrazoles. The structural configurations of all of the novel molecules were done with the help of their structural and analytical data. The formations of the reported molecules were established by comparison with the data reported in the literature. X-ray crystallographic study of compound **6a** was done to establish the structure of the molecules. The biopotential of all these molecules is yet to be explored.

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Disclosure statement

Conflict of interest: The authors declare that they have no conflict of interest.
Ethical approval: All ethical guidelines have been adhered.
Sample availability: Samples of the compounds are available from the author.

CRediT authorship contribution statement

Conceptualization: Jai Narain Vishwakarma; Methodology: Susma Das; Software: Susma Das; Validation: Jai Narain Vishwakarma; Formal Analysis: Susma Das; Investigation: Susma Das; Resources: Jai Narain Vishwakarma; Data Curation: Labet Bankynmaw Marpna; Writing - Original Draft: Susma Das; Writing - Review and Editing: Labet Bankynmaw Marpna; Visualization: Jai Narain Vishwakarma; Funding acquisition: Jai Narain Vishwakarma; Supervision: Jai Narain Vishwakarma; Project Administration: Jai Narain Vishwakarma.

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