One-Pot Multicomponent Synthesis & Characterization of Novel Pyrazolo[5,1-b]Quinazoline Derivatives

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Abstract: *5, 5-dimethylcyclohexane-1, 3-dione (dimedone) is versatile reactant for the synthesis of pyrazoloquinazoline derivatives. Thus, we sought that the reaction of dimedone, an appropriate aldehyde and 5-amino-N-cyclohexyl-3-(methylthio)-1H-pyrazole-4-carboxamide in the presence of base in isopropyl alcohol could be an effective strategy to furnish the novel pyrazoloquinazoline derivatives.*

Key Words: *5, 5-dimethylcyclohexane-1, 3-dione, dimedone, pyrazoloquinazoline, 5-amino-N-cyclohexyl-3-(methylthio)-1H-pyrazole-4-carboxamide.*

1. INTRODUCTION:

Dimedone has been extensively used in the synthesis of partially hydrogenated quinoline rings. Thus, 1,4,5,6,7,8-hexahydroquinolines **(2)**[1-3] were prepared by Hantzsch-like synthesis starting from **(1)**, aromatic or aliphatic aldehydes and *β*-aminocrotonates or *β*-aminocrotonamide[4-7]. Hexahydroquinolines **(2)** were also obtained by ultrasound or microwave (MW) irradiation of a mixture of **(1)**, aromatic aldehydes and *β*-aminocrotonates or ethyl acetoacetate in the presence of ammonium acetate[8-11] or in water in the presence of triethylbenzylammonium (TEBA) chloride[12,13]. When paraformaldehyde was used, *bis*(dimedonyl)methane was isolated as a byproduct[14].

The Hantzch cyclocondensation of the four components **(1)**, aldehydes, ketoesters, and ammonium acetate has attracted much attention for the synthesis of polyhydroquinolines **(3)**. Various catalysts have been used, such as molecular iodine[15], CAN[16], HY-zeolite[16,17], bakersyeast[18], Montmorillonite K10 clay in methanol[19], L-proline in water, or solvent free condition[20], $HClO_4$–ScO_2 under solvent free condition[21], triethybenzylammonium chloride in water[22], scandium triflate[23], $Yb(OTf)_3$[24], and ionic liquids under solvent free conditions such as hexamethylimidazolium tetrafluoroborate {[hmim]BF_4}, decylmethylimidazolium tetrafluoroborate {[dmim]BF4}, hexamethylimidazolium hexafluorophosphate {[hmim]PF6}, as well as hexamethylimidazolium bromide {[hmim]Br}, where the former was the optimum one. Aliphatic aldehydes[25,26] may be used also. X-ray study of the 4-(3-chlorophenyl) derivative showed that the N containing ring adopted a boat conformation and the cyclohexane has a half chair conformation[27]. The corresponding 4-(2-chloro-5-nitrophenyl) derivative has the chloro substituent in a syn periplanar orientation with respect to the pyridine ring plane with the nitro group over it[28]. The use of terephthaldehyde or isophthaldehyde as an aldehyde allowed the presence of two polyhydroquinolines on the benzene ring; the synthesis was achieved under MW irradiation[29].

Four-component cyclocondensation of **(1)**, aromatic aldehydes, malononitrile, and ammonium acetate proceeded under MW irradiation in solvent free conditions to give highly functionalized hexahydroquinolines in excellent yield. The crystal structure of 2-amino-3-cyano-4-phenyl-7,7-dimethyl-5-oxo-1,4,5,6,7,8-hexahydro quinoline was determined[30]. Oxidation of 245 with chromic acid gave tetrahydro derivatives **(5)**[14], that can be also obtained from reaction of **(1)** with 3-amino 2-methylacrylaldehyde[31], or 4-(3-indolyl)pyrimidine **(4)**[32]. Various derivatives of **(3)** and **(5)** were reported for treatment of cardiovascular and cellular proliferative diseases[33-37] **(Figure-1)**.

2. EXPERIMENTAL SECTION:

Synthesis of 2-cyano-*N*-cyclohexylacetamide (3)

In a 250mL round bottom flask equipped with magnetic stirrer and thermometer was placed ethyl 2-cyanoacetate (0.25mol), cyclohexayl amine (0.25mol) and toluene (100mL). The reaction mixture was heated up to 110-120 ^oC for 8 h. The progress of reaction was monitored by thin layer chromatography. The reaction mixture was cooled to room temperature and the solid product was filtered, washed with toluene to afford 90% yield.

Synthesis of 2-cyano-*N*-cyclohexyl-3,3-bis(methylthio)acrylamide (4)

A 100mL conical flask equipped with magnetic stirrer and septum was charged with a solution of 2-cyano-*N*-cyclohexylacetamide (**3**), (10 mmol) in DMF (10 mL). Dry K_2CO_3 (10 mmol) was added and the mixture was stirred at room temperature for 2 h. CS_2 (30 mmol) was added and the mixture was stirred for an additional 2 h at room

temperature. Then, methyl iodide (20 mmol) was added at 0-5 ºC and the mixture was stirred for 4 h at room temperature. The progress of the reaction was monitored by thin layer chromatography. After completion of the reaction, it was poured into 50ml cold water. The precipitated crude product was purified by filtration followed by crystallization from EtOH.

Synthesis of 5-amino-*N*-cyclohexyl-3-(methylthio)-1*H*-pyrazole-4-carboxamide (5)

A 100mL conical flask equipped with magnetic stirrer and septum was charged 2-cyano-*N*-cyclohexyl-3,3-bis(methylthio)acrylamide (**4**) (0.1mol) in isopropyl alcohol (100mL) and hydrazine hydrate (0.1mol). The Reaction mixture was heated to reflux for 2 h. After completion of the reaction, it was poured into 50mL cold water. The precipitated crude product was purified by filtration followed by crystallization from EtOH.

General synthesis of substituted and fused pyrazoloquinoline(8 a-p)

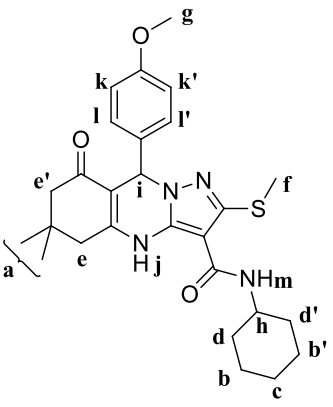
A mixture of 5-amino-*N*-cyclohexyl-3-(methylthio)-1*H*-pyrazole-4-carboxamide (**5**) (3.0mmol), potassium carbonate (6.0mmol),an appropriate aldehyde **(7 a-p)** and dimedone **(6)** (3.0mmol) in isopropyl alcohol (10 mL) was heated to reflux for 7-10 h. The progress of reaction mixture was monitored by TLC. After completion of reaction, the mixture was cooled to room temperature and solid residue was filtered and washed with 10mL of isopropyl alcohol followed by 50 ml of water. The product was crystallized from MeOH to give **(8 a-p)** in 80-90% yield.

Experimental data of synthesized compound [DPA 01 to 16]

N-cyclohexyl-6,6-dimethyl-2-(methylthio)-8-oxo-9-(p-tolyl)-4,5,6,7,8,9-hexahydropyrazolo[5,1-b]quinazoline-3-carboxamide [DPA-01]

White solid; mp >320 ºC, R_f 0.31 (9:1Chloroform: Methanol); IR (KBr): 3309, 3254, 3016, 2925, 1671, 1563, 1473,1287, 1246, 927,831, 807, 758. cm^{-1}; MS (*m/z*): 478 (M^+); Anal. Calcd for $C_{27}H_{34}N_4O_2S$: C, 67.75; H, 7.16; N, 11.71; O, 6.69; S, 6.70

N-cyclohexyl-9-(4-methoxyphenyl)-6,6-dimethyl-2-(methylthio)-8-oxo-4,5,6,7,8,9-hexahydropyrazolo[5,1-b]quinazoline-3-carboxamide [DPA-02]



Creamish solid; mp >320 ºC, R_f 0.40 (9:1Chloroform : Methanol); IR (KBr), ν(cm^{-1}): 3279, 3257 (-NH- stretching), 3016 (aromatic CH stretching), 2928 (asymmetric alkane CH stretching), 2850 (symmetric alkane CH stretching), 1730 (C=O stretching), 1675 (amidic C=O stretching), 1660, 1627, 1591 (aromatic carbon skeleton, C=C stretching), 1481 (alkane CH bending), 1246 (alkane C-C stretching), 1193 (C-O-C stretching), 1111 (C-O stretching), 810 (aromatic CH bending, out of plane), 743 & 667 (aromatic CH bending, out of plane); ^{1}H NMR (400 MHz, DMSO): **(a)**0.99 δppm (s, 6H, 2×-CH_3), **(b)**1.29 δppm (m, 4H, 2×CH_2), **(c)**1.53 δppm (m, 2H, CH_2), **(d)**1.69 δppm (m, 4H, 2×CH_2), **(e)**1.84 δppm (s, 4H, 2×CH_2) **(f)**2.40 δppm (s, 3H, -SCH_3), **(g)**2.89 δppm (s, 3H, -OCH_3), **(h)**3.79 δppm (m, 1H, -CH), **(i)**6.47 δppm (s, 1H, -CH), **(j)**7.01 δppm (s, 1H, -NH-), **(k)**7.19 δppm (dd, 2H, Ar-H, ^{3}J=8.0 Hz), **(l)**7.38 δppm (dd, 2H, Ar-H, ^{3}J=8.0 Hz), **(m)**8.80 δppm (s, 1H, -CONH-cyclohexyle); MS (*m/z*): 494 (M^+, molecular ion peak), 447, 387, 372(base peak, 100%), 357, 348, 325, 315, 297, 289, 274, 259, 247, 231, 214, 192, 175, 156, 141, 135, 121, 98, 91, 77, 56, 55, 41, 40 ; Anal. Calcd for $C_{27}H_{34}N_4O_3S$: C, 65.56; H, 6.93; N, 11.33; O, 9.70; S, 6.48

N-cyclohexyl-6,6-dimethyl-2-(methylthio)-8-oxo-9-phenyl-4,5,6,7,8,9-hexahydropyrazolo[5,1-b]quinazoline-3-carboxamide [DPA-03]

White solid; mp >320 ˚C, R_f 0.48 (9:1Chloroform: Methanol); IR (KBr): 3323, 3026, 2908, 2856, 1674, 1630, 1563, 1473, 1246, 927, 843, 798, 732, cm^{-1}; MS (*m/z*): 464 (M^+); Anal. Calcd for $C_{26}H_{32}N_4O_2S$: C, 67.21; H, 6.94; N, 12.06; O, 6.89; S, 6.90

9-(4-cyanophenyl)-N-cyclohexyl-6,6-dimethyl-2-(methylthio)-8-oxo-4,5,6,7,8,9-hexahydropyrazolo[5,1-b]quinazoline-3-carboxamide [DPA-04]

Creamish solid; mp >320 ˚C, R_f 0.35 (9:1Chloroform: Methanol); IR (KBr): 3379, 3024, 2902, 1651, 1516,1483, 1332, 1166, 954, 852, 822, 748, 709 cm^{-1}; MS (*m/z*): 489 (M^+); Anal. Calcd for $C_{27}H_{31}N_5O_2S$: C, 66.23; H, 6.38; N, 14.30; O, 6.54; S, 6.55.

9-(4-chlorophenyl)-N-cyclohexyl-6,6-dimethyl-2-(methylthio)-8-oxo-4,5,6,7,8,9-hexahydropyrazolo[5,1-b]quinazoline-3-carboxamide [DPA-05]

White solid; mp >320 ˚C, R_f 0.28 (9:1Chloroform: Methanol); IR (KBr): 3430, 3133, 3051, 2922, 1651, 1516, 1483, 1232, 1166, 954, 883, 780, 743, 698 cm^{-1}; MS (*m/z*): 498 (M^+); Anal. Calcd for $C_{26}H_{31}ClN_4O_2S$: C, 62.57; H, 6.26; Cl, 7.10; N, 11.23; O, 6.41; S, 6.42

9-(4-bromophenyl)-N-cyclohexyl-6,6-dimethyl-2-(methylthio)-8-oxo-4,5,6,7,8,9-hexahydropyrazolo[5,1-b]quinazoline-3-carboxamide [DPA-06]

Yellow solid; mp >320 ˚C, R_f 0.29 (9:1 Chloroform: Methanol); IR (KBr): 3421, 3122, 3088, 2922, 1651, 1516, 1483, 1232, 1166, 954, 883, 780, 743, 698 cm^{-1}; MS (*m/z*): 542 (M^+); Anal. Calcd for $C_{26}H_{31}BrN_4O_2S$: C, 57.45; H, 5.75; Br, 14.70; N, 10.31; O, 5.89; S, 5.90.

N-cyclohexyl-9-(4-fluorophenyl)-6,6-dimethyl-2-(methylthio)-8-oxo-4,5,6,7,8,9-hexahydropyrazolo[5,1-b]quinazoline-3-carboxamide [DPA-07]

Creamish solid; mp >320 ˚C, R_f 0.36 (9:1 Chloroform: Methanol); IR (KBr): 3422, 3127, 3085, 2942, 1628, 1483, 1237, 1158, 883, 780, 743 cm^{-1}; MS (*m/z*): 482 (M^+); Anal. Calcd for $C_{26}H_{31}FN_4O_2S$: C, 64.71; H, 6.47; F, 3.94; N, 11.61; O, 6.63; S, 6.64

N-cyclohexyl-9-(3-hydroxyphenyl)-6,6-dimethyl-2-(methylthio)-8-oxo-4,5,6,7,8,9-hexahydropyrazolo[5,1-b]quinazoline-3-carboxamide [DPA-08]

Creamish solid; mp >320 ˚C, R_f 0.41 (9:1Chloroform: Methanol); IR (KBr): 3430, 3133, 3051, 2922, 1651, 1516, 1483, 1232, 1166, 954, 883, 780, 743, 698 cm^{-1}; MS (*m/z*): 480 (M^+); Anal. Calcd for $C_{26}H_{32}N_4O_3S$: C, 64.97; H, 6.71; N, 11.66; O, 9.99; S, 6.67

9-(3-chlorophenyl)-N-cyclohexyl-6,6-dimethyl-2-(methylthio)-8-oxo-4,5,6,7,8,9-hexahydropyrazolo[5,1-b]quinazoline-3-carboxamide [DPA-09]

White solid; mp >320 ˚C, R_f 0.35 (9:1Chloroform: Methanol); IR (KBr): 3279, 3257, 3016, 2928, 2850, 1730, 1660, 1627, 1246, 835, 810, 748 cm^{-1}; MS (*m/z*): 498 (M^+); Anal. Calcd for $C_{26}H_{31}ClN_4O_2S$: C, 62.57; H, 6.26; Cl, 7.10; N, 11.23; O, 6.41; S, 6.42

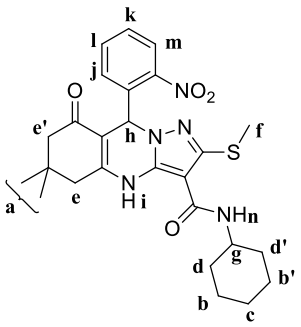
9-(3-bromophenyl)-N-cyclohexyl-6,6-dimethyl-2-(methylthio)-8-oxo-4,5,6,7,8,9-hexahydropyrazolo[5,1-b]quinazoline-3-carboxamide [DPA-10]

White solid; mp >320 ˚C, R_f 0.44 (9:1Chloroform: Methanol); IR (KBr): 3198, 3157, 3042, 2942, 2832, 1734, 1668, 1654, 1257, 832, 806, 742 cm^{-1}; MS (*m/z*): 542 (M^+); Anal. Calcd for $C_{26}H_{31}BrN_4O_2S$: C, 57.45; H, 5.75; Br, 14.70; N, 10.31; O, 5.89; S, 5.90

9-(2-chlorophenyl)-N-cyclohexyl-6,6-dimethyl-2-(methylthio)-8-oxo-4,5,6,7,8,9-hexahydropyrazolo[5,1-b]quinazoline-3-carboxamide [DPA-11]

Creamish solid; mp >320 ˚C, R_f 0.41 (9:1Chloroform: Methanol); IR (KBr): 3398, 3227, 3150, 2902, 2865, 1651, 1516, 1452, 1326, 880, 828, 750, 697 cm^{-1}; MS (*m/z*): 498 (M^+); Anal. Calcd for $C_{26}H_{31}ClN_4O_2S$: C, 62.57; H, 6.26; Cl, 7.10; N, 11.23; O, 6.41; S, 6.42

N-cyclohexyl-6,6-dimethyl-2-(methylthio)-9-(2-nitrophenyl)-8-oxo-4,5,6,7,8,9-hexahydropyrazolo[5,1-b]quinazoline-3-carboxamide [DPA-12]



White solid; mp >320 ˚C, R_f 0.38 (9:1Chloroform: Methanol); IR (KBr), ν(cm^{-1}): 3282 (-NH- stretching), 3055 (aromatic CH stretching), 2933 (asymmetric alkane CH stretching), 2852 (symmetric alkane CH stretching), 1732 (C=O stretching), 1672 (amidic C=O stretching), 1660, 1620, 1602 (aromatic carbon skeleton, C=C stretching), 1552, 1533, 1352, 1317(N-O stretching), 1479 (alkane CH bending), 1099 (C-O stretching), 833, 792 (aromatic CH bending, out of plane), 709 & 669 (aromatic CH bending, out of plane); ^{1}H NMR(400 MHz, DMSO): **(a)**0.99 δppm (s, 6H, 2×-CH_3), **(b)**1.28 δppm (m, 4H, 2×CH_2), **(c)**1.53 δppm (m, 2H, CH_2), **(d)**1.68 δppm (m, 4H, 2×CH_2), **(e)**1.83 δppm (s, 4H, 2×CH_2) **(f)**2.42 δppm (s, 3H, -SCH_3), **(g)**3.79 δppm (m, 1H, -CH), **(h)**6.47 δppm (s, 1H, -CH), **(i)**7.01 δppm (s, 1H, -NH-), **(j)**7.07 δppm (dd, 1H, Ar-H, ^{3}J=8.6 Hz), **(k)**7.20 δppm (dt, 1H, Ar-H, ^{3}J=8.8 Hz, ^{4}J=2.4 Hz), **(l)**7.29 δppm (dt, 1H, Ar-H, ^{3}J=8.6 Hz, ^{4}J=2.4 Hz), **(m)**7.38 δppm (dd, 1H, Ar-H, ^{3}J=8.6 Hz), **(n)**8.80 δppm (s, 1H, -CONH-cyclohexyle); MS (*m/z*): 509 (M^+, molecular ion peak), 492(base peak, 100%), 462, 448, 426, 410, 393, 379, 378, 361, 349, 333, 316, 300, 288, 273, 254, 242, 227, 211, 196, 185, 171, 156, 141, 128, 115, 98, 92 ; Anal. Calcd for $C_{26}H_{31}N_5O_4S$: C, 61.28; H, 6.13; N, 13.74; O, 12.56; S, 6.29

N-cyclohexyl-9-(2,5-dimethoxyphenyl)-6,6-dimethyl-2-(methylthio)-8-oxo-4,5,6,7,8,9-hexahydropyrazolo[5,1-b]quinazoline-3-carboxamide [DPA-13]

Creamish solid; mp >320 ˚C, R_f 0.45 (9:1 Chloroform: Methanol); IR (KBr), ν(cm^{-1}): 3294, 3259 (-NH-stretching), 3097, 3018 (aromatic CH stretching), 2942 (asymmetric alkane CH stretching), 2882 (symmetric alkane CH stretching), 1728 (C=O stretching), 1678 (amidic C=O stretching), 1639, 1589, 1560 (aromatic carbon skeleton, C=C stretching), 1429 (alkane CH bending), 1252 (alkane C-C stretching), 1019, 1006 (C-O stretching), 821 (aromatic CH bending, out of plane), 779 & 661 (aromatic CH bending, out of plane); MS (*m/z*): 524 (M^+, molecular ion peak), 507, 477, 441, 425, 394, 378(base peak, 100%), 375, 361, 346, 320, 304, 288, 274, 257, 241, 221, 201, 185, 172, 156, 138, 114, 98 ; Anal. Calcd for $C_{28}H_{36}N_4O_4S$: C, 64.10; H, 6.92; N, 10.68; O, 12.20; S, 6.11

N-cyclohexyl-9-(3,4-dimethoxyphenyl)-6,6-dimethyl-2-(methylthio)-8-oxo-4,5,6,7,8,9-hexahydropyrazolo[5,1-b]quinazoline-3-carboxamide [DPA-14]

Creamishsolid; mp >320°C, R_f 0.34 (9:1Chloroform: Methanol); IR (KBr): 3460, 3367, 3242, 2956, 2845, 1647, 1538, 1420, 1318, 867, 750, 700 cm^{-1}; MS (*m/z*): 524 (M^+); Anal. Calcd for $C_{28}H_{36}N_4O_4S$: C, 64.10; H, 6.92; N, 10.68; O, 12.20; S, 6.11

N-cyclohexyl-6,6-dimethyl-2-(methylthio)-9-(4-nitrophenyl)-8-oxo-4,5,6,7,8,9-hexahydropyrazolo[5,1-b]quinazoline-3-carboxamide [DPA-15]

White solid; mp >320 °C, R_f 0.23 (9:1Chloroform: Methanol); IR (KBr): 3483, 3242, 3162, 3068, 2902, 1675, 1584,1425, 1332, 1066, 954, 820, 750 cm^{-1}; MS (*m/z*): 509 (M^+); Anal. Calcd for $C_{26}H_{31}N_5O_4S$: C, 61.28; H, 6.13; N, 13.74; O, 12.56; S, 6.29

9-(2-bromophenyl)-N-cyclohexyl-6,6-dimethyl-2-(methylthio)-8-oxo-4,5,6,7,8,9-hexahydropyrazolo[5,1-b]quinazoline-3-carboxamide [DPA-16]

White solid; mp >320 °C, R_f 0.22 (9:1Chloroform: Methanol); IR (KBr): 3503, 3450, 3206, 3068, 2908, 1628, 1548,1420, 1342, 1066, 825, 754 cm^{-1}; MS (*m/z*): 542 (M^+); Anal. Calcd for $C_{26}H_{31}BrN_4O_2S$: C, 57.45; H, 5.75; Br, 14.70; N, 10.31; O, 5.89; S, 5.90

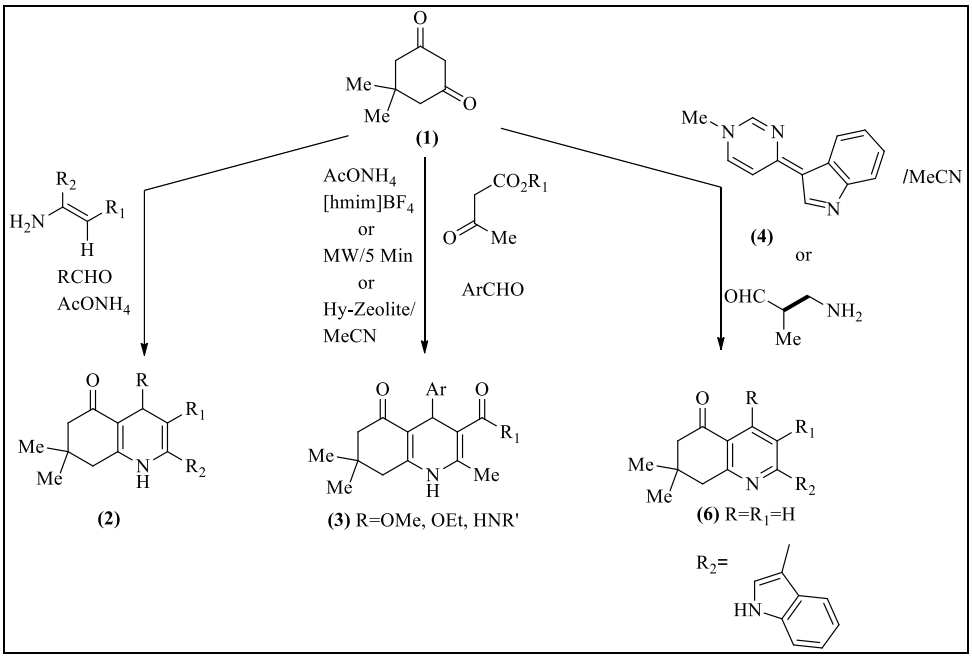
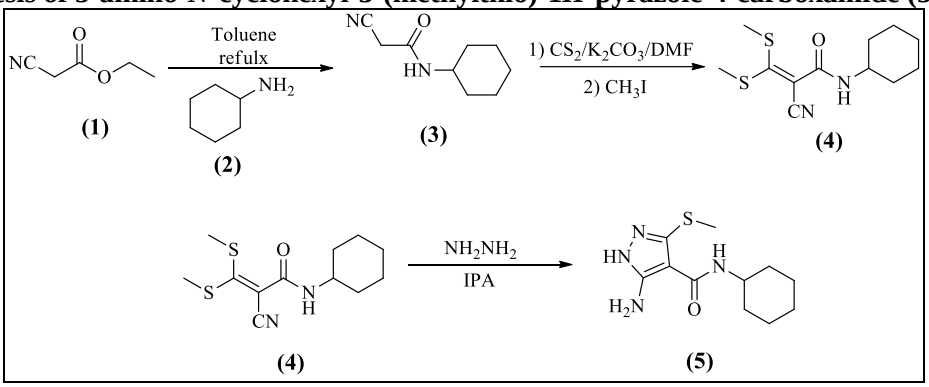


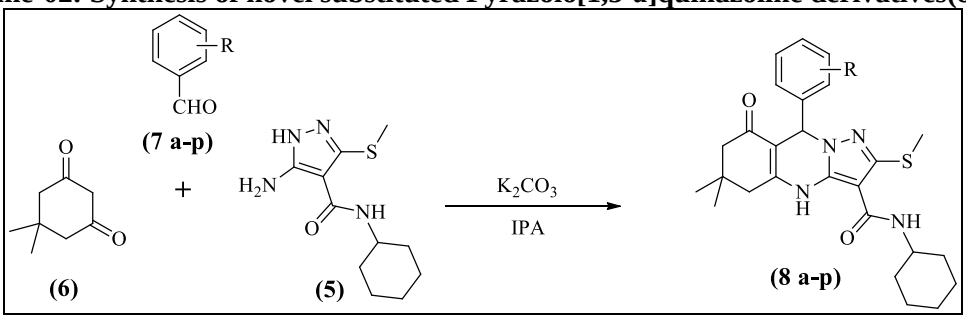
Figure-1

3. RESULTS AND DISCUSSION:

Scheme-01: Synthesis of 5-amino-*N*-cyclohexyl-3-(methylthio)-1*H*-pyrazole-4-carboxamide (5)



Scheme-02: Synthesis of novel substituted Pyrazolo[1,5-*a*]quinazoline derivatives(8 a-p)



Preparation of the target compounds was initiated by the reaction of ethylcynoacetate **(1**) with cyclohexyl amines (**2**) in toluene at reflux temperature to afford the cyanoacetamides (**3)** in 90% yields. This product undergoes reaction with carbon disulfide in the presence of base in DMF followed by methylation to afford corresponding 2-cyano-3,3-bis(methylthio)-*N*-phenylacrylamide (**4**). Which on reaction with hydrazine hydrate undergoes cyclization to form 5-amino-*N*-cyclohexyl-3-(methylthio)-1*H*-pyrazole-4-carboxamide (**5**) (**Scheme-01**).

Dimedone **(6)** is reacted with an appropriate aldehyde (**7 a-p**) and 5-amino-*N*-cyclohexyl-3-(methylthio)-1*H*-pyrazole-4-carboxamide (**5**) in the presence of $NaHCO_3$ and methanol as a solvent to afford highly substituted pyrazolo[1,5-a]quinazoline (**8 a-p**) in law yield (**Table-1)(Scheme-02**).

Table-1: synthesis of novel substituted and fused pyrazoloquinazoline derivatives

Entry	Code	-R	Mol. Formula	Mol. Weight	Time hrs	Yield %
8 a	DPA-01	4-CH_3	$C_{27}H_{34}N_4O_2S$	478	8.5	82
8 b	DPA-02	4-OCH_3	$C_{27}H_{34}N_4O_3S$	494	8.0	76
8 c	DPA-03	-H	$C_{26}H_{32}N_4O_2S$	464	8.5	80
8 d	DPA-04	4-CN	$C_{27}H_{31}N_5O_2S$	489	7.5	73
8 e	DPA-05	4-Cl	$C_{26}H_{31}ClN_4O_2S$	498	7.5	79
8 f	DPA-06	4-Br	$C_{26}H_{31}BrN_4O_2S$	542	9.0	84
8 g	DPA-07	4-F	$C_{26}H_{31}FN_4O_2S$	482	8.0	76
8 h	DPA-08	3-OH	$C_{26}H_{32}N_4O_3S$	480	8.5	80
8 i	DPA-09	3-Cl	$C_{26}H_{31}ClN_4O_2S$	498	8.0	86
8 j	DPA-10	3-Br	$C_{26}H_{31}BrN_4O_2S$	542	7.5	77
8 k	DPA-11	2-Cl	$C_{26}H_{31}ClN_4O_2S$	498	8.0	78
8 l	DPA-12	2-NO_2	$C_{26}H_{31}N_5O_4S$	509	7.5	82
8 m	DPA-13	2,5-di-OMe	$C_{28}H_{36}N_4O_4S$	524	7.5	72
8 n	DPA-14	3,4-di-OMe	$C_{28}H_{36}N_4O_4S$	524	8.5	80
8 o	DPA-15	4-NO_2	$C_{26}H_{31}N_5O_4S$	509	8.5	86
8 p	DPA-16	4-Br	$C_{26}H_{31}BrN_4O_2S$	542	9.0	74

4. CONCLUSIONS:

In summary, the heterocyclizations of dimedone, an appropriate aldehyde with 5-aminopyrazole derivative were studied in details, and the influence of the reaction parameters and the aminoazole structure on the direction of the reaction was established. We found that the reaction of dimedone **(6),** an appropriate aldehyde **(7 a-p)** with 5-aminopyrazole derivative (**5)** were faster and afforded the pyrazolo[5,1-*b*]quinazoline **(8 a-p)** in good yield in the presence of K_2CO_3 as a base and isopropyl alcohol. The results of the study described above have led to the development of a simple approach for synthesis of pyrazolo[5,1-*b*]quinazoline **(8 a-p)**, substances that potentially interesting biological and medicinal properties.

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