Heterocyclic Letters
Vol. 6| No.1|123-132| Nov-Jan| 2016
ISSN : (print) 2231–3087 / (online) 2230-9632
CODEN: HLEEAI
http://heteroletters.org

COMPARATIVE STUDY ON THE USE OF CONVENTIONAL, MICROWAVE AND ULTRASOUND-IRRADIATION FOR THE SYNTHESIS OF PYRANO[3,2-*c*]CHROMENE AND BENZOPYRANO[4,3-*b*]CHROMENE DERIVATIVES IN WATER

Jayvirsinh D. Gohil, Haresh B. Patel, Manish P. Patel*

Department of Chemistry, Sardar Patel University,
Vallabh Vidyanagar 388120, Gujarat, India
E-mail: *patelmanish1069@yahoo.Com*

ABSTRACT
An efficient one-pot synthesis using multi-component system (MRCs) for the preparation of pyrano-chromene and benzopyrano-chromene derivatives from the reaction of 6-(un)substituted-2-(amino triazole/tetrazole)quinoline-3-carbaldehydes **2a-b**/**3a-b**, 4-hydroxy coumarin **5**/4-hydroxy-6-methyl pyran **6** and malononitrile **4a**/methyl cyanoacetate **4b** using water as a solvent and $_{L}$-proline as a catalyst. The reactions were carried out by three different techniques, conventional heating, microwave irradiation and ultrasound irradiation. But ultrasound method is better than the other methods on the basis of their attractive features like mild conditions, high atom-economy, less reaction time and excellent yields. The structures of all compounds were established on the basis of their spectral data.

KEYWORDS
Triazole ; Tetrazole ; Quinoline; $_{L}$-proline ; Chromene ; green media

INTRODUCTION
Today, chemists think about a process in which use of catalyst and solvents should be non toxic and environment friendly. So, water is a solvent which is commonly consider as benign solvent in view of its non toxicity and abundant natural occurrence. For many chemical reactions, it has been sacrificing without regio- and stereo selectivity as well as yield[i,ii]. In multicomponent reaction (MCRs), biologically active molecules and complex products are synthesized from readily available starting materials in a single step process. From this point of view, for organic synthesis and drug discovery MCRs emerged as green and powerful tools[iii-vi]. Moreover, organocatalyzed MCRs in water are of outstanding value in organic synthesis and green chemistry[vii-xii].
Nowadays, synthetic chemists are seeking other methods that help to develop strategies which maximize the atom economy and minimize the waste generation and costs. For these reason, the microwave and ultrasound assisted reactions have many advantages like the environmentally benign and the high reaction selectivity, which was provided more rapid and convenient procedures for the synthesis of combinatorial heterocycles[xiii-xviii]. At present work, the use of triazole, tetrazole and quinoline which have always important both synthetic and biological chemist because of its diverse chemical, pharmacological properties[xix-xxi].

From the literature survey[xxii-xxiii], reported the synthesis of quinoline incorporating structures systems. In present work, we introduced amino triazole/tetrazole at C-2 position of 6-(un)substituted- quinoline-3-carbaldehyde and to synthesis the targeted compounds **7a-h** and **8a-h** by using and compare the three methods such as conventional, microwave and ultrasound irradiation with concept of atom economy, environmental concern and highlighting green chemistry.

EXPERIMENTAL

The solvents used were of analytical grade and the reagents 4H-1,2,4-triazol-4-amine, 1H-tetrazol-5-amine, substituted malononitrile, 4-hydroxy coumarin, 6-methyl pyran and $_{L}$-proline were obtained from Sigma Aldrich. Ultrasonication was performed in D-Compact ultrasonic cleaner with a frequency of 50 kHz and power of 250 W (EIE instrument pvt.ltd. Ahmadabad). The reaction flask was suspended at the centre of ultrasonic bath so as surface of the reactants remained slightly lower than the level of water in the bath. Another instrument like microwave-assisted reactions are conducted in a ‘‘RAGA’s Modified Electromagnetic Microwave System, ’’whereby microwaves are generated by magnetron at a frequency of 2,450 MHz having an adjustable output power levels, i.e., 10 levels from 140 to 700 W, with an individual sensor for temperature control (fiber optic is used as a individual sensor for temperature control) with attachment of reflux condenser with constant stirring thus, avoiding the risk of development high pressure. For monitoring the progress of all reactions with the use of thin-layer chromatography on which aluminum plates precoated with silica gel, $^{60}F_{254}$, 0.25-mm thickness (Merck, Darmstadt, Germany). Elemental analysis (% C, H, and N) was carried out with Perkin–Elmer 2400 series-II elemental analyzer (Perkin–Elmer, USA) and all compounds are within ±0.4 % of theory specified. Mass were recorded on a Shimadzu LC-MS 2010 spectrometer. The IR spectra were recorded in KBr on a Perkin–Elmer Spectrum GX FT-IR Spectrophotometer (Perkin–Elmer, USA) and here, the characteristic peaks are reported in cm^{-1}. ^{1}H NMR and ^{13}C NMR spectra were recorded on a Bruker Avance 400F (MHz) spectrometer (Bruker Scientific Corporation Ltd., Switzerland) at 400 MHz and 100 MHz in DMSO-d_6 solvent.

General procedure for the synthesis of Aldehydes (2a-b and **3a-b).**

Stirred substituted aldehydes (**1a-b**) (15 mmol) with ethylene glycol (45 mmol, 3 equiv) in anhydrous toluene (25 ml), add *p*-TSA (1.5 mmol, 0.1 equiv) as a catalyst. The reaction mixture was heated under reflux for 5–6 h by using a Dean–Stark condenser (TLC, ethyl acetate/petroleum ether 1:9). Solvent was removed under reduced pressure, water (20 mL) was added to the reaction mixture, After the reaction was complete(check by TLC), then the aqueous layer was extracted with ethyl acetate, the combined organic layer was dried over sodium sulphate, and ethyl acetate was evaporated under vacuum. Then, replacement of chloro group by 4-amino triazole and 5- amino tetrazole in the presence of K_2CO_3 in DMF at 100°C for 2-3 hrs. Finally, product **2a-b**/**3a-b** obtained by deprotection of aldehydes under reflux using acid in water for 1 hr.

General procedure for the synthesis of title compounds 7a-h to 8a-h by ultrasonic, microwave irradiation and conventional method.

2-amino triazole/2-amino tetrazole quinoline-3-carbaldehyde **2a-b**/**3a-b** (1mmol) and 4-hydroxy coumarin (1mmol) 5/4-hydroxy-6-methyl-2H-pyran-2-one 6 and $_{L}$-proline (5 mol %) were mixed with water (2 ml). Then add malononitrile/methyl cyanoacetate **4a-b** (1 mmol), Method-1, under sonication for 15 min at 50°C, Method-2, under microwave (420 W) for 20 min and Method-3, 1 h at 80°C for conventional methods. The crude products were allowed

to cool. The precipitates obtained were filtered and washed with water and then with ethanol to afford the pure product. The reaction progress was monitored by TLC.

^{1}H, ^{13}C, IR and Mass spectra of synthesized compound **7a-h** and **8a-h**.

2-(4H-1,2,4-triazol-4-ylamino)quinoline-3-carbaldehyde (TA-1)

White solid ; mp 120-125^{o}C; IR (KBr, $\nu_{max,}$ cm^{-1}) = 2930 (Ar-C-H), 3330 (-NH), 1613 (C=O str.); ^{1}H NMR (400 MHz, DMSO-d_6) δ =7.81-8.45 (m,6H,Ar-H), 8.88 (s,1H,Ar-H), 9.69 (s,1H, Ar-NH), 10.45 (s,1H,CHO) ppm; ^{13}C NMR (100 MHz DMSO-d_6) δ: 121.54, 123.55, 125.36, 126.55, 128.66, 132.55, 140.36, 145.66, 146.87, 148.66, 158.57, 192.33 (C=O); MS Calc. for $C_{12}H_9N_5O$ $[M]^+$ 239.15, found 239.23; Anal. Calc. C, 60.25; H, 3.79; N, 29.27; Found: C 60.40, H 3.70, N 29.10 %

2-(1H-tetrazol-5-ylamino) quinoline-3-carbaldehyde (TA-2)

White solid ; mp 130-135^{o}C ; IR (KBr, $\nu_{max,}$ cm^{-1}) = 3025 (Ar-C-H), 3222 and 3350 (-NH), 1670 (C=O str.) cm^{-1};^{1}H NMR (400 MHz, DMSO-d_6) δ = 7.78-8.44 (m,6H,Ar-H +tetrazole -NH), 9.07 (s,1H,Ar-NH), 10.65 (s,1H,CHO) ppm; ^{13}C NMR (100 MHz DMSO-d_6) δ: 122.48, 123.64, 125.74, 127.12, 130.97, 132.74, 140.69, 147.55, 158.74, 162.52, 193.74 (C=O) ; MS Calc. for $C_{11}H_8N_6O$ $[M]^+$ 240.20, found 240.22; Anal. Calc. C, 55.00; H, 3.36; N, 34.98; Found: C 54.80, H 3.50, N 35.15 %

4-(2-(4H-1,2,4-triazol-4-ylamino)quinolin-3-yl)-2-amino-5-oxo-4,5-dihydropyrano[3,2-*c*]chromene-3-carbonitrile (7a)

White solid ; mp 232°C; IR (KBr, $\nu_{max,}$ cm^{-1}) = 3440 and 3355 (asym. and sym. str. of -NH_2), 2158 (C≡N str.), 1668 (C=O str.); ^{1}H NMR (400 MHz, DMSO-d_6) δ = 5.59 (s,1H,CH), 7.21 (s,2H,Ar-NH_2), 7.42-8.43 (m,10H,Ar-H), 8.57 (s,1H,Ar-H), 9.57 (s,1H,NH) ppm; ^{13}C NMR (100 MHz DMSO-d_6) δ: 34.22 (CH), 59.54 (C–CN), 108.74, 110.87, 115.65, 118.71, 121.70, 124.51, 124.60, 125.88, 127.50, 129.20, 132.02, 133.72, 138.15, 139.52, 142.08, 145.40, 145.49, 150.77, 154.10, 160.92, 169.54 (Ar-C), 193.40 (C=O) ppm; MS Calc. for $C_{24}H_{15}N_7O_3$ $[M]^+$ 449.20, found 449.42; Anal. Calc. C 64.14, H 3.36, N 21.82; Found: C 64.41, H 3.23, N 21.61 %

Methyl 4-(2-(4H-1,2,4-triazol-4-ylamino)quinolin-3-yl)-2-amino-5-oxo-4,5-dihydropyrano[3,2-*c*]chromene-3-carboxylate (7b)

White solid ; mp. 240°C; IR (KBr, $\nu_{max,}$ cm^{-1}) = 3394 and 3279 (asym. and sym. str. of -NH_2), 1696 and 1647 (C=O str.); ^{1}H NMR (400 MHz, DMSO-d_6) δ = 3.23 (s,3H,$COOCH_3$), 5.42 (s,1H,CH), 7.22 (s,2H,Ar-NH_2), 7.45-8.29 (m,10H,Ar-H), 8.39 (s,1H,Ar-H), 9.59 (s,1H, NH) ppm; ^{13}C NMR (100 MHz DMSO-d_6) δ: 36.39 (CH), 52.45 ($COOOCH_3$), 81.08 (C-$COOCH_3$), 109.17, 115.85, 118.31, 120.33, 122.03, 124.83, 126.10, 127.28, 127.64, 128.34, 129.13, 130.00, 131.27, 133.69, 135.94, 136.92, 141.10, 145.22, 145.94, 150.82, 172.53 (Ar-C), 195.86 (C=O) ppm; MS Calc. for $C_{25}H_{18}N_6O_5$ $[M]^+$ 482.12, found 482.45; Anal. Calc. C 62.24, H 3.76, N 17.42; Found: C 62.11, H 4.05, N 17.61 %

4-(2-(4H-1,2,4-triazol-4-ylamino)-6-methoxyquinolin-3-yl)-2-amino-5-oxo-4,5-dihydropyrano[3,2-*c*]chromene-3-carbonitrile (7c)

White solid; mp. 215°C; IR (KBr, $\nu_{max,}$ cm^{-1}) = 3445 and 3350 (asym. & sym. str. of -NH_2), 2220 (C≡N str.),1675 (C=O str.); ^{1}H NMR (400 MHz, DMSO-d_6) δ = 3.56 (s,3H,OCH_3), 5.54 (s,1H, CH), 7.24 (s,2H,Ar-NH_2), 7.45-8.33 (m,9H,Ar-H), 8.45 (s,1H,Ar-H), 9.56 (s,1H,NH) ppm; ^{13}C NMR (100 MHz DMSO-d_6) δ: 35.22 (CH), 55.45 (Ar-OCH_3), 58.93 (C–CN), 107.23, 115.11, 120.12, 121.43, 122.45, 124.46, 125.76, 127.33, 127.85, 128.03, 129.37, 131.63, 133.31, 135.19, 137.85, 140.16, 145.12, 145.96, 148.25, 150.77, 169.43 (Ar-C),194.97 (C=O) ppm; MS Calc. for $C_{25}H_{17}N_7O_4$ $[M]^+$ 479.30, found 479.45; Anal. Calc. C 62.63, H 3.57, N 20.45; Found: C 62.91, H 3.41, N 20.15 %

Methyl 4-(2-(4H-1,2,4-triazol-4-ylamino)-6-methoxyquinolin-3-yl)-2-amino-5-oxo-4,5-dihydropyrano[3,2-*c*]chromene-3-carboxylate (7d)

White solid; mp 222°C; IR (KBr, $\nu_{max,}$ cm^{-1})= 3425 and 3356 (asym. & sym. str. of -NH_2), 1682 and 1652 (C=O str.) ; ^{1}H NMR (400 MHz, DMSO-d_6) δ = 3.31 (s,3H,$COOCH_3$), 3.68 (s,3H OCH_3), 5.59 (s,1H, CH), 7.15 (s,2H,Ar-NH_2), 7.35-8.26 (m,9H,Ar-H), 8.35 (s,1H,Ar-H), 9.458 (s,1H,-NH) ppm; ^{13}C NMR (100 MHz DMSO-d_6) δ: 34.23 (CH), 52.45 ($COOCH_3$), 56.45 (Ar-OCH_3), 79.12 (C-$COOCH_3$), 107.31, 114.85, 118.22, 120.51, 122.56, 124.87, 126.45, 127.28, 128.55, 129.74, 131.56, 133.74, 135.36, 136.34, 138.66, 140.49, 144.74, 145.10, 150.36, 153.46, 172.93 (Ar-C), 194.66 (C=O) ppm; MS calc. for $C_{26}H_{20}N_6O_6$ $[M]^+$ 512.24, found 512.47 ; Anal. Calc. C 60.94, H 3.93, N 16.40; Found: C 60.71, H 3.81, N 16.55 %

4-(2-(4H-1,2,4-triazol-4-ylamino)quinolin-3-yl)-2-amino-7-methyl-5-oxo-4,5-dihydropyrano[4,3-*b*]pyran-3-carbonitrile (7e)

White solid; mp 245°C; IR (KBr, $\nu_{max,}$ cm^{-1}) = 3418 and 3348 (asym. & sym. str. of -NH_2 and -NH), 2199(C≡N str.), 1659 (C=O str.); ^{1}H NMR (400 MHz, DMSO-d_6) δ ppm: 2.31 (s,3H,CH_3), 5.36 (s,1H, CH), 7.29 (s,2H,Ar-NH_2), 7.68-8.31 (m,7H,Ar-H), 8.40 (s,1H,Ar-H), 8.62 (s,1H,Ar-H), 9.18 (s,1H,NH),^{13}C NMR (100 MHz DMSO-d_6) δ; 22.45 (CH_3), 35.15 (CH), 56.95 (C–CN), 108.32, 113.18, 118.97, 122.08, 123.65, 124.68, 125.70, 128.71, 128.80, 131.32, 131.58, 136.26, 138.30, 145.86, 145.92, 157.30, 169.14 (Ar-C), 193.68 (C=O) ppm; MS Calc. for $C_{21}H_{15}N_7O_3$ $[M+1]^+$ 414.40, found 413.39 ; Anal. Calc. C 61.01, H 3.66, N 23.72 ; Found: C 61.30, H 3.32, N 23.51 %

Methyl 4-(2-(4H-1,2,4-triazol-4-ylamino)quinolin-3-yl)-2-amino-7-methyl-5-oxo-4,5-dihydropyrano[4,3-*b*]pyran-3-carboxylate (7f)

White solid; mp 270°C; IR (KBr, $\nu_{max,}$ cm^{-1}) = 3411 and 3332 (asym. & sym. str. of -NH_2), 1662 and 1610 (C=O str.) ;^{1}H NMR (400 MHz, DMSO-d_6) δ ppm: 2.35 (s,3H,CH_3), 3.43 (s,3H,$COOC\underline{H}_3$), 5.42 (s,1H,CH), 7.21 (s,2H,Ar-NH_2), 7.46-8.38 (m,7H,Ar-H), 8.58 (s,1H,Ar-H), 9.04 (s,1H,NH); ^{13}C NMR (100 MHz DMSO-d_6) δ : 20.74 (CH_3), 33.12 (CH), 53.27 ($COOCH_3$), 78.33 (C-$COOCH_3$), 110.11, 114.13, 120.24, 122.46, 123.47, 125.03, 127.74, 128.92, 129.11, 131.36, 132.65, 135.44, 138.12, 144.33, 145.13, 154.78, 170.46 (Ar-C), 194.15 (C=O) ppm; MS Calc. for $C_{22}H_{18}N_6O_5$ $[M]^+$ 446.22, found 446.42; Anal. Calc. C 59.19, H 4.06, N 18.83; Found: C 59.41, H 3.96, N 19.02 %

4-(2-(4H-1,2,4-triazol-4-ylamino)-6-methoxyquinolin-3-yl)-2-amino-7-methyl-5-oxo-4,5-dihydropyrano[4,3-*b*]pyran-3-carbonitrile (7g)

White solid; mp 265°C; IR (KBr, $\nu_{max,}$ cm^{-1}) = 3427 and 3352 (asym. & sym. str. of -NH_2), 2240 (C≡N str.), 1655 (C=O str.) ; ^{1}H NMR (400 MHz, DMSO-d_6) δ ppm: 2.25 (s,3H,CH_3), 3.45 (s,3H,OCH_3), 5.53 (s,1H, CH), 7.14 (s,2H,Ar-NH_2), 7.57-8.34 (m,6H,Ar-H), 8.74 (s,1H,Ar-H), 9.04 (s,1H,NH); ^{13}C NMR (100 MHz DMSO-d_6) δ: 21.34 (CH_3), 33.43 (CH), 55.41 (C–CN), 109.41, 113.45, 118.65, 123.41, 124.55, 126.84, 127.32, 128.11, 129.35, 130.49, 131.56, 133.75, 135.49, 137.54, 145.02, 145.98, 154.41, 165.39 (Ar-C), 193.45 (C=O) ppm; MS Calc. for $C_{22}H_{17}N_7O_4$ $[M]^+$ 443.22, found 443.41; Anal. Calc.C, 59.59; H, 3.86; N, 22.11; Found: C 59.45, H 4.10 N 22.51 %

Methyl 4-(2-(4H-1,2,4-triazol-4-ylamino)-6-methoxyquinolin-3-yl)-2-amino-7-methyl-5-oxo-4,5-dihydropyrano[4,3-*b*] pyran - 3-carboxylate (7h)

White solid; mp 275°C; IR (KBr, $\nu_{max,}$ cm^{-1}) = 3425 and 3364 (asym. & sym. str. of -NH_2), 1674 and 1630 (C=O str.); ^{1}H NMR (400 MHz, DMSO-d_6) δ ppm : 2.10 (s,3H,CH_3), 3.34 (s,3H,$COOCH_3$), 3.58 (s,3H,OCH_3), 5.63 (s,1H, CH), 7.10 (s,2H,Ar-NH_2), 7.82-8.29 (m,6H,Ar-H), 8.47 (s,1H, Ar-H), 9.54 (s,1H,NH) ppm ; ^{13}C NMR (100 MHz DMSO-d_6) δ : 21.71 (CH_3), 35.44 (CH), 52.02 (C–$COOCH_3$), 56.09 (Ar-OCH_3), 78.66 ($\underline{C}$-$COOCH_3$), 108.02, 115.27, 120.04, 121.41, 122.95, 124.68, 126.55, 128.55, 130.65, 133.41, 134.16,

137.21, 140.52, 145.58, 146.04, 151.42, 171.71 (Ar-C), 193.66 (C=O) ppm; MS calc. for $C_{23}H_{20}N_6O_6$ $[M]^+$ 476.61, found 476.44; Anal. calc. C 57.58, H 4.23, N 17.64; Found: C 57.60, H 4.96, N 17.80 %

4-(2-(1H-tetrazol-5-ylamino) quinolin-3-yl)-2-amino-5-oxo-4,5-dihydropyrano[3,2-*c*]chromene-3-carbonitrile (8a)

White solid; mp 230°C; IR (KBr, $\nu_{max,}$ cm^{-1}) = 3394, 3310 and 3209 (asym. & sym. str. of -NH_2 and tetrazole -NH), 2191 (C≡N str.), 1666(C=O str.); ^{1}H NMR (400 MHz, DMSO-d_6) δ = 5.79 (s,1H, CH), 7.42-8.32 (m,11H, Ar-H +NH_2 + tetrazole-NH), 8.72 (s,1H,Ar-H), 9.24 (s,1H,-NH) ppm; ^{13}C NMR (100 MHz DMSO-d_6) δ: 37.68 (CH), 55.66 (C–CN), 109.68, 114.79, 117.95, 120.59, 122.89, 125.02, 127.49, 129.36, 130.91, 133.45, 135.40, 135.65, 139.25, 141.80, 145.81, 146.49, 151.43, 151.69, 154.76, 168.22 (Ar-C), 196.25 (C=O) ppm; MS Calc. for $C_{23}H_{14}N_8O_3$ $[M]^+$ 450.40, found 450.41; Anal. Calc. C 61.33, H 3.13, N 24.88; Found: C 61.15, H 3.31, N 24.75 %

Methyl 4-(2-(1H-tetrazol-5-ylamino) quinolin-3-yl)-2-amino-5-oxo-4,5-dihydropyrano[3,2-*c*]chromene-3-carboxylate (8b)

White solid; mp 248°C; IR (KBr, $\nu_{max,}$ cm^{-1}) = 3418, 3348 and 3245 (asym. & sym. str. of -NH_2 and tetrazole -NH), 1670 and 1632(C=O str.); ^{1}H NMR (400 MHz, DMSO-d_6) δ ppm; 3.43 (s,3H,$COOCH_3$), 5.46 (s,1H, CH), 7.11 (s,2H,Ar-NH_2), 7.44-8.22 (m,9H,Ar-H+tetrazole-NH), 8.36 (s,1H,Ar-H), 9.23 (s,1H,NH) ; ^{13}C NMR (100 MHz DMSO-d_6) δ: 33.12 (CH), 55.23 ($COOCH_3$), 108.13, 112.16, 118.35, 121.48, 123.42, 124.39, 125.71, 128.53, 129.33, 130.69, 131.74, 132.65, 134.78, 135.35, 136.71, 138.22, 145.13, 150.35, 155.68, 159.55, 172.46 (Ar-C), 194.48 (C=O) ppm ; MS Calc. for $C_{24}H_{17}N_7O_5$ $[M]^+$ 483.34, found 483.44; Anal. Calc. C 59.63, H 3.54, N 20.28; Found: C 61.01, H 3.85, N 20.72 %

4-(2-(1H-tetrazol-5-ylamino)-6-methoxyquinolin-3-yl)-2-amino-5-oxo-4,5-dihydropyrano[3,2-*c*]chromene-3-carbonitrile (8c)

White solid; mp 225°C; IR (KBr, $\nu_{max,}$ cm^{-1}) = 3340, 3398 and 3298 (asym. & sym. str. of -NH_2 and tetrazole -NH), 2185(C≡N str.),1670(C=O str.); ^{1}H NMR (400 MHz, DMSO-d_6) δ = 3.46 (s,3H,OCH_3), 5.69 (s,1H, CH),7.12 (s,2H,NH_2),7.47-8.76 (m,8H, Ar-H + tetrazole-NH), 8.76 (s,1H, Ar-H), 9.35 (s,1H, NH) ppm ; ^{13}C NMR (100 MHz DMSO-d_6) δ: 35.22 (CH), 57.84 (C–CN), 105.23, 114.32, 117.45, 121.54, 123.86, 124.78, 126.31, 127.85, 128.91, 130.43, 131.43, 133.48, 134.62, 135.11, 137.35, 142.66, 144.88, 152.54, 154.73, 155.45, 162.45 (Ar-C), 194.21 (C=O) ppm; MS Calc. for $C_{24}H_{16}N_8O_4$ $[M]^+$ 480.31, found 480.44; Anal. Calc. C 60.00, H 3.36, N 23.32; Found: C 59.93, H 3.99, N 23.52 %

Methyl 4-(2-(1H-tetrazol-5-ylamino)-6-methoxyquinolin-3-yl)-2-amino-5-oxo-4,5-dihydropyrano[3,2-*c*]chromene-3-carboxylate (8d)

White solid; mp 250°C; IR (KBr, $\nu_{max,}$ cm^{-1}) = 3410, 3379 and 3229 (asym. & sym. str. of -NH_2,tetrazole -NH), 1696 and 1677 (C=O str.) ;^{1}H NMR (400 MHz, DMSO-d_6) δ ppm: 3.22 (s,3H,$COOC\underline{H}_3$), 3.57 (s,3H,OCH_3), 5.36 (s,1H, CH), 7.29 (s,2H,NH_2), 7.40-8.43 (m,8H, Ar-H + tetrazole-NH), 8.69 (s,1H,Ar-H), 9.25 (s,1H, NH) ppm; ^{13}C NMR (100 MHz DMSO-d_6) δ: 33.19 (CH), 52.56 ($COOCH_3$), 56.75(OCH_3), 111.23, 113.68, 118.65, 120.19, 122.48, 124.67, 126.93, 127.80, 128.32, 130.69, 132.06, 134,29, 135.02, 137.89, 140.67, 138.24, 144.57, 149.23, 152.04, 154.08, 170.67 (Ar-C), 195.59 (C=O) ppm; MS Calc. for $C_{25}H_{19}N_7O_6$ $[M]^+$ 513.21, found 513.46; Anal. Calc. C 58.48, H 3.73, N 19.10; Found: C 58.71, H 3.91, N 19.31 %

4-(2-(1H-tetrazol-5-ylamino) quinolin-3-yl)-2-amino-7-methyl-5-oxo-4,5-dihydropyrano[4,3-*b*]pyran-3-carbonitrile (8e)

White solid; mp 256°C; IR (KBr, $\nu_{max,}$ cm^{-1}) = 3437, 3320 and 3294 (asym. & sym. str. of -NH_2,tetrazole -NH), 2206 (C≡N str.), 1674(C=O str.) ;^{1}H NMR (400 MHz, DMSO-d_6) δ ppm: 2.22 (s,3H,CH_3), 5.67 (s,1H, CH), 7.45 (s,2H,NH_2), 7.32-8.51 (m,6H, Ar-H + tetrazole

NH), 8.83 (s,1H,Ar-H), 9.34 (s,1H,NH); ^{13}C NMR (100 MHz DMSO-d_6) δ ; 22.44 (CH_2), 34.89 (CH), 58.43 (C–CN), 109.27, 113.28, 117.78, 120.91, 122.11, 124.67, 125.33, 128.80, 130.32, 131.69, 133.06, 135,29, 138.24, 144.57, 152.04, 159.67 (Ar-C), 193.59 (C=O) ppm; MS Calc. for $C_{20}H_{14}N_8O_3$ $[M]^+$ 414.55, found 414.38; Anal. Calc. C 57.97, H 3.41, N 27.04; Found: C 57.61, H 3.55, N 26.72 %

Methyl- 4-(2-(1H-tetrazol-5-ylamino)quinolin-3-yl)-2-amino-7-methyl-5-oxo-4,5-dihydropyrano[4,3-*b*]pyran-3-carboxylate (8f)

White solid; mp 284°C; IR (KBr, $\nu_{max,}$ cm^{-1}) = 3371, 3294 and 3180 (asym. & sym. str. of -NH_2,tetrazole -NH), 1697 and 1640(C=O str.); ^{1}H NMR (400 MHz, DMSO-d_6) δ ppm: 2.08 (s,3H,CH_3), 3.59 (s,3H, $COOCH_3$), 5.46 (s,1H,CH), 7.21 (s,2H,NH_2), 7.36-8.79 (m,6H,Ar-H + tetrazole-NH), 8.79 (s,1H,Ar-H) 9.35 (s,1H,NH); ^{13}C NMR (100 MHz DMSO-d_6) δ: 21.44 (CH_3), 33.72 (CH), 53.43 ($COOCH_3$), 111.27, 115.28, 120.78, 121.91, 123.11, 124.43, 125.94, 127.80, 130.45, 132.49, 133.16, 135,74, 137.24, 145.34, 148.23, 153.14, 171.67 (Ar-C), 195.12 (C=O) ppm; MS Calc. for $C_{21}H_{17}N_7O_5$ $[M]^+$ 447.23, found 447.40; Anal. Calc. C 56.38, H 3.83, N 21.91; Found: C 56.61, H 4.13, N 21.77 %

4- (2-(1H-tetrazol-5-ylamino)-6-methoxyquinolin-3-yl)-2-amino-7-methyl-5-oxo-4,5-dihydropyrano[4,3-*b*]pyran-3-carbonitrile(8g)

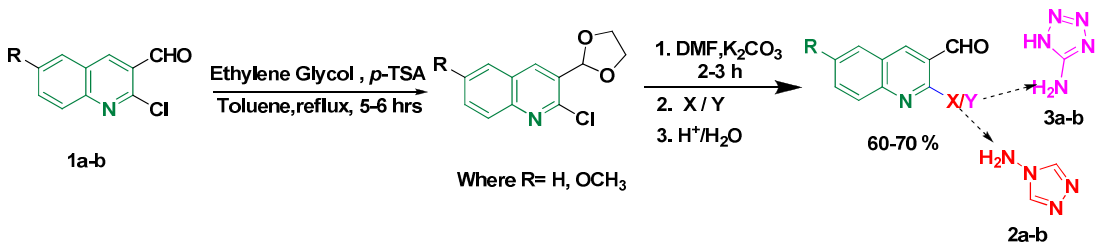
White solid; mp 262°C; IR (KBr, $\nu_{max,}$ cm^{-1}) = 3394, 3310 and 3110 (asym. & sym. str. of -NH_2,tetrazole -NH), 2220 (C≡N str.), 1666(C=O str.); ^{1}H NMR (400 MHz, DMSO-d_6) δ ppm: 2.23 (s,3H,CH_3), 3.36 (s,3H,OCH_3), 5.33(s,1H,CH), 7.23 (s,2H,NH_2), 7.48-8.30 (m,5H,Ar-H+ tetrazole-NH), 8.70 (s,1H,Ar-H), 9.31 (s,1H,NH); ^{13}C NMR (100 MHz DMSO-d_6) δ: 20.95 (CH_3), 35.11 (CH), 54.45(OCH_3), 58.66 (C-CN), 110.33, 114.28, 118.41, 121.93, 122.80, 123.32, 126.69, 127.06, 129.29, 131.02, 133.89, 134.67, 138.24, 144.57, 159.28, 172.23 (Ar-C), 195.59 (C=O) ppm; MS Calc. for $C_{21}H_{16}N_8O_4$ $[M]^+$ 444.11, found 444.40; Anal. Calc. C 56.76, H 3.63, N 25.21; Found: C 56.51, H 3.96, N 24.98 %

Methyl 4-(2-(1H-tetrazol-5-ylamino)-6-methoxyquinolin-3-yl)-2-amino-7-methyl-5-oxo-4,5-dihydropyrano [4,3-*b*] pyran-3-carboxylate (8h)

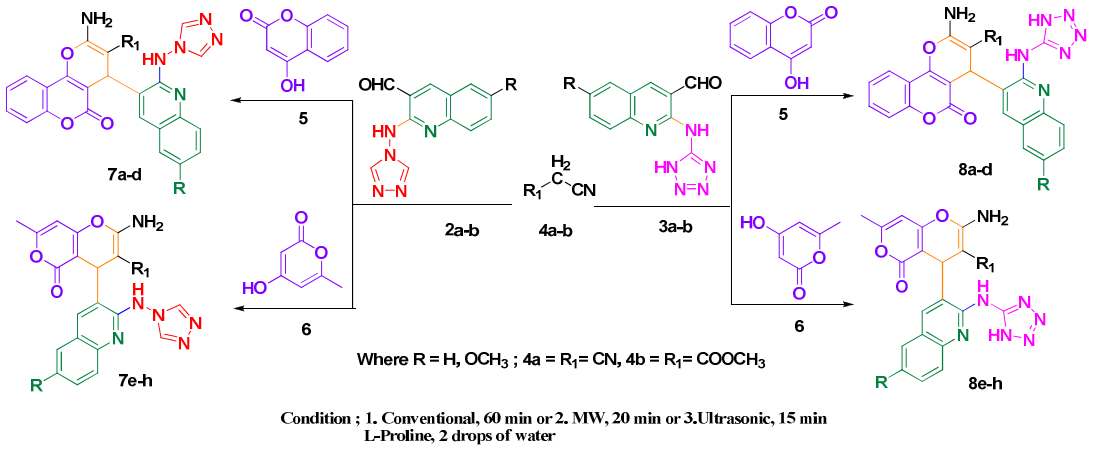
White solid; mp 229°C IR (KBr, $\nu_{max,}$ cm^{-1}) = 3487, 3355 and 3198 (asym. & sym. str. of -NH_2, tetrazole -NH), 1696 and 1656 (C=O str.); ^{1}H NMR (400 MHz, DMSO-d_6) δ ppm: 2.08 (s,3H,CH_3), 3.44 (s,3H,$COOCH_3$), 3.76 (s,3H,Ar-OCH_3), 5.64 (s,1H, CH), 7.39-8.34 (m,7H, Ar-H + NH_2+ tetrazole-NH), 8.72 (s,1H,Ar-H), 9.28 (s,1H,NH); ^{13}C NMR (100 MHz DMSO-d_6) δ: 20.87 (CH_3), 37.45 (CH), 57.79 ($COOCH_3$), 59.20 (OCH_3), 81.15 (C-$COOCH_3$), 110.89, 121.60, 123.05, 125.12, 126.06, 128.40, 128.50, 128.64, 128.75, 131.56, 134.55, 136.85, 141.43, 145.41, 154.07, 169.30 (Ar-C), 195.69 (C=O) ppm; MS Calc. for $C_{22}H_{19}N_7O_4$ $[M]^+$ 477.32, found 477.43; Anal. Calc. C 55.35, H 4.01, N 20.54; Found: C 55.11, H 4.31, N 20.66 %

RESULTS AND DISCUSSION

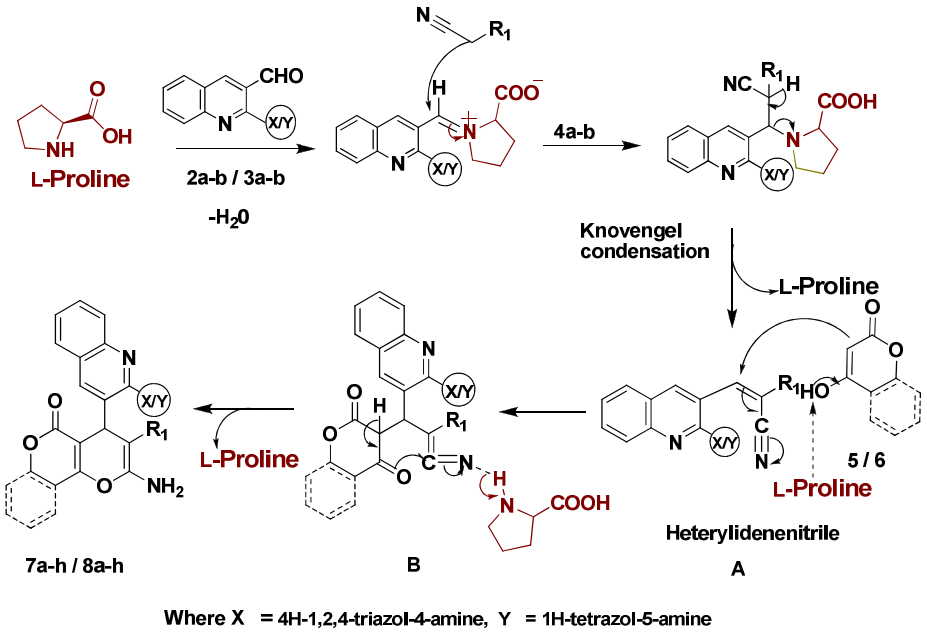
The synthetic approach adopted to obtain 6-(un)substituted-2-(amino triazole/tetrazole) quinoline-3-carbaldehydes **2a-h**/**3a-h** are shown in **Scheme 1**. The starting material 2-chloro-3-formyl quinolines **1a**–**b** were prepared by the Vilsmeier–Haack reaction from acetanilide and were conveniently converted into **2a-b**/**3a-b** by nucleophilic displacement of chloro group at C-2 in **1a**–**b** with 4-amino-1,2,4-triazole/5-amino tetrazole in the presence of anhydrous K_2CO_3 in Dimethyl formamide[xxiv]. Subsequently, the one-pot three-component cyclocondensation of **2a-h**/**3a-h**, 4-hydroxy coumarin 5/4-hydroxy-6-methyl-2H-pyran-2-one 6 and malononitrile **4a**/methyl cyanoacetate **4b** in water containing a catalytic amount of $_L$-proline afforded the targeted compounds **7a**–**h** and **8a**–**h** in good to excellent yields **Scheme 2**.



Scheme-1 Synthetic route for the intermediates 2a-b/3a-b.



Scheme-2: Synthetic route for entitled compounds 7a-h and 8a-h.



Scheme 3 Possible mechanistic pathway for the synthesis of 7a-h or 8a-h

A plausible reaction mechanism for the reaction is provided in **Scheme 3**. The heterylidenenitrile, containing an electron-poor C=C double bond is produced, from the

Knoevenagel condensation between **2a-h**/**3a-h** and malononitrile **4a**/methyl cyanoacetate **4b** followed by dehydration. Subsequent attack of cyclic 1,3-dicarbonyl compounds **5**/**6** to the intermediate A, afforded B which undergoes cyclization to the final products **7a**–**h** and **8a**–**h**.

The structures of all the synthesized compounds were confirmed by ^{1}H NMR, ^{13}C NMR, and FT-IR spectrometry. Mass spectrometry and IR spectrometry were performed for few selected compounds. In the ^{1}H NMR (DMSO-d6) spectrum of compound **7a** and **8a** singlet peak observed at δ = 5.59 and δ = 5.79 of –CH proton, and disappearance of -CHO in TA-1 and TA-2 at δ =10.45, δ =10.65 protons which conformed the cyclization of knoevenagel intermediate, as well as $–NH_2$ protons, for **7a** give singlet at δ =7.21 and for **8a**, its peak merged with aromatic proton at δ =7.42-8.32 ppm that conformed the NH_2 group is present in our targeted molecule. In addition, ^{13}C NMR spectra of compounds **7a** and **8a** a peak observed at around δ = 34.22 and δ = 37.68 ppm for methane carbon (CH) which confirmed the cyclization. In FT-IR spectra, compounds **7a-h** and **8a-h** exhibited an absorption band at around 1580–1697 cm^{-1} for (C=O) stretching. The elemental analysis data are in consonance with theoretical data. Mass spectrometry of the **8a** compounds showed molecular ion peak $[M]^{+}$ corresponding to exact mass.

Table 1 Comparison between the yields obtained in the synthesis of compounds 7a-h & 8a-h using different reaction methodologies.

Entry	R	R_1	Conventional [a] (%)	Microwave irradiation [b] (%)	Ultrasound irradiation [c] (%)	Atom economy (%)
7a	H	CN	75	85	94	96.15
7b	H	$COOCH_3$	75	87	94	96.40
7c	OCH_3	CN	75	86	95	96.38
7d	OCH_3	$COOCH_3$	73	84	95	96.61
7e	H	CN	74	85	95	95.83
7f	H	$COOCH_3$	76	83	91	96.12
7g	OCH_3	CN	73	85	94	96.11
7h	OCH_3	$COOCH_3$	75	84	93	96.36
8a	H	CN	77	88	94	96.15
8b	H	$COOCH_3$	72	85	95	96.41
8c	OCH_3	CN	75	84	93	96.39
8d	OCH_3	$COOCH_3$	76	86	94	96.61
8e	H	CN	72	86	95	95.83
8f	H	$COOCH_3$	74	87	93	96.13
8g	OCH_3	CN	74	88	94	96.10
8h	OCH_3	$COOCH_3$	71	85	92	96.36

[a] H_2O,100°C,60 min, [b] H_2O, 420W, 20 min, [c] H_2O, 50°C, 15 min.
[a,b,c] Isolated yield

The reaction between different aromatic aldehydes **2a-b**/**3a-b**, active methylene **5**/**6** and malononitrile **4a**/methyl cyanoacetate **4b** were carried out in three ways, one of them it was used a conventional system in water as solvent at 100ºC for 60 min. and the other, it was applied microwave irradiation using water at 420W for 20 min. For comparison purposes, the reaction using ultrasonic irradiation not only provided the best yields, but also successfully performed within a short reaction time 15 min at 50ºC, the lowest temperature compare to above methods. The yields obtained for compounds **7a-h** and **8a-h** were synthesized using conventional, microwave and ultrasonic irradiation, along with the percentage of atom economy, is shown in **Table 1**. % Atom economy for ultrasound assisted synthesis compounds **7a-h** and **8a-h** were found in the range of 96-97%, as only one molecules of water was released in the process[xxv].

The conditions under, the ultrasonic irradiation reaction performed which is very important from the environmental point of view. Main aim of green chemistry, to designed method so that all the raw materials after ends up the reaction in the product should be maximum and amount of waste is produced should be minimum. In this work, a reaction can achieve a high percentage yield with a high atom economy. For compounds **7a-h** to **8a-h**, the atom economy values obtained very high (>95% for all compounds), which indicates its environmental relevance and efficiency of this reaction. We also compare the use of different catalyst and time which is required for these synthesis **Table 2**. From the data, ultrasonic irradiation with $_{L}$-proline catalyzed reaction gives a better yield than other catalyst.

Table 2. Comparative data using the ultrasounds method with different catalyst for the synthesis of 7a-b and 8a-b in water.

No	Catalyst	Time(min)	Yield (%)
1	Piperidine	60	70-75
2	pyridine	50	70-75
3	TEA	40	60-70
4	NaOH	45	60-70
5	**L-Proline**	**15**	**80-85**

TEA-Triethyamine ; NaOH -Sodium Hydroxide
Isolated yield

In this study, reaction does not give any undesirable by-products. Moreover, the reaction using ultrasonic irradiation does not required toxic solvents, easy purification and the procedure can be reproduced on a larger scale without loss of efficiency. In addition, not required high temperatures which minimize the risk of accidents, such as explosions, spills and fires. Further efforts to find more uses of quinoline based triazole and tetrazole hybrids and evaluate its biological applications are currently underway in our laboratory.

CONCLUSION

In this study, we developed a mild, highly efficient and improved protocol for the preparation of 2-amino triazole/tetrazole quinoline base pyrano [3,2-c]chromene and benzopyrano[4,3-b]chromene derivatives under conventional, microwave and ultrasonic irradiation experiments. Our sonochemical method offers several advantages over existing methods, cleaner reactions, simple work-up, including improved yields, time consuming, making it a useful and environmentally attractive strategy for the synthesis of chromene derivatives.

ACKNOWLEDGMENT

The authors are thankful to the Head, Department of Chemistry, Sardar Patel University for providing 1H NMR and 13C NMR spectroscopy and research facilities. We are also thankful to the DST-Pursed, for providing mass spectroscopy facilities, Vallabh Vidyanagar, Gujarat, India. One of the authors Jayvirsinh D. Gohil is grateful to UGC, New Delhi for Basic Science Research Fellowship for Meritorious Students.

REFERENCES

i. Li, C.-J., & Chan, T.-H., Organic Reactions in Aqueous Media, Wiley, 1997.
ii. Grieco, P.A. 'Organic Synthesis in Water, Blackie Academic & Professional: London,

1998.
iii. Asghari, S.; Ramezani, S.; Mohseni, M. Chinese Chem. Lett. 2014, 25, 431-434.
iv. Nagarajan, S.; Shanmugavelan, P.; Sathishkumar, M.; Selvi, R.; Ponnuswamy, A.; Harikrishnan, H.; Shanmugaiah, V. Chinese Chem. Lett. 2014, 25, 419-422.
v. Tabatabaeian, K.; Shojaei, A.F.; Shirini, F.; Hejazi, S.Z.; Rassa, M.; Chinese Chem. Lett. 2014, 25, 308-312.
vi. Estevez, V.; Villacampa, M.; Menendez, J.C. Chemical Soc. Rev. 2010, 39, 4402-4421.
vii. Rajguru, D.; Keshwal, B.S.; Jain, S. Chinese Chem. Lett. 2013, 24, 1033-1036.
viii. Tabatabaeian, K.; Shojaei, A.F.; Shirini, F.; Hejazi, S.Z.; Rassa, M Chinese Chem. Lett. 2014, 25, 308-312.
ix. Kandhasamy, K.; Gnanasambandam, V., Multi-component reactions in water. Current Organic Chemistry **2009,** 13, 1820-11841.
x. Rajesh, S.M.; Bala, B.D. Perumal, S.; Menéndez, J.C. Green Chem. 2011, 13, 3248-3254.
xi. Li, Y.; Chen, H.; Shi, C.; Shi, D.; Ji, S. J. Comb. Chem. 2010, 12, 231-237.
xii. Liu, Y.; Liang, J.; Liu, X.H.; Fan, J.C.; Shang, Z.C. Chinese Chem. Lett. 2008, 19, 1043-1046.
xiii. Roshan, A.A.; Mamaghani, M.; Mahmoodi, N.O.; Shirini, F. Chinese Chem. Lett. 2012, 23, 399-402.
xiv. Mobinikhaledi, A.; Foroughifar, N.; Fard, M.A.B.; Moghanian, H.; Ebrahimi, S.; Kalhor, M. Synth. Commun. 2009, 39, 1166-1174.
xv. Agarwal, A. Chauhan, P.M. Tetrahedron lett. 2005, 46, 1345-1348.
xvi. Guo, S.; Yuan, Y. Chinese J.Che. 2010, 28, 811-817.
xvii. Peng, Y.; Song, G. Green Chem. 2001, 3, 302-304.
xviii. Feng, H.; Li, Y.; Van der Eycken, E.V.; Peng, Y.; Song, G. Tetrahedron Lett. 2012, 53, 1160-1162.
xix. Patel, R.V.; Park, S.W. Eur. J. Med. Chem. 2014, 71, 24-30.
xx. Mohite, P.; Bhaskar, V. Int. J. Pharm Tech Res. 2011, 3, 1557-1566.
xxi. Gohil, J. D.; Patel, H. B.; Patel, M. P.; Indian J. Adv. Chem. Sci. 2016, 4 (1), 102-113.
xxii. Fatma, S., Ankit, P., Singh, M., Singh, S. B., & Singh, J. Synth.Commun. 2014, 44, 1810–1816.
xxiii. Heravi, M.M.; Zakeri, M.; Pooremamy, S. and Oskooie, H.A. Synth.Commun. 2011, 41, 113–120.
xxiv. Afghan, A.; Baradarani, M.M.; Jouleb, J.A. Arkivoc, 2009, 2, 20-30.
xxv. Jardosh, H.H., Patel, M.P. Med. Chem. Res. 2013, 22, 905-915.

Received on October 30, 2015.