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ULTRASOUND BASED SYNTHESIS OF SUBSTITUTED 2-AMINO-4-PHENYL-4*H*-BENZO[g]CHROMENE-3-CARBONITRILE BY USING MORPHOLINE AS A CATALYST

Madhuri J. Suthar[a], Prakashbhai V. Bishnoi[ab], Jasmin H. Kumbhani[c], Keyur D. Bhatt[a]*

[a]Faculty of Science, Mehsana Urban Institute of Sciences, Department of Chemistry, Ganpat University, Kherva, Mehsana-384012, Gujarat, India
[b]Pramukh Swami Science and H.D. Patel Arts College Kadi, Mehsana, India
[c]Department of Chemistry, M B Patel Science College Anand, S P University, VV Nagar, India
**Corresponding author: Keyur Bhatt (drkdbhatt@outlook.com)*

ABSTRACT:
High-intensity ultrasonic irradiation is a more environmentally friendly method of increasing the rate of chemical processes. In terms of cost-effectiveness, high efficiency, low waste, low energy requirements, and outstanding yield, ultrasound sonochemistry is more efficient. This article describes an ultrasonic irradiation-catalyzed one-pot multicomponent reaction including morpholine as a catalyst in an aqueous solution with substituted aldehyde, malanonitrile, and -naphthol or -naphthol.

KEYWORDS: 2-amino-4-phenyl-4*H*-benzo[g]chromene-3-carbonitrile, Ultrasound irridation, Morpholine, one pot reaction.

INTRODUCTION:

Ultrasound-based synthesis has emerged as a powerful technique for the efficient and environmentally friendly synthesis of various organic compounds[iii]. More than half of the organic compounds, recognized so far, consist of heterocycles[iv]. Because of their great biological activity[v], these magnificent types of chemicals are significant[vi-vii]. It exhibits potential pharmacological properties[viii], such as anti-inflammatory, antioxidant and anticancer activities, making it highly desirable in the field of medicinal chemistry[ix-x].

Multi-component reactions (MCRs) are attractive valuable tool for synthesizing structurally various molecular objects[xi]. Developing safer and more environment friendly[xii] one-pot multicomponent reactions is an ongoing effort in academia and industry[xiii-xiv]. In MCR approach employment of numerous conversions in an one-pot offers a number of advantages such as, reduction in the number of work-up steps[xv], operational simplicity, energy efficiency, minimization of the purification procedures there by satisfying some of the goals of green and sustainable chemistry[xvi-xvii].

The last aera has seen a incredible outburst in changing chemical processes[xviii] to make them maintainable for the improvement of our environment[xix-xx]. In this situation one of the utmost accomplishments is the contribution of ultrasound in chemical reactions[xxi]. Ultrasonic irradiated methods are much valuable over the old-style current methods[xxii]. Overall, ultrasound-based synthesis utilizing morpholine as a catalyst represents a promising approach for the preparation of substituted 2-amino-4-aryl-4*H*-chromene[xxiii]. This methodology offers several advantages, including shorter reaction times, improved yields[xxiv], and reduced environmental impact, making it a valuable tool in the field of organic synthesis[xxv]

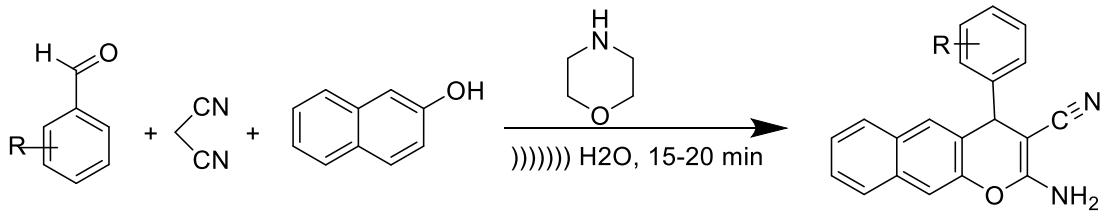
EXPERIMENTAL SECTION:

Melting points were taken on an electrothemal microscopy digital melting point device. TLC plates were used for analytical thin layer chromatography. In an idoine chamberTLC spots were clearly visible. Ethyl acetate and heaxane were taken as a mobile phase. FT IR spectra on bruker was taken in research laboratory of our college itself. 13C NMR spectra were recorded using DMSO solvent in oxygen company. A perkin-Elmer 2400 CHN analyzer confirmed the element analysis (percent C, H and N).

GENERAL PROCEDURE:

For the Synthesis of 2-amino-4-phenyl-4*H*-benzo[g]chromene-3-carbonitrile

A mixture of B-naphthol (0.6 gm, 0.01 mol), malononitrile (0.56 ml, 0.01 mol) and substituted aldehyde (1.40 gm, 0.01 mol) in water (10 ml) with catalytic amount of Morpholine (0.50 ml) was irradiated by an ultrasonic irradiation (33 kHz) at room temperature. The completion of reaction was monitored periodically by TLC using ethyl acetate : n-hexane (60:40 v/v) as mobile phase. The obtained product was filtered, washed with water, dried and recrystallized from ethanol.



Where R = -H
= 2-OH
= 3-OH
= 3-Cl
= 4-Cl
= 4-NO_2
= 4-$N(CH_3)_2$
= furfural
= Indol-3-carboxaldehyde
= 3-OCH_3

Scheme-I

ANALYTICAL DISCUSSION:

Synthesis of 2-amino-4-phenyl-4*H*-benzo[g]chromene-3-carbonitrile (4a)

IR(ATR): 3224, 2950, 2190, 2140, 1250 cm-1 . 1H NMR(400 MHz,DMSO-d6, δ, ppm): δ = 4.73 (s, 1H, CH), 6.72 (s, 2H, NH_2), 7.20-7.86(m, 11H, Ar-H). ^{13}C NMR (100MHz, DMSO-

d6, δ, ppm): δ = 28.8, 58.2, 108.6, 117.4, 123.6, 125.6, 125.8, 127.3, 128.3, 132.6, 140.4, 155.3, 177.2. MS (m/z): 298.35 M+. m.p.: 200-215°C; Yield: 88 %; Anal. Calcd. For $C_{20}H_{14}N_2O$ (296.7): C, 80.52; H, 4.73; N, 9.39; O, 5.36%. Found C, 78.43; H, 4.36; N, 9.30%.

Synthesis of 2-amino-4-(2-hydroxyphenyl)-4*H*-benzo[g]chromene-3-carbonitrile (4b)

IR(ATR): 3350, 3224, 2950, 2190, 2140, 1250 cm^{-1} . 1H NMR(400 MHz,DMSO-d6, δ, ppm): δ = 4.75 (s, 1H, CH), 6.83 (s, 2H, NH_2), 6.78-7.86(m, 10H, Ar-H), 9.67(s, 1H, OH). ^{13}C NMR (100MHz, DMSO-d6, δ, ppm): δ = 23.5, 58.5, 107.6, 115.4, 116.6, 119.6, 123.8, 125.3, 128.6, 132.6, 155.2, 177.5. MS (m/z): 314.11 M^+. m.p.: 150-160°C; Yield: 87%; Anal. Calcd. For $C_{20}H_{14}N_2O_2$(312.7): C, 76.42; H, 4.49; N, 8.91; O, 10.18%. Found C, 74.12; H, 4.36; N, 7.92; O, 9.14%.

Synthesis of 2-amino-4-(3-hydroxyphenyl)-4*H*-benzo[g]chromene-3-carbonitrile (4c)

IR(ATR): 3355, 3324, 2955, 2190, 2140, 1250 cm^{-1}. 1H NMR(400 MHz,DMSO-d6, δ, ppm): δ = 4.73 (s, 1H, CH), 6.80 (s, 2H, NH_2), 6.98-8.96(m, 10H, Ar-H), 9.30(s, 1H, OH). ^{13}C NMR (100MHz, DMSO-d6, δ, ppm): δ = 30.1, 59.2, 113.2, 117.4, 116.6, 123, 126.8, 127.2, 128.8, 129.6, 130, 132.6, 155.3, 177.5. MS (m/z): 314.11 M^+. m.p.: 155-165°C; Yield: 85%; Anal. Calcd. For $C_{20}H_{14}N_2O_2$(312.10): C, 76.42; H, 4.49; N, 8.91; O, 10.18%. Found C, 75.12; H, 4.36; N, 8.86; O, 10%.

Synthesis of 2-amino-4-(3-chlorophenyl)-4*H*-benzo[g]chromene-3-carbonitrile (4d)

IR(ATR): 3351, 3226, 2850, 2220, 2140, 1255, 550 cm^{-1} . 1H NMR(400 MHz,DMSO-d6, δ, ppm): δ = 4.73 (s, 1H, CH), 6.80 (s, 2H, NH_2), 7.09-7.87(m, 10H, Ar-H). ^{13}C NMR (100MHz, DMSO-d6, δ, ppm): δ = 29.2, 59.3, 108.2, 117.3, 123, 125.8, 126.2, 127.8, 128.6, 129.2, 130, 132.6, 134.2, 141.2, 155.2, 177.3. MS (m/z): 332.79 M^+. m.p: 200-265°C; Yield: 80-82%; Anal. Calcd. For $C_{20}H_{13}ClN_2O$ (330.70): C, 72.18; H, 3.94; N, 8.42; O, 4.81; Cl, 10.65%. Found C, 70.12; H, 3.80; N, 8.40; O, 10%.

Synthesis of 2-amino-4-(4-chlorophenyl)-4*H*-benzo[g]chromene-3-carbonitrile (4e)

IR(ATR): 3355, 3206, 2851, 2220, 2150, 1245, 556 cm^{-1} . 1H NMR(400 MHz,DMSO-d6, δ, ppm): δ = 4.72 (s, 1H, CH), 6.82 (s, 2H, NH_2), 7.07-7.89(m, 10H, Ar-H). ^{13}C NMR (100MHz, DMSO-d6, δ, ppm): δ = 29.7, 59.3, 108.3, 116.3, 123.5, 125.7, 126.3, 127.9, 128.5, 129.2, 130.5, 132.5, 133.2, 145.2, 156.2, 177.5. MS (m/z): 332.79 M^+. m.p: 220-265°C; Yield: 83-85%; Anal. Calcd. For $C_{20}H_{13}ClN_2O$ (331.80): C, 72.18; H, 3.94; N, 8.42; O, 4.81; Cl, 10.65%. Found C, 70.10; H, 3.70; N, 8.40; O, 9.60%.

Synthesis of 2-amino-4-(4-nitrophenyl)-4*H*-benzo[g]chromene-3-carbonitrile (4f)

IR(ATR): 3350, 3206, 2851, 2100, 1245, 1550 cm^{-1}. 1H NMR(400 MHz,DMSO-d6, δ, ppm): δ = 4.72 (s, 1H, CH), 6.80 (s, 2H, NH_2), 7.21-8.17(m, 10H, Ar-H). ^{13}C NMR (100MHz, DMSO-d6, δ, ppm): δ = 29.9, 59.3, 108.6, 117.3, 123.6, 125.7, 126.8, 126.9, 127.8, 128.6, 129.3, 132.5, 132.9, 155.5, 177.6. MS (m/z): 343.34 M^+. m.p: 220-265°C; Yield: 83-85%; Anal. Calcd. For $C_{20}H_{13}N_3O_3$ (341.50): C, 69.97; H, 3.82; N, 12.24; O, 13.98%. Found C, 68.10; H, 3.70; N, 11.42; O, 12.50%.

Synthesis of 2-amino-4-(4-dimethylamino)phenyl-4*H*-benzo[g]chromene-3-carbonitrile (4g)

IR(ATR): 3440, 3250, 2198, 1680, 1516 cm^{-1}. 1H NMR(400 MHz,DMSO-d6, δ, ppm): δ = 3.01 (s,6H,-CH3,N,N-dimethyl grop), 4.72 (s, 1H, CH), 6.80 (s, 2H, NH_2), 6.68-7.87 (m, 10H, Ar-H). ^{13}C NMR (100MHz, DMSO-d6, δ, ppm): δ = 29.7, 41.2, 59.3, 108.5, 116.3, 123.5, 125.6, 126.7, 126.8, 127.6, 128.8, 129.4, 132.6, 132.8, 155.3, 177.5. MS (m/z): 341.41 M^+. m.p: 180°C; Yield: 80-85%; Anal. Calcd. For $C_{20}H_{19}N_3O$ (340.38): C, 77.40; H, 5.61; N, 12.24; O, 4.59%. Found C, 68.10; H, 3.70; N, 11.42; O, 4.50%.

Synthesis of 2-amino-4-(furan-2-yl)-4*H*-benzo[g]chromene-3-carbonitrile (4h)

IR(ATR): 3440, 3250, 2851, 2198, 1500, cm^{-1}. 1H NMR(400 MHz,DMSO-d6, δ, ppm): δ = 3.04 (s,6H,-CH3,N,N-dimethyl grop), 4.70 (s, 1H, CH), 6.79 (s, 2H, NH_2), 6.68-7.87(m, 10H,

Ar-H). ^{13}C NMR (100MHz, DMSO-d6, δ, ppm): δ = 29.7, 41.2, 59.2, 108.8, 113.3, 117.3, 123.5, 125.6, 126.8, 127.9, 128.6, 129.3, 132.5, 132.9, 148.5, 155.3, 177.3. MS (m/z): 288.31 M^+. m.p: 180-190°C; Yield: 88%; Anal. Calcd. For $C_{18}H_{12}N_2O_2$(287.30): C, 74.99; H, 4.20; N, 9.72; O, 11.10%. Found C, 73.95; H, 4.10; N, 8.70; O, 10.10%.

Synthesis of 2-amino-4-(1*H*-indol-3-yl)-4*H*-benzo[g]chromene-3-carbonitrile (4i)

IR(ATR): 3450, 3150, 2750, 2195, 1550, cm^{-1}. ^{1}H NMR(400 MHz,DMSO-d6, δ, ppm): δ = 4.73 (s, 1H, CH), 6.80 (s, 2H, NH_2), 10.78 (s, 1H, NH) 6.78-7.95(m, 11H, Ar-H). ^{13}C NMR (100MHz, DMSO-d6, δ, ppm): δ = 29.8, 59.2, 108.8, 112.3, 118.3, 124.5, 125.6, 126.7, 127.8, 128.5, 128.3, 132.5, 132.8, 148.4, 155.5, 176.3. MS (m/z): 337.38 M^+. m.p: 170-180°C; Yield: 85%; Anal. Calcd. For $C_{22}H_{15}N_3O$ (335.30): C, 78.32; H, 4.48; N, 12.46; O, 4.74%. Found C, 77.95; H, 4.45; N, 10.70; O, 4.73%.

Synthesis of 2-amino-4-(3-methoxyphenyl)-4H-benzo[g]chromene-3-carbonitrile (4j)

IR(ATR): 3440, 3250, 2851, 2198, 1500, cm^{-1}. 1H NMR(400 MHz,DMSO-d6, δ, ppm): δ = 3.04 (s,6H,-CH3,N,N-dimethyl grop), 4.70 (s, 1H, CH), 6.79 (s, 2H, NH_2), 6.68-7.87(m, 10H, Ar-H). ^{13}C NMR (100MHz, DMSO-d6, δ, ppm): δ = 29.7, 41.2, 59.2, 108.8, 113.3, 117.3, 123.5, 125.6, 126.8, 127.9, 128.6, 129.3, 132.5, 132.9, 148.5, 155.3, 177.3. MS (m/z): 288.31 M^+. m.p: 180-190°C; Yield: 88%; Anal. Calcd. For $C_{18}H_{12}N_2O_2$(287.30): C, 74.99; H, 4.20; N, 9.72; O, 11.10%. Found C, 73.95; H, 4.10; N, 8.70; O, 10.10%.

RESULT AND DISCUSSION:

Comparison of solvents:

2-amino-4-aryl-4*H*-chromene and its derivatives were synthesized using β-naphthol, Malononitrile and different aldehyde with 1:1:1 in this reaction. stocheometric ratio of 5 mmol morpholine and water was used as a green catalyst. The reaction was carried out in ultrasound irradiation. A reaction was designed as a model in direction to find out the optimum solvent in Table no.1.

Table 1. Comparison of solvents for the reaction of β-naphthol, malononitrile and 3- hydroxy benzaldehyde to synthesize 2-amino-4-(3-hydroxyphenyl)-4H-benzo[g]chromene-3-carbonitrile

No.	Solvent	Time (min)	Yield %
1	Solvent free	12	None
2	Water	13	90
3	Methanol	12	83
4	Ethanol	14	85
5	Acetone	15	78
6	n-hexane	14	70
7	Toluene	20	65

Comparison of ultrasonic irradiation and conventional methods:

A potent technique that is being employed to speed up organic processes is ultrasonic assisted organic synthesis as a green synthetic method.. Ultrasonic irradiation was found to be greater in terms of higher yield, shorter reaction time and mild reaction conditions in compared to the conventional heating. we have compared the outcome of ultrasound to conventional heating for better yields and reaction rates for 2-amino-4-aryl-4*H*-chromene derivatives.

Table 2. Synthesis of 2-amino-4-Phenyl-4*H*-chromene 2 derivatives under sonication and conventional conditions.

No	Compound	-R	Ultrasonic irradiation		Conventional method	
			Time (min)	Yield %	Time (min)	Yield (%)
1	4a	-H	12	85	120	50
2	4b	2-OH	10	90	100	47
3	4c	3-OH	10	92	110	45
4	4d	3-Cl	15	84	90	52
5	4e	4-Cl	12	86	120	55
6	4f	4-NO_2	15	82	150	45
7	4g	4-$N(CH_3)_2$	16	84	130	52
8	4h	furfural	14	80	170	42
9	4i	Indole-3-Carboxaldehyde	14	84	160	45
10	4j	3-OCH_3	13	82	90	50

Table 3. Effect of amount of catalyst on the synthesized product 4c

No	Amount of Morpholine (equiv %)	Time (min)	Yield %
1	Trace	10	Trace
2	5	12	90
3	10	14	85
4	15	15	80
5	20	13	84
6	25	14	82
7	30	15	83

Table 4. Effect of time on the synthesis of the product 4c

No	Solvent	Time (min)	Yield %
1	Water	15	90
2	Water	16	88
3	Water	17	85
4	Water	16	84
5	Water	20	86

Table 5. Effect of temperature on the synthesis of the product 4c

No	Solvent	Temperature (^{0}c)	Time (min)	Yield %
1	Water	30	15	90
2	Water	40	16	88
3	Water	50	17	85
4	Water	60	17	84
5	Water	70	20	86

CONCLUSION:

In this research article we have compared ultrasonic irradiation with conventional method by doing optimization studies. We have endeavoured to emphasize the synthesis of heterocyclic compounds utilizing ultrasonic irradiation. The ultrasonic irradiation has been applied to synthesize the 2-amino 4-aryl-4*H*-chromene derivatives since it dramatically reduces reaction times from days or hours to minutes. Also this technique provides lower cost, excellent yields, greater purity and simple workup as compared to the higher cost, less yields, longer reaction times in the conventional method.

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