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Research Article

A GREEN APPROACH FOR THE SYNTHESIS OF 2-AMINO-4*H*-BENZO [*B*] PYRAN DERIVATIVES USING DBU AS AN EFFICIENT CATALYST

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ABSTRACT

A green, mild, most efficient, eco-friendly and simple procedure has been developed for the synthesis of tetrahydro benzo [*b*] pyran derivatives from one-pot three component cyclocondensation reactions of various aromatic aldehydes, malononitrile and dimedone in aquous ethanol at room temperature by using 1,8-diazabicyclo [*5.4.0*] undec-7-ene (DBU) as an efficient catalyst.

Keywords: Dimedone, Aromatic Aldehydes, Malonitrile, DBU. MCRs.

INTRODUCTION

Multicomponent reactions (MCRs) have been develop in recent years in form of powerful and useful tools in synthetic organic chemistry and have attracted increasing attention because of complex molecules and drugs can be prepared from cheap and easily available starting materials[1-6]. In addition, the implementation of several transformations in a single manipulation is highly compatible with the goals of sustainable and "Green chemistry" [7-8], with the increasing public concern over environmental degradation, the use of environmentally benign solvents like water become most essential. Multicomponent reactions have become very popular in the discovery of biologically active novel compounds because of simple experimentation, atom economy and high yield of the products[9]. 4*H*-Pyrans and 4*H*-pyran-annulated heterocyclic scaffolds have broad spectrum of significant biological activities that include anticancer[10], cytotoxic[11], anti-HIV[6–8], anti-inflammatory[12], antimalarial[13-14], antimicrobial[15], ant hyperglycemic, and antidyslipidemic[16], along with antineuro degenerative disorders like Alzheimer's, Parkinson disease, Huntington's disease[17] and functionalized 4*H*-pyran derivatives have played increasing roles in synthetic approaches to promising compounds in the field of medicinal[18-19], agrochemical[20], cosmetics, and pigment industries[21]. It is worthwhile to mention that currently a number of drug molecules bearing the 4*H*-pyran moiety are in use in the treatment of various infirmity, such as hypertension, asthma, ischemia, and urinary incontinence[22-26].

Literature survey reveals that various catalysts reported for the synthesis of tetra hydro benzo [*b*] pyrans that include potassium sodium tartarate[27], TiO_2[28], ionic liquid[29], lactose[30], (*S*)-proline[31], *L*-proline[32], starch[33], hexadecyl dimethyl benzyl ammonium bromide[34], MgO [35-36] tetrabutyl ammonium bromide[37], lithium bromide[38], supported ionic liquid catalyst (SILC), per-6-amino-β-cyclodextrin, and phenylboronic acid. Although these protocols reported by others find certain merits of their own, still they suffer from a number of demerits such as long reaction time, harsh reaction conditions, heating time, expensive catalyst/reagents, and high catalytic loading.

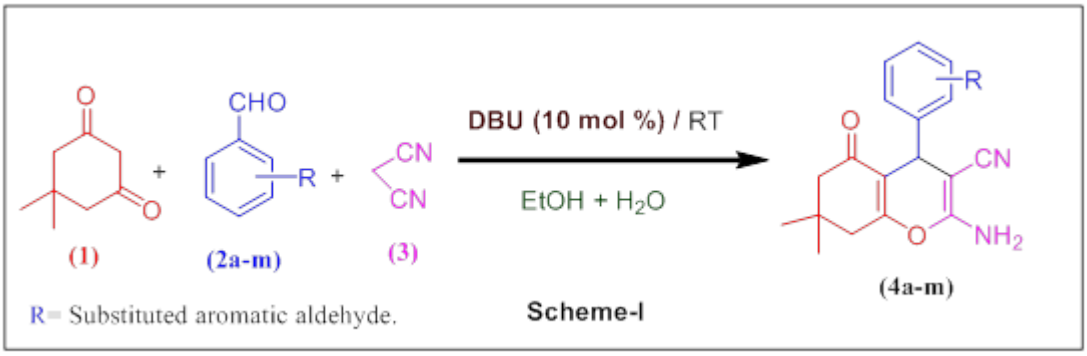
However, catalyst used 1,8-diazabicyclo [*5.4.0*] undec-7-ene (DBU) acts as homogeneous catalyst and it perform much organic transformation under mild condition. Hence, there is a vital need to develop a glowingly organized, simple and yield elevating protocol for the synthesis of tetrahydrobenzo [*b*] pyrans. As a part of our continual efforts toward the development of efficient, economical and new methods using green catalysts and solvents, we investigated the activity of the readily available, renewable, recyclable and environmentally benign DBU as catalyst for the synthesis of tetrahydrobenzo [*b*] pyrans at room temperature.

MATERIAL AND METHODS

General procedure for the synthesis of 2-amino-3-cyano-7, 7-dimethyl-oxo-5, 6,7,8-tetrahydro-4*H*- benzopyran (4a-4m)

A mixture of 5, 5-dimethyl-1,3-cyclohexanedione (Dimedone) **(1)** (1.0 mmol), different substituted aromatic aldehydes **(2a-m)** (1.0 mmol), Malononitrile **(3)**, (1.0 mmol) and 1,8-diazabicyclo[*5.4.0*] undec-7-ene (**DBU**) was stirred on magnetic stirrer in aqueous ethanol for four hours. Progress of reaction was monitored by TLC. Solid precipitate formed was filtered, washed with water and recrystallized from ethanol to give **(4a-m).** These synthesized products **(4a-m)** were completely characterized from IR, ^{1}H-NMR, Mass and ^{13}C-NMR spectroscopic technique and also elemental analysis.

RESULT AND DISCUSSION



In present investigation, we have reported the synthesis of tetrahydro benzo [*b*] pyran derivatives (**4a-m**) via Knoevenagel-Michael condensation pathways. Initially, a model reaction was examined using Dimedone **(1)**, Aromatic benzaldehyde **(2a-m)**, and Malononitrile **(3)** were at room temperature stirred on magnetic stirrer in aqueous ethanol using 1,8-diazabicyclo[*5.4.0*]undec-7-ene (DBU). After four hours, tetrahydro benzo [*b*] pyran product **(4a-m)** was obtained. (**Scheme I**).

Optimization of catalyst can be done by using variable quantity of DBU. It was observed that the excellent yield was obtained by using 10 mol% of DBU**.** Also, we checked the effect of different solvent on yield and reaction time it was found that aqueous ethanol in (1:1) stichometry is appropriate solvent. After investigating the effect of different parameters on the model reaction, we synthesize efficient route for tetrahydro benzo [*b*] pyran derivatives **(4a-m)**, using dimedone (**1**), different substituted aldehydes **(2a-m)**, and malononitrile (**3**) were stirred by using (10 mol%) DBU as mild base catalyst in aqueous ethanol at room temperature (**Scheme I**), and the result are summarized in Table **3**. The desired products (4a-m) were obtained to excellent yields. These synthesized products **(4a-m)** were completely characterized from IR, ^{1}H-NMR, Mass and ^{13}C-NMR spectroscopic technique and also elemental analysis. We proposed tentative plausible mechanism for the formation of tetrahydro benzo [*b*] pyran derivatives **(4a-m)** in the presence of 1,8-diazabicyclo [*5.4.0*] undec-7-ene. The overall, mechanism takes place according to Knoevenagels condensation followed by Michael addition reaction.

Table 1: Optimization of the reaction conditions using different solvents [a]

Entry No	Solvent	Reaction Time (H)	Yield (%)[b]
1	Toluene	7.0	35
2	DCM	8.0	40
3	THF	9.0	50
4	DMF	7.0	45
5	Water	5.5	72
6	Ethanol	6.0	70
7	Ethanol-Water (1:1)	4.0	87

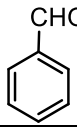
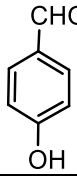
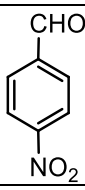
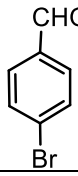
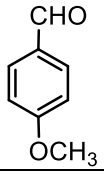
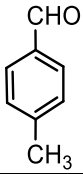
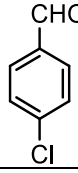
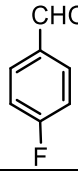
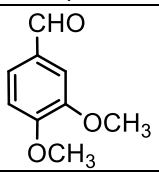
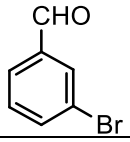
[a] ***Reaction conditions:*** dimedone (**1**) (1.0 mmol), substituted aromatic aldehydes (**2**) (1.0 mmol), and malononitrile (**3**) (1.0 mmol) in aqueous ethanol using DBU as catalyst stirred at RT.[b] Isolated yields.

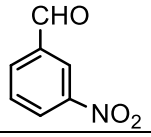
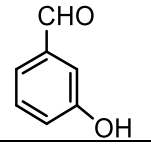
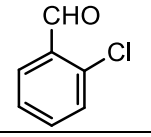
Table 2: Optimization Study for the amount of 1,8-diazabicyclo [*5.4.0*] undec-7-ene DBU. [a]

Entry No	Catalyst (mole %)	Reaction Time (Hours)	Yield (%)[b]
1	01	4.0	42
2	02	4.0	50
3	05	4.0	60
4	08	4.0	71
5	10	4.0	87
6	15	4.0	85
7	20	4.0	85

[a] ***Reaction conditions:*** dimedone (**1**) (1.0 mmol), substituted aromatic aldehydes (**2**) (1.0 mmol), and malononitrile (**3**) (1.0 mmol) in aqueous ethanol using DBU stirred at Room Temperature. [b] Isolated yields.

Table 3: Three component reaction of dimedone (1) (1.0 mmol), substituted aromatic aldehydes (2) (1.0 mmol), and malononitrile (3) (1.0 mmol) for the synthesis of (4a-4m) [a]

Entry	Aldehydes	Time (Hrs)	Yield (%)[b]	M.P. (^{0}C)	
				Found	Lit.[Ref]
4a		3.5	78	227-229	228-230
4b		2.5	87	198-200	201-203
4c		3.0	80	234-236	236-238
4d		3.5	85	202-204	201-203
4e		4.0	84	199-201	198-200
4f		3.5	85	211-213	212-214
4g		4.0	80	198-200	201-203
4h		4.5	78	197-199	200-201
4i		3.0	84	209-211	211-213
4j		4.0	74	228-230	229-231

4k		4.5	76	203-205	201-203
4l		3.0	74	211-213	213-215
4m		4.0	68	220-222	222-224

[a] *Reaction conditions:* dimedone (1) (1.0 mmol), substituted aromatic aldehydes (2) (1.0 mmol) and malononitrile (3) (1.0 mmol) in aqueous ethanol and [b] Isolated yields

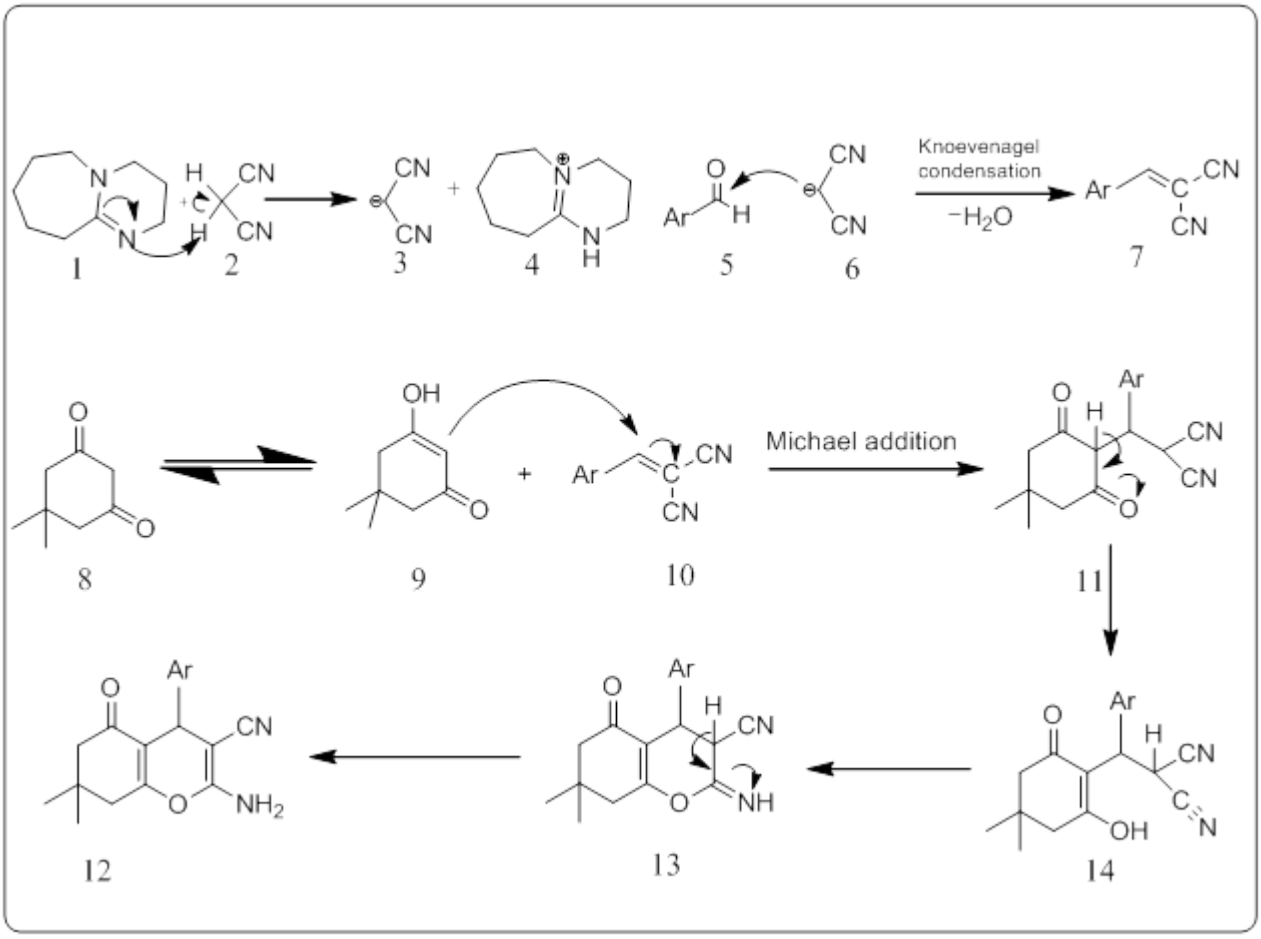


Figure 1: Plausible Tentative mechanism

Experiment

Melting points of synthesized compounds were determined by open capillary tubes and uncorrected. Purity of all the products was routinely checked by thin layer chromatography (TLC) on pre-coated sheets of silica gel-C plates of 0.25 mm thickness using UV Chamber for detection. Perkin-Elmer FT-IR spectra were recorded in KBr pallets on infrared spectrophotometer. Brukner advance spectrophotometer 300 or 400 MHz was used to record ^{1}H and^{13}. C-NMR spectra in DMSO-d_6 using TMS as internal standard. Mass spectra were recorded on FT-VC-7070 H Mass spectrometer using the EI technique at 70 eV.

Spectral Analysis

2-Amino-3-Cyano-5,6,7,8-tetrahydro-7,7-dimethyl-4-phenyl-5-oxo-4*H* benzopyran (4a): IR (KBr / cm^{-1}) 3390, 3220 (-NH_2), 2205 (-CN), 1692 (C=O); ^{1}H NMR (300MHz, DMSO-d_6 / ppm) δ 0.98 -1.06 (2s, 6H, -2CH_3), 2.05 - 2.14 & 2.20-2.26 (2d, 2H, -CH_2), 2.60 (s, 2H, -CH_2), 4.01 (s, 1H, -CH), 6.12 (bs,2H,-NH_2) 7.04-7.92 (m, 5 H, Ar-H) ; EI-MS (m/z: RA %): 295 (M^{+}, 100%). ^{13}C NMR (300 MHz, DMSO–d_6/ ppm) δ: 194 (C=O), 162, 157, 142, 129, 124, 120(-CN),114, 60, 52, 40, 36,30, 28, 24. Elemental analysis**:** Calculated data for $C_{18}H_{18}N_2O_2$; C, 73. 54; N, 09.91. Found: C, 73.52; N, 09.89.

2-Amino-3-Cyano-5,6,7,8-tetrahydro-7,7-dimethyl-4-(4'-hydroxyphenyl)-5-oxo-4*H* benzopyran (4b): IR (KBr / cm^{-1}) 3460 (-OH), 3370, 3230 (-NH_2), 2199 (-CN), 1666 (C=O); ^{1}H NMR (300MHz, DMSO-d_6 / ppm) δ 0.97 -1.09 (2s, 6H, -2CH_3), 2.12 & 2.30 (2d, 2H, -CH_2), 2.50 (s, 2H, -CH_2), 4.22 (s, 1H, -CH), 5.02 (s, 1H, Ar-OH), 5.90 (bs, 2H,-NH_2) 6.60- 7.12 (m, 4 H, Ar-H); EI-MS (m/z: RA %): 311 ($M^{+\cdot}$ 100%). ^{13}C NMR (300 MHz, DMSO–d_6/ ppm) δ: 196 (C=O), 164, 160, 136, 126, 122, 119(-CN), 116, 59, 55, 40, 36, 25,22. Elemental analysis**:** Calculated data for $C_{18}H_{18}N_2O_3$; C, 65.85; N, 08.55. Found: C, 65.84; N, 08.53.

2-Amino-3-Cyano-5,6,7,8-tetrahydro-7,7-dimethyl-4-(4'-nitrophenyl)-5-oxo-4*H*- benzopyran (4c): IR (KBr / cm^{-1}) 3420, 3325 (-NH_2), 2198 (-CN), 1680 (C=O); ^{1}H NMR (300MHz, DMSO-d_6 / ppm) δ 0.96 -1.06 (2s, 6H, -2CH_3), 2.18 & 2.30 (2d, 2H, -CH_2), 2.70 (s, 2H, -CH_2), 4.45 (s, 1H, -CH), 7.18 (bs, 2H,-NH_2) 7.42- 8. 25 (m, 4 H, Ar-H); EI-MS (m/z: RA %): 339 ($M^{+\cdot}$ 100%). ^{13}C NMR (300 MHz, DMSO–d_6/ ppm) δ: 192 (C=O), 163, 160, 150, 140,129, 121(-CN), 116, 60, 55, 45, 40, 32, 29, 24. Elemental analysis**:** Calculated data for $C_{18}H_{17}N_3O_4$; C, 63.72; N, 08.24. Found: C, 63.69; N, 08.22.

2-Amino-3-Cyano-5,6,7,8-tetrahydro-7,7-dimethyl-4-(4'-bromophenyl)-5-oxo-4*H* benzopyran (4d): IR (KBr / cm^{-1}) 3385, 3290 (-NH_2), 2205 (-CN), 1686 (C=O); ^{1}H NMR (300MHz, DMSO-d_6 / ppm) δ 0.93 -1.04 (2s, 6H, -2CH_3), 2.12 & 2.25 (2d, 2H, -CH_2), 2.62 (s, 2H, -CH_2), 4.20 (s, 1H, -CH), 7.10 (bs, 2H,-NH_2) 7.15 & 7.40 (m, 4 H, Ar-H) ; EI-MS (m/z: RA %): 373 (M+2, 98%), 371($M^{+\cdot}$ 100%). ^{13}C NMR (300 MHz, DMSO–d_6/ ppm) δ: 194 (C=O), 162, 159, 145, 130,122(-CN), 128, 60, 55, 40, 32, 29, 24. Elemental analysis**:** Calculated data for $C_{18}H_{17}BrN_2O_2$; C, 65. 86; N, 08.53. Found: C, 65.82; N, 08.51

2-Amino-3-Cyano-5,6,7,8-tetrahydro-7,7-dimethyl-4-(4'-methoxyphenyl)-5-oxo-4H- benzopyran (4e): IR (KBr / cm^{-1}) 3368, 3310 (-NH_2), 2196 (-CN), 1690 (C=O); ^{1}H NMR (300MHz, DMSO-d_6 / ppm) δ 0.96 -1.08 (2s, 6H, -2CH_3), 2.06-2.16 & 2.26-2.38 (2d, 2H, -CH_2), 2.50 (s, 2H, -CH_2), 3.65 (s,3H,-Ar–OCH_3), 4.16 (s, 1H, -CH), 6.98 (bs, 2H,-NH_2) 6.80-6.89 & 7.06-7.10 (m, 4 H, Ar-H) ; EI-MS (m/z: RA %): 323 ($M^{+\cdot}$, 100%). ^{13}C NMR (300 MHz, DMSO–d_6/ ppm) δ: 196(C=O), 164, 160, 158, 130, 120(-CN), 56, 52, 40, 32, 29, 25. Elemental analysis**:** Calculated data for $C_{19}H_{20}N_2O_3$; C, 70. 36; N, 08.63. Found: C, 70.33; N, 08.61.

2-Amino-3-Cyano-5,6,7,8-tetrahydro-7,7-dimethyl-4-(4'-methylphenyl)-5-oxo-4H- benzopyran(4f): IR (KBr / cm^{-1}) 3420, 3320 (-NH_2), 2194 (-CN), 1686 (C=O); ^{1}H NMR (300MHz, DMSO-d_6 / ppm) δ 0.94 -1.12 (2s, 6H, -2CH_3), 2.16 & 2.26 (2d, 2H, -CH_2), 2.30 (s, 3H,-CH_3), 2.62 (s, 2H, -CH_2), 4.21 (s, 1H, -CH), 6.98 (bs, 2H,-NH_2) 7.04- 7.16 (m, 4 H, Ar-H); EI-MS (m/z: RA %): 308 ($M^{+\cdot}$ 100%). ^{13}C NMR (300 MHz, DMSO–d_6/ ppm) δ: 194(C=O), 163, 159, 146, 139,130, 119 (-CN), 110, 54, 45, 40, 35, 29, 26, 20. Elemental analysis**:** Calculated data for $C_{19}H_{20}N_2O_2$; C, 74.05; N, 09.10. Found: C, 74.03; N, 09.08.

2-Amino-3-Cyano-5,6,7,8-tetrahydro-7,7-dimethyl-4-(4'-chlorophenyl)-5-oxo-4H- benzopyran (4g): IR (KBr / cm^{-1}) 3465, 3340 (-NH_2), 2198 (-CN), 1690 (C=O); ^{1}H NMR (300MHz, DMSO-d_6 / ppm) δ 0.99 -1.08 (2s, 6H, -2CH_3), 2.12 & 2.30 (2d, 2H, -CH_2), 2.50 (s, 2H, -CH_2), 4.80 (s, 1H, -CH), 7.09 (bs, 2H,-NH_2) 7.20 - 7.40 (m, 4 H, Ar-H) ; EI-MS (m/z: RA %): 328 ($M^{+\cdot}$ 100%). ^{13}C NMR (300 MHz, DMSO–d_6/ ppm) δ: 193(C=O), 165, 158, 145, 135, 126, 120(-CN), 114, 58, 52, 39, 32, 27. Elemental analysis**:** Calculated data for $C_{18}H_{17}ClN_2O_2$; C, 65.84; N, 08.53. Found: C, 65.82; N, 08.50.

2-Amino-3-Cyano-5,6,7,8-tetrahydro-7,7-dimethyl-4-(4'-fluorophenyl)-5-oxo-4H- benzopyran(4h): IR (KBr / cm^{-1}) 3348, 3318 (-NH_2), 2196 (-CN), 1690 (C=O); ^{1}H NMR (300MHz, DMSO-d_6 / ppm) δ 0.92 -1.06 (2s, 6H, -2CH_3), 2.14 & 2.28 (2d, 2H, -CH_2), 2.42 (s, 2H, -CH_2), 4.26 (s, 1H, -CH), 7.01 (bs, 2H,-NH_2), 7.10-7.19 (d, 2H, Ar-H), δ 7.20-7. 30.(d, 2H, Ar-H); EI-MS (m/z: RA %): 312 ($M^{+\cdot}$ 100%). ^{13}C NMR (300 MHz, DMSO–d_6/ ppm) δ: 194(C=O), 162, 158, 146,130,120(-CN), 118,110, 59, 52, 46, 40, 28, 26. Elemental analysis**:** Calculated data for $C_{18}H_{17}FN_2O_2$; C, 69.22; N, 08.96. Found: C, 69.20; N, 08.94.

2-Amino-3-Cyano-5,6,7,8-tetrahydro-7,7-dimethyl-4-(3,4'-dimethoxyphenyl)-5-oxo-4H- benzopyran (4i): IR (KBr / cm^{-1}) 3410, 3330 (-NH_2), 2198 (-CN), 1686 (C=O); ^{1}H NMR (300MHz, DMSO-d_6 / ppm) δ 0.94 -1.06 (2s, 6H, -2CH_3), 2.16 & 2.29 (2d, 2H, -CH_2), 2.60 (s, 2H, -CH_2), 3.85 (2s, 6H,(-2-OCH_3), 4.21 (s, 1H, -CH), 6.96 (bs, 2H,-NH_2) 6.60-6.72 (dd, 1H, Ar-H), 6.85-6.90(d, 1H, Ar-H), 7.10-7.40(d, 1H, Ar-H) ; EI-MS (m/z: RA %): 354 ($M^{+\cdot}$ 100%). ^{13}C NMR (300 MHz, DMSO–d_6/ ppm) δ: 195 (C=O), 164, 156, 150, 138, 119(-CN), 115, 60, 56, 40, 28, 24. Elemental analysis**:** Calculated data for $C_{20}H_{22}N_2O_4$; C, 67.80; N, 07.89. Found: C, 67.78; N, 07.86.

2-Amino-3-Cyano-5,6,7,8-tetrahydro-7,7-dimethyl-4-(3'-bromophenyl)-5-oxo-4*H*- benzopyran (4j) :IR (KBr / cm^{-1}) 3450, 3310 (-NH_2), 2196 (-CN), 1680 (C=O); ^{1}H NMR (300MHz, DMSO-d_6 / ppm) δ 0.94 -1.04 (2s, 6H, -2CH_3), 2.16 & 2.29 (2d, 2H, -CH_2), 2.60 (s, 2H, -CH_2), 4.30 (s, 1H, -CH), 7.07 (bs, 2H,-NH_2) 7.20- & 7.45 (m, 4 H, Ar-H) ; EI-MS (m/z: RA %): 373 (M+2, 98%), 371($M^{+\cdot}$ 100%). ^{13}C NMR (300 MHz, DMSO–d_6/ ppm) δ: 196(C=O), 162, 150, 145, 130, 128, 120(-CN), 116, 60, 55, 44, 32, 28, 26. Elemental analysis**:** Calculated data for $C_{18}H_{17}BrN_2O_2$; C, 57. 90; N, 07.52. Found: C, 57.88; N, 07.50.

2-Amino-3-Cyano-5,6,7,8-tetrahydro-7,7-dimethyl-4-(3'-nitrophenyl)-5-oxo-4*H*- benzopyran (4k): IR (KBr / cm^{-1}) 3430, 3340 (-NH_2), 2189 (-CN), 1660 (C=O); ^{1}H NMR (300MHz, DMSO-d_6 / ppm) δ 0.96 -1.08 (2s, 6H, -2CH_3), 2.10 & 2.36 (2d, 2H, -CH_2), 2.60 (s, 2H, -CH_2), 4.45 (s, 1H, -CH), 7.20 (bs, 2H,-NH_2) 7.51- 8.12 (m, 4 H, Ar-H) ; EI-MS (m/z: RA %): 339 ($M^{+\cdot}$ 100%). ^{13}C NMR (300 MHz, DMSO–d_6/ ppm) δ: 194(C=O), 164, 160, 150,138,130, 125, 122(-CN), 110, 58, 45, 39, 29, 27. Elemental analysis**:** Calculated data for $C_{18}H_{17}N_3O_4$; C, 63.73 ; N, 08.25. Found: C, 63.71; N, 08.23.

2-Amino-3-Cyano-5,6,7,8-tetrahydro-7,7-dimethyl-4-(3'-hydroxyphenyl)-5-oxo-4H- benzopyran(4l): IR (KBr / cm^{-1}) 3460 (-OH), 3465, 3330 (-NH_2), 2180 (-CN), 1689 (C=O); ^{1}H NMR (300MHz, DMSO-d_6 / ppm) δ 0.95 -1.09 (2s, 6H, -2CH_3), 2.12 & 2.29 (2d, 2H, -CH_2), 2.58 (s, 2H, -CH_2), 4.29 (s, 1H, -CH), 5.10 (s, 1H, Ar-OH), 5.70 (bs, 2H,-NH_2) 6.60- 7.14 (m, 4 H, Ar-H); EI-MS (m/z: RA %): 310 ($M^{+\cdot}$ 100%). ^{13}C NMR (300 MHz, DMSO–d_6/ ppm) δ: 192 (C=O), 160, 159, 136, 130, 128, 120(-CN), 116, 58, 52, 46, 40, 26, 24. Elemental analysis**:** Calculated data for $C_{18}H_{18}N_2O_3$; C, 65.86 ; N, 08.53. Found: C, 65.84; N, 08.51.

2-Amino-3-Cyano-5,6,7,8-tetrahydro-7,7-dimethyl-4-(2'-chlorophenyl)-5-oxo-4H- benzopyran (4m): IR (KBr / cm^{-1}) 3456, 3330 (-NH_2), 2190 (-CN), 1689 (C=O); ^{1}H NMR (300MHz, DMSO-d_6 / ppm) δ 0.96 -1.14 (2s, 6H, -2CH_3), 2.04 & 2.35 (2d, 2H, -CH_2), 2.60 (s, 2H, -CH_2), 4.80 (s, 1H, -CH), 7.04 (bs, 2H,-NH_2) 7.19 - 7.45 (m, 4 H, Ar-H) ; EI-MS (m/z: RA %): 328 ($M^{+\cdot}$ 100%). ^{13}C NMR (300 MHz, DMSO–d_6/ ppm) δ: 195(C=O), 163, 159, 145, 132, 128, 122(-CN), 116, 50, 45, 39,

30,26. Elemental analysis**:** Calculated data for $C_{18}H_{17}ClN_2O_2$; C, 65.81 ; N, 08.51. Found: C, 65.79; N, 08.49.

Antioxidant Activity

DPPH (1, 1-diphenyl-2-picrylhydrazyl) radical scavenging assay

DPPH (1,1-diphenyl-2-picrylhydrazyl) radical scavenging assay was performed as per earlier reported method. The reaction cocktail was prepared by mixing individual newly synthesized organic compounds is added to equal volume of 0.1 mM solution of DPPH radical in absolute ethanol. After 20 minutes of incubation at room temperature, the DPPH reduction was calculated by reading the absorbance at 517 nm using UV-Visible spectrophotometer. Ascorbic acid (1mM) was used as reference compound.

The compound **(4c, 4d, 4g, and 4m)** shows remarkable antioxidant activity against DDPH radical scavenging activity with reference of ascorbic acid (91.4 ± 0.021).

OH-radical scavenging assay

Hydroxyl radicals scavenging activity was measured with Fenton's reaction (Rollet –Labelle et al., 1998). The reaction mixture contained 60 µl of $FeCl_2$ (1mM), 90 µl of 1,10-phenanthroline(1mM), 2.4 ml of phosphate buffer (pH 7.8),150 µl of 0.17M H_2O_2 and 1.5 ml of individual newly synthesized organic compounds (1mM). The reaction mixture was kept at room temperature for 5 minutes incubation and the absorbance were recorded at 560 nm using UV-Visible spectrophotometer. Ascorbic acid (1mM) was used as the reference compound.

The compound **(4c, 4d, 4g, and 4m)** shows good OH radical scavenging activity as compared with Ascorbic acid (89.5 ± 0.021).

Table 4: Antioxidant potential of (4a-d, 5a-c, 6a-d, and 7a-d).

Entry	Compound Code	% Radical scavenging activity	
		DPPH radical scavenging	OH-radical scavenging
1	4a	50.5 ± 1.20	60.2 ± 1.12
2	4b	70.4 ± 0.43	68.0 ± 1.40
3	4c	80.2 ± 1.80	84.1 ± 1.34
4	4d	86.4 ± 1.32	82.4 ± 0.26
5	4e	65.0 ± 0.30	62.2 ± 1.20
6	4f	70. 2 ±1.22	68.2 ± 0.65
7	4g	78. 4 ± 1.86	80.2 ± 1.02
8	4h	75. 6 ± 1.24	76.0 ± 0.32
9	4i	60.3 ± 1.64	62.6 ± 1.62
10	4j	78.4 ± 1.86	76.6 ± 1.28
11	4k	60.4 ± 1.62	64.2 ± 1.23
12	4l	59.4 ± 1.40	60.2 ± 0.24
13	4m	76.2 ± 0.10	79.2 ± 1.44
14	Ascorbic Acid (Standard)	91.4 ± 0.021	**89.5 ± 0.021**

CONCLUSION

In Conclusion, We have developed a novel efficient and eco-friendly synthesis for the preparation of tetrahydro benzo[*b*] pyran derivatives by one-pot three component cyclocondensation reaction of aldehyde, Malononitrile and Dimedone stirred at room temperature by using 1,8-diazabicyclo[*5.4.0*]undec-7-ene DBU in aqueous ethanol. Product formed is recrystallized by ethanol no need of column chromatography, no heating, room temperature, eco-friendly solvent, short reaction time, excellent isolated yields and easy work up make this methodology for the synthesis of benzo[*b*] pyran.

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