An Efficient and Convenient Approach to Synthesis of Tetrahydrobenzo[*b*]pyran Derivatives Using Tetrabutylammonium Bromide as Catalyst

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Abstract: An efficient and convenient approach to the synthesis of 2-amino-3-cyano-4-aryl-7,7-dimethyl-5-oxo-4*H*-5, 6, 7, 8- tetrahydro benzo[*b*]pyran derivatives using tetrabutylammonium bromide (TBABr) as the catalyst is described. This method provides several advantages such as neutral conditions, high yields and simple work procedure.

Keywords: Tetrahydro benzo[*b*]pyran, Tetrabutylammonium bromide, Synthesis.

Introduction

In recent years 4*H* benzo[*b*]pyrans and their derivatives have attracted considerable attention due to their wide range of biological activities¹. Further more these compounds can be employed as pigments, photoactive materials² and they constitute the structural unit of a series of natural products³.

The importance of these compounds has led many workers to synthesize them using methods including microwave⁴, electrosynthesis⁵ or by using catalysts like hexadecyltrimethylammonium bromide (HTMAB)⁶, triethylbenzylammonium chloride (TEBA)⁷, (*s*)-proline⁸, perfluorooctanoate [RE(PFO)₃]⁹ and *N*-methylimidazole¹⁰.

Each of the above methods has its own merits, while some are plagued by limitation of poor yields, difficult work up and toxic effluents. TBABr has been used¹¹ in many organic reactions as a catalyst. However, the use of TBABr as catalyst in the synthesis of tetrahydro benzo[*b*]pyran derivatives has not been reported. In the present investigation we wish to report efficient procedure for the synthesis of tetrahydrobenzo[*b*]pyrans using an inexpensive and commercially available TBABr as catalyst. In addition, water was chosen as a green solvent, which also gives the corresponding products in excellent yields.

Experimental

Materials and methods

All the chemicals were purchased from s.d.fine chem. Limited (India) and were used as such without further purification. Melting points were determined by open capillary method and are uncorrected. Infrared (IR) spectra were recorded on Avatar-330 FTIR spectrometer. ^1H NMR and ^{13}C NMR spectra were obtained on a Bruker AMXC-500MHz Spectrometer in DMSO. Chemical shifts are expressed in δ (ppm) values. The following abbreviations were used to indicate the peak multiplicity s-singlet, d-doublet, t-triplet, q-quartet, and m-multiplet.

Methods A and B

In a typical procedure, equimolar amounts of arylaldehyde **1**, malononitrile **2** and dimedone (5,5-dimethyl-1,3-cyclohexanedione) **3**, were mixed with tetrabutylammonium bromide (10 mol %) in 15 cm³ 90% of ethanol (method A) or in 15 cm³ water (method B) and refluxed with stirring for the specific time indicated in Table 1. After the completion of the reaction, the mixture was cooled to room temperature and poured into ice (method A) or was kept at refrigerator overnight (method B) to get the crude products. The crude products were purified by recrystallization from ethanol.

Table 1. Synthesis of tetrahydrobenzo[*b*]pyrans catalyzed by TBABr.

Product	Ar	Time / min			Yield, %				M. P / °C	
		EtOH	H ₂ O	Grind	EtOH	H ₂ O	Grind	Found	Reported	
4a	C ₆ H ₅	20	60	5	92	88	94	225-227	226-228	⁹
4b	2-Cl-C ₆ H ₄	45	360	30	93	90	90	218-220	217-218	⁶
4c	3-Cl-C ₆ H ₄	60	450	45	90	85	92	235-237	—	
4d	4-Cl-C ₆ H ₄	30	120	10	95	91	92	209-210	209-211	⁸
4e	2-NO ₂ -C ₆ H ₄	60	480	40	91	87	92	215-217	—	
4f	3-NO ₂ -C ₆ H ₄	90	540	50	90	86	88	207-209	208-210	⁶
4g	4-NO ₂ -C ₆ H ₄	40	180	25	92	89	91	175-177	177-178	⁶
4h	4-Me-C ₆ H ₄	75	440	45	90	85	91	214-215	214-216	⁶
4i	N(Me) ₂ -C ₆ H ₄	95	510	53	92	90	92	197-199	198-200	⁵
4j	4-MeO-C ₆ H ₄	120	630	48	87	80	90	199-200	199-201	⁶
4k	3,4-(MeO) ₂ -C ₆ H ₃	140	675	55	90	88	91	158-160	—	
4l	3-Br-C ₆ H ₄	55	340	40	89	90	90	227-229	225-227	¹²
4m	4-F-C ₆ H ₄	45	300	20	95	91	96	176-178	—	
4n	C ₆ H ₅ -CH=CH	140	720	70	90	90	89	205-207	—	
4o	Furfuryl	95	150	35	90	86	91	217-219	218-220	¹³

Method C

A mixture of the reactants as given in methods A and B was grounded for the appropriate time using a dry mortar and pestle. The initial reaction mixture solidified within 5-70 min. The solid was washed with cold water and recrystallized from ethanol.

2-Amino-3-cyano-5,6,7,8-tetrahydro-7,7-dimethyl-5-oxo-4-phenyl-4H-benzopyran (4a)

IR (KBr) cm^{-1} 3396 (NH_2), 3028 (C-H), 2198 (CN), 1682 (C=O), 1601 (C=C); ^1H NMR (DMSO), δ 7.28-7.07(m, 5H), 6.99(s, 2H, NH_2), 4.14(s, 1H, H-4), 2.48(s, 2H, H-8), 2.22(d, 1H, H-6), 2.08(d, 1H, H-6'), 1.01(s, 3H, CH_3), 0.93(s, 3H, CH_3); ^{13}C NMR δ 195.5 (C=O), 162.4 (C-8a), 158.4 (C-2), 119.6(CN), 112.7 (C-4a), 58.3 (C-3), 49.9 (C-6), 39.8 (C-8), 39.0 (C-4), 31.7 (C-7), 28.3 (CH_3), 26.7 (CH_3), 144.6, 128.2, 127.1, 126.5 (Aromatic) Anal. Calcd. for $\text{C}_{18}\text{H}_{18}\text{N}_2\text{O}_2$: C, 73.53; H, 6.16; N, 9.52. Found: C, 73.53; H, 6.31; N, 9.47.

2-Amino-3-cyano-5,6,7,8-tetrahydro-7,7-dimethyl-4-(2-chlorophenyl)-5-oxo-4H-benzopyran (4b)

IR (KBr) cm^{-1} 3469 (NH_2), 2962 (C-H), 2196 (CN), 1600 (C=C); ^1H NMR (DMSO), δ 7.36-7.38 (dd, 1H, Ar-H), 7.26-7.29 (m, 1H, Ar-H), 7.16-7.22 (m, 2H, Ar-H), 7.03 (s, 2H, NH_2), 4.70 (s, 1H, H-4), 2.53(s, 2H, H-8), 2.27 (d, 1H, H-6), 2.09(d, 1H, H-6'), 1.07 (s, 3H CH_3), 0.98 (s, 3H, CH_3); ^{13}C NMR δ 196.0 (C=O), 163.6 (C-8a), 159.1 (C-2), 119.7 (CN), 112.2 (C-4a), 57.3 (C-3), 50.4 (C-6), 40.5 (C-8), 39.4 (C-4), 32.3 (C-7), 28.8 (CH_3), 27.3 (CH_3), 142.0, 130.4, 129.9, 128.6 (Aromatic) Anal. Calcd. for $\text{C}_{18}\text{H}_{17}\text{ClN}_2\text{O}_2$: C, 65.85; H, 5.18; N, 8.54. Found: C, 65.68; H, 5.25; N, 8.49.

2-Amino-3-cyano-5,6,7,8-tetrahydro-7,7-dimethyl-4-(3-chlorophenyl)-5-oxo-4H-benzopyran (4c)

IR (KBr) cm^{-1} 3419 (NH_2), 2961 (C-H), 2191 (CN), 1660 (C=O), 1630 (C=C), 1600 (C=C); ^1H NMR (DMSO), δ 7.32-7.35 (m, 1H, Ar-H), 7.26-7.27 (dd, 1H, Ar-H), 7.16-7.17 (m, 1H, Ar-H), 7.10-7.12 (dd, 1H, Ar-H), 7.09 (s, 2H, NH_2), 4.21 (s, 1H, H-4), 2.53(s, 2H, H-8), 2.27 (d, 1H, H-6), 2.14 (d, 1H, H-6'), 1.03 (s, 3H CH_3), 0.96 (s, 3H, CH_3); ^{13}C NMR δ 196.2 (C=O), 163.3 (C-8a), 159.0 (C-2), 119.9 (CN), 112.5 (C-4a), 58.0 (C-3), 50.3 (C-6), 40.5 (C-8), 39.4 (C-4), 32.3 (C-7), 28.7 (CH_3), 27.2 (CH_3), 147.6, 130.7, 127.5, 126.4 (Aromatic). Anal. Calcd. for $\text{C}_{18}\text{H}_{17}\text{ClN}_2\text{O}_2$: C, 65.85; H, 5.18; N, 8.54. Found: C, 65.73; H, 5.22; N, 8.60.

2-Amino-3-cyano-5,6,7,8-tetrahydro-7,7-dimethyl-4-(4'-chlorophenyl)-5-oxo-4H-benzopyran (4d)

IR (KBr) cm^{-1} 3380 (NH_2), 2960 (C-H), 2188 (CN), 1676 (C=O), 1635 (C=C), 1603 (C=C); ^1H NMR (DMSO), 7.15-7.33 (d, 2H), (d, 2H) Ar-H, 7.06 (s, 2H, NH_2), 4.18 (s, 1H, H-4), 2.54 (s, 2H, H-8), 2.23 (d, 1H, H-6), 2.14 (d, 1H, H-6'), 1.01 (s, 3H, CH_3), 0.93 (s, 3H, CH_3); ^{13}C NMR δ 195.5 (C=O), 163.5 (C-8a), 158.4 (C-2), 119.4 (CN), 112.3 (C-4a), 57.8 (C-3), 49.9 (C-6), 39.9 (C-8), 39.0 (C-4), 31.7 (C-7), 28.2 (CH_3), 26.8 (CH_3), 128.2-131.0 (Aromatic). Anal. Calcd. for $\text{C}_{18}\text{H}_{17}\text{ClN}_2\text{O}_2$: C, 65.85; H, 5.18; N, 8.54. Found: C, 65.75; H, 5.12; N, 8.45.

2-Amino-3-cyano-5,6,7,8-tetrahydro-7,7-dimethyl-4-(2-nitrophenyl)-5-oxo-4H-benzopyran (4e)

IR (KBr) cm^{-1} 3471 (NH_2), 3076 (C-H), 2194 (CN), 1688 (C=O), 1665 (C=C), 1597 (C=C), 1526 (NO_2); ^1H NMR (DMSO), δ 7.80-7.83 (dd, 1H, Ar-H), 7.64-7.68 (m, 1H, Ar-H), 7.41-7.44 (m, 1H, Ar-H), 7.35-7.37 (dd, 1H, Ar-H), 7.19 (s, 2H, NH_2), 4.94 (s, 1H, H-4), 2.55 (s, 2H, H-8), 2.22 (d, 1H, H-6), 2.03 (d, 1H, H-6'), 1.01 (s, 3H, CH_3), 0.88 (s, 3H, CH_3); ^{13}C NMR δ 196.3 (C=O), 163.2 (C-8a), 159.6 (C-2), 119.5 (CN), 112.7 (C-4a), 56.8 (C-3), 50.0 (C-6), 40.5 (C-8), 39.4 (C-4), 32.3 (C-7), 28.7 (CH_3), 27.1 (CH_3), 149.4, 130.7, 128.3, 124.1 (Aromatic). Anal. Calcd. for $\text{C}_{18}\text{H}_{17}\text{N}_3\text{O}_4$: C, 63.72; H, 5.01; N, 8.26. Found: C, 63.90; H, 5.10; N, 8.32.

2-Amino-3-cyano-5,6,7,8-tetrahydro-7,7-dimethyl-4-(3-nitrophenyl)-5-oxo-4H-benzopyran (4f)

IR (KBr) cm^{-1} 3430 (NH_2), 3101 (C-H), 2187 (CN), 1654 (C=O), 1597 (C=C), 1531 (NO_2); ^1H NMR (DMSO), δ 8.07-8.09 (m, 1H, Ar-H), 7.98-7.99 (m, 1H, Ar-H), 7.66-7.68 (m, 1H, Ar-H), 7.61-7.64 (m, 1H, Ar-H), 7.18 (s, 2H, NH_2), 4.42 (s, 1H, H-4), 2.55 (s, 2H, H-8), 2.28 (d, 1H, H-6), 2.13 (d, 1H, H-6'), 1.04 (s, 3H, CH_3), 0.96 (s, 3H, CH_3); ^{13}C NMR δ 196.2 (C=O), 163.6 (C-8a), 159.1 (C-2), 119.8 (CN), 112.2 (C-4a), 57.6 (C-3), 50.3 (C-6), 40.4 (C-8), 39.4 (C-4), 32.2 (C-7), 28.7 (CH_3), 27.2 (CH_3), 148.2, 134.6, 130.4, 122.2 (Aromatic). Anal. Calcd. for $\text{C}_{18}\text{H}_{17}\text{N}_3\text{O}_4$: C, 63.72; H, 5.01; N, 8.26. Found: C, 63.85; H, 5.13; N, 8.19.

2-Amino-3-cyano-5,6,7,8-tetrahydro-7,7-dimethyl-4-(4'-nitrophenyl)-5-oxo-4H-benzopyran (4g)

IR (KBr) cm^{-1} 3407 (NH_2), 2970 (C-H), 2184 (CN), 1671 (C=O), 1630 (C=C), 1594 (C=C), 1520 (NO_2); ^1H NMR (DMSO), δ 8.16-8.18 (m, 2H, Ar-H), 7.44-7.46 (m, 2H, Ar-H), 7.18 (s, 2H, NH_2), 4.36 (s, 1H, H-4), 2.57 (s, 2H, H-8), 2.28 (d, 1H, H-6), 2.13 (d, 1H, H-6'), 1.04 (s, 3H CH_3), 0.95 (s, 3H, CH_3); ^{13}C NMR δ 196.2 (C=O), 163.5 (C-8a), 159.0 (C-2), 119.7 (CN), 112.1 (C-4a), 57.4 (C-3), 50.3 (C-6), 40.4 (C-8), 39.4 (C-4), 32.2 (C-7), 28.7 (CH_3), 27.4 (CH_3), 146.7, 129.0, 124.1 (Aromatic). Anal. Calcd. for $\text{C}_{18}\text{H}_{17}\text{N}_3\text{O}_4$: C, 63.72; H, 5.01; N, 8.26. Found: C, 63.60; H, 5.08; N, 8.19.

2-Amino-3-cyano-5,6,7,8-tetrahydro-7,7-dimethyl-4-(4'-methylphenyl)-5-oxo-4H-benzopyran (4h)

IR (KBr) cm^{-1} 3426 (NH_2), 2956 (C-H), 2191 (CN), 1682 (C=O), 1639 (C=C), 1601 (C=C); ^1H NMR (DMSO), δ 7.08-7.10 (d, 2H, Ar-H), 7.02-7.03 (d, 2H, Ar-H), 6.96 (s, 2H, NH_2), 4.13 (s, 1H, H-4), 2.51 (s, 2H, H-8), 2.24 (s, 3H, CH_3), 2.26 (d, 1H, H-6), 2.10 (d, 1H, H-6'), 1.03 (s, 3H, CH_3), 0.95 (s, 3H, CH_3); ^{13}C NMR δ 196.1 (C=O), 162.7 (C-8a), 158.9 (C-2), 120.2 (CN), 113.3 (C-4a), 58.9 (C-3), 50.4 (C-6), 40.5 (C-8), 39.4 (C-4), 32.2 (C-7), 28.8 (CH_3), 27.2 (CH_3), 21.0 (CH_3 , Aryl), 142.2, 136.1, 129.3, 127.5 (Aromatic). Anal. Calcd. for $\text{C}_{19}\text{H}_{20}\text{N}_2\text{O}_2$: C, 74.03; H, 6.49; N, 9.09. Found: C, 74.23; H, 6.55; N, 9.17.

2-Amino-3-cyano-5,6,7,8-tetrahydro-7,7-dimethyl-4-(4'-N,N-dimethylaminophenyl)-5-oxo-4H-benzopyran (4i)

IR (KBr) cm^{-1} 3382 (NH_2), 2959 (C-H), 2191 (CN), 1687 (C=O), 1655 (C=C), 1608 (C=C); ^1H NMR (DMSO), δ 6.93-6.95 (d, 2H, Ar-H), 6.62-6.64 (d, 2H, Ar-H), 6.88 (s, 2H, NH_2), 4.04 (s, 1H, H-4), 2.84 (s, 6H, $(\text{CH}_3)_2$), 2.53 (s, 2H, H-8), 2.25 (d, 1H, H-6), 2.09 (d, 1H, H-6'), 1.06 (s, 3H, CH_3), 0.95 (s, 3H, CH_3); ^{13}C NMR δ 196.1 (C=O), 162.3 (C-8a), 158.8 (C-2), 120.4 (CN), 112.8 (C-4a), 59.4 (C-3), 50.5 (C-6), 40.6 (C-8), 39.9 (C-4), 32.2 (C-7), 28.9 (CH_3), 27.2 (CH_3), $\text{N}(\text{CH}_3)_2$ merged with solvent peaks, 149.7, 132.9, 128.1 (Aromatic). Anal. Calcd. for $\text{C}_{20}\text{H}_{23}\text{N}_3\text{O}_2$: C, 71.22; H, 6.82; N, 8.31. Found: C, 71.03; H, 6.90; N, 8.23.

2-Amino-3-cyano-5,6,7,8-tetrahydro-7,7-dimethyl-4-(4'-methoxyphenyl)-5-oxo-4H-benzopyran (4j)

IR (KBr) cm^{-1} 3375 (NH_2), 2962 (C-H), 2193 (CN), 1683 (C=O), 1655 (C=C), 1605 (C=C); ^1H NMR (DMSO), δ 6.82-6.84 (d, 2H, Ar-H), 7.01-7.04 (d, 2H, Ar-H), 6.97 (s, 2H, NH_2), 4.11 (s, 1H, H-4), 3.71 (s, 3H, OCH_3), 2.54 (s, 2H, H-8), 2.24 (d, 1H, H-6), 2.08 (d, 1H, H-6'), 1.04 (s, 3H, CH_3), 0.97 (s, 3H, CH_3); ^{13}C NMR δ 195.6 (C=O), 162.0 (C-8a), 158.4 (C-2), 119.7 (CN), 113.6 (C-4a), 58.6 (C-3), 50.0 (C-6), 39.9 (C-8), 39.1 (C-4), 31.7 (C-7), 28.3

(CH₃), 26.7 (CH₃), 54.9 (OCH₃, Aryl), 136.8, 128.1, 113.0 (Aromatic). Anal. Calcd. for C₁₉H₂₀N₂O₃: C, 70.37; H, 6.17; N, 8.64. Found: C, 70.20; H, 6.09; N, 8.72.

2-Amino-3-cyano-5,6,7,8-tetrahydro-7,7-dimethyl-4-(3,4-dimethoxyphenyl)-5-oxo-4H-benzopyran (4k)

IR (KBr) cm⁻¹ 3390 (NH₂), 2955 (C-H), 2193 (CN), 1682 (C=O), 1658 (C=C), 1603 (C=C); ¹H NMR (DMSO), δ 6.86-6.88 (d, 1H, Ar-H), 6.69-6.70 (d, 1H, Ar-H), 6.64-6.67 (dd, 1H, Ar-H), 3.71 (d, 6H, (OCH₃)₂), 6.95 (s, 2H, NH₂), 4.13 (s, 1H, H-4), 2.50 (s, 2H, H-8), 2.24 (d, 1H, H-6), 2.12 (d, 1H, H-6'), 1.04 (s, 3H, CH₃), 0.97 (s, 3H, CH₃); ¹³C NMR δ 196.1 (C=O), 162.7 (C-8a), 158.8 (C-2), 119.5 (CN), 112.2 (C-4a), 59.0 (C-3), 50.4 (C-6), 40.5 (C-8), 39.9 (C-4), 32.2 (C-7), 28.9 (CH₃), 27.1 (CH₃), 55.96, 55.92 (OCH₃, Aryl), 148.9, 137.7, 113.3 (Aromatic). Anal. Calcd for C₂₀H₂₃N₂O₄: C, 67.81; H, 6.48; N, 7.89. Found: C, 67.72; H, 6.40; N, 7.81.

2-Amino-3-cyano-5,6,7,8-tetrahydro-7,7-dimethyl-4-(3-bromophenyl)-5-oxo-4H-benzopyran (4l)

IR (KBr) cm⁻¹ 3343 (NH₂), 2962 (C-H), 2191 (CN), 1687 (C=O), 1657 (C=C), 1603 (C=C); ¹H NMR (DMSO), δ 7.38-7.41 (m, 1H, Ar-H), 7.30-7.31 (m, 1H, Ar-H), 7.26-7.29 (m, 1H, Ar-H), 7.15-7.17 (m, 1H, Ar-H), 7.09 (s, 2H, NH₂), 4.20 (s, 1H, H-4), 2.53 (s, 2H, H-8), 2.24 (d, 1H, H-6), 2.11 (d, 1H, H-6'), 1.03 (s, 3H, CH₃), 0.96 (s, 3H, CH₃); ¹³C NMR δ 196.2 (C=O), 163.3 (C-8a), 159.0 (C-2), 119.6 (CN), 112.5 (C-4a), 58.1 (C-3), 50.3 (C-6), 40.5 (C-8), 39.4 (C-4), 32.3 (C-7), 28.7 (CH₃), 27.2 (CH₃), 147.9, 131.1, 129.9, 126.8 (Aromatic). Anal. Calcd. for C₁₈H₁₇BrN₂O₂: C, 57.91; H, 4.56; N, 7.51. Found: C, 57.78; H, 4.49; N, 7.62.

2-Amino-3-cyano-5,6,7,8-tetrahydro-7,7-dimethyl-4-(4'-fluorophenyl)-5-oxo-4H-benzopyran (4m)

IR (KBr) cm⁻¹ 3343 (NH₂), 2962 (C-H), 2191 (CN), 1687 (C=O), 1657 (C=C), 1603 (C=C); ¹H NMR (DMSO), δ 7.17-7.20 (m, 2H, Ar-H), 7.09-7.13 (m, 2H, Ar-H), 7.03 (s, 2H, NH₂), 4.20 (s, 1H, H-4), 2.51 (s, 2H, H-8), 2.26 (d, 1H, H-6), 2.12 (d, 1H, H-6'), 1.03 (s, 3H, CH₃), 0.94 (s, 3H, CH₃); ¹³C NMR δ 196.1 (C=O), 162.9 (C-8a), 158.9 (C-2), 120.1 (CN), 113.0 (C-4a), 58.5 (C-3), 50.4 (C-6), 40.4 (C-8), 39.4 (C-4), 32.2 (C-7), 28.7 (CH₃), 27.3 (CH₃), 141.1, 129.5, 115 (Aromatic). Anal. Calcd. for C₁₈H₁₇FN₂O₂: C, 69.23; H, 5.45; N, 8.97. Found; C, 69.35; H, 5.38; N, 8.88.

2-Amino-3-cyano-5,6,7,8-tetrahydro-7,7-dimethyl-4-(Phenyl allylidene)-5-oxo-4H-benzopyran (4n)

IR (KBr) cm⁻¹ 3386 (NH₂), 2962 (C-H), 2186 (CN), 1648 (C=O), 1604 (C=C); ¹H NMR (DMSO), δ 7.37-7.39 (d, 2H, Ar-H), 7.29-7.31 (m, 2H, Ar-H), 7.20-7.23 (m, 1H, Ar-H), 7.06 (s, 2H, NH₂), 6.35, 6.10 (2H, CH=CH), 3.83 (s, 1H, H-4), 2.51 (s, 2H, H-8), 2.29 (d, 1H, H-6), 2.23 (d, 1H, H-6'), 1.03 (s, 3H, CH₃), 1.00 (s, 3H, CH₃); ¹³C NMR δ 196.3 (C=O), 162.9 (C-8a), 159.7 (C-2), 120.3 (CN), 112.3 (C-4a), 55.6 (C-3), 50.5 (C-6), 40.5 (C-8), 39.4 (C-4), 32.2 (C-7), 28.6 (CH₃), 27.4 (CH₃), 136.9, 131.5, 129.7, 126.6 (Aromatic). Anal. Calcd. for C₂₀H₂₀N₂O₂: C, 75.01; H, 6.25; N, 8.75. Found: C, 75.17; H, 6.17; N, 8.82.

2-Amino-3-cyano-5,6,7,8-tetrahydro-7,7-dimethyl-4-(2-furfuryl)-5-oxo-4H-benzopyran (4o)

IR (KBr) cm⁻¹ 3396 (NH₂), 2966 (C-H), 2196 (CN), 1680 (C=O), 1660 (C=C), 1603 (C=C); ¹H NMR (DMSO), δ 7.48 (s, 1H, Ar-H), 6.32-6.33 (dd, 1H, Ar-H), 6.05 (d, 1H, Ar-H), 7.08 (s, 2H, NH₂), 4.33 (s, 1H, H-4), 2.50 (s, 2H, H-8), 2.30 (d, 1H, H-6), 2.15 (d, 1H, H-6'), 1.04 (s, 3H, CH₃), 0.99 (s, 3H, CH₃); ¹³C NMR δ 195.9 (C=O), 163.7 (C-8a), 159.7 (C-2), 120.0 (CN),

110.8 (C-4a), 55.8 (C-3), 50.3 (C-6), 40.4 (C-8), 39.4 (C-4), 32.2 (C-7), 28.8 (CH₃), 27.0 (CH₃), 156.1, 142.2, 110.9, 105.5 (Aromatic). Anal. Calcd. for C₁₇H₁₇N₂O₃: C, 68.69; H, 5.72; N, 9.43. Found: C, 68.81; H, 5.80; N, 9.50.

Results and Discussion

A mixture of benzaldehyde, malononitrile and 5,5-dimethyl-1,3-cyclohexanedione (dimedone) were treated with tetrabutylammoniumbromide under three different conditions, namely (i) using ethanol as solvent (method A); (ii) using water as reaction medium (method B); (iii) grinding in a mortar with pestle (method C) at room temperature, to give desired product derivatives (Scheme 1). To explore the scope of this reaction, we extended the reaction to various aromatic aldehydes. The reaction time, yield and the physical constants of various products obtained by the reaction are given in Table 1.

Scheme 1

The yields are, in general, very high regardless of the structural variations in aromatic aldehyde, but show obvious effects in terms of reaction time, under these reaction conditions. Aromatic aldehydes containing electron-donating groups (such as alkoxy group, methyl group and dimethylamino group, **4h-k** in table 1) have taken longer reaction time, whereas the reaction time is less for the aldehyde containing electron-withdrawing groups (such as nitro or halide, **4b-g** and **4l-m** in table 1).

The catalyst plays a crucial role in the success of the reaction in terms of the rate and the yields. For example, benzaldehyde reacts with malononitrile and dimedone in the presence of 1 mol% TBABr in ethanol giving the product **4a** of 70% yield. Increasing the percentage of catalyst to 5 mol% and 10 mol% results the yields 82% and 92% respectively. Higher amounts of the catalyst did not improve the results to a greater extent. Thus, 10 mol% TBABr was chosen as the maximum quantity of catalyst used for these reactions. We performed the reaction in ethanol without the catalyst and isolated the cyano olefin intermediate and unreacted **3**.

A mechanism for the reaction is outlined in Scheme 2. The reaction proceeds via initial formation of cyanoolefin [A] formed by the condensation of aryl aldehyde **1** and malononitrile **2**. Cyanoolefin [A] reacts with the active methylene moiety of **3** giving intermediate [B] which subsequently cyclises to afford the desired compound **4**. The water molecule eliminated in the first step plays a key role in the cyclisation process.

Scheme 2

Conclusion

We have described a general and highly efficient procedure for the preparation of tetrahydrobenzo[*b*]pyrans catalysed by TBABr three component condensation under three different conditions. Among the above methods, the solvent-free procedure (method C) provided the best results. Although the reaction carried out in water (method B) showed similar results as in ethanol (method A), they are less expensive and less toxic than those with organic solvents. Compared to other methods using TBABr as catalyst, has several advantages including high yields, inexpensive operation and minimal environmental impact which make it a useful process for the synthesis of these compounds.

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