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1,3-Dibromo-5,5-dimethylhydantoin (DBH) as a cheap and efficient catalyst for the synthesis of polyhydroquinolines and 12-aryl-8,9,10,12-tetrahydro [a] xanthene-11-ones

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ABSTRACT

1,3-Dibromo-5,5-dimethylhydantoin (DBH), as a cheap and commercially available reagent, is efficiently able to catalyze the synthesis of polyhydroquinoline derivatives and 12-aryl-8,9,10,12-tetrahydro[a] xanthene-11-ones via one-pot multi-component reactions. This novel synthetic method has the advantages of low cost and availability of the catalyst, short reaction times, high to excellent yields, simple and easy work-up and purification of the products compared to the conventional methods reported in the literature.

Keywords*: Multi-component reactions, 1,3-Dibromo-5,5-dimethylhydantoin, Aldehydes, 12-Aryl-8,9,10,12-tetrahydro[a] xanthene-11-ones, Polyhydroquinoline*.

1. Introduction

Design of highly efficient chemical reaction sequences that provides maximum structural complexity and diversity with a minimum number of synthetic steps to assemble compounds with interesting properties is a major challenge of modern drug discovery [1, 2]. Recently, multi-component reactions have emerged as a highly valuable synthetic tool in the context of modern organic synthesis. The atom economy and convergent character, the simplicity of a one-pot procedure, the possible structural variations, the accessible complexity of the molecules, and the very large number of accessible compounds are among the described advantages of multi-component reactions [3, 4]. Thus, they are perfectly amenable to automation for combinatorial synthesis [5-8].

In recent years, many organic chemists paid their attention to the synthesis of 4-substituted 1,4-dihydropyridines (DHPs) owing to their significant biological properties such as calcium channel blockers, vasodilator, bronchodilator, antiatherosclerotics, antitumor, geroprotective and hepatoprotective [9]. In addition, these compounds are one of the most important classes of drugs for the treatment of cardiovascular diseases including hypertension [10]. Furthermore, extensive studies reveal that these compounds exhibit different medicinal applications and are being utilized as neuroprotectant, celebral antischemic activity in the treatment of Alzheimer's disease, platelet anti-aggregatory activity, chemosensitizer in tumor therapy [11], antimalarial, antiinflammatory, anti-asthamatic, antibacterial and tyrosine kinase inhibiting agents [12]. Also, dihydropyridine derivatives have been used as reducing agents for the direct reductive amination of aldehydes and ketones [13].

Classical method for the synthesis of 1,4-dihydropyridines (DHPs) is one-pot condensation of aldehydes with ethylacetoacetate and ammonia in acetic acid or by refluxing in alcohol [14]. However this method involves long reaction time, harsh reaction conditions, use of a large quantity of volatile organic solvents and generally gives low yields.

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In recent years, several new efficient methods have been developed including the use of ceric ammonium nitrate (CAN) [15], $Cs_{2.5}H_{0.5}PW_{12}O_{40}$ [16], $Hf(NPf_2)_4$ [17], $Yb(OTf)_3$ [18], $Sc(OTf)_3$ [19], $K_7[PW_{11}CoO_{40}$ [20], MCM-41 [21], molecular iodine [22], nickel nanoparticle [23], HY-zeolite [24], ionic liquids [25], organo-catalyst [26], p-TSA [27], BINOL-phosphoric acid derivatives [28], $HClO_4.SiO_2$ [29] and Mn(III) complex [30]. Although these methods have their own advantages but most of them suffer from one or more disadvantages such as use of stoichiometric amount of reagents, acidic or basic catalysts, expensive metal precursors, tedious work-up, long reaction times, unsatisfactory product yields, excess of organic solvent, high temperatures, harsh reaction conditions and difficulty in the preparation of the catalyst. Therefore, it is important to find more convenient methods for the synthesis of these types of compounds.

In the past decade, synthesis of xanthenes derivatives has been of considerable interest in organic chemists because they possess various biological and pharmaceutical activities such as antiviral [31], antibacterial [32] and anti-inflammatory [33]. These are being utilized as antagonists for paralyzing action of zoxazolamine [34] and in photodynamic therapy [35]. Furthermore, these compounds can be used as leuco-dyes [36], in laser technology [37] and pH-sensitive fluorescent materials for the visualization of biomolecular assemblies [38]. Among this class of molecules, xanthone is a prominent structural motif found in numerous natural products and synthetic compounds with important biological activity [39-41]. Tetrahydroxanthenones are the most important classes of these compounds due to their distinctive structures and great potential for further transformations [42]. Consequently, the development of novel methods for the synthesis of these heterocyclic compounds has been receiving considerable interest in both organic and medicinal field. Several methods have been reported for the synthesis of 12-aryl-8,9,10,12-tetrahydrobenzo [a] xanthen-11-ones via the condensation of aldehydes, 2-naphtol and cyclic 1,3-dicarbonyl compounds catalyzed by $Sr(OTf)_2$ [43], $NaHSO_4.SiO_2$ [44], $H_3PW_{12}O_2$ [45], p-TSA/ [bmim]BF_4 [46], HBF_4/ SiO_2 [47], $InCl_3$ and/or P_2O_5 [48], N,N'-dibromo-N,N'-1,2- ethanediyl-bis(p-toluene sulfonamide) [BNBTS] [49], Caro's acid.SiO_2 [50] and I_2 [51]. However, these methods suffer from disadvantages such as long reaction times, unsatisfactory yields, harsh reaction conditions, tedious work-up, use of harmful volatile organic solvents, and requirement of excess of reagents or catalysts. Consequently, introduction of new methods and catalysts that addresses these drawbacks is desirable.

2. Experimental

2.1. General

Chemicals were purchased from Fluka, Merck and Aldrich Chemical Companies. All yields refer to the isolated products. The purity determination of the substrate and reaction monitoring were accompanied by thin-layer chromatography (TLC) on silica-gel Polygram SILG / UV 254 plates.

2.2. General procedure for the synthesis of polyhydroquinolines

A mixture of aldehyde (1 mmol), cyclic diketone (1 mmol) *β*-ketoester (1 mmol), ammonium acetate (1.1 mmol), DBH (0.1 mmol) and 3 drop EtOH were heated at 70 ^oC for the appropriate time (Table 1). After completion of the reaction (monitored by TLC), the reaction mixture was cooled to room temperature and dissolved in ethanol and poured into water. The resulting precipitate was filtered and was purified by recrystalization from EtOH to afford the pure products in good to high yields. The physical and spectral data of the compounds were in agreement with those reported in the literature.

2.3. General procedure for the synthesis of 12-aryl-8,9,10,12-tetrahydrobenzo [a] xanthenes-11-ones

A mixture of aldehyde (1 mmol), 2-naphthol (1 mmol), cyclic 1,3-dicarbonyl compound (1.2 mmol), Kaolin (0.1 g) and DBH (0.1 mmol) was heated in an oil bath. After completion of the reaction (monitored by TLC), the reaction was cooled to room temperature, CH_2Cl_2 (15 mL) was added and Kaolin was separated by filtration. Evaporation of the solvent from the filtrate, followed by recrystallization of the residue from EtOH affords the pure products in good to high yields. The physical and spectral data of the know compounds were in agreement with those reported in the literature.

The selected spectral data

Table 1, Entry 1: Pale yellow solid; m.p. 221-223 ^oC; IR (KBr, cm^{-1}): 3295, 2995, 1695, 1643, 1605, 1460, 1375, 1220, 1180; ^{1}H NMR (400 MHz, $CDCl_3$, ppm): δ: 7.1-7.34 (m, 5H, Ar-H), 6.70 (br s, 1H, NH), 5.08 (s, 1H), 4.09 (q, *J*= 7.2 Hz, 2H), 2.36 (s, 3H), 2.15-2.35 (m, 4H) , 1.24 (t, *J* = 7.2 Hz, 3H), 1.08 (s, 3H), 0.95 (s, 3H).

Table 1, Entry 2: Pale yellow solid; m.p. 256-258 ^oC; IR (KBr, cm^{-1}): 3295, 2990, 1692, 1645, 1604, 1475, 1375, 1220, 1180; ^{1}H NMR (400 MHz, $CDCl_3$, ppm): δ: 7.34 (d, *J* = 8.4 Hz, 2H, Ar–H), 7.21 (d, *J* = 8.4 Hz, 2H, Ar–H), 6.12 (br s,1H, NH), 5.04 (s, 1H), 4.08 (q, *J* = 7.2 Hz, 2H), 2.40 (s, 3H), 2.15-2.37 (m, 4H), 1.22 (t,

Table 1. Synthesis of polyhydroquinoline derivatives catalyzed by DBH[a, b]

Entry	Aldehyde	R	R'	Time (min)	Yield (%)	M.P. (°C)	
						Found	Reported [Ref]
1	C_6H_5CHO	Et	Me	65	87	221-223	225-227 [20]
2	4-BrC_6H_4CHO	Et	Me	70	86	256-258	253-255 [17]
3	4-$CH_3OC_6H_4CHO$	Et	Me	60	95	255-257	256-257 [20]
4	3-$NO_2C_6H_4CHO$	Et	Me	95	86	240-242	242-243 [20]
5	3-$NO_2C_6H_4CHO$	Et	Me	100	85	174-175	174-176 [23]
6	4-ClC_6H_4CHO	Et	Me	70	92	241-243	245-247 [23]
7	Furfural	Et	Me	138	87	242-243	242-245 [55]
8	4-$(CH_3)_2CHC_6H_4CHO$	Et	Me	120	88	179-180	180-182 [55]
9	4-ClC_6H_4CHO	Me	Me	75	91	254-255	221-222 [51]
10	4-$(CH_3)_2NHC_6H_4CHO$	Me	Me	85	87	256-258	256-258 [56]
11	4-$CH_3OC_6H_4CHO$	Et	H	100	90	210-212	193-159 [5]
12	4-ClC_6H_4CHO	Et	H	50	89	250-252	234-235 [5]
13	Furfural	Et	H	150	87	240-241	210-220 [5]

[a]The desired products were characterized by their physical data, comparison with authentic samples, and IR and NMR spectroscopy.
[b]Isolated yield.

J = 7.2 Hz, 3H), 1.09 (s, 3H), 0.95 (s, 3H)

Table 1, Entry 3**:** Pale yellow solid; m.p. 241-243 °C; IR (KBr, cm^{-1}): 3295, 2995, 1685, 1650, 1604, 1470, 1378, 1220, 1180; ^1H NMR (400 MHz, $CDCl_3$, ppm) δ: 7.26 (d, *J*= 8.4 Hz, 2H, Ar–H), 7.18 (d, *J*= 8.4 Hz, 2H, Ar–H), 6.50 (br s,1H, NH), 5.05 (s, 1H), 4.08 (q, *J*= 7.2 Hz, 2H), 2.38 (s, 3H), 2.14-2.34 (m, 4H), 1.21 (t, *J*= 7.2 Hz, 3H), 1.09 (s, 3H), 0.94 (s, 3H).

Table 1, Entry 4: Yellow solid; m.p. 240-242 °C; IR (KBr, cm^{-1}): 3290, 2985, 1697, 1645, 1610, 1460, 1378, 1220, 1180; ^1H NMR (400 MHz, $CDCl_3$, ppm): δ: 8.10 (d, *J*= 8.8 Hz, 2H, Ar–H), 7.51 (d, *J* = 8.8 Hz, 2H, Ar–H), 6.72 (br s, 1H, NH), 5.18 (s, 1H), 4.07 (q, *J* = 7.2 Hz, 2H), 2.40 (s, 3H), 2.13-2.37 (m, 4H), 1.24 (t, *J*= 7.2 Hz, 3H), 1.09 (s, 3H), 0.92 (s, 3H).

Table 1, Entry 5: Yellow solid; m.p. 174-175 °C; IR (KBr, cm^{-1}): 3298, 2995, 1695, 1645, 1610, 1480, 1375, 1220, 1180; ^1H NMR (400 MHz, $CDCl_3$, ppm): δ: 8.14 (s, 1H, Ar–H), 7.99 (dd, J_1= 8 Hz, J_2= 1.2 Hz, 1H, Ar–H), 7.74 (d, *J* = 8 Hz, 1H, Ar–H), 7.40 (t, *J*= 8 Hz, 1H, Ar–H), 6.70 (br s, 1H, NH), 5.18 (s, 1H), 4.08 (q, *J* = 7.2 Hz, 2H), 2.40 (s, 3H), 2.14-2.32 (m, 4H), 1.24 (t, *J* = 7.2 Hz, 3H), 1.10 (s, 3H), 0.94 (s, 3H).

Table 1, Entry 6: Pale yellow solid; m.p. 255-257 °C; IR (KBr, cm^{-1}): 3287, 2995, 1695, 1645, 1605, 1487, 1378, 1220, 1180; ^1H NMR (400 MHz, $CDCl_3$, ppm): δ: 7.23 (d, *J* = 8.4 Hz, 2H, Ar–H), 6.75 (d, *J*= 8.4 Hz, 2H, Ar–H), 6.62 (br s, 1H, NH), 5.02 (s, 1H), 4.09 (q, *J* = 7.2 Hz, 2H), 3.74 (s, 3H), 2.36 (s, 3H), 2.18-2.27 (m, 4H), 1.24 (t, *J* = 7.2 Hz, 3H), 1.07 (s, 3H), 0.95 (s, 3H).

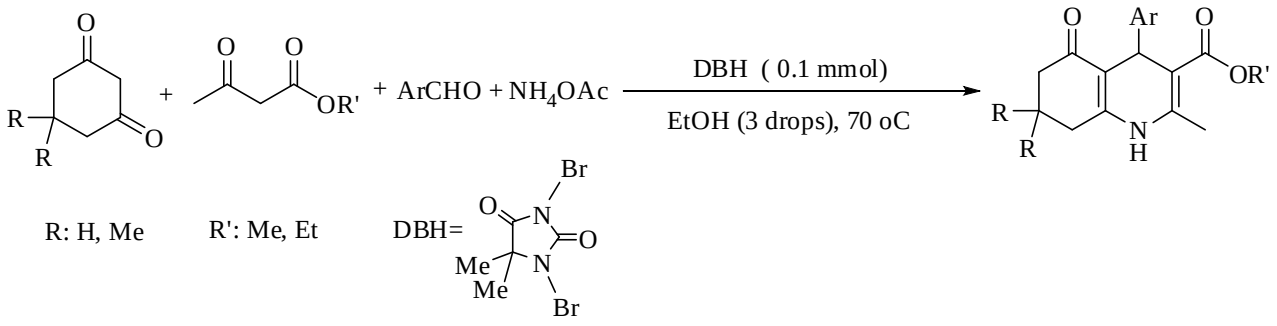
Table 1, Entry 7: Pale yellow solid; m.p. 179-180 °C; IR (KBr, cm^{-1}): 3292, 2995, 1698, 1650, 1610, 1478, ^1H NMR (400 MHz, $CDCl_3$, ppm) δ: 7.22 (d, *J* = 8 Hz, 2H, Ar–H), 7.06 (d, *J* = 8 Hz, 2H, Ar–H), 6.77 (br s, 1H, NH), 5.05 (s, 1H), 4.09 (q, *J* = 7.2 Hz, 2H), 2.79-2.86 (m, 1H), 2.16-2.37 (m, 7H), 1.19-1.28 (m, 9H), 1.09 (s, 3H), 0.98 (s, 3H).

Table 1, Entry 8: Yellow solid; m.p. 242-243 °C; IR (KBr, cm^{-1}): 3295, 2970, 1690, 1605, 1480, 1375, 1220, 1179 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$, ppm): δ: 7.21 (d, *J*= 0.8 Hz, 1H), 6.23 (t, *J* = 3.2 Hz, 1H), 6.04 (d, *J*= 3.2 Hz, 1H), 6.0 (br s, 1H, NH), 5.28 (s, 1H), 4.12-4.22 (m, 2H), 2.20-2.41 (m,6H), 1.25-1.30 (m, 4H), 1.12 (s, 3H), 1.05 (s, 3H).

Table 1, Entry 9: Pale yellow solid; m.p. 254-255 °C; IR (KBr, cm^{-1}): 3295, 2970, 1695, 1610, 1475, 1375, 1220, 1170; ^1H NMR (400 MHz , $CDCl_3$, ppm): δ: 7.26 (d, *J* = 8.4 Hz, 2H, Ar–H), 7.19 (d, *J* = 8.4 Hz, 2H, Ar–H), 6.05 (br s, 1H, NH), 5.06 (s, 1H), 3.64 (s, 3H), 2.41 (s, 3H), 2.16-2.39 (m, 4H), 1.10 (s, 3H), 0.95 (s, 3H).

Table 1, Entry 10: Pale yellow solid; m.p. 256-258 °C; IR (KBr, cm^{-1}): 3298, 2980, 1695, 1600, 1480, 1375, 1220, 1180; ^1H NMR (400 MHz, $CDCl_3$, ppm): δ: 7.18 (d, *J*= 8.8 Hz, 2H, Ar–H), 6.64 (d, *J*= 8.8 Hz, 2H, Ar–H), 6.09 (br s, 1H, NH), 4.99 (s, 1H), 3.64 (s, 3H), 2.90 (s, 6H), 2.39 (s, 3H), 2.17-2.34 (m, 4H), 1.09 (s, 3H), 0.98 (s, 3H).

Table 1, Entry 11: White solid; m.p. 250-252 °C; IR



Scheme 1. Synthesis of polyhydroquinoline derivatives.

(KBr, cm^{-1}): 3298, 2995, 1698, 1645, 1604, 1478, 1378, 1220, 1180; ^{1}H NMR (400 MHz, $CDCl_3$, ppm): δ: 7.26 (d, *J*= 8.4 Hz, 2H, Ar–H), 7.19 (d, *J* = 8.4 Hz, 2H, Ar–H), 6.01 (br s, 1H, NH), 5.09 (s, 1H), 4.08 (q, J= 7.2 Hz, 2H), 2.41 (s, 3H), 2.33-2.48 (m, 7H), 1.94-2.05 (m, 2H), 1.23 (t, *J* = 7.2 Hz, 3H).

Table 1, Entry 12: Pale yellow solid; m.p. 210-212 ^{o}C; IR (KBr, cm^{-1}): 3295, 2970, 1695, 1604, 1480, 1378, 1220, 1179; ^{1}H NMR (400 MHz, $CDCl_3$, ppm): δ: 7.24 (d, *J* = 8.8 Hz, 2H, Ar–H), 6.74-6.78 (m, 3H), 5.06 (s, 1H), 4.08 (q, *J* = 7.2 Hz, 2H), 3.75 (s, 3H), 2.29-2.42 (m, 7H) , 1.91-2.02 (m, 2H), 1.24 (t, *J* = 7.2 Hz, 3H).

Table 1, Entry 13: Yellow solid; m.p. 240-241 oC; IR (KBr, cm^{-1}): 3295, 2995, 1695, 1643, 1603, 1477, 1375, 1218, 1180; ^{1}H NMR (400 MHz, $CDCl_3$, ppm): δ: 7.23 (d, *J* = 0.8 Hz,1H), 6.23 (t, *J* = 2.8 Hz, 1H), 6.14 (br s, 1H, NH), 6.01(d, *J* = 2.8 Hz, 1H), 5.31 (s, 1H), 4.11-4.21 (m, 2H), 2.36-2.51 (m, 7H), 2.02-2.06 (m, 2H), 1.27 (t, *J* = 8.8 Hz, 3H).

Table 3, entry 8: White solid; m.p. 150-152 ^{o}C; IR (KBr, cm^{-1}): 3050, 2950, 2870, 1620, 1590, 1504, 1460, 1363, 1220, 1140, 1115, 1020, 817, 740 ^{1}H NMR (400 MHz, $CDCl_3$, ppm): δ: 8.05 (d, *J* = 8 Hz, 1H, Ar-H), 7. 78 (t, *J* = 10 Hz, 2H, Ar-H), 7.03-7.46 (m, 7H, ar-H), 5.70 (s, 1H), 2.76-2.79 (m, 1H), 2.53 (d, *J* = 45 Hz, 2H), 2.22-2.35 (m, 2H), 1.16 (s, 3H), 1.14 (s, 6H), 1.01 (s, 3H).

Table 3, entry 9: White solid; m.p. 198-199 ^{o}C; IR (KBr, cm^{-1}): 3070, 2956, 2931, 2300, 1650, 1618, 1595, 1500, 1460, 1360, 1220, 1190, 1140, 1020, 840, 805, 742; ^{1}H NMR (400 MHz, $CDCl_3$, ppm): δ: 7.82-7.86 (m, 3H, ArH), 7.41-7.49 (m, 6H, ArH), 7.37 (d, *J* = 8.8 Hz, 1H, ArH), 5.78 (s, 1H), 2.61 (s, 2H), 2.25 and 2.37 (AB system, *J* = 16 Hz, 2H), 1.15 (s, 3H), 0.97 (s, 3H).

Table 3, entry 10: White solid; m.p. 215-217 ^{o}C IR (KBr, cm^{-1}): 3070, 2956, 2931, 1640, 1594, 1505, 1460, 1370, 1220, 1187, 1140, 1020, 810, 740 ^{1}H NMR (400 MHz, $CDCl_3$, ppm): δ: 8.08 (d, *J*= 8 Hz, 1H, ArH), 7.67-7.86 (m, 6H, ArH), 7.50 (d, *J* = 8.4 Hz, 1H, ArH), 7.28-7.44 (m, 5H, ArH), 5.92 (s, 1H), 2.57 (d, *J* = 35.6 Hz, 2H), 2.32 and 2.36 (AB system, *J* = 16.4 Hz, 2H), 1.14 (s, 3H), 0.96 (s, 3H).

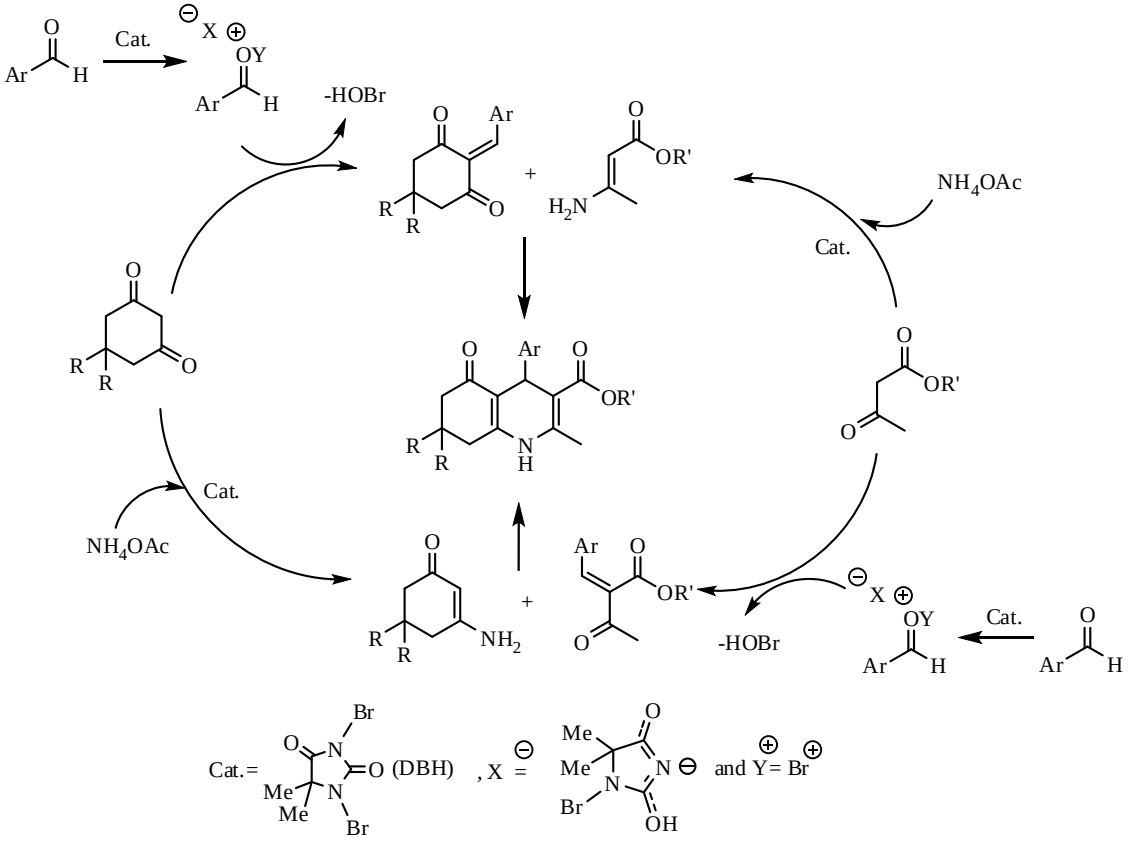
Table 3, entry 16: White solid; m.p. 220-222 ^{o}C; IR (KBr, cm^{-1}): 2950, 1640, 1585, 1480, 1367, 1265, 1220, 1180, 1020, 940, 810, 750; ^{1}H NMR (400 MHz, $CDCl_3$, ppm): δ: 6.66-8.02 (m, 10H, ArH), 5.78 (s, 1H), 3.75 (s, 3H), 2.05-2.74 (m, 6 H).

Table 3, entry 17: White solid; m.p. 216-217 oC; IR (KBr, cm^{-1}): 2950, 1640, 1617, 1590, 1510, 1370, 1220, 1180, 1140, 995, 820, 740; ^{1}H NMR (400 MHz, $CDCl_3$, ppm): δ: 8.04 (d, *J*= 8 Hz, 1H, ArH), 7.8 (t, *J* = 8.4 Hz, 2H, ArH), 7.36-7.48 (m, 3H, ArH), 7.28 (d, *J* = 8.4 Hz, 2H, ArH), 7.06 (d, *J* = 8 Hz, 2H, ArH), 5.76 (s, 1H), 2.05-2.84 (m, 7H), 1.17-1.19 (d, *J* = 5.2 Hz, 6H)

3. Results and Discussion

In recent years, use of bromo reagents in organic transformations, became an important part of our research program [52, 53]. Along this line, we have reported the applicability of 1,3-dibromo-5,5-dimethylhydantoin, as a cheap, stable and commercially available reagent, in the promotion of trimethylsilylation and tetrahydropyranylation of alcohols [54]. In continuation of this study we have found that this reagent is efficiently able to catalyze the synthesis of polyhydroquinoline derivatives via a one-pot four component condensation of aldehydes, alkyl acetoacetates, cyclic 1,3-dicarbonyl compounds and ammonium acetate (Scheme 1).

In order to find the best reaction conditions, we started our study on the synthesis of DPHs using DBH as the catalyst by a model reaction. Benzaldehyde reacted with ethylacetoacetate, 5,5-dimethyl-1,3-cyclohexanedione and ammonium acetate in the presence of various amounts of the catalyst. Different ratios of the substrates were also examined. The optimum amounts were found to be 1:1:1:1.1:0.1 for



Scheme 2. Mechanism of the Hantzsch reaction.

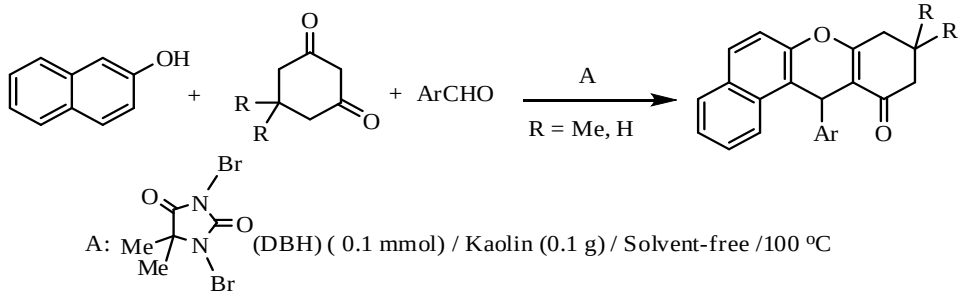
benzaldehyde, ethylacetoacetate,5,5-dimethyl-1,3-cyclohexanedione, ammonium acetate and the catalyst respectively. Next, the model reaction was performed in different solvents such as dichloromethane, acetonitrile and ethanol, and also in the absence of solvent. Our investigations clarified that the best result was obtained when the reaction was performed using 3 drops of EtOH at 70 ^{o}C.

In order to show the catalytic effect of DBH, the reaction of benzaldehyde, ethylacetoacetate, 5,5-dimethyl-1,3-cyclohexanedione and ammonium acetate was also carried out in the absence of the catalysts in 3 drops of EtOH, which result in only 56 % of the corresponding 4-substituted-1,4-dihydropyridine after 4 h. This result indicates that DBH is a highly efficient catalysts in the synthesis of 1,4-dihydropyridines.

After optimization of the reaction conditions and in order to show the general applicability of the method, different types of aldehydes were subjected to the same reaction under the determined conditions. As indicated in Table 1, in all cases the corresponding 1,4-dihydropyridines were obtained in good to excellent yields in appropriate times. To investigate the versatility of the selected method, the reaction of 1,3-cyclohexanedione was also carried out in the presence of DBH with various aldehydes under the selected conditions. It can be easily seen that in all cases, regardless of the substituent, the reaction gave

Table 2. Compared performance of various catalysts in the synthesis of 2,7,7-trimethyl-5-oxo-4-phenyl-1,4,5,6,7,8-hexahydroquinoline-3-carboxylic acid ethyl ester (Table 1, entry 1).

Entry	Catalyst	Conditions	Time (min)	Yield (%)	Reference
1	DBH	3 drops of EtOH/70 °C	65	87	This work
2	$Hf(NPf_2)_4$	$C_{10}F_{18}$/60 °C	3 h	95	17
3	$Yb(OTf)_3$	EtOH/r.t.	5 h	90	18
4	$Sc(OTf)_3$	EtOH/r.t.	4 h	93	19
5	HY-Zeolite	CH_3CN/r.t.	2 h	93	24
6	-	EtOH/r.t.	6.5 h	89	55



Scheme 3. Synthesis of 12-aryl-8,9,10,12-tetrahydrobenzo [a] xanthene-11-ones.

the products in good to high yields during relatively short reaction times. We have also found that the same results were obtained when methylacetoacetate is used in place of ethylacetoacetate. A plausible mechanism of the reaction is shown in Scheme 2. On the basis of this mechanism, the main role of the catalysts is the activation of aldehyde for nucleophilic attack via the coordination of Br^+ with oxygen [54].

Table 2, compares the efficiency of DBH with other catalysts in Hantzsch reaction. It is clear from Table 2 that the present method is simpler, more efficient, and less time consuming for the synthsis of polyhydroquinoline derivatives.

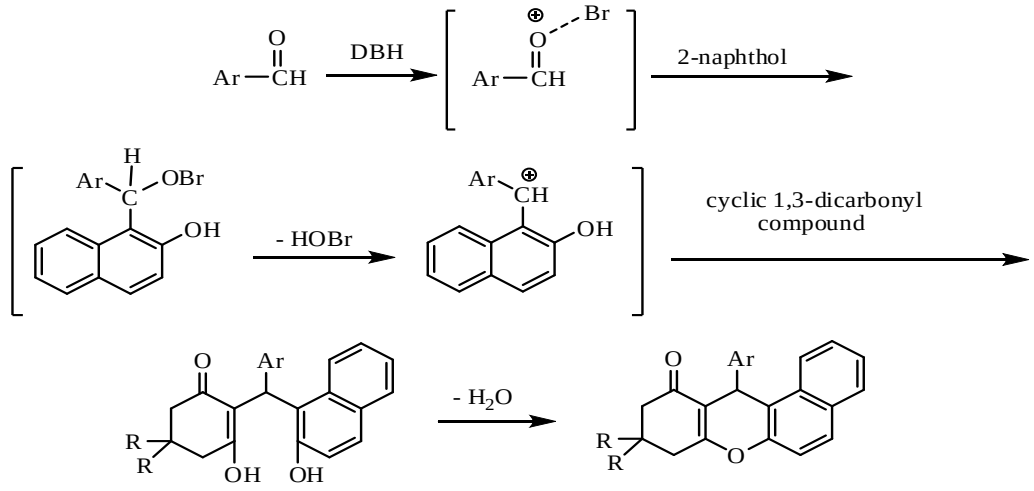
After the above mentioned studies, we were interested to extend the applicability of DBH in the promotion of the other types of the multi-component reactions, by studying the probable one-pot synthesis of 12-aryl-8,9,10,12-tetrahydrobenzo [a] xanthene-11-ones in the presence of this reagent (Scheme 3).

In order to optimize the reaction conditions, we have used DBH as a catalyst for the condensation of benzaldehyde, 2-naphthol and dimedone in the absence of solvent. A highly sticky reaction mixture was obtained with the formation of the desired product in low yield after several hours. Therefore, we studied the catalytic effect of DBH in the presence of ethanol, SiO_2 or Kaolin for the similar reaction. The best result was obtained by carrying out the reaction of benzaldeyhde (1 mmol), 2-naphthol (1 mmol) and dimedone (1.2 mmol) in the presence of 0.1 mmol of DBH and 0.1 g of Kaolin at 100 °C for 90 min in the absence of solvent (Table 3, entry 1) After optimization of the reaction conditions and in order to

Table 3. Synthesis of 12-aryl-8,9,10,12-tetrahydrobenzo[a]xanthene-11-one derivatives [a, b].

Entry	Aldehydes	R	Time(min)	Yield (%)
1	PhCHO	Me	90	90
2	4-BrC_6H_4CHO	Me	75	95
3	4-ClC_6H_4CHO	Me	100	90
4	4-FC_6H_4CHO	Me	80	95
5	4-$NO_2C_6H_4CHO$	Me	60	91
6	3-$NO_2C_6H_4CHO$	Me	60	95
7	4-MeC_6H_4CHO	Me	115	80
8	4-*iso*-Pr-C_6H_4CHO	Me	136	85
9	4-CNC_6H_4CHO	Me	80	98
10	2-Naphthaldehyde	Me	95	95
11	PhCHO	H	130	95
12	4-BrC_6H_4CHO	H	120	92
13	4-ClC_6H_4CHO	H	160	98
14	2-ClC_6H_4CHO	H	120	93
15	4-MeC_6H_4CHO	H	170	95
16	3-$MeOC_6H_4CHO$	H	150	95
17	4-*iso*-Pr-C_6H_4CHO	H	180	85

[a]The desired products were characterized by their physical data, comparison with authentic samples, and IR and NMR spectroscopy.
[b]Isolated yield



Scheme 4. Mechanism of the reaction.

show the general applicability of the method, different types of aldehydes were subjected to the same reaction under the determined conditions under the determined conditions. As shown in Table 3, the corresponding 12-aryl-8,9,10,12-tetrahydrobenzo [a] xanthene-11-ones derivatives were obtained during relatively short reaction times in good to excellent yields. It is notable that the electron property of the group on aromatic ring of aldehydes has a delicate effect on the reaction time. As shown in Table 3, aromatic aldehydes containing electron-withdrawing groups showed higher reactivity than those containing electron-donating groups. Because of the formation of unidentified products the method is not suitable for the synthesis of ATXOs from aliphatic aldehydes.

A plausible mechanism of the reaction is shown in Scheme 4, based on the reported pathway in literature [49, 54], our observations and obtained results.

In order to show the merit of this method, Table 4 compares the results obtained from the synthesis of ATXOs derivative of 4-chlorobenzaldehyde and 3-nitrobenzaldehyde by our method with some of those reported in literature

4. Conclusion

In conclusion, in this study, we have developed a simple and efficient method for the synthesis of 4-substituted-1,4-dihydropyridines and 12-aryl-8,9,10,12-tetrahydrobenzo [a] xanthene-11-ones in the presence of 1,3-dibromo-5,5-dimethylhydantoin. The present method has some valuable advantages such as short reaction times, mild reaction conditions, simple work-up and high yields of products, no side reactions, in combination with stability, availability, cheapness and efficiency of the catalysts which make this method a valid contribution to the existing processes in the field of 1,4-dihydropyridines and 12-aryl-8,9,10,12-tetrahydrobenzo [a] xanthene-11-ones synthesis.

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Table 4. Comparison of the results obtained from the synthesis of ATXOs derivative of 4-chlorobenzaldehyde and 3-nitrobenzaldehyde in the presence of various catalysts.

Entry	Catalyst	Time(min) / Yield [a]	Time(min) / Yield [b]	Reference
1	$Sr(OTf)_2$	300/88	300/86	43
2	Proline Triflate 10 mol%	300/76	330/72	59
3	$NaHSO_4 \cdot SiO_2$	300/91	--	44
4	BNBTS	93/97	95/87	49
5	DBH	100/90	60/95	This article

[a]Times and yields refer to ATXOs synthesis from 4-chlorobenzaldehyde.
[b]Times and yields refer to ATXOs synthesis from 3-nitrobenzaldehyde.

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