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Mild and green synthesis of tetrahydrobenzopyran, pyranopyrimidinone and polyhydroquinoline derivatives and DFT study on product structures

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Abstract The multicomponent synthesis of 4*H*-benzo[*b*]pyran, pyranopyrimidinone and polyhydroquinoline derivatives has been achieved using catalytic amounts of calcium hydrogen phosphate in aqueous medium as a green, inexpensive and environmentally benign media. The process is operationally simple and has good to excellent yields. Moreover, computational parameters of some products were obtained using density functional theory at the B3LYP/6-311++G(*d*,*p*) basis set and correlated to experimental results.

Keywords Green synthesis · Benzopyran · Pyranopyrimidinone · DFT study

Introduction

Environmentally benign and clean synthetic procedures have great importance in organic syntheses. Reactions in solvent-free or aqueous media are environmentally safe, devoid of any carcinogenic effects, have a simple work up and are especially important in industry. Thus, development of multicomponent reactions (MCRs) without the use of any harmful organic solvents and catalysts has become the goal of present day chemical reactions [1].

Tetrahydrobenzo[*b*]pyran, pyranopyrimidinone and polyhydroquinoline derivatives are an important class of heterocyclic drugs and pharmaceuticals, and are widely used as antiallergic, antibacterial, antifungal, diuretic, spasmolytic, hepatoprotective, vasodilator, bronchodilator, antiatherosclerotic, antidiabetic, antitumor, antihypertensive, antimalarial and antianaphylactic agents [2–8]. Numerous methods have been reported for the synthesis of these heterocycles [9–19]. However,

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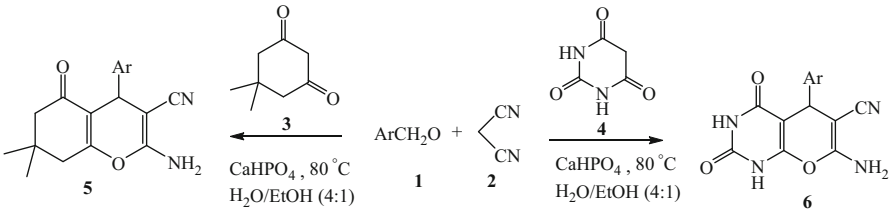
some of these methods have drawbacks, such as long reaction times, use of stoichiometric and/or relatively expensive reagents, low yields, harsh reaction conditions, effluent pollution and tedious workup procedures. Because of the drawbacks mentioned above, the search for improved and less hazardous conditions for the synthesis of these compounds has prime importance.

Hydrogen phosphate slats are inexpensive, easily available and safe salts that are used in some organic transformations [20–24]. As a continuation of our research devoted to the development of green organic chemistry and one-pot multicomponent reactions (MCRs) for the synthesis of various heterocyclic compounds [25, 26] and our interest in computational chemistry, herein we wish to report an efficient and green procedure for the preparation of 4*H*-benzo[*b*]pyrans, pyrano[2,3-*d*]pyrimidinones and polyhydroquinolines via a domino Knoevenagel cyclocondensation reaction using calcium hydrogen phosphate as an efficient and inexpensive catalyst in aqueous medium, and theoretical study on product structures (Schemes 1, 2).

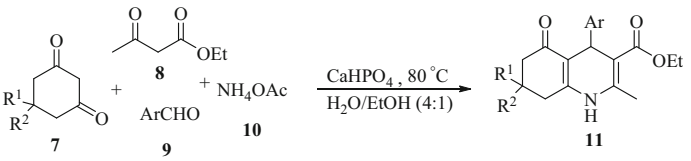
Results and discussion

At first, we optimized reaction condition using various solvent and hydrogen phosphate salts at different temperatures. For optimization benzaldehyde, dimedone and malononitrile were chosen as a model reaction and various conditions were evaluated (Scheme 3). The best reaction condition for this reaction was 10 wt% $CaHPO_4$ as a catalyst, Water/ethanol (4:1) as a green solvent, 2 h time and 80 °C (Table 1, entry 12). To determine the efficiency of catalyst, the model reaction was carried out in the absence of catalyst and it was revealed that the reaction was not completed in the absence of catalyst (Table 1, entry 14). The reaction is clean and efficient, and the experimental procedure is very simple. This method does not require high temperature. Moreover, the catalyst can be conveniently handled and also recovered and reused for at least three times without loss of its activity (Table 1, entry 12).

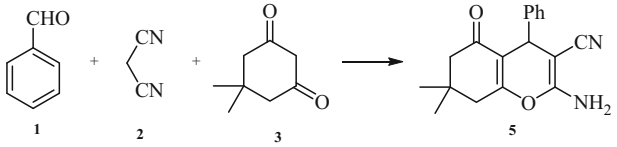
We used this optimized condition for the synthesis of tetrahydrobenzo[*b*]pyran, pyrano[2,3-*d*]pyrimidinone and polyhydroquinoline derivatives. The various aromatic aldehydes bearing electron-donating and electron-withdrawing substituent underwent the condensation with malononitrile and diketone smoothly to afford a wide range of desired products in good yields. The results are indicated in Tables 2, 3 and 4.



Scheme 1 The efficient synthesis of tetrahydrobenzopyran and pyranopyrimidinone derivatives



Scheme 2 The efficient synthesis of polyhydroquinolines



Scheme 3 The model reaction for optimization of reaction condition

Table 1 Optimization of reaction condition

Entry	Solvent	Catalyst	Temp. (°C)[b]	Yield (%)[a]
1	H_2O	$CaHPO_4$ (20 %)	25	N.C. [c]
2	H_2O	$CaHPO_4$ (20 %)	80	N.C.
3	CH_3OH	$CaHPO_4$ (20 %)	Reflux	N.C.
4	$CH_3CH_2CH_2OH$	$CaHPO_4$ (20 %)	Reflux	N.C.
5	$CHCl_3$	$CaHPO_4$ (20 %)	Reflux	N.C.
6	CH_3CN	$CaHPO_4$ (20 %)	Reflux	N.C.
7	DMF	$CaHPO_4$ (20 %)	Reflux	N.C.
8	Toluene	$CaHPO_4$ (20 %)	Reflux	N.C.
9	C_2H_5OH	$CaHPO_4$ (20 %)	Reflux	84
10	H_2O/EtOH (4:1)	$CaHPO_4$ (20 %)	25	50
11	H_2O/EtOH (4:1)	$CaHPO_4$ (20 %)	80	92
12	H_2O/EtOH (4:1)	$CaHPO_4$ (10 %)	80	91, 89, 90[d]
13	H_2O/EtOH (1:1)	$CaHPO_4$ (10 %)	80	90
14	H_2O/EtOH (4:1)	None	Reflux	N.C.
15	H_2O/EtOH (4:1)	$(NH_4)_2HPO_4$ (20 %)	80	N.C.
16	H_2O/EtOH (4:1)	$NaHPO_4$ (20 %)	80	N.C.
17	H_2O/EtOH (4:1)	$KHPO_4$ (20 %)	80	N.C.

N.C. means: The reaction was not completed

[a] Isolated yields

[b] All reactions carried out in 2 h

[c] Not completed, as indicated by TLC

[d] Catalyst reused for three consecutive reactions

A possible explanation for the mechanism of the one-pot reaction between aldehyde, malononitrile and dimedone or barbituric acid in the presence of $CaHPO_4$, is presented in Scheme 4. We suggest that $CaHPO_4$ is an effective catalyst for the

Table 2 Synthesis of tetrahydrobenzo[*b*]pyrans in green media

Entry	ArCHO	Product	M.P (°C)	Yield (%)[a]
1	C_6H_5–	5a	226–228	91
2	4-MeO–C_6H_4–	5b	202–205	90
3	4-$(Me)_2N$–C_6H_4–	5c	224–226	95
4	4-Cl–C_6H_4–	5d	212–215	92
5	3-NO_2–C_6H_4–	5e	210–212	90
6	2,4-Cl_2–C_6H_3–	5f	182–184	93
7	4-Br–C_6H_4–	5g	204–206	91
8	3-Cl–C_6H_4–	5h	228–230	89
9	2-NO_2–C_6H_4–	5i	223–226	91
10	3-OH–C_6H_4–	5j	230–233	91

[a] Yields refer to isolated products

Table 3 Synthesis of pyrano[2,3-*d*] pyrimidinones in green media

Entry	ArCHO	Product	M.P (°C)	Yield (%)[a]
1	C_6H_5–	6a	226–228	89
2	4-Cl–C_6H_4–	6b	212–215	92
3	3-NO_2–C_6H_4–	6c	270–272	90
4	3-Cl–C_6H_4–	6d	239–241	87
5	2,4-Cl_2–C_6H_3–	6e	242–245	93
6	4-NO_2–C_6H_4–	6f	241–243	91
7	4-Br–C_6H_4–	6g	226–229	91

[a] Yields refer to isolated products

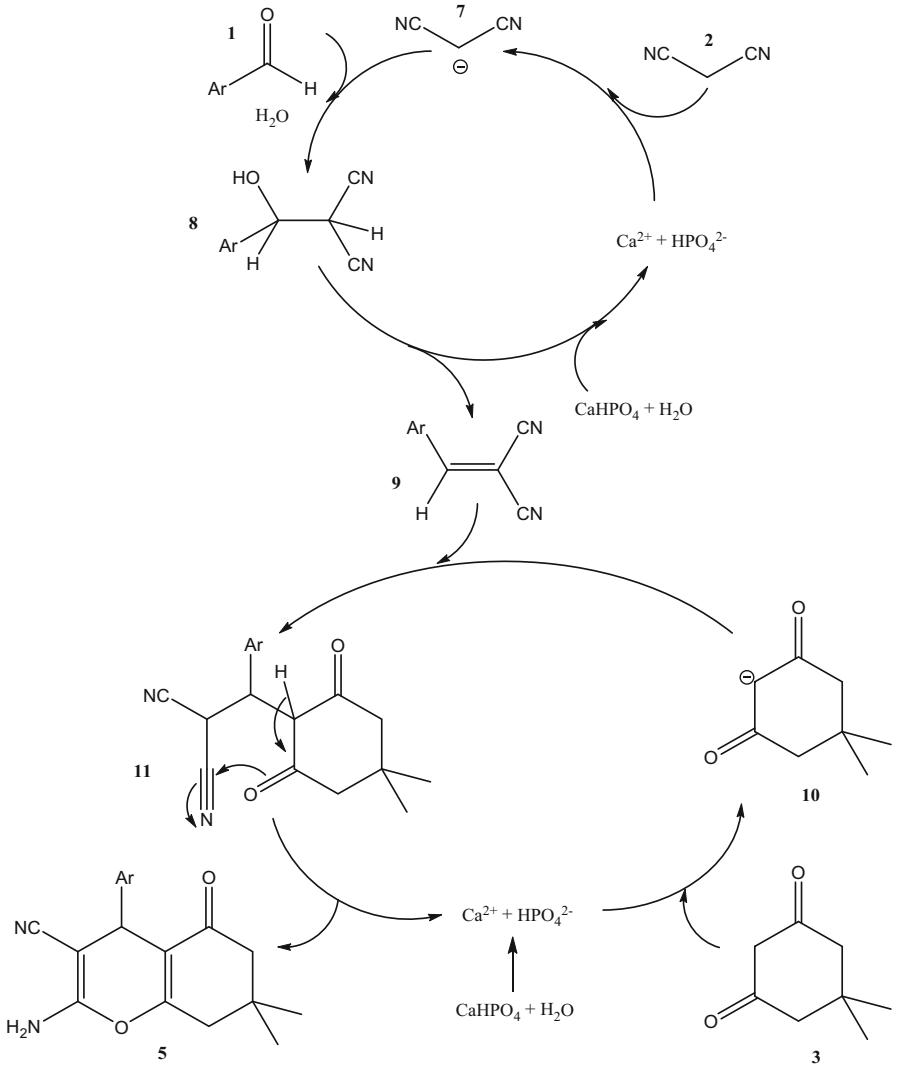
Table 4 Synthesis of polyhydroquinolines in green media

Entry	ArCHO	R^1	R^2	Product	M.P (°C)	Yield (%)[a]
1	C_6H_5–	H	H	11a	238–240	89
4	4-Cl–C_6H_4–	H	H	11b	235–238	92
5	4-Me–C_6H_4–	H	H	11c	242–245	90
5	3-NO_2–C_6H_4–	H	H	11d	201–203	91
5	C_6H_5–	CH_3	CH_3	11e	203–205	90
2	4-MeO–C_6H_4–	CH_3	CH_3	11f	252–255	91
3	4-$(Me)_2N$–C_6H_4–	CH_3	CH_3	11g	260–263	91
4	4-Cl–C_6H_4–	CH_3	CH_3	11h	242–245	90
5	3-NO_2–C_6H_4–	CH_3	CH_3	11i	178–180	88
6	2,4-Cl_2–C_6H_3–	CH_3	CH_3	11j	240–243	92
7	4-Br–C_6H_4–	CH_3	CH_3	11k	253–255	91
8	3-NO_2–C_6H_4–	CH_3	CH_3	11l	180–183	88
9	2-Cl–C_6H_4–	CH_3	CH_3	11m	203–205	91
10	4-Me–C_6H_4–	CH_3	CH_3	11n	260–263	93

[a] Yields refer to isolated products

formation of malonate anion 7 and facilitates Knoevenagel condensation between aryl aldehyde 1 and malononitrile 2, which proceeds via intermediate 7 and produces intermediate 8, which after dehydration produces olefin 9. $CaHPO_4$ also catalyzes the generation of a proposed enolate intermediate 10, which is formed from dimedone 3. Enolate intermediate 10 adds to olefin 9 to generate product 5, after intramolecular cyclization, proton transfer and tautomerization of intermediate 11 (Scheme 4).

A DFT study has been carried out on selected molecules of desired products **5a**, **6g** and **11a** at 6-311++G(*d*,*p*) basis set by assuming Cs point group symmetry.



Scheme 4 The proposed mechanism for the reaction in the presense of $CaHPO_4$

Also, the natural bond orbital (NBO) has been done on the optimized structures at B3LYP/6-311++G(*d,p*) level. The GIAO/DFT calculations were performed to obtain computational ^{13}C chemical shifts for products at B3LYP level with 6-311++G(*d,p*) basis set. The optimized structures bearing charge density on atoms

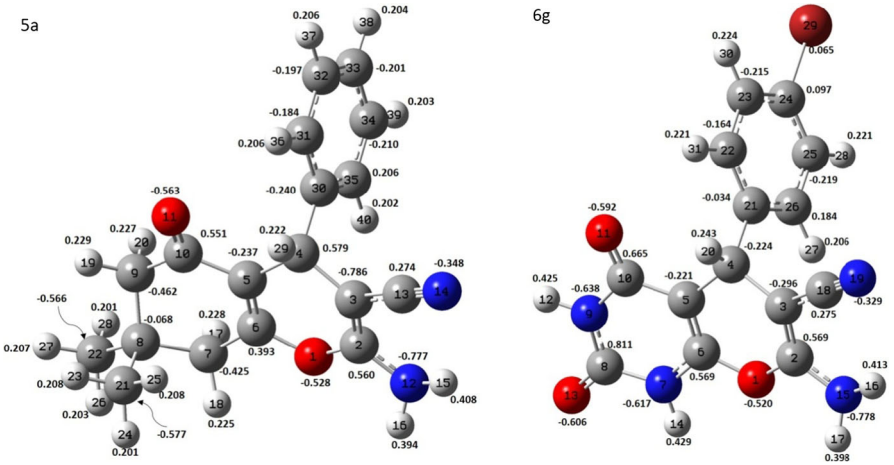


Fig. 1 Molecular structure of products **5a** and **6g**, along with numbering and charge density of atoms

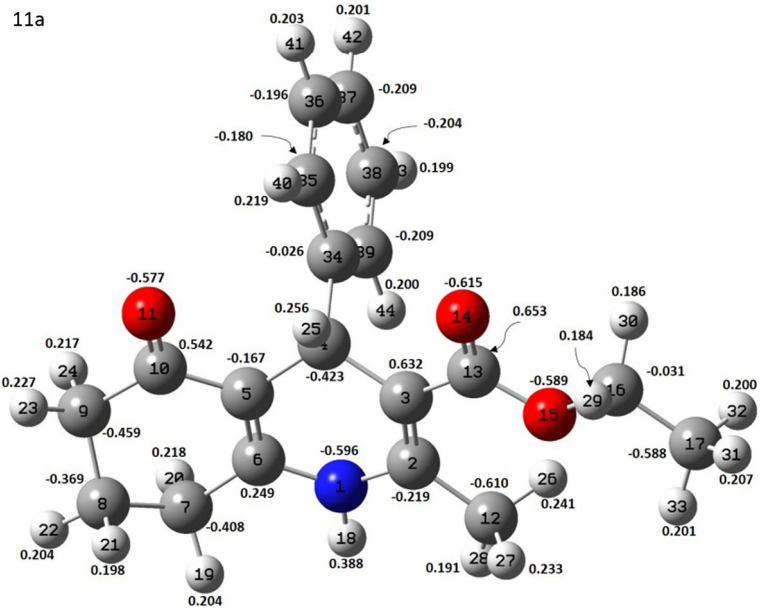


Fig. 2 Molecular structure of product **11a**, along with numbering and charge density of atoms

Table 5 Calculated optimized parameter values of product **5a**

Bond label	Bond length (Å)	Bond label	Bond length (Å)	Bond label	Bond length (Å)
O1–C2	1.368	C7–H17	1.098	C9–H20	1.099
C2–C3	1.358	C7–H18	1.094	C10–O11	1.218
C2–N12	1.366	C7–C8	1.546	C10–C5	1.480
N12–H15	1.010	C8–C21	1.542	C30–C31	1.396
N12–H16	1.010	C21–H23	1.093	C31–H36	1.084
C3–C13	1.415	C21–H24	1.094	C31–C32	1.394
C13–N14	1.160	C21–H25	1.093	C32–H37	1.084
C3–C4	1.521	C8–C22	1.537	C32–C33	1.393
C4–H29	1.093	C22–H26	1.095	C33–H38	1.084
C4–C38	1.534	C22–H27	1.094	C33–C34	1.395
C4–C5	1.516	C22–H28	1.094	C34–H39	1.084
C5–C6	1.344	C8–C9	1.544	C34–C35	1.393
C6–O1	1.378	C9–C10	1.520	C35–H40	1.085
C6–C7	1.498	C9–H19	1.092	C35–C30	1.399

Table 6 Calculated NBO charges on atoms of product **5a** in the gas phase

Atom	Charge	Atom	Charge	Atom	Charge
O1	−0.528	H15	0.408	H29	0.222
C2	0.560	H16	0.394	C30	−0.240
C3	−0.786	H17	0.228	C31	−0.184
C4	0.579	H18	0.225	C32	−0.197
C5	−0.237	H19	0.229	C33	−0.201
C6	0.393	H20	0.227	C34	−0.201
C7	−0.425	C21	−0.577	C35	−0.210
C8	−0.068	C22	−0.566	H36	0.212
C9	−0.462	H23	0.208	H37	0.206
C10	0.551	H24	0.201	H38	0.204
O11	−0.563	H25	0.208	H39	0.203
N12	−0.777	H26	0.203	H40	0.202
C13	0.274	H27	0.207		
N14	−0.348	H28	0.201		

are depicted in Figs. 1 and 2. Bond orders, charge density on all atoms and ^{13}C-NMR data are indicated in Tables 5, 6, 7, 8, 9, 10, 11, 12, and 13. Computational parameters obtained for product **5a** showed that in 4*H*-benzo[*b*]pyrans, the C5-C6 bond length is shorter than that of the C2–C3 bond that referred to lone pair electron sharing from 2-amino group to the C2–C3 double bond and electron demanding of the 3-cyano substituent (Table 5). On the other hand, NBO analysis indicates maximum positive charge density on C2 and highly negative charge density on C3 that confirmed the resonance between NH_2 moiety and C2–C3 double bond (Table 6). The normal ^{13}C-NMR signals of olefinic carbons often appear in the

range of 110–140 ppm, but GIAO/DFT calculated ^{13}C-NMR predicted the C3 signal to appear in high magnetic field, and C2 signal to appear in low magnetic field, which is in consistent with experimental data and confirmed the highly negative charge density on C3 and the positive charge on C2 (Table 7). Also, a

Table 7 Calculated ($\delta_{Theo.}$) and experimental ($\delta_{Exp.}$) ^{13}C NMR chemical shifts for product **5a**

Atom	Experimental	GIAO/DFT B3LYP/6-311++G(*d,p*)		$\delta_{Exp}-\delta_{Theo}$
		Gas phase	DMSO	
C21	26.33	25.542	25.091	1.209
C22	27.62	32.019	31.046	−3.446
C8	31.27	38.382	39.143	−7.943
C4	35.04	40.77	40.257	−5.257
C7	39.83	43.266	42.812	−3.012
C9	49.91	53.958	54.678	−4.778
C3	60.33	66.698	62.925	−2.625
C13	113.07	119.548	119.605	−6.605
C5	118.41	120.804	124.274	−5.874
C33	126.11	131.575	131.659	−5.559
C32	126.65	132.536	132.191	−5.591
C34	126.65	132.732	133.664	−7.064
C35	127.52	132.773	133.693	−6.193
C31	127.52	136.555	135.133	−7.633
C30	143.21	150.402	151.616	−8.416
C2	157.73	164.566	168.277	−10.577
C6	161.37	166.948	171.635	−10.335
C10	195.17	200.905	205.622	−10.522
$\delta_{Exp} = 0.957\ \delta_{Theo} - 1.606$				$R^2 = 0.998$

Table 8 Calculated optimized parameter values of product **6g**

Bond label	Bond length (Å)	Bond label	Bond length (Å)	Bond label	Bond length (Å)
O1–C2	1.378	C5–C6	1.348	C22–H31	1.084
C2–C3	1.357	C6–N7	1.370	C22–C23	1.394
C2–N15	1.362	N7–H14	1.010	C23–H30	1.082
N15–H16	1.010	N7–C8	1.395	C23–C24	1.390
N15–H17	1.010	C8–O13	1.210	C24–Br29	1.918
C3–C18	1.416	C8–N9	1.381	C24–C25	1.392
C18–C19	1.159	N9–H12	1.012	C25–H28	1.082
C3–C4	1.523	N9–C10	1.411	C25–C26	1.392
C4–H20	1.094	C10–O11	1.216	C26–H27	1.085
C4–C5	1.512	C4–C21	1.534		
C5–C10	1.458	C21–C22	1.396		

Table 9 Calculated NBO charges on atoms of product **6g** in the gas phase

Atom	Charge	Atom	Charge	Atom	Charge
O1	−0.520	H12	0.425	C23	−0.215
C2	0.569	O13	−0.606	C24	0.097
C3	−0.296	H14	0.429	C25	−0.219
C4	−0.224	N15	−0.778	C26	0.184
C5	−0.221	H16	0.413	H27	0.206
C6	0.569	H17	0.398	H28	0.221
N7	−0.617	C18	0.275	Br29	0.065
C8	0.811	N19	−0.329	H30	0.224
N9	−0.638	H20	0.243	H31	0.221
C10	0.665	C21	−0.034		
O11	−0.592	C22	−0.164		

Table 10 Calculated ($\delta_{Theo.}$) ^{13}C NMR chemical shifts for the compound **6g**

Atom	Experimental	GIAO/DFT B3LYP/6-311++G(*d,p*)		$\delta_{Exp}-\delta_{Theo}$
		Gas phase	DMSO	
C4	32.25	40.641	40.134	−7.884
C3	58.38	68.680	64.581	−6.201
C5	87.97	96.618	96.638	−8.668
C18	118.95	118.856	123.661	−4.711
C26	119.73	132.390	134.320	−14.59
C23	129.63	136.485	135.788	−6.158
C25	129.63	136.855	136.836	−7.206
C22	131.07	137.487	137.367	−6.297
C21	131.07	146.845	144.655	−13.585
C24	143.52	146.960	149.141	−5.621
C8	149.44	149.019	144.655	4.785
C6	152.32	154.593	156.984	−4.654
C10	157.60	163.918	165.844	−8.244
C2	162.40	163.979	167.993	−5.593
$\delta_{Exp} = 1.012\ \delta_{Theo} - 8.369$				$R^2 = 0.986$

weak resonance has been found among O1–C6–C5 atoms, which gives a slight negative charge density on C5 (Table 6). The same results have been seen in pyranopyrimidinone **6g** (Tables 8, 9, 10).

Computational parameters obtained for product **11a** showed that there is no difference between C5–C6 and C2–C3 bond lengths, and they are approximately identical. NBO analysis indicates a slightly negative charge density on C5 due to weak resonance between the N1 atom and the C5–C6 double bond. The effective resonance in the ester functional group among O15 and the C13–O14 double bond and the highly negative charge density on O14 atom can be a good reason for

Table 11 Calculated optimized parameter values of product **11a**

Bond label	Bond length (Å)	Bond label	Bond length (Å)	Bond label	Bond length (Å)
N1–C2	1.395	C7–H19	1.096	C17–H31	1.093
N1–H18	1.008	C7–H20	1.099	C17–H32	1.093
C2–C3	1.359	C7–C8	1.532	C17–H33	1.093
C2–C12	1.508	C8–H21	1.095	C34–C35	1.398
C12–H26	1.088	C8–H22	1.094	C35–H40	1.083
C12–H27	1.092	C8–C9	1.530	C35–C36	1.394
C12–H28	1.094	C9–H23	1.092	C36–H41	1.085
C3–C4	1.527	C9–H24	1.098	C36–C37	1.394
C4–H25	1.090	C9–C10	1.525	C37–H42	1.084
C3–C13	1.475	C10–O11	1.222	C37–C38	1.394
C4–C34	1.535	C13–O14	1.213	C38–H43	1.085
C4–C5	1.520	C13–O15	1.361	C38–C39	1.394
C5–C6	1.356	O15–C16	1.448	C39–H44	1.085
C5–C10	1.469	C16–H29	1.092	C39–C34	1.400
C6–N1	1.383	C16–H30	1.092		
C6–C7	1.506	C16–C17	1.516		

Table 12 Calculated NBO charges on atoms of product **11a** in the gas phase

Atom	Charge	Atom	Charge	Atom	Charge
N1	−0.596	C16	−0.031	H31	0.207
C2	−0.219	C17	−0.588	H32	0.200
C3	0.632	H18	0.388	H33	0.201
C4	−0.423	H19	0.204	C34	−0.026
C5	−0.167	H20	0.218	C35	−0.180
C6	0.249	H21	0.198	C36	−0.196
C7	−0.408	H22	0.204	C37	−0.209
C8	−0.369	H23	0.227	C38	−0.204
C9	−0.459	H24	0.217	C39	−0.209
C10	0.542	H25	0.256	H40	0.219
O11	−0.577	H26	0.241	H41	0.203
C12	−0.610	H27	0.233	H42	0.201
C13	0.653	H28	0.191	H43	0.199
O14	−0.615	H29	0.184	H44	0.200
O15	−0.589	H30	0.186		

inefficient resonance in N1–C2–C3 bonds. The calculated ^{13}C-NMR signal of olefinic carbons in polyhydroquinoline in contrast to previous products (**5a** and **6g**) has not appeared in high field (Table 13), and good correlation has been found among theoretical and experimental data.

Table 13 Calculated ($\delta_{Theo.}$) 13C NMR chemical shifts for the compound **11a**

Atom	Experimental	GIAO/DFT B3LYP/6-311++G(*d,p*)		$\delta_{Exp}-\delta_{Theo}$
		Gas phase	DMSO	
C17	14.10	14.483	13.946	0.154
C12	19.26	24.417	24.257	−4.997
C8	21.50	26.645	26.636	−5.136
C7	27.25	31.484	30.945	−3.695
C9	33.48	39.83	40.994	−7.514
C4	36.88	41.59	41.697	−4.817
C16	58.80	63.852	64.431	−5.631
C3	105.85	113.158	110.477	−4.627
C5	113.54	121.331	119.148	−5.608
C37	124.98	130.232	130.391	−5.411
C36	128.05	131.928	131.437	−3.387
C38	128.25	132.027	133.096	−4.846
C39	128.05	132.036	133.717	−5.667
C35	128.25	137.781	134.1	−5.850
C2	143.05	147.497	153.716	−10.666
C6	147.00	151.534	155.261	−8.261
C34	148.85	154.203	158.416	−9.566
C13	167.05	171.16	173.626	−6.576
C10	195.20	197.717	202.67	−7.470
$\delta_{Exp} = 0.977\ \delta_{Theo} - 3.356$				$R^2 = 0.999$

Experimental method

Chemicals were purchased from Merck and Acros chemical companies. All of the products are known compounds and were identified by their physical and spectroscopic data reported in literature. Melting points were measured by using capillary tubes on an electro-thermal digital apparatus and are uncorrected. The progress of reactions was monitored by thin-layer chromatography (TLC) using *n*-hexane/EtOAc (3:1 v/v) as eluent. IR spectra were recorded as KBr disc on a galaxy series FT-IR 5030 spectrometer. NMR spectra were recorded on a 300 MHz Bruker spectrometer in DMSO-d_6 with TMS as an internal standard.

Theoretical calculations were performed using the GAUSSIAN 98 package and the Gauss-View molecular visualization program on a personal computer [27]. The geometry optimization of the products and corresponding energy and harmonic vibrational frequencies were calculated at 6-311++G(*d,p*) basis set by assuming Cs point group symmetry [28, 29]. The absence of imaginary frequency verified that optimized geometry for the title molecule was a true minimum on the potential energy surface at their respective levels of theory. The natural bond orbital (NBO) technique was performed on the optimized structures at B3LYP/6-311++G(*d,p*)

level [30]. The GIAO/DFT method at B3LYP level with 6-311++G(*d,p*) basis set was used for ^{13}C chemical shifts predictions [31, 32].

General procedure for the synthesis of tetrahydrobenzo[b]pyrans

A mixture of an aromatic aldehyde (1 mmol), malononitrile (1 mmol), dimedone (1 mmol) and $CaHPO_4$ (10 mol%) in 5 ml H_2O/EtOH (4:1) was heated at 80 °C with stirring for an appropriate time. After completion of the reaction was confirmed by TLC, for catalyst removal, 10 ml ethanol was added and stirred for 5 min and filtered. Water (5–10 ml) was added to filtration and the mixture cooled in a fridge to give the precipitate. The solid product was filtered and washed with cold water (2 × 10 ml). The pure product was obtained by recrystallization from ethanol:water (4:1).

General procedure for the synthesis of pyrano[2,3-d]pyrimidinones

A mixture of barbituric acid (1 mmol), malononitrile (1 mmol), aromatic aldehyde (1 mmol), and $CaHPO_4$ (10 mol%) was added to a round bottomed flask and 5 ml H_2O/EtOH (4:1) was added to it and heated on a hot plate at 80 °C. After completion of the reaction was confirmed by TLC, for catalyst removal, 10 ml ethanol was added and stirred for 5 min and filtered. Water (5–10 ml) was added to filtration and the mixture cooled in a fridge to give the precipitate. The solid product was filtered and washed with cold water (2 × 10 ml). The pure product was obtained by recrystallization from ethanol:water (4:1).

General procedure for the synthesis of polyhydroquinolines

A mixture of dimedone (1 mmol), ethylacetoacetate(1 mmol), aromatic aldehyde (1 mmol), ammonium acetate (1.2 mmol) and $CaHPO_4$ (10 mol%) was added to a round bottomed flask and 5 ml H_2O/EtOH (4:1) was added to it and heated on a hot plate at 80 °C. After completion of the reaction was confirmed by TLC, for catalyst removal, 10 ml ethanol was added and stirred for 5 min and filtered. Water (5–10 ml) was added to filtration and the mixture cooled in a fridge to give the precipitate. The solid product was filtered and washed with cold water (2 × 10 ml). The pure product was obtained by recrystallization from ethanol:water (4:1).

Physical and spectroscopic data for selected compounds

Compound **5a** (Table 2) IR (KBr) (ν_{max}): 3393, 3317, 3185, 2958, 2196, 1687, 1652, 1367 cm^{-1}; ^1H-NMR (300 MHz, DMSO-d_6): δH: 0.94 (3H, s, CH_3), 1.04 (3H, s, CH_3), 2.08 (1H, d, $J = 16.0$ Hz, H(C-6)), 2.23 (1H, d, $J = 16.0$ Hz, H(C-6)), 2.50 (2H, m, CH_2), 4.11 (1H, s, H-4), 7.06 (2H, br s, NH_2), 7.19 (3H, m, H_{Ar}), 7.33 (2H, m, H_{Ar}) ppm; ^{13}C-NMR (75 MHz, DMSO-d_6) δC: 26.33 (C21), 27.62 (C22), 31.27 (C8), 35.04 (C-4), 39.83 (C7), 49.91 (C9), 60.33 (C3–CN), 113.07 (C5), 118.41 (CN), 126.11 ($\underline{C}H_{Ar}$), 126.65 (2$\underline{C}H_{Ar}$), 127.52 (2$\underline{C}H_{Ar}$), 143.21 (C6),

157.73 (C2–NH_2), 161.37 (C_{Ar}), 195.17 (C=O) ppm; Anal. Calcd. for $C_{18}H_{18}N_2O_2$: C, 73.45; H, 6.16; N, 9.52. Found: C, 73.61; H, 6.31; N, 9.41.

Compound **5c** (Table 2) IR (KBr) (ν_{max}): 3381, 3321, 3209, 2962, 2191, 1682, 1656, 1367 cm^{-1}; ^{1}H-NMR (300 MHz, DMSO-d_6): δH: 0.97 (3H, s, CH_3), 1.06 (3H, s, CH_3), 2.10 (1H, d, $J = 16.0$ Hz, H(C-6)), 2.27 (1H, d, $J = 16.0$ Hz, H(C-6)), 2.47–2.55 (2H, m, CH_2), 2.87 (6H, s, –$N(Me)_2$), 4.06 (1H, s, H-4), 6.66 (2H, d, $J = 8.7$ Hz, H_{Ar}), 6.95 (2H, br s, NH_2), 6.97 (2H, d, $J = 8.7$ Hz, H_{Ar}) ppm; Anal. Calcd. for $C_{20}H_{23}N_3O_2$: C, 71.19; H, 6.87; N, 12.45. Found: C, 71.33; H, 6.75; N, 12.33.

Compound **5f** (Table 2) IR (KBr) (ν_{max}): 3533, 3364, 3153, 2966, 2193, 1685, 1658, 1367 cm^{-1}; ^{1}H-NMR (300 MHz, DMSO-d_6): δH: 1.00 (3H, s, CH_3), 1.06 (3H, s, CH_3), 2.11 (1H, d, $J = 16.0$ Hz, H(C-6)), 2.27 (1H, d, $J = 16.0$ Hz, H(C-6)), 2.47–2.61 (2H, m, CH_2), 4.70 (1H, s, H-4), 7.15 (2H, br s, NH_2), 7.25 (1H, d, $J = 8.4$ Hz, H_{Ar}), 7.39 (1H, d, $J = 8.4$ Hz, H_{Ar}), 7.56 (1H, s, H_{Ar}) ppm; ^{13}C-NMR (75 MHz, DMSO-d_6): δC: 19.0, 27.4, 28.8, 32.2, 33.1 (C7), 50.3 (C9), 56.5 (C3–CN), 111.8 (C5), 119.5 (CN), 128.1 (C_{Ar}), 129.2 (C_{Ar}), 131.9 (C_{Ar}), 132.2 (C_{Ar}), 133.5 (C_{Ar}), 141.2 (C6), 159.1 (C2–NH_2), 163.8 (C_{Ar}), 196.1 ppm; Anal. Calcd. for $C_{18}H_{16}Cl_2N_2O_2$: C, 59.52; H, 4.44; N, 7.71. Found: C, 59.79; H, 4.56; N, 7.63.

Compound **5g** (Table 2) IR (KBr) (ν_{max}): 3398, 3319, 3211, 2966, 2191, 1683, 1656, 1369 cm^{-1}; ^{1}H-NMR (300 MHz, DMSO-d_6): δH: 0.97 (3H, s, CH_3), 1.06 (3H, s, CH_3), 2.12 (1H, d, $J = 16.0$ Hz, H(C-6)), 2.28 (1H, d, $J = 16.0$ Hz, H(C-6)), 2.54 (2H, m, CH_2), 4.21 (1H, s, H-4), 7.13 (2H, br s, NH_2), 7.15 (2H, d, $J = 8.5$ Hz, H_{Ar}), 7.50 (2H, d, $J = 8.5$ Hz, H_{Ar}) ppm; Anal. Calcd. for $C_{18}H_{17}BrN_2O_2$: C, 57.92; H, 4.59; N, 7.51. Found: C, 58.11; H, 4.71; N, 7.43.

Compound **6e** (Table 3) IR (KBr) (ν_{max}): 3389, 3305, 3184, 3078, 2193, 1718, 1676, 1410, 1282 cm^{-1}; ^{1}H-NMR (300 MHz, DMSO-d_6): δH: 4.75 (1H, s, H-5), 7.25 (2H, br s, NH_2), 7.38 (2H, s, H_{Ar}), 7.57 (1H, s, H_{Ar}), 11.13 (1H, br s, NH), 12.17 (1H, br s, NH) ppm; ^{13}C-NMR (75 MHz, DMSO-d_6): δC: 32.91 (C4), 56.76 (C3–CN), 87.22 (C5), 118.74 (C≡N), 127.66 ($\underline{C}H_{Ar}$), 128.81 ($\underline{C}H_{Ar}$), 132.03 ($\underline{C}H_{Ar}$), 133.23 (C_{Ar}–Cl), 140.05 (C_{Ar}–Cl), 149.62 (C6), 152.87 (C=O), 152.90 (C2–NH_2), 157.94 (C=O), 162.41 (C_{Ar}) ppm; Anal. calcd. for $C_{14}H_8Cl_2N_4O_3$: C, 47.89; H, 2.30; N, 15.96. Found: C, 47.72; H, 2.41; N, 15.85.

Compound **6g** (Table 3) IR (KBr) (ν_{max}): 3391, 3302, 3188, 3072, 2197, 1718, 1674, 1408, 1280 cm^{-1}; ^{1}H-NMR (DMSO-d_6): δH: 4.26 (1H, s, H-5), 7.20 (2H, br s, NH_2), 7.22 (2H, d, $J = 8.2$ Hz, H_{Ar}), 6.51 (2H, d, $J = 8.2$ Hz, H_{Ar}) 11.12 (1H, br s, NH), 12.14 (1H, br s, NH) ppm ^{13}C-NMR (75 MHz, DMSO-d_6): δC: 35.25 (C4), 58.38 (C3–CN), 87.97 (C5), 118.95 ($\underline{C}$≡N), 119.73 (C–Br), 129.63 (2 $\underline{C}H_{Ar}$), 131.07 (2 $\underline{C}H_{Ar}$), 143.52 (C6), 149.44 (C=O), 152.32 (C2–NH_2), 157.60 ($\underline{C}$=O), 162.40 (C_{Ar}) ppm; Anal. Calcd. for $C_{14}H_9BrN_4O_3$: C, 46.56; H, 2.51; N, 15.51. Found: C, 46.81; H, 2.63; N, 15.39.

Compound **11a** (Table 4) IR (KBr) (ν_{max}): 3284, 3140, 1691, 1608, 1479, 1379, 1222, 1180, 1072 cm^{-1}; ^{1}H-NMR (300 MHz, DMSO-d_6): δH: 1.12 (3H, t,

$J = 7.0$ Hz, CH_3), 1.87–2.27 (6H, m, CH_2), 2.46 (3H, s, CH_3), 3.97 (2H, q, $J = 7.0$ Hz, CH_2), 4.90 (1H, s, CH), 7.04–7.20 (5H, m, H_{Ar}), 9.14 (1H, s, NH) ppm; ^{13}C-NMR (75 MHz, DMSO-d_6): δC: 14.10, 19.26, 21.50, 27.25, 33.48, 36.88, 58.80, 105.85, 113.54, 124.98, 128.05, 128.25, 143.05, 147.00, 148.75, 167.05, 195.20 ppm; Anal. Calcd. for $C_{19}H_{21}NO_3$: C, 73.29; H, 6.80; N, 4.50. Found: C, 73.51; H, 6.85; N, 4.48.

Compound **11e** (Table 4) IR (KBr) (ν_{max}): 3288, 2962, 1699, 1610, 1485, 1381, 1211, 1072 cm^{-1}; ^{1}H-NMR (300 MHz, DMSO-d_6): δH: 0.84 (3H, s, CH_3), 1.00 (3H, s, CH_3), 1.13 (3H, t, $J = 7.1$ Hz, CH_3), 2.14–2.50 (4H, m, CH_2), 3.97 (2H, q, $J = 7.1$ Hz, CH_2), 4.84 (1H, s, CH), 7.03–7.20 (5H, m, H_{Ar}), 9.07 (1H, s, NH) ppm; Anal. Calcd. for $C_{21}H_{25}NO_3$: C, 74.31; H, 7.42; N, 4.13. Found: C, 74.48; H, 7.51; N, 4.06.

Compound **11 k** (Table 4) IR (KBr) (ν_{max}): 3280, 3217, 3065, 2951, 1695, 1637, 1608, 1489, 1381, 1263, 1210, 1092 cm^{-1}; ^{1}H-NMR (300 MHz, DMSO-d_6): δH:0.82 (3H, s, CH_3), 1.00 (3H, s, CH_3), 1.12 (3H, t, $J = 7.0$ Hz, CH_3), 1.94–2.44 (4H, m, CH_2), 2.29 (3H, s, CH_3), 3.96 (2H, q, $J = 7.0$ Hz, CH_2), 4.82 (1H, s, CH), 7.08–7.39 (4H, m, H_{Ar}), 9.12 (1H, s, NH) ppm; Anal. Calcd. for $C_{21}H_{24}BrNO_3$: C, 60.29; H, 5.78; N, 3.35. Found: C, 60.41; H, 5.89; N, 3.43.

Compound **11n** (Table 4) IR (KBr) (ν_{max}): 3277, 3207, 3078, 2962, 1701, 1647, 1604, 1493, 1381, 1280, 1215, 1090 cm^{-1}; ^{1}H-NMR (300 MHz, DMSO-d_6): δH: 0.84 (3H, s, CH_3), 1.00 (3H, s, CH_3), 1.14 (3H, t, $J = 7.1$ Hz, CH_3), 1.98–2.44 (4H, m, CH_2), 2.24 (3H, s, CH_3), 2.29 (3H, s, CH_3), 3.96 (2H, q, $J = 7.1$ Hz, CH_2), 4.79 (1H, s, CH), 6.95–7.03 (4H, m, H_{Ar}), 9.03 (1H, s, NH) ppm; Anal. Calcd. for $C_{22}H_{27}NO_3$: C, 74.76; H, 7.70; N, 3.96. Found: C, 74.88; H, 7.81; N, 3.81.

Conclusion

In conclusion, we have demonstrated a simple and efficient method for the synthesis of tetrahydrobenzo[*b*]pyran, pyrano[2,3-*d*]pyrimidinone and polyhydroquinoline derivatives. The present method has many obvious advantages compared to those reported in the previous literature, such as the avoidance of discharging harmful organic solvents, the simplicity of the methodology and the use of a commercially available and inexpensive catalyst. Good yields of products and reusability of catalyst are other advantages of this methodology. Furthermore, DFT-NBO and GIAO/DFT analysis revealed some facts and good correlation in theoretical and experimental data for the desired products.

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