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One Pot Synthesis of Benzopyrans in Water as Green Solvent

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A convenient synthesis of polyfunctionalized benzopyran derivatives using tricaprylyl methyl ammonium chloride (aliquate-336) as a catalysts (10 mol %) is described. The catalyst found to be an effective for the synthesis of various benzopyran derivatives. The method has several advantages such as good to excellent yields, minimum environmental impact and simplest work up procedure.

Key Words: Benzopyrans, Tricaprylyl methyl ammonium chloride (aliquate-336) and synthesis.

INTRODUCTION

Recently, Wander[1] defined the ideal synthesis as one in which the target component is produced in one step in quantitative yield from readily available and inexpensive starting materials in source effective and environmentally acceptable process. Environmental concerns about today's chemical research and industry are ever increasing. The challenge for sustainable environment calls for clean reaction processes that avoid the use of hazardous and harmful organic solvents. With the increasing environmental consciousness and regulatory constrains faced in the pharmaceutical and different chemical industries, development of environmentally benign organic reaction has become a crucial, indispensable and demanding research area in the field of modern organic chemical reserach[2]. One pot multi component condensation represents a possible instrument to perform a near ideal synthesis, because it may posses the qualities like possibilities of building up complex molecules with maximum simplicity and brevity[3]. The synthesis of the heterocyclic nucleus is of much current importance. The art of performing efficient chemical transformation coupling three or more components in a single operation by a catalytic process avoiding stoichiometric toxic reagents, large amount of solvents and expensive different purification techniques represent a fundamental target of the modern organic synthesis[4].

Benzopyrans constitute structural units of series of natural products[5] which are widely distributed in the plant kingdom. Members of this group display a broad range of applications[6,7] as fragrances, additives to food and cosmetics, potential biodegradable agrochemicals[8], optical brightening agents, dispersed fluorescent and tunable dye lasers[9]. In recent years, polyfunctionalized benzopyran derivatives have

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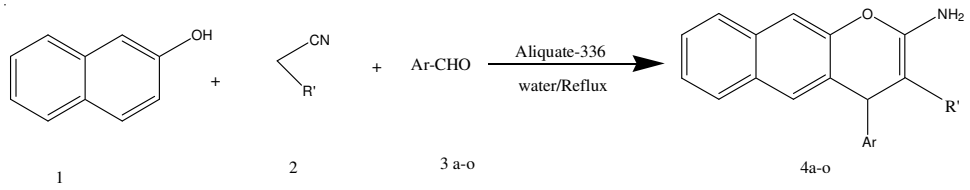
attracted strong interest due to their useful biological and pharmacological properties. A number of benzopyrans are endowed with large number of biological activities such as anticoagulant, antianaphylactic, anticancer, spasmolytic, diuretic, antibacterial, antifungal and insecticidal[10].

Many conventional synthetic methods which are useful to prepare polyfunctionalized benzopyrans involve three component, one pot condensation of ethyl cyanoacetate with an aldehyde and activated phenol using base or amide as catalyst[11]. But some of these methods are plagued by the limitation of poor yields, affluent pollution and difficult work up. As a good phase transfer catalyst aliquate-336 have been used in number of organic reactions. However much less work has been reported on the use of aliquate-336 as catalysts in the synthesis of polyfunctionalized benzopyrans. Hence the development of alternative environmentally friendly synthetic method of these derivatives is of interest. Based on these observations, we report a general and highly effective route for the synthesis of benzopyrans using inexpensive and commercially available aliquate-336 as catalyst (**Scheme-I**).



Scheme-I

EXPERIMENTAL

The mixture of aromatic aldehyde (1 mol), alkyl cyanoacetates (1 mol), naphthol (1 mol), aliquate-336 (10 mol %) and water was heated under reflux for 4 h. TLC was checked. The resulting benzopyran derivative was extracted with ethyl acetate and the solvent layer was washed with water, dried over Na_2SO_4 concentrated and recrystallized from 95 % ethanol (Table-1). All the compounds obtained were characterized fully by spectroscopic (IR and ^{1}H NMR), elemental analysis[12], simple workup procedure and product isolation.

4p: IR (KBr, ν_{max}, cm^{-1}): 3404, 3296, 2989, 2938, 2904, 1671, 1615, 1525, 1402, 1306, 1219, 1072, 825, 815, 743, ^{1}H NMR (300 MHz, $CDCl_3$): δ, 1.41 (3H, t, J = 7.2Hz, CH_3), 4.28 (2H, q, CH_2), 5.64 (1H, s, CH), 6.35 (2H, brs, NH_2), 7.10-8.80 (11H, m, Ar-H). Mass M. wt (345): M^+, 346.4, 317.4 (M-C_2H_5), 300.4 (M-C_2H_5 and -NH_2). Anal. calcd. (%) for $C_{22}H_{19}NO_3$: C, 76.50; H, 5.54; N, 4.06. Found (%): C, 76.48; H, 5.50; N, 4.10.

4q: IR (KBr, ν_{max}, cm^{-1}): 3404, 3191, 2924, 2716, 2209, 1716, 1610, 1549, 1496, 1407, 1299, 1276, 1128, 1080, 754. ^{1}H NMR (300 MHz, $CDCl_3$): δ, 1.33 (3H, t, J = 9Hz, CH_3), 3.90 (2H, q, CH_2), 7.42-9.74 (10H, m, Ar-H), 7.28 (2H, brs, NH_2), 9.10 (1H, s, CH). Anal. calcd. (%) for $C_{22}H_{18}NO_3F$: C, 72.72; H, 4.99; F, 5.23; N. 3.85. Found (%): C, 72.68; H. 5.01; F, 5.20; N, 3.89.

TABLE-1
ALIQUATE-CATALYZED SYNTHESIS OF BENZOPYRAN REPORTED

S. No.	Phenol	R^1	Ar	Product	Yields (%)[a]	m.p. (ºC)[b]
1	1-Naphthol	-CN	C_6H_5	**4a**	90	205-207[12]
2	1-Naphthol	-CN	2-Cl-C_6H_4	**4b**	87	235-237[12]
3	1-Naphthol	-CN	3-Cl-C_6H_4	**c**	89	220-222[12]
4	1-Naphthol	-CN	4-Cl-C_6H_4	**d**	93	229-230[11]
5	1-Naphthol	-CN	2,4-$Cl_2C_6H_3$	**e**	85	215-217[12]
6	1-Naphthol	-CN	3-NO_2-C_6H_4	**4f**	82	216-218[11]
7	1-Naphthol	-CN	4-NO_2-C_6H_4	**4g**	87	236-238[12]
8	1-Naphthol	-CN	4-OH-C_6H_4	**4h**	90	245-247[11]
9	1-Naphthol	-CN	4-CH_3O-C_6H_4	**4i**	92	184-186[11]
10	2-Naphthol	-CN	C_6H_5	**4j**	92	274-276[12]
11	2-Naphthol	-CN	4-CH_3-C_6H_4	**4k**	77	255-257[12]
12	2-Naphthol	-CN	4-NO_2-C_6H_4	**4l**	81	187-189[12]
13	2-Naphthol	-CN	4-CH_3O-C_6H_4	**4m**	83	191-193[11]
14	2-Naphthol	-CN	2-CH_3O-C_6H_4	**4n**	81	115-117[12]
15	2-Naphthol	-CN	2-Cl-C_6H_4	**4o**	79	260-262[11]
16	2-Naphthol	-COOEt	C_6H_5	**4p**	93	165-167
17	2-Naphthol	-COOEt	4-F-C_6H_4	**4q**	86	237-239
18	2-Naphthol	-COOEt	2-NO_2-C_6H_4	**4r**	87	248-250
19	2-Naphthol	-COOEt	4-CH_3O-C_6H_4	**4s**	88	213-215
20	2-Naphthol	-COOEt	2-Cl-C_6H_4	**4t**	89	246-248

[a]Isolated yields. [b]The melting points are carried in open capillaries and are uncorrected.

4r: IR (KBr, ν_{max}, cm^{-1}): 3468, 3332, 3095, 3016, 1682, 1600, 1524, 1436, 1404, 1353, 1305, 1276, 1251, 1220, 1069, 822, 721. ^{1}H NMR (300 MHz, $CDCl_3$): δ, 1.29 (3H, t, *J* = 7.5 Hz, CH_3), 4.02 and 4.37 (2H, m, CH_2), 6.45 (2H, brs, NH_2), 6.58 (H, s, CH), 7.14-8.72 (10H, m, Ar-H). Anal. calcd. (%) for $C_{22}H_{18}N_2O_5$; C, 67.69; H, 4.65; N, 7.18. Found (%): C, 67.65; H, 4.68; N, 7.16.

4s: IR (KBr, ν_{max}, cm^{-1}): 3418, 3305, 3207, 2979, 2958, 2933, 2831, 1660, 1627, 1612, 1515, 1504, 1456, 1407, 1371, 1310, 1262, 1243, 1227, 1159, 1098, 1061, 805, 792, ^{1}H NMR (300 MHz, $CDCl_3$): δ, 1.20 (3H, t, *J* = 6 Hz, CH_3), 3.49 (3H, s, OCH_3), 4.06 (2H, q, CH_2), 4.83 (1H, s, CH), 6.36 (2H, brs, NH_2), 6.47-7.26 (10H, m, Ar-H). Anal. calcd. (%) for $C_{23}H_{21}NO_4$: C, 73.58; H, 5.64; N, 3.73. Found (%): C, 73.55; H, 5.66; N, 3.80.

4t: IR (KBr, ν_{max}, cm^{-1}): 3403, 3293, 2998, 2977, 2956, 1667, 1519, 1401, 1221, 1074, 740. ^{1}H NMR (300 MHz, $CDCl_3$): δ 1.29 (3H, t, *J* = 7.2 Hz, CH_3), 4.27 (2H, q, CH_2), 6.02 (1H, s, CH), 6.42 (2H, brs, NH_2), 6.99-8.36 (10H, m, Ar-H). Anal. calcd. (%) for $C_{22}H_{18}NO_3Cl$: C, 69.57; H, 4.78; Cl, 9.33; N, 3.69. Found (%): C, 69.56; H, 4.75; Cl, 9.31; N, 3.71.

RESULTS AND DISCUSSION

The general experiment procedure for the preparation of benzopyrans is the mixture of active methylene group, aromatic aldehyde and an activated phenol in water was heated under reflux in the presence of catalyst, resulting benzopyran derivative was recrystallized from suitable solvent.

It was observed that the nature of the substitutions does not play vital role in terms of yields under this reaction conditions and the there component cyclo condensation reactions procedure smoothly to give the required benzopyran derivatives in high yields. Aromatic aldehyde containing electron with drawing groups were employed and reacted well to give the corresponding pyrans in good yields.

The catalyst plays a crucial role in the success of the reaction in terms of the rate and the yields. It was observed that increasing the quantity of catalyst gradually from 1-10 mol % results in accelerating the reaction yields from 60-90 %. The use of 10 mol % of aliquate-336 in refluxing water is sufficient to push the reaction forward. It was quite interesting to note that more than 10 mol % of the catalyst did not improve the results and the structural variation in aromatic aldehyde has absolutely no effect on the reactions resulting higher yields of the product. Hence 10 mol % aliquate-336 was chosen as a quantitative catalyst for present reaction carried in the water as green solvent. It was also observed there the above reactions gave very poor yields (less than 30 %), when it was carried out in absence of catalyst.

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