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Basic ionic liquid-catalyzed one-pot synthesis of the spiroacenaphthylene derivatives in water medium

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The basic ionic liquid (benzyl)(dimethyl)(*N*,*N*-dimethylaminoethyl)ammonium chloride was found to be an efficient and reusable catalyst for the synthesis of spiroacenaphthylenes *via* the multicomponent reaction between acenaphthenequinone, malononitrile and α-methylenecarbonyl compounds (β-diketones, pyrazolones) in water.

Since the global attention for environmental protection increasing during the last decades, more and more green chemical processes with less pollution have been developed. As a green reaction media, water could strongly enhance the rate of many organic reactions due to its hydrophobic effects.[1] Organic reactions in water without using harmful organic solvents have being focused on and many multicomponent reactions have been reported.[2]

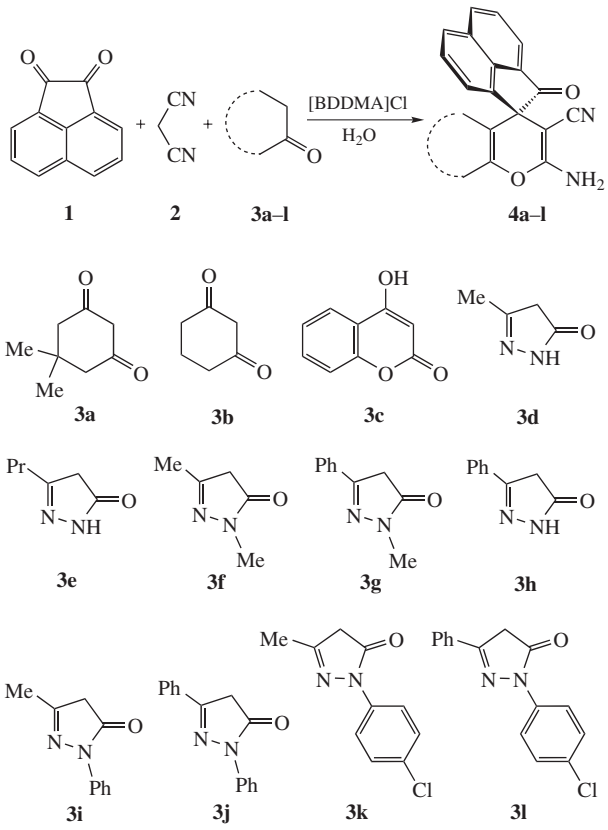
As an important class of naturally occurring substances, spiro compounds were characterized by highly pronounced biological properties.[3] On the other hand, heterocyclic compounds containing pyran ring also possess a wide spectrum of biological activities such as spasmolytic, anticoagulant, diuretic, anticancer, *etc*.[4] Syntheses of spiro heterocycles, including the use of microwave,[5] ultrasonic irradiation technology,[6] and catalysts such as $KAl(SO_4)_2{\cdot}12H_2O$,[7] NH_4Cl,[8] $InCl_3$,[9] L-proline,[10] β-cyclodextrin,[11] sodium stearate,[12] *etc.*, were reported. But, to the best of our knowledge, there are just a few reports on the synthesis of spiroacenaphthylenes catalyzed by Et_3N.[13]

Due to the biological activities of spiro compounds containing pyran moieties, we take interest in developing an environmentally benign approach for synthesis of spiroacenaphthylene derivatives. As efficient catalyst and solvent, ionic liquids play an increasingly key role in organic reactions.[14] Recently, we reported (benzyl)(*N*,*N*-dimethylaminoethyl)dimethylammonium chloride {[BDDMA]Cl, $Me_2N^+(Bn)(CH_2)_2NMe_2Cl^-$} as an efficient, fast, and convenient catalyst for the synthesis of 2-amino-2-chromenes under solvent-free conditions.[15] Some other basic ionic liquids were successfully used in three-component pyran assembling.[16]

Herein, we found that basic ionic liquid [BDDMA]Cl could also efficiently promote the one-pot three-component condensation between acenaphthenequinone, malononitrile and various α-methylenecarbonyl compounds, especially pyrazolones, in water. Moreover, several novel spiroacenaphthylene derivatives containing pyrazole ring were prepared successfully by this protocol (Scheme 1).†

Initially, we used acenaphthenequinone **1**, malononitrile **2** and 4-hydroxycoumarin **3c** as model reaction to explore the influence of temperature and the amount of catalyst on the reaction outcome (Table 1, entries 1–10). We just only obtained the Knoevenagel condensation product when the reaction was carried out at room temperature with (Table 1, entry 1) or in the absence of catalyst (entry 6). As shown in Table 1, the best result was achieved when the reaction was performed with 15 mol% of catalyst at 80 °C.

Under the optimized reaction conditions, a series of spiroacenaphthylene derivatives **4a–l** was successfully synthesized



Scheme 1

† *Typical procedure for the synthesis of 2'-amino-7',7'-dimethyl-2,5'-dioxo-5',6',7',8'-tetrahydro-2*H*-spiro[acenaphthylene-1,4'-chromene]-3'-carbonitrile* **4a**. An equimolar (1.0 mmol) mixture of acenaphthenequinone **1**, malononitrile **2**, dimedone **3a** and ionic liquid (15.0 mol%) in 5.0 ml water was stirred at 80 °C for the specified time (Table 2). Upon completion (monitored by TLC), the solid was filtered off and washed with water (2×5 ml) and cold ethanol (2×2 ml) to obtain sufficiently pure product (TLC pure). The thus obtained material was further purified by recrystallization from ethanol or ethanol–acetone. The catalyst contained in the filtrate can be used in next run without further purification.

4a: yellow solid, mp 256–257 °C. ^{1}H NMR (300 MHz, DMSO-d_6) δ: 1.03 (s, 3H, Me), 1.04 (s, 3H, Me), 2.08 (q, 2H, CH_2, J 36.0 Hz), 2.63 (s, 2H, CH_2), 7.34 (s, 2H, NH_2), 7.39–8.28 (m, 6H, H_{Ar}). IR (KBr, ν/cm^{-1}): 3369, 3293, 3245, 3182, 2954, 2193, 1717, 1665, 1600, 1347.

For characteristics of compounds **4b–l**, see Online Supplementary Materials.

Table 1 Optimization of reaction conditions.[a]

Entry	Cat. (mol%)	*T*/°C	Time/h	Yield (%)[b]
1	10	25	5	Knoevenagel product
2	10	45	5	Incomplete
3	10	60	3	89
4	10	80	2	90
5	10	100	2	89
6	0	80	5	Knoevenagel product
7	5	80	5	85
8	15	80	1.5	90
9	20	80	1.5	87
10	25	80	1.5	88

[a] The reaction was carried out with acenaphthenequinone **1** (1 mmol), malononitrile **2** (1 mmol), 4-hydroxycoumarin **3c** (1 mmol) and [BDDMA]Cl as catalyst in water (5 ml). [b] Isolated yield of **4c**.

Table 2 Synthesis of spiroacenaphthylene derivatives **4**.[a]

Entry	Compound **3**	Product	Time/h	Yield (%)[b]	Mp/°C
1	**3a**	**4a**	1	89	256–257[8]
2	**3b**	**4b**	1	80	242–244[8]
3	**3c**	**4c**	1.5	90	>300
4	**3d**	**4d**	1	89	>300
5	**3e**	**4e**	2	75	234–236
6	**3f**	**4f**	2	77	201–203
7	**3g**	**4g**	3	66	183–186
8	**3h**	**4h**	2	92	264–266
9	**3i**	**4i**	2	75	159–161
10	**3j**	**4j**	2	92	215–217
11	**3k**	**4k**	3	79	172–174[13(*a*)]
12	**3l**	**4l**	4	71	194–196

[a] *Reaction conditions*: acenaphthenequinone **1** (1 mmol), malononitrile **2** (1 mmol), α-methylenecarbonyl compounds **3** (1 mmol), [BDDMA]Cl (15 mol%) as catalyst, water (5 ml), 80 °C. [b] Isolated yield.

(Table 2). Reactions with various substrates **3** including 1,3-diketones and pyrazolones proceeded smoothly to furnish the corresponding products **4**. All the substrates afford good to excellent yields in short time, and among the products, compounds **4e–j**,**l** are new spiroacenaphthylene derivatives.

Then we chose the reaction of acenaphthenequinone **1**, malononitrile **2** and 4-hydroxycoumarin **3c** to further examine the reusabilities of [BDDMA]Cl. After filtering, the catalyst contained in the filtrate could be directly used in the subsequent run without further treatment under the mentioned conditions. The yield of product **4c** was 89, 90, 90, 89 and 88% in consecutive 1 to 5 runs, respectively, which indicated that the catalyst could be reused for at least 5 runs without loss of the activities.

To show the advantage of this work in comparison with previously described procedures, we took synthesis of **4c** for a representative example. As shown in Table 3, in comparison with reported protocols, our catalytic system has merits of higher yield, shorter time, without using organic solvent as co-solvent, and efficient reusablilites.

In conclusion, we have developed a practical and efficient one-pot synthesis of various spiroacenaphthylene derivatives in water with a reusable basic ionic liquid as the catalyst. This method offers the advantages of environmental compatibility, mild reaction conditions, short reaction times, high yields and operational simplicity.

Table 3 Catalytic systems for synthesis of **4c**.

Catalyst (mol%)	Solvent	*T*/°C	Time/h	Yield (%)	Reference
Alum (10)	EtOH–H_2O	60	5	63	7
Alum (10)	EtOH–H_2O	25	24	53	7
Et_3N (200)	EtOH	reflux	4	60	13(*a*)
[BDDMA]Cl (15)	H_2O	80	1.5	90	This work

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Online Supplementary Materials

Supplementary data associated with this article can be found in the online version at doi:10.1016/j.mencom.2012.05.012.

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