Tandem reaction of Morita–Baylis–Hillman alcohols derived from acrylic nitrile with 2-aminobenzimidazole in ionic liquid [BMIM]Cl/H_2O

Yan Wang, Li Liu, Dong Wang, and Yong-Jun Chen

Abstract: The tandem reaction of Morita–Baylis–Hillman (MBH) alcohols **1a**–**1l** derived from acrylic nitrile with 2-aminobenzimidazole (**2**) in ionic iquid (IL) [BMIM]Cl/H_2O without additional catalyst was developed for the efficient synthesis of benzimidazol[1,2-*a*]pyrimidin-7(8*H*)-imine compounds. The tandem reaction included aza-Michael addition and intramolecular addition of an amino group to the cyano group in one pot. The combination of ionic liquid and water was found to be the best reaction medium, which played a role for accelerating the tandem reaction.

Key words: Morita–Baylis–Hillman, ionic liquids, catalyst-free, aza-Michael addition.

Résumé : Comme méthode de synthèse efficace des dérivés de la benzimidazo[1,2-*a*]pyrimidine-7(8*H*)-imine, on a mis au point une réaction en tandem de Morita–Baylis–Hillman (MBH) d'alcools **1a**–**1l** dérivés de l'acrylonitrile avec du 2-aminobenzimidazole (**2**) dans un liquide ionique (LI) formé de chlorure de 1-butyl-3-méthylimidazolium (BMIM) et d'eau, sans addition de catalyseur. La réaction en tandem comporte une addition d'aza-Michael et une addition intramoléculaire du groupe amino sur le groupe cyano dans une réaction monotope. On a trouvé que la combinaison du liquide ionique et de l'eau est le meilleur milieu réactionnel qui joue un rôle d'accélérateur dans la réaction en tandem.

Mots-clés : Morita–Baylis–Hillman, liquides ioniques, sans catalyseur, addition d'aza-Michael.

[Traduit par la Rédaction]

Introduction

The Morita–Baylis–Hillman (MBH) reactions have proved to be one of the most successful methods for C–C bond-forming reactions. Since three functionalized groups, the hydroxyl group, the double bond, and the carbonyl (cyano) group, lie closely in one molecule, the MBH adducts are suitable precursors for the synthesis of many heterocycles and biologically active molecules.[1] Particularly, the Michael addition of the amine to the double bond of an MBH adduct's molecule and the subsequent functionalization have been employed in the synthesis of many aza-heterocycles.[2]

Imidazo[1,2-*a*]pyrimidines are very important intermediates and are widely used in the pharmaceutical chemistry, such as for the synthesis of the antianxiety drug divaplon (**A**) (Fig. 1).[3] Among them, several 7-amino-imidazo[1,2-*a*]pyrimidine derivatives also exhibited interesting biological activities including as $GABA_A$ receptors (**B**) (Fig. 1).[4] Recently, we reported the efficient synthesis of benzimidazo[1,2-*a*]pyrimidinone via a catalyst-free tandem reaction of MBH adducts bearing an ester unit with 2-aminobenzimidazole.[5] In general, the reaction containing the nitrile compound as a substrate is one of the most efficient approaches for introducing an amino group into a molecule. We envisioned that the tandem reaction of MBH alcohols derived from acrylic nitrile with 2-aminobenzoimidazole should be very interesting for the development of an efficient protocol accessible to the novel fused aza-heterocyclic compounds.

On the other hand, in recent years, ionic liquids (ILs) have attracted considerable attention as an alternative solvent in organic reactions because of their tunable physical properties, such as their almost nonvolatile nature, high thermal stability, strong solvating ability to a great number of organics, inorganics and polymers, reusability, and recyclability. Several ILs have been successfully used as solvents and promoters in a lot of chemical transformations.[6]

Herein, we will report a tandem reaction of MBH alcohols derived from acrylic nitrile and aldehydes with 2-aminobenzimidazole[7] in ILs with a small amount of water without any additional catalyst to produce novel fused aza-heterocyclic compounds.

Results and discussion

Initially, under the condition that is similar to the reaction of MBH alcohol derived from acrylic ester with 2-aminobenzimidazole (**2**),[5] the reaction of MBH alcohol **1h** derived from benzaldehyde and acrylic nitrile with **2** was carried

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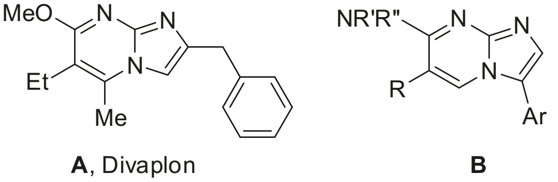
Fig. 1. Divaplon (**A**) and GABA$_A$ receptors (**B**).



out in dioxane at 80 °C (Table 1, entry 1). However, the yield of the product **3h** was very low. Although various organic solvents were used, the yields of **3h** were unsatisfactory either (Table 1, entries 2–6), even in the presence of K_2CO_3 as a catalyst (Table 1, entry 7). But the reaction of **1h** with **2** could proceed smoothly in water (Table 1, entry 8). Unfortunately, when the aqueous condition was employed to other substrates, such as **1a**, the reaction with **2** became sluggish and the products were complicated (Table 2, entries 1 and 2). This is probably attributed to the poor solubility and stability of the MBH alcohol **1a** in water at high temperature. To improve the solubility of the MBH alcohols and **2**, the ionic liquids were selected to be reaction media. If ionic liquid [BMIM]Cl was used as a medium for the reaction of **1a** with **2** at 100 °C, a homogeneous solution was formed and the product, 6-(4-chlorophenylhydroxylmethyl)-5,6-dihydro-benzimidazo-[1,2-*a*]pyrimidin-7(8*H*)-imine (**3a**), was obtained in 53% yield (Table 2, entry 3). To our delight, the addition of a small amount of water to the medium ([BMIM]Cl/H_2O = 11:1) led the yield of **3a** to increase (Table 2, entries 4 and 5). It was probably that the small amount of water could promote this reaction.[8] The tandem reaction did not need any additional catalyst for the high yield of the final product **3a**. However, when the water percentage in the reaction medium was increased to 4:1 ([BMIM]Cl/H_2O), the yield of **3a** was decreased sharply to 6%. It is proposed that the substrate **1a** decomposed under the conditions with such a large amount of water (Table 2, entry 6).

Based on these results, various ILs (Fig. 2) were employed in the reaction of **1a** with **2** as reaction media containing a small amount of water (IL/water = 11:1). As shown in Table 2 for the same cation ([BMIM]$^+$), the anions of the ILs used strongly influnced the yields of the product **3a** (Table 2, entry 5 vs entries 7–9). Moreover, with the same anion (BF_4^-) the molecular structure of the ammonium ion also has a strong effect on the reaction. It was found that [EMIM]$^+$ bearing an *N*-ethyl group and [OMIM]$^+$ bearing an *N*-octyl group provided poor yields of **3a** (Table 2, entries 10 and 11, respectively), but for [BMIM]$^+$ bearing an *N*-butyl group a 74% yield of **3a** was obtained (Table 2, entry 9). In comparison with [BMIM]$^+$, the change of the N′-substituent from a methyl to a vinyl group ([BEIM]$^+$) and introduction of a second methyl group ([BDMIM]$^+$) provided a complicated product mixture and very poor yield of **3a** (Table 2, entries 12 and 13) despite having the same core structure of imidazole. The employment of the pyridine unit ([NBPD]$^+$) as a cation part did not improve the yield of **3a** at all (Table 2, entry 14). Interestingly, the use of organic solvents with a small amount of water (Sol/H_2O = 11:1) also afforded a complicated mixture of the products (Table 2, entries 15 and 16). In summary, the IL [BMIM]Cl/water was determined to be the most efficient reaction medium for this tandem reaction.

With optimized conditions in hand, we examined the scope of the MBH alcohols derived from acrylic nitrile[9] with **2** in IL [BMIM]Cl/H_2O (11:1) at 100 °C in the absence of any additional catalyst (Scheme 1). The results are summarized in Table 3. As shown in Table 3, the reactions of various MBH alcohols (**1a**–**1l**) derived from acrylic nitrile proceeded smoothly in a period of 6 h to form the corresponding products **3a**–**3l** in good yields. The electronic properties of the substituents of MBH alcohols had no effect on the reaction. The MBH alcohol **1k** bearing the steric group also generated the product **3k** in 89% yield (Table 3, entries 11). Although much a longer reaction time (48 h) was needed, alkyl-substituted MBH alcohol **1l** could also give the expected product **3l** in good yield (75%) (Table 3, entry 12).

In terms of a plausible mechanism for the nucleophilic reaction with imidazole,[7b] the route of the reaction of MBH alcohols **1** derived from acrylic nitrile with 2-aminobenzimidazole (**2**) was proposed as shown in Scheme 2. In the first step, the nitrogen atom at the 3 position of 2-aminobenzimidazole attacked at the α,β-unsaturated carbon atom of the MBH alcohol in a Michael-addition manner to generate an intermediate **I** (path A). In this step, ILs, especially [BMIM]Cl containing a small amount of water, played the roles of both reaction medium and accelerator.[8] It was noteworthy that since the MBH alcohols **1** derived from acrylic nitrile were unstable to water and could be decomposed through retro-MBH reaction at high temperature, the water percentage in the IL was confined to a small range: H_2O:IL = 1:11 ~ <1:4. In the second step (path B), the intermediate **I** underwent an intramolecular addition reaction of an amino group to the cyano group, giving cyclization product **3**. In general, for the addition reaction of an amino group to the cyano group a suitable catalyst or a relatively higher reaction temperature were required. Thus, in a catalyst-free system a high reaction temperature (100 °C) had to be employed unavoidably.

Conclusion

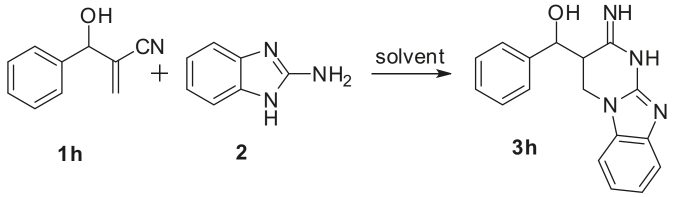
In conclusion, we have developed an efficient method for the synthesis of fused aza-heterocyclic compounds, benzimidazo[1,2-*a*]pyrimi-din-7(8*H*)-imine derivatives in good to excellent yields via a tandem reaction of BMH alcohols (**1a**–**1l**) with 2-aminobenzoimidazole in IL/H_2O. The developed protocol was simple and catalyst free. The reaction underwent the Michael addition reaction, followed by intramolecular cyclization in a one-pot process. The produced fused heterocyclic compounds provided an opportunity to enhance the diversity of benzimidazo[1,2-*a*]pyrimidine compounds by further derivation.

Experimental

Typical procedure for the reaction of MBH alcohol (1) with 2-aminobenzimidazole (2)

To a solution of MBH alcohol **1a** (97 mg, 0.5 mmol) and **2** (100 mg, 0.75 mmol) in 0.5 mL of IL [BMIM]Cl was added water (40 μL, 2.5 mmol). The resulting mixture was heated at 100 °C until completion as indicated by TLC. Then the reaction mixture was extracted by ethyl acetate and

Table 1. The reaction of Morita–Baylis–Hillman (MBH) alcohol **1h** with **2**.



Entry	Solvent	T (°C)	Time (h)	Yield (%)[a]
1	Dioxane	80	14	45
2	MeOH	Reflux	14	10
3	THF	Reflux	14	18
4	DCM	Reflux	14	44
5	CH_3CN	80	14	18
6	Toluene	80	14	20
7[b]	Toluene	50	24	30[c]
8	H_2O	80	14	100

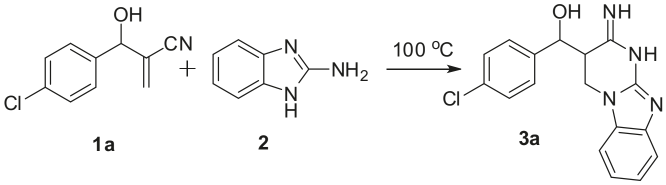
Note: Reaction conditions: **1h** (0.5 mmol), **2** (0.75 mmol), and solvent (0.5 mL).

[a] Determined by ^{1}H NMR.

[b] With K_2CO_3 (10 mol%).

[c] Isolated yield.

Table 2. The reaction of Morita–Baylis–Hillman (MBH) alcohol **1a** with **2**.



Entry	Reaction medium	Time (h)	Yield (%)[a]
1	H_2O	6	—[b]
2[c]	H_2O	6	—[b]
3	[BMIM]Cl	1	53
4[d]	[BMIM]Cl	1	66
5[d]	[BMIM]Cl	4	85
6[e]	[BMIM]Cl	4	6
7[d]	$[BMIM]SbF_6$	3	—[b]
8[d]	$[BMIM]PF_6$	3	46
9[d]	$[BMIM]BF_4$	3	74
10[d]	$[EMIM]BF_4$	4	50
11[d]	$[OMIM]BF_4$	4	—[b]
12 [d]	$[BEIM]BF_4$	4	—[b]
13[d]	$[BDMIM]BF_4$	4	—[b]
14 [d]	$[NBPD]BF_4$	4	—[b]
15 [d]	MeOH	6	—[b]
16 [d]	THF	5	—[b]

Note: Reaction conditions: **1a** (0.5 mmol), **2** (0.75 mmol), and solvent (0.5 mL), at 100 °C or reflux.

[a] Isolated yield.

[b] complicated products with poor yield of **3a**.

[c] At 80 °C.

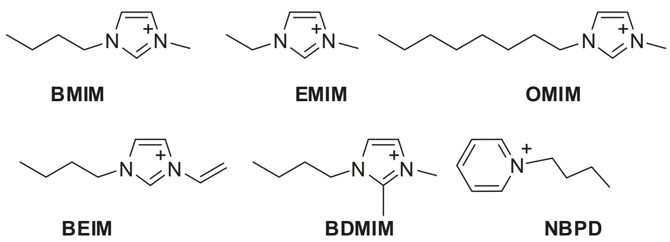
[d] H_2O (2.5 mmol) was added.

[e] [BMIM]Cl (0.4 mL) : H_2O (0.1 mL) = 4:1.

water. The organic phase was dried by Na_2SO_4 and purified by column chromatography over silica gel (eluent: DCM–MeOH = 100:2) to afford a light yellow solid **3a** (139 mg, 85%).

3a, light yellow solid, mp 161–163 °C. ν_{max} (KBr, cm^{-1}): 3471, 3371, 3055, 1547. δ_H (300 MHz, DMSO-d_6, TMS): 3.53–3.67 (1H, m, –CH), 4.21–4.54 (2H, m, –CH_2), 4.89–4.98 (1H, m, –CH), 6.47–6.56 (3H, m, –NH, –NH, –OH), 6.88–6.98 ($2H_{arom}$, m), 7.03–7.27 ($2H_{arom}$, m), 7.46–7.49 ($4H_{arom}$, m). δ_C (300 MHz. DMSO-d_6, TMS): 40.4, 41.2, 68.4, 70.3, 107.7, 107.8, 114.9, 118.0, 118.2, 118.3, 118.7, 120.7, 127.6, 128.2, 128.3, 128.6, 132.2, 132.7, 133.9,

Fig. 2. Ionic liquids employed in the reaction of Morita–Baylis–Hillman (MBH) alcohols with **2**.



134.2, 140.0, 141.0, 142.6, 142.7, 154.7, 154.8. HRMS (EI) *m/z* calcd for $C_{17}H_{16}ClN_4O$ $(M + 1)^+$: 327.1007; found: 327.1004.

3b, light yellow solid, mp 138–140 °C. ν_{max} (KBr, cm^{-1}): 3444, 3353, 3058, 1547. δ_H (300 MHz, DMSO-d_6, TMS): 3.57–3.59 (1H, m, –CH), 4.26–4.51 (2H, m, –CH_2), 4.91–5.00 (1H, m, –CH), 6.46–6.56 (3H, m, –NH, –NH, –OH), 6.88–6.98 (2H_{arom}, m), 7.04–7.59 (6H_{arom}, m). δ_C (300 MHz, DMSO-d_6, TMS): 40.5, 41.3, 68.4, 70.4, 107.8, 107.9, 114.8, 118.0, 118.4, 118.4, 118.7, 120.8, 124.4, 125.5, 125.7, 126.6, 127.6, 128.1, 130.1, 133.0, 133.1, 133.9, 134.2, 142.4, 142.6, 143.6, 144.5, 154.8. HRMS (EI) *m/z* calcd for $C_{17}H_{16}ClN_4O$ $(M + 1)^+$: 327.1007; found: 327.1007.

3c, light yellow solid, mp 108–110 °C. ν_{max} (KBr, cm^{-1}): 3444, 3353, 3060, 1546. δ_H (300 MHz, DMSO-d_6, TMS): 3.53–3.65 (1H, m, –CH), 4.47–4.55 (2H, m, –CH_2), 4.89–5.39 (1H, m, –CH), 6.44–6.57 (3H, m, –NH, –NH, –OH), 6.87–7.02 (2.5H_{arom}, m), 7.13–7.17 (1H_{arom}, m), 7.28–7.48 (3.5H_{arom}, m), 7.73–7.70 (1H_{arom}, m). δ_C (300 MHz, DMSO-d_6, TMS): 38.0, 38.3, 40.6, 65.2, 67.4, 107.6, 107.8, 114.9, 117.5, 118.3, 118.6, 118.7, 121.0, 127.3, 127.6, 128.0, 128.6, 129.1, 129.3, 129.6, 129.9, 130.1, 131.7, 133.7, 134.2, 138.2, 138.8, 142.2, 142.3, 154.7, 154.8. HRMS (EI) *m/z* calcd for $C_{17}H_{16}ClN_4O$ $(M + 1)^+$: 327.1007; found: 327.1003.

3d, light yellow solid, mp 149–151 °C. ν_{max} (KBr, cm^{-1}): 3477, 3371, 3054, 1546. δ_H (300 MHz, DMSO-d_6, TMS): 3.50–3.70 (1H, m, –CH), 4.20–4.53 (2H, m, –CH_2), 4.86–4.96 (1H, m, –CH), 6.45–6.54 (3H, m, –NH, –NH, –OH), 6.85–6.99 (2H_{arom}, m), 7.03–7.27 (2H_{arom}, m), 7.39–7.63 (4H_{arom}, m). δ_C (300 MHz, DMSO-d_6, TMS) 40.4, 41.2, 68.5, 70.3, 107.7, 107.9, 114.8, 114.8, 118.0, 118.2, 118.3, 118.7, 120.8, 121.3, 128.0, 129.0, 131.1, 131.2, 133.9, 134.2, 140.5, 141.4, 142.5, 142.7, 154.7, 154.8. HRMS (EI) *m/z* calcd for $C_{17}H_{16}BrN_4O$ $(M + 1)^+$: 371.0497; found: 371.0502.

3e, light yellow solid, mp 152–154 °C. ν_{max} (KBr, cm^{-1}): 3452, 3368, 3065, 1552. δ_H (300 MHz, DMSO-d_6, TMS): 3.57–3.69 (1H, m, –CH), 4.25–4.51 (2H, m, –CH_2), 4.89–4.96 (1H, m, –CH), 6.45–6.54 (3H, m, –NH, –NH, –OH), 6.88–6.99 (2H_{arom}, m), 7.02–7.73 (6H_{arom}, m). δ_C (300 MHz, DMSO-d_6, TMS): 41.0, 41.9, 68.9, 70.9, 108.3, 108.4, 115.4, 118.5, 118.9, 119.3, 121.3, 122.1, 122.3, 125.3, 126.4, 129.1, 130.0, 130.9, 131.0, 131.5, 134.4, 134.8, 143.0, 143.1, 144.3, 145.3, 155.3, 155.4. HRMS (EI) *m/z* calcd for $C_{17}H_{16}ClN_4O$ $(M + 1)^+$: 371.0497; found: 371.0502

3f, light yellow solid, mp 171–173 °C. ν_{max} (KBr, cm^{-1}): 3444, 3352, 3057, 1546. δ_H (300 MHz, DMSO-d_6, TMS) 3.48–3.71 (1H, m, –CH), 4.27–4.60 (2H, m, –CH_2), 4.81–5.32 (1H, m, –CH), 6.49–6.60 (3H, m, –NH, –NH, –OH), 6.86–6.99 (2.3H_{arom}, m), 7.12–7.16 (1H_{arom}, m), 7.22–7.34 (1.7H_{arom}, m), 7.45–7.54 (1.7H_{arom}, m), 7.65–7.74 (1.3Harom, m). δ_C (300 MHz, DMSO-d_6, TMS): 16.9, 37.2, 37.9, 38.3, 40.5, 67.3, 69.8, 107.6, 107.8, 114.8, 114.9, 117.3, 118.3, 118.5, 118.6, 118.7, 120.3, 120.9, 121.0, 122.2, 127.8, 128.1, 128.3, 128.8, 130.0, 130.3, 132.3, 132.6, 133.5, 133.7, 134.3, 139.7, 140.1, 142.1, 142.3, 154.4, 154.8. HRMS (EI) *m/z* calcd for $C_{17}H_{16}BrN_4O$ $(M + 1)^+$: 371.0497; found: 371.0502

3g, light yellow solid, mp 129–131 °C. ν_{max} (KBr, cm^{-1}): 3444, 3352, 3150, 1547. δ_H (300 MHz, DMSO-d_6, TMS): 3.52–3.66 (1H, m, –CH), 4.27–4.54 (2H, m, –CH2), 4.88–4.98 (1H, m, –CH), 6.42–6.56 (3H, m, –NH, –NH, –OH), 6.91–7.27 (6H_{arom}, m), 7.48–7.55 (2H_{arom}, m). δ_C (300 MHz, DMSO-d_6, TMS): 40.6, 41.2, 68.5, 70.3, 107.7, 107.8, 114.8, 118.0, 115.1, 115.2, 118.1, 118.2, 118.3, 118.8, 120.7, 127.7, 128.2, 127.8, 128.7, 128.8, 133.9, 134.3, 137.3, 138.1, 138.2, 142.6, 142.7, 154.7, 154.9, 160.0, 160.3. HRMS (EI) *m/z* calcd for $C_{17}H_{16}FN_4O$ $(M + 1)^+$: 311.1299; found: 311.1302.

3h, light yellow solid, mp 171–173 °C. ν_{max} (KBr, cm^{-1}): 3462, 3374, 3062, 1548. δ_H (300 MHz, DMSO-d_6, TMS): 3.51–3.69 (1H, m, –CH), 4.22–4.55 (2H, m, –CH_2), 4.85–4.95 (1H, m, –CH), 6.38–6.61 (3H, m, –NH, –NH, –OH), 6.86–7.01 (2.5H_{arom}, m), 7.13–7.16 (1H_{arom}, m), 7.24–7.45 (5.5H_{arom}, m). δ_C (300 MHz, DMSO-d_6, TMS): 41.1, 41.8, 69.4, 71.5, 108.3, 115.2, 118.7, 119.4, 121.3, 126.2, 127.2, 128.2, 128.7, 134.4, 134.7, 141.6, 142.5, 142.9, 155.2. HRMS (EI) *m/z* calcd for $C_{17}H_{17}N_4O$ $(M + 1)^+$: 293.1393; found: 293.1397.

3i, light yellow solid, mp 150–152 °C. ν_{max} (KBr, cm^{-1}): 3430, 3354, 3221, 1546. δ_H (300 MHz, DMSO-d_6, TMS): 3.53–3.67 (1H, m, –CH), 3.76–3.78 (3H, m, –OCH_3), 4.22–4.54 (2H, m, –CH_2), 4.83–4.94 (1H, m, –CH), 6.37–6.57 (3H, m, –NH, –NH, –OH), 6.89–7.34 (8H_{arom}, m). δ_C (300 MHz, DMSO-d_6, TMS): 39.3, 40.5, 41.3, 55.0, 55.0, 68.9, 70.9, 107.7, 107.8, 111.6, 112.2, 112.9, 113.7, 114.9, 117.9, 118.2, 118.9, 120.7, 129.3, 129.4, 134.0, 134.3, 131.5, 142.6, 142.7, 143.7, 154.7, 154.9, 159.2, 159.2 HRMS (EI) *m/z* calcd for $C_{18}H_{19}N_4O_2$ $(M + 1)^+$: 323.1498; found: 323.1503.

3j, light yellow solid, mp 173–175 °C. ν_{max} (KBr, cm^{-1}): 3444, 3354, 3053, 1546. δ_H (300 MHz, DMSO-d_6, TMS): 3.55–3.70 (3H, m, –CH_3), 3,81 (1H, s, –CH), 4.10–4.57 (2H, m, –CH_2), 4.82–5.30 (1H, m, –CH), 6.09–6.55 (3H, m, –NH, –NH, –OH), 6.81–7.27 (7H_{arom}, m), 7.53–7.55 (1H_{arom}, m). δ_C (300 MHz, DMSO-d_6, TMS): 14.0, 20.7, 37.8, 37.9, 40.8, 54.9, 55.4, 59.7, 63.4, 65.2, 107.4, 107.8, 110.2, 110.9, 114.8, 114.9, 118.2, 118.2, 118.3, 119.1, 120.2, 120.4, 120.7, 120.8, 126.2, 127.4, 128.7, 129.3, 129.7, 133.8, 134.3, 142.6, 142.7, 154.8, 154.9, 155.9. HRMS (EI) *m/z* calcd for $C_{18}H_{19}N_4O$ $(M + 1)^+$: 307.1549; found: 307.1553.

3k, light yellow solid, mp 168–170 °C. ν_{max} (KBr, cm^{-1}): 3444, 3353, 3221, 1546. δ_H (300 MHz, DMSO-d_6, TMS): 1.89 (1.5H, m, –CH_3), 2.30–2.33 (4.5H, m, –CH_3), 3.37–3.64 (1H, m, –CH), 4.34–4.60 (2H, m, –CH_2), 4.79–5.16 (1H, m, –CH), 6.17–6.59 (3H, m, –NH, –NH, –OH), 6.88–7.30 (6H_{arom}, m), 7.41–7.47 (1H_{arom}, m). δ_C (300 MHz, DMSO-d_6, TMS): 17.4, 18.5, 20.7, 20.9, 38.5, 40.5, 40.9, 65.0, 67.5, 107.7, 107.8, 114.9, 115.0, 118.0, 118.3, 118.5, 118.7, 120.8, 120.8, 126.4, 127.0, 128.1, 128.5, 130.1,

Scheme 1 The reactions of Morita–Baylis–Hillman (MBH) alcohols with **2**.

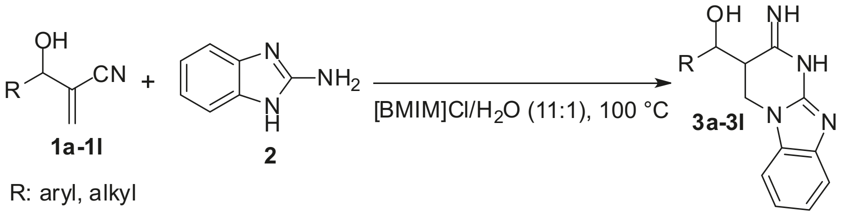
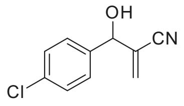
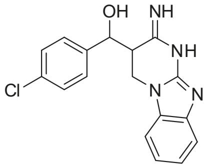
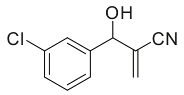
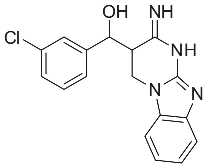
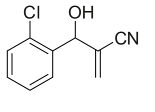
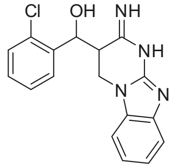
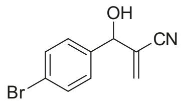
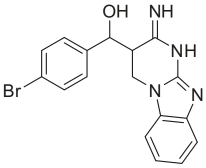
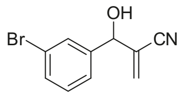
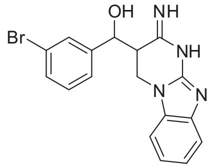
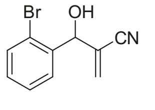
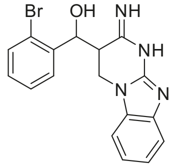
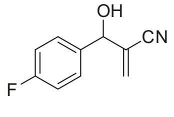
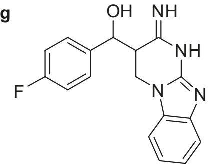


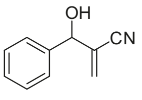
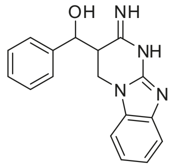
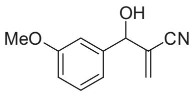
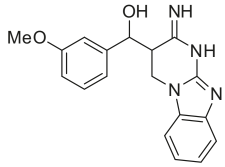
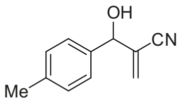
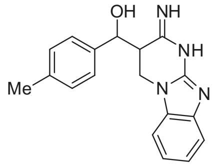
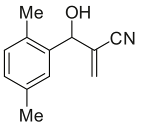
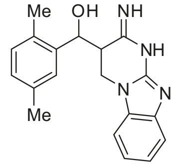
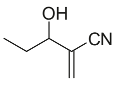
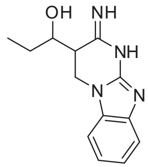
Table 3. The reaction of Morita–Baylis–Hillman (MBH) alcohols **1a**–**1l** with **2** in IL/H_2O without catalyst (IL, ionic liquid).

Entry	MBH alcohol	Time (h)	Product	Yield (%)
1	**1a** 	4	**3a** 	85
2	**1b** 	1.5	**3b** 	88
3	**1c** 	3	**3c** 	83
4	**1d** 	4	**3d** 	75
5	**1e** 	1.5	**3e** 	91
6	**1f** 	2	**3f** 	80
7	**1g** 	4	**3g** 	85

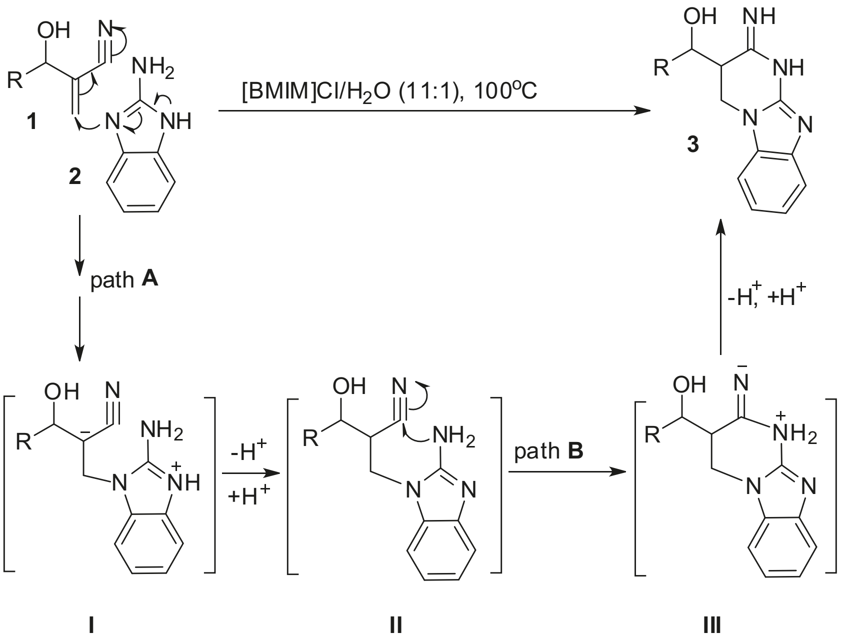
130.2, 131.9, 134.0, 134.4, 134.6, 135.0, 139.3, 139.6, 142.6, 142.8, 154.8, 155.0. HRMS (EI) *m*/*z* calcd for $C_{19}H_{21}N_4O$ $(M + 1)^+$: 321.1706; found: 321.1710.

3l, light yellow solid, mp 110–112 °C. ν_{max} (KBr, cm^{-1}): 3430, 3352, 2966, 1547. δ_H (300 MHz, DMSO-d_6, TMS): 0.86–0.98 (3H, m, $-CH_3$), 1.46–1.76 (2H, m, $-CH_2$), 3.21 (1H, m, –CH), 3.51–3.59 (1H, m, –CH), 4.17–4.44 (2H, m, $-CH_2$), 5.48–5.60 (1H, m, –CH), 6.51 (3H, s, –NH, –NH, –OH), 6.88–6.99 ($2H_{arom}$, m), 7.41–7.24 ($2H_{arom}$, m). δ_C (300 MHz, DMSO-d_6, TMS): 10.0, 10.0, 16.8, 28.2, 37.7,

Table 3. (*concluded*).

Entry	MBH alcohol	Time (h)	Product	Yield (%)
8	**1h** 	5	**3h** 	83
9	**1i** 	4	**3i** 	88
10	**1j** 	3	**3j** 	76
11	**1k** 	6	**3k** 	89
12	**1l** 	48	**3l** 	75

Scheme 2. Plausible mechanism.



38.2, 39.8, 40.8, 68.7, 69.5, 107.9, 114.8, 114.9, 118.3, 118.3, 118.8, 119.3, 120.7, 120.8, 134.0, 134.2, 142.5, 142.7, 154.8, 154.8. HRMS (EI) *m/z* calcd for $C_{13}H_{16}N_4O$ $(M + 1)^+$: 245.1395; found: 245.1397.

Acknowledgement

We are grateful to the National Natural Foundation of China, Ministry of Science and Technology (No. 2009ZX09501-006), and the Chinese Academy of Sciences for financial support.

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