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Hydroxyl ionic liquid (HIL)-immobilized quinuclidine for Baylis–Hillman catalysis: synergistic effect of ionic liquids as organocatalyst supports

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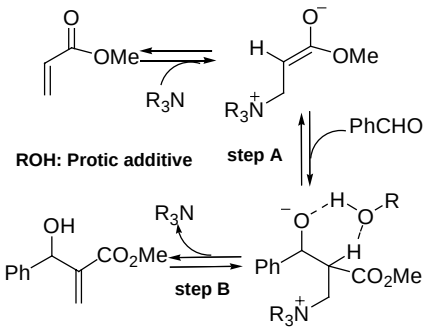
Abstract—Hydroxyl ionic liquid (HIL) has been explored as a novel support for Baylis–Hillman catalyst. The HIL-supported catalyst showed a better catalytic activity compared to other IL-immobilized catalyst that has no hydroxyl group attached to the IL scaffold. The hydroxyl group linked on IL played an important role in facilitating efficient catalysis under solvent-free conditions. The corresponding Baylis–Hillman and aza-Baylis–Hillman adducts were obtained in good to excellent yields in all cases examined. The HIL-supported quinuclidine can be readily recovered and reused for six times without significant loss of catalytic activity.

1. Introduction

The tertiary amine-catalyzed C–C bond-forming reaction of aldehydes with activated alkenes is widely referred to as Morita–Baylis–Hillman reaction, which has become one of the most popular C–C bond-forming reactions due to its many advantages regarding to atomic economy, non-metal catalysis, mild conditions, as well as the promising utility of the multifunctional products.[1] Recent efforts in this area have been focused largely on developing efficient reaction systems and exploring asymmetric Baylis–Hillman reactions.[1b,2] These studies have shown that the use of protic solvents or protic additives could accelerate the coupling reaction quite significantly and provide the presently most efficient Baylis–Hillman reactions.[3,4] In addition, a general inspection of the successful asymmetric catalysts reveals that the catalysts all bear a common structure motif with a 'proton'-donating moiety, which may be viewed as a critical determinant for chiral transduction.[2] Altogether, it seems likely that the involvement of a protic medium or a protic additive may be the prerequisite for developing efficient Baylis–Hillman synthesis and asymmetric catalysis. The recent finding that a protic additive could mediate intramolecular proton transfer (Scheme 1, step B) rather than enolate–aldehyde coupling (step A) as the rate-determining step in the initial stage of a Baylis–Hillman reaction,[5] is clearly in line with this proposal.



Scheme 1.

Another important area of current research is the development of supported Baylis–Hillman reactions and the recyclable catalysts.[6] This became of our recent focus because excess or stoichiometric small Lewis base catalysts have to be used under normal homogeneous B–H conditions. Progresses in literature along this line now include the exploration of poly-DMAP and the synthesis of supported phosphines for Baylis–Hillman catalysis.[6a,b] In our previous work, we have developed ionic liquid-supported quinuclidines for Baylis–Hillman catalysis on

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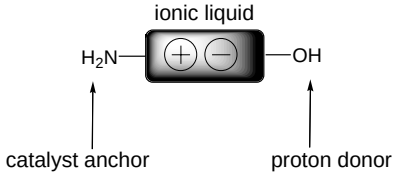
the basis of the biphasic strategy.[7] An inspection revealed that optimal result was achieved when using methanol as reaction medium, which is similar to the accelerating effect of protic solvent in other Baylis–Hillman reactions as highlighted above.[3,4] We could then speculate that the use of a hydroxyl containing ionic liquid alone may exert a similar accelerating effect. If this is the case, it will offer additional advantages such as elimination of a protic solvent, reduction of the catalyst loading, and a more efficient catalyst recycling for the Baylis–Hillman reactions. This deduction was considered to be reasonable because it was observed previously that a hydroxyl group in an amine type catalyst did exert accelerating effect on some coupling reactions.[8,9] In the present work, we explored the use of HILs as organocatalyst support. To our delight, we indeed observed a significant beneficial effect of the HIL catalyst over its non-hydroxyl counterpart. The first example of such type of Baylis–Hillman catalysts and their successful applications are hereby reported.

The ionic liquid precursor consists of a hydroxyl group and an amino group at the two ends of each alkyl chain, respectively, of which the amino group was linked to a quinuclidine moiety (Scheme 2). The synthesis of the HIL-supported quinuclidines was straight forward as depicted in Scheme 3. Reductive amination of 3-quinuclidinone with the synthetic bifunctional ionic liquid afforded the desired HIL-bound quinuclidines (**1a**–**1c**, **2a**–**2c**) as colorless or pale yellow viscous liquid. This new type of ionic liquids was characterized by ^{1}H, ^{13}C NMR, IR and MS.[10]

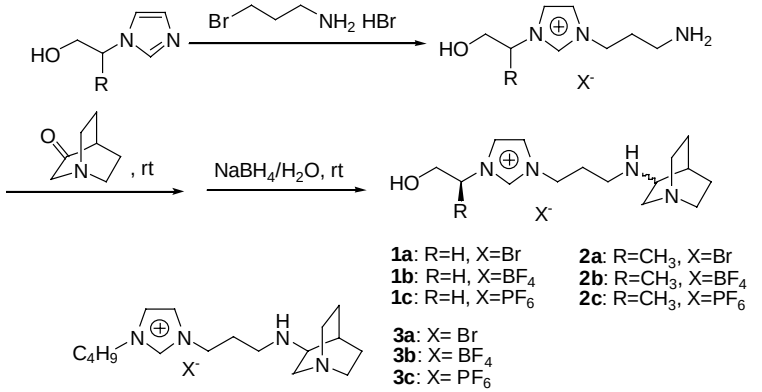


Scheme 2.

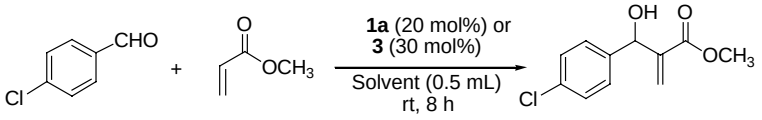
First, catalytic capability of the hydroxyl ionic liquid-immobilized quinuclidines was tested using **1a** as a representative catalyst and the reaction of *p*-chlorobenzaldehyde and methyl acrylate as a model B–H reaction (Scheme 4); the results were summarized in Table 1. As therein revealed, the reactions proceeded quite smoothly in the presence of 20 mol% of **1a** and showed a significant acceleration effect when conducted in protic solvents. For example, the reaction in methanol afforded 72% yield of the desired Baylis–Hillman product in 8 h, while the same reaction in THF provided only 32% of yield (Table 1, entry 1 vs entry 4).

It was also show that the HIL-supported quinuclidine **1a** had a better catalytic activity than its non-hydroxyl-bearing counterpart **3a** (or **3b**), regardless of the reaction media (Table 1). Considering the similarity of their structures of **1a** and **3**, it was envisioned that the hydroxyl group in the ionic liquid support **1a** must be responsible for its higher activity. It was conceived that the HIL support itself may serve as a protic additive to promote the Baylis–Hillman reaction in a manner similar to the protic additives in conventional cases. Indeed, further optimization of reaction conditions revealed that the reaction under solvent-free conditions provided the best result (90% in 8 h, Table 1, entry 11). In sharp contrast, the same reaction in the presence of a similar amount of non-HIL **3** was very sluggish and afforded less than 10% of the B–H product in 8 h under solvent-free conditions (Table 1, entry 11). These results indicated that the hydroxyl group linked on the ionic liquid played a critical role in promoting the reaction.[5]

Previously, ionic liquids have been shown in a few cases to exert positive effect on the Baylis–Hillman reaction rate when serving as reaction media.[6d–i,11] In our study, the use of hydroxyl containing ionic liquid as reaction media was found to give moderate accelerating effect in the presence of non-HIL-supported catalyst **3a** (Scheme 5, compared with Table 1, entries 7–11). Based on these results, further exploration led to the identification of hydroxyl containing



Scheme 3.



Scheme 4.

Table 1. Reactions of *p*-chlorobenzaldehyde with methyl acrylate in the presence of ionic liquid-supported quinuclidine **1a** (0.2 equiv) or **3** (0.3 equiv) in 0.5 mL of solvent for 8 h[a]

Entry	Solvent	Catalyst/yield (%)[b]	
		1a	**3a**
1	CH_3OH	72	37
2	C_2H_5OH	63	36
3	CH_3CN	43	18
4	THF	32	8
5	CH_2Cl_2	48	5
6	$CHCl_3$	29	9
7	$[BMIM]BF_4$	43	13[c]
8	$[BMIM]PF_6$	47	13[c]
9	$[bupy]BF_4$	69	21[c]
10	$[BMMIM]BF_4$	53	15[c]
11	None	90[d]	<10[c,d]

[a] Carried out on 0.5 mmol scale in the presence of 0.2 equiv of the catalyst **1a** at room temperature. Molar ratio of *p*-chlorobenzaldehyde/methyl acrylate=1:1.5.
[b] Isolated yields of pure product.
[c] Compound **3b** was employed instead of **3a**.
[d] Molar ratio of *p*-chlorobenzaldehyde/methyl acrylate=1:2.0.

IL-immobilized quinuclidine **1** as highly efficient Baylis–Hillman catalyst. The observations that the hydroxyl-bearing ionic liquids as catalyst supports could significantly promote the B–H reactions may be interpreted by suggesting a key role of the hydroxyl group on the IL support in activating aldehyde carbonyl or promoting an intramolecular proton transfer (or both) in a similar way to that suggested by Aggarwal.[5] However, the detailed mechanism as to how exactly the hydroxyl group is functioning in the B–H transition state is still unclear at the present stage and will need further investigation. Nevertheless, the finding that the HILs could serve as a synergistic reagent and support as well as a recoverable medium for Baylis–Hillman reactions provides a useful clue for designing highly efficient and recyclable catalysts for Baylis–Hillman reactions.

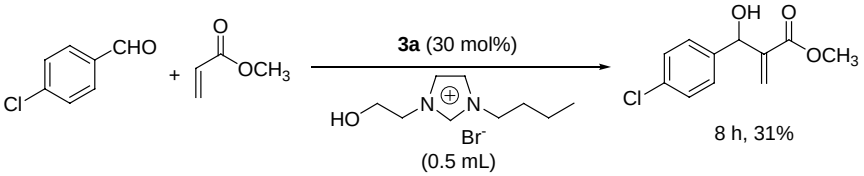
Under solvent-free conditions, several other hydroxyl ionic liquid-supported quinuclidines were also examined (Scheme 6, Table 2). The HILs with different counter ions showed little effect on the reactions (Table 2, entries 1–5). Among all the HILs examined, **1a** provided slightly better results in terms of reaction yields, and thus was selected as the catalyst for subsequent experiments. Increasing the loading of the catalyst did not lead to an increase in the yields (Table 2, entries 2 and 3), probably due to the formation of byproducts.

The immobilized chiral ionic liquids **2** were synthesized starting from L-alanine. The diastereoisomers obtained were inseparable and used directly as the B–H catalyst. As revealed in Table 2, the HIL-supported quinuclidines **2** maintained a comparable activity as **1** (Table 2, entries 6–8), but with poor enantioselectivity (<10% ee). The low selectivity may arise from an improper distance between the nucleophilic center and the protic moiety,[2a,b] thus the structure of catalyst should be further optimized.

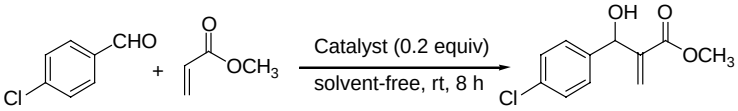
The HIL-supported catalysts can be readily recovered after the reaction using the biphasic strategy (i.e., homogeneous reaction and heterogeneous separation). The catalyst can then be reused directly for the following runs. It was found that **1a** could be recycled for at least six times without significant loss of its catalytic activity (Table 2, entries 9–13).

Under the optimized conditions established above, we then examined the Baylis–Hillman reactions of acrylates with a variety of aldehydes under solvent-free conditions (Scheme 7, Table 3). As shown therewith, both aliphatic and aromatic aldehydes can undergo very efficient Baylis–Hillman reactions with acrylates in the presence of 20 mol% of **1a**, giving the corresponding Baylis–Hillman adducts **4a**–**4s** in good to excellent yields (55–98%, 0.5–24 h). These results demonstrated that the HIL-supported quinuclidines were excellent Baylis–Hillman catalysts, with activities comparable to or better than some of the currently best catalytic systems in the literature.[3h] For example, the present system with 20 mol% of **1a** could provide fairly good isolated B–H adduct yields even for the reactions of inert substrates *p*-anisaldehyde (55%, Table 3, entry 11). In comparison, a similar reaction of *p*-anisaldehyde under the optimal conditions of the literature in the presence of 100 mol% quinuclidine gave 67% yield after 48 h.[3h] In addition, no apparent side reactions of aldehydes (such as aldol) were observed.

The analogous reactions of acrylonitrile with various aromatic aldehydes were also investigated (Scheme 8, Table 4). High yields were achieved for all the reactions in less reaction time. As shown in Table 4, catalyst **1a** was much more effective than **3b** in the cases tested. For example, for the commonly known inert substrate *p*-anisaldehyde, the yield of 83% was achieved in 8 h in the presence of 20 mol% of **1a** (Table 4, entry 4). In contrast, only 69% yield was obtained after 24 h when using **3b** (30 mol%) as the catalyst. For more active aldehydes such



Scheme 5.

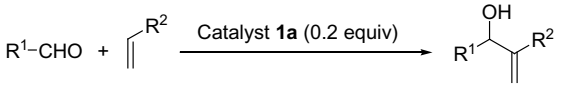


Scheme 6.

Table 2. Reactions of *p*-chlorobenzaldehyde with methyl acrylate in the presence of various HIL-supported quinuclidines[a]

Entry	Catalyst	Time (h)	Yield (%)[b]
1	**1a**	8	90
2	**1a**[c]	8	88
3	**1a**[d]	4	74
4	**1b**	8	86
5	**1c**	8	86
6	**2a**	8	79
7	**2b**	8	84
8	**2c**	8	86
9[e]	**1a** (2nd)	8	88
10[e]	**1a** (3rd)	8	88
11[e]	**1a** (4th)	8	82
12[e]	**1a** (5th)	12	86
13[e]	**1a** (6th)	12	84

[a] Carried out on 0.5 mmol scale in the presence of 0.2 equiv of the catalyst (except those specified) at room temperature. Molar ratio of *p*-chlorobenzaldehyde/methyl acrylate = 1:2.
[b] Isolated yields of pure product.
[c] 0.3 equiv of **1a** was used.
[d] 0.5 equiv of **1a** was used.
[e] Reuse of catalyst **1a** from 1 to 6 run.



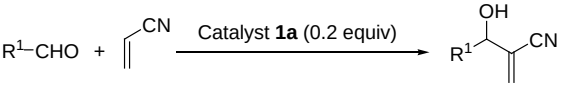
4a 4r (55 98%)

Scheme 7.

Table 3. Baylis–Hillman reactions of aldehydes (1.0 equiv) and acrylates (2.0 equiv) catalyzed by ionic liquid-supported quinuclidine **1a** (0.2 equiv) at room temperature[a]

Entry	R^1	R^2	Time (h)	Product	Yield (%)[b]
1	*n*-C_3H_7	$COOCH_3$	12	**4b**	79
2	*i*-C_4H_9	$COOCH_3$	12	**4c**	74
3	*n*-C_6H_{13}	$COOCH_3$	12	**4d**	80
4	Ph	$COOCH_3$	8	**4e**	94
5	*p*-ClPh	$COOC_2H_5$	8	**4f**	88
6	*p*-ClPh	$COOC_4H_9$	8	**4g**	86
7	*o*-ClPh	$COOCH_3$	8	**4h**	91
8	*m*-ClPh	$COOCH_3$	8	**4i**	84
9	*p*-CH_3Ph	$COOCH_3$	8	**4j**	72
10	*p*-*i*PrPh	$COOCH_3$	10	**4k**	70
11	*p*-CH_3OPh	$COOCH_3$	24	**4l**	55
12	*o*-NO_2Ph	$COOCH_3$	1	**4m**	97
13	*m*-NO_2Ph	$COOCH_3$	1	**4n**	94
14	2-Pyridyl	$COOCH_3$	0.5	**4o**	95
15	3-Pyridyl	$COOCH_3$	0.5	**4p**	98
16	4-Pyridyl	$COOCH_3$	0.5	**4q**	97
17	2-Furyl	$COOCH_3$	1	**4r**	93

[a] The reaction was carried out in 0.5 mmol scale.
[b] Isolated yields.



5a–5h (83–97%)

Scheme 8.

Table 4. Baylis–Hillman reactions of aldehydes (1.0 equiv) and acrylonitrile (2.0 equiv) in the presence of **1a** (0.2 equiv) at room temperature[a]

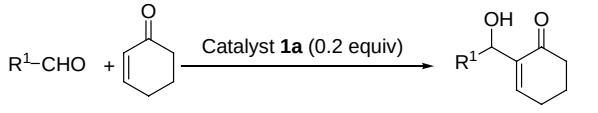
Entry	R^1	Time (h)	Product	Yield (%)[b]
1	Ph	1.5	**5a**	96
2	*p*-ClPh	1.5	**5b**	97
3	*p*-CH_3Ph	4	**5c**	91
4	*p*-CH_3OPh	8 (24)[c]	**5d**	83 (69)[c]
5	*p*-NO_2Ph	0.5	**5e**	85
6	2-Pyridyl	10 min	**5f**	98
7	3-Pyridyl	10 min	**5g**	98
8	4-Pyridyl	10 min	**5h**	98

[a] Carried out on 0.5 mmol scale.
[b] Isolated yields.
[c] Results using 30 mol% of **3b** as catalyst in 2.0 equiv of methanol.

as pyridinecarboxaldehydes, almost all substrates were quantitatively converted to the desired Baylis–Hillman products in only 10 min (Table 4, entries 6–8).

The Baylis–Hillman reactions involving the poor Michael acceptors, cyclic enones, were usually quite sluggish under normal conditions. Many attempts have been made to explore efficient catalysts to accelerate this kind of reaction.[7,12] In our previous work, we found that the reaction of 2-cyclohexenone could undergo quite effective (fair to high yields) B–H reactions in methanol using ionic liquid-supported quinuclidine **3b** as the catalyst.[7] In the present work, comparable or better results were obtained in the presence of 20 mol% of **1a** (Scheme 9, Table 5). No apparent aldol byproducts, except for the case of piperanol (Table 5, entry 5), were observed. In contrast, there were substantial aldol adducts in most cases when using **3b** as the catalyst.[7] Furthermore, the inert *p*-anisaldehyde could also undergo quite efficient Baylis–Hillman reaction with the inert Michael acceptor 2-cyclohexenone, giving 51% yield in quite a short reaction time (Table 5, entry 4). These results indicated that the HIL-bound catalyst **1a** of the present work was a very efficient catalyst for the Baylis–Hillman reactions involving 2-cyclohexenone.

The aza-Baylis–Hillman reaction was also examined (Scheme 10, Table 6). With 20 mol% of **1a**, the aza-



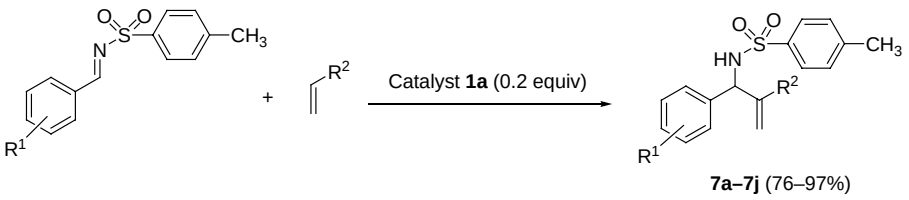
6a–6e (51–84%)

Scheme 9.

Table 5. Baylis–Hillman reactions of aldehydes (1.0 equiv) and 2-cyclohexenone (2.0 equiv) in the presence of **1a** (0.2 equiv) at room temperature[a]

Entry	R^1	Time (h)	Product	Yield (%)[b]
1	Ph	8	**6a**	77
2	*p*-ClPh	8	**6b**	84
3	*p*-CH_3Ph	12	**6c**	65
4	*p*-CH_3OPh	16	**6d**	51
5	Piperonal	16	**6e**	73 (9)[c]

[a] Carried out on 0.5 mmol scale.
[b] Isolated yields.
[c] The number in parentheses is the yield of aldol byproduct.



Scheme 10.

Baylis–Hillman reactions of *N*-sulfonated imines (i.e., *N*-arylmethylidene-4-methylbenzenesulfonamides) with various B–H substrates such as methyl acrylate and acrylonitrile were promoted to give exclusively the desired aza-Baylis–Hillman adducts (76–97%). Even the relatively inert *N*-4-methyoxyphenylmethylidene-4-methylbenzenesulfonamide could undergo efficient aza-B–H reaction with methyl acrylate and acrylonitrile in good to excellent yields (Table 6, entries 5 and 10).

Table 6. Aza-Baylis–Hillman reactions of aldehydes (1.0 equiv) and electrophiles (5.0 equiv) in the presence of **1a** (0.2 equiv) at room temperature[a]

Entry	R^1	R^2	Time (h)	Product	Yield (%)[b]
1	4-Cl	$COOCH_3$	4	**7a**	91
2	H	$COOCH_3$	2	**7b**	76
3	2-Cl	$COOCH_3$	4	**7c**	84
4	4-CH_3	$COOCH_3$	4	**7d**	88
5	4-CH_3O	$COOCH_3$	8	**7e**	96
6	4-Cl	CN	2	**7f**	94
7	H	CN	1	**7g**	90
8	2-Cl	CN	2	**7h**	92
9	4-CH_3	CN	2	**7i**	83
10	4-CH_3O	CN	4	**7j**	97

[a] Carried out on 0.2 mmol scale.
[b] Isolated yields.

In summary, we have disclosed HILs as novel supports for Baylis–Hillman catalyst. The HIL-bound quinuclidine demonstrated better catalytic activity than its non-hydroxyl ionic liquid analogues and was well applied to a range of Baylis–Hillman substrates under solvent-free conditions. This beneficial matrix effect of HIL was ascribed to the presence of hydroxyl group in the proximity of active sites, which accelerated the reaction via hydrogen-bonding activation and/or assisting intramolecular proton transfer. The HIL-bound catalysts possess all the advantages of the non-HIL-bound catalysts and can be readily recovered from the reaction mixture and reused for at least six times without significant loss of catalytic activity. The solvent-free reaction system provided a highly efficient Baylis–Hillman synthesis under environmentally friendly conditions.

2. Experimental

2.1. General procedure

In a 5 mL vial, **1a** (36 mg, 0.1 mmol), aldehyde (0.5 mmol) and activated alkene (1.0 mmol) were mixed. The resulted homogeneous solution was stirred at ambient temperature and monitored by TLC. After the indicated reaction time, the solution was extracted with diethyl ether. The ether extract was rotary-evaporated and the crude product was purified by flash chromatography on silica gel to afford the desired product. The remaining layer was further vacuumed to dryness and the resulting catalyst was reused directly for next run. The reactions using the recycled catalyst were conducted in the same manner.

2.1.1. Synthesis of HIL-bound quinuclidine 1a (R=H, X=Br). The synthesis of hydroxyl containing amino ionic liquid (R=H) followed our previous procedure:[7] to a stirred solution of 2-imidazol-1-yl ethanol (5.6 g, 50 mmol) in 50 mL of dry ethanol was added 3-bromopropylamine hydrobromide (10.95 g, 50 mmol). The solution was heated to reflux for 24 h. The ethanol was then removed under vacuo and the solid residue was dissolved in a minimal quantity of water and was brought to about pH=10 by the addition, in small portions, of solid KOH. The water solution was then concentrated to dryness and the residue was extracted with ethanol–THF. The combined extracts were concentrated to give the desired product (11.33 g, 91%) as a pale yellow viscous liquid. ^{1}H NMR (CD_3OD, 300 MHz): 7.20 (s, 1H), 6.98 (s, 1H), 4.15 (t, 2H, J=4.8 Hz), 3.91 (t, 2H, J=5.1 Hz), 3.83 (t, 2H, J=5.1 Hz), 2.73–2.69 (m, 2H), 2.08 (t, 2H, J=7.2 Hz); ^{13}C NMR (CD_3OD, 75 MHz): δ 139.2, 124.2, 123.6, 62.5, 60.8, 53.5, 39.1, 33.9; MS for $C_8H_{16}N_3O^+$ (M^+), calcd 170.13, found 170.47; Br^- (M^-), calcd 78.92, found 78.93.

To a solution of the synthetic hydroxyl containing amino imidazolium bromide (2.5 g, 10 mmol) in 20 mL of dry methanol was added 3-quinuclidinone (1.88 g, 15 mmol). After stirring for 12 h at ambient temperature, the reaction was cooled to 0 °C and sodium borohydride (0.855 g, 22.5 mmol) was added in small portions. The solution was stirred for 4 h, followed by adding small quantity of water. The resulting mixture was then stirred for additional 30 min and concentrated to dryness. The residue was extracted with chloroform and the extracts was concentrated, followed by extensive washing with diethyl ether to provide the expected product **1a** (3.09 g, 86%) as a pale yellow viscous liquid. IR (KBr, cm^{-1}): 3397, 2945, 1581, 1457, 1399, 1164, 1075. ^{1}H NMR (CD_3CN, 300 MHz): 7.51 (s, 1H), 7.06 (s, 1H), 6.89 (s, 1H), 4.27 (t, 2H, J=5.4 Hz), 3.90 (t, 2H, J=4.5 Hz), 3.17–3.09 (m, 2H), 2.86–2.73 (m, 4H), 2.68–2.60 (m, 3H), 2.45–2.39 (m, 2H), 2.13–2.08 (m, 3H), 1.90–1.85 (m, 2H), 1.76–1.71 (m, 1H), 1.61–1.53 (m, 2H), 1.48–1.40 (m, 2H); ^{13}C NMR (CD_3CN, 75 MHz): δ 138.8, 124.1, 123.6, 68.1, 62.5, 61.0, 58.1, 56.7, 55.8, 53.3, 44.6, 31.2, 26.7, 25.7, 20.3; MS for $C_{15}H_{27}N_4O^+$ (M^+), calcd 279.22, found 279.61; Br^- (M^-), calcd 78.92, found 78.98; HRMS for $C_{15}H_{27}N_4O^+$ (M^+), calcd 279.2185, found 279.2179.

2.1.2. Synthesis of hydroxyl based ionic liquid-bound quinuclidine 1b (R=H, X=BF_4). The sodium tetrafluoroborate (2.47 g, 22.5 mmol) was added to a solution of the synthetic hydroxyl containing amino imidazolium bromide (R=H, 3.75 g, 15 mmol) in ethanol/THF and stirred for 3 days. The suspension was filtered to remove the precipitated bromide salt and the organic phase was concentrated. The residue was then re-dissolved in a small amount of chloroform, and filtered to remove the inorganic salt. The solvent was removed under vacuo to afford a pale yellow liquid (3.12 g, 57%). ^{1}H NMR (CD_3OD, 300 MHz): 7.19 (s, 1H), 6.98 (s, 1H), 4.13 (t, 2H, J=5.1 Hz), 3.91 (t, 2H, J=4.8 Hz), 3.82 (t, 2H, J=5.4 Hz), 2.91–2.83 (m, 2H), 2.18 (t, 2H, J=7.2 Hz); ^{13}C NMR (CD_3OD, 75 MHz): δ 139.2, 124.3, 123.5, 62.5, 61.0, 53.4, 38.3, 31.6; MS for $C_8H_{16}N_3O^+$ (M^+), calcd 170.13, found 170.40; BF_4^- (M^-), calcd 87.00, found 87.03.

The synthesis of **1b** followed similar procedure as that of **1a**. With 3.12 g of imidazolium tetrafluoroborate (8.5 mmol), 2.57 g of **1b** (82%) was obtained as a colorless viscous liquid. IR (KBr, cm^{-1}): 3396, 2947, 1501, 1396, 1164, 1091. ^{1}H NMR (CD_3OD, 300 MHz): 7.19 (s, 1H), 6.98 (s, 1H), 4.35 (t, 2H, J=4.8 Hz), 3.92 (t, 2H, J=4.8 Hz), 3.17–3.10 (m, 2H), 2.82–2.77 (m, 4H), 2.68–2.59 (m, 3H), 2.46–2.44 (m, 2H), 2.14–1.09 (m, 3H), 1.93–1.89 (m, 2H), 1.77–1.72 (m, 1H), 1.61–1.55 (m, 2H), 1.48–1.40 (m, 2H); ^{13}C NMR (CD_3OD, 75 MHz): δ 138.8, 124.1, 123.6, 68.3, 62.5, 61.0, 58.1, 56.7, 55.9, 53.4, 44.6, 31.2, 26.7, 25.6, 20.3; MS for $C_{15}H_{27}N_4O^+$ (M^+), calcd 279.22, found 279.57; BF_4^- (M^-), calcd 87.00, found 87.03; HRMS for $C_{15}H_{27}N_4O^+$ (M^+), calcd 279.2185, found 279.2177.

2.1.3. Synthesis of hydroxyl based ionic liquid-bound quinuclidine 1c (R=H, X=PF_6). The potassium hexafluorophosphate (2.76 g, 15 mmol) was added to a solution of the synthetic hydroxyl containing amino imidazolium bromide (R=H, 2.5 g, 10 mmol) in ethanol/THF and stirred for 3 days. The suspension was filtered to remove the precipitated bromide salt and the organic phase was concentrated. The residue was then re-dissolved in a small amount of chloroform, and filtered to remove the inorganic salt. The solvent was removed under vacuo to afford a pale yellow liquid (2.15 g, 51%). ^{1}H NMR (CD_3OD, 300 MHz): 7.19 (s, 1H), 6.98 (s, 1H), 4.12 (t, 2H, J=5.4 Hz), 3.89 (t, 2H, J=4.8 Hz), 3.82 (t, 2H, J=4.8 Hz), 2.91–2.86 (m, 2H), 2.19 (t, 2H, J=7.2 Hz); ^{13}C NMR (CD_3OD, 75 MHz): δ 137.7, 124.2, 123.5, 65.6, 60.4, 56.8, 38.5, 31.8, 18.6; MS for $C_8H_{16}N_3O^+$ (M^+), calcd 170.13, found 170.42; PF_6^- (M^-), calcd 144.96, found 145.13.

The synthesis of **1c** followed the similar procedure as that of **1a**. With 2.15 g of imidazolium hexafluorophosphate (5.1 mmol), 2.67 g of **1c** (92%) was obtained as a colorless viscous liquid. IR (KBr, cm^{-1}): 3158, 2946, 1561, 1457, 1398, 1164, 1078, 847. ^{1}H NMR (CD_3OD, 300 MHz): 7.18 (s, 1H), 6.98 (s, 1H), 4.33 (t, 2H, J=5.1 Hz), 3.90 (t, 2H, J=5.1 Hz), 3.16–3.10 (m, 2H), 2.85–2.73 (m, 4H), 2.70–2.60 (m, 2H), 2.45–2.40 (m 2H), 2.12–2.07 (m, 3H), 1.93–1.88 (m, 2H), 1.77–1.73 (m, 1H), 1.61–1.55 (m, 2H), 1.48–1.40 (m, 2H); ^{13}C NMR (CD_3OD, 75 MHz): δ 138.8, 124.1, 123.6, 68.2, 62.5, 61.0, 58.1, 56.6, 55.8, 53.3, 44.6, 31.2, 26.7, 25.7, 20.3; HRMS for $C_{15}H_{27}N_4O^+$ (M^+), calcd 279.2185, found 279.2179; MS for $C_{15}H_{27}N_4O^+$ (M^+), calcd 279.22, found 279.55; BF_4^- (M^-), calcd 144.96, found 145.15.

2.1.4. Synthesis of hydroxyl based ionic liquid-bound quinuclidine 2a (R=CH_3, X=Br). The synthesis of hydroxyl containing amino ionic liquid (R=CH_3) still followed our previous procedure: to a stirred solution of 2-(1-imidazolyl)propanol (8.64 g, 68 mmol) in 68 mL of dry ethanol was added 3-bromopropylamine hydrobromide (14.88 g, 68 mmol). The solution was heated to reflux for 24 h. The ethanol was then removed in vacuo and the solid residue was dissolved in a minimal quantity of water and brought to about pH=10 by the addition, in small portions, of solid KOH. The water solution was then concentrated to dryness and the residue was extracted with ethanol–THF. The combined extracts were concentrated to give the desired product (R=CH_3, 17.29 g, 96%) as a pale red viscous liquid. ^{1}H NMR (CD_3OD, 300 MHz): 7.24 (s, 1H), 6.98 (s, 1H), 4.69–4.58 (m, 1H), 4.43–4.38 (m, 2H), 3.78–3.71 (m, 2H), 3.66–3.59 (m, 2H), 2.26–2.13 (m, 2H), 1.60 (d, 3H, J=6.9 Hz); ^{13}C NMR (CD_3OD, 75 MHz): δ 137.7, 123.7, 126.6, 65.6, 60.4, 56.8, 38.5, 31.8, 18.6; MS for $C_9H_{18}N_3O^+$ (M^+), calcd 184.14, found 184.42; Br^- (M^-), calcd 78.92, found 78.97.

To a solution of the synthetic hydroxyl containing amino imidazolium bromide (R=H, 2.64 g, 10 mmol) in 20 mL of dry methanol was added 3-quinuclidinone (1.88 g, 15 mmol). After stirring for 12 h at ambient temperature, the reaction was cooled to 0 °C and sodium borohydride (0.855 g, 22.5 mmol) was added in small portions. The solution was stirred for 4 h, followed by adding a small quantity of water. The resulting mixture was then stirred for an additional 30 min and concentrated to dryness. The residue was extracted with chloroform and the extract was concentrated, followed by extensive washing with diethyl ether to provide the expected product **2a** (3.48 g, 93%) as a pale yellow viscous liquid. IR (KBr, cm^{-1}): 3137, 2944, 2874, 2312, 1558, 1457, 1400, 1167, 1046. ^{1}H NMR (CD_3OD, 300 MHz): 7.90 (s, 1H), 7.01 (s, 1H), 6.97 (s, 1H), 4.61–4.56 (m, 1H), 4.38–4.33 (m, 2H), 3.89–3.84 (m, 1H), 3.75–3.58 (m, 2H), 3.33 (br, 1H), 3.18–3.11 (m, 1H), 2.80 (br, 3H), 2.66–2.59 (m, 3H), 2.45–2.41 (m, 1H), 2.10 (t, 2H, J=6.9 Hz), 1.90 (br, 2H), 1.74 (br, 2H), 1.59 (d, 3H, J=6.9 Hz); ^{13}C NMR (CD_3OD, 75 MHz): δ 136.2, 122.0, 120.8, 67.3, 64.5, 58.9, 58.9, 56.3, 54.9, 48.0, 47.4, 46.4, 28.3, 24.8, 19.0; HRMS for $C_{16}H_{29}N_4O^+$ (M^+), calcd 293.2336, found 293.2339; MS for $C_{16}H_{29}N_4O^+$ (M^+), calcd 293.23, found 293.49; Br^- (M^-), calcd 78.92, found 78.93.

2.1.5. Synthesis of hydroxyl based ionic liquid-bound quinuclidine 2b (R=CH_3, X=BF_4). The sodium tetrafluoroborate (3.29 g, 30 mmol) was added to a solution of the synthetic hydroxyl based amino imidazolium bromide (R=CH_3, 5.28 g, 20 mmol) in ethanol/THF and stirred for 3 days. The suspension was filtered to remove the precipitated bromide salt and the organic phase was concentrated. The residue was then re-dissolved in a small amount of chloroform, and filtered to remove the inorganic salt. The solvent was removed under vacuo to afford a pale yellow liquid (2.51 g, 46%). ^{1}H NMR (CD_3OD, 300 MHz):

7.79 (s, 1H), 7.61 (s, 1H), 4.69–4.59 (m, 1H), 4.45–4.40 (m, 2H), 3.89–3.85 (m, 2H), 3.66–3.59 (m, 2H), 2.37–2.27 (m, 2H), 1.59 (d, 3H, $J=8.4$ Hz); ^{13}C NMR (CD_3OD, 75 MHz): δ 137.0, 124.1, 122.7, 65.8, 60.3, 58.4, 37.8, 29.2, 18.5; MS for $C_9H_{18}N_3O^+$ (M^+), calcd 184.14, found 184.37; BF_4^- (M^-), calcd 87.00, found 87.05.

The synthesis of **2b** followed a similar procedure to that of **2a**. With 2.22 g of imidazolium tetrafluoroborate (8.2 mmol), 1.92 g of **2b** (86%) was obtained as a colorless viscous liquid. IR (KBr, cm^{-1}): 3132, 2942, 2871, 1558, 1457, 1400, 1115, 1045. ^{1}H NMR (CD_3OD, 300 MHz): 7.22 (s, 1H), 6.98 (s, 1H), 4.63–4.58 (m, 1H), 4.39–4.34 (m, 2H), 3.89–3.85 (m, 1H), 3.76–3.70 (m, 2H), 3.37 (br, 1H), 3.18–3.10 (m, 1H), 2.79 (br, 3H), 2.68–2.56 (m, 3H), 2.46–2.40 (m, 1H), 2.12 (t, 2H, $J=$ 6.9 Hz), 1.90 (br, 2H), 1.74 (br, 2H), 1.59 (d, 3H, $J=6.9$ Hz); ^{13}C NMR (CD_3OD, 75 MHz): δ 137.6, 123.6, 122.3, 68.1, 66.8, 60.3, 58.1, 56.7, 55.8, 48.1, 47.5, 47.1, 29.1, 25.3, 19.6; HRMS for $C_{16}H_{29}N_4O^+$ (M^+), calcd 293.2336, found 293.2336; MS for $C_{16}H_{29}N_4O^+$ (M^+), calcd 293.23, found 293.56; BF_4^- (M^-), calcd 87.00, found 87.06.

2.1.6. Synthesis of hydroxyl based ionic liquid-bound quinuclidine 2c ($R=CH_3$, $X=PF_6$). The potassium hexafluorophosphate (4.14 g, 22.5 mmol) was added to a solution of the synthetic hydroxyl based amino imidazolium bromide ($R=CH_3$, 3.96 g, 15 mmol) in ethanol/THF and stirred for 3 days. The suspension was filtered to remove the precipitated bromide salt and the organic phase was concentrated. The residue was then re-dissolved in a small amount of chloroform, and filtered to remove the inorganic salt. The solvent was removed under vacuo to afford a pale yellow liquid (2.96 g, 60%). ^{1}H NMR (CD_3OD, 300 MHz): 7.24 (s, 1H), 6.98 (s, 1H), 4.60–4.54 (m, 1H), 4.39–4.34 (m, 2H), 3.88–3.84 (m, 2H), 3.62–3.53 (m, 2H), 2.31–2.21 (m, 2H), 1.58 (d, 3H, $J=6.9$ Hz); ^{13}C NMR (CD_3OD, 75 MHz): δ 137.6, 123.5, 122.5, 65.5, 60.3, 56.8, 38.4, 31.6, 17.9; MS for $C_9H_{18}N_3O^+$ (M^+), calcd 184.14, found 184.34; PF_6^- (M^-), calcd 144.96, found 145.14.

The synthesis of **2c** followed a similar procedure to that of **2a**. With 2.8 g of imidazolium hexafluorophosphate (8.5 mmol), 2.58 g of **2c** (92%) was obtained as a colorless viscous liquid. IR (KBr, cm^{-1}): 3162, 2946, 2875, 2310, 1558, 1457, 1396, 1166, 1052, 845. ^{1}H NMR (CD_3OD, 300 MHz): 7.22 (s, 1H), 6.97 (s, 1H), 4.60–4.54 (m, 1H), 4.36–4.31 (m, 2H), 3.87–3.83 (m, 1H), 3.75–3.69 (m, 2H), 3.37 (br, 1H), 3.17–3.13 (m, 1H), 2.78 (br, 3H), 2.67–2.54 (m, 3H), 2.44–2.40 (m, 1H), 2.10 (t, 2H, $J=6.9$ Hz), 1.89 (br, 2H), 1.76 (br, 2H), 1.58 (d, 3H, $J=6.9$ Hz); ^{13}C NMR (CD_3OD, 75 MHz): δ 137.6, 123.6, 122.3, 68.2, 66.5, 60.3, 58.1, 56.6, 55.7, 47.5, 47.0, 44.6, 29.0, 26.7, 20.3; MS for $C_{16}H_{29}N_4O^+$ (M^+), calcd 293.23, found 293.58; Br^- (M^-), calcd 144.96, found 145.13.

All the Baylis–Hillman products are known compounds.[4,7,13]

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