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N^1,N^1,N^2,N^2-tetramethyl-N^1,N^2-bis(sulfo)ethane-1,2-diaminium Chloride ([TMBSED][Cl]$_2$): An Efficient Ionic Liquid Catalyst for the One-pot Synthesis of Dihydropyrrol-2-ones and Tetrahydropyridines

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N^1,N^1,N^2,N^2-tetramethyl-N^1,N^2-bis(sulfo)ethane-1,2-diaminium chloride ([TMBSED][Cl]$_2$) was synthesized as an acidic ionic liquid and characterized using FT-IR, ^{1}H and ^{13}C NMR, mass spectroscopy, TG, DTG, and DTA techniques. This ionic liquid was employed as an efficient catalyst for the extremely facile and efficient synthesis of dihydropyrrol-2-ones and functionalized tetrahydropyridines. One-pot four-component reaction of amines, dialkyl acetylenedicarboxylates, and formaldehyde in the presence of [TMBSED][Cl]$_2$ in ethanol at ambient temperature provides substituted dihydropyrrol-2-ones in good to high yields. This ionic liquid catalyst was also found to be useful for the synthesis of functionalized tetrahydropyridines using a multi-component reaction of amines, aldehydes, and β-ketoesters in methanol.

Keywords: Dihydropyrrol-2-one, Tetrahydropyridine, Multi-component reaction, Ionic liquid, [TMBSED][Cl]$_2$

INTRODUCTION

Development of novel methodologies to reduce the pollution in chemical synthesis has received considerable attention due to increasing environmental concerns. In this context, one active area is the utilization of eco-friendly ionic liquid catalysts instead of conventional, toxic and polluting Brönsted acid catalysts. Ionic liquids have attracted considerable attention due to their unique properties such as good solvating ability, a wide liquid range, tunable polarity, negligible vapor pressure, and high thermal stability [1,2]. They have been used in all areas of the chemical industries including solvents and catalysts in synthesis, matrices for mass spectroscopy, separation and extraction, lubricants, plasticizers, and electrolyte in batteries [3,4].

Dihydropyrrol-2-one and its derivatives are key compounds for the synthesis of bioactive molecules such as chaetoglobosin A and C [5], and clausenamide [6]. Moreover, dihydropyrrol-2-ones have been successfully used as HIV integrase [7], herbicidal [8], pesticides [9], anti-tumor and anticancer agents [10], mitomycin antibiotics [11], and also inhibitor of DNA polymerase [12]. Recently, multi-component reactions have been used for one-pot synthesis of dihydropyrrol-2-ones using catalysts such as AcOH [13,14], I_2 [15], benzoic acid [16], TiO_2 nanopowder [17] and $Cu(OAc)_2{\cdot}H_2O$ [18]. However, some of these methods displayed drawbacks, such as using excess amount of catalyst, purification of products by preparative TLC, long reaction times and need to column chromatography for products purification.

On the other hand, tetrahydropyridine and their analogues have received attention owing to their biological activities such as antimalarial [19], antihypertensive [20], antibacterial [21], anticonvulsant, and anti-inflammatory agents [22]. Additionally, substituted tetrahydropyridines have also been established as therapeutic agents such as clebopride, cisapride, bamipine, fentanyl, α-methylfentanyl

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and indoramine [23]. To date, methods for the synthesis of functionalized tetrahydropyridines have been reported using multi-component reactions in the presence of L-proline/TFA [19], $InCl_3$ [24], VCl_3 [25], bromodimethylsulfonium bromide (BDMS) [26], tetrabutylammonium tribromide (TBATB) [27], I_2 [28], cerium ammonium nitrate (CAN) [29], $Bi(NO_3)_3{\cdot}5H_2O$ [30], $ZrOCl_2{\cdot}8H_2O$ [31], and $BF_3{\cdot}SiO_2$ [32]. However, owing to the importance of dihydropyrrol-2-ones and tetrahydropyridines from pharmaceutical and biological view points, there is still the need to develop efficient protocols for the synthesis of these heterocycles. Therefore, in this work, N^1,N^1,N^2,N^2-tetramethyl-N^1,N^2-bis(sulfo)ethane-1,2-diaminium chloride ([TMBSED][Cl]$_2$) was utilized as an efficient ionic liquid catalyst for the synthesis of dihydropyrrol-2-ones and functionalized tetrahydropyridines.

EXPERIMENTAL

Preparation of [TMBSED][Cl]$_2$

To a stirred solution of chlorosulfonic acid (10 mmol) in CH_2Cl_2 (30 ml), a mixture of N^1,N^1,N^2,N^2-tetramethyl ethan-1,2-diamine (5 mmol) in CH_2Cl_2 (30 ml) was added drop wise at 10 °C over 10 min. The mixture was then allowed to warm up to room temperature and stirred for 4 h. The solvent was evaporated under reduced pressure, and the residue was washed with petroleum ether (3 × 10 ml) and dried at 90 °C under vacuum conditions. Then, [TMBSED][Cl]$_2$ was obtained as viscose pale yellow oil in 97% yield [33]. IR (Nujol, cm^{-1}): ν = 3300-2400, 1291, 1146, 1023, 856; ^{1}H NMR (250 MHz, DMSO-d_6): 2.82 (12H, s, 4CH_3), 3.48 (4H, s, 2CH_2), 12.50 (2H, br s, 2H) ppm; ^{13}C NMR (62.5 MHz, DMSO-d_6): 42.5 (s, CH_3), 50.4 (CH_2) ppm; MS (EI, 70 eV): *m/z* (%) = 349 (M^+, 8).

General Procedure for the Synthesis of Dihydropyrrol-2-ones (5)

A mixture of amine 1 (1 mmol) and dialkyl acetylenedicarboxylate 2 (1 mmol) in ethanol (3 ml) was stirred for 30 min. Next, aromatic amine 3 (1 mmol), formaldehyde 4 (37% solution, 1.5 mmol) and [TMBSED][Cl]$_2$ (20 mol%) were added successively. The reaction mixture was allowed to stir at ambient temperature for the appropriate time. The progress of the reaction was monitored by TLC. After completion, the solid precipitate was filtered off and washed with ethanol to afford the pure product 5.

General Procedure for the Synthesis of Functionalized Tetrahydropyridines (9)

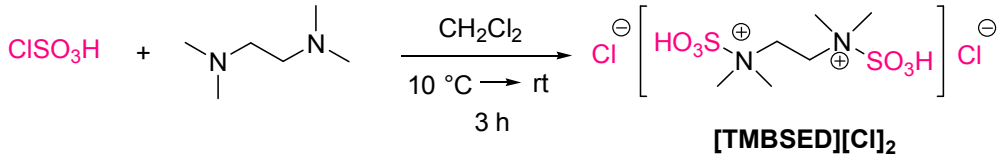
First, a solution of aromatic amine 6 (2 mmol) and *β*-ketoester 7 (1 mmol) in methanol (5 ml) was stirred for 30 min in the presence of [TMBSED][Cl]$_2$ (25 mol%) at ambient temperature. Next, the aromatic aldehyde 8 (2 mmol) was added and the reaction mixture was allowed to stir for an appropriate time under reflux conditions. After completion of the reaction (monitored by TLC), the reaction mixture was cooled to room temperature and the precipitate was filtered off and washed with ethanol to give the pure product 9.

Physical and Spectral Data for the Selected Products

Methyl-2,5-dihydro-5-oxo-1-phenyl-4-(phenyl-amino)-1*H*-pyrrole-3-carboxylate (5a, Table 2, entry 1). White solid; ^{1}H NMR (400 MHz, $CDCl_3$): δ = 3.76 (s, 3H, OCH_3), 4.57 (s, 2H, CH_2-N), 7.16-7.23 (m, 4H, ArH), 7.35 (t, J = 7.6 Hz, 2H, ArH), 7.42 (t, J = 7.6 Hz, 2H, ArH), 7.81 (t, J = 8.0 Hz, 2H, ArH), 8.05 (br s, 1H, NH); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 48.4, 51.5, 102.9, 120.0, 122.9, 124.5, 125.8, 128.5, 129.4, 137.7, 138.7, 143.1, 163.7, 164.4.

Ethyl-4-(4-Chlorophenylamino)-1-(4-chlorophenyl)-2,5-dihydro-5-oxo-1*H*-pyrrole-3-carboxylate (5f, Table 2, entry 6). White solid; ^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.29 (t, J = 7.2 Hz, 3H, OCH_2CH_3), 4.27 (q, J = 7.2 Hz, 2H, OCH_2CH_3), 4.52 (s, 2H, CH_2-N), 7.09 (d, J = 8.8 Hz, 2H, ArH), 7.29 (d, J = 8.4 Hz, 2H, ArH), 7.37 (d, J = 8.8 Hz, 2H, ArH), 7.76 (d, J = 8.8 Hz, 2H, ArH), 8.07 (br s, 1H, NH); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 14.2, 48.2, 60.6, 104.2, 120.2, 123.9, 128.4, 129.2, 129.9, 130.2, 137.1, 137.2, 142.6, 163.6, 164.5.

Ethyl-1-(4-bromophenyl)-3-(butylamino)-2,5-di-hydro-5-oxo-1*H*-pyrrole-3-carboxylate (5k, Table 2, entry 11). White solid; ^{1}H NMR (400 MHz, $CDCl_3$): δ = 0.97 (t, J = 7.2 Hz, 3H, CH_3), 1.35 (t, J = 7.2 Hz, 3H, OCH_2CH_3), 1.43 (sextet, J = 7.6 Hz, 2H, CH_2), 1.61 (quintet, J = 7.6 Hz, 2H, CH_2), 3.87 (t, J = 7.2 Hz, 2H, CH_2-



Scheme 1. Preparation of N^1,N^1,N^2,N^2-tetramethyl-N^1,N^2-bis(sulfo)ethane-1,2-diaminium chloride ([TMBSED][Cl]$_2$)

NH), 4.28 (t, J = 7.2 Hz, 2H, OCH_2CH$_3$), 4.40 (s, 2H, CH_2-N), 6.72 (br s, 1H, NH), 7.52 (d, J = 8.8 Hz, 2H, ArH), 7.71 (d, J = 8.8 Hz, 2H, ArH); ^{13}C NMR (100 MHz, CDCl$_3$): δ = 13.8, 14.5, 19.8, 33.4, 42.8, 47.8, 59.8, 98.1, 117.8, 120.5, 132.0, 137.9, 164.6, 165.5.

Methyl-4-(4-fluorophenylamino)-1-(4-fluorophenyl)-2,6-bis(4-methylphenyl)-1,2,5,6-tetrahydropyridine-3-carboxylate (9d, Table 4, entry 4). White solid; ^{1}H NMR (400 MHz, CDCl$_3$): δ = 2.36 (s, 3H, CH$_3$), 2.38 (s, 3H, CH$_3$), 2.66 (dd, J = 15.1, 2.8 Hz, 1H, H'-5), 2.86 (dd, J = 15.1, 6.0 Hz, 1H, H''-5), 3.95 (s, 3H, OCH$_3$), 5.08 (d, J = 4.0 Hz, 1H, H-6), 6.25-6.28 (m, 2H, ArH), 6.33 (s, 1H, H-2), 6.43-6.48 (m, 2H, ArH), 6.77-6.84 (m, 4H, ArH), 7.05-7.20 (m, 8H, ArH), 10.17 (s, 1H, NH); ^{13}C NMR (100 MHz, CDCl$_3$): δ = 21.0, 21.1, 33.6, 51.0, 55.4, 58.1, 98.0, 113.6 (d, J = 7.0 Hz), 115.2 (d, J = 22.0 Hz), 115.6 (d, J = 22.0 Hz), 126.4 (d, J = 23.0 Hz), 128.0 (d, J = 8.0 Hz), 129.0, 129.4, 133.9 (d, J = 3.0 Hz), 136.0, 136.9, 139.7, 140.6, 143.5, 155.0 (d, $^1J_{CF}$ = 233.0 Hz), 156.2, 160.7 (d, $^1J_{CF}$ = 244.0 Hz), 168.6.

Ethyl-4-(4-methylphenylamino)-1,2,6-tri(4-methylphenyl)-1,2,5,6-tetrahydropyridine-3-carboxylate (9g, Table 4, entry 7). White solid; ^{1}H NMR (400 MHz, CDCl$_3$): δ = 1.49 (t, J = 7.0 Hz, 3H, OCH$_2$CH_3), 2.20 (s, 3H, CH$_3$), 2.31 (s, 3H, CH$_3$), 2.36 (s, 3H, CH$_3$), 2.38 (s, 3H, CH$_3$), 2.78 (dd, J = 15.1, 2.4 Hz, 1H, H'-5), 2.87 (dd, J = 15.1, 5.6 Hz, 1H, H''-5), 4.37 (dq, J = 10.4, 7.2 Hz, 1H, OCH$_a$H$_b$), 4.48 (dq, J = 10.4, 6.8 Hz, 1H, OCH$_a$H$_b$), 5.13 (d, J = 3.6 Hz, 1H, H-6), 6.23 (d, J = 8.4 Hz, 2H, ArH), 6.42 (s, 1H, H-2), 6.49 (d, J = 8.8 Hz, 2H, ArH), 6.89 (d, J = 10.8 Hz, 2H, ArH), 6.93 (d, J = 7.6 Hz, 2H, ArH), 7.08-7.29 (m, 8H, ArH), 10.26 (s, 1H, NH); ^{13}C NMR (100 MHz, CDCl$_3$): δ = 14.8, 20.1, 20.9, 21.0, 21.1, 33.6, 55.0, 57.9, 59.5, 97.8, 112.8, 124.8, 125.9, 126.4, 126.6, 128.9, 129.2, 129.3, 129.4, 135.4, 135.6, 136.4, 140.0, 141.4, 145.0, 156.4, 168.3.

Methyl-4-(4-chlorophenylamino)-1-(4-chlorophenyl)-2,6-bis(4-methylphenyl)-1,2,5,6-tetrahydropyridine-3-carboxylate (9l, Table 4, entry 12). White solid; ^{1}H NMR (400 MHz, CDCl$_3$): δ = 2.35 (s, 3H, CH$_3$), 2.37 (s, 3H, CH$_3$), 2.74 (dd, J = 15.0, 1.6 Hz, 1H, H'-5), 2.88 (dd, J = 15.0, 5.6 Hz, 1H, H''-5), 3.96 (s, 3H, OCH$_3$), 5.10 (d, J = 3.8 Hz, 1H, H-6), 6.22 (d, J = 8.8 Hz, 2H, ArH), 6.36 (s, 1H, H-2), 6.46 (d, J = 8.8 Hz, 2H, ArH), 7.02-7.21 (m, 12H, ArH), 10.23 (s, 1H, NH); ^{13}C NMR (100 MHz, CDCl$_3$): δ = 21.0, 21.2, 33.5, 51.1, 55.1, 58.1, 98.6, 114.0, 121.1, 126.5, 126.7, 127.0, 128.6, 129.0, 129.7, 131.5, 136.1, 136.4, 137.0, 139.2, 140.2, 145.9, 155.5, 168.4.

RESULTS AND DISCUSSION

First, for preparation of the catalyst, chlorosulfonic acid was reacted with N^1,N^1,N^2,N^2-tetramethyl ethan-1,2-diamine in dichloromethane to afford [TMBSED][Cl]$_2$ as viscose pale yellow oil (Scheme 1) [33].

The structure of acidic ionic liquid catalyst was fully characterized by IR, ^{1}H and ^{13}C NMR, Mass, TG, DTG and DTA techniques. The FT-IR spectrum of [TMBSED][Cl]$_2$ exhibited characteristic absorptions at around 856 cm^{-1} (N-S), 1146 and 1291 cm^{-1} (S=O), and 2400-3300 cm^{-1} (SO$_3$H) groups. The ^{1}H NMR spectrum of [TMBSED][Cl]$_2$ showed two singlet peaks at 2.82 and 3.48 ppm for methyl and methylene groups, respectively. A fairly broad singlet was observed at 12.50 ppm for two acidic OH groups. In ^{13}C NMR of the catalyst two distinct singles observed at 42.5 and 50.4 ppm in agreement with the proposed structure. The mass spectrum of [TMBSED][Cl]$_2$ displayed the molecular ion peak (M$^+$) at m/z = 349 which was consistent with the 1:2 adduct of N^1,N^1,N^2,N^2-tetramethyl ethan-1,2-diamine and chlorosulfonic acid, respectively

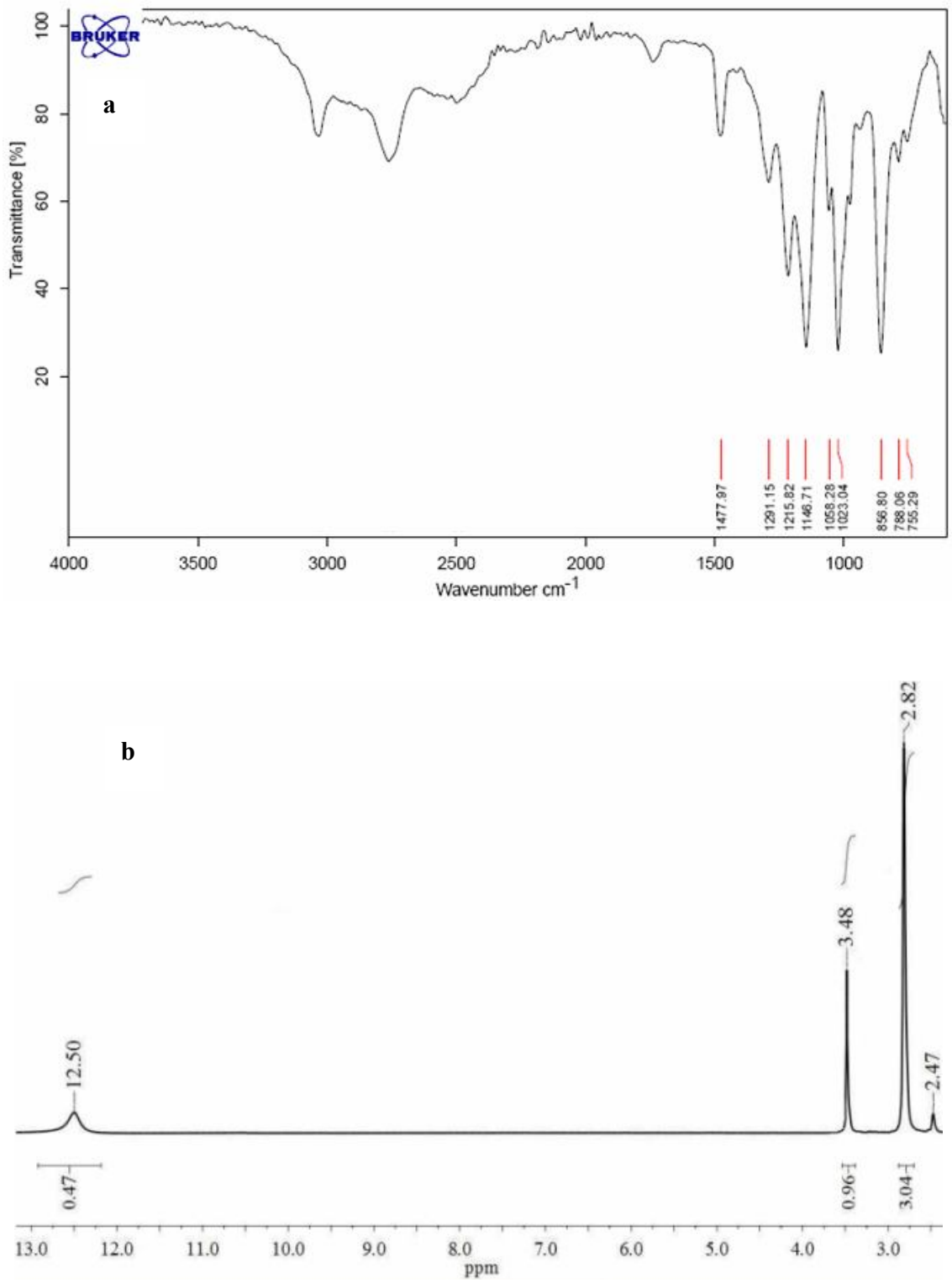


Fig. 1. (a) FT-IR, (b) ^{1}H NMR, (c) ^{13}C NMR and (d) mass spectra of [TMBSED][Cl]$_2$.

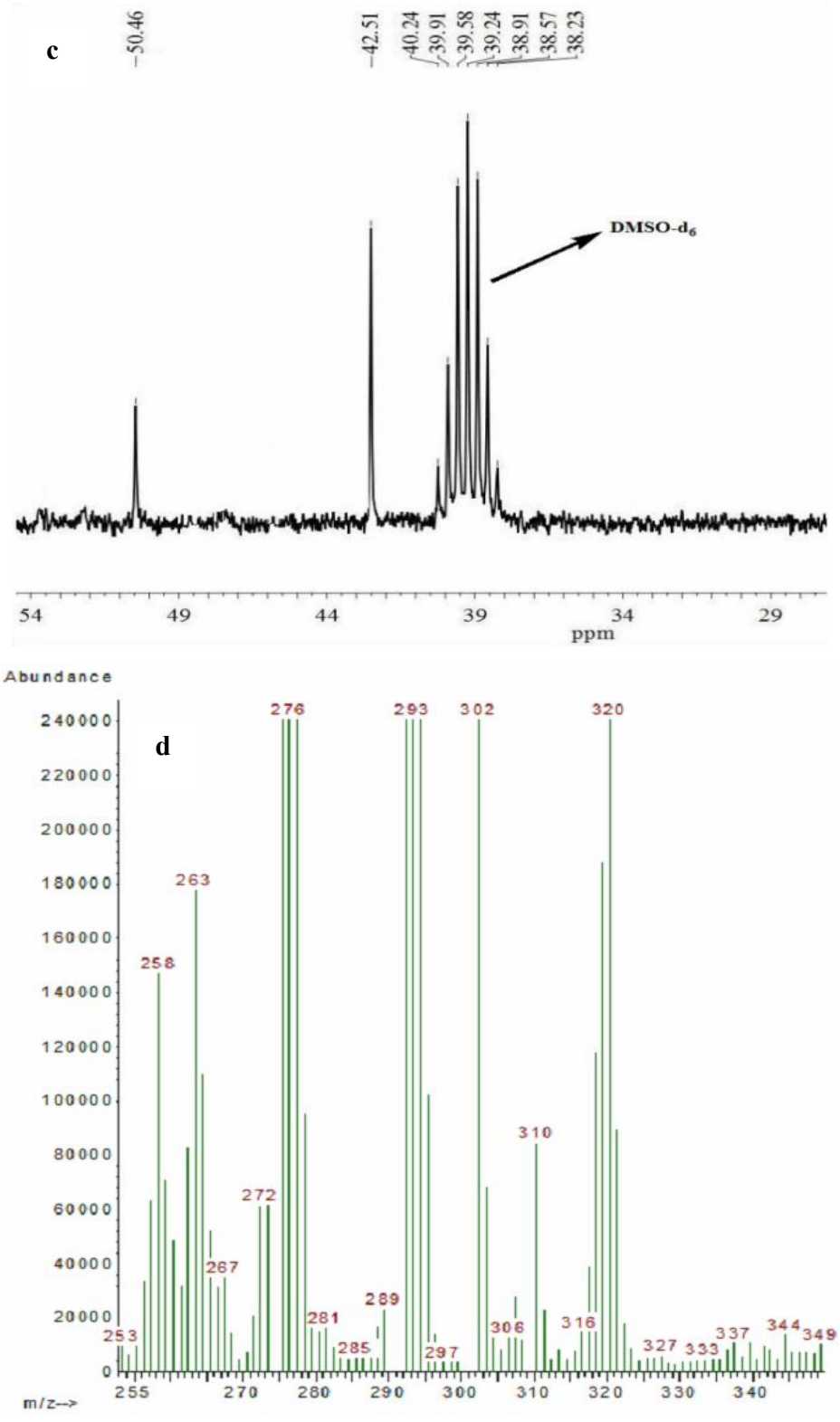


Fig. 1. Continued.

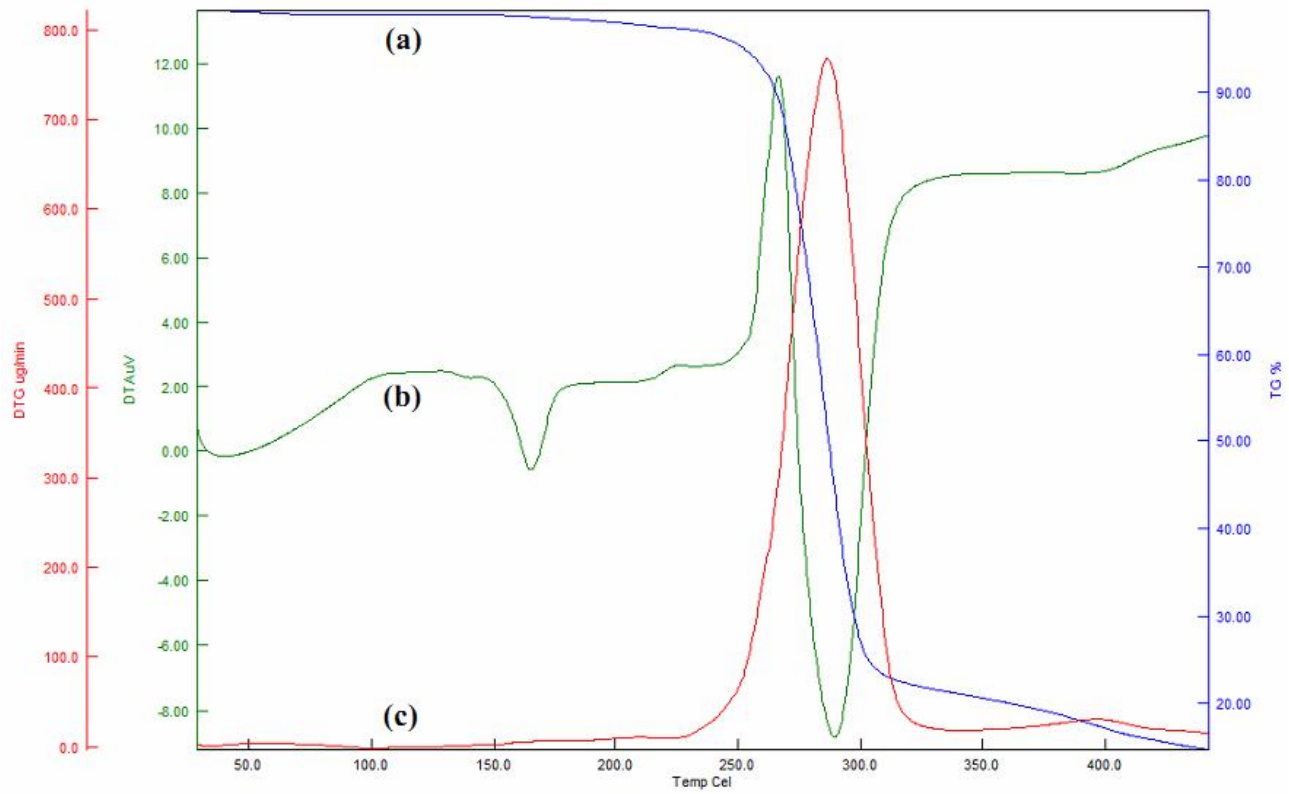
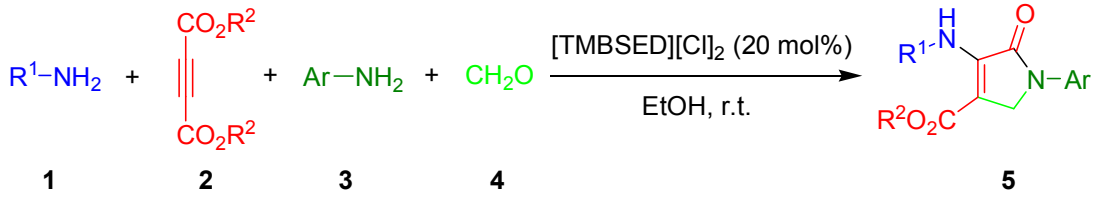


Fig. 2. (a) TG, (b) DTA, and (c) DTG spectra of $[TMBSED][Cl]_2$.



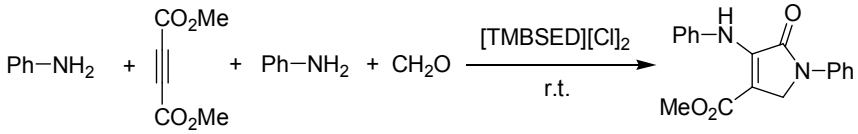
Scheme 2. Synthesis of highly substituted dihydropyrrol-2-ones, 5

(Fig. 1).

Thermogravimetry (TG), derivative thermogravimetry (DTG), and differential thermal analysis (DTA) diagrams of $[TMBSED][Cl]_2$ in a range of 25-450 ºC indicate the ionic liquid showed one weight loss at about 250-320 ºC (Fig. 2). In continuation of our work on heterocycles synthesis, especially synthesis of dihydropyrrol-2-ones [34-38], $[TMBSED][Cl]_2$ was employed as an efficient catalyst for the one-pot four-component synthesis of dihydropyrrol-2-ones in ethanol at ambient temperature (Scheme 2).

To find the optimal conditions, the reaction of aniline, dimethyl acetylendicarboxylate (DMAD) and formaldehyde was performed in the presence of different quantities of $[TMBSED][Cl]_2$ in various solvents at ambient temperature (Table 1). The use of 20 mol% of the catalyst in ethanol gave the highest yield of the corresponding product in 5 h (Table 1, entry 1). The reaction in the absence of the catalyst showed a trace yield of the product 5a (Table 1, entry 9). Under the optimized reaction conditions, various anilines

Table 1. Optimization of the Reaction Conditions for the Synthesis of 5a



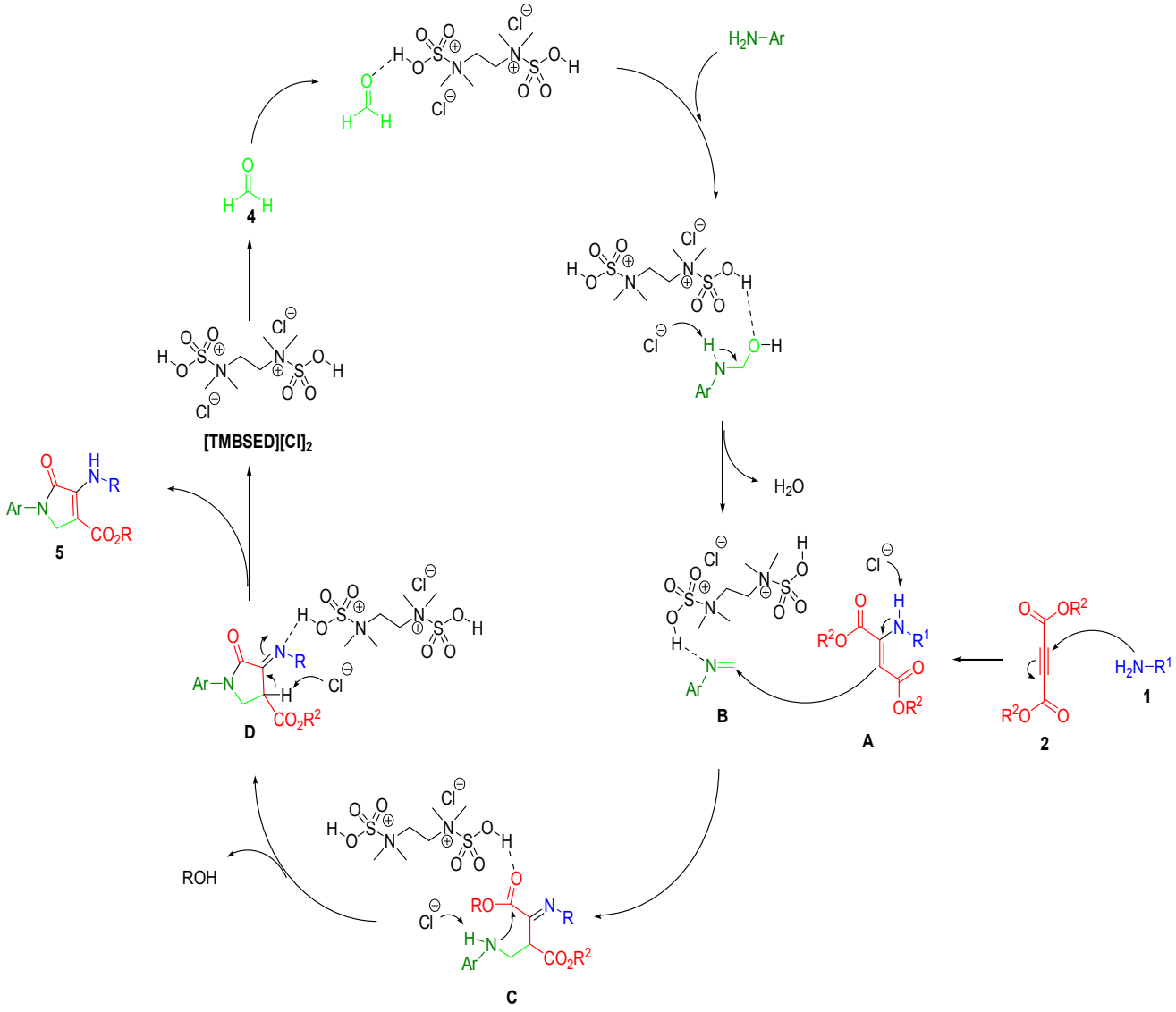
Entry	Solvent	Catalyst (mol%)	Time (h)	Yield (%)[a]
1	EtOH	20	5	89
2	MeOH	20	7	64
3	MeCN	20	8	69
4	THF	20	12	23
5	EtOH	10	8	36
6	EtOH	15	7	45
7	EtOH	25	5	89
8	EtOH	30	5	90
9	EtOH	No catalyst	24	Trace

[a]Yield of isolated product.

Table 2. Synthesis of Dihydropyrrol-2-ones 5a-k

Entry	R^1	R^2	Ar	Product	Time (h)	Yield (%)[a]	M.p. (°C) (lit. mp)[b]
1	Ph	Me	Ph	5a	5	89	153-155 (155-156)[15]
2	4-Cl-C_6H_4	Me	4-Cl-C_6H_4	5b	5	94	170-172 (173-174)[15]
3	4-Me-C_6H_4	Me	4-Me-C_6H_4	5c	6	81	164-166 (168-170)[15]
4	4-Br-C_6H_4	Me	4-Br-C_6H_4	5d	3	90	184-186 (179-180)[15]
5	Ph	Et	Ph	5e	7	78	133-135 (138-140)[13]
6	4-Cl-C_6H_4	Et	4-Cl-C_6H_4	5f	3	88	168-170 (168-170)[36]
7	4-Br-C_6H_4	Et	4-Br-C_6H_4	5g	5	92	164-166 (169-171)[13]
8	4-OMe-C_6H_4	Et	4-OMe-C_6H_4	5h	10	89	152-154 (151-153)[35]
9	$PhCH_2$	Me	Ph	5i	4.5	82	138-140 (140-141)[13]
10	$PhCH_2$	Me	4-Me-C_6H_3	5j	5	85	144-146 (144-146)[37]
11	*n*-C_4H_9	Et	4-Br-C_6H_4	5k	5	85	92-95 (94-96)[34]

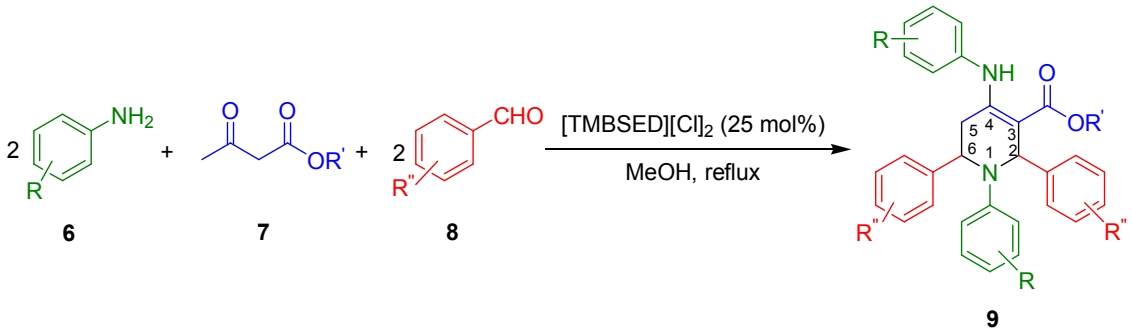
[a]Isolated yield. [b]Literature references for the known compounds.



Scheme 3. Suggested mechanism for the synthesis of dihydropyrrol-2-one 5 in the presence of $[TMBSED][Cl]_2$

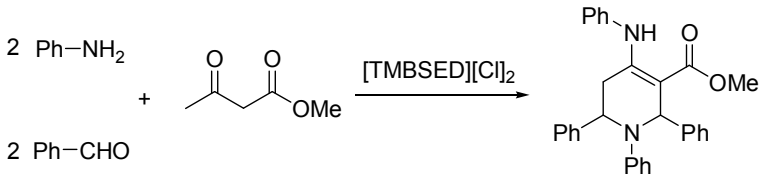
and dimethyl and/or diethyl acetylenedicarboxylates were used to test the versatility of this reaction; the results are summarized in Table 2. This protocol efficiently coupled anilines with electron donating and/or withdrawing groups to produce the expected products 5a-h in good to high yields (Table 2, entries 1-8). Additionally, aliphatic amines such as benzyl amine and *n*-butyl amine reacted smoothly with dialkyl acetylenedicarboxylates, aromatic amines and formaldehyde to generate the desired products including two different amine groups in high yields (Table 2, entries 9-11).

A reasonable mechanism for the synthesis of dihydropyrrol-2-one 5 was proposed in Scheme 3. The reaction between amine 1 and dialkyl acetylenedicarboxylate 2 gives intermediate A. Next, the reaction of amine 3 with formaldehyde 4 produce imine B. Attack of A on B leads to intermediate C which converts to intermediate D by intramolecular cyclization. In the final step, tautomerization of intermediate D produces the corresponding dihydropyrrol-2-one 5.



Scheme 4. Synthesis of tetrahydropyridine 9

Table 3. Optimization of the Reaction Conditions for the Synthesis of 9a



Entry	Solvent/Conditions	Catalyst (mol%)	Time (h)	Yield (%)[a]
1	EtOH/r.t.	20	22	65
2	MeOH/r.t.	20	5	77
3	MeCN/r.t.	20	7	60
4	THF/r.t.	20	24	Trace
5	EtOH/Reflux	20	16	85
6	MeOH/Reflux	20	2	85
7	MeCN/Reflux	20	7	80
8	MeOH/Reflux	10	4	62
9	MeOH/Reflux	15	3	79
10	MeOH/Reflux	25	1	92
11	MeOH/Reflux	30	1	93
12	MeOH/Reflux	No catalyst	12	20

[a]Yield of isolated product.

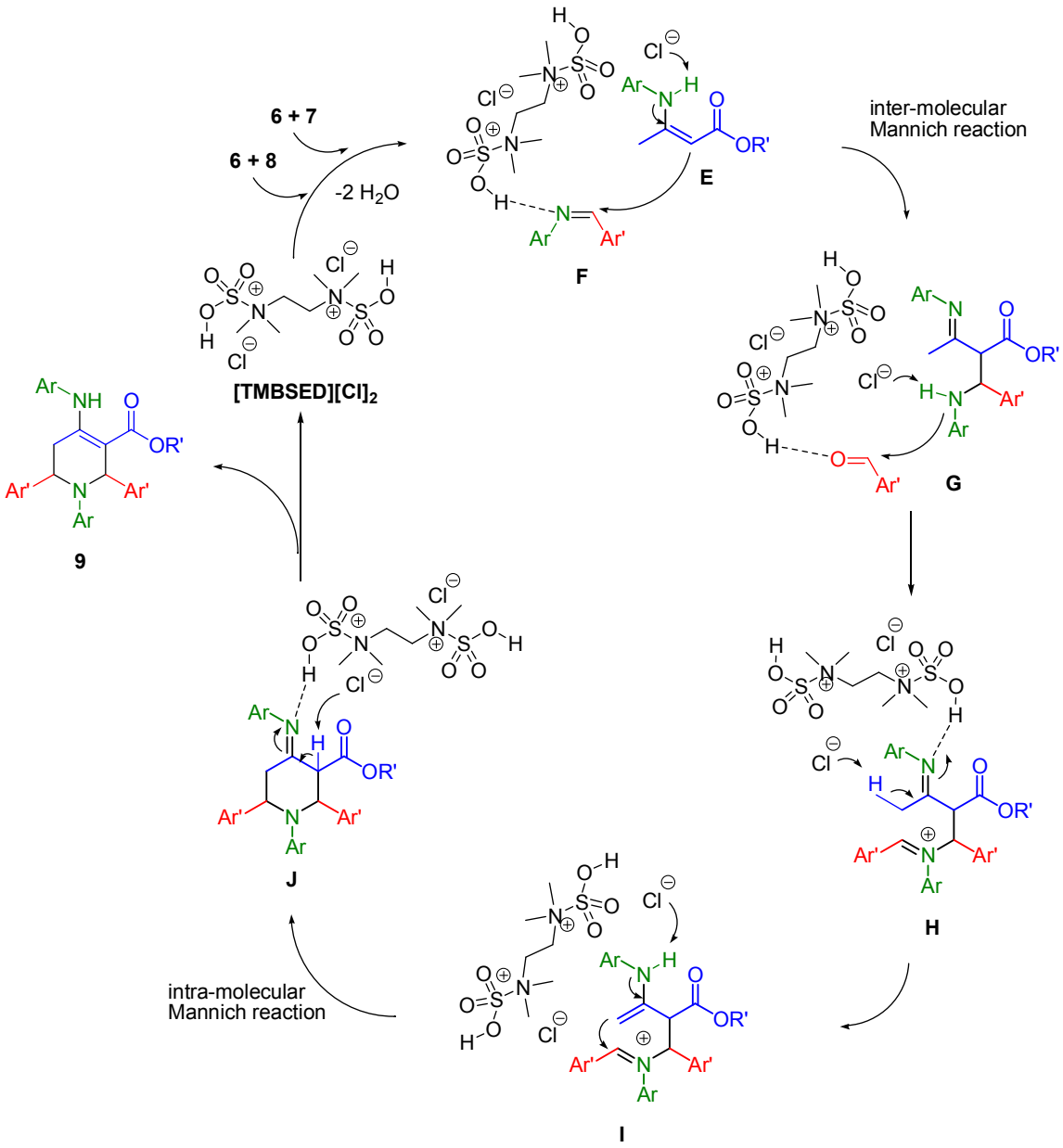
Table 4. Synthesis of Substituted Tetrahydropyridines 9a-m

Entry	R	R′	R″	Product	Time (h)	Yield (%)[a]	M.p. (ºC) (lit. mp)[b]
1	H	Me	H	9a	1	92	186-188 (185-186)[28]
2	H	Me	4-Cl	9b	3	90	220-222 (225-227)[28]
3	H	Me	4-Me	9c	1	84	210-212 (215-217)[28]
4	4-F	Me	4-Me	9d	1	94	198-200 (199-201)[42]
5	4-Me	Me	H	9e	1	83	186-188 (190-192)[35]
6	4-Me	Et	H	9f	5	91	190-193 (196-198)[30]
7	4-Me	Et	4-Me	9g	1	90	169-171 (169-171)[39]
8	4-Cl	Me	4-Br	9h	4	91	163-165 (159-161)[25]
9	4-OMe	Me	3-Cl	9i	4	88	160-162 (162-163)[29]
10	4-Me	Me	4-Me	9j	1	92	201-203 (206-208)[28]
11	H	Me	4-OMe	9k	4	80	181-183 (186-188)[28]
12	4-Cl	Me	4-Me	9l	2	84	204-206 (204-206)[43]
13	H	Me	4-NO_2	9m	5	45	233-235 (239-241)[28]

[a]Isolated yield. [b]Literature references for known compounds.

Recently, we have reported the effective synthesis of piperidine derivatives using multi-component reactions [39-43]. Motivated from the efficient catalytic activity of $[TMBSED][Cl]_2$ for the synthesis of dihydropyrrol-2-ones, its catalytic activity was examined for the synthesis of substituted tetrahydropyridines, 9, *via* one-pot three-component reaction of amines, aldehydes and β-ketoesters in methanol under reflux conditions (Scheme 4).

At the outset, the reaction between benzaldehyde (2 mmol), aniline (2 mmol) and methyl acetoacetate (1 mmol) was carried out in the presence of $[TMBSED][Cl]_2$ (20 mol%) in ethanol at room temperature. The reaction proceeds smoothly to generate the corresponding highly substituted tetrahydropyridine 9a in 65% yield after 22 h. In order to optimize the reaction conditions, this reaction was considered as the model (Table 3). The best result was achieved in the presence of 25 mol% $[TMBSED][Cl]_2$ in methanol under reflux conditions (Table 3, entry 10). To illustrate the need for catalytic amounts of $[TMBSED][Cl]_2$ in these reactions, the model reaction was also studied in the absence of the catalyst in methanol, where product was obtained in a trace yield even after 12 h (Table 3, entry 12).



Scheme 5. Proposed mechanism for the synthesis of tetrahydropyridines 9 in the presence of $[TMBSED][Cl]_2$

Using the optimized reaction conditions, a series of functionalized tetrahydropyridines were prepared in good to high yields from the reaction between aromatic aldehydes, anilines and methyl/ethyl acetoacetate. As indicated in Table 4, anilines containing electron withdrawing and/or electron donating groups reacted efficiently with benzaldehyde and substituted benzaldehydes to give the corresponding products 9 in good to high yields.

On the basis of the previous literature [26-29], the proposed mechanism for the formation of tetrahydropyridine 9 is illustrated in Scheme 5. First, aniline 6 reacts with *β*-ketoester 7 and aldehyde 8 in the presence of $[TMBSED][Cl]_2$ to give enamine E and imine F, respectively. Next, the reaction between enamine E and

Table 5. Comparison Results of $[TMBSED][Cl]_2$ with Previously Reported Catalysts [12]

Compound	Conditions	Time (h)	Yield (%)	Ref.
5a	I_2 (10 mol%), MeOH, r.t.	1	82	[15]
	$Cu(OAc)_2 \cdot H_2O$ (0.4 mmol), benzaldehyde (2 mmol, as additive), MeOH, r.t.	6	91	[18]
	$Al(H_2PO_4)_3$ (0.1 g), MeOH, r.t.	5	81	[35]
	[TMG][Ac] (25 mol%), MeOH, r.t.	5	81	[38]
	$[TMBSED][Cl]_2$ (20 mol%), EtOH, r.t.	5	89	This work
9a	$InCl_3$ (33.5 mol%), CH_3CN, r.t.	24	60	[24]
	BDMS (10 mol%), CH_3CN, r.t.	3	75	[26]
	TBATB (10 mol%), EtOH, r.t.	24	74	[27]
	I_2 (10 mol%), MeOH, r.t.	8	81	[28]
	CAN (15 mol%), CH_3CN, r.t.	20	82	[29]
	$ZrOCl_2 \cdot 8H_2O$ (20 mol%), EtOH, reflux	3.5	80	[31]
	p-$TsOH \cdot H_2O$ (0.11 g), EtOH, r.t.	10	78	[40]
	$BF_3 \cdot SiO_2$ (15 mol%), MeOH, 65 °C	9	78	[32]
	$Bi(NO_3)_3 \cdot 5H_2O$ (10 mol%), EtOH, r.t.	12	81	[30]
	L-proline/TFA (20 mol%), CH_3CN, r.t.	17	70	[19]
	$[TMBSED][Cl]_2$ (20 mol%), MeOH, reflux	1	92	This work

activated imine F leads to intermediate G through intermolecular Mannich-type reaction. The intermediate G reacts with aldehyde 8 to generate intermediate H. Then, tautomerization of H generates intermediate I, which immediately undergoes intramolecular Mannich-type reaction to produce intermediate J. Eventually, tautomerization of the intermediate J. generates the desired tetrahydropyridine 9 due to conjugation with the ester group. The results of this work are compared with the previously reported methods in Table 5. Considering the reaction time and amount of the catalyst, the presented work can be useful for preparation of these important compounds.

In general, at the beginning of both reactions for the synthesis of dihydropyrrol-2-ones and tetrahydropyridines, the reagents were completely soluble in reaction medium to form a homogeneous mixture. However, at the end of the reaction, the products 5 and 9 were precipitated and separated by simple filtration. No column chromatography

technique was used for the products purification. This avoids use of large amounts of volatile organic solvents, as the solvent is generally the main source of waste and the environmental pollutants.

CONCLUSIONS

This work shows that N^1,N^1,N^2,N^2-tetramethyl-N^1,N^2-bis(sulfo)ethane-1,2-diaminium chloride, which can be prepared by simple operation from commercially available and cheap starting materials, is an efficient catalyst for one-pot and multi-component synthesis of dihydropyrrol-2-ones and substituted tetrahydropyridines. The noteworthy aspects of these procedures are high atom economy, good to high yields, readily available starting material, and operational simplicity. Moreover, all products were obtained through simple filtration without need to column chromatography, which in turn reduces the waste and environmental pollutants.

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