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Abstract

Nicotine-based ionic liquid has been prepared and used as a green, alternative recyclable solvent as well as catalyst for pyridine-catalyzed Huisgen reaction. It involves pyridine promoted addition of dimethylacetylenedicarboxylate to aldehydes or *N*-tosylimines leading to efficient synthesis of 2-benzoylfumarates and 1-azadienes respectively. The same reactions repeated under pyridine free odorless ionic liquid conditions. The improved results were obtained in terms of enhanced yields, with minimal work up.

Introduction

Pyridine is well known versatile liquid organic compound which is employed as a solvent as well as an organocatalyst for many vital organic transformations. [1] Pyridine is polar aprotic liquid containing nitrogen with a lone pair of electron which impart basic and nucleophillic character to it. Consequently the pyridine in many reactions acts as a proton scavenger due to its basic nature and as a good nucleophile with a donor number of 33.1. The presence of nucleophillic nitrogen in pyridine enables it to catalyze many reactions like acylation of alcohols, amines and thiols.[2] It is especially suitable for the elimination reactions like dehydrohalogenation, where it acts as the base and scavenges the hydrogen halide to facilitate the formation of elimination product and prevents the other possible side reactions. In esterification and acylation reactions, the pyridine activates the acid anhydrides and acts as an active acylating agent. In addition to this, some condensation reactions have also been achieved through pyridine such as Knoevenagel condensations where it acts as a base.[3a] To make these reactions more efficient, more active the pyridine derivatives like 4-dimethylamino pyridine (DMAP) and 4-(1-pyrrolidinyl) pyridine have been prepared and used in different reaction. [3b] DMAP is a more powerful derivative of pyridine which acts as an efficient

nucleophillic catalyst for a variety of useful reactions such as esterifications with anhydrides, the Baylis-Hillman reaction, hydrosilylations, tritylation, the Steglich rearrangement, Staudinger synthesis of *β*-lactams and many more. Chiral DMAP analogues are also used in kinetic resolution experiments of mainly secondary alcohols and Evans auxiliary type amides.[3c-d]

Another remarkable aspect of pyridine applications is that some reactive chemical reagents are used in form of complexes of pyridine to make them stable and selective for various reactions. For example Pyridine-borane, $C_5H_5NBH_3$ (m.p. 10–11 °C) is a mild reducing agent with improved stability versus $NaBH_4$ in protic solvents and also exhibits the improved solubility in aprotic organic solvents.[4] Pyridine-sulfur trioxide, $C_5H_5NSO_3$ (m.p. 175 °C) is a sulfonation agent used to convert alcohols to sulfonates, which in turn undergo C-O bond scission upon reduction with hydride reagents.[5] Pyridinium chlorochromate (PCC) is a mild oxidizing agent used for oxidation of primary and secondary alcohols. It contains chromium trioxide in stable form as complex with pyridine.[6] Pyridine *N*-oxide is stable source of electrophillic oxygen which can be used to achieve various selective oxidations.[7] Apart from acting as a solvent and reagents, the pyridine is also used as a starting material for the synthesis of some useful scaffolds. These are further used as starting material for synthesis of certain useful commercial compounds such as insecticides, herbicides, pharmaceuticals, food flavorings, dyes, rubber chemicals, adhesives, paints, explosives and disinfectants.[8] Despite of these amazing properties and wide range of applications, the use of pyridine is often minimized and restricted due to its toxicity and hazardous effects on human health. The carcinogenic pyridine can be absorbed through skin thus poses greater health risk. [9] Available data indicates that "exposure to pyridine in drinking-water led to reduction of sperm motility at all dose levels in mice and increased estrous cycle length at the highest dose level in rats".[10]

Many alternative reagents and methods have been devised to circumvent the use of pyridine. Nevertheless the use of pyridine seems to be unavoidable under certain conditions; therefore it is better to conceive some ionic liquid substitute of pyridine. Ionic liquids are replacing, wherever possible, the traditional toxic organic solvents in the synthesis because of their non volatility, nonflammability, thermal stability and ease of recyclability.[11] Task specific ionic

liquid is special class of ionic liquids that contains specific functionalities which are capable of promoting some key organic transformations. These ionic liquids are prepared by attaching certain suitable organocatalyst to imidazolium ring which is common cationic part of such ionic liquids**.** This strategy leads to some valuable advantages over routine methods such as improved catalyst efficiency, green reaction conditions and procedural convenience. A large number of task specific ionic liquids have been designed and synthesized for many organocatalyzed reactions and used successfully with good results. [12] For example, Beckmann rearrangement,[13] Brönsted acidic reactions,[14] quinuclidine-catalyzed Morita-Baylis-Hillman reactions,[15] asymmetric Michael addition reactions, [16] Swern oxidation, [17] Claisen–Schmidt reaction, [18] Mannich reaction, [19] ionic liquid-supported NHPI complex.[20] Apart from this, we have introduced a novel concept of "multipurpose ionic liquids" which can promote more than one different types of reactions. For this, we have reported the synthesis and applications of novel (Dimethylformamide) DMF-like ionic liquid for promoting all DMF-dependent reactions.[21] Due to its ability to promote myriad type of reactions, this has become the first example of "multipurpose ionic liquids". In contrast to other reported ionic liquids which are "task specific" in nature means they are designed for one specific reaction only, the DMF-like ionic liquid is "multipurpose" in sense that it can facilitate many different types of reactions. We have reported numerous highly useful applications of "multipurpose" DMF-like ionic liquid as a solvent and as a solvent-cum-reagent. Vilsmier reagent is one of the well known and powerful organoreagent used to achieve some useful organic transformations. Normally this is prepared from DMF, its ionic liquid version been prepared from DMF-like ionic liquid which is more stable and efficient. This ionic liquid version of Vilsmier reagent has been used for various Vilsmier reagent catalyzed reaction such as direct iodination of alcohols,[22] many more applications have also been reported.[23]

Handy et al have reported nicotine-based ionic liquid (Figure1) and investigated its potential as an ionic liquid based nucleophillic solvent for acylation of different types of alcohols with acetic anhydride (Scheme 1).[24] The nicotine-based task specific ionic liquid contains active pyridine unit with nucleophillic nitrogen which is non-volatile, stable and free from all hazardous effects of pyridine. In addition to this, the nicotine-based ionic liquid demonstrates the enhanced reactivity which leads to efficient results i.e. rapid reaction rates and enhanced

product yields. This observation arises from marginal stabilization of transition states or reactive intermediates associated with reactions performed under ionic liquid conditions. The formation of polar transition states and charged reactive intermediates in ionic liquids is encouraged by the greater stabilization effect of ionic liquid arising from its highly polar and saline nature. Consequently the nicotine-based ionic liquid was proved to be an efficient substitute of ordinary pyridine as a green solvent as well as stable and recyclable organocatalyst for acetylation of alcohols with acetic anhydride.

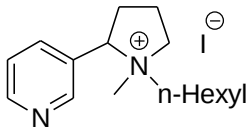
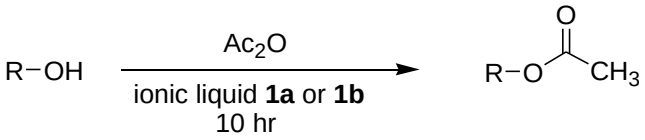


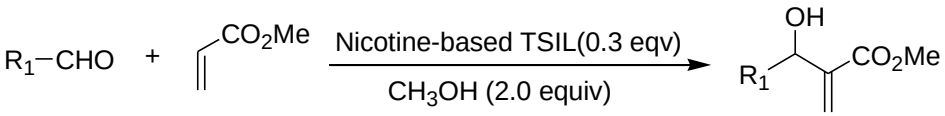
Fig. 1

According to the reported claim the nicotine-based task specific ionic liquid TSIL (Figure 1) was investigated for acylation of various types of alcohols. It effectively mediated the acylation of simple primary and secondary alcohols as well as relatively more hindered alcohol like 2-phenylethanol with acetic anhydride. However no reaction was observed with a tertiary alcohol at room temperature and modified condition were used to achieve its acylation (Scheme 1).



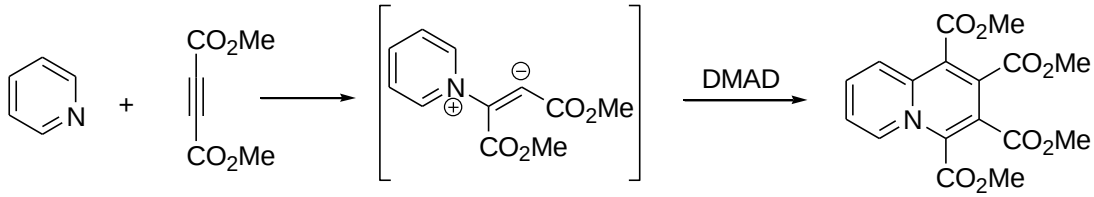
Scheme-1

The success of this reaction tempted us to believe that other pyridine-catalyzed reaction can also be carried out with nicotine based TSIL. In order to make this nicotine-based ionic liquid another "multipurpose ionic liquid" for all pyridine catalyzed reactions, we carried out extensive literature survey to collect all related reactions. As a result we have already reported a successful use of nicotine-based task specific ionic liquid (TSIL) in achieving pyridine-dependent Baylis-Hilmann reaction with improved results and procedural convenience (Scheme 2). [25]



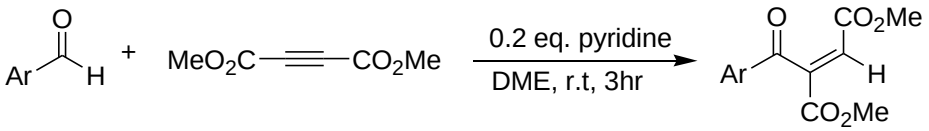
Scheme-2

In continuation of our efforts to widen the scope of applications of nicotine-based (TSIL) and to prove it to be "multipurpose" in its function, we are reporting another pyridine-catalyzed reaction known as Huisgen cycloaddition reaction. This reaction involves the pyridine mediated cycloaddition reaction of dimethylacetylenedicarboxylate (DMAD) with dipolarophiles like aldehydes or *N*-tosylimines leading to the efficient synthesis of 2-benzoylfumarates and 1-azadienes respectively [26]. The process involves the nucleophillic attack of pyridine on DMAD to form highly reactive 1,3-dipolar intermediate that reacts with dipolarophiles like aldehydes or *N*-tosylimines to give 2-benzoylfumarates or highly substituted 1-azadienes respectively with *in situ* elimination of pyridine (Scheme 7). Diels and Alder have already established the ability of pyridine to attack dimethyl acetylenedicarboxylate (DMAD) to form a 1,3-dipolar intermediate which reacts further with one more DMAD to form an adduct called 4H-quinolizine (Scheme 3). [27]



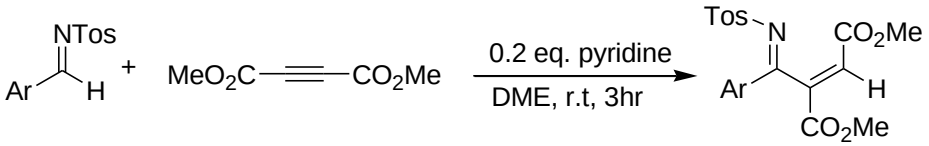
Scheme-3.

This reaction has been studied in detail by Acheson, who has further proved the existence of the 1,3-zwitterionic intermediate (Scheme 3). [28] He showed that pyridine reacts feasibly with dimethylacetylenedicarboxylate (DMAD) forming 1,3-dipolar zwitterion which can be trapped with suitable dipolarophiles to form corresponding adducts. V. Nair et al identified the potential of this reaction for construction of heterocyclic systems by trapping the 1,3-zwitterionic intermediates with carbonyl compounds.[29] He demonstrated that trapping the 1,3-dipole with aryl aldehydes afforded the corresponding aroyl fumarate (Scheme 4).



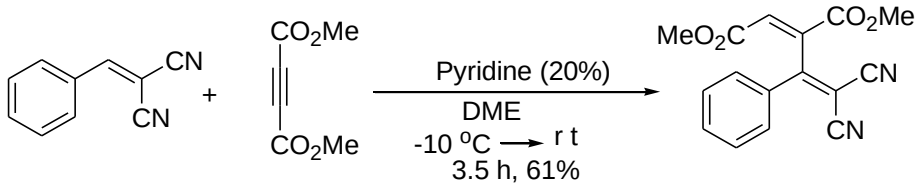
Scheme-4.

Similarly the same reaction with *N*-tosylimines as a dipolarophile produced 1-azadienes in quantitative amounts (Scheme 5).



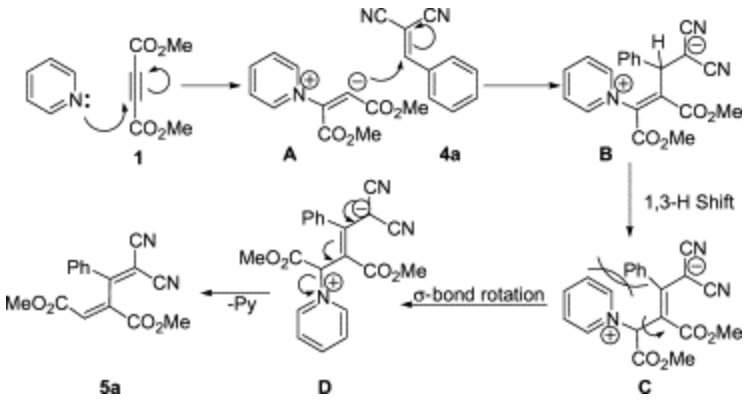
Scheme-5

In case of using arylmethylidenemalononitrile (*β*-dicyanostyrene) as dipolarophile afforded a highly substituted 1,3-butadiene with complete stereoselectivity (Scheme 6). [30]



Scheme-6

Mechanism: Mechanistically, the reaction involves [2 + 2] cycloaddition of the 1,3-zwitterion generated from pyridine and DMAD to the carbonyl group of the aldehyde to give an unstable oxetene, which undergoes stereospecific ring opening to give the *Z*-isomer.



Scheme-7

In this paper we are have investigated the potential of nicotine-based TSIL catalyzed formation of 1,3-zwitterion from DMAD and its subsequent reaction with various active unsaturated compounds like carbonyls, *N*-tosylimines and arylmethylidenemalononitriles (β-dicyanostyrenes) to form corresponding adducts.

Experimental

All the reagents and solvents were pure and of analytical grade chemicals purchased from Aldrich and were used without further purification. Melting/boiling points were determined with a Buchi 510 melting point apparatus (Flawi/SG, Switzerland) and are uncorrected. Electron impact (EIMS) mass spectra were determined with a Finniggan MAT-312 (Bremen, Germany), Vrain MAT-112 (Bremen, Germany) double focusing mass spectrometer connected to a PDP 11/34 (DEC) computer system. The 1H-NMR spectra were recorded in CD_3OD and $CDCl_3$ with Bruker AM 300 and 400 spectrometers (Rheinstetten-Forchheim, Germany) operating at 300 and 400 MHz, respectively. 1H-NMR chemical shifts are reported in δ (ppm) and coupling constants in Hz. The purity of the products was checked on TLC plates (Merck, Darmstadt, Germany), coated with silica gel PF254 and the spots were characterized with UV light at 254 and 366 nm and by spraying with ninhydrin and iodine tank.

Procedure for preparation of Nicotine based task specific ionic liquid

Preparation of Compound 8b

The nicotine **8a** (10 g, 0.079 mole) and benzyl bromide (13.5 g, 0.079 mole) were dissolved in 60 ml acetonitrile in 150 ml round bottom flask. The reaction mixture was refluxed and progress of reaction was monitored by TLC analysis. The reaction was completed during 15 hrs. After cooling, the solvent was removed in *vacuo*. The residual material was extracted with ether (5 × 15 mL) and the ether layer decanted. The remaining ionic liquid layer was dissolved in 5 mL of methylenechloride and filtered through Whatman #1 filter paper. Removal of the solvent in *vacuo* afforded 19.32 g (94%) of compound **8b** as a pale orange liquid.

^{1}HNMR (400MHz, $CDCl_3$) (ppm) 7.17 – 7.32 (m, 5H), 6.17(s, 2H), 7.24 – 9.37(m, 4H), 2.18 (s, 3H), 2.86(t, J = 7.35 Hz, 1H), 1.50 – 2.06 (dt, J = 7.35 Hz, J = 3.8 Hz, 2H), 1.80 – 206 (tt, J = 7.3 Hz, J = 3.8 Hz, 2H), 2.46 – 3.23 (t, J = 6.51 Hz, 2H) **^{13}CNMR (300MHz, CDCl3) (ppm)** Pyrrolidine 93.23(N-CH3), 54.32(CH2), 22.68(CH2), 34.54(CH2), 69.20(CH) Pyridine 132.09(C), 137.84(CH), 143.58 (CH), 124.29(CH), 140.11(CH), 62.33(N-CH2) Phenyl 134.69 (C), 128.23 (CH), 128.25(CH), 127.00(CH), 128.25(CH), 128.23(CH**)** **HRMS(EI)** C_{17} H_{21} N_2 Br calcd. 333.362; found 333.371

Preparation of Compound 8c

The Bromide salt **8b** (19.32 g, 0.058 mole) and hexyliodide (12.30g, 0.058 mole) were dissolved in 60 ml acetonitrile in 150 ml round bottom flask. The reaction mixture was refluxed for 20 hrs. After completion of reaction, as confirmed by TLC, yellow crystalline product was filtered from reaction mixture 0^{o}C, washed with acetone and recystallised twice from H_2O/acetone (15:85). The salt was dried in desiccators to give 40.04 g (95%) of desired product **8c**.

^{1}HNMR (400MHz, CDCl3) (ppm) 0.88 – 1.74(m, 11H), 3.11 – 3.32(t, J = 7.00 Hz, 2H), 7.17 – 7.32 (m, 5H), 6.17(s, 2H), 7.24 – 9.37(m, 4H), 3.11 (s, 3H), 4.55 (t, J = 9.00 Hz, 1H), 2.20 – 2.27 (dt, J = 9.00 Hz, J = 7.4 Hz, 2H), 2.20 – 2.27 (tt, J = 7.95 Hz, J = 7.45 Hz, 2H), 3.64 – 3.71 (t, J = 7.95 Hz, 2H) **^{13}CNMR (300MHz, $CDCl_3$) (ppm)** Pyrrolidine 48.77(N-CH3), 66.26(CH2), 20.75(CH2), 27.63(CH2), 81.01(CH) N-Hexyl 59.79(CH2), 23.93(CH2), 26.26(CH2), 31.20(CH2), 22.35(CH2), 13.80(CH3), Pyridine 138.61(C), 131.06(CH), 143.90 (CH), 123.55(CH), 138.35(CH), 62.33(N-CH2) Phenyl 134.69 (C), 128.23 (CH), 128.25(CH), 127.00(CH), 128.25(CH), 128.23(CH**)** **HRMS (EI)** C_{23} H_{34} N_2 Br I calcd.545.532; found 545.534.

Preparation of Compound 8d

The salt **8c** (30.04 g, 0.055 mole) and triphenylphosphine (14.42 g, 0.055 mole) were dissolved in 65 mL methanol in 150 mL round bottom flask. The reaction mixture was refluxed for 6 hrs. After completion of reaction as indicated by TLC, the solvent was concentrated under *vacuo*. The residue was extracted with (5x10 mL) diethyl ether. The ether was concentrated and ether residue was washed with water and dried with Na_2SO_4 to give 19.72 g (92%) of compound **8d**. **^{1}HNMR (400MHz, $CDCl_3$) (ppm)** 0.88 – 1.74(m, 11H), 3.11 – 3.32(t, J = 7.00 Hz, 2H), 9.48(s, 1H), 8.54(d, J 4.85Hz, 1H), 6.76(m, 1H), 8.81(m, 1H), 3.11 (s, 3H), 4.55 (t, J = 9.00 Hz, 1H), 2.20 – 2.27 (dt, J = 9.00 Hz, J = 7.4 Hz, 2H), 2.20 – 2.27 (tt, J = 7.95 Hz, J = 7.45 Hz, 2H), 3.64 – 3.71 (t, J = 7.95 Hz, 2H). **^{13}CNMR (300MHz, $CDCl_3$) (ppm)** Pyrrolidine 48.77(N-CH3), 66.26(CH2), 20.75(CH2), 27.63(CH2), 81.01(CH) N-Hexyl 59.79(CH2), 23.93(CH2), 26.26(CH2), 31.20(CH2), 22.35(CH2), 13.80(CH3), Pyridine 124.45(C), 141.13(CH), 145.69 (CH), 118.05(CH), 129.19(CH) **HRMS(EI)** $C_{17}H_{30}N_2I$ calcd. 389.434; found 389.438.

Preparation of Compound 8e

Lithium triflimide (14.40 g, 0.050 mmol) of was dissolved in 25 mL of water. And in a separate flask, 19.72 g (0.051 mol) of iodide 8d was dissolved in 65 mL of water. Both solutions were heated to 70 °C and then combined. The combined solution was allowed to cool to room temperature while stirring was continued for 3 h. The top aqueous layer was decanted and extracted with methylenechloride (2×5 mL). These washes were combined with the original remaining ionic liquid layer and washed with water (2×5 mL). The organic layer was filtered through a short plug of basic alumina and the solvent removed in *vacuo*. The residue was dried on a vacuum line overnight to afford 0.2193 g (72%) of 5 as a pale yellow liquid. Its purity was checked by both **^{1}HNMR** and **^{13}CNMR** as well as elemental analysis. **HRMS (FAB)** $C_{19}H_{30}N_3O_2F_6S_2Li$ calcd. 563.434, found 563.434

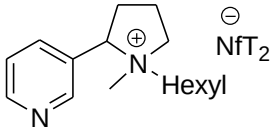
General Representative Procedure: A solution of dimethylacetylenedicarboxylate (1 equiv) and aldehyde (1 equiv) in dry acetonitrile (2 mL) was cooled to 0 °C. To this, nicotine-based (TSIL) **8e** (20 mol %) was added, and the reaction mixture was stirred at room temperature until completion of reaction as evident from TLC. The solvent was then removed under vacuum, the product as extracted from ionic liquid by ether. Ether was removed under *vacuo* to

get 2-oxo-3-benzylidenesuccinates. The nicotine-based TSIL was washed with distilled water then dried under *vacuo* and reused for next run.

Results and discussion

Synthesis of Nicotine based task specific ionic liquid

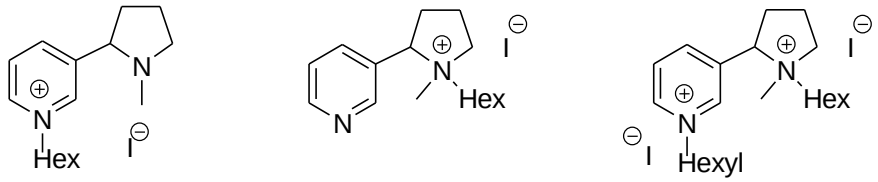
The required nicotine based task specific ionic liquid was synthesized according to the reported procedure. [31] The nicotine based task specific ionic **4e** was synthesized as shown in (scheme 4).



8e

Fig. 1

In theory, there are three possible types of room temperature ionic liquids (RTILs) available from nicotine i.e., two different monocations (**2a** and **2b**) and one dication **2c** (Figure 2). Of the two possible monocationic species only **2b** has active nucleophillic nitrogen to perform catalysis.

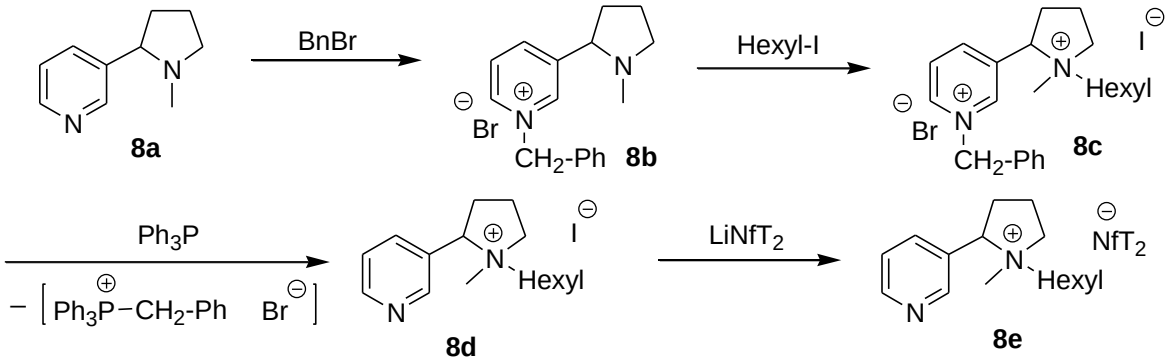


2a **2b** **2c**

Fig. 2

Selective preparation of nucleophillic nicotine ion **2b** is not quite as simple. The procedure requires the selective alkylation of the pyrrolidine moiety as reported by Shibagaki.[32] The procedure starts with regioselective *N*-benzylation of pyridine of nicotine **8a** with benzyl bromide to give **8b**. The bromide salt **4b** is then treated with hexyl iodide for *N*-alkylation of pyrrolidine to form dicationic salt **8c**. Treatment of *N*-benzyl-*N*'-alkylnicotinium dihalides **8c**

with Ph_3P provided a synthetic route to *N*'-hexylnicotinium salts **8d** with nucleophillic pyridine. The final iodide salt **8d** was highly viscous liquids at room temperature. The anionic metathesis of iodide ion in salt **8d** with triflimide produced was relatively less viscous liquid qualitatively.



Scheme-8

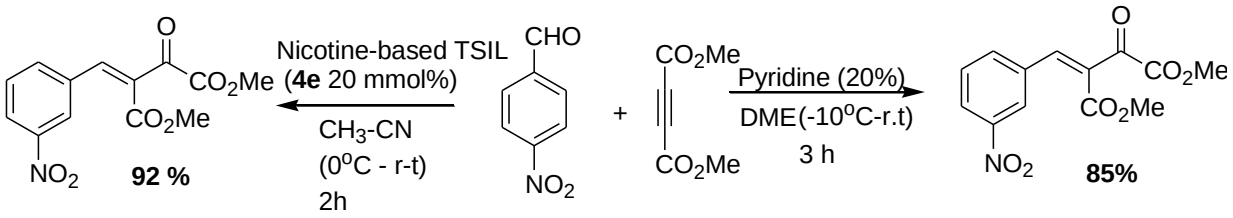
The triflimide salts was prepared by stirring the of iodide salt **8d** with lithium triflimide in distilled water. The water immiscible ionic liquid **8e** formed a separate layer with water and was isolated by simple decantation. The resulting ionic liquid **8e** was characterized by ^{1}H NMR and ^{13}C NMR, and MS. The choice of an ionic liquid with the NTf_2 anion followed from the its ability to depress the melting point of salt, its hydrophobic character, its resistance to air and moisture and weak coordination character. The ionic liquids containing this anion are known to be more chemically and thermally stable than the ionic liquids with BF_4- or PF_6- anions, which are prone to hydrolysis forming of hydrogen fluoride. NTf_2 anions also impart lower viscosity to ionic liquids which considerably facilitates use of ionic liquid.[33,34]

Reactions tested

Nicotine based TSIL-catalyzed reaction of dimethylacetylenedicarboxylate with Aldehydes

Catalytic Conditions. The Huisgen cycloaddition reaction of DMAD with 3-nitro benzaldehyde in the presence of nicotine-based TSIL was selected as model reaction to set the

standard conditions (Scheme 9). The 1 equivalent of DMAD was treated with nicotine-based TSIL (20 mol %) in acetonitrile at 0 °C and stirred for 30 minutes. Then 1 equivalent of 3-nitrobenzaldehyde was added to stirring mixture. After this, the reaction was allowed to stir initially at 0 °C for 30 minutes and then temperature was gradually increased to room temperature. The progress of reaction was monitored by thin layer chromatography (TLC) analysis. The reaction was found to be completed after 2 hr as indicated by TLC. After completion of reaction the acetonitrile was removed under *vacuo* and product was isolated from ionic liquid phase by extraction with diethyl ether. The removal of ether provided the required product 2-oxo-3-benzylidenesuccinate in 92% yield.



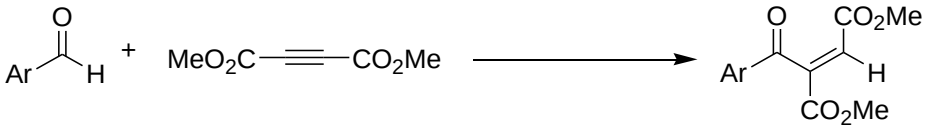
Scheme-9

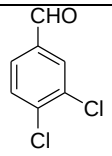
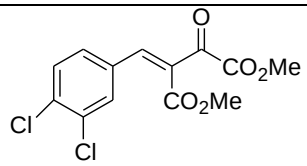
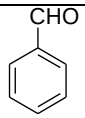
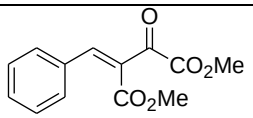
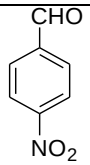
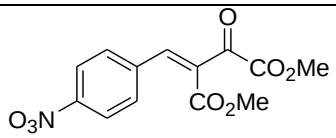
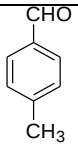
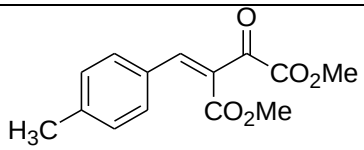
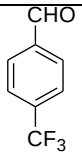
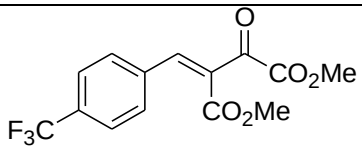
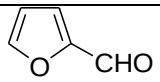
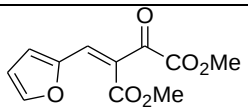
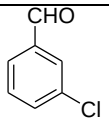
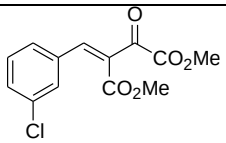
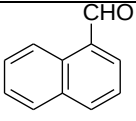
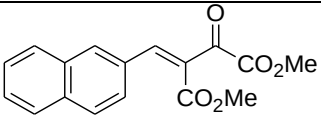
The excellent yield obtained in lesser time indicates the worth of the reaction conditions employed. And these conditions were used as standard conditions for further studies. The comparison of results obtained under ionic liquid condition with those of normal reported procedure indicates the superiority of new methodology over the reported one. The markable aspects associated with current methodology include the rapid reaction rate, highest yeild of products procedural convenience. The major reason for improved results obtained under ionic liquid conditions is the significant stabilization of 1,3-dipolar intermediate by solvating effects of ionic liquid.

We tested the scope of nicotine-based task specific ionic liquid as a green recyaclable catalyst using same compounds as reported under normal proecdure for sake of comparision. The results obtained were consistantly excellent. Apart from other typical advantages associated with use of task specific ionic liquid procedure like operational convenience, green reaction conditions, rapid reaction rates, we got relatively enhanced yields of the products under new protocol as compared to reported one. as shown in the (**Table 1).** Various derivatives of benzaldehyde were treated with DMAD in presence of nicotine-based TSIL. The pyridine ring

present in nicotine moiety having active nucleophilic nitrogen was responsible for converting DMAD into zwitterion intermediate. The rapid reaction rate of each entry and higher yield of the product obtained under new protocol can be rationalized with fact that zwitterion being highly charged intermedate was stabilized by greater solvation effects of highly polar nature of ionic liquid. This factor promoted the formation of zwitterion intermediate thus enhancing the reaction rate and led to higher yield of products. The benzaldehyde with electron withdrawing groups gave excellent yields (**Table 1**, entry 3, 5).

Table 1 Reaction of aldehydes with DMAD in the presence of a catalytic amount of and pyridine and Nicotine-based TSIL

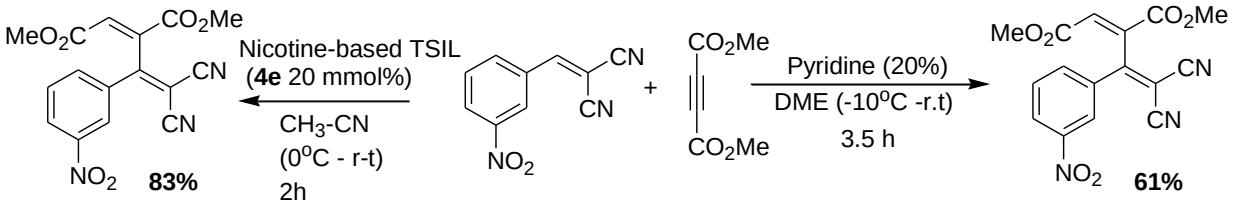


Entry	Aldehyde	Product	Yield(%)[a]	Yield(%)[b]
1			**89**	**84**
2			**62**	**44**
3			**92**	**72**
4			**56**	**43**
5			**96**	**84**
6			**83**	**61**
7			**76**	**66**
8			**66**	**43**

[a]Isolated product with TSIL, [b]Isolated yield in normal conditions

Nicotine based TSIL-catalyzed reaction of dimethylacetylenedicarboxylate with benzylidenemalononitrile.

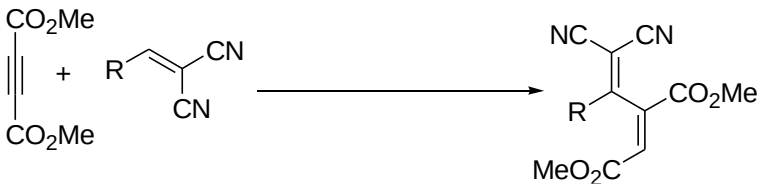
After aldehydes, we decided to explore the potential of other reactive alkenes to form adduct with DMAD. As a test reaction, we chose the reaction of DMAD with 3-nitrobenzylidenemalononitrile in the presence of nicotine-based TSIL (20 mol %) in acetonitrile as a model reaction. On completion of reaction, we isolated a highly substituted butadiene derivative in 83 % yield as compared to 61 % yield reported under normal reported procedure (Scheme 10).

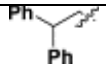


Scheme-10

A variety of dicyanostyrenes were found to participate in this reaction affording the corresponding 1,3-dienes in good to excellent yields. The results are summarized in (**Table 2**). The values of the yields reported under normal conditions are just taken from the reported literature and no such reaction was performed. The better results obtained under present protocol, can be ascribed to same reasons as given above. The successful reaction of different reactive alkenes like arylmethylidenemalononitriles with same 1,3-dipolar intermediate reflects the power and capacity of nicotine based TSIL to facilitate the various versions of a given type of reaction. Again the electron withdrawing effect of substituents on aromatic ring resulted in enhanced yields of corresponding products.

Table 2 Reaction of arylmethylidenemalononitriles with DMAD catalysed by pyridine and nicotine-based TSIL



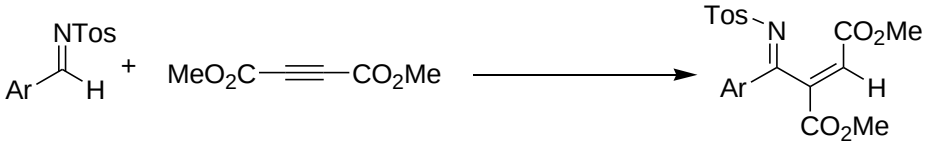
Entry	Styrene, R =	Yield (%)[a]	Yield (%)[b]
1	4-Fluorophenyl,	93	82
2	3-Nitrophenyl,	85	71
3	4-Chlorophenyl,	97	87
4	1-Naphthyl,	98	92
5	3,4-Dichlorophenyl,	89	82
6	4-Methoxyphenyl,	84	78
7	trans-Cinnamyl,	64	45
8		54	43
9	3-Benzyloxyphenyl,	87	75

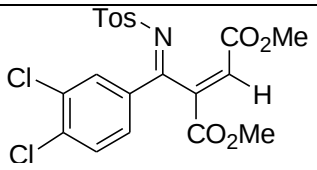
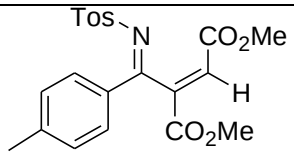
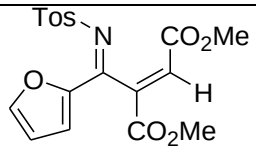
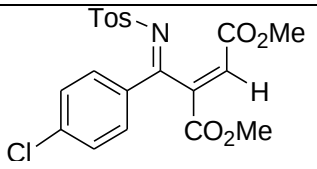
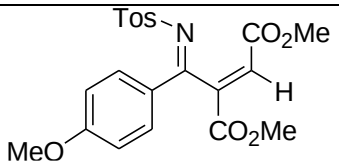
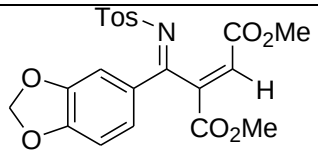
[a] isolated yield in TSIL, [b] Isolated yield in normal conditions

The pyridine-catalyzed reaction of dimethylacetylenedicarboxylate with *N*-Tosylimines

In order to further explore the scope of nicotine based TSIL, we investigated the *N*-tosylimines as third different type of dipolarophile to react with 1,3-dipolar intermediate resulting from reaction between DMAD nicotine based TSIL. Various tosylimines under given reaction conditions led to the efficient synthesis of corresponding 1-azadienes and *N*-substituted isatins. The results obtained under this new protocol were compared with those reported under normal conditions (**Table 3**).

Table 3 Reaction of Tosylimines with DMAD catalyzed by pyridine and Nicotine-based TSIL



Entry	Product	Yield[a](%)	Yield[b](%)
1		93	84
2		56	43
3		78	61
4		98	86
5		88	70
6		87	78

[a] isolated yield in TSIL, [b]Isolated yield in normal conditions

The improved yields of products and reduced reaction time imply the relatively higher nucleophilicity of pyridine in nicotine. The greater stabilization of zwittorionic intermediates in ionic liquid conditions contributed to the efficiency of the reaction. The easy recovery of the product and recycling of the catalyst and replacement of obnoxious and toxic pyridine are

additional advantages. The new protocol was equally beneficial for variety of structural variants of aldehydes.

The products were characterized by latest spectroscopic methods. The reported data of the experiments of Huisgen reaction performed under ordinary condition were taken as it is. And it was compared with the data obtained from the replica of those experiments in proposed nicotine based task specific ionic liquid. The data is compared in form of table which indicates the relatively enhanced yields of the isolated products as compared to that obtained using original conventional methodology. Relative increase in product yield can be attributed to the polar nature of the reactive intermediates which are stabilized by the highly polar and saline nature of ionic liquid. The nicotine-based ionic liquid reacted efficiently with DMAD to form kinetically controlled 1,3-dipolar intermediate due to its stabilization by highly polar environment of ionic liquid. The intermediate was treated with variety of dipolarophiles which reacted effectively with it form corresponding products. This observation indicates the wide scope Huisgen cycloaddition when performed under ionic liquid conditions.

Recycling

The one of the important aspect of green reagents is their recyclability. We investigated the opportunity of recovering and recycling of nicotine based TSIL for present reaction conditions. For this, we chose the cycloaddition reaction of 4-nitrobenzaldehyde with DMAD in presence of nicotine based TSIL. The results are summarized in (**Table 4**), which show that the product yields are quite consistent. The recovered ionic liquid maintains its catalytic efficiency up to four recycles.

Table 4 Recycling studies of nicotine-based ionic liquid

Recycle times	**1**	**2**	**3**	**4**
Product yield (%)	92	88	84	81
Recovered ionic liquid (%)	98	97	97	95

Conclusion

The nicotine based task specific ionic liquid was found to be very efficient facilitator of cycloaddition reaction of dimethylacetylenedicarboxylate (DMAD) with various dipolarophiles like aldehyde, benzylidenemalononitrile, and *N*-Tosylimines forming corresponding adducts with improved yields leading to very useful scaffolds. The ionic liquid has been shown as a best substitute of toxic pyridine for pyridine promoted reactions. In addition it was recyclable and with appreciable retention of catalytic efficiency.

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