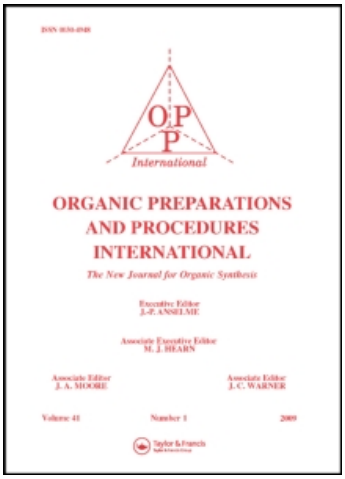

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AN EFFICIENT AND CHEMOSELECTIVE SYNTHESIS OF ALDEHYDE 1,1-DIACETATES USING MORPHOLINIUM BISULFATE AS A BRÖNSTED ACIDIC IONIC LIQUID UNDER SOLVENT-FREE CONDITIONS

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AN EFFICIENT AND CHEMOSELECTIVE SYNTHESIS OF ALDEHYDE 1,1-DIACETATES USING MORPHOLINIUM BISULFATE AS A BRÖNSTED ACIDIC IONIC LIQUID UNDER SOLVENT-FREE CONDITIONS

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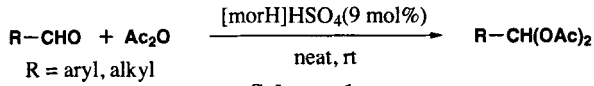
Ionic liquids (IL) have frequently been used as a green solvent in place of conventional organic solvents and being[1-5] superior due to their extremely low vapor pressure, excellent thermal stability, reusability and ability to dissolve many organic and inorganic substrates.[6] The application of ionic liquids as solvent and catalyst has been reported for a variety of functional group transformations but their use as acid catalysts under solvent-free conditions deserves more attention.[7] Ionic liquids with Brönsted acidic counter ions such as 1-hexyl-3-methylimidazolium bisulfate ([hmim][HSO_4]),[8] 1-butyl-3-methylimidazolium dihyrogen phosphate ([bmim][H_2PO_4]),[8] 1-[2-(2-hydroxy-ethoxy)ethyl]-3-methylmidazolium bisulfate ([heemim][HSO_4]),[8] 1-butyl-3-methylimidazolium chloroaluminate ([bmim]Cl $2AlCl_3$),[9] and 1-butyl-3-methylimidazolium bisulfate ([bmim][HSO_4])[10] have been used as acid catalysts and provide a useful medium under solvent-free conditions because of their polar nature.

Protection and deprotection of carbonyl groups are often essential steps in organic syntheses.[11] 1,1-Diacetates (acylals) are useful carbonyl protecting groups due to their stability under neutral, basic and acidic conditions.[12] The diacetates of α,β-unsaturated aldehydes are not only basic starting materials for Diels-Alder reactions[13, 14] but they can also be converted into compounds with other functional groups by reaction with appropriate nucleophiles.[15, 16] Some of the reported methods for the preparation of 1,1-diacetates from aldehydes and acetic anhydride include sulfuric acid,[17] triflic acid,[18] PCl_3,[19] I_2,[20] $FeCl_3$,[12, 21] NBS,[22] $Sc(OTf)_3$,[23] $Cu(OTf)_2$,[24] $Bi(OTf)_3$,[25] CAN,[26] $AlPW_{12}O_{40}$,[27] β-Zeolite,[28] $LiBF_4$,[29] Zn-Montmorillonite,[30] $In(OTf)_3$,[31] H_2NSO_3H,[32] $ZrCl_4$,[33] $Bi(NO_3)_3$•$5H_2O$,[34] Wells-Dawson acid ($H_6P_2W_{18}O_{62}$•$24H_2O$)[35] and silica sulfuric acid.[36] Although some of these methods have been used for conversion of aldehydes to the corresponding diacetates in good to high yields, the majority of these methods suffer at least from one of several disadvantages such as reaction under oxidizing conditions, use of strong acid, high temperatures, long reaction times, sensitivity to moisture and the high cost and high toxicity of the reagents. This paper describes a straightforward and efficient method for the preparation of the acidic IL morpholinium bisulfate ([morH]HSO_4) and its use with acetic anhy-

dride for conversion of aldehydes to the corresponding acylals. This catalyst in comparison to the reported ionic liquids with Brönsted acidic counter ions can be prepared from inexpensive starting material and is quite stable at room temperature. The reaction is easily carried out at room temperature under solvent-free conditions using 9 mol % of the ionic liquid (*Scheme 1*).



Scheme 1

Table 1. Preparation of Acylals in the Presence of [morH]HSO_4 under Solvent-Free Conditions at Room Temperature.[a]

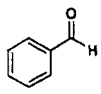
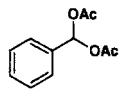
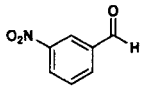
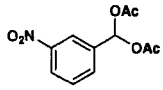
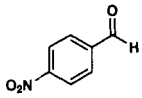
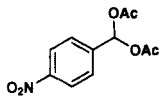
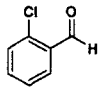
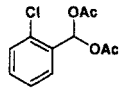
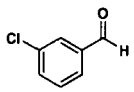
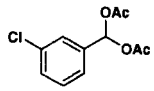
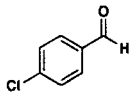
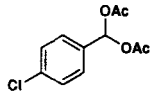
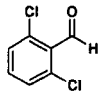
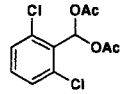
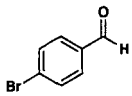
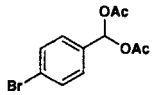
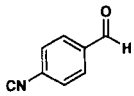
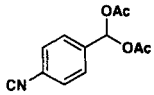
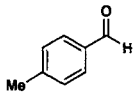
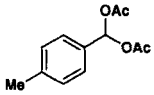
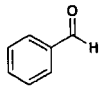
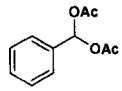
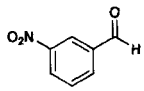
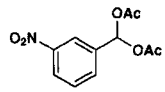
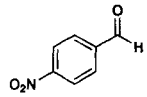
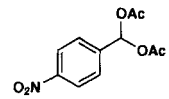
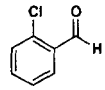
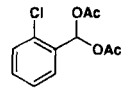
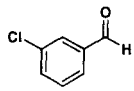
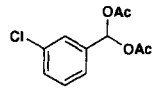
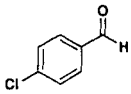
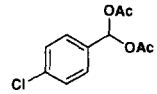
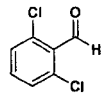
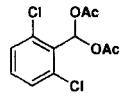
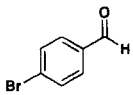
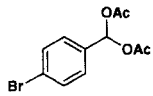
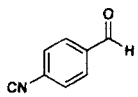
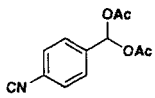
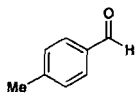
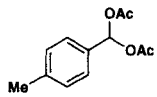
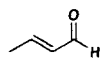
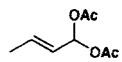
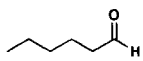
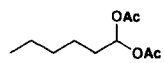
Entry	Substrate	Product	Time (min)	Yield (%)	mp. (°C) Found	mp. (°C) Reported
1			3	85	44-46	44-45[36]
2			5	85	65-67	65-66[36]
3			5	92	124-126	125-127[36]
4			5	95	51-52	52-53[36]
5			4	94	64-65	64-65[36]
6			5	99	81-82	82-83[36]
7			10	98	89-90	88-90[36]
8			5	90	93-95	92-95[36]
9			10	90	100-101	100-102[36]
10			2	95	80-82	81-82[36]

Table 1. Continued...

Entry	Substrate	Product	Time (min)	Yield (%)	mp. (°C) Found	mp. (°C) Reported
11			3	85	68-70	73-74[36]
12			5	92	193 (630)	193 (630)[36]
13			7	80	65-66	64-65[36]
14			10	80	101-102	101-103[36]
15			10	85	90-92	89-90[36]
16			2	95	70-72	72-74[36]
17			3	95	107-108	110[36]
18			20	70	52-53	52-53[36]
19			3	97	90-92	95[36]
20			2	97	84-86	84-85[36]
21			3	83	Oil	112-114(28)[37]
22			4	80	Oil	184 (630)[36]
23			5	92	Oil	127-129 (2)[38]

a) The products were characterized from their spectra (IR, ^{1}H NMR, and MS) and comparison with authentic samples.[36-38]

For optimization of the reaction conditions, we studied the conversion of benzaldehyde (1 mmol) to 1,1-diacetoxy-1-phenylmethane in the presence of catalytic amounts of [morH]HSO_4 (9 mol %) and acetic anhydride (2 mmol) in various solvents and also under solvent-free conditions. The yield under solvent-free conditions is higher and the reaction times shorter in comparison to conventional methods. Thus these conditions were employed for conversion of various aldehydes to the corresponding acylals (*Table 1*). Aliphatic and α,β-unsaturated aldehydes produced acylals in very good yields (*Table 1, Entries 20-23*). Acid sensitive substrates such as furfural and 5-methylfurfural were also protected as diacetates in good yields (*Table 1, Entries 18 and 19*).[32] The reaction of 2-hydroxybenzaldehyde and 4-hydroxybenzaldehyde under these conditions led to acetylation of both the carbonyl group and phenolic -OH. 4-(Dimethylamino)benzaldehyde, cyclohexanone, butanal and acetophenone failed react even at 180°C.

When equimolar amounts of aldehyde and of ketone were mixed in the presence of two equivalents of acetic anhydride and 9 mol % of catalyst and stirred at room temperature for 10 min, only the aldehydes were completely converted to the corresponding acylal derivatives and the ketones remained intact. The method also demonstrated chemoselectivity for aldehydes with electron-withdrawing group over those substrates with electron-donating group on the benzene ring (*Entries 3 and 4*).

EXPERIMENTAL SECTION

All yields refer to isolated products after purification. All of the products were characterized by comparison of their spectral (IR, ^{1}H-NMR, combustion analysis, TLC and GC) and physical data (melting and boiling points) **(Tables 1 and 2)** with those of authentic samples. [36] All ^{1}H-NMR spectra were recorded at 300 MHz in $CDCl_3$ relative to TMS as an internal standard. All ^{13}C-NMR spectra were recorded at 75 MHz in $CDCl_3$ relative to TMS as an internal standard.

Preparation of Morpholinium Bisulfate [morH]HSO_4.- A 25 mL round-bottom flask was charged with morpholine (0.87 mL, 10 mmol) and cooled to 0°C. Then a stoichiometric amount of conc. sulfuric acid (97%, 0.53 mL, 10 mmol) was added dropwise and the mixture was stirred for 10 min at 0°C and then for 20 min at room temperature. The acidic ionic liquid was washed repeatedly with cyclohexane (3 x 3 mL) to remove non-ionic residue and dried under reduced pressure to afford a colorless, viscous liquid (1.12 g, 80%, 8 mmol). This procedure may be scaled up to 100 g with no difficulty in temperature control.

Preparation of 1,1-Diacetoxy-1-(3-nitrophenyl)methane. Typical Procedure.- To a stirred solution of 3-nitrobenzaldehyde (1 mmol, 0.15 g) in freshly distilled acetic anhydride (2 mmol, 0.19 mL) was added [morH]HSO_4 (0.017 g, 9 mol %) and the reaction mixture was stirred at room temperature for 5 min. The progress of reaction was followed by TLC (*n*-Hexane: EtOAc, 9:1). After completion of the reaction, the mixture was diluted with ethyl acetate and was washed with a 10% $NaHCO_3$ solution, water and then dried over anhydrous Na_2SO_4. The solvent was

evaporated under reduced pressure to give 0.21 g (85%) of 1,1-diacetoxy-1-(3-nitrophenyl)methane. This procedure was scaled up to 50 mmol of 3-nitrobenzaldehyde (7.5 g) to give 1,1-diacetoxy-1-(3-nitrophenyl)methane in 82% yield.

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FACILE SYNTHESIS OF ANXIOLYTIC BUSPIRONE

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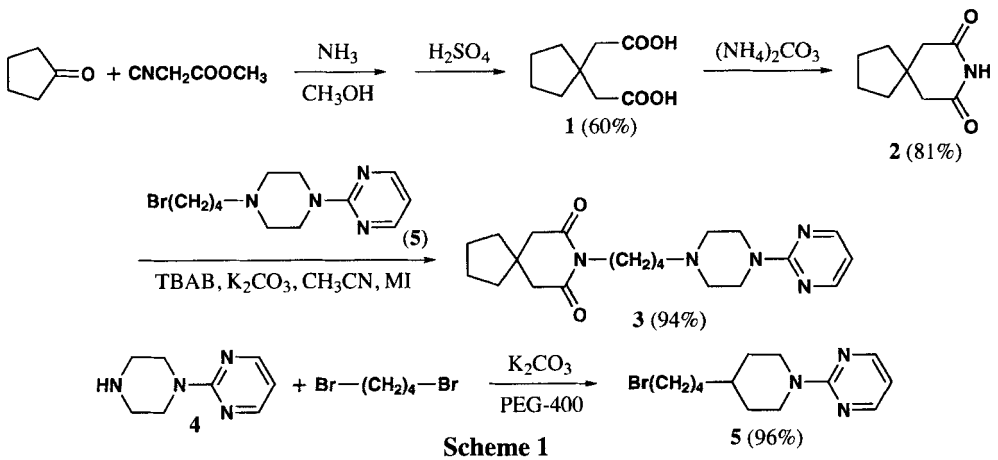
Buspirone (**3**·HCl) is an anxiolytic and antidepressant drug widely used in therapy.[1-5] Although several approaches to buspirone have been reported in the patent literatures with varying degrees of success, there are some drawbacks such as harsh reaction conditions, tedious workup, high reaction temperatures, lengthy steps, poor overall yields, and difficulties in the separation of the product from the resulting mixture.[6] Herein, we report a facile and high-yield synthesis of buspirone **3** (*Scheme 1*) under mild conditions from readily available reagents.



Scheme 1