



Effective preparation of hexahydroquinolines under ambient and solvent-free conditions



Mahdi Ghorbani ^{a,*}, Hamid Reza Shaterian ^a, Soheila Noura ^a, Fereshte Khammar ^a, Kazem Behbodi ^b, Bahareh Reisi ^c, Mohsen Oftadeh ^d

^a Department of Chemistry, Faculty of Sciences, University of Sistan and Baluchestan, PO Box 98135-674, Zahedan, Iran

^b Department of Chemistry, Shahreza Branch, Islamic Azad University, 311-86145 Shahreza, Isfahan, Iran

^c Department of Chemistry, Yasouj University, Yasouj 75918-74831, Iran

^d Chemistry Department, Payame Noor University, 19395-4697 Tehran, Iran

ARTICLE INFO

Article history:

Received 6 October 2014

Received in revised form 5 January 2015

Accepted 8 January 2015

Available online 10 January 2015

Keywords:

Ionic liquid

Catalysis

Dimedone

Aldehyde

Solvent free

ABSTRACT

The mild acidic ionic liquids such as *N*-methyl-2-pyrrolidonium dihydrogen phosphate [NMP][H₂PO₄], *N*-methyl-2-pyrrolidonium hydrogen sulfate [NMP][HSO₄], Triethylamine hydrogen sulfate [Et₃N-H][HSO₄], *l*-prolinium sulfate [L-Pro₂][SO₄] and *l*-prolinium nitrate [L-Pro][NO₃] were used as efficient catalysts for the one-pot four-component condensations of aromatic aldehydes, dimedone, ethyl acetoacetate, and ammonium acetate under solvent-free conditions. Some derivatives of ethyl 4-(aryl)-2,7,7-trimethyl-5-oxo-1,4,5,6,7,8-hexahydroquinoline-3-carboxylate were obtained under solvent-free conditions in high yields. Simple reaction, mild condition and easy work-up procedures are advantages of the present work. Also, the ionic liquids can be recycled several times without significant loss of their activity.

© 2015 Published by Elsevier B.V.

1. Introduction

Multicomponent reactions (MCRs) in ionic liquids (ILs) are important in organic synthesis [1]. Ionic liquids act as solvent, co-catalyst, or catalyst [2]. IL-MCR causes the rapid synthesis of highly functionalized heterocyclic molecules with high potential applications in medicinal chemistry [3,4]. Yielding the one-pot multi-component symmetrical 1,4-dihydropyridines (1,4-DHPs) during Hantzsch reaction was first established in 1881 [5]. 1,4-DHPs form a class of heterocyclic compounds which present interesting pharmacological and biological properties [6]. In order to research on ionic liquids and their application on IL-MCRs [7], recently several alternate and more efficient methods including the use of microwaves [8], autoclave [9], ionic liquids [10], iodine [11], metal triflates [12], ceric ammonium nitrate (CAN) [13], *l*-proline [14], PTSA-SDS [15] and BINOL-phosphoric acid derivatives [16] have been developed for the synthesis of polyhydroquinoline derivatives. Herein, we report the new application of some ILs such as *N*-methyl-2-pyrrolidonium dihydrogen phosphate [NMP][H₂PO₄], *N*-methyl-2-pyrrolidonium hydrogen sulfate [NMP][HSO₄], Triethylamine hydrogen sulfate [Et₃N-H][HSO₄], *l*-prolinium sulfate [L-Pro₂][SO₄], and *l*-prolinium nitrate [L-Pro][NO₃] as catalysts (Fig. 1) for the preparation of some functionalized ethyl 4-(aryl)-2,7,7-trimethyl-5-oxo-1,4,5,6,7,8-

hexahydroquinoline-3-carboxylate derivatives during the reaction of aromatic aldehydes, dimedone, ethyl acetoacetate, and ammonium acetate under solvent-free conditions for the first time (Scheme 1).

2. Experimental

All reagents were purchased from Merck and Aldrich and used without further purification. The mild acidic ionic liquids such as *N*-methyl-2-pyrrolidonium hydrogen phosphate [NMP][H₂PO₄] [17], *N*-methyl-2-pyrrolidonium hydrogen phosphate [NMP][HSO₄] [18], Triethylamine hydrogen sulfate [Et₃N-H][HSO₄] [19], [L-Pro₂][SO₄] [20] and [L-Pro][NO₃] [20] as catalysts were prepared according to the reported procedure. The NMR spectra were recorded on a Bruker Avance DPX 300 or 400 MHz instrument. IR spectra were recorded on a JASCO FT-IR 460 plus spectrophotometer. Melting points were determined in open capillaries with a BUCHI 510 melting point apparatus. TLC was performed on silica-gel Poly Gram SIL G/UV 254 plates. All yields refer to isolated products after purification.

2.1. General procedure for the synthesis of ethyl 4-(aryl)-2,7,7-trimethyl-5-oxo-1,4,5,6,7,8-hexahydroquinoline-3-carboxylate derivatives under solvent-free conditions

The mixture of the aldehydes (10 mmol), dimedone (10 mmol), ethyl acetoacetate (10 mmol) and ammonium acetate (15 mmol) and

* Corresponding author.

E-mail address: ghorbani.mahdi@gmail.com (M. Ghorbani).

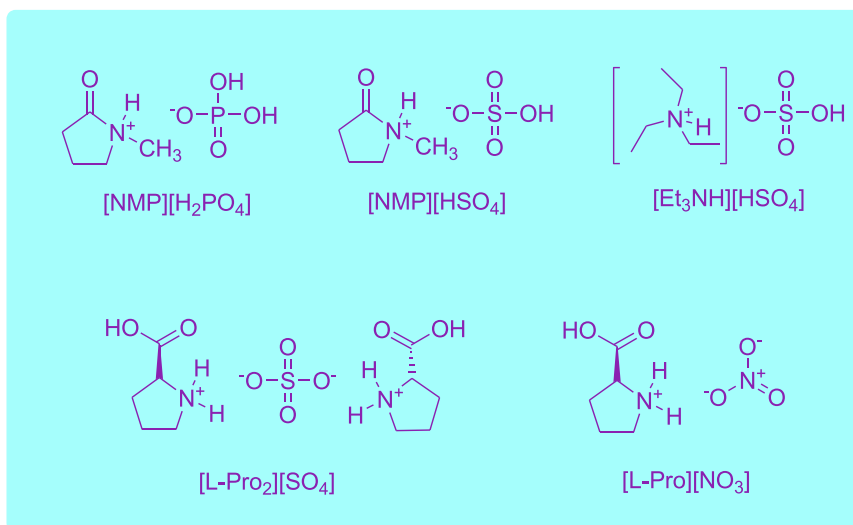
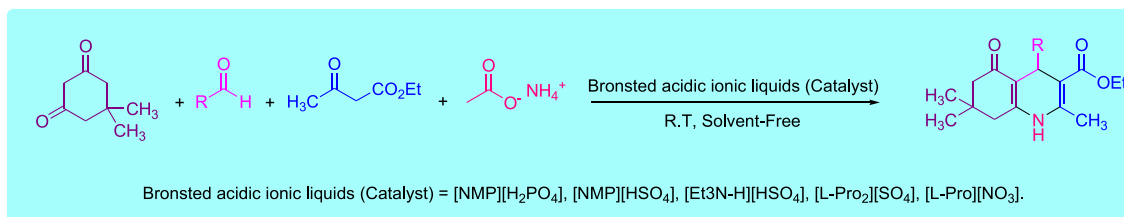


Fig. 1. The molecular structure of [NMP][H₂PO₄], [NMP][HSO₄], [Et₃N-H][HSO₄], [L-Pro₂][SO₄] and [L-Pro][NO₃].



Scheme 1. The preparation of ethyl 4-(aryl)-2,7,7-trimethyl-5-oxo-1,4,5,6,7,8-hexahydroquinoline-3-carboxylate derivatives.

ILs containing [NMP][H₂PO₄] (10 mol%), [NMP][HSO₄] (10 mol%), [Et₃N-H][HSO₄] (10 mol%), [L-Pro₂][SO₄] (10 mol%) and [L-Pro][NO₃] (10 mol%) as mild acidic ionic liquid catalysts was stirred at room temperature for the specific time. At the end of the reaction, it was cooled to room temperature. Then, 5 mL of water was added to the mixture. The ionic liquid was dissolved in water, and filtered for separation of the crude product. The separated product was washed twice with water (2 × 5 mL). The solid product was purified by recrystallization procedure in ethanol. All of the desired products were characterized by comparison of their physical and spectral data (melting points, IR, ¹H NMR) with those of known compounds [1,22,24,26]. For recycling the catalysts, after washing the solid products with water completely, the water containing the ionic liquid (IL is soluble in water) was evaporated under reduced pressure and the ionic liquid was recovered and reused.

All of the spectral data have been presented in the supported information and the selected spectra for three known products are given below:

Ethyl 4-(4-methoxyphenyl)-2,7,7-trimethyl-5-oxo-1,4,5,6,7,8-hexahydroquinoline-3-carboxylate (Table 2, entry 6): m.p = 256–258 °C; IR (KBr): ν_{\max} = 3276, 2956, 1703, 1648, 1606, 1496, 1381, 1215, 1031, 765 cm⁻¹. ¹H NMR (300 MHz, DMSO-d₆): δ (ppm) 0.85 (s, 3H), 1.00 (s, 3H), 1.14 (t, *J* = 7.0 Hz, 3H), 1.96 (d, *J* = 16.0 Hz, 1H), 2.15 (d, *J* = 16.1 Hz, 1H), 2.27 (s, 3H), 2.37–2.49 (m, 2H), 3.66 (s, 3H), 3.97 (q, *J* = 7.0 Hz, 2H), 4.79 (s, 1H), 6.73 (d, *J* = 8.3 Hz, 2H), 7.05 (d, *J* = 8.3 Hz, 2H), 8.99 (s, 1H); ¹³C NMR (75 MHz, DMSO-d₆): δ (ppm) 14.6, 18.7, 26.9, 29.6, 32.6, 35.4, 50.6, 55.3, 59.4, 104.4, 110.7, 113.5, 128.8, 140.5, 145.1, 149.7, 157.7, 167.4, 194.7.

Ethyl 4-(4-hydroxyphenyl)-2,7,7-trimethyl-5-oxo-1,4,5,6,7,8-hexahydroquinoline-3-carboxylate (Table 2, entry 8): m.p = 229–231 °C;

Table 1
Optimal amounts of A: [Et₃N-H][HSO₄], B: [NMP][HSO₄], C: [NMP][H₂PO₄], D: [L-Pro₂][SO₄] and E: [L-Pro][NO₃] as catalysts in four-component synthesis of ethyl 4-(aryl)-2,7,7-trimethyl-5-oxo-1,4,5,6,7,8-hexahydroquinoline-3-carboxylate from the reaction of aldehydes, dimedone, ethyl acetoacetate, and ammonium acetate under solvent-free and ambient conditions.

Entry	Catalyst (mol%)	Temp (°C)	Time (min)					Yield (%) ^a				
			A	B	C	D	E	A	B	C	D	E
1	–	25	120	120	120	120	120	Trace	Trace	Trace	Trace	Trace
2	5	25	9	10	11	9	12	90	89	87	88	85
3	10	25	8	9	9	8	10	92	91	92	91	89
4	15	25	7	6	7	6	9	95	96	94	95	92
5	20	25	5	5	6	4	7	96	97	95	96	94

^a Yields refer to isolated pure product based on the reaction of aldehydes (10 mmol), dimedone (10 mmol), ethyl acetoacetate (10 mmol) and ammonium acetate (15 mmol).

Download English Version:

<https://daneshyari.com/en/article/5411160>

Download Persian Version:

<https://daneshyari.com/article/5411160>

[Daneshyari.com](https://daneshyari.com)