



Short communication

The Synthesis of α,α' -bis(arylidene)Cycloalkanones using Sulfonic Acid Functionalized Pyridinium Chloride



Ahmad Reza Moosavi-Zare^a*, Mohammad Ali Zolfigol^b*, Zahir Rezanejad^b

^a Sayyed Jamaledin Asadabadi University, Asadabad, 6541861841, I. R. Iran

^b Faculty of Chemistry, Bu-Ali Sina University, Hamedan, 6517838683, Iran

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Sulfonic acid functionalized pyridinium chloride

Cross-aldol condensation

α,α' -bis(arylidene)cycloalkanone

Solvent-free

ABSTRACT

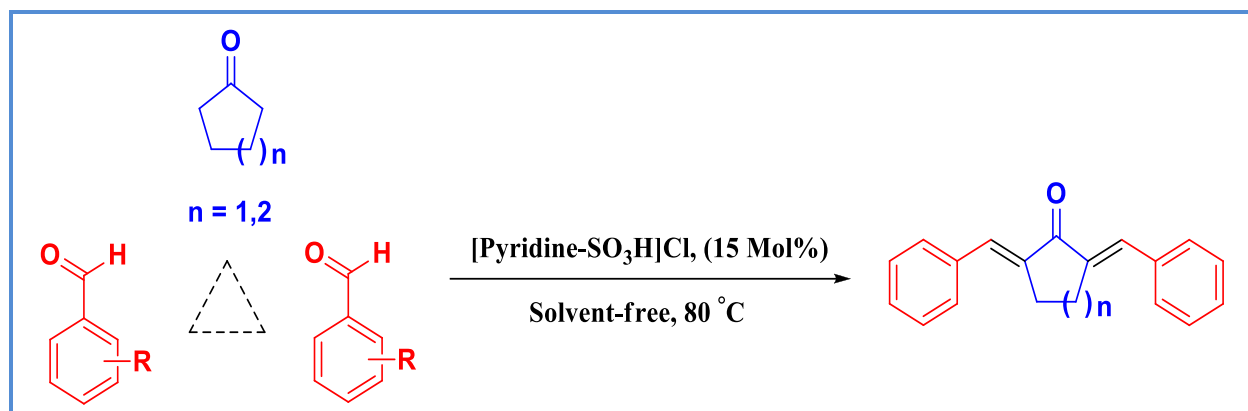
In this study, condensation reaction of the aldehydes with various ketones in the presence of sulfonic acid functionalized pyridinium chloride [pyridine- SO_3H] Cl as an ionic liquid and catalyst were carried out to prepare the α,α' -bis(arylidene)cycloalkanone under the solvent free conditions. The purity and yield of the products were high and their identification was performed by the spectroscopic analysis and comparison of the physical information with known compounds in the previous literature.

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*Corresponding author: E-mail: moosavizare@yahoo.com, Sayyed Jamaledin Asadabadi University, Asadabad, 6541861841, I. R. Iran, Tel: 8123237450; E-mail: mzolfigol@yahoo.com, Faculty of Chemistry, Bu-Ali Sina University, Hamedan, 6517838683, Iran, Tel: 09181113831

Graphical Abstract



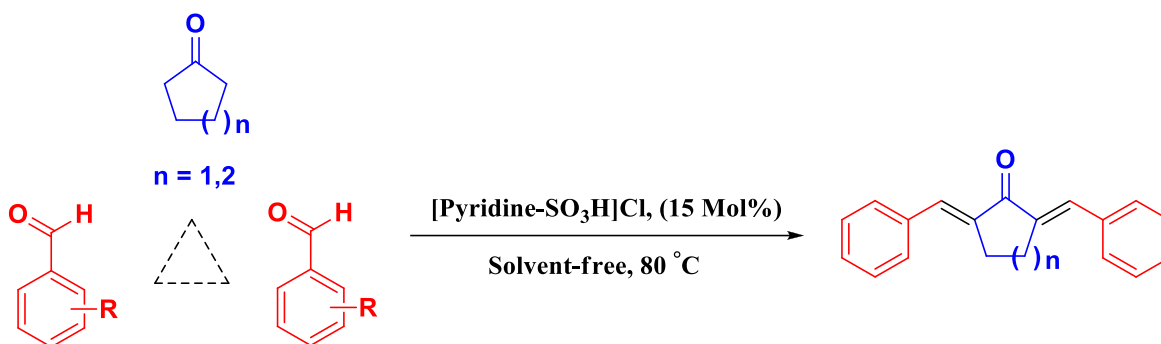
Introduction

Recently, sulfonic acid functionalized pyridinium chloride $[\text{pyridine-SO}_3\text{H}]\text{Cl}$ as a Brønsted acidic ionic liquid which collected solid acids behavior with ionic liquids properties, has been introduced as a suitable acidic condition and efficient catalyst in organic transformations [1, 2]. $[\text{Pyridine-SO}_3\text{H}]\text{Cl}$ as an ionic liquid has important properties such as non-flammability, non-volatility, wide liquid-state temperature range, high thermal and chemical stability [3]. In the role of a catalyst, simple application, high efficacy, high solubility in water to separate it from the organic materials and high miscibility with organic matters is other advantages of this ionic liquid [4]. $[\text{Pyridine-SO}_3\text{H}]\text{Cl}$ was used as an efficient catalyst for the preparation of hexahydroquinolines [1], 3-methyl-1-phenyl-1H-pyrazol-5(4H)-ones [2], 1,2,4,5-tetrasubstituted imidazoles [3] and bis-coumarin derivatives [4]. Solvent-free organic reactions have been used as important protocols in organic synthesis. Solvent-free reactions under thermal or microwave conditions often considered due to shorter reaction times, increased yields and easier workup, in addition to working well in green chemistry protocols, and raising the regio- and stereoselectivity of reactions [5-12].

The cross-aldol condensation has been introduced for carbon-carbon bond formation in organic synthesis [13]. By this reaction between the cycloalkanones and arylaldehydes, α, α' -bis(arylidene)cycloalkanone derivatives were prepared [14]. Also, arylidene cycloalkanones have been used for the synthesis of important intermediate organic compounds such as, bis-spiropyrrolidines [15], bis-spiroisoxazolines [16] and perfumes [17]. The synthesis of α, α' -bis(arylidene)cycloalkanone derivatives were reported by various catalysts such as,

silica-supported, phosphorus-containing reagents [14], KOH [18], 1-methyl-3-(2-(sulfooxy)ethyl)1H-imidazol-3-ium chloride [19], 2-hydroxyethylammonium acetate [20], [Msim]FeCl₄ [21], bromodimethylsulfonium bromide [22] and molecular iodine [23].

Due to the significant properties of these compounds, new methods for the synthesis of α,α' -bis(arylidene)cycloalkanones are still needed. Having above facts, we have used the [pyridine-SO₃H]Cl as an efficient acidic ionic liquid and catalyst for the preparation of α,α' -bis(arylidene)cycloalkanones by the condensation reaction of aldehydes with various ketones under solvent-free conditions (Scheme 1).



Scheme 1. The preparation of α,α' -bis(arylidene)cycloalkanones

Experimental

General procedure for the synthesis of the α,α' -bis(arylidene)cycloalkanones. To a 15 mL round-bottomed flask containing [pyridine-SO₃H]Cl (0.0292 g, 15 mol%) was added cycloalkanone (1 mmol) and aldehyde (2 mmol) and connected to a reflux condenser. The resulting mixture was stirred in an oil-bath at 80 °C under solvent-free conditions. After completion of the reaction, as monitored by TLC, the reaction mixture was extracted by warm ethyl acetate and separated from the catalyst. Finally, for further purification, the crude product was purified by recrystallization from ethanol (95%).

(2E,6E)-2,6-bis(4-chlorobenzylidene)cyclohexanone (2)

M.p.: 143-145 °C; IR (KBr): ν 1600, 1667, 2928, ¹H NMR (90 MHz, CDCl₃): δ 1.53 (s, 2H), 2.62 (s, 4H), 7.10 (s, 8H), 7.44 (s, 2H).

(2E,6E)-2,6-bis(3-bromobenzylidene)cyclohexanone (4)

M.p.: 116-119 °C; IR (KBr): ν 1662, 2865, 2937, ¹H NMR (90 MHz, CDCl₃): δ 1.8 (s, 2H), 2.89 (s, 4H), 7.33-7.67 (m, 10H).

(2E,6E)-2,6-bis(2-nitrobenzylidene)cyclohexanone (6)

M.p.: 148-152 °C; IR (KBr): ν 1601, 1667, 2943, ^1H NMR (90 MHz, CDCl_3): δ 1.72 (s, 2H), 2.58 (s, 4H), 7.28-7.57 (m, 8H), 7.97-8.09 (m, 2H).

(2E,6E)-2,6-bis(4-methoxybenzylidene)cyclohexanone (7)

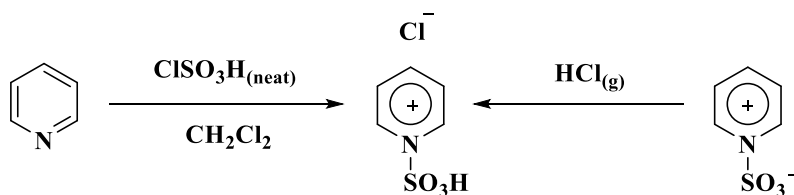
M.p.: 161-164 °C; IR (KBr): ν 1594, 1658, 2828, 2938, ^1H NMR (90 MHz, CDCl_3): δ 1.51 (s, 2H), 2.64 (s, 4H), 3.56 (s, 6H), 6.60-7.48 (m, 10H).

(2E,5E)-2,5-bis(4-chlorobenzylidene)cyclopentanone (8)

M.p.: 223-225 °C; IR (KBr): ν 1590, 1693, 2858, 3089, ^1H NMR (90 MHz, CDCl_3): δ 2.83 (s, 4H), 7.13-7.28 (m, 10H).

Results and discussion

Sulfonic acid functionalized pyridinium chloride [pyridine- SO_3H]Cl was prepared by the reaction of pyridine with the chlorosulfonic acid in dry dichloromethane as a viscous colorless oil and ionic liquid. In another procedure for the synthesis of the [pyridine- SO_3H]Cl, sulfur trioxide pyridine complex was reacted with hydrogen chloride to prepare the [pyridine- SO_3H]Cl (Scheme 2) [2]. In two mentioned procedures, the same product was prepared in high yield which the N-S bond formation was carried out in this compound.



Scheme 2. The preparation of [pyridine- SO_3H]Cl

To optimize the reaction conditions for the synthesis of the α,α' -bis(arylidene)cycloalkanone derivatives, the reaction of 4-chlorobenzaldehyde and cyclohexanone as a model reaction was chosen as a model reaction and examined in the presence of different amounts of [pyridine- SO_3H]Cl, at range of 25-100 °C under solvent-free conditions (Table 1). Table 1 indicates that, 15 mol% of the [pyridine- SO_3H]Cl was suitable to provide the desired products at 80 °C with high yields in short reaction times (Table 1, entry 3). Moreover, various solvents including, the ethanol, toluene, dichloromethane, acetonitrile, ethyl acetate and hexane were tested

on the model reaction in comparison with solvent-free condition which the results were not acceptable (Table 1).

Table 1. Effect of the catalyst amounts, temperature and solvents on the reaction between 4-chlorobenzaldehyde and cyclohexanone

Entry	Catalyst amount (g)	Solvent	Temperature (°C)	Time (min)	Yield ^a (%)
1	10	-	80	60	67
2	15	-	80	20	91
3	20	-	80	20	91
4	15	-	25	90	trace
5	15	-	60	28	20
6	15	-	100	20	91
7	15	Ethanol	Reflux	270	trace
8	15	Toluene	80	270	27
9	15	Dichloromethane	Reflux	270	35
10	15	Acetonitrile	Reflux	270	55
11	15	Ethyl acetate	Reflux	270	40
12	15	Hexane	Reflux	270	56

^a Isolated yield

After the optimization of the reaction conditions, to show the efficiency and generality of the catalyst, the reaction of various cycloalkanones including cyclohexanone and cyclopentanone, with various arylaldehydes such as benzaldehyde as well as the aldehydes containing electron-withdrawing substituents, electron-releasing substituents or halogens was tested in the presence of [pyridine-SO₃H]Cl at 80 °C under solvent-free conditions (Table 2). Table 2. Demonstrates that, the desired products were prepared with high yields in short reaction times.

Table 2. The preparation of α,α' -bis(arylidene)cycloalkanones using [pyridine-SO₃H]Cl

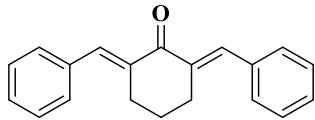
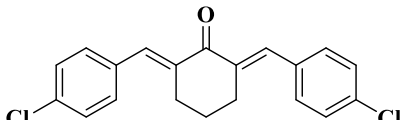
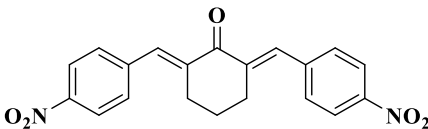
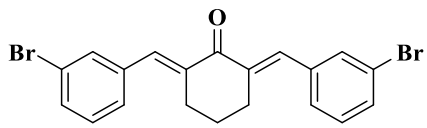
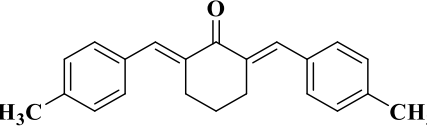
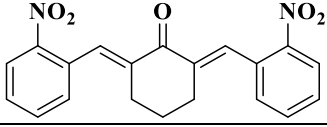
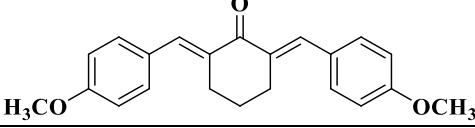
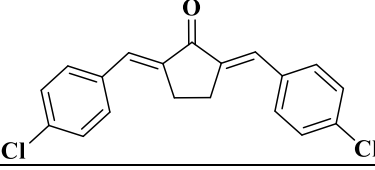
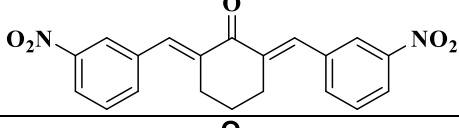
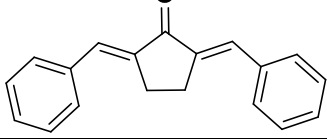
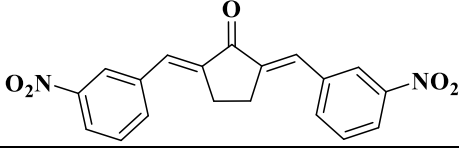
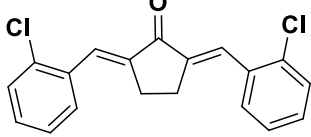
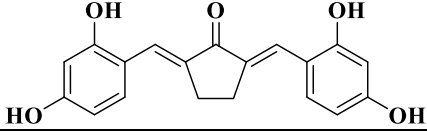
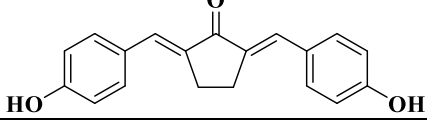
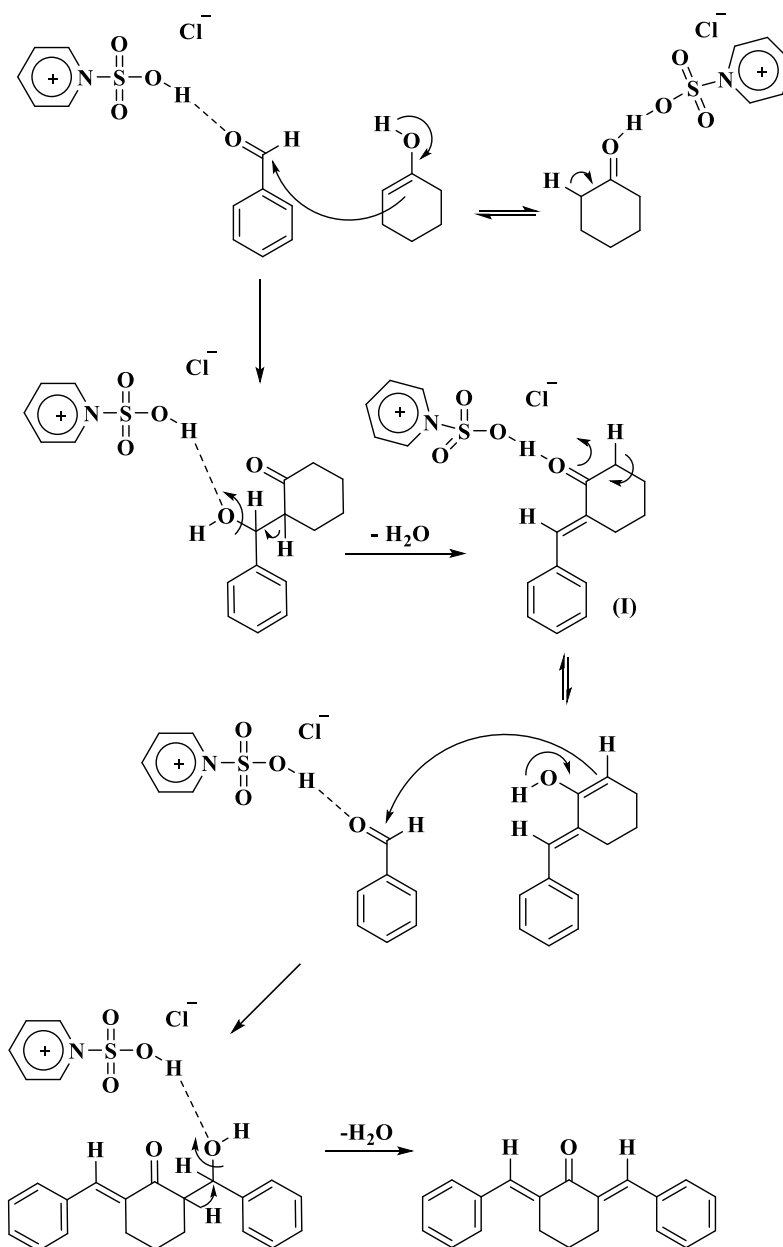
Entry	Product	Time (min)	Yield ^a (%)	Mp °C (Lit.)
1		15	82	112-115 (115-118) [18]
2		20	91	143-145 (147-149) [18]
3		20	89	208-210 (208-210) [18]

Table 2. Continued

4		15	85	116-119 (118-119) [19]
5		20	90	151-155 (168-171) [18]
6		20	87	148-152 (151-154) [18]
7		16	88	161-164 (160-161) [18]
8		20	87	223-226 (223-226) [18]
9		20	85	194-196 (193-196) [18]
10		20	80	188-191 (188-191) [18]
11		17	86	223-225 (224-226) [18]
12		15	85	152-154 (157-160) [18]
13		15	93	240-243 (-) [24]
14		14	90	294-297 (288-290) [20]

^a Isolated yield

In a suggested mechanism which is confirmed by the previous literature [11-15], the carbonyl group of cyclohexane was activated by [pyridine-SO₃H]Cl and converted to enol form and then reacted with activated aromatic aldehyde by acidic group of [pyridine-SO₃H]Cl to prepare (I) after removing one molecule of H₂O. In the second step, (I) was converted to the enol form and then reacted with another molecule aldehyde which was activated by the catalyst to give the expected product after removing of one molecule of H₂O (Scheme 3).



Scheme 3. The purposed mechanism for the synthesis of α,α' -bis(arylidene)cycloalkanones

Conclusions

In this research study, we used the sulfonic acid functionalized pyridinium chloride [pyridine-SO₃H]Cl, as an efficient catalyst and ionic liquid, for the cross-aldol condensation reaction between the cycloalkanones, including, cyclohexanone and cyclopentanone, and various arylaldehydes such as benzaldehyde as well as the aldehydes containing electron-withdrawing substituents, electron-releasing substituents or halogens to furnish the α,α' -bis(arylidene)cycloalkanones at 80 °C under solvent-free conditions. The high yields, short reaction times, simple work up, easy purification, adaptation to green chemistry protocols were found to be some important advantages of this work.

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