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Highly Efficient Green Diels-Alder Reaction Between Isoprene and 2-Cyclopentene-1-One Under Microwave Irradiation

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Abstract
A solid supported synthetic technique has been established for the Diels-Alder reaction between isoprene and 2-cyclopentene-1-one using solid supports as energy transfer medium under microwave irradiation in 3-methyl-1-octyl-imidazolium tetrachloroaluminate ionic liquid. The experimental results obtained by microwave irradiation technique were compared with those attained by the conventional method. This solvent-free technique coupled with the excellent yields and short reaction time makes this procedure environmentally benign for synthesis.

1. Introduction

The stress-free way of synthesizing a six membered cyclic compound is applying Diels-Alder reaction, known as one of the examples of pericyclic reactions, between a conjugated diene and a dienophile to form a substituted cyclohexene adduct [1]. Conventional synthetic methods of consuming massive volumes of organic solvents for the preparation of organic compounds have been creating pollution issue and global warming around the globe. These drawbacks make ionic liquids as smart substitute to the conventional synthesis processes. The suitable and essential alternative to initiate the construction of pollution less environment was green processing. In recent years various techniques such as mixers, microreactors, spin disc reactor, oscillated flow reactors, microwave irradiation, ultrasonication, multifunctional membranes and coiled flow inverter have been applied for the green synthetic processes [2]. Although various techniques are available for green synthesis, microwave irradiation technique was selected for the present work up of Diels-Alder reaction between isoprene and 2-cyclopentene-1-one at various reaction conditions. The main features of utilizing this microwave technology are performing at easy work-up conditions, setting up and monitoring of reaction temperature, pressure, reaction time, rapid reaction rates and excellent yields [3]. Due to these benefits microwave techniques have widely been used already for the synthesis of number of compounds [4, 5].

In addition to microwave technology, solid supports such as $LiNTf_2$, $Y(OTf)_3$, $Sc(OTf)_3$, etc. have also played outstanding performance in acceleration of several Diels-Alder reactions conducted in ionic liquids. The use of these type of solid supports is essential for a smooth reaction [6]. In this presently reported experiments, 3-methyl-1-octyl-imidazolium tetrachloroaluminate ionic liquid was selected as reaction medium as it has excellent activity than imidazolium based tetrafluoroborate ionic

liquids [3]. It is well known that the rate acceleration in most of the reactions are resulted from the thermal/kinetic effect achieved from microwave irradiation [7]. It is evident that from results of the experiments of the past twenty years, microwave irradiated reactions are 1,000-fold faster than conventional heating techniques [8]. All the reactions can be carried out in ionic liquids under mild reaction conditions with shorter duration of reactions giving excellent yield [9-12]. Although water is a good solvent for organic reactions, there is a probability of unwanted hydrolysis during the process [13].This drawback can be resolved by using ionic liquid instead of water and also can be used repeatedly after subjecting it to recycling process without significant loss of activity [14].

The first microwave assisted synthesis of ionic liquid was carried out by Varma et al. in 2001 [3]. The ionic liquid, 3-methyl-1-octyl-imidazolium tetrachloroaluminate used in our study was also prepared using a household microwave oven.

In the present work, we focused on understanding the role of solid supports and microwave irradiation on the rate enhancements in addition to the catalytic activity of 3-methyl-1-octyl-imidazolium tetrachloroaluminate ionic liquid. We have also focused in conducting Diels-Alder reactions between isoprene and 2-cyclopentene-1-one in conventional and microwave irradiation techniques with obeying the green chemistry principles [15].

2. Materials and Methods

2.1. Chemicals and Instruments Required

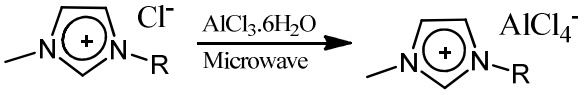
^{1}H and ^{13}C NMR (300 MHz) spectra were measured on Bruker AVANCE spectrometer (Bruker Bio Spin AG, Fällanden, Switzerland; 300 MHz). TMS was used as internal standard having the chemical shift value δ=0.00 ppm. The chemical shifts for all NMR spectra were recorded as δ in ppm. FT-Infrared spectra were measured in the range 4000-400 cm^{-1} on a Perkin Elmer (Model-Frontier) FT-IR spectrophotometer (Waltham, MA, USA) using a 1 cm (10 mm) quartz cell, concentration: 0.5 mmol mL^{-1} (Acetone). Absorption spectra were recorded on a UVPC absorption spectrophotometer (Perkin Elmer, Lambda 35, USA) using a 1 cm (10 mm) quartz cuvette, concentration: 0.0001 mmol mL-1 (Acetone) in the range 190 nm to 1100 nm. Gas Chromatography-Mass Spectroscopy (GC-MS) analysis was performed by means of a Thermo LCQ Deca XP MAX GC – MS instrument equipped with electrospray (ESI) and APCI ionization (positive or negative mode) sources. Boiling point was determined by ThermoCal / µThermoCal10 automatic capillary point apparatus. All microwave assisted Diels-Alder reactions were performed on a Biotage microwave reactor (Power range: 0-300 W at 2.45 MHz) at 60 ^{o}C. All the conventional reactions were carried out on a calibrated magnetic stirrer (Remi) at 25 ^{o}C. Isoprene **1** and 2-cyclopentene-1-one **2** (Scheme 2) were purchased from Aldrich Chemical Company Inc. and used without further purification. All other reagents were purchased from Merck-Millipore Company and used without further purification.

The progress of all the reactions were examined by GC-MS (Thermo LCQ Deca XP MAX) spectrometer.

2.2. Experimental Section

2.2.1. General Procedure for Synthesis of Ionic Liquid

The ionic liquid, 3-methyl-1-octyl-imidazolium tetrachloroaluminate, [MOIM] $AlCl_4$ was synthesized (Scheme 1) from 3-methyl-1-octyl imidazolium chloride and aluminium chloride hexahydrate using a household microwave oven (IFB, 700 W) following the simple work-up procedure given in the literature [16].



Where R = Octyl

Scheme 1. *Preparation of ionic liquid [MOIM] $AlCl_4$.*

2.2.2. Spectral Data of Ionic Liquid

^{1}H-NMR (300 MHz, D_2O, ppm, δ) of [MOIM] $AlCl_4$: 0.72 (3H, t, $N(CH_2)_7CH_3$), 1.13 (10H, m, $N(CH_2)_2(CH_2)_5CH_3$), 3.78 (3H, s, NCH_3), 3.82 (2H, t, $NCH_2(CH_2)_6CH_3$), 4.11 (2H, m, $CH_2CH_2(CH_2)_5CH_3$), 7.37 (2H, s, 2NCH), 8.62 (1H, s, N_2CH).

2.2.3. General Procedure for Synthesis of the Diels-Alder Adduct a in Conventional Method

2 mL of [MOIM] $AlCl_4$ ionic liquid was taken in a 25 mL round bottom flask. Appropriate quantity of solid support was added to it and stirred well for 30 s to undergo homogenization of the reaction medium. 2.2 mmol of isoprene **1** and 2 mmol of 2-cyclopentene-1-one **2** were mixed with the reaction medium. The reaction mixture was subjected to calibrated magnetic stirring (REMI) till the time mentioned (Table 1, Table 2 and Fig. 1). The progress of the reaction was monitored by GC-MS spectrometer. After completion of the reaction, the Diels-Alder adduct was extracted by solvent extraction using diethyl ether (5 X 6 mL). After extraction, the ethereal solution was allowed to evaporate to half volume under vacuum in a rotary evaporator. Then it was filtered using a silica gel bed (3 cm) to remove any contamination of ionic liquid present in the organic layer. The Diels-Alder adduct was separated by allowing the organic solution to evaporate up to dryness. Whenever further purification was necessary, it was purified by chromatography. Finally, the product was analyzed by ^{1}H NMR, ^{13}C NMR, FT-IR, UV-Vis, and GC-MS spectroscopy.

2.2.4. General Procedure for Synthesis of the Diels-Alder Adduct a in Microwave Method

2 mL of [MOIM] $AlCl_4$ ionic liquid was taken in a 20 mL microwave-vial. Appropriate quantity of corresponding solid

support was added to it. 2.2 mmol of isoprene **1** and 2 mmol of 2-cyclopentene-1-one **2** were mixed with the reaction medium. The reaction medium was subjected to pre-mixing for 30 s to undergo homogenization of the reaction medium. The reaction mixture was subjected to microwave irradiation at 60 ^{o}C using Biotage microwave reactor (300 W) for a pre-programmed time mentioned (Table 1, Table 2 and Fig. 2). The course of the reaction was monitored by GC-MS spectrometer. After completion of the reaction, the product was extracted by solvent extraction and purified as previously described work-up (Section 2.2.4). The product was analyzed by ^{1}H NMR, ^{13}C NMR, FT-IR, UV-Vis and GC-MS spectroscopy.

2.2.5. Spectral Data of 5-Methyl-2,3,3a,4,7,7a-Hexahydro-1*H*-Inden-1-One (a)

Yellow liquid, BP: 232 ^{o}C. ^{1}H-NMR (300 MHz, $CDCl_3$, ppm, δ) = 1.67 (3H, s, -CH_3), 2.15 (1H, m, -CH_2), 2.20 (1H, m, -CH_2), 2.70 (1H, m, -CH), 2.76 (1H, td, -CH), 4.85 (1H, m, -CH_2),5.10 (1H, t, =CH), 5.76 (1H, dd, -CH_2).

^{13}C-NMR (300 MHz, $CDCl_3$, ppm, δ) = 22.468, 26.019, 28.723, 29.583, 31.545, 36.227, 50.151, 122.217, 135.927, 217.003.

GC-MS (m/z) (R. Time 18.714) +ESI: $[M]^+$ = 150.0, 144.0, 139.1, 132.0, 127.0, 122.0, 113.1, 104.0.

IR (NaCl)v: at 3437.50 cm^{-1} (=C-H), 2255.54 cm^{-1} (C-H, methyl), 1629.85 cm^{-1} (C=O), 1360.79 cm^{-1} (C-H def. in methyl), 744.14 cm^{-1} (vinyl C-H).

UV/Vis λ_{max} ($CDCl_3$) =250.48 nm.

3. Results and Discussion

3.1. Designing the Starting Materials

Designing a suitable medium is an important aspect in creating an ideal environment to conduct a chemical reaction smoothly. In this study, 3-methyl-1-octyl-imidazolium tetrachloroaluminate ionic liquid was selected as green medium for conducting all the Diels-Alder reactions. The various reasons for selection of this medium are: (a) It can be synthesized rapidly using a household microwave oven on direct addition of aluminium chloride hexahydrate with 3-methyl-1-octyl-imidazolium chloride. (b) No any byproduct was formed while synthesizing this ionic liquid. So there is no stress of eliminating the contamination of byproducts. (c) Hundred percent yield of ionic liquid is formed in household microwave oven synthetic procedure.

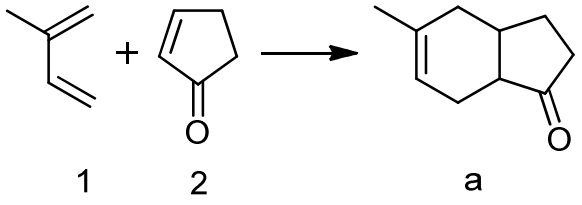
5-methyl-2,3,3a,4,7,7a-hexahydro-1*H*-inden-1-one a (Scheme 2) was synthesized using isoprene **1** and 2-cyclopentene-1-one **2** following the conventional and microwave (MW) synthetic methods. Aluminium oxide (Al_2O_3-activated, neutral, Brockmann I-150), silica gel (SiO_2-60), montmorillonite (K-10), bis(trifluoromethane)sulfonimide lithium ($LiNTf_2$), scandium trifluoromethanesulfonate [$Sc(OTf)_3$] and yttrium trifluoromethanesulfonate [$Y(OTf)_3$] were used as solid supports for conventional and microwave irradiation methods.

3.2. Role of Solid Supports

Although all the ionic liquids have remarkable catalytic properties their efficiency still to be improved to accelerate the reaction rates remarkably without omitting the green chemistry principles [17]. In our study six types of solid supports have been investigated in order to explore the efficiency of individual solid supports in enhancing the rates of Diels-Alder reactions marvelously. In our investigation bis(trifluoromethane)sulfonimide lithium ($LiNTf_2$), scandium trifluoromethanesulfonate [$Sc(OTf)_3$] and yttrium trifluoromethanesulfonate $Y(OTf)_3$ showed almost equivalent and efficient performances over rest of three solid supports. When these three ($LiNTf_2$, $Sc(OTf)_3$, $Y(OTf)_3$) solid supports were compared the bis(trifluoromethane)sulfonimide lithium showed the best activity in microwave irradiation method and the role of scandium trifluoromethanesulfonate was dominant in conventional method of synthesis. A quick review of the results reveals that, aluminium oxide showed the least performance among all the solid supports.

3.3. Contribution of Microwave Energy in Enhancing the Reaction Rates

Continuing the effort to improve the reaction rate and yield, the effect of an exposure of the reaction medium to microwave energy is reported here. Microwave energy is transferred to the reaction medium through dipole rotation and ionic conduction mechanism. This process is not possible in conventional thermal heating method. It reveals the advantage of microwave method over conventional method where the same reaction gives poor yield while performing under same temperature and pressure conditions [3]. In our experiment, a comparison of conventional and microwave irradiation methods clearly showed that the microwave-irradiation method was a much superior one since it resulted in excellent yields and impressively condensed reaction time involving more shortened and cleaner approach avoiding longer duration, unlike conventional method where magnetic stirrer was used.



Scheme 2. *Synthesis of 5-methyl-2,3,3a,4,7,7a-hexahydro-1H-inden-1-one.*

In a model Diels-Alder reaction, isoprene **1** and 2-cyclopentene-1-one **2** in 3-methyl-1-octyl-imidazolium tetrachloroaluminate ionic liquid mixed with corresponding solid support were stirred at room temperature (25 ^{o}C) in conventional method. After completion of the reaction as monitored on GCMS, the typical work-up affords clean Diels-

Alder adduct. The reactions proceeded neatly at 60 ºC temperature in microwave method and at room temperature (25 ºC) in conventional method. However, at room temperature the conventional reactions proceeded in long time period (0.30-3.30 h) while the time period of microwave reaction is 60 s only (Table 1). This ionic liquid plus solid supported green medium in combination with microwave energy proved to be very effective to induce the cyclo-addition reaction dramatically. After completion of reaction, accumulation of water and diethyl ether to the reaction mixture effects in the formation of a two-phase system: the organic layer at the top, ionic liquid mingled with the aqueous layer at the bottom. The product was isolated from the organic layer by solvent extraction using diethyl ether followed by decantation. Isolation of product is made stress-free, since imidazolium ionic liquids have extraordinary solvent properties.

3.4. Effect of Recycling and Reuse of Green Medium

Generally ionic liquids are called as green medium because of its non-volatile behavior. But only this behavior will not fulfil the green chemistry principles unless proper recycling methods was not well-known. In addition, recycling of ionic liquids provides the opportunity to synthesize organic compounds more economically. In our experiment, the recyclability of the green medium was studied. 3-methyl-1-octyl-imidazolium tetrachloroaluminate ionic liquid containing 0.750 g of solid support ($LiNTf_2$) used in Diels-Alder reaction was recovered and reused for five times in successive reactions without significant loss of activity in both conventional and microwave techniques (Fig. 1 and Fig. 2).

Table 1. *Diels-Alder reaction between 1 and 2 using various solid supports.*

Entry	Solid Support[a]	Conventional[b]		Microwave[c]	
		Time, h	Yield, %[d]	Time, s	Yield, %[e]
1	$LiNTf_2$	0.30	97	60	99
2	$Sc(OTf)_3$	0.45	99	60	97
3	$Y(OTf)_3$	1.30	93	60	96
4	K-10	2.00	88	60	91
5	SiO_2-60	2.30	86	60	89
6	Al_2O_3	3.30	83	60	86

Reaction conditions: [a]amount of solid support = 0.750 g, [b]temperature = 25 ºC, [c]temperature=60 ºC, [d,e]isolated yield.

Table 2. *Diels-Alder reaction between 1 and 2 using $LiNTf_2$.*

Entry	Amount of $LiNTf_2$, g	Conventional[a]		Microwave[b]	
		Time, h	Yield, %[c]	Time, s	Yield, %[d]
1	0.050	0.30	39	60	57
2	0.125	0.30	78	60	88
3	0.250	0.30	82	60	92
4	0.500	0.30	88	60	95
5	0.750	0.30	97	60	99
6	1.000	0.30	97	60	99

Reaction conditions: [a]temperature = 25 ºC, [b]temperature=60 ºC, [c,d]isolated yield.

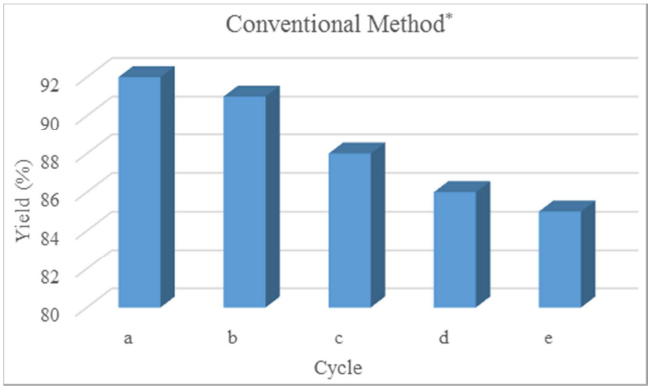


Fig. 1. *Recyclability of the system, ionic liquid [MOIM] $AlCl_4$ mixed with $LiNTf_2$ for the reaction between 1 and 2 in conventional method.*

*Reaction conditions: 2 ml of [MOIM] $AlCl_4$, 0.750 g of LiNTf2, temperature = 25 ºC, time = 0.30 h, isolated yield,

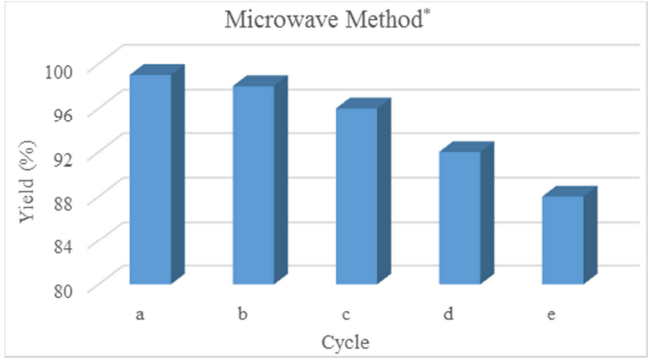


Fig. 2. *Recyclability of the system, ionic liquid [MOIM] $AlCl_4$ mixed with $LiNTf_2$ for the reaction between 1 and 2 under microwave irradiation.*

*Reaction conditions: 2 ml of [MOIM] $AlCl_4$, 0.750 g $LiNTf_2$, temperature = 60 ˚C, microwave, time = 60 s, isolated yield.

3.5. Outstanding Performance of Bis(trifluoromethane)sulfonimide Lithium

Table 2 shows the examination of discovering the efficiency of $LiNTf_2$ at different load study. From the data, it is observed that the maximum rate of conversion was achieved while using 0.750 g or 1 g of bis (trifluoromethane) sulfonimide lithium ($LiNTf_2$). It should be noted that in conventional method, scandium trifluoromethanesulfonate have participated in maximum conversion rate among other solid supports where as in microwave technique the role of $LiNTf_2$ have the major part in obtaining high yield. Our main aim is to synthesize organic compounds rapidly and smoothly with high yield. So, it should be noted that bis(trifluoromethane)sulfonimide lithium has given significant contribution in enhancing the reaction rates in microwave irradiation method. We have achieved 99 % conversion of substrates within 60 s in this technique.

In our experiments, all the products were characterized by ^{1}H NMR, ^{13}C NMR, FT-IR, UV-Vis, and GC-MS spectrometers. The overall work-up revealed that the microwave energy has played an outstanding part in the rate enhancement several fold over the conventional method.

4. Conclusion

In conclusion, we describe a novel convenient and rapid procedure for the synthesis of 5-methyl-2,3,3a,4,7,7a-hexahydro-1*H*-inden-1-one **a** through an Diels-Alder reaction between isoprene and 2-cyclopentene-1-one by conventional method in 0.30-3.30 h and under microwave irradiation involves time duration of only 60 s while using solid supports in the ionic liquid with improved yield. So that the microwave irradiation method has been developed as an easy and convenient synthetic procedure for the preparation of 5-methyl-2,3,3a,4,7,7a-hexahydro-1*H*-inden-1-one by coupling microwaves with 3-methyl-1-octyl-imidazolium tetrachloroaluminate ionic liquid under solvent free conditions keeping innovation and simplification of traditional procedure, to avoid consuming massive amount of volatile or toxic solvents.

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