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Free Solvent Synthesis Characterization and Kinetics Studies of N-phenyl Aziridine Catalyzed by Maghnite (Algerian MMT) under Effect of Microwave Irradiation

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Abstract

Aziridination reactions of aniline (heterocyclic and primary amine) with ethylene glycol or Di-bromo ethane catalysed by green and ecologic catalyst called Maghnite (Algerian MMT) under micro wave irradiation were investigated and discussed. The original synthesis of heterocyclic Aziridine itself takes place in one step. In this step aniline and ethylene glycol or Di-bromoethane are reacted with maghnite- Na^+ (basics and clay fin) in free solvent under microwave irradiation at (180°C in 3 MN) to form the N-phenyl Aziridine. The Aziridination method described afforded very good yields of easily purified products using only a slight excess of sodium hydroxide.

Keywords: Phenyl Aziridine; Maghnite- H^+ ; Aniline; Ethylene glycol; Dibromoethane; Microwave irradiation

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Introduction

In general, most organic reactions have been heated using traditional heat transfer equipment such as oil baths, sand baths and heating jackets [1]. These heating techniques are however rather slow and a temperature gradient can develop within the sample [2]. In addition, local overheating can lead to product, substrate and reagent decomposition [3]. In the early days of microwave synthesis household microwave ovens were used in chemical laboratory [4]. Although nowadays dedicated instrumentation is available there are still chemists who use kitchen microwave ovens for scientific purposes [5]. In inorganic chemistry, microwave technology has been used since the late 1970s, while it has only been implemented in organic chemistry since the mid 1980s [6]. The development of the technology for organic chemistry has been rather slow compared, to for example, combinatorial chemistry and computational chemistry [7]. This slow up takes of the technology has been principally attributed to its lack of controllability and reproducibility [8]. Recent developments in microwave accelerated solvent less organic synthesis are summarised. This expeditious and solvent-free approach involves the exposure of neat reactants to Microwave

(MW) irradiation in conjunction with the use of supported reagents or catalysts which are primarily of mineral

origin [9]. The salient features of these high yield protocols are the enhanced reaction rates, greater selectivity and the experimental ease of manipulation [10]. The chemistry of heterocyclic such as aziridine and its derivatives has attracted the attention in the organics synthesis. This is due to the high reactivity of these heterocyclic, which makes them versatile species in organic synthesis [11]. Aziridine are important building blocks in the synthesis of polyamines and polymers that are typically prepared by elimination of a leaving group from haloamines [12] and similar molecules [13] are used in organic synthesis as polymers and copolymers [14] and as anticancer drugs [15]. Aziridine attract most of the synthetic chemists due to their tremendous potential and versatility in organic synthesis and medicinal chemistry [16]. They exhibit highly regio and stereoselective ring opening reactions which provide a convenient entry to the stereoselective preparation of functionalized amino compounds [17]. Various biologically important compounds such as amino acids, β -lactam, antibiotics and alkaloids are derived from aziridine [18]. In addition, aziridine have also found applications

as chiral auxiliaries and lately also as chiral ligands in asymmetric catalysis [19]. Even though highly reactive, the aziridine skeleton occurs in several natural products [20]. Numbers of molecules possessing an aziridine ring have shown to exhibit potent biological activity [21]. They are most attractive synthetic targets since they may exhibit anti tumor or antibiotic activity or still other biological properties [22]. The main target of this study was to synthesize functionalized nitrogen-containing three membered rings (phenyl aziridine) when we used maghnite-Na⁺ (Algerian MMT) as catalyst. The current state of the art features catalytic, highly enantioselective aziridination, reliable ring-opening transformations, and stereoselective cycloadditions [23] all of which illustrate the unique reactivity of aziridine.

Experimental section

Materials

Aniline, ethylene glycol, dibromoethane, chloroform and sodium hydroxide were purchased from Sigma Aldrich and used as received. Maghnite (Algerian MMT) used in this work comes from a quarry located in Maghnia (North West of Algeria) and was supplied by the company "ENOF" (Algerian manufacture specialized in the production of non-ferric products and useful substances). This catalyst can be easily separated from the product and regenerated by heating at a temperature above 105°C.

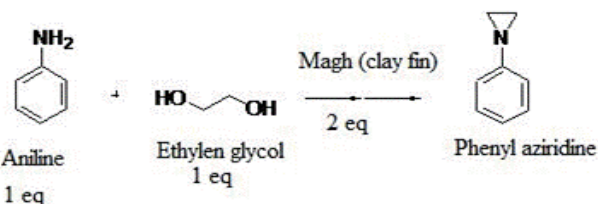
Synthesis of N-phenyl aziridine

All reactions was performed using the same methodology described below, with however, a variation of time for the 2% by weight of Mag-Na⁺ /monomers at 3 MN reaction. In a round bottom flask fitted with a condenser was mixed 1 g of Aniline and 2 g Mag-Na⁺(basics clay fin) previously dried at 105°C and 1 g of ethylene glycol or dibromoethane was added. The mixture was heated under microwave irradiation (180°C at 3 MN). Upon the addition of the Mag-Na⁺ a colour change was witnessed from clear to brown before finally becoming dark black. After 3 MN of heating a yellow oil was formed, and the suspension was cooled to room temperature. The residual yellow oil was dried at 80°C overnight to remove any monomer traces.

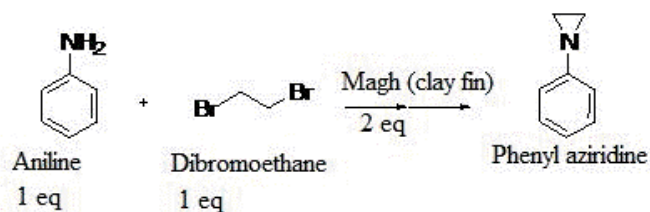
Results and Discussion

Kinetics studies

N-phenyl aziridine was prepared firstly by reaction of aniline with ethylen glycol followed by a treatment with sodium hydroxide solution (**Scheme 1**) and secondary by reaction of aniline with dibromoethane (**Scheme 2**) in equimolar ratio and in free solvent under microwave irradiation. The conditions of the reaction and results of some selected experiments are summarized in (**Table 1**). The product (oil yellow liquid) was found to be soluble in water and organic solvents [24]. Here we wish to report an expeditious, catalytic route for the synthesis of substituted Aziridine directly from aniline and dibromoethane or ethylen



Scheme 1 Catalytic route for the synthesis of phenyl aziridine directly from aniline and ethylene glycol using Maghnite (Algerian MMT) as a catalyst.



Scheme 2 Catalytic route for the synthesis of phenyl aziridine directly from aniline and dibromoethane using Maghnite (Algerian MMT) as a catalyst.

Table 1 Effect of reagents amount on the synthesis of N-phenyl aziridine from aniline/dibromoethane and maghnite under MW irradiation.

Entry	Solvent	Aniline (equiv.)	Dibromoethane (equiv.)	Maghnite-Na ⁺ (equiv.)	Yield (%)
1	free	2	1	2	trace
2	-	1.5	1	2	9.32
3	-	1	1.5	2	15.78
4	-	1	1	2	85.09
5	-	1	2	2	trace
6	-	2	2	2	71.26

glycol using Maghnite (Algerian MMT) as a catalyst. We have carried out the initial reaction by adding a solution of aniline (1 equivalent) to a maghnite (2 equivalent) and dibromoethane or ethylene glycol (1 equivalent) under microwave irradiation. We observed that the reaction is very fast and the corresponding aziridine was isolated in 85.83% yield after 3 min of reaction. In order to find out the best reaction condition, we have investigated the effect of catalyst, temperature and time on the product yield. The reaction was also studied with varying amount of catalyst (**Tables 1 and 2**). Yields of the corresponding aziridine were found to be lower when the amount of the catalyst decries. Here we wish to report an expeditious, catalytic route for the synthesis of substituted aziridine directly from aniline and dibromoethane or ethylen glycol using Maghnite (Algerian MMT) as a catalyst. Finally, the use of (2 equiv) of catalyst was found to be optimum for the best result [25]. In order to find out the best reaction condition, we have investigated the effect of various solvents on the product yield (**Tables 3 and 4**). When tetrahydrofuran and

dimethylformamide were used as a solvent the reaction did not produce the expected product after 3 min at 180°C of reaction. Further investigation on the reaction using ethyl ether as a solvent gave the best result of 88.59% isolated yield of the corresponding aziridine. When we studied with chloroform or acetonitrile, under the same reaction conditions, interestingly it gave 42.38% to 45.56% yield of aziridine form (Tables 3 and 4). So we selected ethyl ether as the best solvent [26]. Table 4 and Figure 1, shows the effect of the amount of Mag-Na⁺ on the reaction yield under effect of microwave irradiation. Indeed, using various amounts of Mag-Na⁺ : 1%, 1.5%, 2%, 2.5% and 3% by weight, the reaction was carried under microwave irradiation in free solvent at 200°C with excess of ethylene glycol or dibromoethane and in basics medium. The reaction yield increased with the amount of Mag-Na⁺, thus clearly showing the effect of Mag-Na⁺ as a catalyst. This phenomenon is probably the result of an increase in the number of "initiating active sites" responsible of inducing reaction [27]. Effect of temperature on the yield of aziridation reaction of aniline under effect of maghnite-Na⁺ (2% by weight) for 3 min in microwave irradiation is shown in Table 5 and Figure 2. The aziridation yield reach maximum value around 180°C. On the other hand, with the increase in the reaction temperature above 180°C, viscosity of the obtained aziridine increase and decrease

Table 2 Effect of reagents amount on the synthesis of N-phenyl aziridine form aniline/ethylene glycol and maghnite under MW irradiation.

Entry	Solvent	Aniline (equiv.)	Ethylene glycol (equiv.)	Maghnite-Na ⁺ (equiv.)	Yield (%)
1	free	1	1	1	46.28
2	-	1	1	1.5	54.95
3	-	1	1	2	84.88
4	-	1	1	2.5	72.12
5	-	1	1	3	67.11
6	-	1	1	3.5	52.63

Table 3 Effect of solvent on reaction d'aziridation of aniline with dibromoethane under microwave irradiation.

Entry	Solvent	Aniline (equiv.)	Dibromoethane (equiv.)	Maghnite-Na ⁺ (equiv.)	Yield (%)
1	THF	1	1	2	trace
2	DMF	1	1	2	trace
3	ACN	1	1	2	42.38
4	CDCl ₃	1	1	2	45.56
5	EthE	1	1	2	82.59
6	free	1	1	2	88.92

Table 4 Effect of solvent on reaction d'aziridation of aniline with ethylen glycol under microwave irradiation.

Entry	Solvent	Aniline (equiv.)	ethylen glycol (equiv.)	Maghnite-Na ⁺ (equiv.)	Yield (%)
1	THF	1	1	2	15.25
2	DMF	1	1	2	trace
3	ACN	1	1	2	39.05
4	CDCl ₃	1	1	2	51.35.
5	EthE	1	1	2	80.83
6	Free	1	1	2	85.73

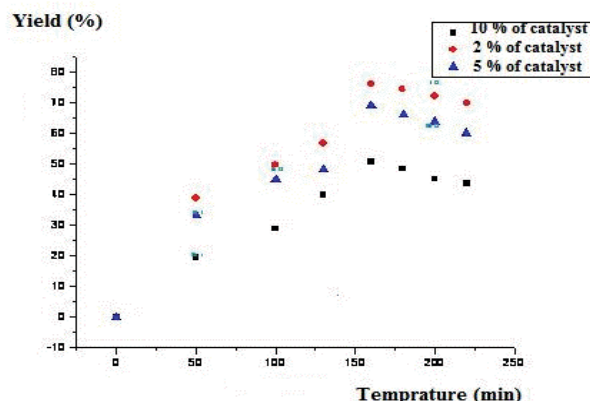


Figure 1 Effect of amount of catalyst on reaction d'aziridation of aniline with dibromoethane under microwave irradiation.

Table 5 Effect of amount of catalyst on reaction d'aziridation of aniline with dibromoethane under microwave irradiation.

Time (min)	1	2	3	4	5
Catalyst (%)	1	1.5	2	2.5	3
Yield (%)	38.89	78.88.86	88.93	87.73	86.95

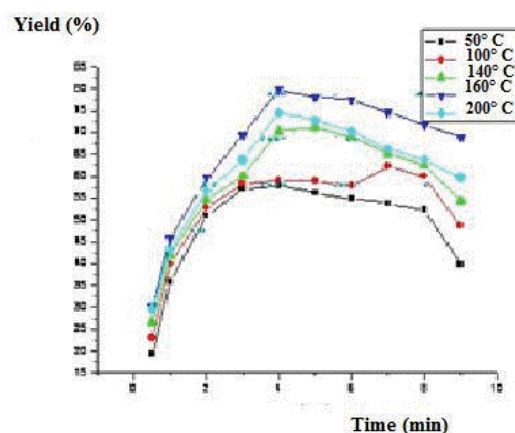


Figure 2 Effect of temperature on aziridation reaction of aniline with dibromoethane under microwave irradiation.

the molecular weight of the product progressively, suggesting the possible occurrence of thermal degradation [28]. On the basis these results, subsequent aziridations were carried out at 180°C under effect of microwave irradiation in free solvent and with excess of ethylene glycol or dibromoethane.

Structure analysis

The product was analyzed after chromatographic separation by HNMR and FTIR spectroscopic analysis. In the proton NMR spectra of the aziridine from aniline and dibromoethane or ethylen glycol, all aromatic protons were appeared in the range 7-8 ppm as multiples [29]. For the aromatic group attached to the azote atom, the protons appeared as two doublets in the aromatic

region. By FTIR spectroscopic analysis as show in (Figures 3 and 4), this compounds has both a phenyl ring, you can detect the familiar sp³ C-H peaks below 3000 cm⁻¹, the phenyl ring usually shows multiple C-H peaks between 3100 and 3000 cm⁻¹

and phenyl rings almost always show a weaker sharp peak right at 1600 cm⁻¹ [30]. The (CH₂) group appeared as a singlet at around 2.3 ppm (Figures 5 and 6). Want three more pieces of proof that you have a phenyl ring. Phenyl rings generally show two very

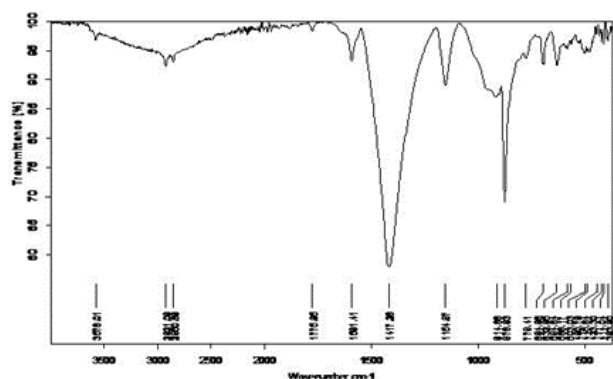


Figure 3 FT-IR spectra of N-phenyl aziridine obtained by the intercalated method between Aniline/dibromoethane and Maghnite-H⁺ under MW irradiation.

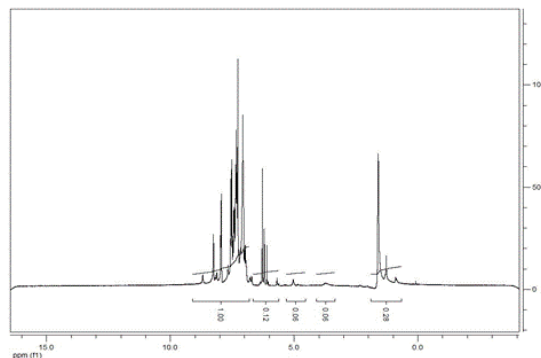


Figure 5 H-NMR spectra of N-phenyl aziridine obtained by the intercalated method between Aniline/ dibromoethane and Maghnite-H⁺ under MW irradiation.

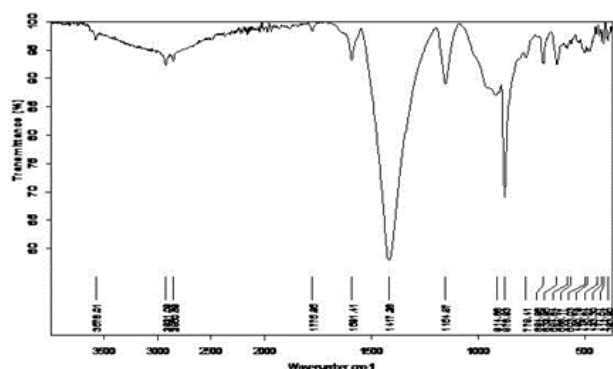


Figure 4 FT-IR spectra of N-phenyl aziridine obtained by the intercalated method between Aniline/ ethylen glycol and Maghnite-H⁺ under MW irradiation.

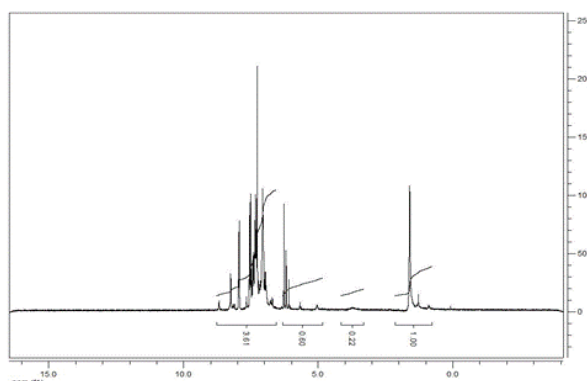
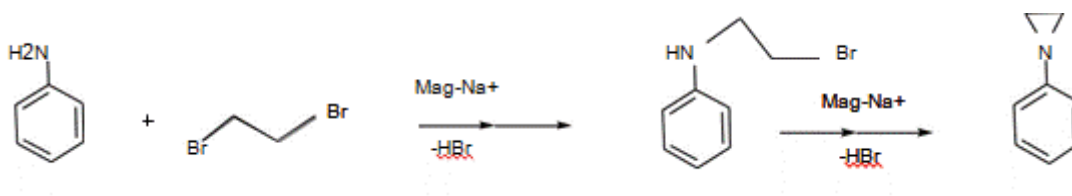
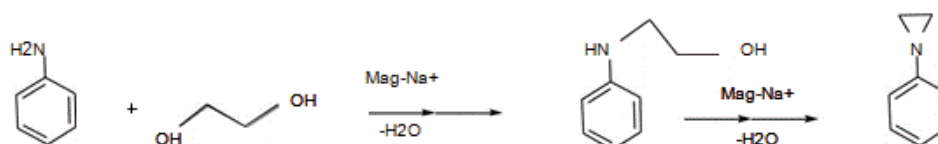


Figure 6 H-NMR spectra of N-phenyl aziridine obtained by the intercalated method between Aniline/ ethylen glycol and Maghnite-H⁺ under MW irradiation.



Scheme 3 Proposed mechanism of N-phenyl aziridine obtained by the intercalated method between Aniline/dibromoethane and Maghnite-H⁺ under MW irradiation.



Scheme 4 Proposed mechanism of N-phenyl aziridine obtained by the intercalated method between Aniline/ethylen glycol and Maghnite-H⁺ under MW irradiation.

narrow peaks at 1450 and 1500 cm^{-1} . Phenyl rings always have a strong, sharp peak in the region of 700 to 800 cm^{-1} . Also, phenyl rings almost always show jagged craziness (it's weak) between 2000 and 1650 cm^{-1} [31,32].

Proposed mechanism

There is a strong possibility of generation of benzoyl nitrene from aniline and dibromoethane in the presence of maghnite- Na^+ (clay). Initial step of the reaction is the abstraction of the Br by the clay which subsequently loses NaBr to form the nitrene with evaporation of HBr (Schemes 3 and 4). We observed that the solution becomes very turbid at the end of the reaction which is due to the precipitation of NaBr [33,34].

Conclusion

In this study, we have developed a new method for the synthesis of N-phenyl aziridine and synthesized two N-substituted aziridine

derivatives of the same nature. In the first reaction we started by the aziridation of aniline with ethylene glycol and in the other by the aziridation of aniline with dibromoethane. The method developed in this study begins with the direct cyclization of aniline under the effect of maghnite- Na^+ (basics clay fin) in free solvent. The reaction of dialcohols or dibromo compounds with aliphatic or aromatic primary amines gave the same aziridine (N-phenyl aziridine) in a yield of 88.7% to 88.8%. The main advantage of our reaction is in free solvent, catalyzed by green catalyst and the time (reactions are finished in 5 MN under MW). The aziridination method described afforded very good yields of easily purified products using only a slight excess of sodium hydroxide

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