

Short Communication

**Thin Layer Chromatography-A Tool to Investigate Kinetics of Michael
Addition Reaction**

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Abstract

Thin layer chromatography (TLC), a tool for defining identity, purity, and quantitation of a compound, has also been proved useful for monitoring the progress of a chemical reaction. However, the technique is yet to be exploited for investigating the kinetics of a reaction systematically. In this work, we used TLC for measuring the time for consumption of a reactant in Michael addition reaction of acetylacetone with 2-cyclohexene-1-one. Average rate of the model reaction was determined using a definite initial concentration of acetylacetone for a series of catalyst systems like NaOH, 1,8-diazabicyclo[5.4.0]undec-7-ene (DBU), DBU based protic ionic liquids (PILs) 1,8-diazabicyclo[5.4.0]undec-7-ene-8-ium hydroxide ([HDBU]OH) and 1,8-diazabicyclo[5.4.0]undec-7-ene-8-ium acetate ([HDBU]CH₃COO), a DBU based aprotic ionic liquid (AIL), 8-hexyl-1,8-diazabicyclo[5.4.0]undec-7-ene-8-ium hydroxide ([C₆DBU]OH), and binary systems of the ionic liquids with molecular solvents, such as, water, DBU, and acetic acid. The kinetic data on the performance of the chosen catalysts were interpreted on the basis of the established mechanism of the reaction. Finally, the prospect of the method based on TLC as a suitable technique for kinetic study of chemical reactions has been discussed.

Keywords: Thin layer chromatography; Michael addition reaction; Catalyst; Average rate.

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1. Introduction

Thin layer chromatography (TLC) is one of the easiest and most versatile methods of separating a mixture of chemicals into its components [1]. This method is simple, quick, sensitive, and reproducible. The mobile phase in TLC is a liquid, in general, mixtures of polar and nonpolar organic solvents, alcohol/water/acid, alcohol/water/base etc. [2] and

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the stationary phase is a thin layer of materials for instance, silica gel, alumina, cellulose etc. [3] on top of a thin and flat plate like paper, glass, plastic, and aluminum. The mobile phase transports the solutes through the stationary phase and the speed of transportation depends on the force of the mobile phase as it dissolves the solute and moves it up the plate. The speed of transportation of solutes also depends on the resistance of the adsorbent material as it pulls the solute out of solution and back into the adsorbent. Solute that are strongly attracted to the adsorbent move slowly and those less attracted to the solid layer move quickly [4]. Therefore, different compounds with different properties can be separated by using the diverse interactions of the solutes with the adsorbent and the mobile phase.

The mechanism of separation in TLC follows: adsorption, partition, ion exchange, and size exclusion or gel permeation [5]. Generally adsorbents are polar; therefore more polar solutes move more slowly than nonpolar solutes. By increasing the polarity of the mobile phase, the polar solutes can be drawn to increase separation [6]. Although techniques commonly employed for separation of components from a mixture including paper chromatography (PC), gas chromatography (GC), and high performance liquid chromatography (HPLC) have been popular, considerations of disappearance of peaks, presence of ghost peaks, and broadening of peaks from highly retained substances to result in the poorer resolution, give TLC supremacy over these techniques. Samples can be analyzed simultaneously using TLC with higher analytical precision and accuracy and at lower cost per analysis. In addition, highly retained substances form tightest zones and are detected with high sensitivity to make TLC adaptable, cheap, faster, and simple for analytical applications [1].

Quite reasonably, the application of the technique TLC to monitor the progress of a chemical reaction has drawn significant attention in synthetic organic chemistry. In practice, the progress of a reaction is monitored by following the consumption of reactant(s). In other words, absence of reactant(s) in the reaction mixture indicates the completion of the reaction which can be performed with ease using TLC. A TLC plate spotted with reactant(s) and reaction mixture can provide information about the absence/presence of reactant(s) in the reaction mixture after developing the plate and ultimately the completion of the reaction is indicated. This opens the avenue to exploit the potential of TLC to investigate the kinetics of a reaction. In fact, the time for completion of a reaction can be measured using TLC method and used to evaluate the average rate for the reaction for the initial concentration of the reactant used. The literature so far reports only the use of chromatographic techniques for indication of the completion of a reaction and emphasizes on the yield [7-12]. The reaction completion time has been reported in few instances [8-10], but has not been focused on the kinetics of a reaction. The study to exploit the reaction completion time for evaluating average rate and to systematically investigate the rate of a chemical reaction is yet to be explored. It would be worth evaluating different systems as catalysts through kinetic investigations and comparing their catalytic performances for practical applications. In a recent study, we have investigated the use of an aprotic ionic liquid (AIL), 8-hexyl-1,8-diazabicyclo[5.4.0]-

undec-7-ene-8-ium hydroxide ([C₆DBU]OH) for studying the kinetics of a Michael addition reaction using TLC. The applicability of the TLC as a versatile tool for studying the kinetics of a reaction and comparing the performances of a range of catalysts is very important and has been a demanding task.

In this work, kinetic investigation of Michael addition reaction of acetylacetone and 2-cyclohexen-2-one was made employing TLC technique using a range of catalyst systems and the average rate of the reaction was evaluated in each case. The reaction was carried out by using NaOH, 1,8-diazabicyclo[5.4.0]undec-7-ene (DBU), two DBU based protic ionic liquids (PILs) 1,8-diazabicyclo[5.4.0]undec-7-ene-8-ium hydroxide ([HDBU]OH) and 1,8-diazabicyclo[5.4.0]undec-7-ene-8-ium acetate ([HDBU]CH₃COO), one DBU based AIL [C₆DBU]OH, and the binary systems of the ILs with molecular solvents (water, DBU, and acetic acid) as catalysts and average rates of the reaction for the different catalyst systems were compared. Finally, kinetic results of the Michael addition reaction were interpreted in the light of the mechanism of the reaction to establish the efficacy of the TLC technique as a tool for kinetic studies.

2. Materials and Methods

2.1. Chemicals

Acetylacetone (Scharlau, Spain), 2-cyclohexen-1-one (Sigma-Aldrich), DBU (Sigma-Aldrich), sodium hydroxide (Merck Chemicals Ltd.), chloroform (Fisher Scientific), *n*-hexane (RCI Labscan Ltd., Thailand), acetic acid (RCI Labscan Ltd., Thailand) and absolute ethanol (Merck Chemicals Ltd., Germany) were used as received without further purification. Ultrapure water from HPLC grade water purification system (BOECO, Germany; specific conductivity = 0.055 $\mu\text{S cm}^{-1}$) was used for the preparation of the binary mixtures of the ILs.

2.2. Kinetic study

A mixture of acetylacetone (5 mmol) and 2-cyclohexen-1-one (5 mmol) was taken in a test tube. In general, 0.5 mmol of a catalyst was mixed in the test tube and the mixture was magnetically stirred at room temperature (≈ 20 °C). The progress of the reaction was followed by TLC and reaction completion time was measured. Crystalline product, 3-(3-cyclohexanonyl) pentyl-2,4-dione was obtained as characterized by chemical and FTIR, ¹H NMR, and ¹³C NMR spectral analyses [13].

Commercially available aluminum TLC plates coated with silica gel 60 F₂₅₄ were used as the stationary phase and mixture of chloroform and *n*-hexane (1:1 by volume) was used as the eluent. A line at the edge of the TLC plate, ≈ 1 cm from the bottom of the plate was marked using a pencil. This is the baseline of the TLC plate. Samples (two reactants: acetylacetone and 2-cyclohexen-1-one and the reaction mixture) were spotted onto the baseline of the plate using a capillary tube. The spots of the samples were labeled as "A"

for acetylacetone, “C” for 2-cyclohexene-1-one and “P” for the reaction mixture/product (Fig. 1a).

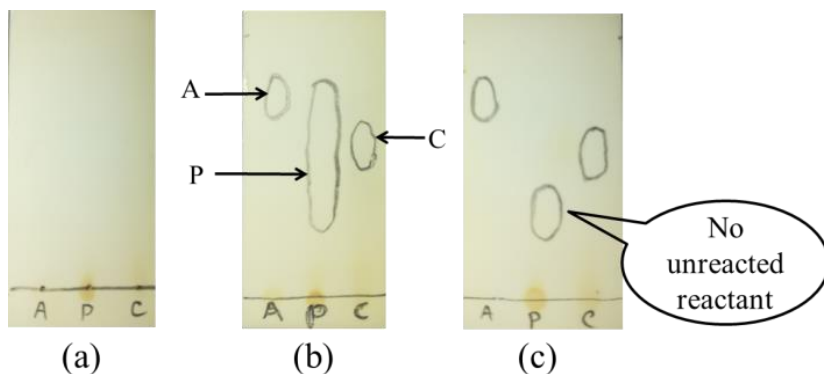


Fig. 1. Spotting and labeling of a TLC plate: (a) prior to developing; (b) developed at the initial stage of the reaction, and (c) after completion of the reaction.

The eluent, mixture of chloroform and *n*-hexane, was taken in a chamber to a depth of about 5 mm so that the base line of the TLC plate would be above the level of the eluent. The spotted plate was placed in the chamber to develop. The chamber was covered to prevent evaporation of the eluent. When the eluent reached near the top of the plate, the plate was removed from the chamber. The position of the solvent front was marked by using pencil and the plate was allowed to dry. The spots on developed plate were visualized under UV light and the spots were marked by pencil for record (Fig. 1). TLC analysis of the product mixture was carried out at different time intervals (5–30 min) in order to determine the time for the complete consumption of reactants. The product mixture showed the presence of spots for both the reactants and the product on the plate after few min from the beginning of the reaction (Fig. 1b). When the product mixture showed no spots for reactant(s), the reaction was assumed to be completed (Fig. 1c) and the time was taken as the reaction completion time (t). The initial concentration of the substrate, acetylacetone ($[A]_0$) was 3.791 mol L^{-1} , and the average rate was evaluated using, $v = \frac{[A]_0}{t}$.

3. Results and Discussion

The reaction of acetylacetone and 2-cyclohexene-1-one at equimolar concentration was carried out using NaOH, DBU, aprotic IL, $[\text{C}_6\text{DBU}]\text{OH}$, protic ILs, $[\text{HDBU}]\text{OH}$, $[\text{HDBU}]\text{CH}_3\text{COOH}$, and the binary systems of the ILs with molecular solvents, DBU, water and acetic acid as catalysts at room temperature (ca. 20°C). Table 1 summarizes the kinetic results using $[A]_0 = 3.791 \text{ mol L}^{-1}$.

The Michael addition reaction of acetylacetone and 2-cyclohexene-1-one in the absence of any catalyst was extremely slow and the average rate could not be measured even after few days using TLC method. Once NaOH was added to the reaction mixture, the average rate, albeit still slow enough, was enhanced and could be conveniently

measured (Table 1). NaOH takes a proton from the acetylacetone generating a carbanion to initiate the reaction. Large amount of ethanol was however, required for preparation of solution in this case. The average rate with DBU as the base was found to be almost identical with that with NaOH and it was completely miscible with both of the reactants. But with ILs, [HDBU]OH and [C₆DBU]OH, the average rates were higher and ILs served both as the medium and the catalyst requiring no additional solvent. These kinetic results were very significant. Ranu and coworkers also reported the use of a basic ionic liquid for a Michael addition reaction and showed that [BMIm]OH serves as a good catalyst with significant increase in the yield of the reaction and reduction in reaction completion time measured by TLC [8]. Using the initial concentration of the reactants and the reported reaction completion time in their study, we have evaluated the average rate of the reaction which compares well with the kinetic results in our case. This also showed the potential of the use of the technique for kinetic investigation of the Michael addition reaction and comparing the catalytic performances [8-10]. The low average rate with the IL [HDBU]CH₃COO may be ascribed to the less basicity of the anion CH₃COO⁻ compared to OH⁻ [14]. It is very interesting to note that when binary mixtures of the ILs were used as catalysts, the rate was higher than those for the pure ILs. This is due to the fact that the molecular solvents (water, DBU, and acetic acid) in binary systems make significant changes in the arrangement of the ions in IL through different molecular interactions to make the anion of IL efficient for catalysis [13].

Table 1. Reaction completion time and average rate for different catalyst systems and reaction media for Michael addition reaction of acetylacetone and 2-cyclohexene-1-one at ca. 20 °C.

Systems used as catalyst (0.5 mmol)	Reaction completion time (min)	Average rate (v) (mol L ⁻¹ s ⁻¹) $\times 10^4$
NaOH	250	2.53
DBU	240	2.63
[HDBU]OH	180	3.51
[HDBU]CH ₃ COO	270	2.34
[C ₆ DBU]OH	170	3.72
[[HDBU]OH]/[H ₂ O]=2/6	120	5.27
[[HDBU]OH]/[DBU]= 2/6	110	5.74
[[HDBU]CH ₃ COO]/[CH ₃ COOH]=2/6	160	3.95
[[HDBU]CH ₃ COO]/[DBU]= 2/6	152	4.16
[[C ₆ DBU]OH]/[H ₂ O]= 5/5	50	12.64

The catalytic performances of different systems for the Michael addition reaction were compared. The average rate of the reaction using ILs was faster compared to the pure bases (Table 1). The anion of the ILs acted as the base and similar mechanism was followed by both the base and IL [8,15]. The difference originates from the ability of the formation of hydrogen bonds between the reactants and ions. The formation of hydrogen bond with the carbanion enhances its nucleophilic ability and the hydrogen bond with the α,β -unsaturated carbonyl compound increases its electrophilic ability [16]. The reaction

thereby becomes more favorable and requires lower time for completion when IL was used as the catalyst instead of NaOH or DBU.

Among the five catalysts used, the rate of the reaction was observed to be highest when the AIL, [C₆DBU]OH was used as the catalyst. The cation C₆DBU⁺ of [C₆DBU]OH comprises a hexyl group and plays the key role in enhancing the reaction rate. The interactive forces of such an IL varies depending on the alkyl chain length and the cumulative effect of the electrostatic interaction between the ionic species and the induction interactions between the ions, aggregates, and clusters determine the properties of ILs [17]. The packing of cations and anions in [C₆DBU]OH is probably loose due to large size of the cation with the hexyl group. Moreover the hexyl group is nonpolar and hydrophobic in nature which also disturbs the close packing of ions [13]. Therefore, the anion is more mobile in [C₆DBU]OH and available for catalysing the reaction. The average rate is thus faster for [C₆DBU]OH and its binary system with water compared to the PIL systems as well as bases.

4. Conclusion

The average rates for the Michael addition reaction of acetylacetone and 2-cyclohexen-1-one could be successfully determined using TLC for measuring the time for completion of the reaction. Rates were determined for a range of catalysts such as, NaOH, DBU, ILs: [HDBU]OH, [HDBU]CH₃COO, and [C₆DBU]OH and their binary systems with water, acetic acid, and DBU. The observed kinetic results of the Michael addition reaction using different catalytic systems have been shown to be in conformity with the established mechanism of the title reaction and the average rates compare very well with the fundamental aspects of catalysis and the mechanism of the reaction. The technique may be efficiently used for investigation of the kinetics of other organic reactions as well where the reactants or products may be identified by the spots on the suitable TLC plates. By varying plate materials, solvent system, development technique, and method of detection, the scope of TLC may be extended to a wide variety of systems including super base, ionic liquid and even non-conventional catalysts for kinetic studies. Although the applicability may be somewhat restricted for fast reactions, the technique works very well for reactions with moderate rates and has the prospect to serve as a sensitive and reliable tool for kinetic study of organic reactions.

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