Meta-Stable Enamines: Synthesis of Simple Enamines via Catalytic Isomerization of Allylic Amine Substrates and Their Polymerization Behavior

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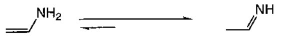
As is the case with enols, primary and secondary enamines are thermodynamically unstable species that exist in an unfavorable equilibrium with their imine tautomer (eq 1).[1] Simple ali-



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phatic enamines in the absence of extraordinary steric or electronic factors are particularly unstable and have proved to be most difficult to prepare. Secondary enamines have been generated in nonequilibrium concentrations by the controlled methanolysis or hydrolysis of trimethylsilyl, tin, magnesium, or lithium derivatives.[2] Primary enamines have been prepared in small quantities by a retro-Diels−Alder approach from the thermolysis of anthracene adducts for spectroscopic observation.[3] Vinylamine, the prototypical enamine, has been formed in only a few rare situations, further illustrating the unfavorable thermodynamics of simple enamines.[4] Currently there is a lack of an effective and efficient synthesis for simple enamines, and therefore their chemistry remains largely unexplored. One such area we believe these enamines to be particularly interesting is in the direct (co)polymerization of these "vinylamine" equivalents as a route to poly(vinylamine) analogues. In this communication, we describe the preparation and observed stability of aliphatic enamines using a mild, catalytic method from allylic substrates, and the further use of these meta-stable compounds as monomers for polymerization.

Poly(vinylamine) (PVAm) is not prepared from the vinylamine monomer. Instead, approaches to PVAm have had to rely on indirect methods such as the chemical modification of preexisting polymers and the polymerization-deprotection of protected vinylamine monomers.[5] Despite the difficulty of their preparation, polyamines are useful in applications ranging from paper sizing to pharmaceutical practices.

Not being capable of undergoing tautomerization, the catalytic isomerization of various tertiary allylamines to form stable enamines has been successfully performed by using strong bases (t-BuOK, KNH_2 on alumina, and KOH on alumina)[6] and heterogeneous basic metal oxides (MgO, CaO, SrO, and BaO)[7] as well as homogeneous transition-metal complexes of Mo, Co, Rh, and Ru.[8] Much of this work employs conditions (acidic or basic, long reaction times, high temperatures) which we believe to be incompatible with simple enamines. Lacking the mild conditions potentially more amicable to enamine stability, reaction attempts with primary and secondary allylamines generally resulted in the exclusive formation of the more stable imine products.[8] Indeed, to the best of our knowledge the only observation of an isomerized enamine was reported by Hiraki et al. for the isomerization of *N*-methyl allylamine (**1b**) in a modest 10% yield with a ruthenium(II) complex, $RuHCl(CO)(PPh_3)_3$.[9] Despite this lack of precedent, the very unfavorable thermodynamics governing enamine/imine behavior can be, in principle, circumvented by accessing appropriate kinetic pathways.[10] In the context of this study, controlled double-bond migration in primary and secondary allylamine substrates affords the opportunity to form the enamine product provided that the isomerization rate (k_1) is greater than that of the tautomerization (k_2).

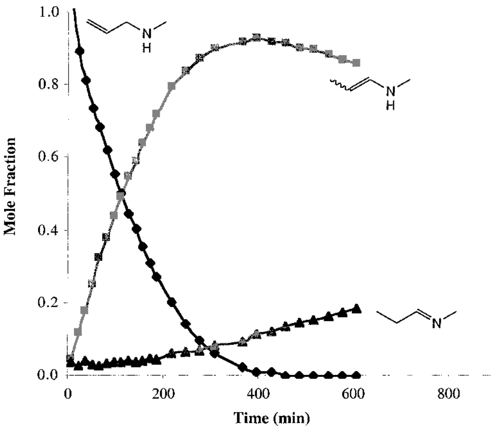

Figure 1. The concentration profiles of reactants and products during the room temperature isomerization of *N*-methyl allylamine (**1b**) with $RhH(CO)(PPh_3)_3$ in benzene-d_6 at 22 °C.

In our own attempts to further optimize through variants of the above ruthenium(II) catalyst system, we were unable to obtain complete conversion of the allylic substrate while maximizing enamine formation the tautomerization rates were far too competitive. Although cationic rhodium(I) complexes were extremely

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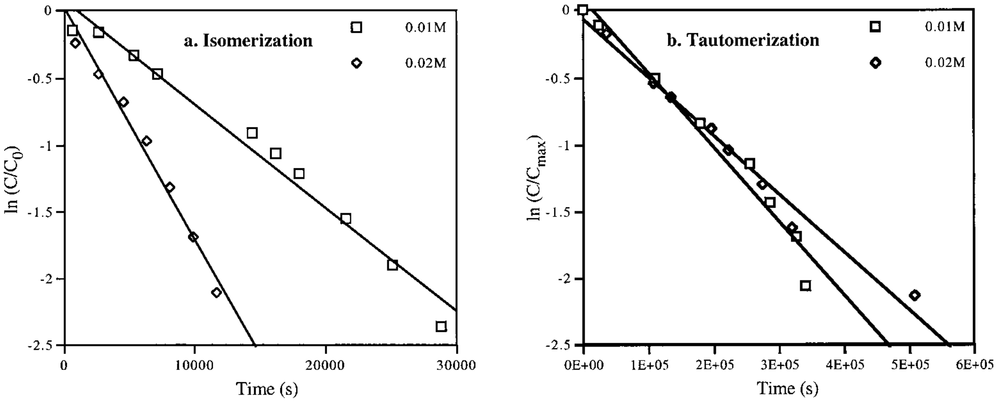
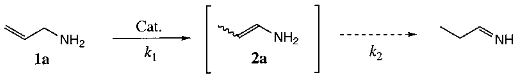


Figure 2. The kinetic plots of isomerization (a) of allylamine (**1a**) to the enamine (**2a**), and subsequent tautomerization (b) as a function of catalyst concentration, $HRh(CO)(PPh_3)_3$ (22 °C, benzene-d_6, Teflon tube). The tautomerization is first order in catalyst and the tautomerization is zero order.

efficient for allyl alcohol and tertiary allylamines,[11] we found that they were ineffective at room temperature for primary and secondary allylamines. During this survey, we discovered the neutral rhodium(I) complex $HRh(PPh_3)_4$ was a very active isomerization catalyst under mild conditions (22 °C), but unfortunately it also catalyzed a nearly equal tautomerization rate (e.g., for allylamine (**1a**) at 22 °C, $k_1/k_2 = 4.3$ and $k_2 = 8.7 \times 10^{-5}$ s^{-1}). However, and for reasons not well understood, we found the isoelectronic $HRh(CO)(PPh_3)_3$ compound to be a highly selective catalyst for the double-bond migration of **1a** and **1b** under mild conditions (eq 2) to form high concentrations of the



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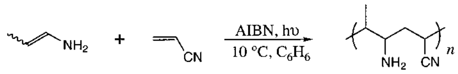
corresponding enamines (Figure 1). ^1H NMR kinetic studies of the room temperature isomerization of allylamines **1a** and **1b** in benzene (following the loss of the **1** methylene protons) were performed with $HRh(CO)(PPh_3)_3$ as a catalyst.[12] The reagents were handled in the inert atmosphere of a drybox and the reaction vessel consisted of a sealed NMR tube equipped with a fluorinated poly(ethylene-propylene) liner.[13] These studies show a first order dependence on both the concentration of **1** and catalyst (rate α $[cat.]^1$) for the double-bond migration to form enamine (**2**) as a mixture of cis and trans isomers (Figure 2a). At 22 °C, the fast rate of isomerization (7.1×10^{-5} s^{-1}), relative to the secondary reaction of tautomerization (4.8×10^{-6} s^{-1}), enabled the formation of significant concentrations of **2**. Subsequently, the tautomerization rates of **2a** and **2b** were determined through the continued observation of the original reaction mixture. Furthermore, the tautomerization rate was found to be independent of catalyst concentration (rate α $[cat.]^0$) (Figure 2b). It is significant to find a catalyst that does not catalyze the tautomerization of the enamine. Enamine is only formed at a background rate that is highly dependent on the presence of protic sources. This rate can be minimized by using Teflon liners, stainless steel vessels, or silylated glassware, and half-lives of enamines **2a** and **2b** of 1.7 and 1.9 days at 22 °C, respectively, have been measured. This decoupling of the tautomerization step from the catalyst concentration also allows for the use of high catalyst loadings in this system to increase the rate of isomerization relative to tautomerization. To date, no other complex has shown this behavior.

It was necessary to increase the scale of the isomerization reactions to generate quantities of enamine suitable for polymerization studies. We have been able to successfully isomerize large-scale batches of 1.0 M allylamine solutions through the use of stainless steel vessels charged with $HRh(CO)(PPh_3)_3$. Once the isomerization reaction was completed, the volatile enamine solution was then isolated by vacuum transfer (again underscoring the kinetic stability of these enamines) and the catalyst reused for succeeding reactions.

The availability of enamines allows for the direct incorporation of amines into polymeric structures without the need for protection-deprotection strategies. To this end, we have found that **2a** successfully copolymerizes with acrylonitrile (AN) under free radical conditions to yield the one-to-one alternating copolymer (eq 3). Enamine **2a** was isolated as a 0.8 M solution in benzene



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by vacuum transfer after complete isomerization of allylamine with $HRh(CO)(PPh_3)_3$ in a stainless steel trap-to-trap apparatus. The reaction vessel was charged with 0.101 g (1.9 mmol) of acrylonitrile, 2.4 mL of the **2a** solution (1.9 mmol) ,and AIBN (3.8 10^{-6} mol), sealed ,and irradiated with a 350 nm UV source for 10 h at 10 °C. The isolated material was characterized as an alternating copolymer of **2a** and AN typical of electron rich/poor monomer combinations.

In conclusion, this study has shown that the appreciable formation of primary and secondary enamines is indeed possible. As a result of this catalytic pathway and increased stability, further investigations into the chemistry of these otherwise unstable enamines is now possible. The copolymerization of **2a** with acrylonitrile is the first example of the ability to incorporate an unprotected vinylamine directly into a polymeric structure.

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(13) Typical conditions: [**1**] = 0.10 M, [cat.] = 0.01 M d_6-benzene, $T =$ 22 °C.

(14) Our observations suggest that the surface of the glass NMR tubes contains protic contaminates which catalyze tautomerization and are hence detrimental to the enamine. To avoid this interaction, PTFE inserts in the NMR tubes were used.