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Nucleophilic Substitution of Benzyl Halides with in Ammonium Acetate in Presence of Glycerol as Green Solvent

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Glycerol was employed as a green solvent in the nucleophilic substitution of benzyl halides and ammonium acetate. As a solvent, glycerol facilitated the solubility of both organic molecules and salt and it enabled easy separation of the product.

Key Words: Nucleophilic substitution, Glycerol, Green solvent.

INTRODUCTION

As environmental concerns have become a high priority, cleaner synthetic procedures that reduce the reliance on hazardous compounds and minimize energy consumption are highly sought after in the chemical industry[1]. One way to achieve this aim is to use more environmentally friendly solvents in chemical syntheses[2]. Because it dictates reaction conditions and the extent of mass and heat transfer as well as product recovery techniques, the solvent usually plays an important role in any synthesis. Furthermore, in many reaction systems, the solvent also affects reaction rate and selectivity, which, in turn, also affect separation procedure.

From economical and environmental points of view, water is without a doubt the solvent of choice. Yet the low solubilities of many organic compounds in water limit its applicability as a solvent. Several green solvents, such as ionic liquids[3] and supercritical carbon dioxide[4], were successfully used in numerous catalytic and non-catalytic reactions over the past decade as alternatives to hazardous and volatile petroleum based organic solvents. We recently showed that glycerol, which is usually produced as a by-product of the transesterification of a triglyceride in the production of biodiesel, is an environmentally benign reaction medium that is a viable, attractive alternative[5-8]. Glycerol, which is a polar, non-toxic, biodegradable and recyclable liquid, has promising physical and chemical properties that facilitate the dissolution of inorganic salts, acids and bases and of organic compounds that are poorly miscible in water. In addition, the incorporation of glycerol in the reaction enables product removal by simple extraction with hydrophobic organic solvents or by distillation.

Nucleophilic substitution, a fundamental reaction class in organic chemistry[9,10], usually involves a non-polar organic compound and a polar ionic salt, thereby requiring a solvent that can dissolve both reagents[11-13]. Alternatively, biphasic reaction systems can also be employed, but because biphasic reactions are limited by mass transfer, phase transfer catalysts are commonly added to these systems to increase reaction rate[12,13]. However, the use of phase transfer catalysts is accompanied by troublesome purification issues.

In this study, glycerol was used as a green solvent in the nucleophilic substitution of benzyl halides with ammonium acetate to produce benzyl acetate (Fig. 1). The use of glycerol increased the solubility of the aromatic in the solution and facilitated easy product separation.

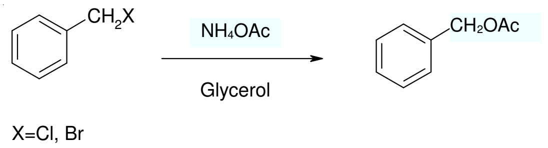

Fig. 1. Nucleophilic substitution of benzyl halide with ammonium acetate

EXPERIMENTAL

In a typical nucleophilic substitution procedure, 0.71 mmol (0.1 g) of benzyl chloride and the corresponding amount of salt were added together to 5 mL of solvent (all purchased from Aldrich). After mixing, the reaction mixture was heated in an oil bath to the required temperature (60-100 ºC). The reactions time varies between 0.5-5.0 h and the mixtures were then allowed to cool. The product was separated after cooling by extraction with 2 mL of diethyl ether. The organic phase was concentrated under reduced pressure and to determine product yield, the resulting crude was analyzed by gas chromatography (GC) using an HP-1 column.

RESULTS AND DISCUSSION

As previously mentioned, nucleophilic substitution reactions involve non-polar, organic compounds and an ionic salt that must be dissolved together in the solvent. Thus the negligible solubility of benzyl chloride in water restricts the use of water, which generates mass transfer limitation. Hence, the investigation began by testing the yields of benzyl acetate in the nucleophilic substitution of benzyl chloride and bromide with ammonium acetate in water and several polar organic solvents like DMSO, glycerol and 1-butyl-3-methylimidazolium tetrafluoroborate as the representative ionic liquid (Table-1). As expected benzyl bromide exhibits markedly higher activity than benzyl chloride in all the tested solvents. In addition, the reactions in all the polar organic solvents (entries 2-4) and especially in DMSO (entry 4), are faster than the reaction in water (entry 1), since the solubility of benzyl halide, which is negligible in water, increases in organic solvents. Yet, although the yield of benzyl acetate in DMSO is higher than in glycerol, the use of glycerol as a natural, biodegradable and green organic solvent is advantageous.

TABLE-1
NUCLEOPHILIC SUBSTITUTION OF BENZYL CHLORIDE TO BENZYL ACETATE IN POLAR SOLVENTS*

Entry	Solvent	Yield (%)**	Yield (%)***
1	Water	38.1	14.75
2	Glycerol	60.3	20.00
3	Ionic liquid****	59.2	19.90
4	DMSO	100.0	62.30

*Reaction conditions: 0.8 mmol benzyl halide, 0.88 mmol ammonium acetate, 5 mL solvent, 70 ºC, 1 h. **Benzyl bromide. ***Benzyl chloride; ****1-Butyl-3-methylimidazolium tetrafluoroborate

Tests of the effect of reaction temperature on the progress of the reaction over time showed that the yield of benzyl acetate increased with both the reaction temperature and time, as expected (Fig. 2). However, at a low temperature (60 ºC), the conversion changed only slightly as the reaction progressed, while at temperatures above 60 ºC the effect of reaction time on benzyl acetate yield was substantial. This effect may be attributable to an energy barrier that can be overcome above 60 ºC and to the decrease, as the temperature increased, in the viscosity of glycerol, which served to increase both mass and heat transfer.

As base loading was expected to affect catalytic performance, we tested the change in benzyl acetate yield with changing base amounts in both glycerol and water (Fig. 3). The results show that increased ammonium acetate loading augmented the yield of benzyl acetate correspondingly in both water and glycerol, in the latter of which the activity was consistently higher.

Because the reaction rate may also depend on the concentration of the organic substrate, the effect of benzyl chloride loading on the product yield was also tested in glycerol and water with and without preserving relative ammonium acetate amounts (Fig. 4). When the amount of salt was not changed, the total amount of benzyl acetate in glycerol and water increased slightly with benzyl chloride concentration, while increasing the concentration of benzyl chloride and preserving the ammonium acetate/benzyl chloride ratio at a constant value linearly increased the reaction rate up to 100 % conversion. These observations imply that the concentrations in the solvent of both benzyl chloride and ammonium acetate affect the reaction rate.

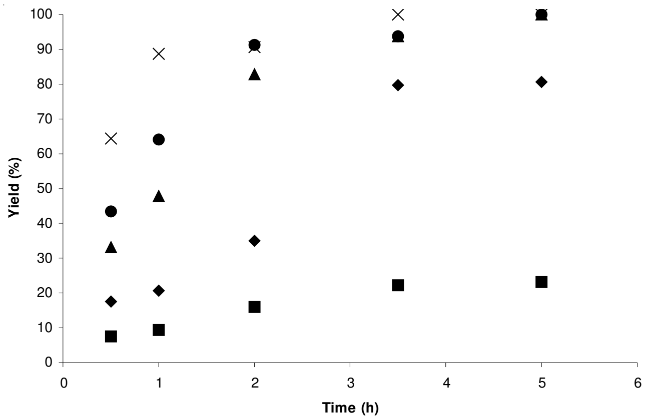

Fig. 2. Effect of reaction temperature on reaction progress. Reaction conditions: 0.71 mmol benzyl chloride, 0.85 mmol ammonium acetate, 5 mL glycerol. (■) 60 ºC; (◆) 75 ºC; (▲) 85 ºC; (●) 90 ºC; (x) 100 ºC

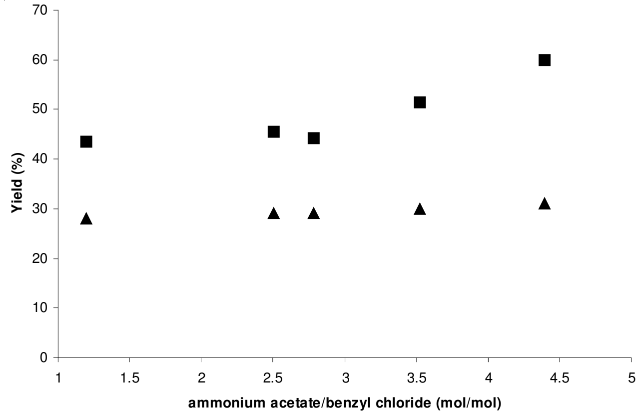

Fig. 3. Effect of ammonium acetate loading on benzyl acetate yield. Reaction conditions: 0.71 mmol benzyl chloride, 90 ºC, 0.5 h; (■) 5 mL glycerol; (▲) 5 mL water

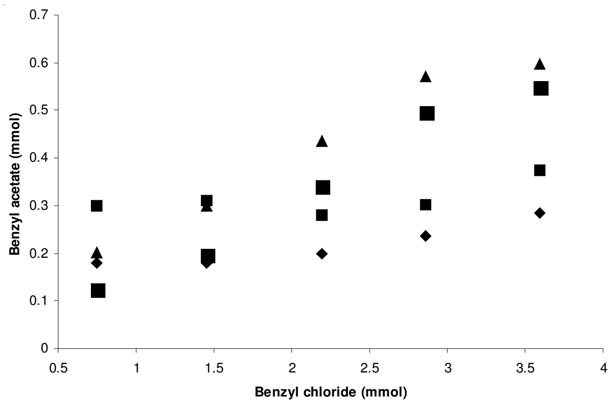

Fig. 4. Effect of benzyl chloride content on the amount of benzyl acetate produced. Reaction conditions: 90 ºC, 0.5 h. (■ 5 mL glycerol, 0.85 mmol ammonium acetate; (◆) 5 mL water, 0.85 mmol ammonium acetate; (▲) 5 mL glycerol, 1.0/1.2 mmol benzyl chloride/mmol ammonium acetate; (x) 5 mL water, 1:1.2 mmol benzyl chloride/mmol ammonium acetate

Conclusion

Benzyl acetate was successfully produced *via* the nucleophilic substitution of benzyl halides on reaction with ammonium acetate in presence of glycerol. In addition to the benefits of using glycerol as a green solvent, it also facilitated the solubilities of both ammonium acetate and the benzyl halides excluding the use of phase transfer catalyst. The reaction rate was affected by the amounts of salt and benzyl halide and by the reaction temperature. As a solvent, glycerol also allowed for easy product recovery.

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