ELECTROCHEMICAL STUDIES OF THE FRIES REARRANGEMENT IN A ROOM-TEMPERATURE MOLTEN SALT

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ABSTRACT

The importance of Lewis acids in promoting the Fries rearrangement has been studied by observing the rearrangement of phenyl benzoate in the aluminum chloride : 1-ethyl-3-methylimidazolium chloride (EMIC) molten salt system. Additions of the Lewis acidic species $\text{Al}_2\text{Cl}_7^{2-}$ to phenyl benzoate in a neutral melt gave an estimate of the K value (140) for the interaction. The rearrangement did not occur at 20°C in the basic melt; however, the reaction went to completion in 12 hours at 77°C in a weakly acid melt. The rearrangement products were 4-hydroxybenzophenone and 2-hydroxybenzophenone, formed in a 3 to 1 mole ratio, as is typical of this reaction in other solvent systems. Further studies were carried out in the neutral buffered melt, under which conditions the reaction required 3 days for completion at 77°C, with the same product distribution. In crossover experiments, addition of benzene to the neutral buffered melt produced only the usual hydroxybenzophenone products; however, addition of m-cresol gave mostly methylhydroxybenzophenone products, strongly suggesting that the Fries rearrangement is intermolecular in the neutral buffered melt.

INTRODUCTION

The Fries rearrangement involves the conversion of a phenolic ester into an aromatic ketone and is typically carried out in the presence of a Lewis acid (1). The Fries rearrangement of phenyl benzoate (PB) is illustrated in Figure 1. Considering that a Lewis acid is typically employed in the reaction, it seems appropriate to study this reaction in molten salt systems based on aluminum chloride. In this paper, the Fries rearrangement of phenyl benzoate has been studied in the aluminum chloride : 1-ethyl-3-methylimidazolium chloride (EMIC) room-temperature molten salt system. Of particular interest is the ability to change the chloride concentration (melt acidity) in the melt over several orders of magnitude simply by changing the molar proportions of EMIC and aluminum chloride (2). Recent work has shown that buffering can be accomplished in this system by addition of sodium chloride to an acidic melt, thereby forming a neutral buffered melt (3). The resulting system possesses a “latent acidity” which promotes interactions between Lewis base solutes and the melt (4,5), thereby providing another avenue of exploration in reactions involving Lewis acid/base chemistry.
EXPERIMENTAL

The melts used in this study were prepared by addition of aluminum chloride to 1-ethyl-3-methylimidazolium chloride (EMIC), which was prepared as described previously (2). Protonic impurities were removed from the melts by placing melts under vacuum at 75°C. Cyclic voltammograms were recorded at Tokai GC-20 (3 mm diameter) vitreous carbon electrodes. Potentials are referenced to an aluminum wire immersed in a 1.5 :1.0 acidic melt (N = 0.60). All reactions were carried out in a Vacuum Atmospheres drybox. Basic melts have a molar excess of EMIC over AlCl₃, neutral melts have equimolar amounts of the components, and acidic melts contain a molar excess of AlCl₃ (2). The anionic species vary as melt composition is changed, tetrachloroaluminate being present at all compositions, with chloride in basic melts and Al₂Cl₇⁻ in acidic melts. Product workup involved either extraction of the melt with hexane, or extraction of the hydrolyzed melt (water addition) with benzene. GC/MS spectra were obtained on a Hewlett-Packard 5890/5971 instrument. All chemicals were obtained from Aldrich Chemical Corporation and used as received.

RESULTS AND DISCUSSION

The behavior of phenyl benzoate in the AlCl₃:EMIC molten salt system illustrates the remarkable acidity changes encountered in the melt as the composition is changed from the basic to the acidic regions. As seen in Figure 2, phenyl benzoate undergoes reduction in the 0.80 : 1.00 basic melt (molar excess of EMIC) at −1.86 V. No further work has been carried out on the reduction process itself; however, the reduction products are evidently not electrochemically active in the basic melt potential window. As expected, the basic melt did not promote the rearrangement of phenyl benzoate, there being no decrease in peak current for the reduction process after three days at 72°C. In order to assess the degree of interaction between phenyl benzoate and Al₂Cl₇⁻, a solution of phenyl benzoate in a neutral melt was titrated with 1.5:1.0 acidic melt from a microliter syringe (Figure 3). As the acidic melt was added, the reduction peak at −1.86 V was found to decrease, and another peak was seen to appear at −0.78 V. Previous studies have shown that this potential shift corresponds to complexation of the carbonyl group by aluminum chloride (6). In this case, this complexation is apparently necessary for the rearrangement to proceed, because rearrangement was not observed in the basic melt. From the titration, it was apparent that an amount of Al₂Cl₇⁻ equivalent to phenyl benzoate was not sufficient to fully complex the ester. From the plot in Figure 4, complete conversion to the complexed ester does not occur until addition of ~80 μL of acidic melt, 18 μL being the equivalent amount. It is not likely that the ester is complexed by more than one AlCl₃ molecule, so it appears that the reaction simply does not go to completion at acidity levels equimolar to phenyl benzoate. From the initial concentration of phenyl benzoate and the peak current values for the reduction of PB: AlCl₃, the equilibrium constant for the reaction

\[
P \text{B} + \text{Al}_2\text{Cl}_7^- \leftrightarrow \text{PB: AlCl}_3 + \text{AlCl}_4^- \quad [1]
\]

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was found to be $140 \pm 20$ at $20^\circ C$. This rather low $K$ value is consistent with the comparatively large amount of acidic titrant required to convert PB to PB: AlCl$_3$. In addition, a small oxidation peak at approximately $0.0 \text{ V}$, which is apparently due to aluminum oxidation, becomes apparent about half-way through the titration, indicating the presence of excess Al$_2$Cl$_7$ in the solution which undergoes reduction to aluminum. It should be noted here that addition of a $0.8 : 1.0$ basic melt solution ($1/4$ the molar amount of added Al$_2$Cl$_7$) caused partial reappearance of the PB reduction peak at $-1.9 \text{ V}$, showing that the reaction above is reversible.

At this point in the titration experiment, the total amount of Al$_2$Cl$_7$ added to the melt was three times the molar amount of PB. With a PB concentration of $34 \text{ mM}$, and some complexation of PB by Al$_2$Cl$_7$, this is only a mildly acidic melt, with a small stripping peak observed for aluminum oxidation. After 15 hours at $22^\circ C$, very little decrease in the PB:AlCl$_3$ reduction peak was observed, indicating that no significant Fries rearrangement had occurred. After twelve hours at $77^\circ C$, however, the PB:AlCl$_3$ reduction peak at $-0.78 \text{ V}$ had gradually been replaced by another reduction process at $-0.20 \text{ V}$. After making the melt basic by addition of EMIC, the melt was reacted with water and extracted with benzene. GC/MS characterization of the product mixture showed 4- and 2-hydroxybenzophenone as major and minor products, respectively (3:1 molar ratio). These rearrangement products are usually observed for the Fries rearrangement in other solvents (7). These results demonstrate the feasibility of using voltammetric studies, coupled with the usual compound characterization techniques, to study Lewis acid-catalyzed reactions in the AlCl$_3$ : EMIC system. In more acidic melts, aluminum reduction obscures the reduction processes for PB and PB:AlCl$_3$, so no extensive studies were carried out in the more acidic melt compositions.

In recent years, a considerable amount of work has been carried out in the neutral buffered melt in an attempt to provide a stable medium with neutral properties (3,4,5). The buffering action is provided by introducing sodium ions into the melt, accomplished by adding sodium chloride to an acidic melt. The resulting reaction produces sodium tetrachloroaluminate, providing a rather high concentration of sodium ions in the melt. Upon subsequent introduction of chloride ions into the melt, the low solubility of NaCl in the melt effectively removes the chloride, preventing basic conditions from developing. In later studies, it was found that there is a low concentration (approximately $3 \text{ mM}$) of Al$_2$Cl$_7$ in the neutral buffered melt, so that the melt is actually very weakly acidic (9). In addition, the presence of sodium ions in the melt can promote interaction of solutes acting as Lewis bases, such as carbonyl functional groups, with AlCl$_4^-$ in the melt to produce solutes complexed by aluminum chloride, the displaced chloride ion being removed by formation of insoluble NaCl (4,5):

$$\text{PB + AlCl}_4^- + \text{Na}^+ \rightarrow \text{PB:AlCl}_3 + \text{NaCl} (s) \quad [2]$$

This interaction illustrates the "latent acidity" of the neutral buffered melt, and such processes have been observed for other solutes (4). Upon addition of PB to a neutral buffered melt, a reduction process at $-0.83 \text{ V}$ was observed, similar to the potential observed in the slightly acidic melt. Reaction times for the Fries rearrangement, however, were somewhat longer, requiring three days at $77^\circ C$ for completion. As seen in Figure 5, a product peak at $-0.51 \text{ V}$ is evident after several hours. It was found that all three
hydroxybenzophenone isomers undergo reduction at this potential, so that only the general extent of reaction can be surmised from this peak height. Upon making the melt basic, however, the 2-hydroxybenzophenone isomer undergoes reduction in a separate process (-0.93 V) from that of the 3- and 4- isomers (-1.35 V). For product workup, neutral buffered melts were made basic after the rearrangement reaction was complete, followed by extraction with hexane or hydrolysis with water and extraction with benzene. The rearrangement products were formed in good yield, giving 4-hydroxybenzophenone as major product and lesser amounts of the 2-hydroxy-benzophenone isomer, essentially the same as in the slightly acidic melt. In another study, the effect of temperature on the product distribution was investigated by running the reaction at 120°C. In most solvent systems, an increase in temperature leads to a higher yield of the 2-isomer; however, in this case, 4-hydroxybenzophenone was almost exclusively formed.

In the Fries rearrangement, the mechanism usually proposed (Figure 1) involves formation of an acyl cation, which then attacks either the phenoxy moiety from the same ester molecule (intramolecular pathway) or that from another ester molecule (intermolecular pathway). Considerable effort has been directed toward determination of the pathway involved in particular ester systems (1,8). In an attempt to assess the pathway under the present conditions, the phenyl benzoate reaction was carried out in the neutral buffered melt in the presence of a large amount (12% mass percent) of benzene, with which the melt is miscible. At 77°C, the decrease of the reduction peak for the PB:AlCl₃ complex was complete in less than 24 hours, considerably faster than observed for the reaction in the neutral buffered melt itself. This is perhaps due to the decreased viscosity of the melt. Workup of the reaction mixture (hydrolysis, benzene extract, GC/MS) showed that the 2- and 4-hydroxybenzophenone isomers were formed in amounts similar to those in the neutral buffered melt without benzene, and that the crossover product, benzophenone, was detected in only very small amounts (<5% yield). This result by itself implies that the pathway is intramolecular, although it is possible that benzene is simply not as reactive toward the acyl cation as is the phenoxy species. In order to test this latter possibility, m-cresol (3-methylphenol) was added to a neutral buffered melt in a 5 : 1 cresol : PB mole ratio, and the reaction was again carried out at 77°C. As in the melt with added benzene, the reaction was complete in less than 20 hours; however, the hydrolyzed benzene extract now consisted mostly (97%) of cresol crossover products as two major isomers. Observation of these cross-over products strongly suggests that the Fries rearrangement of phenyl benzoate in the neutral buffered melt occurs in an intermolecular pathway.

CONCLUSIONS

It has been shown that phenyl benzoate undergoes a complexation reaction with Al₂Cl₇ in a weakly acidic melt to form the complexed form of the ester, which then undergoes the Fries rearrangement at 77°C to form 4-hydroxybenzophenone and 2-hydroxybenzophenone. In the neutral buffered melt, a similar interaction takes place, as is evident from the presence of almost identical potentials for the ester reduction process in the two systems. The rearrangement occurs more slowly in the neutral buffered melt, however, requiring three days for complete reaction compared to only twelve hours in the acidic melt. A considerable effort has been made to establish whether the reaction
mechanism is inter- or intramolecular. Addition of m-cresol to the reaction mixture in the neutral buffered melt produced mostly cresol crossover products, suggesting that the pathway is intermolecular. This finding implies that the melt structure, with its rather large ions, is not particularly confining to the reaction intermediates in the case of phenyl benzoate.

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Figure 1. Fries rearrangement pathway of phenyl benzoate
Figure 2. Cyclic voltammogram of 12 mM phenyl benzoate in 0.8 : 1.0 basic melt. 50 mV/s vitreous carbon 21°C

Figure 3. Cyclic voltammograms of phenyl benzoate (PB) titration with acidic melt solution (1.5 : 1.0, or N = 0.60, melt) vitreous carbon 50 mV/s 20°C
Figure 4. Plot of reduction peak currents during PB: Al₂Cl₇ titration.

Figure 5. Cyclic voltammograms taken at vitreous carbon, at various times after addition of phenyl benzoate (PB) to a neutral buffered melt at 77°C. 50 mV/s