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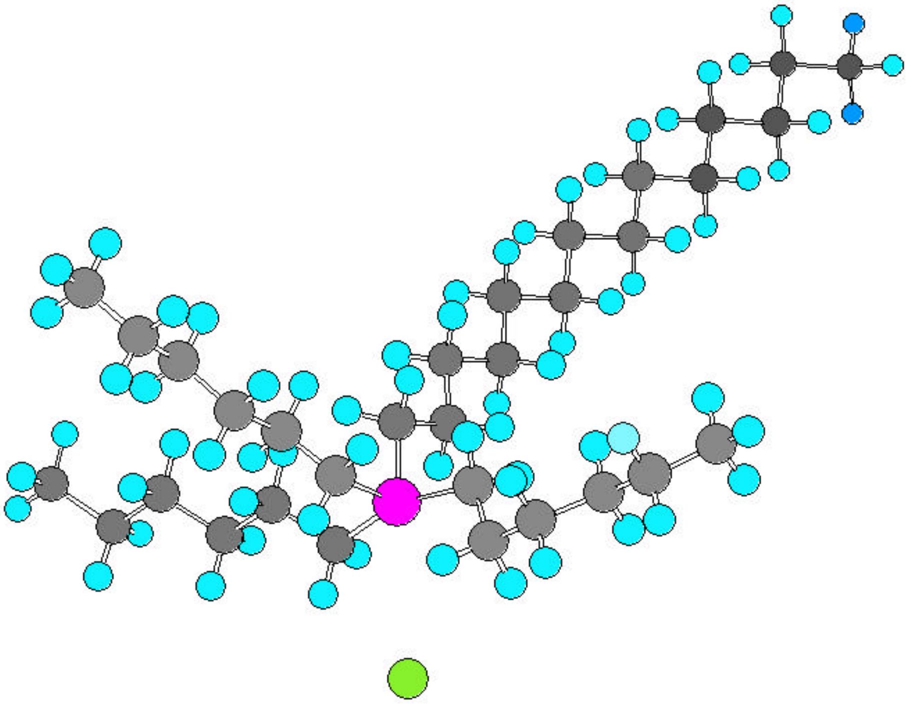
CYPHOS® IL 101
Phosphonium Ionic Liquid



Introduction:

Why consider a "phosphonium" ionic liquid?

Soon after the discovery that certain nitrogen based room temperature liquid salts were found to be useful as battery electrolytes (1a,1b,), interest in these and similar salts as novel fluids and solvents developed. There were a scant number of papers during the 1980s and early 1990s but mainly due to the efforts of the group at The Queen's University – Belfast, headed up by Professor Ken Seddon, there has been an exponential rise in interest and number of publications in the last 7 to 8 years. (2) Indeed, almost an entire issue of Green Chemistry (3) has been devoted to ionic liquids.

Perhaps one of the most influential publications to direct industrial attention to ionic liquids was a feature article entitled "Designer Solvents" in C&E News – March 30,1998 in which Ken Seddon, Robin Rogers, Tom Welton, Helene Olivier and others elaborated on the potential of ionic liquids. While the article dealt almost entirely with nitrogen based ionic liquids, there was a brief reference by Ken Seddon which alluded to the fact that phosphonium salts are also a potential source of numerous ionic liquids. This brief reference to phosphonium ionic liquids is very much representative of the current fraction of publications relating to phosphonium based ionic liquids. With the exception of several papers and patents by George Parshall in the mid 1970s using stannate and germanate salts and John Knifton et al in the early 1990s which centre on the use of molten tetrabutylphosphonium bromide as an ionic solvent, almost the entire volume of ionic liquid literature deals with nitrogen based systems and in particular, those based on 2-methylimidazolium salts.

There was a good reason for the lack of phosphonium based ionic liquid publications – availability of the starting material! While Cytec has been commercially producing phosphine derivatives since 1971, it was not until 1990 that tributylphosphine was produced on a large commercial scale. Since that time, not only has tetrabutylphosphonium chloride and bromide become available in multi ton scales, many other trialkylphosphines and the corresponding quaternary phosphonium salts are or can be manufactured on a large scale.

The phosphonium cation contains four substituents and the various combinations along with the multitude of various available anions represents an enormous number of possible salts. Even when one restricts the cation to the generic formula – $[PR_3R']^+$, the number is still very large. Of course, not all such phosphonium salts are liquid at room temperature, but by a judicious selection of R and R' as well as the appropriate anion, there are many phosphonium salts which are in fact liquid at room temperature and many more which fall within the broad general definition of ionic liquids as salts which are low melting – that is less than 100 °C.

There are several reasons why one might consider a phosphonium ionic liquid. The most important one for those contemplating an industrial process is availability and cost. Phosphonium salts can meet both of these demands – already Cytec is manufacturing phosphonium salts on a multi ton scale and because of the high volumes, costs will be relatively low. For commercial products, chemical inventory registration is also part of the availability equation. While, most of the possible phosphonium ionic liquids are still not registered, several are already listed on EINECS, TSCA, EEC, AICS, PICCS and DSL.

Ionic liquids, in general, are not going to be outrageously expensive, but they will not be in the same league as toluene, 2-hydroxypropane (IPA) or tetrahydrofuran (THF). This means that to be economically viable, they must be chemically as well as thermally very stable for multiple recycle use. Even 0.5 to 1% decomposition can lead to major losses after 10 to 20 cycles. Not only will there be solvent losses but there will also be contamination of the ionic liquid solvent and/or products with decomposition byproducts.

In this regard, phosphonium salts are much more thermally stable than the corresponding ammonium salts and even have an edge on imidazolium salts. This is very important for processes which operate at temperatures greater than 100 °C. In addition to being slightly less thermally stable, the imidazolium cation contains protons which are not entirely inert. They are some what acidic which can result in carbene formation. Phosphonium salts, on the other hand have no such acidic protons.

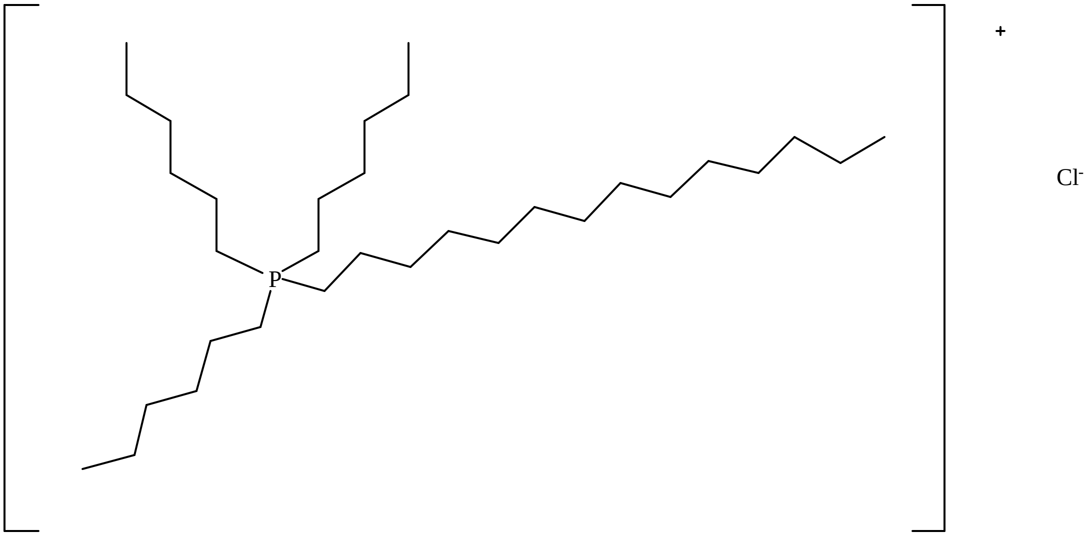
The fact that alkylphosphonium salts are, in general, less dense than water can be beneficial in product work-up steps while decanting aqueous streams which contain inorganic salt byproducts. Imidazolium salts, on the other hand are more dense than water.

Trade Name: **CYPHOS IL 101 phosphonium ionic liquid**

Chemical Name: tetradecyl(trihexyl)phosphonium chloride

C.A.S. Number: [258864-54-9]

Registration: None



Density and Miscibility:

CYPHOS IL 101 phosphonium ionic liquid is a slightly viscous room temperature ionic liquid. It is less dense than water (Figure 1), is colorless to pale yellow and is immiscible with water although it is sparingly soluble in water and can dissolve up to 8% water. When dry, it is totally miscible with a wide range of organic solvents such as indicated in Table 1

Table 1

CYPHOS IL 101 Miscibility

Diluent	**Miscible**
water	No
hexane	Yes
toluene	Yes
2-hydroxypropane (IPA)	Yes
diethylether	Yes
tetrahydrofuran	Yes
dichloromethane	Yes

CYPHOS IL 101 has unique miscibility properties which can be utilized to separate organic products from metal catalysts and byproduct inorganic salts. When dry, it is totally miscible with non polar solvents such as hexane, however when an excess of water is added to the system, three liquid phases form. The upper phase is essentially hexane which can contain the organic reaction product. The middle layer is CYPHOS IL 101 saturated with water and will contain any metal/ligand catalyst. The lower layer is essentially water but will contain any byproduct inorganic salts. (4,5, Figure 2)

When fully saturated, CYPHOS IL 101 will contain 14.0% water. The solubility of CYPHOS IL 101 in water has not been determined but is expected to be much less.

VISCOSITY:

The only negative comment concerning most long alkyl chain phosphonium based ionic liquids is that they are “viscous”. While they are somewhat more viscous than typical imidazolium salts, once in service – that is, when organic substrates are added, the viscosity decreases by an order of magnitude. This is illustrated in Figure 3 in which the addition of hexane or water simulates a reagent or product. Additionally, the viscosity drops off exponentially with temperature. At a typical reaction of 80 to 100 °C and with the addition of 10% of a substrate, the entire system becomes very water-like.

This phenomenon is not unusual. In addition to changing the anion and carbon chain length, small amounts of solutes – diluents or otherwise - have a profound effect on the viscosity as well as the density of ionic liquids (6).

Glass Transition Temperature - T_g

The glass transition temperature (T_g) for CYPHOS IL 101 has been retorted as -56 °C (13).

Thermal Stability:

Typically standard TGA plots are used to indicate the relative thermal stability of ionic liquids. Heating rates of 5 to 10 °C per minute either under an inert atmosphere or under oxidative conditions such as air are usually reported. Under these conditions, the onset for weight loss for CYPHOS IL 101 is approximately 350 and 290 °C under dinitrogen and air respectively. (Figure 4). However, in reality, the true temperature at which an ionic liquid is thermally stable is much lower. Figures 5 and 6 are isothermal TGA plots under dinitrogen and air respectively. The respective safe operating temperatures would appear to be 160 and 140 °C. The latter is still more than adequate for most organic reactions.

As a comparison, the corresponding isothermal TGA for tetrahexylammonium chloride is presented in Figure 7. Even at 120 °C there is an unacceptable weight loss. A safe operating temperature for this salt would be less that 100 °C. $[\text{bmim}]^+$ Cl^-, while more thermally stable than the corresponding ammonium salt, shows signs of serious decomposition at 180 °C (Figure 8), whereas CYPHOS IL 101 does not.

With the exception of $[\text{PF}_6]^-$ salts, the thermal decomposition of phosphonium salts are accompanied by an endotherm. This is a very important safety feature when operating on a large scale.

Electrochemical Window:

Phosphonium ionic liquids are noted for their wide electrochemical windows. A cyclic voltammogram for CYPHOS IL 101 is given in Figure 9. The very stable tetraalkylphosphonium ion is not reduced until -3.0 volts, whereas oxidation at the anodic limit does not occur until +2.5 volts. The total electrochemical window is thus 5.5 volts. (10). This window is at least 0.5 V wider than corresponding imidazolium salts. It is expected that in general, the cathodic limit for most phosphonium salts will remain relatively constant at -3.0 volts and the anodic limit will be dependant on the oxidative potential of the anion.

Applications:

Although there are many potential applications for CYPHOS IL 101 it is especially recommended for palladium catalyzed Suzuki and Heck coupling reactions (4, 9). Both authors have demonstrated that the catalyst/solvent system can be recycled with fresh substrate without loss of activity.

CYPHOS IL 101 has successfully been used as a solvent for the Michael addition of primary and secondary amines to acrylate esters. Essentially quantitative yields have been reported for the addition of aniline, butylamine, hexylamine, morpholine and dioctylamine to both methyl and ethylacrylates. (11)

Quantitative palladium catalyzed carbonylation of iodobenzene with CO/EtOH to ethylbenzoate (12) demonstrates a further important application for CYPHOS IL 101.

CYPHOS IL 101 is an exceptionaly good solvent for the palladium acetate catalyzed Heck coupling reaction. Quantative yields are obtained for aryl iodides in two hours at 50 °C, while conbersions for aryl bromides range from 80 to 90% in four hours at 100 °C (14). Likewise, CYPHOS IL 101 is also an excellent solvent for Suzuki cross coupling reactions between boronic acids and aryl halides (4).

The stability of phosphonium ionic liquids under highly reducing conditions has been demonstrated by Clyburne et al (15). Here CYPHOS IL 101 remains inert as it is used as a solvent to electrochemically and chemically reduce the imidazolium cation to a carbene. This has implications for using phosphonium ionic liquids in highly reductive environments. For example in a more recent paper (16), Clyburne et. al. have demonstrated the compatibility of commercial Grignard reagents in phosphonium ionic liquids such as CYPHOS IL 101. Consequently they were able to convert phenylmagnesium bromide to biphenyl, benzaldehyde, benzyl alcohol, bromobenzene and dimethylbenzyl alcohol in CYPHOS IL 101. The products were readily isolated after adding water and hexane which formed three liquid phases. The products partitioned into the upper hexane layer while the magnesium salts were directed to the lower aqueous phase. In the same paper, they also reported an equally successful $NaBH_4$ reduction of benzaldehyde. Benzyl alcohol was the only detectable product.

Bio-transformations are often limited to the concentration of either the substrate or products due to toxicity effects on either the enzymes or organisms. For example, 1500 mg/l of phenol is toxic to Pseudomonas putida. However, the bio-degradation can be carried out in a two phase system such as CYPHOS IL 101 /(aqueous phenol), in which the phenol will partition into the IL phase at a concentration which is non-toxic to P. putita. This organism is totally compatible with CYPHOS IL 101 and is thus able to consume the phenol from the aqueous phase as it gradually partitions into the IL phase (19).

Ionic Liquid Intermediate:

With the addition of $AlCl_3$ or transition metal salts such as $FeCl_3$, $TiCl_3$ or $CuCl_2$, various tetradecyl(tributyl)phosphonium ionic liquids with complex metal halide anions can be formed. Using the proper solvent (usually water) the chloride anion can be converted via metathesis to hexafluorophosphate, tetrafluoroborate, triflate, bistriflamide or almost any other cation provided the free acid or alkali metal salt is available. (7,8,17,18)

Analysis:

CYPHOS IL 101 typically assays 96 to 97% $[P\ R_3R']^+Cl^-$ (R = hexyl and R' = tetradecyl). However, the product will also contain traces (0 .1 to .4 %) of tetradecene isomers, 0.1 to 0.5% HCl and 0.1 to 1.2% $[PR_3H]^+\ Cl^-$. Titration with standardized $AgNO_3$ in a 75% aqueous 2-hydroxypropane (IPA) solvent will yield the total chloride content. This result when combined with a corresponding NaOH titration will yield the $[PR_3H]^+ Cl^-$, HCl and $[PR_3H]^+ Cl^-$ content. The volatile content (tetradecene isomers) are determined by an internal standard G.C. analysis of an octane extract.

^{31}P NMR is generally not suitable for precise analysis. However, the distinctive signal at +33 ppm can be useful for qualitative analysis.

While electrospray mass spectral analysis (ESMS) is generally not available in every laboratory, this also a very useful tool for both quantitative and qualitative analysis.

LC/MS is the most universal tool to identify and quantify cations and anions (20).

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Figure 1

CYPHOS IL 101 - Density vs. Temperature

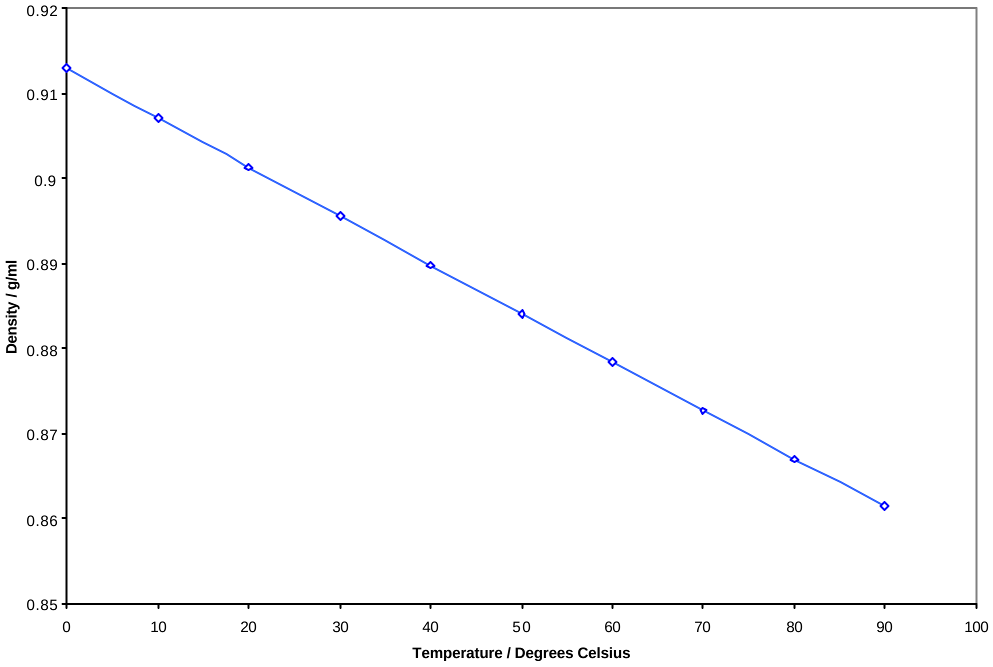


Figure 2

CYPHOSIL 101 - Product Recovery & Catalyst/IL Recycle

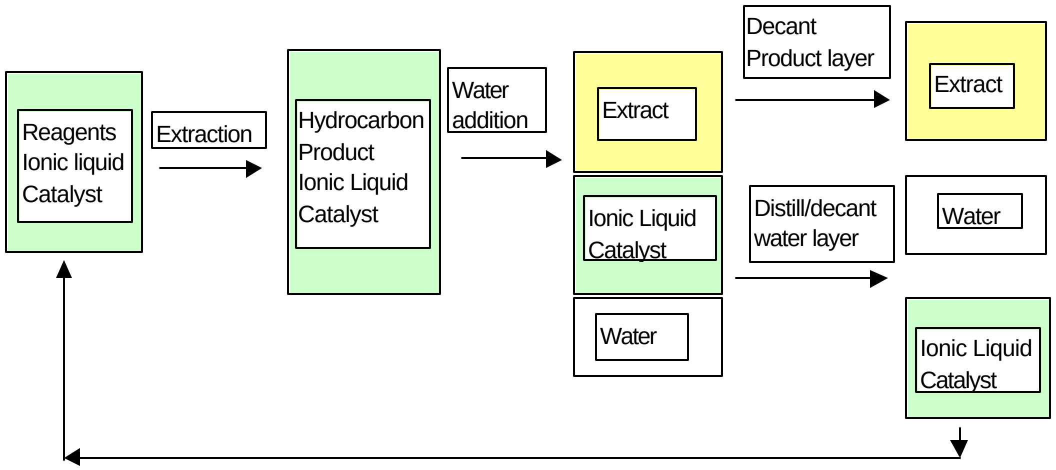


Figure 3

Effect of Solute on CYPHOS IL 101 Viscosity

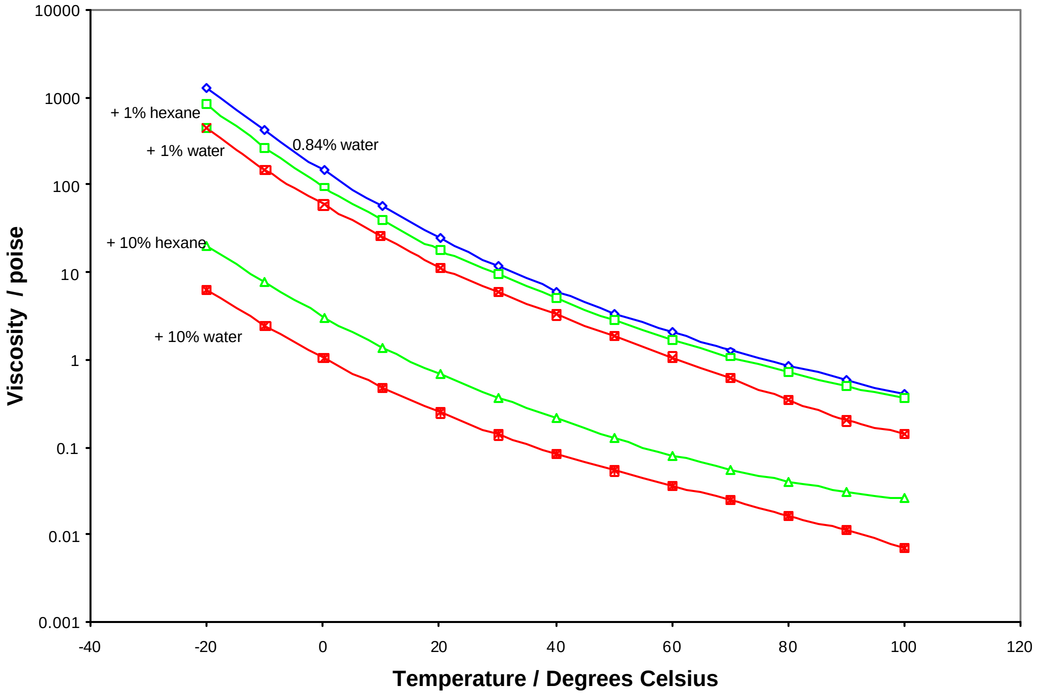


Figure 4

CYPHOS IL 101 – Standard TGA Plots under N_2 and Air

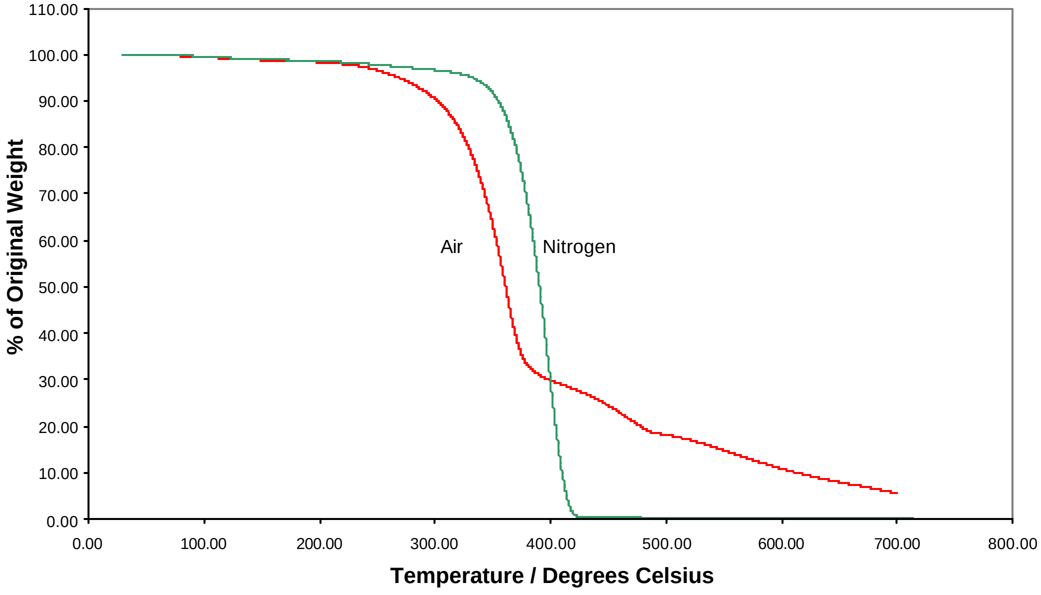


Figure 5

CYPHOS IL 101 – Isothermal TGA Plots under Air

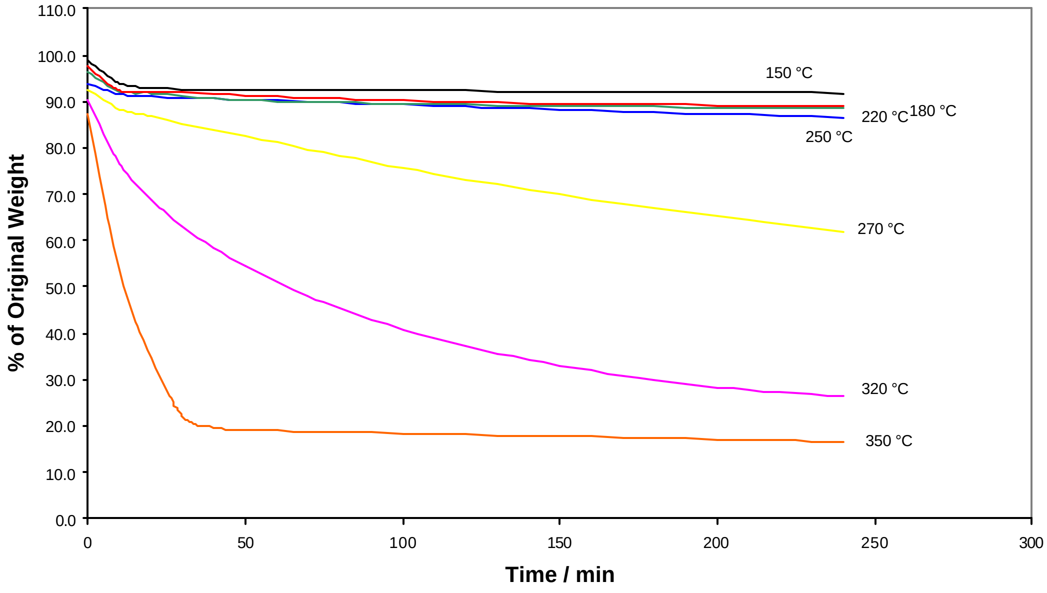


Figure 6

CYPHOS IL 101 – Isothermal TGA Plots under N_2

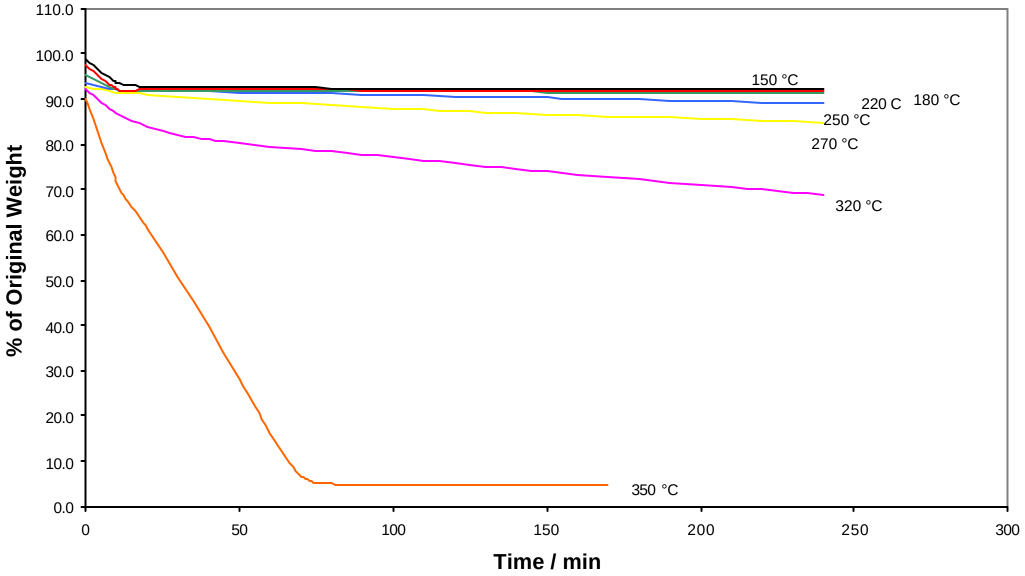


Figure 7

Tetrahexylammonium chloride – Isothermal TGA Plots under N_2

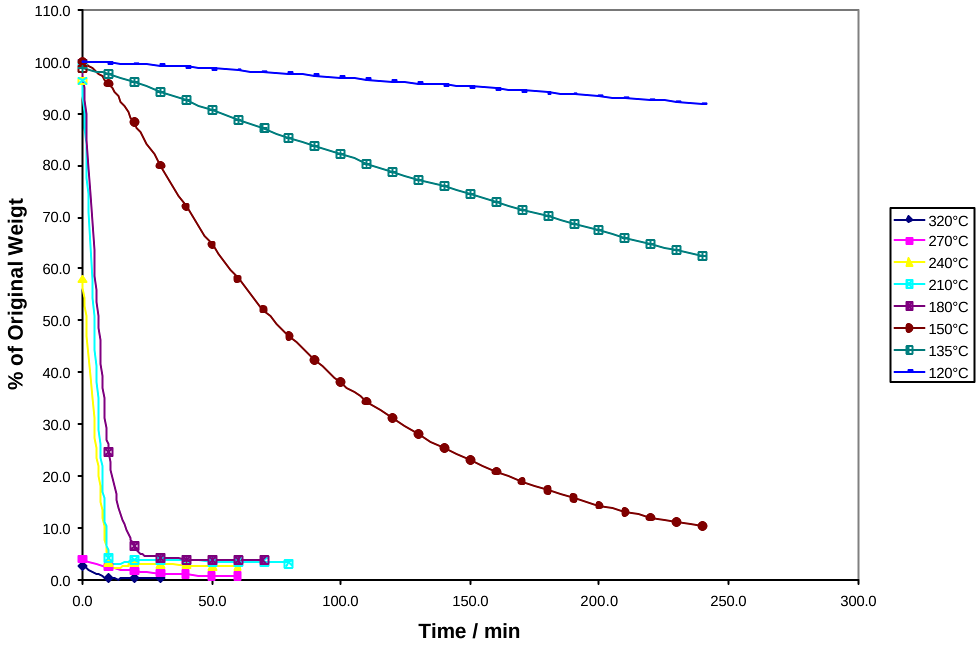


Figure 8

$[bmim]^+$ Cl^- - Isothermal TGA Plots under N_2

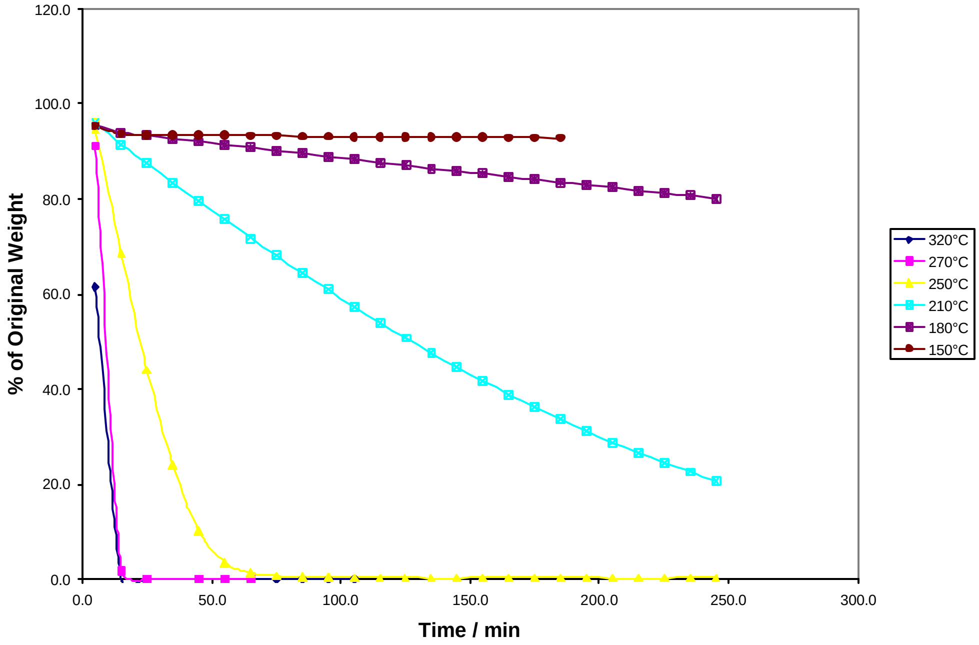
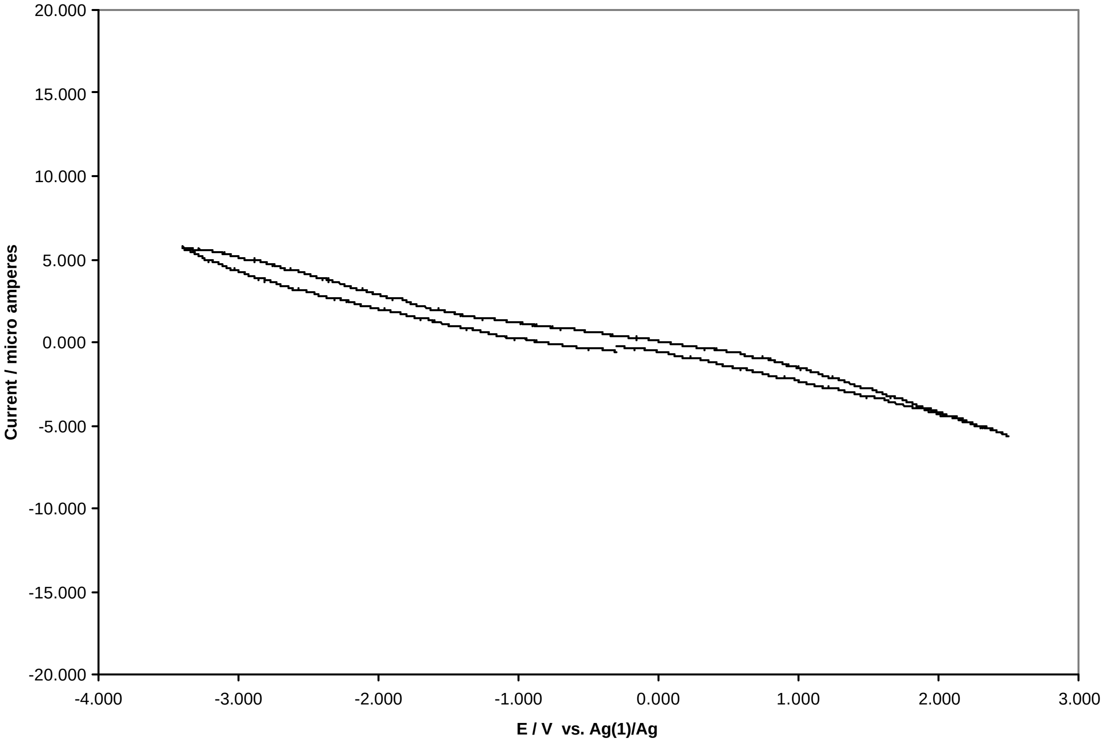


Figure 9

CYPHOS IL 101 – Cyclic Voltammogram



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