

SWITCHABLE SOLVENTS FOR NOVEL CHEMICAL PROCESSING

A Thesis
Presented to
The Academic Faculty

by

Joshua David Grilly

In Partial Fulfillment
of the Requirements for the Degree
Master's of Science in the
School of Chemical and Biomolecular Engineering

Georgia Institute of Technology
December, 2005

SWITCHABLE SOLVENTS FOR NOVEL CHEMICAL PROCESSING

Approved by:

Dr. Charles Eckert, Advisor
School of Chemical and Biomolecular Engineering
Georgia Institute of Technology

Dr. Charles Liotta, Co-Advisor
School of Chemical and Biomolecular Engineering
Georgia Institute of Technology

Dr. Rigoberto Hernandez
School of Chemistry
Georgia Institute of Technology

Date Approved: August 11, 2005

ACKNOWLEDGEMENTS

I would like to start by thanking my advisors, Dr. Charles Eckert and Dr. Charles Liotta and my other committee member, Dr. Rigoberto Hernandez. I would have never gotten to this point without Dr. Eckert's constant wisdom and guidance. His constant question of, "What do we win if we win" always helped me to see the big picture. Dr. Liotta's ever-present humor and knowledge of all things chemistry have greatly enhanced my experience here on both a personal and professional level.

I would like to thank Deborah Babykin, who always had time to help me with whatever I needed.

I would like to thank all of the current and former members of the Eckert-Liotta group. They have made my time here much more enjoyable. Specifically, I would like to thank Josh Brown, who could fix anything; Jason Hallett, who always seemed to know what was going on in the lab and on the baseball diamond; Josh Aronson and Colin Thomas for their invaluable assistance on these projects, and Laura Nunez for all of her hard work.

I would also like my family for supporting me, even when I'm a thousand miles away. Finally, I would like to thank my fiancée, Lisa Harris. I don't know where I would be without her.

TABLE OF CONTENTS

	Page
ACKNOWLEDGEMENTS	iii
LIST OF TABLES	vi
LIST OF FIGURES	vii
SUMMARY	viii
<u>CHAPTER</u>	
I INTRODUCTION	1
II THIIRANE OXIDE AS A SWITCHABLE SOLVENT	3
Introduction	3
Thiirane Oxide	5
Solvent Parameters	6
Experimental Materials	8
Thiirane Oxide Synthesis	8
Apparatus and Procedure	9
Et(30) Determination	9
Kamlet-Taft Parameter Determination	10
Reaction of Benzyl Chloride with Potassium Thiocyanate	10
Product Isolation	11
Results and Discussion	12
Solvent Properties	12
Demonstration Reaction	12
Product Isolation	14
Conclusions	16

References	18
III PIPERYLENE SULFONE AS A SWITCHABLE SOLVENT	19
Introduction	19
Experimental Materials	21
Piperylene Sulfone Synthesis	22
Apparatus and Procedure	22
Results and Discussion	23
Solvent Parameters	23
Demonstration Reaction	24
Decomposition Studies	24
Conclusions	25
References	27
IV CAGE REACTIONS IN GAS-EXPANDED LIQUIDS	28
Introduction	28
Cage Effect	29
Experimental Goals	31
Experimental Materials	31
Conclusions	33
References	34
V CONCLUSIONS AND RECOMMENDATIONS	35
Conclusions	35
Recommendations	36
Switchable Solvents	36
Gas-Expanded Liquids	38

LIST OF TABLES

	Page
Table 2-1: Solvent property comparison for DMSO vs. thiirane oxide.	12
Table 2-2: Kinetic data for BzCl + KSCN in DMSO & thiirane oxide. Error is uncertainty in rate constant; duplicate runs are averaged.	13
Table 2-3: Thermodynamic properties of example reaction.	14
Table 3-1: Solvent properties for piperylene sulfone and comparison with DMSO & thiirane oxide.	23

LIST OF FIGURES

	Page
Figure 2-1: Reaction of DBU with CO ₂ to form adduct.	3
Figure 2-2: Reaction of CO ₂ in the presence of water to form carbonate salt.	4
Figure 2-3: Example of reversible ionic liquid.	4
Figure 2-4: Decomposition of thiirane oxide to form ethylene and SO.	5
Figure 2-5: Nucleophilic substitution of benzyl chloride by potassium thiocyanate.	6
Figure 2-6: Second order rate constant of BzCl + KSCN as a function of temperature. Δ = thiirane oxide; O = DMSO.	13
Figure 2-7: TGA for thiirane oxide. Heating rate = 20 °C/min.	15
Figure 2-8: DSC for thiirane oxide. Heating rate = 20 °C/min.	16
Figure 3-1: Decomposition of piperylene sulfone to form diene and SO ₂ .	19
Figure 3-2: Sulfone decomposition rates.	20
Figure 3-3: TGA for piperylene sulfone. Heating rate = 20 °C/min.	24
Figure 3-4: DSC for piperylene sulfone. Heating rate = 20 °C/min.	25
Figure 4-1: Cage reaction probe with trityl peroxide.	31
Figure 4-2: Reaction of trityl chloride in Zn dust and cyclohexane to form trityl chloride. T = 25 °C, 30 min, open to the atmosphere.	32
Figure 4-3: Reaction of trityl peroxide with potassium superoxide in 18-crown-6 and benzene.	32
Figure 5-1: Reaction of DBU, alcohol, and CO ₂ to form ionic liquid.	37
Figure 5-2: Decomposition of propylene carbonate to di-ol and CO ₂ .	37

SUMMARY

The chemical industry is constantly moving to find newer and more environmentally benign methods for chemical synthesis. This work is aimed at developing novel solvents for sustainable technology. Specifically, this thesis addresses two different types of solvents. The first type has been dubbed “switchable solvents”. The goal is to develop a solvent specifically designed for a reaction that can be easily removed by decomposition with some type of “switch”, such as heat, UV light, CO₂ pressure, or some other external stimulus. The decomposition products would then be collected and reformed to make the solvent. The second type of solvent is a gas-expanded liquid (GXL). Many organic solvents swell with the addition of a gas such as carbon dioxide. CO₂ itself is a poor solvent, but its combination with an organic solvent enables the ability to tune many of the solvent’s properties, such as viscosity, dielectric constant, and polarity. This allows reaction conditions to be changed to fit the requirements for each individual process.

CHAPTER I

INTRODUCTION

Many synthetic chemical systems are hampered by either solubility limitations in the solvent system, or by problems with product separation. The development of new solvent systems that combine appropriate solvents with advantageous separations schemes would greatly benefit the chemical industry. My work aims to develop these types of solvents in order to bridge the gap between reactions and separations.

Switchable / cleavable solvents are a relatively new type of solvent that change properties with the application of an external stimulus such as heat, UV light, pH, or CO₂ pressure. The goal is to design a solvent that has good properties for the chemical reaction, but with a built-in switch to make separations easier. Chapter II details my work with our first foray into the switchable solvent field, thiirane oxide.

While thiirane oxide was useful as a proof of concept, it became clear that a solvent with better separations characteristics was needed. Specifically, we needed a solvent whose decomposition products could be reformed into the original solvent. Thus, we moved on to piperylene sulfone. Chapter III shows the work to date with piperylene sulfone. Piperylene sulfone offers a number of separations advantages over thiirane oxide.

Gas-expanded liquids (GXL's) also show great promise as a reaction medium. GXL's are created by pressurizing an organic liquid with a gas, typically carbon dioxide. The pressure of the gas has a large effect on the physical properties of the bulk solvent such as density, viscosity, and polarity. This "tunability" offers immense control over the reaction conditions. Chapter IV discusses our research into the microstructure of gas-expanded liquids.

Finally, Chapter V summarizes the importance of the research and suggests some directions for the research to go. Switchable solvents offer many possibilities for cleaner solvents and while scant research exists on the topic, this work provides a working example of a solvent of this type.

CHAPTER 2

THIIRANE OXIDE AS A SWITCHABLE SOLVENT

Introduction

The solubility of materials in a solvent depends on, among other parameters, the relative polarities of solute and solvent. If a polar solvent will dissolve a species, then a nonpolar solvent likely will not dissolve that same species. It would be advantageous for a solvent to dissolve the chemical species under reaction conditions, change polarity with a switch, then precipitate out remaining species. A molecule that decomposes to lose a polar species while leaving a nonpolar species would satisfy this criterion. This change in polarity can be abrupt, as with the decomposition of the solvent, or it can be smooth transition with tunable properties. The magnitude of the polarity change as well as the type of change will dictate the appropriate applications for the solvent.

Information on switchable solvents is scarce, though in 1978, Iwatani et al claimed that the amidine 1,8-diazobicyclo-[5.4.0]-undec-7-ene (DBU) reversibly formed an adduct with CO_2 [1] as shown in Figure 2-1.

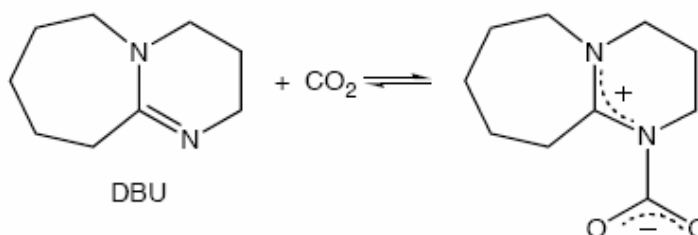


Figure 2-1. Reaction of DBU with CO_2 to form adduct.

However, spectroscopic evidence in a recent paper [2] has shown that instead of the adduct being formed, the reaction of DBU with CO_2 actually forms a bicarbonate salt while in the presence of water (Figure 2-2).

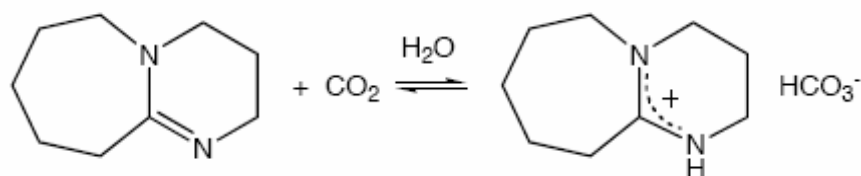


Figure 2-2. Reaction of CO_2 in the presence of water to form carbonate salt.

In the absence of water, no reaction occurs. Jessop et al [3] have recently reported a reversible ionic liquid formed from DBU, an alcohol, and CO_2 (Figure 2-3). This is discussed in more detail in Chapter V.

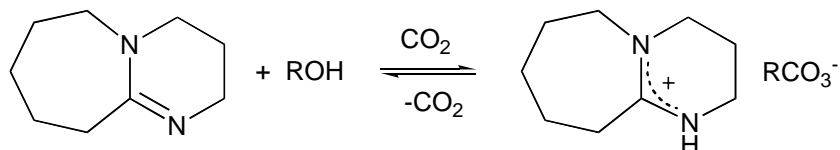


Figure 2-3. Example of reversible ionic liquid.

One difficult separations scheme is the reaction of an organic with a salt. Typically, a phase transfer catalyst (PTC) such as a quaternary salt is utilized [4]. After the reaction, the PTC, which is often toxic and expensive, must be separated from the product. Under these biphasic conditions, maximum contact between the phases is required to minimize the mass transfer barrier between the phases. In addition, significant amounts of water are required to wash the PTC, yielding much aqueous waste. As a result, it would be both economically and ecologically advantageous to find a better option than a PTC. Another option is to use a dipolar, aprotic solvent such as DMSO, DMF, or HMPA which will dissolve both species. However, dipolar, aprotic solvents have high boiling points which makes distillation difficult. DMSO, DMF, and HMPA

are also such a good solvents that liquid extraction is difficult. As a result, we sought to develop a solvent with DMSO-like properties, but with a switch for easy removal. The solvent should have a number of properties advantageous for use as a reaction medium, including the following:

- Useable liquid range (preferably room temperature)
- Chemical stability for the reactions (i.e. the solvent doesn't react)
- Dissolve both organics and salts

The solvent should also have a number of characteristics advantageous for separations, including the following:

- Decomposition at moderate conditions with reasonable rate
- Decomposition products have very low or very high vapor pressure
- Easy recombination to form solvent

The first example of a switchable solvent is thiirane oxide.

Thiirane Oxide

Thiirane oxide represents the cyclic analog to DMSO, as shown in Figure 2-4. Thiirane oxide has similar solvent strength parameters to DMSO, which can be applied to solvent systems.

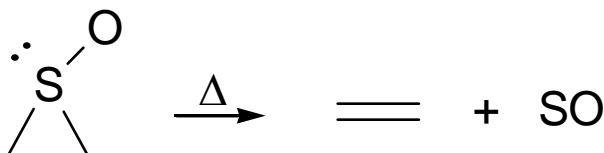


Figure 2-4. Decomposition of thiirane oxide to form ethylene and SO.

Unlike DMSO, thiirane oxide decomposes at temperatures above 100 °C to form ethylene and sulfur oxide. This represents the unique separations advantage conferred by thiirane oxide over DMSO. We can use thiirane oxide's exceptional solvent ability for reactions and its unique decomposition for separations. Theoretically, the reverse reaction of sulfur oxide and ethylene to reform thiirane oxide is possible; however, the rapid disproportionation of SO to form various sulfur products makes this reversal impossible. Still, this "cleavable" solvent is useful as a proof of concept and may find uses in specialty applications where reaction and product isolation are difficult.

This work seeks to characterize the relevant solvent properties of thiirane oxide and to determine its decomposition characteristics. In addition, thiirane oxide was tested as the solvent in a nucleophilic substitution reaction shown in Figure 2-5.

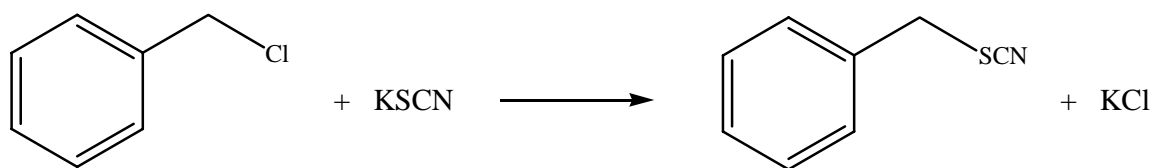


Figure 2-5. Nucleophilic substitution of benzyl chloride by potassium thiocyanate.

This reaction provides a means of comparison between thiirane oxide and a standard dipolar, aprotic solvent such as DMSO in terms of overall solvent ability. However, the critical aspect of thiirane oxide is the ability to remove it with a "switch".

Solvent Parameters

Several experimentally determined parameters can be used to characterize the solvent's properties. The Et(30) solvent strength and Kamlet-Taft parameters α , β , & π^* [5,6,7] are based on the solvent-induced shift in absorbance of a probe dye. This phenomenon is known as solvatochromism and is often used to probe the molecular

interactions between solvent and solute. The final solvent parameter is the dielectric constant ϵ , which is the permittivity of a medium relative to a vacuum. The dielectric constant is related to a solvent's polarity and represents its ability to separate ions in solution.

Et(30)

The solvent's Et(30) value represents the molar transition energy, which is the energy required to bring one mole of the standard dye dissolved in the solvent from electronic ground state to the first excited state [8]. The Et(30) value is the most general measure of a solvent's strength. It is a combination of dipolarity / polarizability and hydrogen bond donating ability and is based on the wavelength of maximum absorbance of Reichardt's dye (2,6-diphenyl-4-(2,4,6-triphenylpyridinium-1-yl) phenolate dihydrate, $C_{41}H_{29}NO \cdot 2H_2O$).

Kamlet-Taft

The parameter π^* value is a measure of dipolarity / polarizability and represents the ability of a solvent to stabilize charges and dipoles. We can then correlate the solvent's ability to stabilize the respective ground states and excited states of the probe molecule, N,N-dimethyl-4-nitroaniline by observing the longest wavelength absorption band of the π to π^* transition in the UV spectrum.

The parameter α represents the acidity, or hydrogen bond donating (HBD) ability of the solvent. It is a measure of the solvent's ability to donate a proton in a solute-to-solvent hydrogen bond. Rather than measure α directly, we can isolate α based on two

other solvatochromic parameters. $E_t(30)$ is a measure of dipolarity / polarizability and HBD acidity, and π^* is a measure of dipolarity / polarizability. Thus we can decouple the effect of acidity from a combination of these two parameters.

The final Kamlet-Taft parameter, β , represents the hydrogen bond accepting ability of the solvent. The numerical value of β is based on the UV absorbance of 4-nitroaniline.

Experimental Materials

All chemicals used were purchased from Sigma Aldrich, unless otherwise noted, and used without further purification. The chemicals used were ethylene sulfide (98%), *m*-chloroperbenzoic acid ($\geq 77\%$), methylene chloride (HPLC grade, $> 99.8\%$), anhydrous ammonia ($\geq 99.99\%$), magnesium sulfate (Fisher, certified anhydrous), 4-nitroaniline (99+ %), Reichardt's dye ($\sim 90\%$), N,N-dimethyl aniline (99%), potassium thiocyanate (reagent), benzyl chloride (99%), dimethyl sulfoxide (99.7%), cyclohexane (99.5%). ^1H and ^{13}C NMR spectra were recorded using a Varian Mercury Vx 400 spectrometer using residual CHCl_3 peak as an internal reference. Gas chromatography was performed on an Agilent 6580 GC with an FID detector. TGA and DSC data were acquired using a Netzsche Model STA-409PC. The dielectric constant was measured using a Model 870 Dielectric Constant Meter by Scientifica.

Thiirane Oxide Synthesis

This procedure was modified from the method described by Kondo et al [9]. 10 mL of ethylene sulfide was added to 50 mL CH_2Cl_2 and stirred. A prepared solution of

30 g. 3-chloroperbenzoic acid ($\leq 77\%$) in 250 mL CH_2Cl_2 was added via addition funnel to the ethylene sulfide solution over 3 hours at room temperature. After stirring for another hour, the addition funnel was replaced with a dry ice/acetone cooled condenser fitted with a septum at the top. Approximately 6 mL anhydrous ammonia was condensed and added as liquid to the vigorously stirred reaction mixture two times. The solution was filtered, the solids washed with CH_2Cl_2 , and the filtrate dried with MgSO_4 . The solvent was removed by rotary evaporation, then by high vacuum. Distillation of the crude material at $70\text{ }^\circ\text{C}$ $\sim 10^{-2}$ torr on a short-path, vacuum distillation apparatus with condenser cooled to $-15\text{ }^\circ\text{C}$ yields analytically pure thiirane oxide in 56% recovered yield based on ethylene sulfide. ^1H NMR: Complex multiplets are centered at 1.99 ppm and 2.41 ppm. ^{13}C NMR: EI-MS: $m/z = 76$.

Apparatus and Procedures

Et(30) Determination

The Et(30) value is based on the wave number of the maximum UV absorption of Reichardt's dye in the solvent. The energy of transition can be calculated using equation 2-1, where Et(30) is the energy of transition in J/mole, h is Planck's constant in Js /molecule, c is the speed of light in cm/s, ν is the wavenumber in cm^{-1} , and N_A is Avagadro's number in molecules/mole.

$$Et(30) = hc\nu N_A \quad \text{Equation 2-1}$$

Kamlet-Taft Parameter Determination

For the parameter π^* , I dissolved N,N-dimethyl-4-nitroaniline in the solvent at a concentration of approximately 5×10^{-3} mol/L. The maximum absorbed wavelength was observed, and π^* was then calculated based on equation 2-2, where λ is the wavelength of maximum absorbance. Cyclohexane is used as a reference and is arbitrarily assigned a value of 0, while DMSO is assigned a value of 1.

$$\pi^* = \frac{\nu(\text{thiiraneoxide}) - \nu(\text{cyclohexane})}{\nu(\text{DMSO}) - \nu(\text{cyclohexane})} \quad \text{Equation 2-2}$$

The acidity α is decoupled from the $E_t(30)$ and π^* values, as shown in equation 2-3.

$$\alpha = -14.7 - 0.532\pi^* + 0.0508E_t(30) \quad \text{Equation 2-3}$$

The method for β was similar to that of π^* . Again, cyclohexane was assigned a value of 0 while DMSO was assigned its literature value of 0.76.

Reaction of Benzyl Chloride with Potassium Thiocyanate

I studied the reaction in Figure 2-4 as a means of comparing the relative solvent ability of thiirane oxide to a standard solvent, in this case DMSO. The kinetic experiments in DMSO were performed as follows: 0.29g of KSCN was added to 50 mL DMSO in a stainless steel Parr reactor and stirred until the KSCN appeared to be dissolved. The vessel was heated to reaction temperature (40 °C to 70 °C, +/- 1 °C) and approximately 0.12 g to 0.18 g benzyl chloride was added. Samples were taken at regular intervals and dissolved in toluene to quench the reaction. The results were quantified by GC / FID analysis (HP 6890).

The kinetic experiments in thiirane oxide were performed as follows: 0.016 g of KSCN was added to 1.3 mL thiirane oxide in a round-bottom flask in a heated oil bath, and stirred until the KSCN appeared to be dissolved. The flask was heated to reaction temperature (40 °C to 60 °C, +/- 1 °C) and approximately 7 mg to 10 mg of benzyl chloride was added. Samples were taken at regular intervals and dissolved in toluene to quench the reaction. The results were quantified by GC / FID analysis. The integrated second-order rate equation is shown in Equation 2-4, where x is conversion, θ is initial molar ratio of KSCN to benzyl chloride, k is the second order rate constant in L/mol/s, C_{Ao} is the initial molar concentration of benzyl chloride in mol/L, and t is the time in s.

$$\ln \left(\frac{1-x}{1-\frac{x}{\theta}} \right) = -k * C_{Ao} * t * (\theta - 1) \quad \text{Equation 2-4}$$

Thus a plot of $\ln \left(\frac{1-x}{1-\frac{x}{\theta}} \right)$ vs. t yields a straight line with slope equal to $[-k * C_{Ao} * (\theta - 1)]$.

Product Isolation

The key to the use of this cleavable solvent is our ability to remove the solvent by decomposition. After one of the kinetic runs, the solvent mixture with reactants and products remaining in solution was added to a heated round-bottom flask at 100 °C and 2 torr absolute until all of the liquid solvent had decomposed.

Since the decomposition of thiirane oxide produces several species that are not gases, TGA data is not suitable for determination of decomposition rate. The

decomposition data obtained using benzyl thiocyanate as an internal reference for ^1H NMR shows that at 100 °C the half-life is 52 minutes, and at 120 °C it is 18 minutes.

Results and Discussion

Solvent Properties

Table 2-1 show the solvatochromic properties and dielectric constant for thiirane oxide and compares them to DMSO. The values for thiirane oxide are very similar to the values for DMSO, which is expected given their related structures.

Table 2-1. Solvent property comparison for DMSO vs. thiirane oxide

	DMSO	Thiirane Oxide
α	0	0
β	0.76	0.74
π^*	1.00	1.02
E_T30	189 kJ/mol	191 kJ/mol
ϵ	46.7	45.0

Demonstration Reaction

The reaction between benzyl chloride and potassium thiocyanate shows a rate of reaction that is slightly higher in DMSO than in thiirane oxide. Table 2-2 shows a comparison of the kinetic data I recorded.

Table 2-2. Kinetic data for BzCl + KSCN in DMSO & thiirane oxide. Error is uncertainty in rate constant; duplicate runs are averaged.

DMSO		Thiirane Oxide	
T, °C	$k \times 10^3, \text{L mol}^{-1} \text{s}^{-1}$	T, °C	$k \times 10^3, \text{L mol}^{-1} \text{s}^{-1}$
44.8	0.97 ± 0.04	40	0.42 ± 0.02
49.5	1.46 ± 0.14	43	0.56 ± 0.04
57.4	2.63 ± 0.04	52	0.97 ± 0.06
61.2	3.35 ± 0.12	61	1.62 ± 0.12
62	3.33 ± 0.11	62	1.61 ± 0.12
68.5	5.65 ± 0.19		
70	6.54 ± 0.18		

A plot of the $\ln(k)$ vs. $1/T$ will yield a slope that is proportional to the activation energy of the reaction in the solvent. Figure 2-6 depicts this plot.

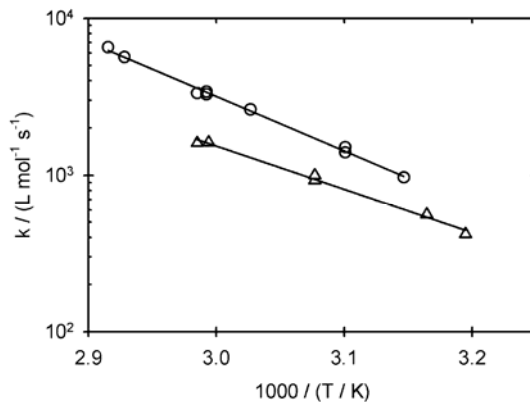


Figure 2-6. Second order rate constant of BzCl + KSCN as a function of temperature. Δ = thiirane oxide; O = DMSO

An analysis of the kinetic data also allows us to determine other thermodynamic properties of the reaction, as shown in Table 2-3. The activation energy in DMSO is higher than that in thiirane oxide, which suggests that the reaction rate should be slower in DMSO. However, the data indicate that this is not true. But we speculate that if we consider the relative acidity of the protons in DMSO compared to thiirane oxide, the greater acidity of thiirane oxide (due to the increased s character of the hybrid orbitals due to ring angle) would solvate the ^-SCN ion more strongly and thus inhibit the reaction.

Table 2-3. Thermodynamic properties of example reaction.

	ΔG^\ddagger KJ/mol	ΔH^\ddagger KJ/mol	ΔS^\ddagger KJ/mol
DMSO	66.6 ± 1.6	63.7	-0.8
Thiirane oxide	53.2 ± 2.3	50.3	-2.5

Product Isolation

One of the decomposition products, sulfur monoxide, is unstable and disproportionates according to equation 2-5 [10].



Although the thiirane oxide was completely decomposed, some sulfurous materials remained in the flask. The remaining materials were extracted with methylene chloride and analyzed for benzyl chloride and benzyl thiocyanate. The overall yield was > 48% recovery of benzyl thiocyanate and unreacted benzyl chloride, as determined by GC/FID.

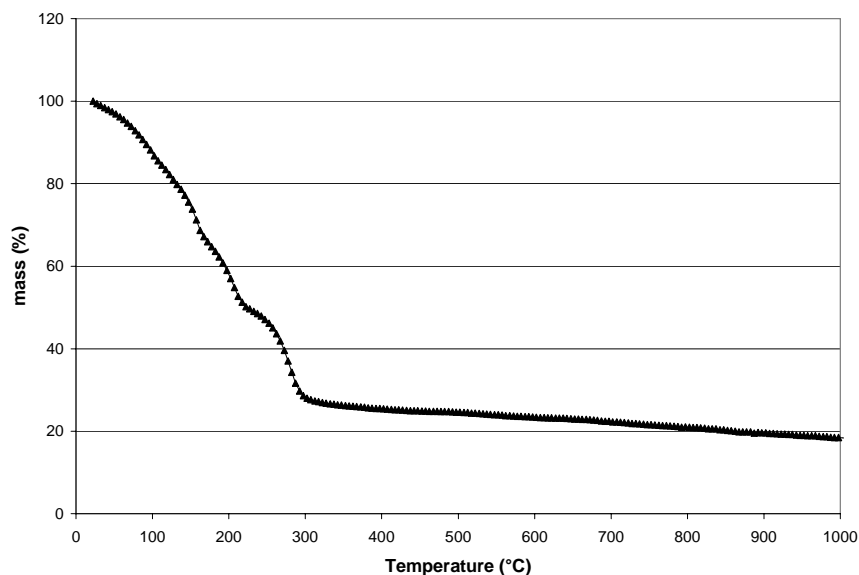


Figure 2-7. TGA for thiirane oxide. Heating rate = 20 °C/min.

Figure 2-7 is a thermogravimetric analysis (TGA) for thiirane oxide. The graph shows that at temperatures over 300 °C, approximately 20% of the original mass is still remaining. This is consistent with the results of the decomposition experiment where we observed sulfurous mass remaining in the flask after decomposition.

Differential scanning calorimetry (DSC) is another method for characterizing the decomposition. Figure 2-8 shows DSC results for thiirane oxide.

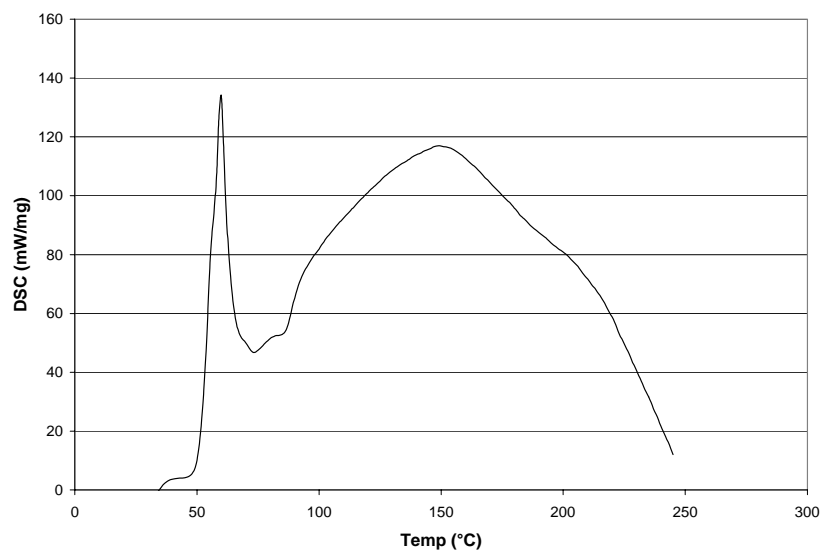


Figure 2-8. DSC for thiirane oxide. Heating Rate = 20 °C/min.

The DSC shows a sharp exotherm at 60 °C and another broad exotherm around 150 °C. DSC and TGA together can give important information about the mechanism and rate of decomposition. The first exotherm in the DSC does not show a corresponding mass loss in the TGA, suggesting that this exotherm is indicative of a bond breaking step. The broad exotherm in the DSC does correspond to mass loss in TGA, indicating the release of ethylene and / or sulfur oxide. Additional DSC / TGA data at different heating rates will allow us to better characterize the decomposition process and give us more accurate data on the decomposition rate and mechanism.

Conclusions

This work has demonstrated a new cleavable solvent that combine advantages for both reactions and separations. These types of solvents represent a new paradigm in product isolation. This thesis summarizes the solvent properties and characteristics of thiirane oxide and found that its solvent properties were very near to those of its cyclic

analog, DMSO. This work also shows a nucleophilic substitution reaction that would be typically run in a dipolar, aprotic solvent such as DMSO and found that the reaction rate in thiirane oxide corresponds well to the rate in DMSO. This work also shows that thiirane oxide can be removed by decomposition by heating it at temperatures above 100 °C, which is much lower than the temperature required to remove DMSO and did not cause degradation of the product.

Thiirane oxide meets all of the requirements for a switchable solvent, save for one. TGA data show that thiirane oxide does not decompose cleanly to form two gases that are then easily removed. The reactivity of sulfur monoxide to form sulfurous products renders this solvent a one-way switch. We desire to have a solvent whose decomposition products can be recombined to form the solvent again. Although thiirane oxide does not meet this criterion, it is still very useful as the first demonstration of a switchable solvent.

References

- [1] Iwatani, M.; Kudo, K.; Sugita, N.; Takezaki, Y. *Sekiyu Gakkaishi* **1978**, 21, 290-296.
- [2] Heldebrant, D. J.; Jessop, P. G.; Thomas, C. A.; Eckert, C. A.; Liotta, C. L. *Nature*, Submitted.
- [3] Jessop, P. G.; Heldebrant, D. J.; Li, X.; Eckert, C. A.; Liotta, C. L.; *Nature*, Galley Proof No. 1884.
- [4] Starks, C. M.; Liotta, C. L.; Halpern, M. & Editors **1994**.
- [5] Kamlet, M. J.; Abboud, J. L.; Taft, R. W.; *Journal of the American Chemical Society* **1977**, 99, 6027-6028.
- [6] Kamlet, M. J.; Taft, R. W.; *Journal of the American chemical Society* **1976**, 98, 377-383.
- [7] Kamlet, M. J.; Taft, R. W.; *Journal of the American chemical Society* **1976**, 98, 2886-2894.
- [8] Reichardt, C.; VCH **1990**.
- [9] Kondo, K.; Negishi, A.; Fukuyama, M. *Tetrahedron Letters* **29**, 2461-2464.
- [10] Herron, J. T.; Huie, R. E.; *Chemical Physics Letters* **1980**, 76, 322-324.

CHAPTER III

PIPERYLENE SULFONE AS A SWITCHABLE SOLVENT

Introduction

Due to the inherent limitations of thiirane oxide outlined in Chapter II, we sought to develop a better solvent. Our design criteria were the same, i.e. useable liquid range, chemical stability, ability to dissolve both organics and salts, decomposition at moderate conditions, decomposition products with appropriate vapor pressures, and easy recombination of decomposition products to reform the solvent. To this end, we are developing the use of piperylene sulfone for switchable applications.

Piperylene sulfone decomposes with temperature to form the diene piperylene and sulfur dioxide, as shown in Figure 3-1.

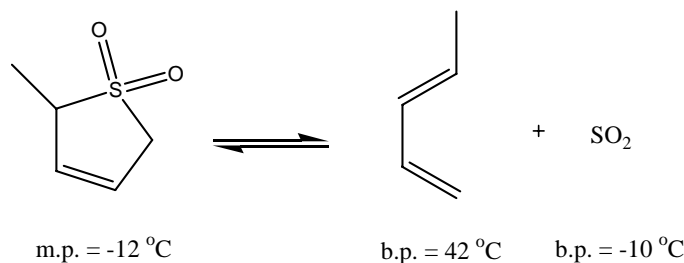


Figure 3-1. Decomposition of piperylene sulfone to form diene and SO₂.

Piperylene sulfone is a liquid at room temperature. The decomposition products have appreciably different boiling points, making separation much easier. Piperylene sulfone is also synthesized from piperylene and sulfur dioxide, so the reverse reaction should be possible. Piperylene sulfone is also reported to have a reasonable decomposition rate at

moderate temperatures, especially when compared to other sulfones as shown in Figure 3-2 [1].

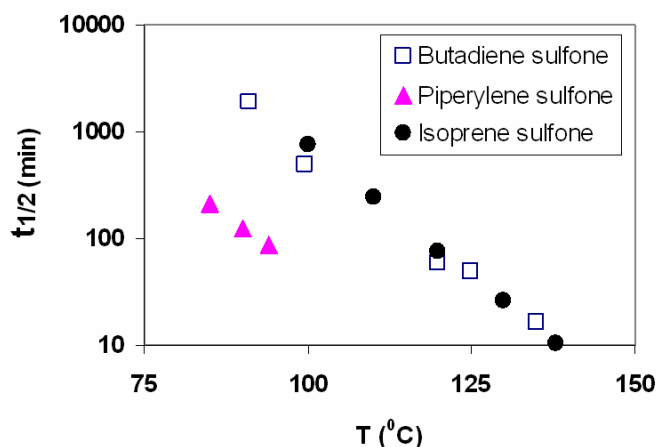


Figure 3-2. Sulfone decomposition rates.

These rates indicate that the decomposition rate should be acceptable to our goals.

The goal of this work is to characterize the solvent in a manner similar to thiirane oxide. As most of the background information on the solvent parameters was covered in Chapter II, it will not be repeated here. I have measured the Et(30) value, Kamlet-Taft parameters, and dielectric constant of piperylene sulfone. I have also shown that piperylene sulfone is a capable medium for the reaction of benzyl chloride with potassium thiocyanate.

The Kamlet-Taft β value procedure was modified slightly from the previous experiment. Since piperylene sulfone absorbance in the UV renders 4-nitroaniline unusable, I used the dye pair N,N-dimethyl-4-nitrosoaniline and N-methyl-nitrosoaniline for β determination. Piperidine ($\beta = 1.04$) and cyclohexane ($\beta = 0$) were used as the reference solvents, and the equation is modified as shown, where v_{diff} is the difference in

wave numbers for a solvent between the maximum absorbance of the two dye probes, and -809 is based on the reference solvents used.

$$\beta_{\text{piperylenesulfone}} = \frac{V_{\text{diff, piperylenesulfone}} - V_{\text{diff, cyclohexane}}}{-809} \quad \text{Equation 3-1}$$

The procedures for α , π^* , Et(30) and the dielectric constant all stayed the same.

It was also necessary to show that piperylene sulfone could support a chemical reaction such as the nucleophilic substitution between benzyl chloride and potassium thiocyanate shown in Figure 2-4.

Experimental Materials

All chemicals used were purchased from Aldrich and used without further purification unless otherwise noted. 1,3-pentadiene (piperylene) (mixture of *cis* and *trans*, 90%), sulfur dioxide ($\geq 99.9\%$), N-phenyl-1-naphthylamine (98%), chloroform (CHROMASOLV Plus HPLC 99.9%), water (HPLC grade), 4-nitroaniline (99+ %), Reichardt's dye (~90%), N,N-dimethyl aniline (99%), potassium thiocyanate (reagent), benzyl chloride (99%), dimethyl sulfoxide (99.7%), cyclohexane (99.5%), piperidine (99.0%), N,N-dimethyl-4-nitrosoaniline (97%), N-methyl-4-nitrosoaniline. ^1H and ^{13}C NMR spectra were recorded using a Varian Mercury Vx 400 spectrometer using residual CHCl_3 peak as an internal reference. Gas chromatography was performed on an Agilent 6580 GC with an FID detector. TGA and DSC data were acquired using a Netzsche Model STA-409PC. The dielectric constant was measured using a Model 870 Dielectric Constant Meter by Scientifica.

Piperylene Sulfone Synthesis

This method was adapted from Krug and Rigney [2]. 25 mL (0.25 mol) of piperylene and 2.75 g. (0.0125 mol) of phenyl- β -naphthylamine was added to a 750 mL stainless steel bomb. 200 to 250 mL of liquid SO₂ (3.9 to 4.9 mol; < 5 bar pressure) was added and the mixture was shaken at room temperature for 2 days. The vessel was vented slowly. Approximately 36 g. of a red oil was recovered and to that was added 10 mL of CHCl₃. The crude material was extracted three times with 50 mL of HPLC grade water. The aqueous layers were combined and extracted three times with 10 mL of CHCl₃. The organic layer was dried over MgSO₄ and the solvent was removed *in vacuo* to yield 7.4 g. of piperylene sulfone. A second aqueous extraction of the crude product and back extraction into CHCl₃ yielded another 4.3 g. The combined samples were distilled at ~10-2 torr at 65 °C to yield a clear, colorless oil. ¹H NMR (ppm): δ = 1.36 (d, 3H), 3.69 (m, 3H), 5.96 (m, 2H). ¹³C NMR (ppm): 12.9, 54.8, 59.4, 122.5, 131.4.

Apparatus and Procedures

The procedures for α , β , π^* , Et(30) and the dielectric constant all stayed the same as they were for thiirane oxide. The kinetic experiments performed in piperylene sulfone were also done using the same procedure.

In order to show the switchable nature of this solvent, we need to be able to decompose it into piperylene and sulfur dioxide. One of the problems with piperylene is that it tends to polymerize. As a result, we need to pay special considerations to ensure that a significant amount of the piperylene does not become unusable in this manner. I propose to decompose the piperylene sulfone at elevated temperatures and shuttle the

resulting piperylene and sulfur dioxide into a “sea” of liquid SO₂. By keeping the path between the decomposition and the liquid SO₂ as short as possible, I believe that we can suppress the polymerization and ensure that if the piperylene does react, that it will react with SO₂ to reform the solvent.

Results and Discussion

Solvent Parameters

The solvent properties for piperylene sulfone are listed in Table 3-1. The α , π^* , Et(30), and dielectric constant are all similar to DMSO and thiirane oxide. The value of α is higher than expected, but there is some uncertainty in the measurements and this may not be an anomaly at all.

Table 3-1. Solvent properties for piperylene sulfone and comparison with DMSO & thiirane oxide

	DMSO	Thiirane Oxide	Piperylene Sulfone
α	0	0	0.07
β	0.76	0.74	0.46
π^*	1.00	1.02	0.87
E _T 30	189 kJ/mol	191 kJ/mol	189 kJ/mol
ϵ	46.7	45.0	42.6

These results show that piperylene sulfone has solvent properties similar to other dipolar, aprotic solvents.

Demonstration Reaction

I also performed the nucleophilic displacement reaction between benzyl chloride and potassium thiocyanate. At 50 °C, the reaction rate constant $k = 1.12 \times 10^{-3} \text{ L mol}^{-1} \text{ s}^{-1}$. This is approximately the same rate constant that was obtained for thiirane oxide at this temperature. Thus, piperylene sulfone is an acceptable solvent for our demonstration reaction. Data at additional temperatures will allow the determination of activation properties and give a more thorough comparison to a standard solvent such as DMSO.

Decomposition Studies

Figure 3-3 shows a thermogravimetric analysis (TGA) for piperylene sulfone.

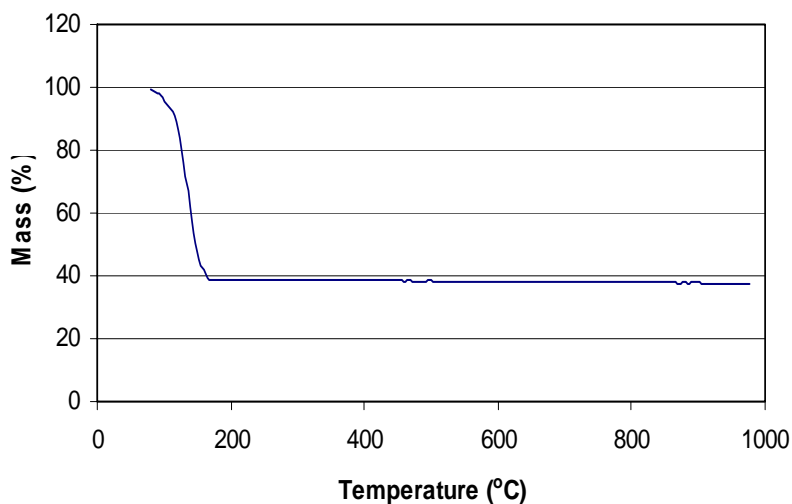


Figure 3-3. TGA for piperylene sulfone. Heating rate = 20 °C/min.

The graph shows that decomposition is complete at about 160 °C. However, about 40% of the original mass is still remaining. This was unexpected and we do not yet know the composition of the remaining mass. It is possible that the piperylene polymerized and remained behind. Further tests are needed, especially at lower heating rates.

Figure 3-4 shows the corresponding differential scanning calorimetry (DSC) results.

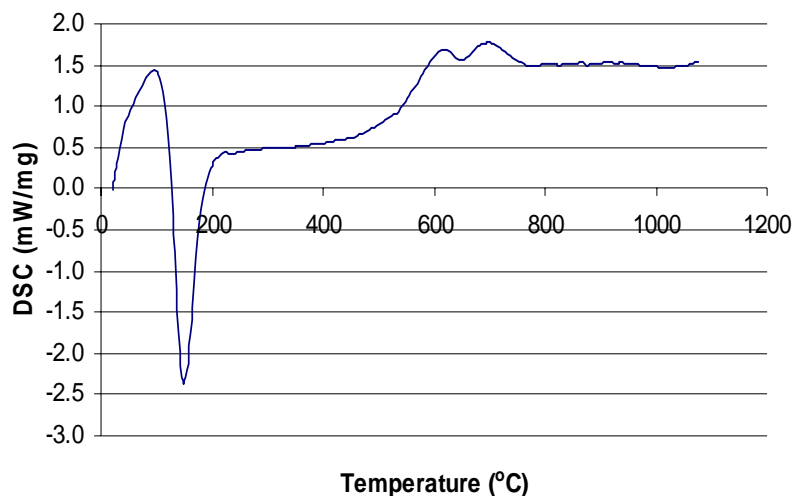


Figure 3-4. DSC for piperylene sulfone. Heating rate = 20 °C/min.

TGA and DSC data at more than one heating rate can yield even more clues as to the method and rate of decomposition.

Conclusions

This work has sought to characterize the use of piperylene sulfone as a solvent. Piperylene sulfone exhibits properties that are similar to another dipolar, aprotic solvent. The reaction rate of a demonstration nucleophilic substitution reaction is comparable to the rate of the same reaction in DMSO and thiirane oxide. These qualities mean that piperylene sulfone shows promise as a dipolar, aprotic solvent.

The key for piperylene sulfone is the ability to “switch” it by heating to form piperylene and sulfur dioxide. Since piperylene sulfone can be synthesized from these two components, in principle we should be able to decompose and reform our solvent. Although the TGA data did show considerable mass remaining, we do not yet know if this is a barrier. More TGA data at different heating rates is required for any determination to be made. The polymerization of piperylene may also be a problem. Indeed, piperylene is packaged along with a polymerization inhibitor. The polymerization of this diene must be suppressed or stopped in order for this solvent to find a practical use. Decomposing the solvent into liquid SO₂ may solve this problem. The current results show that piperylene sulfone has excellent solvent qualities and has promise for use in switchable applications.

References

- [1] Drake, L. R.; Stowe, S. C.; Partanksy, A. M.; *Journal of the American Chemical Society* **1946**, 68, 2521-2524

- [2] Krug, R. C.; Rigney, J. A.; *Journal of Organic Chemistry* **1959**, 23, 1697-9.

CHAPTER IV

CAGE REACTIONS IN GAS-EXPANDED LIQUIDS

Introduction

The recent shift toward environmentally friendly solvents has led many researchers to carbon dioxide, which is relatively inexpensive, non-toxic, and non-flammable. However, compressed carbon dioxide is a poor solvent. Intermediate between conventional organic solvents and pure carbon dioxide are gas-expanded liquids (GXL's). GXL's are formed by dissolving a gas, generally CO₂, into the organic liquid. The solubility of CO₂ in many organic solvents is quite high and this allows properties such as dielectric constant, polarity, viscosity, and solubility of a third component to be tuned [1]. This tunability means that solvent systems can be optimized in terms of rate, selectivity, and solubility.

GXL's have the potential to be an extremely useful solvent medium for reactions and separations. However, before these solvents can be used effectively, we must first understand the molecular structure of the systems. While many experiments have measured bulk, or average, properties of GXL's, compressible and incompressible fluids show local compositions that differ from the bulk compositions. It is this cybotactic region where the solvent structure is influenced by solute-solute, solute-solvent, and solvent-solvent interactions [2] that I will be studying. I will use the cage effect to study the local diffusivity of gas-expanded liquids and compare this local property to the bulk diffusivity. These results will be coupled with theoretical molecular modeling results as

well as molecular rotor results that probe local viscosity in order to obtain an understanding of the local composition of GXL's.

Cage Effect

A pair of radicals that are produced within a solvent “cage” can either recombine within the cage or diffuse out of the cage. Studies in both conventional solvents [3] as well as supercritical fluids [4] have shown that the extent with which the radicals react within the cage is directly proportional to the viscosity of the medium [3]. However, there may be additional factors that influence the cage effect in supercritical fluids. Studies have shown that cage lifetimes may be enhanced near the critical point because of an increase in the local solvent density around the solute [5]. This “solvent / solute clustering” may affect the rates of chemical phenomena [6,7]. It is for this reason that we wish to explore the cage effect in GXL's.

I had planned to use trityl peroxide as the probe molecule for the cage reactions. Trityl peroxide has several major advantages over other types of molecules typically used to probe cage reactions:

- Trityl peroxide does not release a gas upon cage recombination, which could complicate the cybotactic region.
- The O-O bond in trityl peroxide can be easily broken with UV light.
- The cage recombination product is different from the starting material.

Figure 4-1 is a schematic of the reaction.

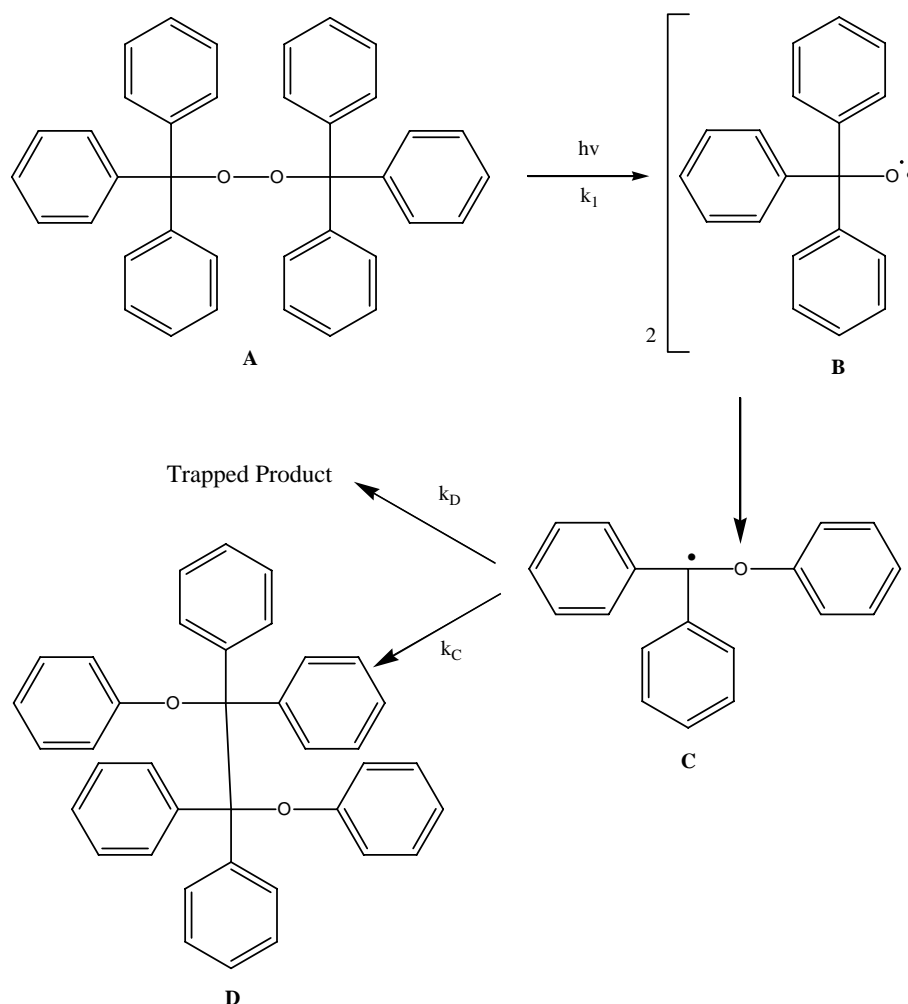


Figure 4-1. Cage reaction probe with trityl peroxide.

The trityl peroxide (A) is first irradiated with UV light. This will form a pair of radicals (B) in the cage with rate constant k_1 . The oxygen radical is not stable, and one of the phenyl groups will immediately migrate to form the carbon radical (C). The radicals can then either diffuse out of the cage with rate constant k_D where they can be trapped, or they can recombine inside the cage (D) with rate constant k_C . Herein lies the advantage of using this peroxide as a probe molecule: the rearranged product is different from the starting material, meaning the analysis is straightforward and the reaction does not need

to be followed with exotic methods such as laser flash photolysis. The ratio of the concentration of the trapped product to the concentration of the recombined product is a direct measure of the cage effect.

Experimental Goals

My goal was to explore the cage effect in a number of gas-expanded solvents. I wanted to investigate the effect of CO₂ pressure on the extent of the cage reactions. I planned to also use a number of different solvents including toluene, acetonitrile, hexane, and DMSO. This will help elucidate chemical effects. Protic solvents may complicate the cybotactic region due to H-bonding, so they were to be avoided. I also wanted to investigate branched versus unbranched alkanes to separate the effect of viscosity. These results, combined with microviscosity probes, bulk viscosity measurements, and molecular dynamics simulations that other members of our group are doing, will provide us with an understanding of the factors affected by CO₂ pressurization. We can then use this information to design processes that take advantage of the alterations to rate and selectivity afforded by local enhancements in the cybotactic region.

Experimental Materials

Trityl peroxide is not commercially available, so we attempted to synthesize it in the lab. Several syntheses are published in the literature, but we were unsuccessful in recreating all of them. Henry-Riyad and Tidwell report [8] that trityl chloride and Zn dust in cyclohexane and open to the atmosphere will make trityl peroxide in 30 minutes at room temperature, as shown in Figure 4-2.

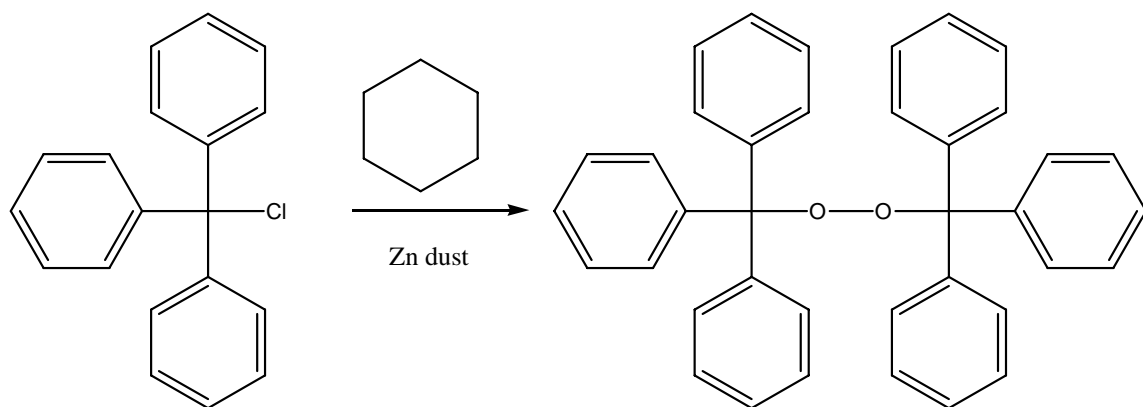


Figure 4-2. Reaction of trityl chloride in Zn dust and cyclohexane to form trityl peroxide. T = 25 °C, 30 min, open to the atmosphere.

We ran the reaction under the specified conditions with no yield. We also ran the reaction with conditions up to 60 °C, 60 hours, and stirred with an air bubbler, and no reaction. Upon further inspection of the reported NMR characterization, we discovered that their reported product values exactly matched our starting material NMR.

We also attempted to synthesize trityl peroxide using potassium superoxide, trityl chloride, and 18-crown-6 in benzene, as shown in Figure 4-3.

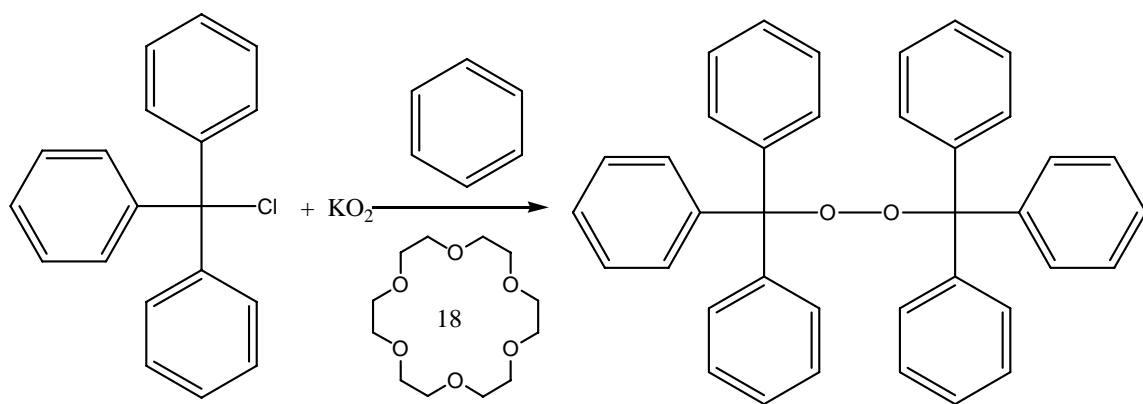


Figure 4-3. Reaction of trityl chloride with potassium superoxide in 18-crown-6 and benzene.

Our first attempt at room temperature and 3 hours gave approximate 75% yield of trityl peroxide. However, subsequent attempts at times up to 72 hours showed no product formation.

As an alternative to trityl peroxide, we propose to use bis(triphenylsilyl) peroxide. Bis(triphenylsilyl) peroxide is structurally similar to trityl peroxide, the only difference being that the two central carbons are replaced with Si atoms. The synthesis and characterization of this molecule are reported in the literature [9]. This molecule is also expected to undergo a rearrangement to a new molecule.

Conclusions

GXL's offer a number of environmental, reaction, and processing advantages over traditional organic solvents. They are tunable, allowing for a wide range of reaction conditions. They also show rate enhancements in the cybotactic region. It is for this reason that we wish to study the solute-solvent and solute-solute interactions in GXL's. We have chosen to study the cage effect by use of a peroxide probe molecule that has a different product distribution depending on whether it diffuses out of the cage or recombines within the cage. However, we were unsuccessful in synthesizing the peroxide for laboratory use. We feel that the silicon derivative of trityl peroxide is a promising alternative to use as a probe molecule.

References

- [1] De la Fuente Badilla, J. C.; Peters, C. J.; de Swann Arons, J.; *Journal of Supercritical Fluids* **2000**, 19, 13-23.
- [2] Zagrobelny, J.; Bright, F. V.; *Journal of the American Chemical Society* **1992**, 114, 7821-7826.
- [3] Niki, E.; Kamiya, Y.; *Journal of the American Chemical Society* **1974**, 7, 2129-2133.
- [4] Tanko, J. M.; Pacut, R.; *Journal of the American Chemical Society* **2001**, 24, 5703-5709.
- [5] Brennecke, J. F.; Chatcauneuf, J. E.; *Chem. Rev.* **1999**, 99, 433-452.
- [6] Rhodes, T. A.; Fox, M. A.; *Journal of Physical Chemistry* **1996**, 100, 17931-17939.
- [7] Kajimoto, O.; Futakami, M.; Kobayashi, T.; Yamasaki, J.; *Journal of Physical Chemistry* **1988**, 92, 1347-1352.
- [8] Henry-Riyad, H.; Tidwell, T. T.; *Journal or Physical Organic Chemistry* **2003**, 16, 559-563.
- [9] Shubber, A. K.; Dannley, R. L.; *J. Org. Chem* **1971**, 36, 3784-3787.

CHAPTER V

CONCLUSIONS AND RECOMMENDATIONS

Conclusions

My work has focused on new solvents to both enhance chemical reactions and improve the separation of products. One part of my work is switchable solvents. The goal of these solvents is to be able to run troublesome reactions such as a nucleophilic substitution reaction between an organic and a salt. Rather than use costly separations techniques or toxic PTC's, we would like to be able to combine the entire process into one save, environmentally benign, cost-effective system. The solvent will contain a built-in switch for facile separation of the product.

Thiirane oxide represents the cyclic analog to DMSO. As one would expect from the structure, thiirane oxide has similar properties in polarity, acidity, basicity, and solvent strength. I have also shown that thiirane oxide is a capable solvent for our demonstration nucleophilic substitution reaction. The keys to the use of a switchable solvent are the ability to remove, isolate, and reform the solvent. I have shown that thiirane oxide can be removed by simple heating; however, the disproportionation of SO into various sulfur products renders the back reaction impossible. For this reason we sought to develop a new solvent.

Piperylene sulfone is another dipolar, aprotic solvent with good solvent properties. It also gave a reaction rate constant for the demonstration reaction that was similar to DMSO. Piperylene sulfone is synthesized from piperylene and sulfur dioxide,

so in principle we should be able to decompose and subsequently reform the solvent if the polymerization of the piperylene can be suppressed. Piperylene sulfone offers promise as a viable switchable solvent.

Recommendations

Switchable Solvents

Switchable solvents show a lot of promise as a viable reaction medium. Thiirane oxide proved to be a very good dipolar, aprotic solvent that we could remove by heating. However, the inability to reform the solvent from the reverse reactions makes thiirane oxide unusable in most applications, except for possibly a few specialty systems. Piperylene sulfone shows a great deal of promise. It has good solvent characteristics, and the reverse reaction is certainly possible.

Even if piperylene sulfone does prove to be a viable switchable solvent, there is room for improvement. One of the products is sulfur dioxide, which is decidedly unfriendly to the environment. The goal of the switchable solvent is the same: to create a molecule that can drastically change properties on demand. I think that we should be looking at a number of different options for the next generation of switchable solvents.

Dr. Philip Jessop at Queen's University has worked to characterize a reversible ionic liquid that his group has developed. Ionic liquids are salts that are liquid at (or near) room temperature and they have gained attention over the last several years due to their abilities as solvents, as well as their vanishingly low vapor pressures. It is this characteristic of their low vapor pressures that makes them attractive as environmentally

benign solvents. Dr. Jessop has developed a solvent that turns from a molecular (non-ionic) liquid into an ionic liquid upon exposure to CO₂ gas, and then turns back to the molecular liquid upon exposure to N₂ or Ar gas. Specifically, he has found that exposing a 1:1 mixture of DBU (1,8-diazabicyclo-[5.4.0]-undec-7-ene) and an alcohol to carbon dioxide will form an ionic liquid, as in Figure 5-1.

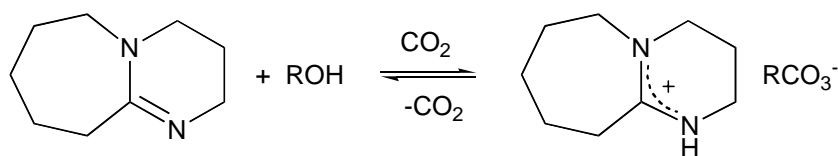


Figure 5-1. Reaction of DBU, alcohol, and CO₂ to form ionic liquid

The molecular liquid has markedly different properties from the ionic liquid. Theoretically, one could run a one step of a reaction in the less polar molecular liquid, and then convert to the ionic liquid for a subsequent step or easier separation. This would eliminate the need to remove and change solvents for each reaction step. The ionic liquid has been characterized spectroscopically. Dr. Jessop reports an E_T30 value of 184 kJ / mol for the liquid under N₂ pressure and a value of 222 kJ / mol under CO₂ pressure.

Another example of the type we are investigation is the cyclization of a carbonate, as in Figure 5-2.

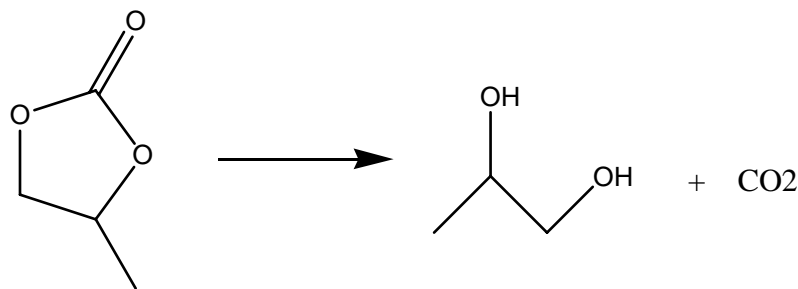


Figure5-2. Decomposition of propylene carbonate to di-ol and CO₂.

Propylene carbonate is very polar and has a dielectric constant of 62.9 and an Et(30) value of 195 kJ / mol. It decomposes to form the di-ol and carbon dioxide, both of which are nonpolar. If we could find a way to make the reverse reaction, then this would represent an ideal candidate since propylene carbonate is already used as a green solvent. While this specific reaction may not be exactly the goal, it represents the type of reaction that we should look at: a drastic change in solvent properties. The molecule goes from a highly polar molecule to two nonpolar molecules.

Gas-Expanded Liquids

Gas-expanded liquids are becoming increasingly popular in research. They offer the potential to greatly enhance reaction rates, while making product separation easier. We were unsuccessful in synthesizing our probe for the microstructure, trityl peroxide. I believe that the silicon derivative will afford us the same advantages as trityl peroxide, yet with an easier synthesis.