Reaction Monitoring in Supercritical Fluids by Flow Injection Analysis with Fourier Transform Infrared Spectrometric Detection

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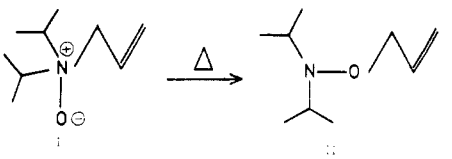
The advantages of direct reaction monitoring using supercritical fluids as solvents in conjunction with Fourier transform infrared spectrometry (FTIR) are illustrated. A capillary system was used in the "flow-injection analysis" mode for the study of the decomposition of allyldiisopropylamine oxide. The solvation effects of supercritical carbon dioxide were monitored as a function of solvent density.

Owing to certain unique physical properties of supercritical fluids (systems above their critical temperatures and near critical pressures), numerous benefits may be found in their use as solvent media. The possible uses of supercritical fluids in organic chemistry were recently discussed by Squires et al (*1*). The mass transfer processes in supercritical fluids are approximately 2 orders of magnitude faster than those in liquids; this fact translates itself into advantages for certain (mass-transfer limited) reactions, extraction processes, and fast chromatography. The solvating power of supercritical fluids, being a sensitive function of pressure, can be easily controlled during such processes. For example, Liphard and Schneider (*2*) showed that the solubility of squalane in supercritical carbon dioxide varies by a factor of 10^{10} when the pressure is increased from 0 to 395 atm. Significant changes in the solvation properties of supercritical fluids with increasing pressure are also indicated by appreciable changes in the dielectric constant. At 50 °C, the static dielectric constant of CO_2 varies from 1 to 1.8 over the pressure range of 0 to 1700 atm (*3*). By use of supercritical fluids as solvents, a wide range of interactions can be studied without changing the chemical nature of a solvent or temperature.

Advantages to be gained from Fourier transform infrared spectrometry (FTIR) in studying various chemical processes are well-known: (1) excellent sensitivity at fast spectral acquisition; (2) the capability to simultaneously monitor the variation of absorption bands. Since certain supercritical fluids (e.g., carbon dioxide or xenon) are relatively transparent in FTIR, they can serve as convenient solvents while a great variety of other organic molecules are monitored in such media.

In the first communication on capillary supercritical fluid chromatography (SFC), a suggestion was made (*4*) that appropriate mobile phases could facilitate solute measurements in the infrared spectral region. The following experiments have demonstrated that supercritical carbon dioxide (*5*, *6*) and xenon (*7*) permit an effective combination of capillary SFC and FTIR spectrometry. The purpose of this communication is yet another demonstration of the advantages of the capillary flow systems, this time for direct reaction monitoring. In this capacity, an earlier described (*6*) capillary supercritical-fluid chromatographic system was used in a "flow injection analysis" mode (*8*) for kinetic measurements on a model reaction.

Just as with capillary SFC (*6*), a capillary flow apparatus with a short, uncoated fused silica column provides a convenient addition to high-pressure FTIR spectrometry, since high pressures are easily contained at extremely small volumes (of the order of microliters) and the flow rates used (microliters per minute). The combined use of supercritical fluids as solvents and FTIR for detection, therefore, may provide a powerful means for studying closely various kinetic and structural parameters. Alternatively, reaction product separation and analysis could be accomplished by capillary SFC/FTIR. As an example presented here, the unimolecular conversion of allyldiisopropylamine oxide (I) to *O*-allyl-*N*,*N*-diisopropylhydroxylamine (II) was monitored using supercritical carbon dioxide as the solvent.



EXPERIMENTAL SECTION

A schematic of the experimental setup is shown in Figure 1. While the system pressure was controlled by a Varian 8500 high-pressure pump, a Varian 1200 gas chromatographic oven controlled the capillary temperature. Details of the high-pressure flow cell have been described in a previous publication (*6*).

A 0.2-μL plug of reactant (sample obtained through courtesy of J. J. Gajewski of our department) was injected, without dilution, into a 1-m section of a 250 μm, i.d., fused silica capillary. The capillary was maintained at 50 ± 0.5 °C with a gas chromatographic oven, which served as the inlet to the high-pressure IR flow cell (nominal volume of 2 μL, optical path length of 1 mm, and cross sectional area of 2 mm^2). The flow cell was also maintained at 50 ± 1 °C. The outlet of the flow cell was a section of 250 μm, i.d., capillary. A shut-off valve (used to trap sample in the IR flow cell) was placed between the outlet fused silica and a 20-m section of 50 μm, i.d., glass capillary restrictor (flow controlling device). The infrared spectrometer used in these experiments was an IBM IR/85 instrument (IBM Instruments, Inc., Danbury, CT) equipped with a narrow bandwidth (4000–669 cm^{-1}) mercury cadmium telluride (MCT) detector with $D^* = 5.96 \times 10^9$ cm $Hz^{1/2}$ W^{-1}. (The D^* is a figure of merit associated with the detector. The larger the value of D^*, the more sensitive the detector. A detailed comparison of detectors may be found elsewhere (*9*).) Because the reaction was thermally induced, the sample was maintained at −77 °C until injection time. The sample was then warmed to liquid state (by allowing it contact with the ambient temperature) and injected neat into the Valco high-pressure valve. The large heat transfer rate across the small capillary ensured a quick rise in the sample temperature from −77 °C to the reaction temperature. Total time from −77 °C bath to reaction temperature was typically less than 2 min.

During the kinetic experiments, the reactant (N-oxide) was passed into the high-pressure flow cell, and trapped there by stopping the flow. Approximately 40 interferograms were accumulated at a rate of 2.5 interferograms/s, every 3 min, over the total run times of typically 4–6 h. Each set of 40 interferograms

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Table I. Variation of Rate Constant as a Function of Solvation

solvent	solubility parameter	pressure, atm	temp, °C	density,[c] g/cm³	k + std,[d] s^{-1} pathway I	k + std,[d] s^{-1} pathway II
CO_2	2.62[a]	68.0	50	0.18	$(8.2 + 0.4) \times 10^{-5}$	
	4.88[a]	98.67	50	0.45		$(1.8 + 0.2) \times 10^{-4}$
	6.42[a]	115.7	50	0.68		$(1.1 + 0.1) \times 10^{-4}$
$CDCl_3$	9.3[b]		17.2	liquid	1.12×10^{-4}	

[a] Reference 10. [b] Reference 11. [c] Reference 12. [d] Standard deviation.

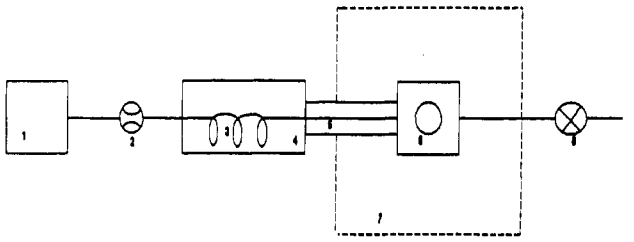


Figure 1. Schematic of the flow injection analysis system with high-pressure FTIR: (1) Varian 8500 syringe pump; (2) Valco injection valve with 0.2-μL loop; (3) 1-m section of fused silica capillary; (4) Varian 1200 gas chromatographic oven; (5) heated transfer line; (6) a heated high-pressure flow cell; (7) IBM Model IR-85 spectrometer; (8) on–off valve.

was coadded before the transform was taken to produce the 4-cm^{-1} IR spectrum. A spectrum of supercritical carbon dioxide was used as the measure of the incident light intensity. No data manipulation such as spectral subtraction or base line correction was used in this study.

RESULTS AND DISCUSSION

Solvation effects may broadly be classified in terms of chemical forces (complex formation, hydrogen bonding, etc.) and weak physical forces of the van der Waals type. An intent of this study was to evaluate the effect of increasing physical forces on the model reaction by increasing the density of supercritical carbon dioxide. This solvent medium was chosen because carbon dioxide is relatively transparent to mid-IR radiation over an appreciable density range (*6*).

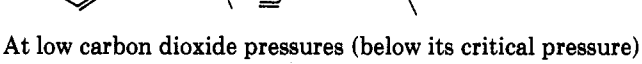
Substantial solvent effects were observed as a function of pressure and, therefore, density variation. Table I provides a summary of experiments included in this study. Initially, at a carbon dioxide density of 0.18 g/cm³, the measured spectra showed an absorbance band at 1218 cm^{-1}, forming and increasing in intensity as a function of time. The intensity of the 1218-cm^{-1} band [due to C–O stretching of the reaction product (II)] was plotted against the intensity of the 2978-cm^{-1} band (C–H stretching) to compensate for changes in concentration of the reacting mixture in the cell as a function of time. From the slope of a plot of the log (absorbance at 1218-cm^{-1} band/absorbance at 2978-cm^{-1} band) vs. time, the reaction rate constant was determined to be $(8.2 \pm 0.4) \times 10^{-5}$ (rate constant ± standard error).

When the density of carbon dioxide was increased to 0.45 g/cm³, no absorbance band formed at 1218 cm^{-1}; instead, two bands appeared and increased as a function of time at 1728 cm^{-1} and 1610 cm^{-1}. These bands correspond to the C=O stretching and C=C stretching of a conjugated aldehyde and alkene system. With the increased density of solvent, no further *O*-allyl-*N*,*N*-diisopropylhydroxylamine was detected. The absorbance bands listed above are those of acrolein when solvated by supercritical carbon dioxide, as found in a separate experiment. The formation of an aldehyde as a product in the decomposition of an N-oxide was unexpected. To our knowledge, there is only one other report of this type of reaction, that for the decomposition of benzyldiethylamine oxide (*13*). The rate constant determined by monitoring the increase in the 1610-cm^{-1} band $[(1.8 \pm 0.2) \times 10^{-4}\ s^{-1}]$ was approximately equal but opposite in sign to the rate constant determined by monitoring the decrease in the 920-cm^{-1} band (N–O stretching of allydiisopropylamine oxide).

The final solvent conditions studied were 115.7 atm (P_R = 1.59) and 50 °C (T_R = 1.06) corresponding to a carbon dioxide density of 0.68 g/cm³. At these conditions two bands, 1728 cm^{-1} and 1610 cm^{-1}, increase with increasing time. Under these circumstances, acrolein was the primary product with a rate constant of $(1.1 \pm 0.1) \times 10^{-4}\ s^{-1}$.

The solvation effects of supercritical carbon dioxide on the thermal decomposition of allyldiisopropylamine oxide seem complex in that both rearrangement and elimination reactions occur as a function of solvent density variation. When liquid deuterated chloroform was the solvent, only the rearrangement pathway was observed using proton NMR detection (*14*). The rate constant (*14*) for the rearrangement reaction in deuterated chloroform (T = 17.2 °C) is also shown in Table I. Additionally, Table I lists the Hildebrand (or one-component) solubility parameters (*10*, *11*, *15*, *16*) for the solvents studied. The solubility parameter is a measure of the cohesive forces holding a liquid together. It is primarily a measure of "physical" forces and therefore does not include solvation effects such as solvent–solute interactions. As the density of carbon dioxide increases, its solubility parameter also increases and begins to approach that of chloroform. Roughly speaking then, if the physical forces of solvation (the molecular cohesive energy) dominate, then the high-pressure carbon dioxide experiment should compare favorably with the experiment in which deuterated chloroform was used. This was not the case, as only for the lowest density of carbon dioxide was the rearrangement reaction dominant. This seems to imply that "chemical" forces such as more intimate solute–solvent interactions significantly affect the thermal decomposition of allyldiisopropylamine oxide in supercritical carbon dioxide.

The most likely explanation for the kinetic data is that the reaction follows two pathways.



At low carbon dioxide pressures (below its critical pressure) pathway I dominates. Pathway II proceeds so slowly at this pressure that over the time scale studied (approximately 3 h) no elimination occurs. When the pressure of carbon dioxide is increased above the critical point, pathway I becomes much faster, but the elimination reaction rate is increased to a much greater extent to the point that no *N*,*N*-diisopropyl(allyloxy)amine is detected. If this proposed mechanism is true, then the measured rate constants would be due primarily to the rearrangement reaction because the rearrangement is the rate-limiting step in the high-pressure reactions. The transition state for the rearrangement reaction (pathway I) is believed to involve charge separation (*14*) and, therefore, an increase in reaction rate is predicted for increasing solvent density. A consistent trend in rate constant variation with increasing solvent density was not discernible. It may be of interest to compare the course of this reaction in more nonpolar supercritical fluids, such as xenon.

While further studies are necessary to identify the exact mechanism for the decomposition of allyldiisopropylamine oxide, the present study has shown the value of combining a capillary flow system with high-pressure FTIR spectrometry for reaction monitoring. Other spectroscopic techniques may be adaptable to similar measurements, as indicated by the recently reported combinations of capillary SFC with a mass spectrometer (*17*) or a photodiode array system (*18*). In addition, the setup described in this communication may represent the smallest flow injection analysis (*8*) system reported to date.

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LITERATURE CITED

(1) Squires, T. G.; Renier, C. G.; Aida, T. *Fluid Phase Equilib.* **1983**, *10*, 261-268.
(2) Liphard, K. G.; Schneider, G. M. *J. Chem. Thermodyn.* **1975**, *7*, 805-814.
(3) Michels, A.; Kleerkoper, L. *Physica (Amsterdam)* **1939**, *6*, 586-590.
(4) Novotny, M.; Springston, S. R.; Peaden, P. A.; Fjeldsted, J. C.; Lee, M. L. *Anal. Chem.* **1981**, *53*, 407A-414A.
(5) Shafer, K. H.; Griffiths, P. R. *Anal. Chem.* **1983**, *55*, 1939-1942.
(6) Olesik, S. V.; French, S. B.; Novotny, M. *Chromatographia* **1984**, *18*, 489-495.
(7) French, S. B.; Novotny, M. *Anal. Chem.* **1986**, *58*, 164-166.
(8) Ruzicka, J.; Hansen, E. L. "Flow Injection Analysis", in *Chemical Analysis*; Elving, P. J., Winefordner, J. D., Eds.; Wiley: New York, 1981; Vol. 62.
(9) *Optical and Infrared Detectors*; Keys, R. J., Ed.; Springer-Verlag: Berlin, 1977.
(10) Schoenmakers, P. J. *J. Chromatogr.* **1984**, *315*, 1-18.
(11) Barbon, A. F. M. *Chem. Rev.* **1975**, *75*, 731-753.
(12) IUPAC *International Thermodynamic Tables of the Fluid State, Carbon Dioxide*; Pergamon Press: Oxford, 1976.
(13) Culvenor, C. C. J. *Rev. Pure Appl. Chem.* **1953**, *3*, 83-114.
(14) Emrani, J.; Gajewski, J. J., Department of Chemistry, Indiana University, private communication, September 1984.
(15) Dack, M. R. J. *J. Chem. Educ.* **1974**, *51*, 231-234.
(16) Schoenmakers, P. J.; Billiet, H. A. H.; de Galan, L. *Chromatographia* **1982**, *15*, 205-214.
(17) Smith, R. D.; Felix, W. D.; Fjelsted, J. C.; Lee, M. L. *Anal. Chem.* **1982**, *54*, 1883-1885.
(18) Gluckman, J.; Sheily, D.; Novotny, M. *Anal. Chem.* **1985**, *57*, 1546-1552.

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Versatile Automatic Development System for Flow Injection Analysis

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A computer-controlled automatic analyzer has been developed to facilitate the rapid development of novel analytical methods based on flow injection analysis (FIA) through the use of mathematical techniques such as modified simplex optimization. The apparatus allows variation of flow rates, pH, and reagent concentration in one or more sample or carrier streams and can accommodate spectrophotometric or electrochemical detectors. The system software, written in BASIC, is menu-driven and interactive. It includes a modified simplex optimization procedure that has permitted automated optimization of analytical methods, yielding an improvement in sensitivity equal to that obtained in earlier manual experiments. The results obtained are discussed, as are the design and execution of the apparatus and software.

One of the crucial problems of automatic analysis is how to speed up or automate the development of an automated method or system. The difficulty is especially acute if one has such diversity of workload that an automatic method needs to be up and running quickly and is subsequently discarded after a month or so of intensive use.

Flow injection analysis (FIA) systems (*1-3*) afford a means of studying the general problem in a concrete way; they are versatile, easy to configure, have a rapid response, and can simulate many other systems. However, in developing a method based on even a simple FIA system, one may need to adjust five or more variables in order to establish optimum conditions for the analysis. This can be very time-consuming if a conventional univariate optimization is undertaken manually, and indeed where interactions exist between the variables, one is unlikely to find the true optimum (*4*).

One solution to this problem would lie in the use of an automated instrument, in which the experimental conditions of concentration, flow rate, pH, etc. may be varied according to a preprogrammed pattern under computer control. The ability to control the system parameters in this way would allow a conventional univariate optimization to be performed much more quickly than is possible by manual means.

In this approach, however, the number of experiments to be performed is still extremely large (*4*). A more economical scheme would be to use the automatic control facilities to carry out a modified-simplex optimization (*5, 6*). This optimization

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