Tetrahedron Letters,Vol.29,No.18,pp 2171-2174,1988
Printed in Great Britain

0040-4039/88 $3.00 + .00
Pergamon Press plc

A METHOD FOR THE FLASH VACUUM THERMOLYSIS OF NON-VOLATILE COMPOUNDS

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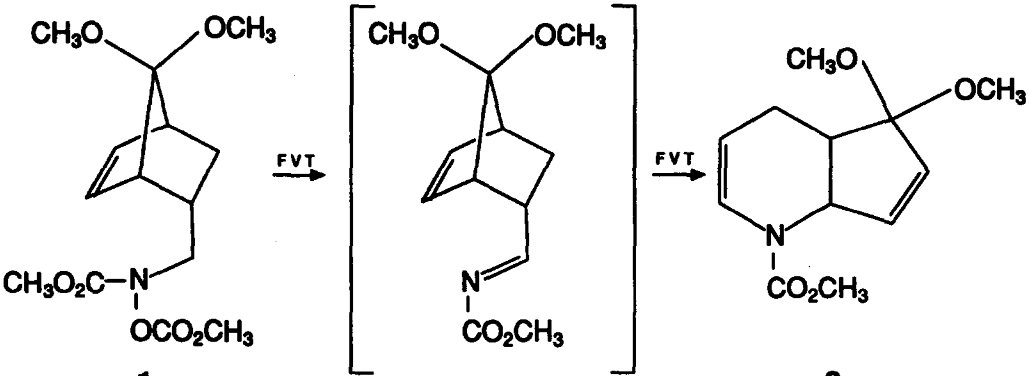
SUMMARY: A method for evaporation of non-volatile compounds is described. Examples are given of the application of this method to flash vacuum thermolysis of organic compounds.

The evaporation of a substrate through a hot tube at low pressure (Flash Vacuum Thermolysis, FVT) is a simple although effective technique for performing thermal chemistry.[1] In contrast to thermal reactions performed in the condensed phase, the high dilution of the gas phase suppresses unwanted side reactions such as polymerization. Furthermore, the rapid cooling of the condensate to low temperature [$N_2(l)$, -196°] allows for the isolation of reactive compounds. The ability of Flash Vacuum Thermolysis to prepare unusual molecular arrangements[1] as well as to probe reaction pathways[2] is impressive. For example, FVT has been a key step in preparations of fundamentally important molecules such as vinyl amine,[3] vinyl alcohol,[4] silaethenes[5] and nitrosyl hydride[6] to name a few.

The primary difficulty in the general application of FVT to problems in chemistry is the transformation of the reactant from the condensed to the gas phase. Many complex molecules of interest have a negligible vapor pressure at room temperature requiring the application of heat to induce evaporation. Unfortunately, this step frequently causes the decomposition of a large number of compounds before evaporation occurs. The use of inert carrier gases,[7] evaporation from thin films, and special methods such as "spray thermolysis"[8] are examples of techniques that have been used to address this problem.

We have also been concerned with this problem in our research program[9] and have discovered that solvent assisted sublimation can be very effective at transferring non-volatile compounds into the gas phase *without* decomposition. The procedure is relatively simple. The reactant is dissolved in an inert solvent that sublimes rather than distills under the evaporating conditions. The solution is frozen in $N_2(l)$ and the thermolysis apparatus[10] is evacuated to the desired pressure. The flask containing the frozen solution is then heated to a high temperature (350-450°C). The frozen solution in contact with the hot surface evaporates carrying the dissolved substrate into the thermolysis oven. The temperature of the thermolysis oven can be adjusted[11] to a temperature necessary to induce the desired thermal reaction. Convenient sample sizes are usually 200 mg or less although larger quantities can be used.[12]

For example, in connection with a project concerned with the 1-aza Cope rearrangement, we were interested in preparing the pyridine **2** from the hydroxamic acid derivative **1**. Unfortunately, **1** was not sufficiently volatile and all attempts to directly evaporate it resulted in its decomposition. However, the conversion of **1** to **2** could be readily accomplished by employing the above evaporation technique. Evaporation of a frozen benzene solution containing 10% of **1** gave, after work-up, a 27% yield of the desired pyridine **2**.

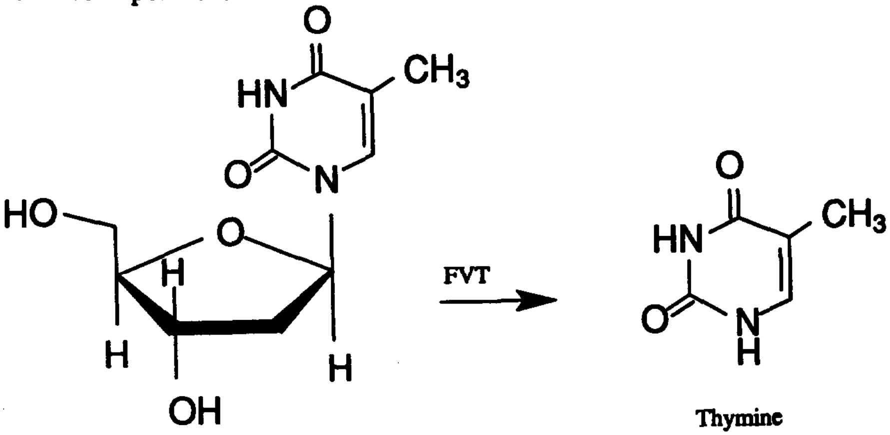


1 **2**

The success of this method for the evaporation of non-volatile compounds[13] is probably due to a number of factors, among which are: 1. Reactive substrate molecules are isolated from each other by the frozen matrix and most of the substrate, except for sample in direct contact with the hot surface, remains cool.[14] 2. The sample that does experience the hot surface evaporates rapidly with the solvent acting as a carrier gas.

The major requirements for suitable solvents for this technique are that they be inert and sublime under the evaporation conditions. We have observed that cyclohexane and *t*-butanol, in addition to benzene, meet these criteria. Inspection of its phase diagram indicates that water, a potentially valuable solvent for the evaporation of polar samples, should be a successful evaporation solvent. However, initial experiments were discouraging. The sample adhered to the evaporation flask allowing rapid heat transfer causing rapid evaporation. This rapid evaporation increased the local pressure which caused the sample to melt and the solvent ultimately distilled. This problem was solved simply by silylation of the evaporation flask. This procedure presumably created a hydrophobic layer on the surface of the evaporating flask.[15]

For example, using water as a solvent, a 5% solution of thymidine was evaporated through the thermolysis oven. If the oven temperature was adjusted to 350°C, then essentially all of the thymidine was recovered unchanged. Increasing the oven temperature resulted in the appearance of thymine as a component of the product mixture. With an oven temperature of 500°C, essentially all of the thymidine had disappeared producing an 80% yield of thymine. Although the structures of the other organic compounds are under investigation, the importance of these preliminary experiments is that they demonstrate that a polar non-volatile molecule, such as thymidine, can be introduced into the gas phase without decomposition.



Thymidine

Thymine

In summary, solvent assisted sublimation can be an important method for the transformation of non-volatile compounds into the gas phase. There are a number of applications for which this method should be useful. For example, synthetic chemistry as well as mechanistic studies can benefit by use of this method because it considerably extends the range of compounds to which gas phase reactions can be applied. Another possible application is in mass spectroscopy where the introduction of non-volatile compounds into the ionization chamber has been a continuing problem. Also, the deposition of materials from the vapor phase is developing as an important technique in solid state chemistry.[16]

Acknowledgement. Support for this research from the National Science Foundation and the Petroleum Research Fund, administered by the American Chemical Society are gratefully acknowledged. We also thank Xinqi Zhao of the Beijing Institute of Technology for some contributions to the experimental part of this paper.

References and Footnotes

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(7) See reference 1e.

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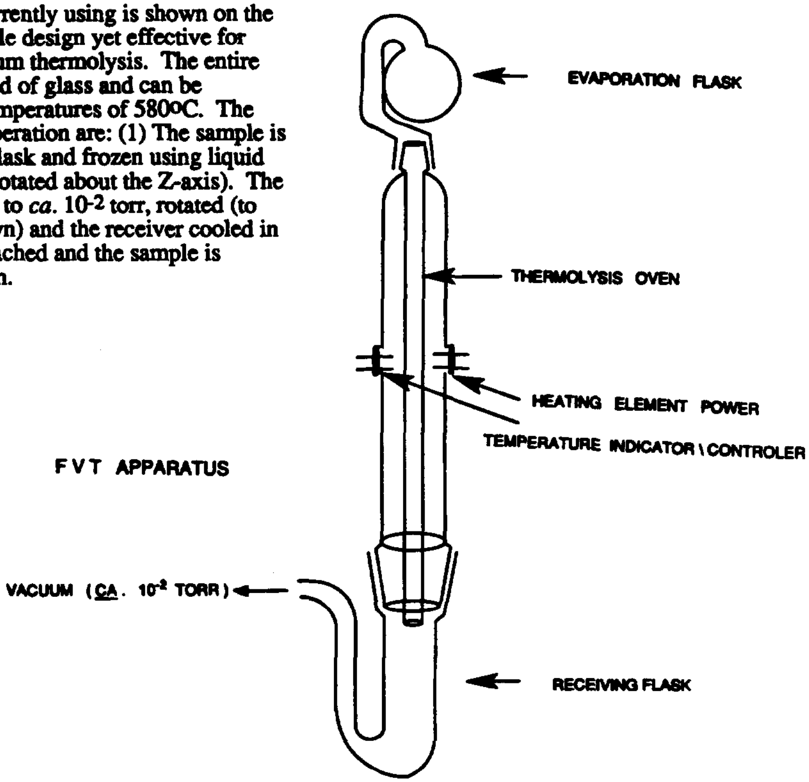
(10) The apparatus we are currently using is shown on the right. It is a very simple design yet effective for performing flash vacuum thermolysis. The entire apparatus is constructed of glass and can be operated up to oven temperatures of 580°C. The steps involved in its operation are: (1) The sample is added to the receiver flask and frozen using liquid N_2 (The apparatus is rotated about the Z-axis). The apparatus is evacuated to *ca.* 10^{-2} torr, rotated (to the configuration shown) and the receiver cooled in N_2(*l*). The oven is attached and the sample is heated using a heat gun.



FVT APPARATUS

(11) We use a solid state temperature controller with a type K thermocouple (model D921K35F20) available from Omega Engineering, P.O. Box 4047, Stamford, CT 06907. The heater for the thermolysis oven was constructed by from 18 gauge resistance wire (ca 0.41 ohms/ft.).

(12) There can be problems with large samples using our method. This is because it is difficult to control the *rate* of evaporation, which is dictated mainly by the surface area of the sample. Higher evaporation rates result in shortened contact times requiring higher oven temperatures to induce the thermal chemistry. For example, the elimination of acetic acid from a 0.5 mL sample of a 10% benzene solution of cholesterol acetate required 500-525°C whereas a sample size of 12 mL required 575-600°C. The sample recoveries are usually very good, 98% or better.

(13) This method is also useful for controlling volatility when applying FVT to very volatile compounds (such as cycloheptatriene: Klump, K.N. and Chesick, J.P. *J. Am. Chem. Soc.* **1963**, *85*, 130.)

(Received in USA 9 December 1987)