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# Thermal Hazard Evaluation of Vilsmeier Reaction with DMF and MFA

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## Abstract:

**The Vilsmeier reaction is one of the important reactions in the organic photoconductor industry, and quantitative information of thermal hazards of the reaction is needed for process control and safety. In this report, the thermal hazards of Vilsmeier reaction are investigated, and heats of reaction are measured using reaction calorimeters. It is found that the thermal decomposition of the Vilsmeier complex is the maximum hazard in this reaction and that the selection of reaction procedure and solvent might be a key for the suitable reaction.**

## 1. Introduction

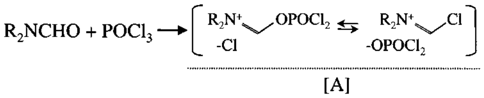
Formylation of aromatic compounds using the Vilsmeier complex is a popular reaction in the chemical industry, especially in inorganic photoconductor manufacturing. However, it is well-known that the complex has a thermal instability;[1,2] a quantitative understanding is needed for the process safety and optimization. The Vilsmeier complex, shown as [A] in Scheme 1, is usually prepared by the reaction of phosphorus oxychloride ($POCl_3$) and *N*,*N*-dimethylformamide (DMF) or *N*-methylformamide (MFA).[3,4]

Immonium salt such as [B] is an intermediate in the Vilsmeier reaction, and it is converted into formyl compound by hydrolyzation according to Schemes 2 and 3.

Since the theoretical calculation of the heat of decomposition of the complex is generally difficult because of its structure, experimental measurement of thermal behavior using the reaction calorimetry technique is useful for the hazard evaluation of this system.

When the Vilsmeier complex is produced, it is considered that $POCl_3$ is solvated, with coordination to DMF.[5] The reaction heat of the Vilsmeier complex depends on the temperature of the system. Furthermore, the equilibrium position of the complex formation may also depend on the temperature, and a shift in this equilibrium position may generate heat.

***Scheme 1.*** **Preparation of Vilsmeier complex**



***Scheme 2.*** **Typical Vilsmeier reaction (formation of immonium salt)**

$$\mathrm{ArH} + [\mathrm{A}] \longrightarrow \underbrace{\mathrm{ArCH{=}N^{+}R_2{\bullet}O^{-}POCl_2}}_{[\mathrm{B}]} + \mathrm{HCl}$$

***Scheme 3.*** **Typical Vilsmeier reaction (hydrolyzation of immonium salt)**

$$[\mathrm{B}] + \mathrm{H_2O} \longrightarrow \mathrm{ArCHO}$$

In the chemical industry, two typical procedures of the formylation process using the Vilsmeier reaction are considered. In the first procedure, the Vilsmeier complex is formed, and the substrate is added to the solution in which the complex is solved to form the salt; after that aldehyde is obtained by hydrolyzation of the salt. In the second procedure, the substrate is dissolved in the solvent, and $POCl_3$ is dosed into the solvent to form the salt and the complex simultaneously; consequently, the formyl compound is obtained by the hydrolyzation. The thermal hazard of the Vilsmeier reaction is different in the operation procedure of formylation.

In this report, the thermal hazard of the Vilsmeier reaction is examined by using reaction calorimeters such as RC1, C80, and ARC, and the physical and chemical heats of reaction are determined. The adequate procedure is investigated by the worst-case scenario in this reaction.

## 2. Materials

$POCl_3$ (99 wt % purity) and DMF (99.5 wt % purity, water-free) or MFA (98 wt % purity, water-free) were used as the Vilsmeier complex reagents, and allylic amine compound TPD (99 wt % purity, solid) was used as the substrate. Formylation of TPD with the Vilsmeier reaction is shown in Scheme 4.

## 3. Experimental Section

The reaction calorimeter Mettler-Toledo RC1 was used. Figure 1 shows a schematic drawing of RC1. RC1 works to measure the temperature difference between the contents of reactor and the heat-transfer fluid in the reactor jacket, and it controls the fluid temperature according to the desired control mode such as $T_r$ mode, $T_j$ mode, or adiabatic mode. At $T_r$ mode, the temperature of the reactants is kept constant,

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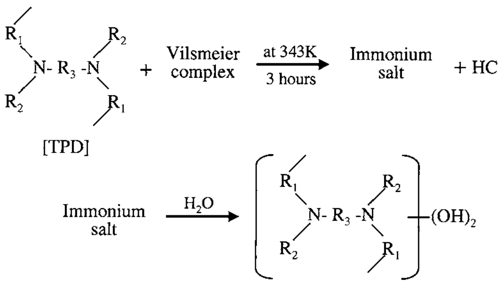
***Scheme 4.*** **Formylation of TPD with Vilsmeier reaction**



and the temperature of the jacket is kept constant at $T_j$ mode. The heat release rate is determined on the basis of the heat and mass balances in the reactor. In addition, the reactor was equipped with temperature sensors, calibration heaters, and a reflux unit. The SV01-type glass reactor with the volume of 0.8 L equipped with a paddle stirrer was used.

Experiments were carried out in semi-batch operation as follows. At first, an adequate solution such as DMF, MFA, or TPD dissolved DMF was heated to the desired temperature in the RC1 reactor. After obtaining thermal equilibrium at the desired temperature, $POCl_3$ was added dropwise into the reactor with a transfer pipet, and then the heat generation was measured. Figure 2 shows the typical heat-release rate versus time profile measured by RC1. Experiments were performed as shown below, respectively.

1. The reaction heat ($Q$) of the Vilsmeier complex in the DMF/$POCl_3$ system at isothermal condition ($T_r$ mode) was examined at a constant temperature between 288 and 323 K. The volumes of DMF and $POCl_3$ were 200 and 10 mL, respectively, and the duration of dosing was 2 min.

2. The dissolution heat of the Vilsmeier complex was measured by adding 10 g of $H_2O$ into the solution above at 298 K.

3. Formylation using the Vilsmeier complex proceeded in a manner similar to that above. First 2.0 or 5.0 g of TPD was dissolved in 200 mL of DMF; 10 mL of $POCl_3$ was added dropwise for 2 min at 343 and 323K, and the heat generation was measured for several hours. Then adequate $H_2O$ was added for hydrolyzation at 298 K in the solution of DMF with immonium salt and Vilsmeier complex, and the heat generation was recorded for several hours, also. Aldehyde was then obtained

The thermal behavior of the Vilsmeier complex was also measured with a heat conduction calorimeter: Setaram C80. The Vilsmeier complex that was formed in DMF/$POCl_3$ system at 298 K was heated to 333 K at a heating rate of 2 K $min^{-1}$. A SUS-316 stainless steel pressure vessel with an inner glass vessel was used.

The thermal stability of the Vilsmeier complex was also investigated using an adiabatic calorimeter (Arthur D Little), accelerating rate calorimeter ARC. Since the thermal stability of the Vilsmeier complex of the DMF/$POCl_3$ system has already been reported,[1,5] the measurement was carried out for the complex of MFA/$POCl_3$ system. ARC was operated in a heat−wait−search mode with steps of 5-K. A titanium bomb was used, and the sample mass was approximately 4 g.

## 4. Results and Discussion

**4.1. Thermal Hazards of the Vilsmeier Complex.** From the results of RC1 experiments, the heat of generation of the Vilsmeier complex in DMF/$POCl_3$ system at $T_r$ mode between 288 and 323 K showed a constant value as −57 kJ/mol at any temperature.

Although the heat generation was observed during formation of the Vilsmeier complex, neither exotherm nor endotherm was found by C80 scanning of the complex. It is considered that the equilibrium of the Vilsmeier complex does not depend on the temperature, otherwise the complex phase does not exist.

**4.2. Influence of the Solvent on the Thermal Stability of the Vilsmeier Complex.** From the ARC data, exothermic peaks of the Vilsmeier complex of MFA/$POCl_3$ system appeared at 339 and 488 K. Table 1 shows the ARC test results compared with those for the DMF/$POCl_3$ system about the first exothermic peak. As a result, the maximum heating rate and the onset temperature of the complex in the MFA system showed values similar to those of the DMF system. However, the heat of generation of the complex in MFA system measured by RC1 was −27kJ/mol, half of that in the DMF system. Since the thermal stability of the Vilsmeier complex of MFA system is the same level as that of DMF system, it is stated that the thermal hazard of the MFA system is lower than that of DMF system.

**4.3. Heats of Reaction in Formylation using the Vilsmeier Reaction.** Table 2 shows the heats of reaction of formylation (DMF/$POCl_3$ = 6/1) at 323 K. From RC1 data the heats of reaction of the Vilsmeier reaction such as generation and hydrolyzation of the Vilsmeier complex were determined. Although the heats of generation and hydrolyzation of the immonium salt of substrate TPD were also able to calculated from the data of formylation, those were expressed in k $Jg^{-1}$ because the molecular weight of TPD was not well-specified. In this experiment the obtained data involved the heats of the Vilsmeier complex and immonium salt when $POCl_3$ was dosing into the DMF solution in which TPD was dissolved in advance. When hydrolyzation of the immonium solution occurred, the experimental data involved the heats of hydrolyzation of the Vilsmeier complex and immonium salt, likewise. Each heat of reaction could be separated as shown in Table 2. On the other hand the result of chemical analysis of the reaction products with liquid chromatography showed that TPD conversion was nearly 100%.

Next, the influence of the temperature of thermal decomposition of the Vilsmeier complex was investigated. The Vilsmeier complex of 298 K was added dropwise into DMF which was kept at 373, 393, and 413 K. The concentration of Vilsmeier complex was held constant at DMF/$POCl_3$ = 6/1 throughout experiment. Although the heat-release rate showed a sharp dive due to the vaporization of the solution just after dosing the complex at 413 K, it gradually decreased after dosing at 373 K and 393 K as shown in Figure 3. It means that the heat generation at 413 K depends on the dosing rate, and those in other cases depend on the reaction rate. Heats of thermal decomposition of the Vilsmeier

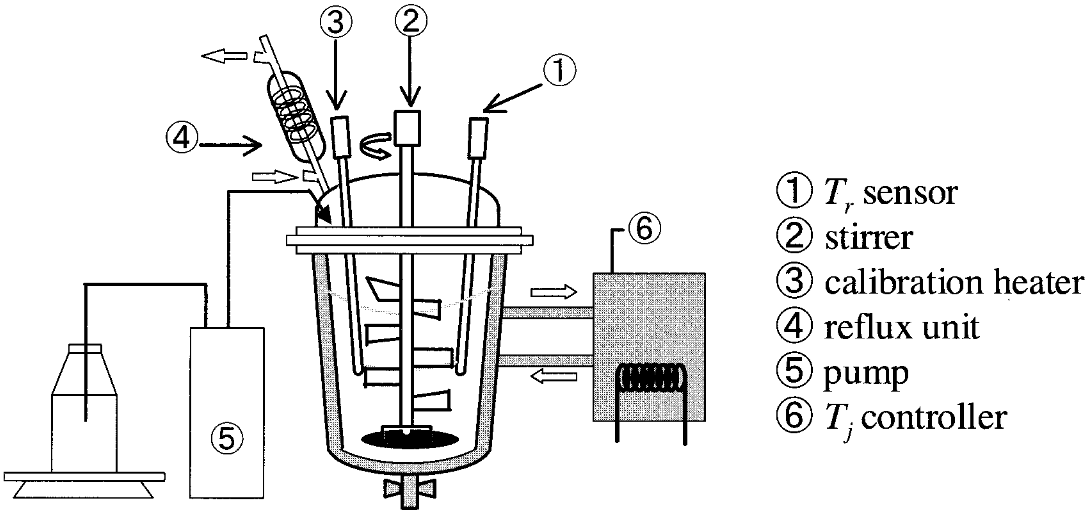


***Figure 1.*** **Schematic drawing of Mettler-Toledo RC1.**

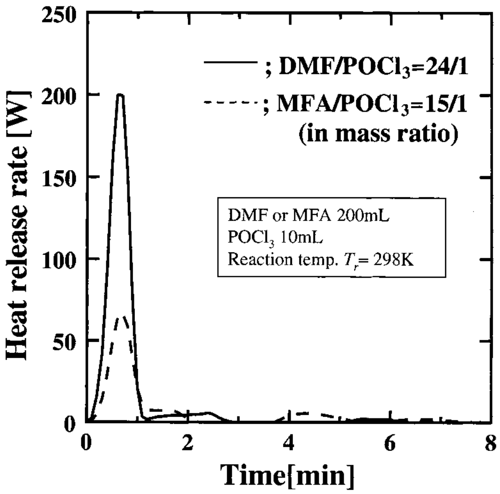


***Figure 2.*** **Heat-release rate versus time profiles of DMF/POCl$_3$ and MFA/POCl$_3$ systems.**

***Table 1.*** **ARC test results of the Vilsmeier complex in different solvent system**

| solvent | POCl$_3$/ solvent | onset temp $T$ [K] | $(dT/dt)_{max}$ [K min$^{-1}$] | thermal inertia [−] |
|---|---|---|---|---|
| DMF [3] | 1/14.4 | 334.3 | 0.071 | $\varphi = 1.57$ |
| MFA | 1/14.9 | 339.5 | 0.102 | $\varphi = 1.59$ |

***Table 2.*** **Heats of reaction ($Q$) in formylation at 323 K**

| reaction | $Q$ |
|---|---|
| generation of Vilsmeier complex | −57 kJ mol$^{-1}$ |
| hydrolyzation of Vilsmeier complex | −178 kJ mol$^{-1}$ |
| generation of immonium salt | −1.13 kJ g$^{-1}$ |
| hydrolyzation of immonium salt | −1.16 kJ g$^{-1}$ |

complex at 37, 393, and 413 K were obtained as 165, 277, and 167 kJ mol$^{-1}$ respectively. From the above data it is concluded that the Vilsmeier reaction at high temperatures can be done safely by controlling the heat balance between the thermal decomposition and vaporization.

Figure 4 shows the ARC results for the complex of DMF/POCl$_3$ = 6/1. The exothermic peaks of the Vilsmeier complex of DMF/POCl$_3$ system appeared at 393 and 453 K. These peaks indicate that the Vilsmeier complex has at least two decomposition pathways, and the self-heat rate shows the coincidence with the pressure release.

From RC1 and ARC results, the following conclusions can be drawn.

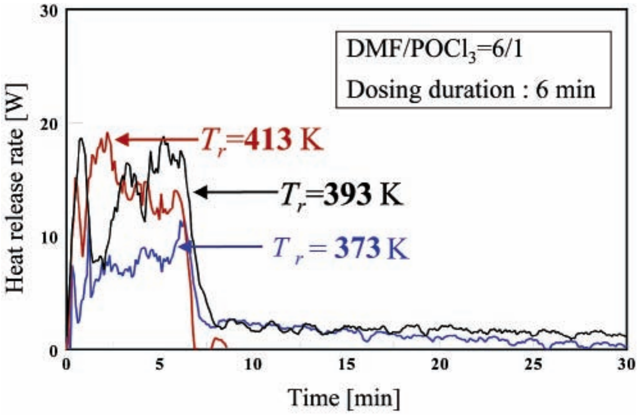


***Figure 3.*** **Influence of reaction temperature on the heat-release rate of the Vilsmeier reaction.**

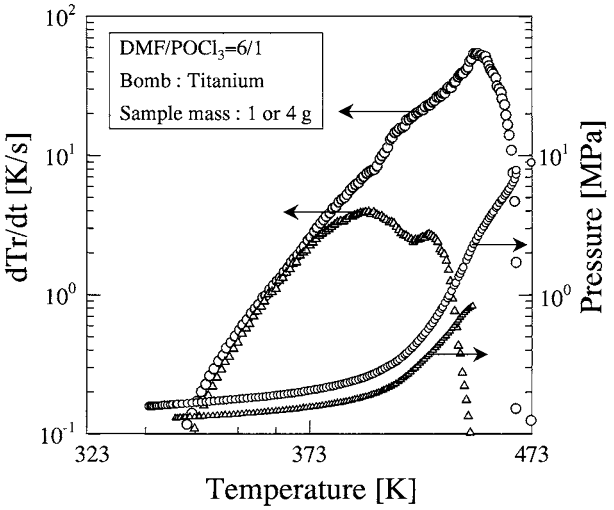


***Figure 4.*** **ARC results of the Vilsmeier complex.**

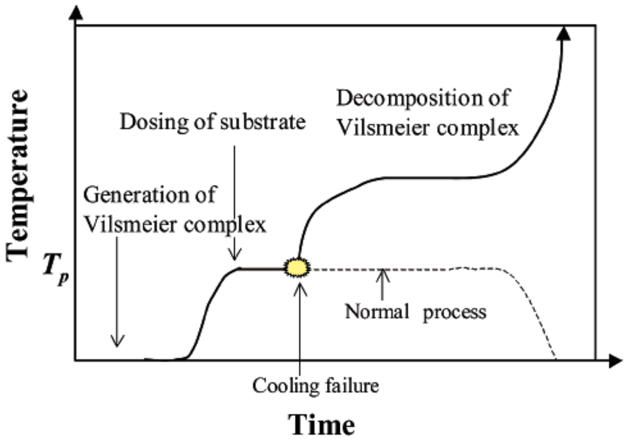


***Figure 5.*** **Worst-case runaway scenario of the Vilsmeier reaction.**

1. Heat-release rate after dosing the complex at 373 and 393 K corresponds to a part of the reaction of the first peak or the reaction of the second peak at ARC.

2. The result from the RC1 at 413 K is a single reaction. This reaction corresponds to the reaction of the second peak at ARC.

3. There are two reasons why the heat of reaction at 413 K is less than that at 393 K.

(1) Since the bubbles were observed in the reactor of RC1 experiment at 413 K and the ARC result shows a pressure rise in the neighborhood of 403 K, the decrease in the heat of reaction is due to the heat of vaporization of the gas generated.

(2) Heat of decomposition at 413 K itself is small.

Therefore, it is concluded from the experiments that the apparent total heat of reaction does not become large at a temperature higher than 413 K.

**4.4. The Worst-Case Scenario in the Vilsmeier Reaction.** Figure 5 shows one of the worst-case scenarios: a runway reaction of the Vilsmeier reaction. In this scenario an undesired reaction is caused by the thermal decomposition of the Vilsmeier complex.[6−8] In the case of adding substrate into the solution in which the Vilsmeier complex is formed in advance, there is a high potential hazard of thermal decomposition of the Vilsmeier complex. For example, adding the substrate solution with water may raise the temperature in the reactor because of the heat of dissolution or hydrolyzation of the complex or the heat of dilution of substrate solution, and then it leads the decomposition of the complex.

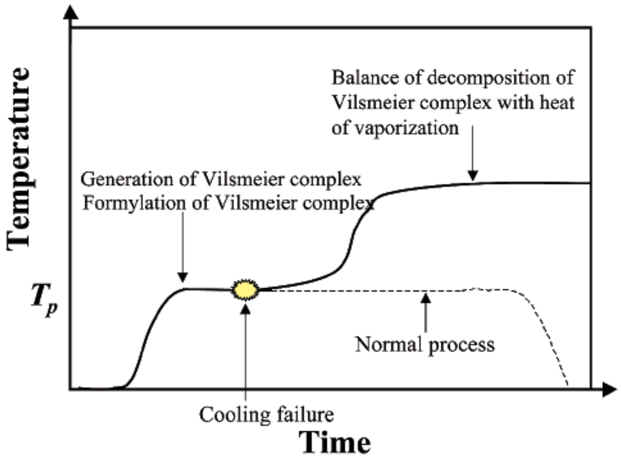


***Figure 6.*** **Moderate runaway scenario of the Vilsmeier reaction.**

On the other hand, as shown in Figure 6, in the case of adding $POCl_3$ into the solution in which the substrate is dissolved in advance, the Vilsmeier complex is consumed immediately by formylation of substrate. The heat of hydrolyzation of the Vilsmeier complex is so large that the excess mass of the Vilsmeier complex will induce a runaway reaction of the system if the water exists. In the RC1 experiment, the thermal decomposition was controlled by choosing the suitable feeding rate of $POCl_3$ when the experiments were carried out at a higher temperature. The heat of reaction is also less because of the energy loss due to the vaporization of solvent. Therefore, the second procedure is the safer method for the Vilsmeier reaction.

## 5. Conclusions

Several kinds of heat regarding the formylation of the Vilsmeier reaction were determined with reaction calorimetric experiments, and the potential hazard scenario of the reaction system was investigated. It is concluded that the thermal decomposition of the Vilsmeier complex is the maximum hazard in the reaction system and that it may cause a runaway reaction. The selection of reaction procedure and solvent might be a key for the suitable reaction, and MFA is more preferable than DMF as a solvent in the Vilsmeier reaction system.

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