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DEVELOPMENT OF A NEW ANALYTICAL METHOD FOR THE EVALUATION OF HAZARDS FROM SLOW DECOMPOSITION OF WASTE STREAMS AND PROCESS SOLUTIONS

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A wide variety of liquid streams are generated as part of the process research and development effort. Frequently these streams are drummed off, either as intermediates that must be held for processing or as wastes that must be sent off-site for disposal. Because of the long times and low concentrations often involved, current thermoanalytical techniques were inadequate to detect the potential of streams to generate gas. A custom-made apparatus, the gas evolution test cell (GETC), was developed in the Merck Research Laboratories to measure the gas generation potential of various streams under precisely defined conditions, is the key innovation for the development of a quantitative gas-generation test method.

Keywords: *gas, isothermal, pressure, safety, storage*

Background

Sodium borohydride is a common reagent used for the reduction of organic compounds, and it is frequently quenched with acid after use. However this aqueous hydrolysis can be slow, and species with boron–hydrogen bonds may be present is a waste stream. If a gas-producing reaction were to occur in a closed container, only a small amount of decomposition could produce potentially dangerous bulging, container failure, and a splashing and spraying hazard. To produce 35 kPa of pressure in a 90% full container, which could cause it to bulge, would require the reaction of only $1.5 \cdot 10^{-3}$ mol L^{-1} (this corresponds to a boron level of 16 mg L^{-1}) via the reaction.

$$(R–O–)_2BH+3H_2O \rightarrow 2R–O–H+B(OH)_3+H_2 \quad (1)$$

This reaction can be very slow, and take days or weeks to go to completion.

In a pharmaceutical research environment there are a variety of streams that may need to be stored for extended periods. These streams include intermediate solutions being held before processing in a subsequent step, streams being sent off-site for disposal, or waste streams being sent to storage tanks. Because of safety and environmental concerns, these storage containers are usually closed.

As part of the Operation Hazard Evaluation Laboratory's (OHEL) evaluation of a process, any stream to be stored in closed containers that had an exotherm with an initiation temperature below 75°C was considered a potential risk. In addition, streams produced by certain types of chemistry which use a reagent associated with gas production, either by itself or when quenched (borohydride reductions, peroxide oxidations, etc.), were considered potentially high-risk. However, if a quench procedure existed along with an analytical method for verifying that the quench was complete, the stream was not considered a risk. For example, streams treated with sulfite following a peroxide reaction were considered acceptable if no peroxide could be detected using a test strip.

The issue was whether these high-risk samples could produce pressure in storage and be a risk under normal storage conditions. The thermoanalytical techniques previously used by the OHEL all possess drawbacks when addressing this issue (Table 1). Some of the limitations of the ARC and DSC are described in [1].

History

The test equipment and method were not originally developed to study the formation of gas during storage conditions, but rather to study a surface-catalyzed decomposition at elevated temperatures.

Molybdenum-containing alloys are listed as incompatible with hydrazine [2]. There was a concern that the incompatibility was due to catalytic decomposition to hydrogen and nitrogen:

$$N_2H_4 \rightarrow N_2+2H_2 \quad (2)$$

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Table 1 Limitations of OHEL techniques for slow gas-generating reactions

Tecnique	Limitations
DSC	• No pressure detection; low heat flow sensitivity (0.1 mW/5 mg). (Typical expected heat flow is 0.01 mW for a 50 mg sample) • The GETC method does not rely on heat flow detection. Pressure sensitivity of the GETC is 0.012 Pa m^{-1} g^{-1}.
CRC	• Heat flow and sensitivity (1 mW/2 g), currently no pressure measuring capability. • The GETC method does not rely on heat flow detection. Pressure sensitivity of the GETC is 0.012 Pa m^{-1} g^{-1}.
RSST, adiabatic dewar	• Open system, small liquid to headspace ratio (10 mL liquid/350 mL headspace). • Limit of P-rate detection=23 Pa m^{-1} g^{-1}. • The GETC method does not rely on heat flow detection. Pressure sensitivity of the GETC is 0.012 Pa m^{-1} g^{-1}.
ARC, VSP2	• Low pressure transducer sensitivty (10–58 Pa/bit), non-reusable test cells. • Limit of P-rate detection=1.4 Pa m^{-1} g^{-1}. • The GETC method does not rely on heat flow detection. Pressure sensitivity of the GETC is 0.012 Pa m^{-1} g^{-1}.
Isothermal aging	• Small exotherm size, low rate of reaction at ambient temperatures. • The GETC method does not rely on heat flow detection. Pressure sensitivity of the GETC is 0.012 Pa m^{-1} g^{-1}.

It was desired to measure the decomposition of hydrazine/water/alcohol solutions in contact with Hastelloy® C-22, and to see if nitrogen and / or hydrogen were being produced.

A test was desired that would allow accurate measurements of gas production at 95°C. The equipment should also minimize handling and provide easy cleanup and decontamination. It was realized that charging the hydrazine/water/alcohol mixture into a sealed Hastelloy® sample cylinder equipped with a pressure gauge and safety valve would meet our testing requirements. It would provide a reproducible liquid volume to wetted surface area ratio, minimize sample handling, and could be run at 95°C safely.

A charge volume could be calculated to ensure that the predicted peak pressure would be less than the burst pressure of the safety device. The test cell was also easy to clean by flushing with hydrogen peroxide, then water and acetone. This design was the prototype for the gas evolution test cell (GETC).

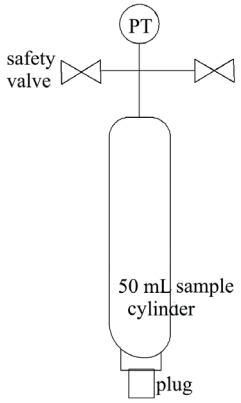

Fig. 1 Sketch of original GETC test cell design

It became apparent that many of the features of the device used for the hydrazine testing would make this test setup an ideal tool to study slow gas-producing reactions in general. The initial design added a pressure bleed-off valve on the side stem, but still used an analog pressure gauge and a safety valve (Fig. 1).

By maintaining the test cell at a constant temperature, it is possible to separate pressure changes due to temperature effects (vapor pressure, gas expansion, liquid expansion) from pressure effects due to slow reactions (gas generation, liquid-phase composition change). A standard test temperature of 35±0.1°C was selected as representative of the worst case scenario, a drum standing on a storage pad during the summer. Temperature control is provided by a circulating bath in which the test cell is immersed up to the crosspiece. The ambient air temperature which will contact the headpiece varies in an unpredictable manner between 16 and 23°C, but the effect of air temperature variations does not interfere with detecting slow pressure generation over 24 h or longer with the bath at 35°C.

Validation

The initial design was validated with two systems known to decompose with the release of gas. Both 3% hydrogen peroxide (Fig. 2) and 1% $NaBH_4$ in 0.1 M NaOH (Fig. 3) showed pressure generation, linear in time, with a lower rate at 20–22 than at 35°C. After both tests a static test was run, showing that the cell was leak-tight with 140–175 kPa gauge of internal nitrogen pressure. Once the validation of the GETC was complete, it was introduced into service in the OHEL.

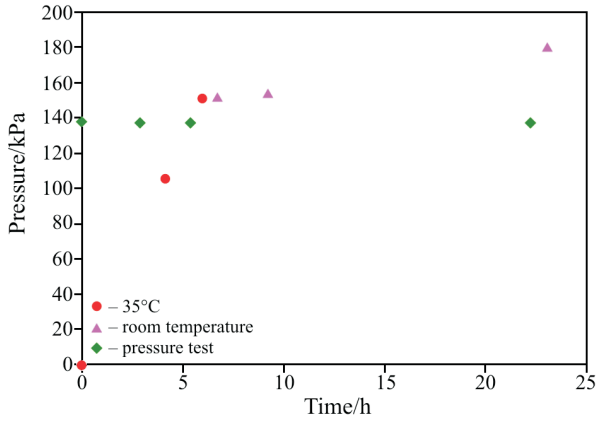

Fig. 2 Test results for 3% hydrogen peroxide in water

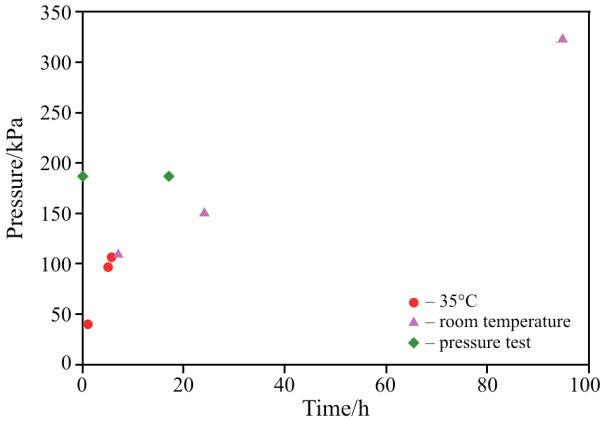

Fig. 3 Test results for 1% $NaBH_4$ in 0.1 M NaOH

Several improvements were made to the device to increase its usefulness, based on issues identified during operation. The first improvement was the elimination of the safety valve. When organic streams were first tested the rubber components of the safety valve failed. Exceeding the design pressure of the GETC (700–7000 kPa) was considered unlikely, since the majority of streams submitted for testing would be generating gas slowly, and autocatalysis was not considered likely for the types of reactions being studied. Observing the pressure during the first 15 min to 1 h while the filled test cell was at room temperature would be sufficient to determine whether the cell would be safe to heat.

It was then decided to re-orient the valve and pressure sensor. The valve was positioned in the 12 o'clock position on the top cross, and the pressure gauge was placed at the 3 o'clock position. This allowed the cell to be assembled fully, and then the test solution charged (and emptied) via a straight syringe needle slid down through the ball valve. This allowed static pressure tests to be run without needing to disassemble anything between the pressure test and the actual run. Once the run is complete, the test solution can

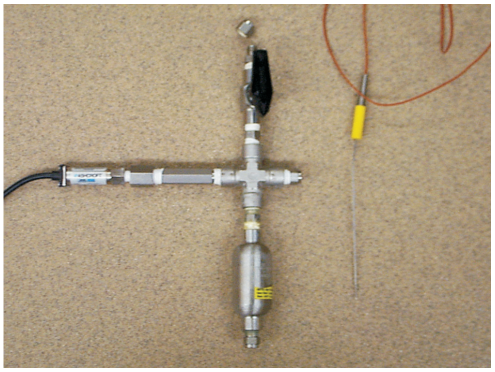

Fig. 4 The GETC prior to a run

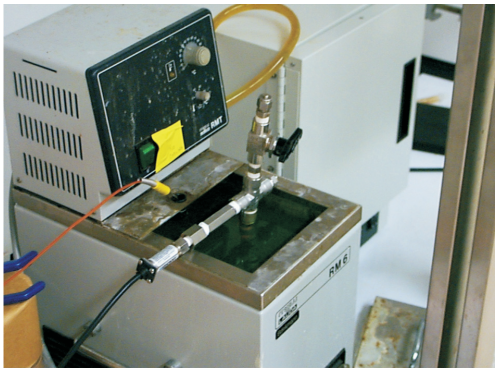

Fig. 5 The GETC in operation

be removed via syringe, and preliminary cleaning and decontaminating agents such as peroxide or bleach introduced through the valve via syringe.

The last development was the replacement of the analog pressure gauge with a digital pressure sensor and a data acquisition system. A FAI RSST unit is currently being used as the data acquisition system. The original 0–3500 kPa Ashcroft pressure transducer was replaced with a 0–420 kPa transducer to increase the sensitivity. With the data acquisition system in place, data could be collected every 15 s over 24 h, allowing for better determination of pressure rise rates, as well as detecting leaks or the leveling out of the pressure signal. The components of the current GETC are shown in Fig. 4. Either a 50 mL 316 L stainless steel or a 150 mL Hastelloy® C-22 sample cylinder can be used for testing. Figure 5 shows the current GETC during operation.

Examples of use

In a recent process, a sodium borohydride reduction was used to convert a ketone to an alcohol. As part of the process, the reaction mixture was stirred with tartaric acid to quench excess sodium borohydride. The aqueous layer after this treatment was examined in the GETC and shown to produce no pressure. However a bulging drum was observed with a

downstream waste following further processing steps. Investigation of the stream that caused the drum to bulge using GETC testing showed that the sample could generate pressure. Headspace and atomic analysis showed that the gas evolved was hydrogen, and that there was significant boron content in the organic stream. The organic stream was traced through the various steps, and GETC testing revealed that the activated organoboron species travels more or less intact through several process steps after the reduction. A waste treatment process that involved heating the waste organic with mineral acid was shown to be effective in destroying the organoboron species, thus eliminating the risk or drum bulging from hydrogen pressure build-up. Figure 6 summarizes the GETC results.

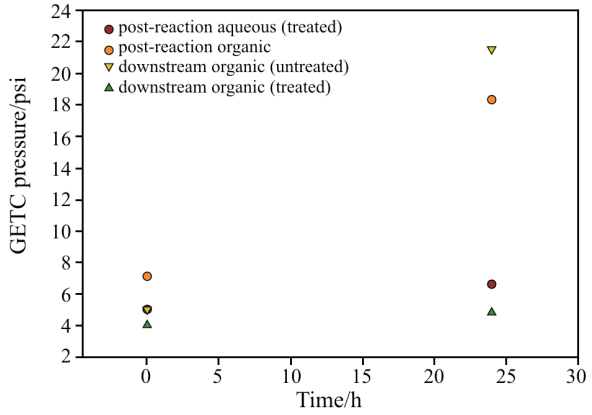

Fig. 6 Results of GETC testing for streams from a borohydride reduction

In another case, potassium iodate was used to oxidize a keto-alcohol to a ketal, and there was concern over potential generation of oxygen from the excess iodate in an aqueous layer. A GETC test was set up using the end-of-reaction solution and tested at 35°C (Fig. 7).

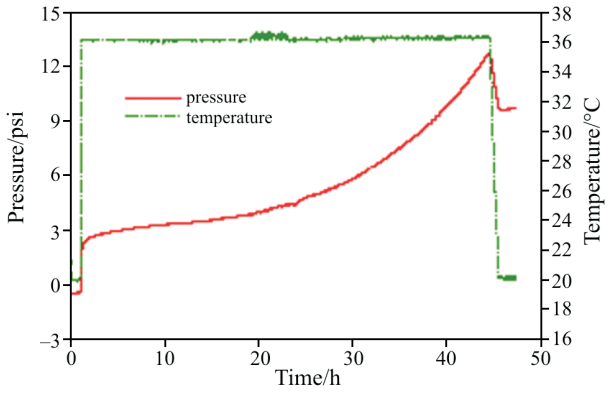

Fig. 7 Aqueous waste later from ketone oxidation process – original GETC evaluation

As can be seen, there was a cause for concern, as the solution, although initially generating only 21 kPa of pressure, began to develop pressure at an increasing rate after 16 h. Another sample generated via the same process was tested at higher temperatures to evaluate the feasibility of thermal treatment, and the maximum possible pressure generation (Fig. 8).

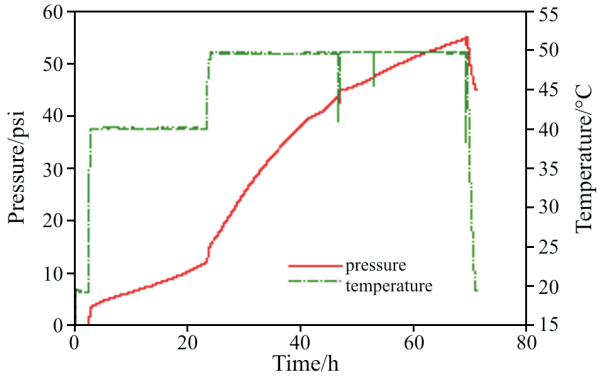

Fig. 8 Aqueous waste later from ketone oxidation process – stressed GETC evaluation

The first 24 h, at 40°C, showed similar behavior to the original test, but when heated to 50°C, the pressure accumulation showed that the reactant was nearing complete consumption. This argued that a sufficient combination of temperature and time could eliminate the pressure potential from the aqueous layer. 46 h at 70°C was tried, and found to be effective (Fig. 9).

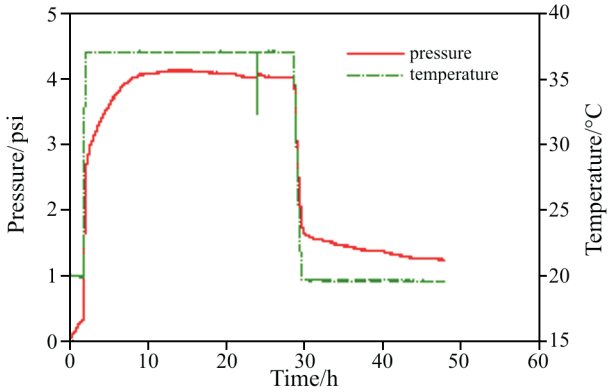

Fig. 9 Aqueous waste later from ketone oxidation process – after 46 h at 70°C

An instrument (Fast Thermal Analysis Instrument (FTAI™), based on similar principles has been used to assess storage safety and vent sizing for hydrogen peroxide [3].

Conclusions

The GETC has extended the OHEL's ability to provide data for safe operation of Merck's research Pilot Plant facilities and to address potential storage issues prior to scale-up for manufacturing. The GETC allows the direct measurement of pressure generation, or as is sometimes more important, the lack of pressure generation, from a material that is to be stored in a closed container. This allows causes of bulging drums to be investigated, potential remedies to be evaluated and the efficacy of large-scale treatment to be demonstrated in the lab. It can also be used to see whether a treatment method is needed before drumming is allowed.

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