Microwave Reactor using Solid-State Oscillator and Resonant Cavity, and its Application to Chemical Synthesis

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1 Introduction

Application of Microwaves (MW) to chemistry started more than 20 years ago, and more than 5,000 articles have been published worldwide. They pointed out MW chemistry has great merits such as lowering the reaction temperature, drastic reduction of the reaction time and so on. But MW chemistry used in production processes has been limited, because of the limited penetration depth, poor controllability, poor reproducibility and other factors. Recently due to the progress of the telecommunication industry, it becomes realistic to apply solid state MW amplifier to chemical equipment, because the output power has steadily been increasing and has reached 250W or more.

Pacific Microwave Technologies (PMT) has been developing apparatus to make it possible to use MW for production process of chemicals by integrating power electronic devices and resonant cavity technology, which is leading to the possibility of large volume production, new chemical reaction spaces and unprecedented reactions by MW.

In this article, we report the details of the MW flow reactor apparatus developed and the possibility to apply this new technology to various chemical reactions.

2 Details of the MW flow reactor system

2.1 Basic structure of the MW flow reactor system

The MW flow reactor system shown in Fig. 1 is composed of an oscillation & irradiation unit (center), a controller unit (left) and a pumping unit (right). Controller unit is connected with PC.

2.2 Oscillation & irradiation unit

The oscillation & irradiation unit is composed of mainly MW generator shown in Fig. 2 and irradiation cavity. As shown in Fig. 3, Voltage Controlled Oscillator (VCO), Variable Attenuator (VAT) and High Power Amplifier (HPA) are the key devices composing the generator. The MW power is irradiated into the cavity via a coaxial cable, a coax waveguide converter and a waveguide.

Figure 1: MW Flow Reactor

Figure 2: MW generator
where it generates the TM110 mode of MW field in the quadrangular shape cavity.

2.3 Reactor

The MW flow reactor system has a structure to be able to insert the reactor tube made of glass as shown in Fig. 4 from the top of the quadrangular cavity along with the axis of the cavity. The reactor has a helical structure, as to generate the appropriate resonant mode within the cavity.

2.4 Control unit and PC

The dielectric properties inside the cavity change depending on the kind of reagent, and temperature of the reagent. The frequency at resonance ($f_r$) differs with the above factors. By using a magnetron it is almost impossible to change its oscillating frequency. But by the use of solid state oscillator, it is possible to change oscillating the frequency within a very broad, covering the ISM 2.4-2.5 GHz frequency range.

By installing an antenna within the cavity, $f_r$ can be rapidly set by sweeping the frequency and detecting the E-field strength in the cavity along with the sweep. Then the oscillating frequency is always kept at $f_r$ by applying such a frequency tuning at every several seconds.

Reaction conditions, such as MW power, flow rates of pumps and so on, are entered from the PC connected via a USB with the controller unit. Reaction status, such as forward and reflected MW power, $f_r$, pressure, etc., are shown up in the monitor of the PC, and automatically recorded in the PC.

As the system accelerates chemical reaction under extremely high temperature and high pressure conditions, safety measures are introduced. When the device detects an irregular condition, the system cuts off the MW power and the flow of the reagent stops within seconds.

2.5 Pumping unit

The pumping unit is composed mainly of 2 units of High Performance Liquid Chromatography (HPLC) pump and Back Pressure Regulator (BPR). There are several types of pumps available to install, from about 10ml/min to a maximum of 100ml/min. Reagent is pressurized when flowing from the pump through BPR, up to 2.5MPa as specification. 2 units of pressure gauges are equipped in between pump and BPR, before and after the reactor tube, monitoring continuously the pressure and change of the pressure.
3 Resonant cavity

The resonant cavity focuses the MW energy within the reagent flowing through the tube. The operation of the resonant cavity depends crucially on the value of the Q-factor. If the Q value is too low, the effect of resonant operation becomes poor. On the other hand if Q value is extremely high, it becomes possible to apply very high E-field to the material to be heated, however, it becomes difficult to control. Once $f_r$ deviates from its prescribed value, the E-field drops considerably and the reflected power from the cavity increases.

The Q value of the resonance depends not only on the dielectric property of the reagent, but also on the shape & volume of the reactor, the temperature of the reagent to be heated up, and so on. Taking into consideration all the above factors we have established that Q values in the range 20 and 200 gives good operational performance. Furthermore, the MW Flow Reactor System has the constraint to keep the oscillating frequency within the ISM band.

TM110 mode cavity has an E-field distribution of half of Sine wave for x and y axis, and constant for z-axis. Such E-field distribution, establishes a very high E-field in the central axis of the TM110 cavity.

4 3D EMF simulation

Taking various factors into consideration, designing by trial and error such an irradiation unit and reactor system was considered not an efficient manner. Therefore computer simulation was considered the only way forward.

By developing a three dimensional Electro-Magnetic Field (3D EMF) simulation software with various data as library, it becomes possible to make simulation of one design condition without much effort. Output from the 3D EMF simulation software is shown in Fig. 5.

By using this simulation software, recording various data such as cavity size, reactor size, dielectric property data on various reagents as library, without designing and making cavity and/or reactor, it becomes possible to identify $f_r$, heating property, Q value.

5 Peak finder

It was almost impossible to identify whether the frequency is at $f_r$ and it is within the ISM band without using expensive equipment such as a network analyzer. For chemists, it is not easy to use a network analyzer, monitoring continuously the status of resonance of MW reactor.

To give a solution to such a problem, PMT developed application software system named “Peak Finder” which is simpler than using a network analyzer.

Before starting the operation of chemical reaction, run “Peak Finder” software, then the software instructs the user, whether $f_r$ lies within the ISM band or not, and the Q value based on the combination of reactor and reagent as shown in Fig. 6. By running this software user can select suitable reactor, suitable reagent to meet the resonant cavity to use.

![Figure 5: 3D EMF Simulation](image)

![Figure 6: Peak Finder](image)
In addition to the function, “Peak Finder” proved more valuable as shown in Fig. 7, since it can measure the changes of the dielectric properties along with temperature increase.

Figure 7: MW Absorption change on Temp.

6 Basic performance, heating various solvents

Table 1 shows the result of heating various solvents by using the 200W MW Flow Reactor System with flow rate of 20ml/min. By having BPR and high E-field of resonant cavity, solvents are easily heated up to near the boiling point temperature under 2.5MPa pressure conditions. The temperatures are extremely higher temperatures than the boiling temperatures under atmospheric pressure conditions.

Table 1: Heating of Various Solvents

<table>
<thead>
<tr>
<th>Solvent</th>
<th>Temperature @ exit (°C)</th>
<th>Boiling point @ 1.0 atm (°C)</th>
</tr>
</thead>
<tbody>
<tr>
<td>n-Hexane</td>
<td>100</td>
<td>69</td>
</tr>
<tr>
<td>Cyclopentyl methyl ether</td>
<td>148</td>
<td>106</td>
</tr>
<tr>
<td>MeOH</td>
<td>178</td>
<td>65</td>
</tr>
<tr>
<td>EtOH</td>
<td>185</td>
<td>79</td>
</tr>
<tr>
<td>n-PrOH</td>
<td>198</td>
<td>97</td>
</tr>
<tr>
<td>AcOH</td>
<td>200</td>
<td>118</td>
</tr>
<tr>
<td>CH3CN</td>
<td>206</td>
<td>82</td>
</tr>
<tr>
<td>N,N-Dimethylformamide</td>
<td>220</td>
<td>153</td>
</tr>
<tr>
<td>N,N-Dimethylacetamide</td>
<td>225</td>
<td>165</td>
</tr>
<tr>
<td>Dimethyl sulfoxide</td>
<td>&gt;250</td>
<td>189</td>
</tr>
</tbody>
</table>

7 Technical feasibility applying to new reaction spaces

7.1 Applications to low yield, time consuming reactions

Fischer Indole reaction shown in Fig. 8. Indole is contained in more than 400 drugs which is a typical model reaction tested in MW-assisted synthesis. In this reaction, one needs to finish the multi-step reactions in a short time. To do so, Hamashima group of Univ. of Shizuoka expected that the substrate and intermediate with polar functionality absorb MW efficiently, so that the reaction could be accelerated.

Figure 8: Fischer Indole Reaction

To find optimum reaction conditions, the group screened the flow rate and irradiation power carefully by using a real time Flow IR monitoring. As a result, the group found the optimum flow rate and irradiation power and reported that it achieved indole at 3kg/day.

Diels-Alder reaction shown in Fig. 9. In a usual batch reaction, retro-Diels–Alder reaction is a major problem, so the reaction should be carried out carefully at less than 110 degree C and a long reaction time is required to obtain the satisfactory yield.

Hamashima group of Univ. of Shizuoka assumed that high yield can be achieved as result of rapid heating followed by rapid cooling of the flow within the MW system. As assumed, MW accelerated the reaction, and high chemical yield was achieved under the optimized conditions. Thus,
acetylene-dicarboxylate was consumed within only 1.2 minutes to afford the product in 76% isolated yield.

In principle, the product can be synthesized to more than 1 kg scale in a day.

### 7.4 Selective heating of substrate chemicals using non polar solvent

Based on the result of the above tests, various reaction experiments using non polar solvents have already started. The experiments currently under way are as follows:

- Claisen rearrangement
- Synthesizing Fullerene derivatives

### 7.5 Concerted reaction with fixed bed catalyst and MW

Catalytic reactions are considered very important for specialty chemicals. Currently such reactions are done by batch systems having catalyst homogeneously mixed with reagents. This process requires the process to separate the catalyst from the reagent after the reaction process, which needs additional equipment, time and increases manufacturing cost.

To give solution to the problem, Sajiki group of Gifu Pharmaceutical Univ. as shown in Fig. 11, found that Heck Mizorogi reaction can be considerably accelerated with fixed bed Pd catalyst and small power of MW irradiation under flow condition. In addition to the research done by
traditional catalysts, new type of catalyst using nanomaterial has started. It is also expected major improvements on reactions by using such a new catalyst and MW power under flow condition as described in this paper.

### 7.6 Transition metal free coupling reaction

It was considered necessary to use very expensive transition metal to complete the coupling reactions. But Hamashima group found and reported that it is possible to do coupling reaction without using transition metal if MW flow system is used, which is shown in Fig. 12.

![Figure 12: Transition metal free coupling reaction](image)

### 8 High speed optimization of reaction by mathematics

One of the biggest merits of MW system using solid state power device is that it is possible to change its conditions easily in a very short time. Gradient mode and step mode are embedded as application software in the MW flow reactor system. That can change MW power gradually or step wise.

Combining the step mode with Design of Experiments (DoE), and also real time flow monitor using a MW Flow Reactor System, it made possible to gather many data on various experimental conditions from the monitor in a short time continuously. After such data logged into the computer, immediately run Multi Variable data Analysis (MVA), then computer system rapidly finds the best optimized condition. The sample of the result of MVA is shown in Fig. 13 Mase group reported considerable reduction of the time necessary for optimization of one chemical reaction process. It considered to take longer than 5 days necessary to complete with small size batch specimen and stand-alone monitor system with manual operation. But such optimization could be shortened less than half a day by using the system described above even though transmission of data from flow monitor to PC is done manually.

Currently with the combined PC system and flow monitor to capture in-situ real time product data directly and automatically has been developed, and the system is now being evaluated. Such optimization by integration chemistry with mathematics is realized and achieved mainly by following two key features. First, is the merit of MW, that can give very high level of activating energy focusing onto the material to be heated uniformly in a very short time from within the material. And, secondly is the merit of using solid state devices that can change the reaction conditions within a very short time.

![Figure 13: MVA (Multi Variable data Analysis)](image)

### 9 Technologies of the future

#### 9.1 Impedance matching

When non-polar solvents are considered, the reflected microwave power from cavity increases. In the worst case, higher than 50% power from MW the generator is reflected from cavity and wasted by termination without contributing to the reaction.

To solve this problem, a new type of impedance matching system shown in Fig. 14 has been developed. By introducing this impedance matching system, reflection MW power could be reduced to less than 10% even though the non-polar Toluene is used as solvent.

#### 9.2 Pulse width modulation (PWM)

By the introduction of solid state power device, it is becomes possible to switch MW power ON-OFF within m-secs. PWM shown in Fig. 15 technology has been developed and started trial experiment. By introducing PWM technology, much higher E field...
could be applied to the chemicals within a short time period.

Figure 14: Impedance Matching

Figure 15: Pulse Width Modulation

9.3 Introduction of higher power amplifier

In 2017, the maximum power of broadband HPA that can cover the 2.45GHz range by a single chip is 250W LD-MOS. The efficiency of LD-MOS has recently been improved a lot, achieving a figure of around 60%. Manufacturers of solid state devices have announced the introduction next year of a 500W device.

In the 915MHz range, HPA delivering higher than 500W by single chip has already been introduced in the market.

It is also announced that 300W type GaN HPA, with an efficiency of higher than 70%, covering 2.45GHz range, will shortly be introduced on to the market.

It seems that very high efficient and green chemical process is possible by keeping the reflection of MW power at a minimum by higher power HPA with higher efficiency and the utilization of resonant cavity technology

10 Summary

PMT succeeded in developing new generation of MW chemical reaction system by incorporating solid state power devices, resonant cavity technology and advanced system control technologies. The system makes it possible to apply MW technology not only to basic research but also to production process as shown in Fig. 16 for various pharmaceutical and specialty chemical applications.

The system makes it possible to proceed the development from basic research to production based on one technology that can considerably shorten the time needed for development.

Figure 16: From Research to Production
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For further reading


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