Technology

Development of Flow Synthesis Method for Deuterated Aromatic Compounds

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1. Introduction

Organic Light Emitting Diode (OLED) device have excellent features such as self-luminescence, thinness, light weight, are widely used in various applications such as TVs and smartphone displays.

OLED materials have been founding improvement of the luminous efficiency and durability of devices by deuteration technology [1], we also have been continuing the development of deuteration technology for aromatic compounds targeting at OLED materials since 2007. In recent years, OLED panel manufacturers also applied deuterated OLED materials in their products and released them on the market. So that, the deuteration has tended to become common trend key technology to improve functions and durability more.

On the other hand, we have been facing with two issues for a long time. One is small production capacity, and the another is the cost of deuterated compounds.

In order to resolve two issue, needs to improve production throughput and enehance reaction efficiency. Then, we have developed new synthesis technology for deuterated aromatic compounds using a flow synthesis method. This paper reports the developed synthesis method.

2. Synthesis method for deuterated aromatic compounds

2.1 Conventional synthesis method

Generally, deuterated aromatic compounds are synthesized by H-D exchange reaction with heavy water (D_2O) and the original aromatic compounds under high temperature and high pressure conditions. This batch type method has some issues to increase production amounts, such as the limitations of production scale by reaction vessel size, the long tact time caused by lower heating and cooling efficiency, and the complexity of filtration and extraction process.

2.2 New synthesis method using microwaves technology and flow type reactors

We have been reserching so far to resolves those issues, then having been developing new chemical reaction system with microwave as a heating source for chemical reactions. The principle of generation heat is by the vibrational and rotational motion of molecules with dipole moments such as water, and enabling direct and fast uniform heating. Therefore, the synthesis method using microvave is expected to improve the heating and reaction efficiency [2]. So far, we have had a great deal of experience for the synthesis of deuterated aromatic compounds using batch microwave reactor [3,4].

Meanwhile, we have extensive skill of a flow synthesis method also, which can be easily scaled up. Our gas plants have already started to use flow synthesis method to produce mass products. The flow synthesis method feeds raw material compounds to mixer continuously and mixing uniformly, then completes the chemical reaction at a subsequent reactor. The flow synthesis method expects higher production efficiency than the batch synthesis method. Other advantages of the flow synthesis method are the flexibility of setting reaction conditions with high temperature and high pressure, superior thermal efficiency, the adaptability of automation, and the high safety design [5].

Based on the above two key our technologies, we developed new flow-type microwave reactor to achieve mass production targeting at deuterated aromatic compounds.

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3. Flow synthesis method for deuterated aromatic compounds

3.1 Basic deuteration test with 1-Naphthol

Figure 1 shows a schematic diagram of the synthesis method. This synthesis process consisted of flow-type microwave reactor with a glass reaction tube, the raw material dissolved in an organic solvent, D_2O, pump unit to supply them, a back pressure valve, and a liquid-liquid separator to separate the organic layer and water after the reaction. The glass reaction tube was filled with a commercially available platinum on alumina catalyst. Deuterated compounds were synthesized by microwave irradiation heating under 2 MPa feeding the raw material solution and D_2O. After the reaction, the organic layer and water were cooled up to the room temperature and separated by a liquid-liquid separator. The solution of the target deuterated compound and H_2O were collected.

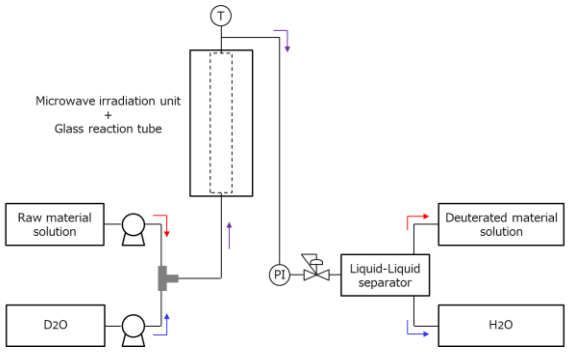
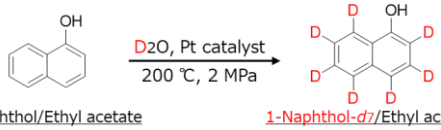


Figure 1. Schematic diagram of flow synthesis method

The H-D exchange reaction of 1-Naphthol was researched as a model reaction to compare the performance between flow synthesis method and batch synthesis method. Both reactors supplied the solution (1-Naphthol/ethyl acetate) to the each microwave irradiation units respectively at a flow rate of 0.55 g of 1-Naphthol per minute. and D_2O [99.8 atom%D] was also supplied there, so that the theoretical deuteration ratio (the theoretical number of deuterium atoms in the reaction system divided by the sum of the number of light and heavy hydrogen atoms) to 1-Naphthol was by 81.2 atom%D.

As a result, the H-D exchange reaction efficiency of 1-Naphthol using the batch-type microwave reactor was only 27% for 10 minutes, whereas the reaction efficiency using the flow-type microwave reactor reached 91% for a residence time (the reaction time in the flow reactor which is the heating time in the microwave irradiated catalyst section) of 3 minutes. The H-D exchange reaction efficiency using the flow-type microwave reactor proceeded 10 times more than using batch-type microwave reactor when both reactions were evaluated in terms of deuterated reaction efficiency per hour (Table 1).

Table 1. Results of H-D exchange reaction of 1-Naphthol using microwave reactor



1-Naphthol/Ethyl acetate　　1-Naphthol-*d*7/Ethyl acetate

MW Reactor	Theoretical deuteration ratio [atom%D]	Reaction time (Residence time)	1-Naphthol-*d*7 deuteration ratio [atom%D]	H-D exchange reaction efficiency [%]	H-D exchange reaction efficiency per time [%/min.]
Batch	94.9	**10 min.**	26.2	27	2.7
Flow	**81.2**	**(3.3 min.)**	**74.1**	**91**	**28**

Reaction scale (1-Naphthol) : Batch : 0.3 g, Flow : 0.55 g/min.
H-D exchange reaction efficiency [%]
= 1-Naphthol-*d*7 deuteration ratio [atom%D]/Theoretical deuteration ratio [atom%D]×100

In addition, the flow-type microwave reactor had very high heating efficiency. The conventional heating method using a tube furnace at the same flow rate required about 60 minutes for reaching 200 °C. On the other hand, this equipment was able to reach 200 °C in only 90 seconds and started the reaction. This means that the use of microwaves can reduce the power consumption by 30%.

These results indicate that the flow-type microwave reactor is an excellent reaction system with very high reaction and heating efficiencies for the synthesis of deuterated aromatic compounds.

3.2 Future plan with this new sytnehesis method

Figure 2 compares the production process between the developed flow synthesis method and the conventional batch synthesis method. The flow synthesis method can quickly raise the temperature of the reaction section due to the highly efficient heating capability of microwaves. In addition, the high cooling efficiency due to the large surface area of the flow path allows the liquid to be cooled in a short time after the reaction. Furthermore, the flow synthesis method does not require filtration of the solid catalyst after each reaction, whereas the batch

synthesis method does. Also, the liquid separation process with a separating funnel can be eliminated by using a liquid-liquid separator. As a result, the flow synthesis method allows the entire process from raw material preparation to purification to be carried out in a single step, thus greatly reducing the process time.

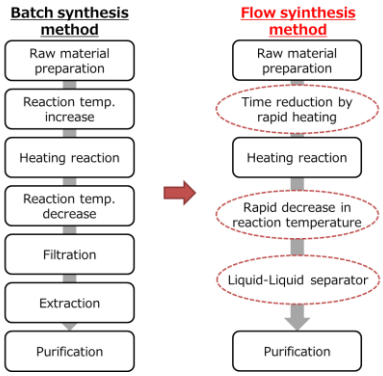


Figure 2. Comparison of production processes between flow synthesis method and batch synthesis method

When synthesizing deuterated aromatic compounds with high deuterated ratio by H-D exchange reaction using D_2O, the amount of expensive D_2O used can be reduced more in a reaction system where the target deuteration ratio is reached by stepwise H-D exchange reactions than single H-D exchange reaction.

The developed flow synthesis method can be possible to get higher deuteration ration with one pass by adding several reactors in series as shown in Figure 3. We are currently able to produce 1-Naphthol-*d7* [94.3 atom%D] at 1 kg/month by using two reactors. We will continue to develop ways to further increase the production scale and automate the system to accomplish the cost reduction.

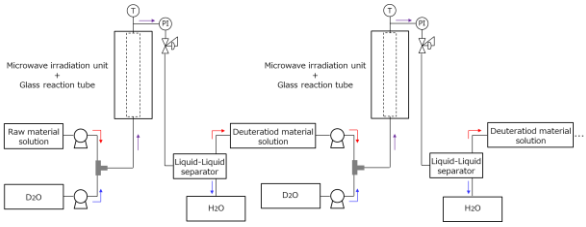


Figure 3. Continuous multi-stage flow synthesis method

3.3 Deutterated products lineup

We have already confirmed that the high efficiency H-D exchange reaction proceeds for Aniline, Toluene, 2-Hydroxycarbazole, etc. other than 1-Naphthol.

Also, we prospect that various deuterated aromatic compound such as Carbazole and 8-Quinolinol can be synthesized using this new method with other chemical skills accumulated so far (Figure 4).

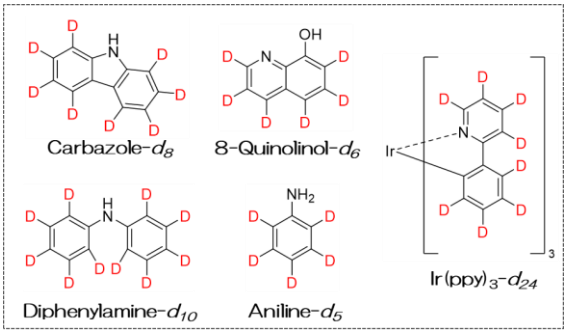


Figure 4. Example of deuterated aromatic compounds

Futhermore, as the sole agent in Japan for US company ISOTEC, the world's largest manufacturer of stable isotopes, we are able to provide more than 3,000 types of stable isotope products.

4. Conclusion

We developed a flow synthesis method for deuterated aromatic compounds. It was confirmed that the synthesis method using flow-type microwave reactor had higher reaction efficiency and throughput than the conventional method.

On the other hand, reaction systems using conventional high-pressure reaction vessels and batch-type microwave reactor also still have some advantages such as reactions can be carried out under very higher pressure conditions and small-volume reactions can be performed easily. Therefore, we will continue to consider best way to produce each deuterated aromatic compounds on demand by combing various chemical skills and technologies with on the new synthesis method.

References

1) Yoko Sugiyama, Haruki Shimodaira, Synthesis and Evaluation of Deuterated OLED Material, Taiyo Nippon Sanso Technical Report No. 32, 2013, p5-8
2) Shozo Yanagida, Takeko Matsumura, Microwave Thermal Catalysts Change Chemistry, 1st edition, Kagakudojin, 2004, p84
3) Japanese Patent
Kyoto University, Taiyo Nippon Sanso Corporation.
Production method of phenol derivatives, Patent No. 6544595, 2019-07-17.
4) Japanese Patent
Taiyo Nippon Sanso Corporation, National Institute of Advanced Industrial Science and Technology
Production method for compounds with deuterated aromatic or heterocyclic rings, Patent No. 5464395, 2014-04-09.
5) Junichi Yoshida, Flow Micro Synthesis - Basic to Practical Synthesis and Production, 1st edition, Kagakudojin, 2014, p288.