THALESNano

Using Flow Chemistry in Agrochemical Applications

Similarly to other major chemical industries, the agrochemical market also faces several changes and challenges. The three major challenges for the industry are:

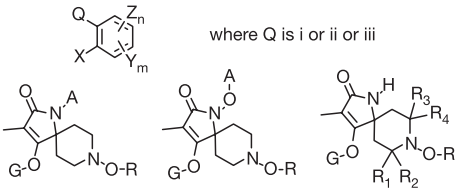
1. The resistance of pests and the impact of this to the long term performance of agrochemical products.
2. More stringent regulatory environment.
3. Increasing cost of goods.

These are in line with the declining number of new molecules' introduction in this field. This is in spite of the increased number of compounds synthesized (2.7 times more) and the increased R&D cost (from U.S. $152 million in 1995 to $256 million in 2005). In order to overcome these challenges the use of different techniques, such as structure-, fragment-, and target based design of active compounds are needed, together with performing intensified and more efficient synthesis techniques [1.].

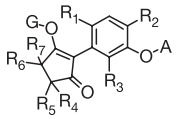
In this application note we provide information from patents from major agrochemical companies, Syngenta and Dow Agrosciences, where flow chemistry was used for the synthesis of active compounds to overcome these challenges. Flow chemistry reactors are ideal tools for chemists to reduce energy and material usage, consequently reducing production costs. The short residence time within these reactors allows users to synthesize molecules rapidly and, owing to the expanded chemical space, provides access to novel structures for new compound submission.

The presented reactions are examples for:

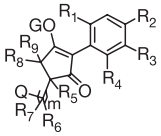
1. Processes for the preparation of novel insecticidally active thietane derivatives to combat and control insect, acarine, nematode, and mollusc pests
2. The synthesis of substituted pyrimidine derivatives to control undesired plant growth in crops
3. A method description of enhancing a crop by applying to the crop or a locus thereof a compound of



4. The synthesis of compounds with a core structure of

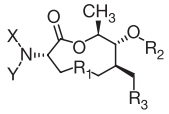


5. The synthesis of compounds with a core structure of

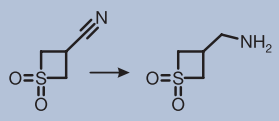
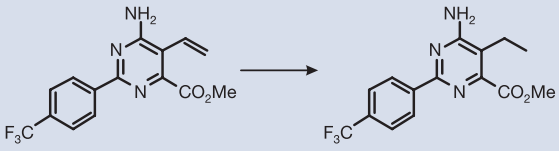
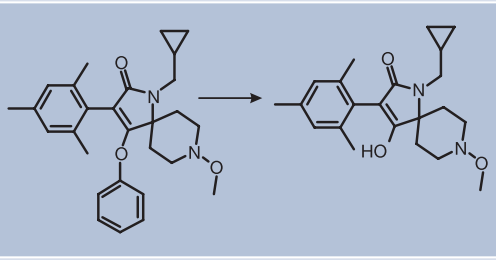
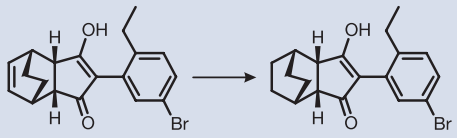
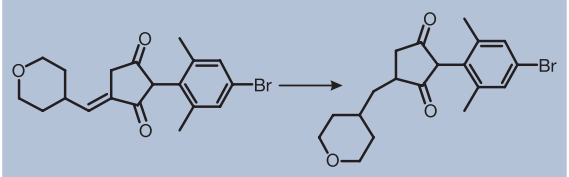
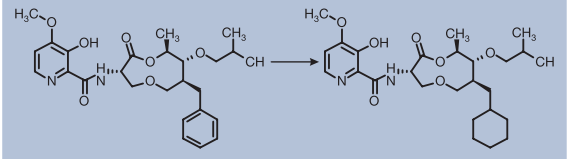


containing them in controlling insects, acarines, nematodes or molluscs

6. The synthesis of macrocyclic picolinamides, and their use as fungicides.



In these experiments the R&D awarding H-Cube® continuous flow reactor was used. The members of the H-Cube family combine in-situ hydrogenation capabilities with a wide temperature and pressure range, and easy automation, making them an ideal screening platform. The research processes are also easily scalable, making research to production translation fast and efficient.

#	Patent number	Equation	Reaction condition	Result
Applications from Syngenta				
1	EP 2748154 A1		v = 1 mL/min RaNi catalyst p = 50 bar T = RT 0.1 g SM in 45 mL MeOH	60 mg
2	EP 2396306 A1		v = 1 mL/min Pd/C (30 mm) p = 20 bar T = 30 °C 38 mg SM in 10 mL MeOH	38 mg, 99%
3	WO 2011151146 A1		v = 1 mL/min 5% Pd/C p = 2-3 bar T = 35 °C 546 mg SM in 47 mL MeOH Twice pumped through	215 mg
4	EP2389066 A1		v = 1 mL/min 10% Pd/C p = 30 bar T = 25 °C 3.87 g SM in 135 mL MeOH:45 mL EtOAc	2.484 g
5	WO 2011073060 A2		v = 1 mL/min 10% Pd/C p = 20 bar 0.1 g SM in 100 mL MeOH	0.09 g
Application from Dow Agrosciences				
6	**US 8835462 B2**		v = 1 mL/min 5% Rh/C p = 100 bar T = 100 °C 25 mg SM in 1.2 mL THF	21 g, 83%

[1.] Lamberth et al. Science; ***2013****; 341; 742-746*

For more information on how flow chemistry can benefit you, please visit www.thalesnano.com

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