

encourage precise and powerful probing of data relationships matter? One potentially relevant example is the Challenger spacecraft, where project engineers failed to spot what the data could have told them about the link between launch pad ambient temperature and O-ring erosion⁵.

Targeted methodologies and promising models for the fusion of experiments and informatics are emerging. Also emerging is a newly enriched scientific commons with a multi-disciplinary vernacular. Related enterprise data communication and analysis systems are taking shape. Only when these communication networks are in place to facilitate data-enriched dialog does it seem fair to judge whether the scientific technology platforms have been part of the problem or part of the solution.

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More microwave reactors required ▼

Microwave energy was first shown to accelerate organic reactions in the 1980s. There were, however, major

concerns with the use of this technology as there was a lack of available systems with adequate temperature control, and there were risks associated with the use of flammable organic solvents. As time moved on, safe microwave heating equipment was brought onto the market that enabled both accurate temperature and pressure control, as well as convenient monitoring of reactions. As a consequence, the total number of articles appearing in the literature describing rapid chemical synthesis promoted by microwave irradiation has grown from ~200 in 1995 to ~1000 in 2001. Excellent reviews have been also published on microwave-assisted chemistry¹.

Pharmaceutical companies are under pressure to speed-up their drug discovery programmes and to drive down the cost of discovering new medicines. We are aware of the interest that has been generated from combinatorial and high-throughput chemistry as a potential means of speeding up the drug discovery process. These techniques have been embraced widely by the pharmaceutical industry, but there is room for further increases in the speed with which we carry out drug discovery. The use of microwave energy to accelerate organic transformations is one route to increasing efficiency.

The majority of microwave-promoted organic synthesis has been performed in multi-mode domestic ovens. For safety reasons, the use of microwave reactors designed for organic chemistry is strongly recommended. One drawback of the present design of safe ovens is that the reaction size is more or less fixed at a relatively small volume.

There have been several procedures using microwave-assisted chemistry for the production of compounds of relevance to medicinal chemistry. One example used microwave irradiation to achieve rapid alkylation of a range of piperidines and piperazines to generate a library using parallel synthesis². This

library was screened in a herpes simplex virus-1 (HSV-1) helicase ATPase assay and confirmed hits were identified.

This is just one example where the advantages of parallel synthesis have been combined with the reaction acceleration possible with microwave-promoted organic synthesis. This synergy has tremendous potential for the future in impacting on the generation of compound libraries for biological screening. One area which will need addressing is to ensure microwave-assisted chemistry does not suffer from limitations of throughput, if library sizes running into many thousands of individual compounds is a goal.

There are other reaction types that have proven suitable for microwave acceleration but have not, to date, been exploited in the context of library production. Many other reactions have potential for automated medicinal and combinatorial chemistry, traditionally performed with long reaction times, and might be dramatically accelerated by microwave heating. Carbonylative reactions are one example.

It is unfortunate that only a few modern microwave reactors designed for safe automated synthesis are currently available. It is up to end-users to demonstrate an increased desire to use such equipment. In doing so, this will ensure the commercial production of single-mode cavity based synthesizers, satisfying the requirements of academia and the pharmaceutical industry.

References

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