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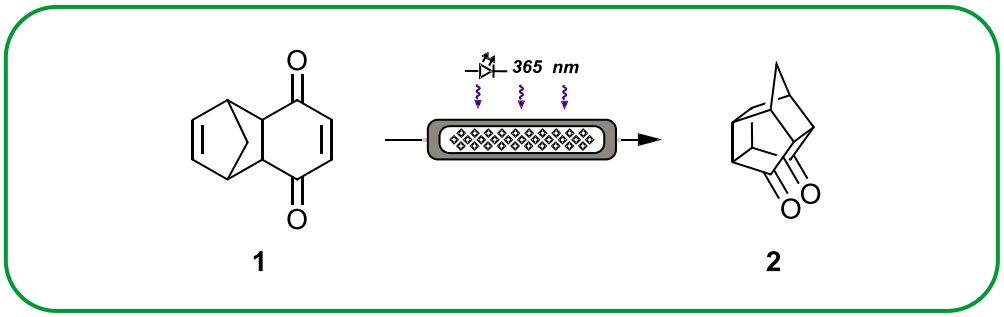
Application Note 1

Synthesis of Cookson's diketone via intramolecular [2+2]-photocycloaddition

Data courtesy of EcoSynth, authored by dr. ir. Wouter Debrouwer

1. ABSTRACT



Scheme 1. Intramolecular [2+2]-photocycloaddition

The intramolecular [2+2]-photocycloaddition leading to Cookson's diketone **2** was performed in the HANU-reactor with a productivity of 2.3 kg/d.

2. BACKGROUND

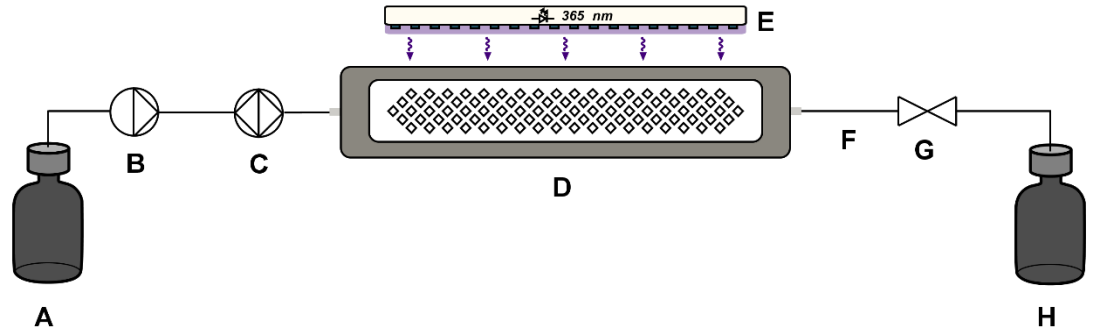
The formation of the strained pentacyclic cage compound **2** (pentacyclo[5.4.0.0^{2,6}.0^{3,10}.0^{5,9}]undecane-8,11-dione, CAS 2958-72-7) was first reported by Cookson and co-workers in their work on the photochemical cyclization of Diels-Alder adducts in 1964 (*J. Chem. Soc.*, **1964**, 3062-3075). The preparation of this cage compound was introduced as a benchmark for comparing photoreactors by Loubière *et al.* (*Chem. Eng. Process.*, **2013**, 64, 38-47).

3. EXPERIMENT

3.1 Setup

The setup with the HANU-reactor is depicted in Scheme 2. The reactor base has cubic static mixing elements, an irradiated volume of 14 mL and is made of stainless steel 316L (Model: *HANU*BASE CUB-15-316L). The recipients and transparent tubing were shielded from light by means of aluminum foil.

The photon flux entering the reactor amounted to 2.7 x 10^{-4} einstein/s as determined by ferrioxalate actinometry.



A. Recipient with starting material
B. Metering pump
C. Pulsator
D. HANU-reactor with *HANU*BASE CUB-15-316L
E. High-power 365 nm LED light source
F. 1.6 mm ID x 3.2 mm OD PFA tubing
G. Dome-loaded BPR (set to 2 bar)
H. Recipient with crude product

Scheme 2. Setup of the experiment

3.2 Procedure

A recipient was filled with 250 mL 0.50 M solution of **1** (9.4 wt%) in EtOAc. The starting mixture was pumped into the system and any residual air pockets were removed. Subsequently, the BPR was pressurized to 2 barg and the flow rate was set to 18.7 mL/min, which corresponds to an irradiation time of 45 seconds. The pulsation frequency was 3 Hz and center-to-peak amplitude in the reactor 4.2 mm. The 365 nm LEDs were placed on top of the reactor lid and switched on. The reaction was performed at ambient temperature. After 135 seconds (3x residence time), collection was started.

3.3 Results

Using the setup in Scheme 2, HPLC-analysis of the crude showed that > 99.8% conversion of Diels-Alder adduct **1** had taken place, while > 99% yield of Cookson's diketone was obtained according to GC-FID. This corresponds to a productivity of 97 g/h or 2.3 kg/d, resulting in a space-time-yield of 6.9 kg/L/h.

4. CONCLUSION

In summary, 2.3 kg/d of Cookson's diketone could be produced with a lab scale 14 mL reactor.

This demonstrates that the HANU-reactor is a compelling photochemical tool which enables the user to generate large outputs of product.

For more detailed information about this application note or the HANU-reactor in general, please contact Creaflow at info@creaflow.be.