



Use of the EvoluChem Photoredox box duo at Domainex

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Domainex

- A pharmaceutical research company
 - Based in Cambridge, UK.
 - Currently 70+ employees.
 - 2000 m² of lab space.
- Provide integrated drug discovery services and consultancy - from target to candidate drug.

- The company has a range of services including,



- Constantly reviewing new technologies to expand our capabilities within synthetic chemistry.



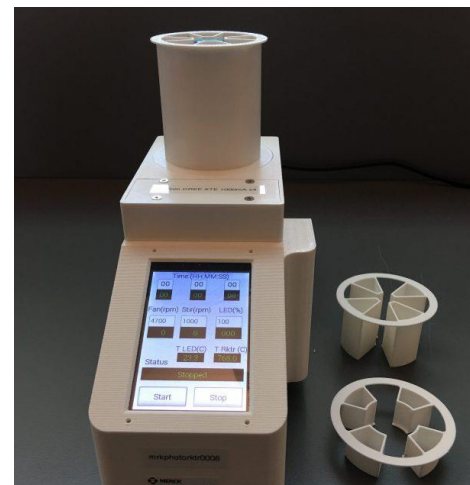
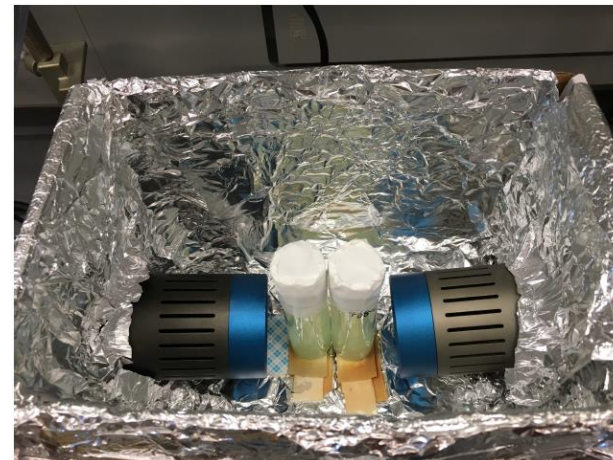
Amongst our clients are:

- 50% of the **Top 10 pharma** companies
- World's **#2 agrochemical** company
- **Global biotechnology** companies
- Major **academic** institutions
- Including...

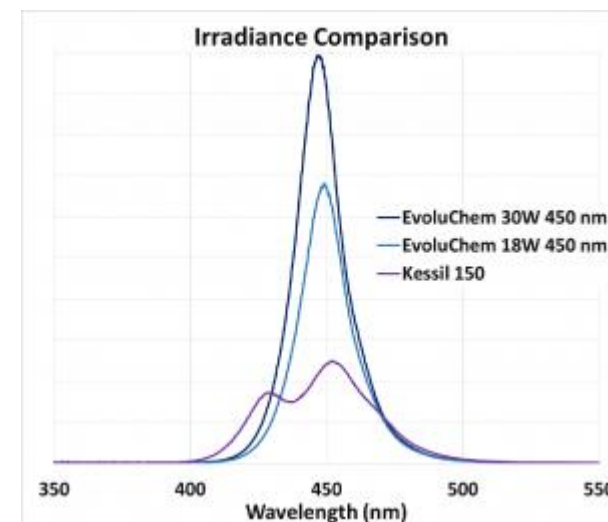
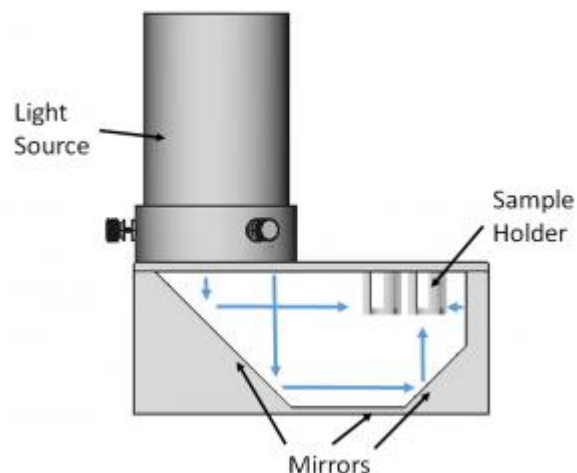
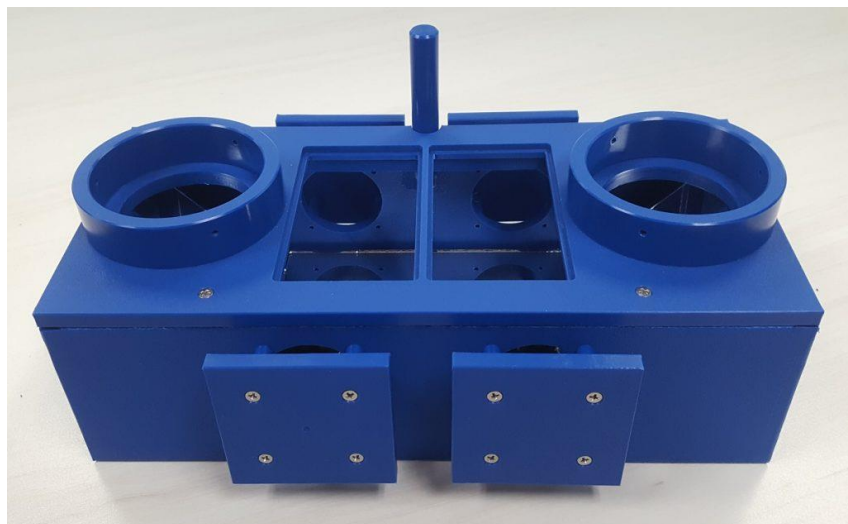


Our interest in photochemistry

- Rise in popularity in the last 5-10 years. Extensive literature now exists.
- Photochemical reactions are typically mild and many reactions are carbon-carbon bond forming.
- A wide range of photochemical equipment is available, from homemade apparatus to automated flow systems.
- We desired equipment that
 - Enable reproducible conditions.
 - Could run reactions in parallel – to allow screening of reaction conditions and explore SAR.
 - Run reactions up in the 100 mg to 1 g range – the scale of most interest to medicinal chemists.
 - Easy to use.



Summary of the photoredox box duo

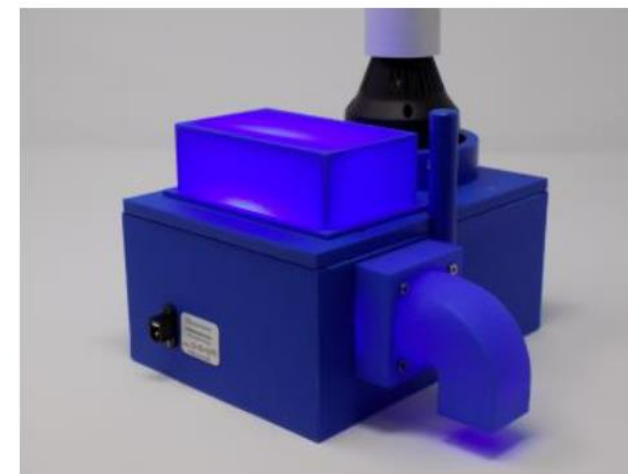
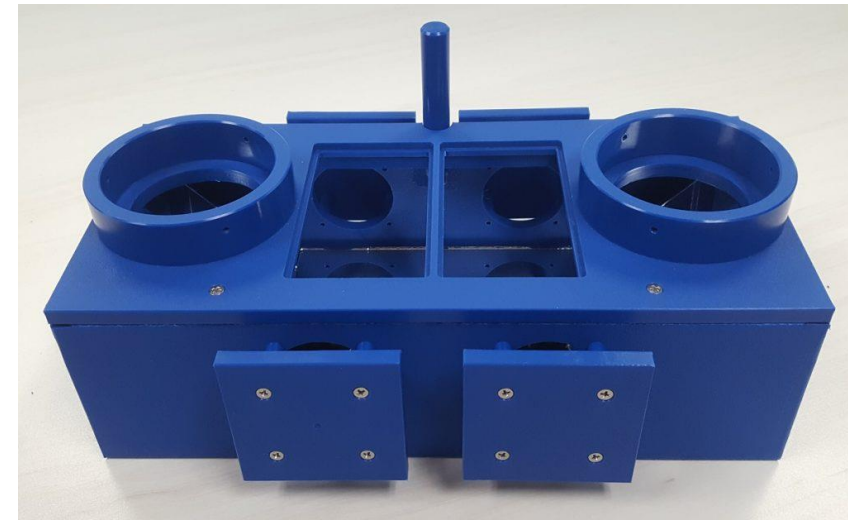


- 2 fans to keep the reaction cool.
- 2 positions to place vials each position can hold 8 × 2, 4 or 8 mL vials or 2 × 20 mL vials.
- Our PhotoRedox Box Duo has 2 × 18W blue (450 nm) LED lights (total power 36W vs 40W using the Merck system).
- Many different wavelengths available, as are more powerful 30W LEDs

Going to focus this talk on the aspects of PhotoRedox Box Duo we have used at Domainex

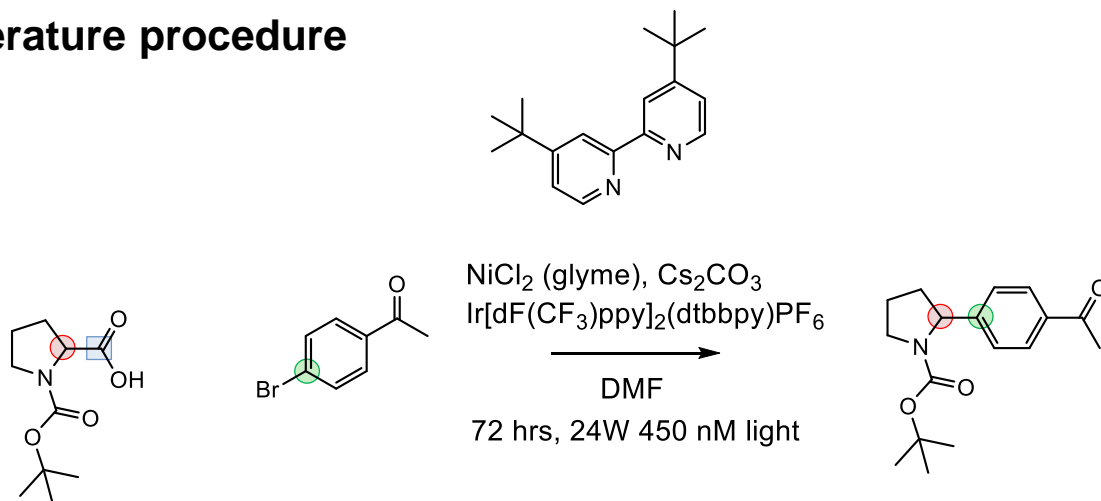
Any issues with the equipment?

- There are no major problems with the equipment. It appears to deliver an improvement on many “homemade” literature set ups.
- Fans keep the reactor cool as described,
 - The fan power adapter looks a bit fragile.
 - No indicator that fans are running.
- Stirring is driven by a separate heater stirrer.
- Lights arrive without connectors (UK only) and have to be purchased separately.
- Including the hotplate, fans, and both lights 4 plugs are required.
- The PhotoRedox Box Duo is quite open so light leakage is a problem. However, an upgrade kit is now available.



Sp2-Sp3 cross coupling 1

Literature procedure



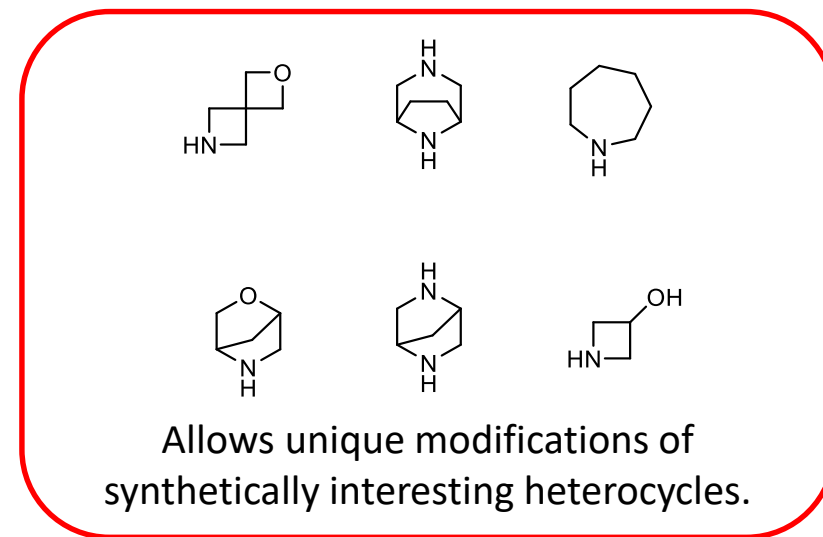
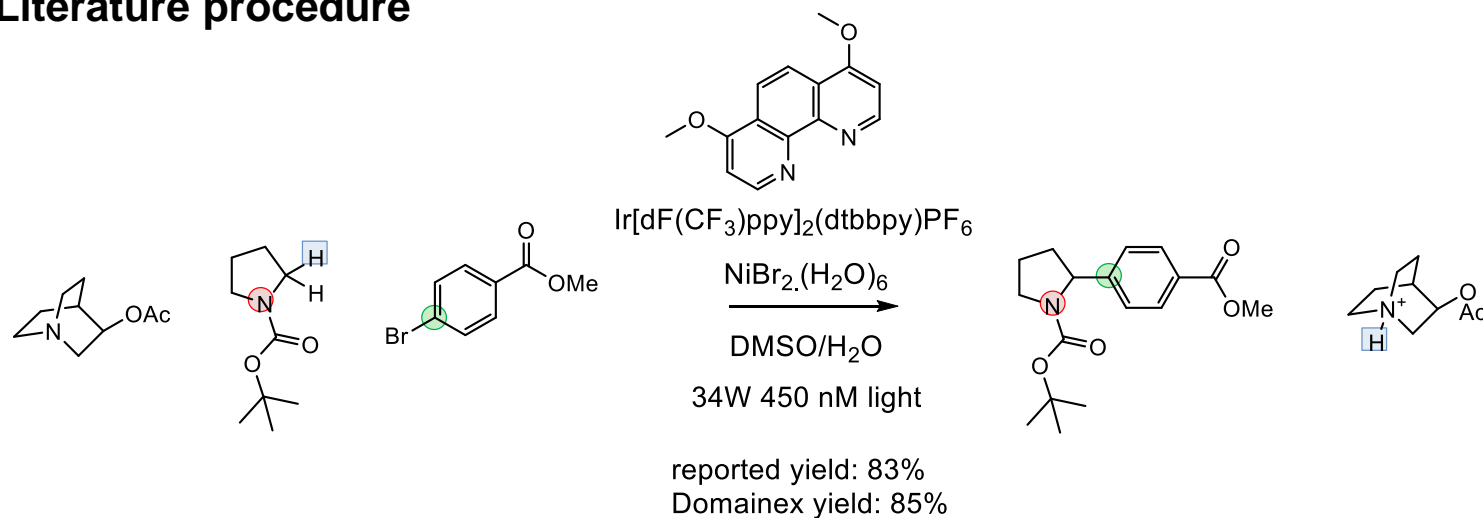
- This reaction was of particular interest to us as it allows modification of a common chemical-feedstock in a carbon-carbon bond forming process.
- The PhotoRedox Box Duo increases the light available to the reaction compared to the literature procedure.

Carboxylic acid	Bromide	Lit yield	In house yield
		84%	82% (isolated)
		N/A	60% (isolated)
		76%	80% (conversion)
		54%	50% (conversion)
		58%	65% (conversion)

Reported substrate scope was repeated successfully. Gratifyingly reaction times were greatly reduced, typically to 18-20 hrs.

Sp2-Sp3 cross coupling 2

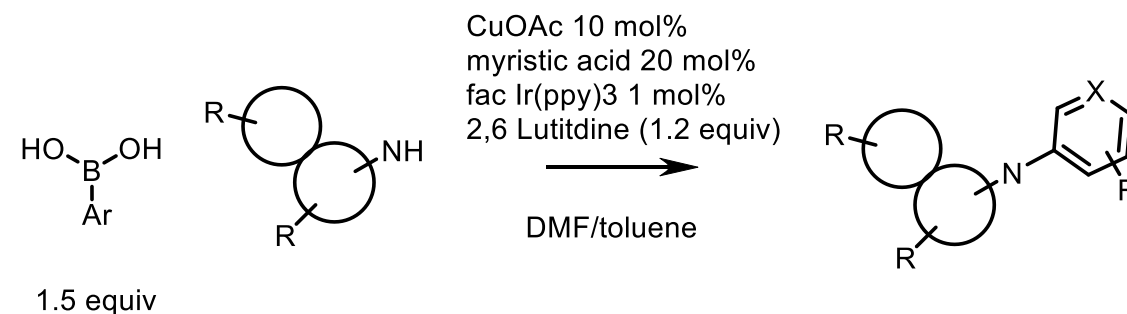
Literature procedure



- Another reaction of obvious interest, direct CH activation for carbon-carbon bond formation.
- This was of particular interest for synthesis of novel fragments and fragment-hit expansion.
- At Domainex we have been able to reproduce the literature procedure above and the reported yield. We have now expanded our investigation to non-literature substrates.

Photochemical procedure for Chan-Lam coupling

- A thermal procedure worked acceptably for phenyl boronic acid. The reaction was generally low yielding for other substrates.
- A photochemical procedure was adapted from a literature reaction to access several heterocyclic substrates.
- Neither the aniline, nor the boronic acid were precededented in the original paper.
- The PhotoRedox Box Duo gave increased light power compared to the literature procedure, 36W vs 18W.



Aryl group	Photochemical reaction Yield	Thermal reaction yield
Phenyl	44%	56%
4 methoxy 3 pyridyl	68%	<5%
3 methoxy 4 pyridyl	56%	<5%
3 Nitrile	0%	<5%

In this example a literature procedure was adapted for use on unreported substrates to synthesise novel products inaccessible using a conventional approach.

Scope for further use at Domainex

- The system is easy to use and chemists have not reported any major problems. Generally literature procedures work as reported and the PhotoRedox Box readily standardises conditions across different substrates.
- Photo Redox is currently being used to expand our fragment library collection both in terms of novel fragments and fragment-hit expansion. Several non-literature compounds have now been synthesised.
- A flow chemistry module is also available we are currently exploring it's use.
- Reaction screening kits are also available which allow many different reaction conditions to be screened in parallel, we are interested in these but we have not done this yet.
- There are also temperature controlled versions of PhotoRedox Box are now available, (Not tried at Domainex).

Conclusions

- Whilst many photochemical transformations are attractive synthetically it is easy to be put off by the need to use unfamiliar (or bespoke) equipment, as well as new methods or practises.
- The PhotoRedox Box Duo fulfils our needs for a photochemical reactor and has been successfully used on several projects.
- The light power (36W) compares well to other “bench top” systems on the market although it is lower than integrated flow systems. However, in our opinion, the single light system would be underpowered with a single 18W lamp.
- Light leakage can be a problem, but upgrade kit is available.
- Price of the PhotoRedox Box Duo was good (about £1500 with delivery and vial holders lamps etc).
- Quality of the PhotoRedox Box Duo is good, especially for the price.

Acknowledgements

- Thanks to all the scientists at Domainex, in particular to Andy Tuffnell, Mel Bayford and Luci Guetzoyan on the new technologies team.
- Thank you to the UKASF for the invite to speak.
- Thank you to EvoluChem for providing some extra details on recent improvements to the PhotoRedox Box duo.
- Any Questions?