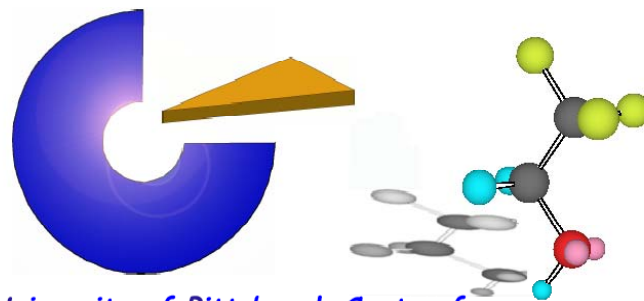


# *Improvements in the Synthesis and Purification of Small Molecule Libraries*

*- MAOS and Reagents/Scavengers on Solid Support -*



*University of Pittsburgh Center for  
Chemical Methodologies & Library Development*

*Stefan Werner*

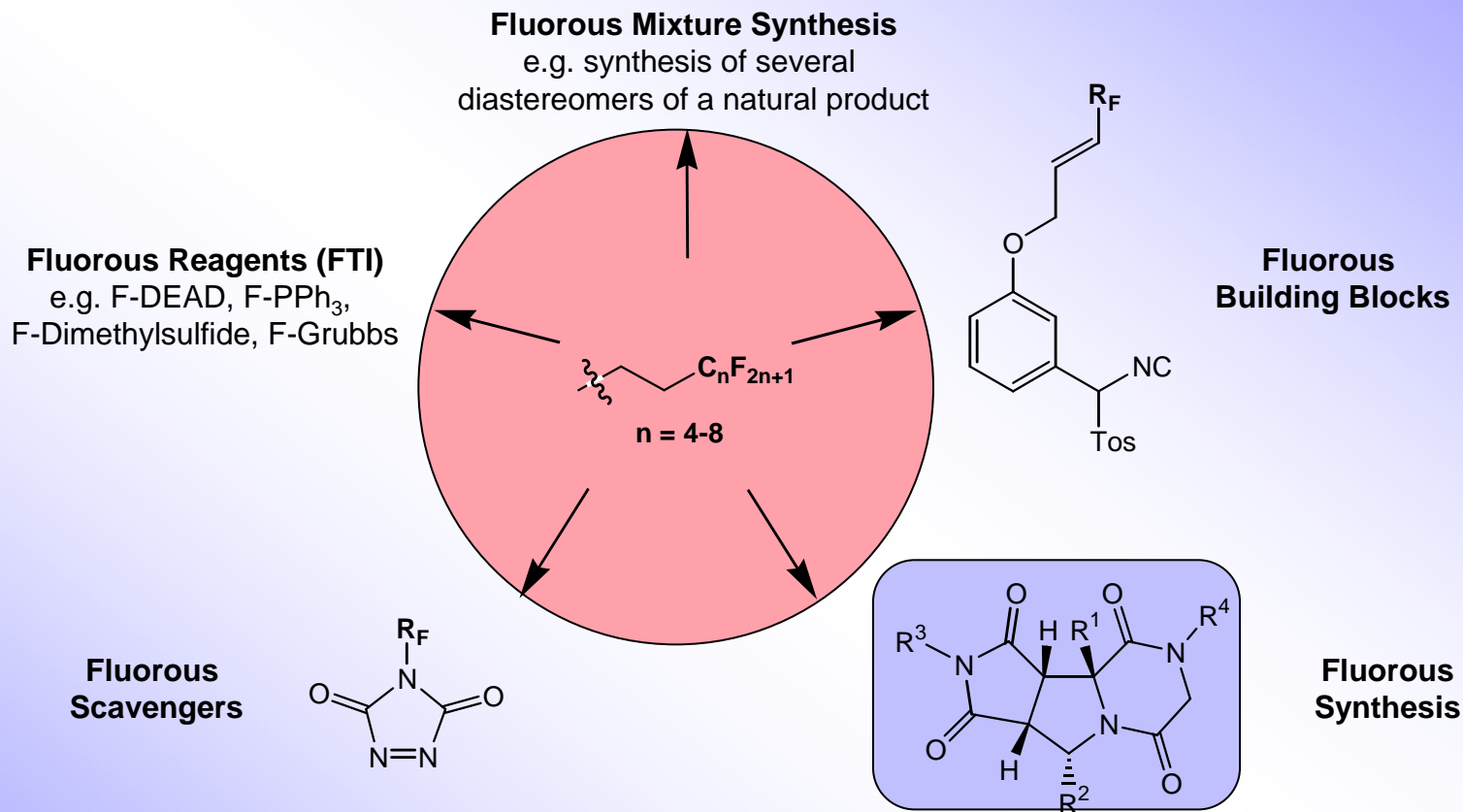
*Associate Director of the UPCMLD*

Drug Discovery Chemistry 2007, CHI, La Jolla, CA

May 14<sup>th</sup>, 2007

# Application of Fluorous Chemistry to the Synthesis of Compound Libraries

Chemical  
Methodologies



Curran, D. P. *Angew. Chem.* **1998**, *110*, 1230-1255.

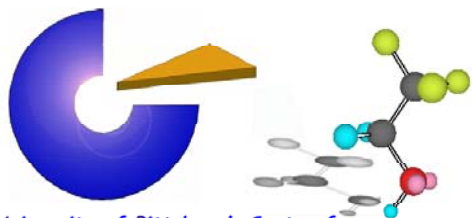
Zhang, W. *Tetrahedron* **2003**, *59*, 4475-4489.

Werner, S.; Curran, D. P. *Org. Lett.* **2003**, *5*, 3293-3296.

Curran, D. P.; Dandapani, S.; Werner, S.; Matsugi, M. *Synlett* **2004**, 1545-1548.

Gladysz, J. A.; Curran, D. P.; Horváth, I. T. *Handbook of Fluorous Chemistry*, Wiley-VCH, New York, **2004**.

Fukui, Y.; Brückner, A.; Shin, Y.; Balachandran, R.; Day, B. W.; Curran, D. P. *Org. Lett.* **2006**, *8*, 301-304.



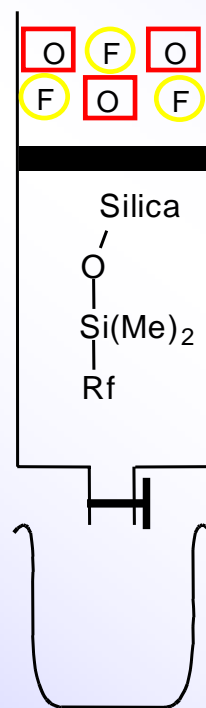
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# FSPE

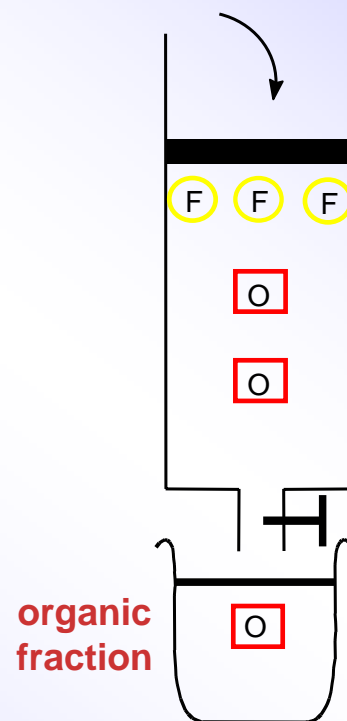
Chemical  
Methodologies



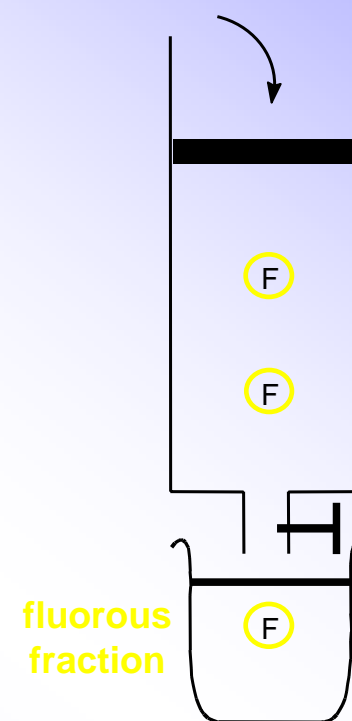
fluorous  
silica gel

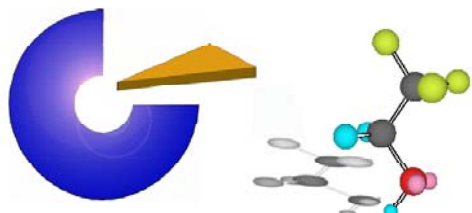


Fluorophobic  
Solvent  
(MeOH-H<sub>2</sub>O)



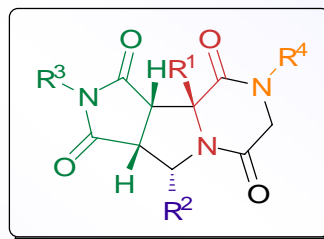
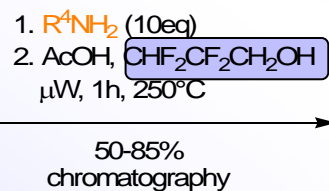
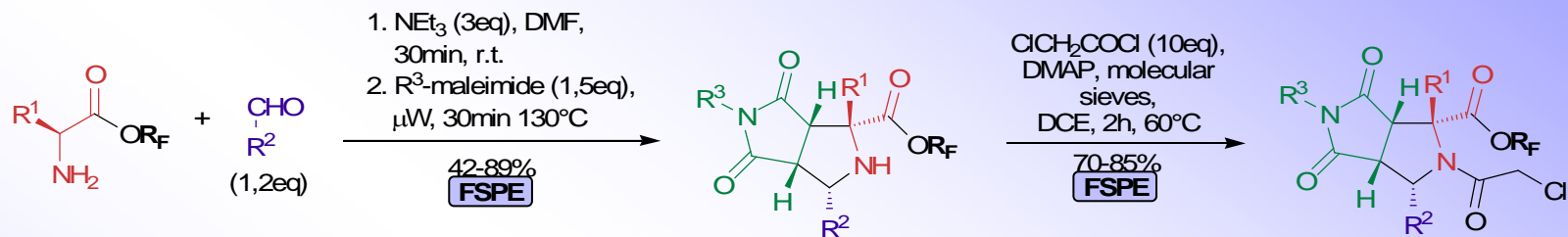
Fluorophilic  
Solvent  
(MeOH or Et<sub>2</sub>O)



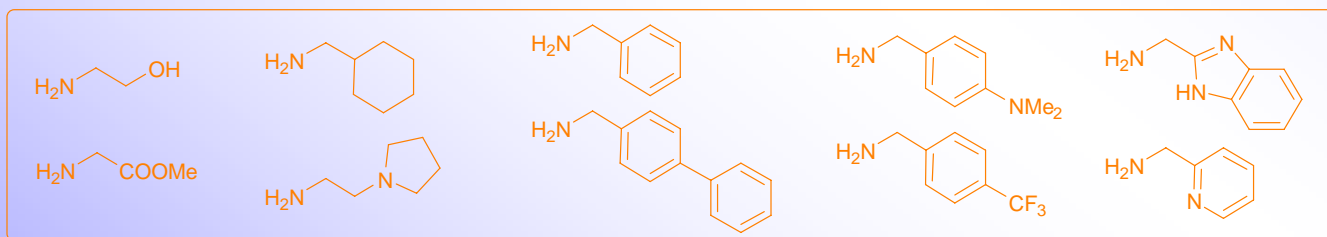
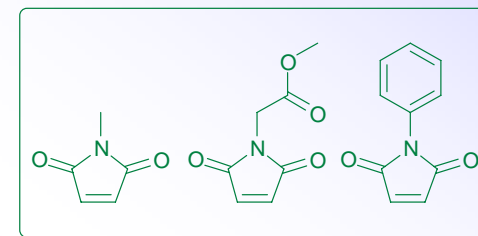
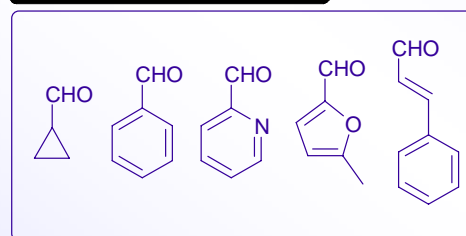
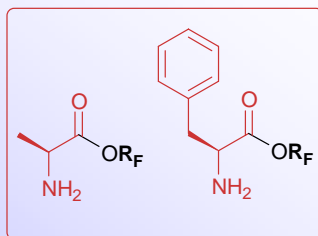


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# Fluorous Synthesis of Piperazinediones



**FSPE = Fluorous Solid  
Phase Extraction**



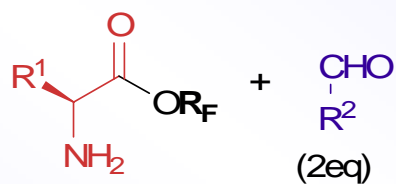
Library  
Development

Zhang, W.; Lu, Y.; Chen, C. H. T.; Curran, D. P.; Geib, S. *Eur. J. Org. Chem.* **2006**, 2055, 2059.  
Werner, S.; Turner, D. M.; Nielsen, S. D.; Curran, D. P. *unpublished*.



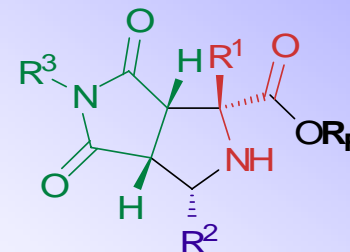
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# FSPE-Purification

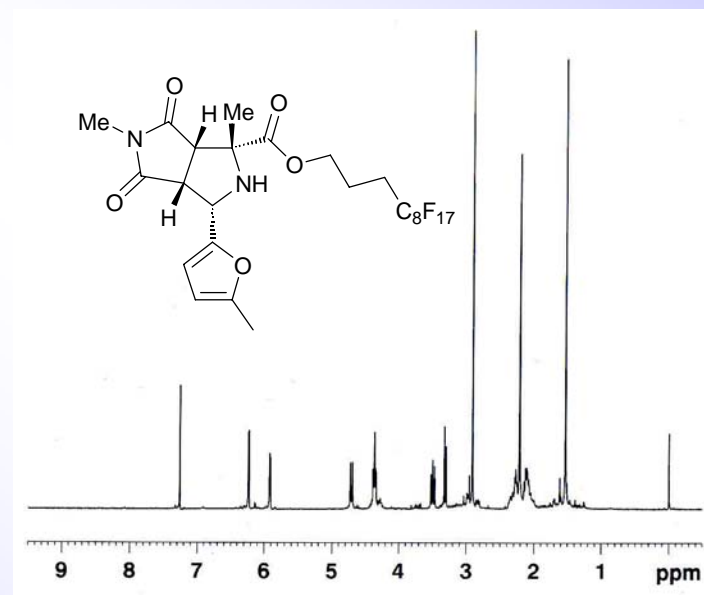
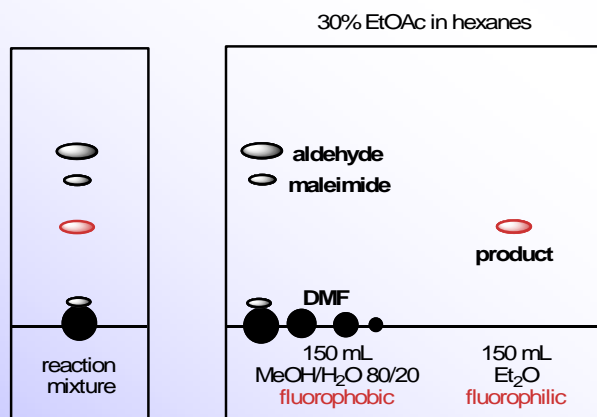


1.  $\text{NEt}_3$ , DMF, 30min, r.t.
2.  $\text{R}^3$ -maleimide (2eq),  $\mu\text{W}$ , 30min 130°C

50-83%  
**FSPE**



Library  
Development



Werner, S.; Turner, D. M.; Nielsen, S. D.; Curran, D. P. *unpublished*.