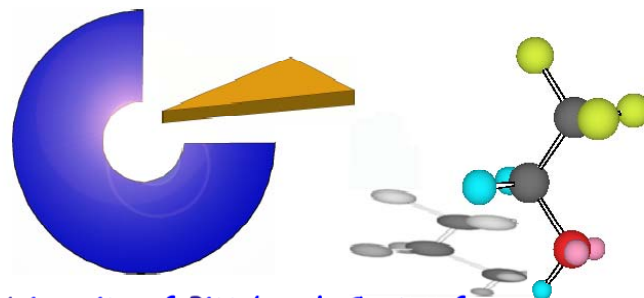


Improvements in the Synthesis and Purification of Small Molecule Libraries

- MAOS and Reagents/Scavengers on Solid Support -



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

Stefan Werner

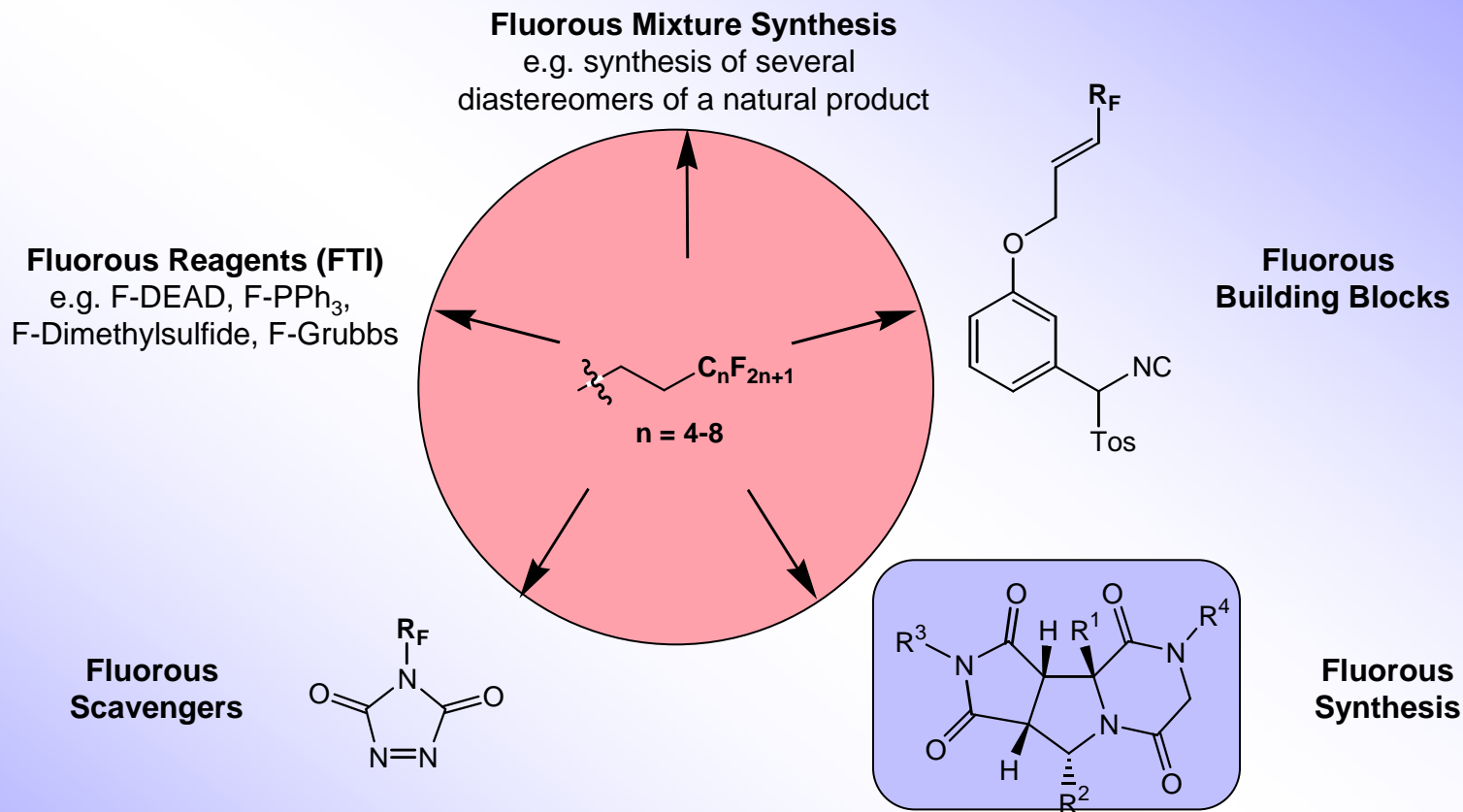
Associate Director of the UPCMLD

Drug Discovery Chemistry 2007, CHI, La Jolla, CA

May 14th, 2007

Application of Fluorous Chemistry to the Synthesis of Compound Libraries

Chemical
Methodologies



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

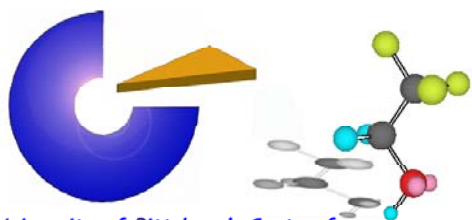
Zhang, W. *Tetrahedron* **2003**, *59*, 4475-4489.

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.



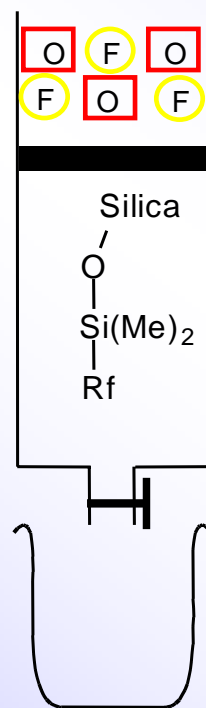
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FSPE

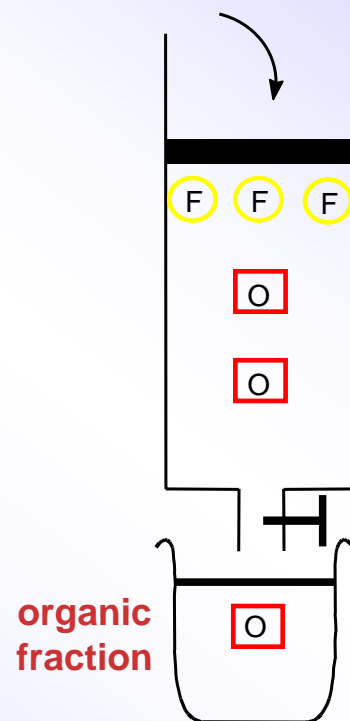
Chemical
Methodologies



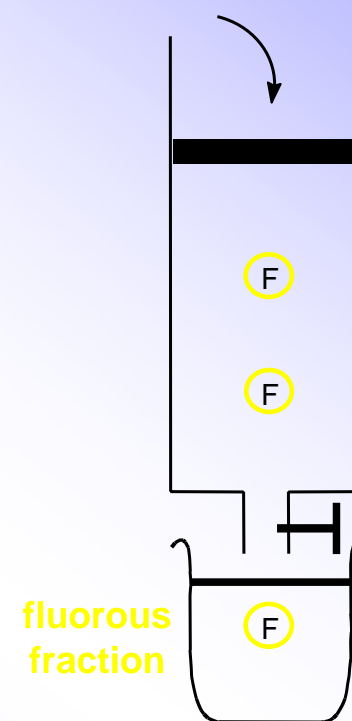
fluorous
silica gel

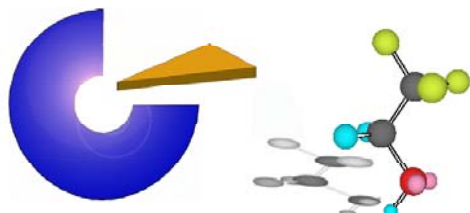


Fluorophobic
Solvent
(MeOH-H₂O)



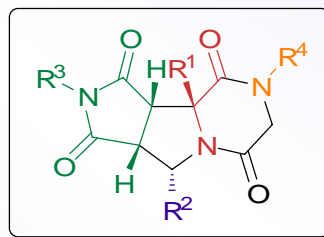
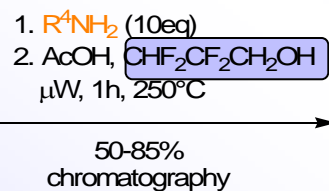
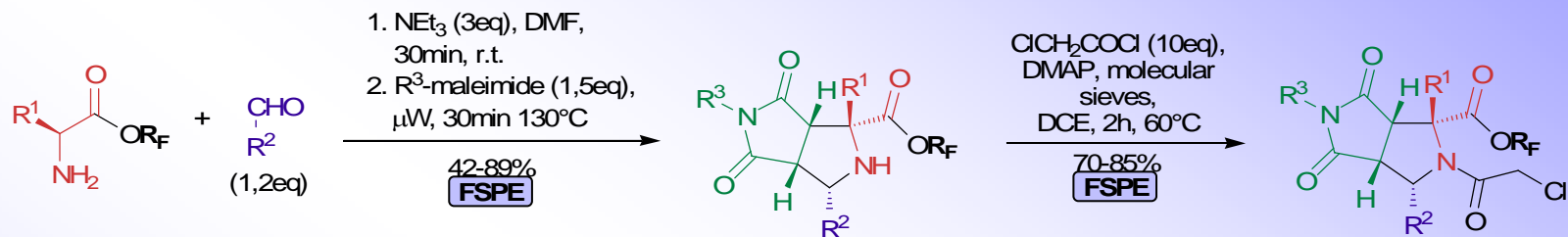
Fluorophilic
Solvent
(MeOH or Et₂O)



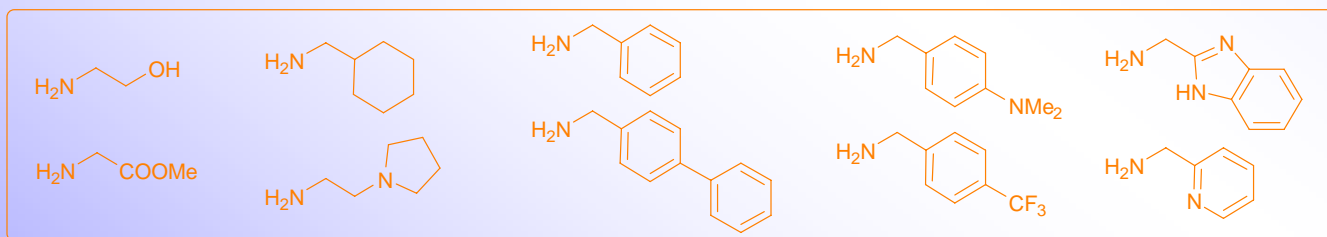
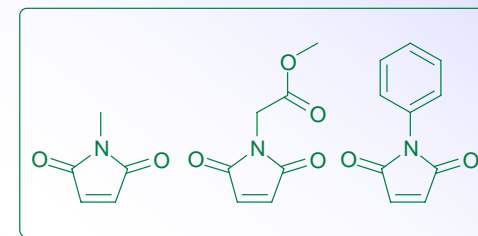
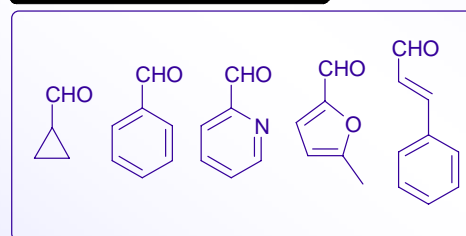
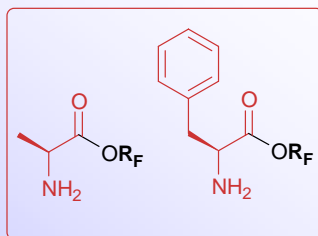


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Fluorous Synthesis of Piperazinediones

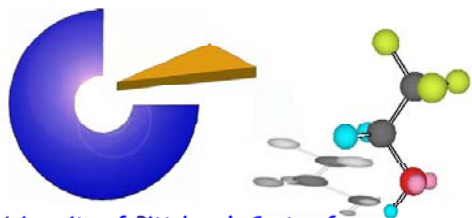


**FSPE = Fluorous Solid
Phase Extraction**



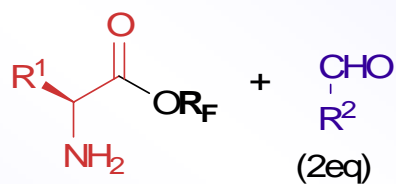
Library
Development

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*.



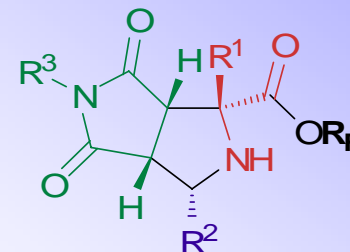
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FSPE-Purification

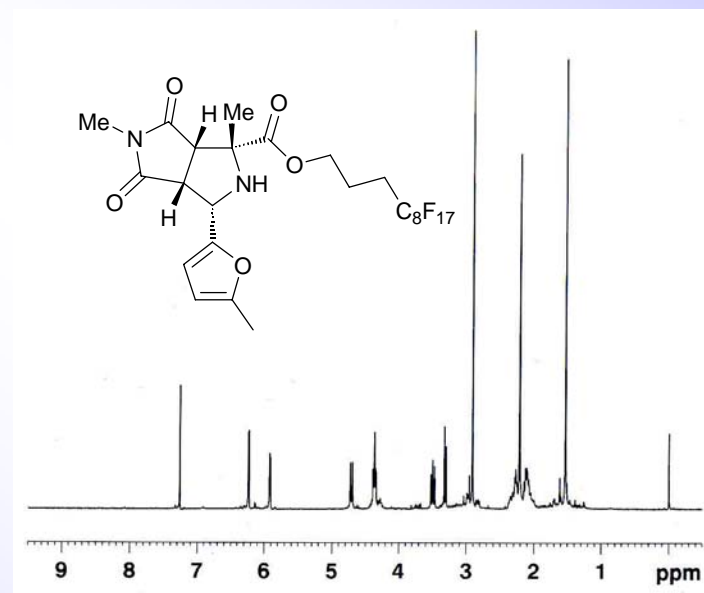
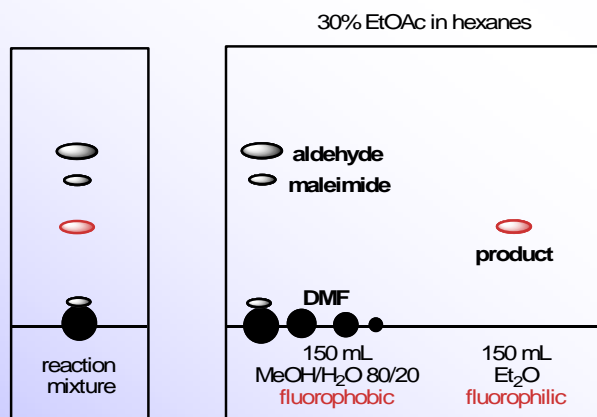


1. NEt_3 , DMF, 30min, r.t.
2. R^3 -maleimide (2eq), μW , 30min 130°C

50-83%
FSPE



Library
Development



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