

Application of the arachno™ technology inside Educational fields: the introduction of parallel synthesis concepts inside an undergraduated lab.

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DIPARTIMENTO DI SCIENZA E
TECNOLOGIA DEL FARMACO
UNIVERSITÀ DEGLI STUDI DI TORINO

**UNIVERSITÀ
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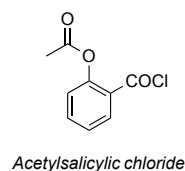
FALC

Parallel synthesis and the arachno™ project

The parallel synthesis is a powerful tool in Drug Design, usually applied to the obtainment of a library of molecules during hit-to-lead processes. Its application, because the expensive technology involved, is restricted to high technological research laboratories. **arachno™** (www.arachnoscience.com) is a revolutionary, easy-to-get low cost technology that allows the performance of up to six organic experiment at the same time. Being inexpensive, **arachno™** can be easily introduced at educational level. In this occasion is presented its application in the parallel preparation of a library of Aspirin analogues. Inside a full day labtime, each student will be able to obtain six different Aspirin amide analogues, each compound in isolated pure form. This exercise will offer the possibility to practically introduce to the class, beside the parallel synthesis concept itself, also concepts of practical organic synthesis, TLC, ¹H-, ¹³C-NMR and MS, being all the obtained compounds fully characterized.

Educational goals:

- Introduction of the parallel synthesis concept at Undergraduated level
- Quickly synthesis of six ASA analogues.
- Introduce the concepts of lipoflicity (ClogP), solubility and chromatography. Comparison of the structure obtained at spectroscopic level (NMR, MS, IR and UV).



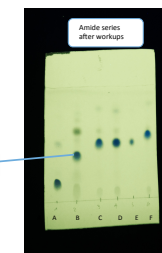
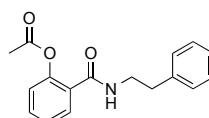
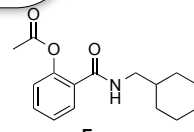
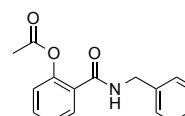
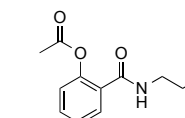
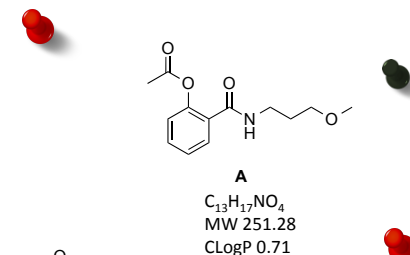
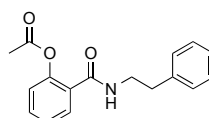
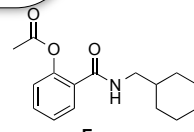
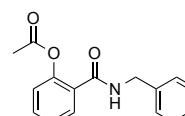
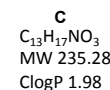
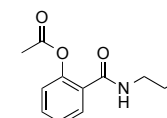
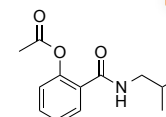
Acetylsalicylic chloride

arachno™: application of a parallel synthesis methodology to the preparation of six ASA analogues

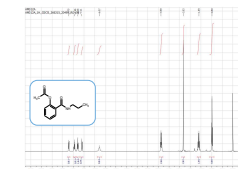


arachno
no more excuses

arachno™: application of parallel workup and purification techniques



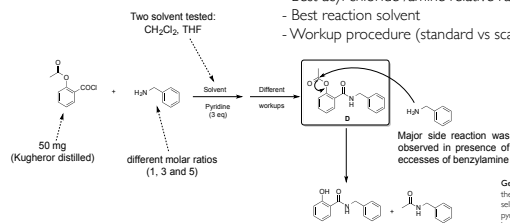
Inside the amide series, the rising ClogPs allow a nice correlation with the TLC Rf's. The substitution allow also the discussion of the NMR/MC/IR profiles.



Optimization of the synthetic scheme: synthesis of benzyl acetylsalicylamide (D)

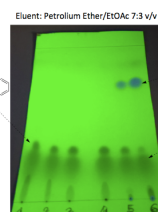
The benzyl amide D was firstly prepared in order to optimize the reaction conditions. Using arachno, six different reaction conditions as well as specific workups were tested. Using just six parallel experiments were checked:

- Best acyl chloride /amine relative ratio
- Best reaction solvent
- Workup procedure (standard vs scavenger)

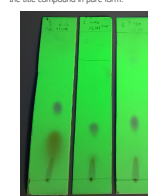


Flask #	Acyl Chloride	Benzyl amine	Pyridine	Solvent	Workup
1	50 mg, 0.252 mmol	27 mg, 27.5 µl, 0.252 mmol; 1 eq	60 mg, 60 µl, 0.504 mmol; 3 eq	CH ₂ Cl ₂ (3 mL)	Standard
2	Idem	Idem	Idem	THF (3 mL)	Standard
3	Idem	Idem	Idem	CH ₂ Cl ₂ (3 mL)	Scavenger
4	Idem	Idem	Idem	THF (3 mL)	Scavenger
5	Idem	81 mg, 82 µl, 0.756 mmol; 3 eq	Idem	THF (3 mL)	Standard
6	Idem	135 mg, 137 µl, 1.26 mmol; 5 eq	Idem	THF (3 mL)	Standard

General procedure: to a solution of the acyl chloride (50 mg) in the selected solvent (3 mL) was added pyridine then the selected amount of benzyl amine. The formation of a white precipitate is immediately observed. The reaction evolution was checked by TLC (Petroleum ether 40:60 EtOAc: 7.3 v/v) observing a complete conversion inside 1 h. In the experiments 5 and 6, where an excess of benzylamine was used (3 and 5 equivalent respectively) a side reaction occur affording the formation of a higher Rf product **D1**. It can be observed how the formation of the side product **D1** is correlated to a reduced D formation. This side product was isolated and characterized as the benzyl salicylamide.



Application of parallel workup and purification techniques



Workup (Resin scavenger): to a slowed stirred mixture, Amberlist 15(H) (320 mg, 1.52 mmol, cationic exchange, loading 4.7 meq/g) was added. This treatment is able to scavenge the basic species present inside the mixtures. After 30 min, to the filtered mixture Amberlist A-21 (110 mg, 0.504 mmol, anionic exchange, loading 4.6 meq/g) was added in order to scavenge the acidic species. The resulting mixture was then carefully stored for 15 min, filtered and the resulting clear solution was concentrated under reduced pressure to afford the title compound in pure form.

arachno is a patented technology developed by **beenext s.r.l.** (www.arachnoscience.com), an University of Torino SpinOff, and represented/distributed on the market by **FALC INSTRUMENT s.r.l.** (www.falcinstruments.it)

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