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UNIVERSITAS SCIENTIARUM SZEGEDIENSIS

# Synthesis, transformation and application of isopulegol and neoisopulegol-based bi-and tridentate chiral ligands

Fatima Zahra Bamou, Tam Minh Le, Bettina Volford, András Szekeres and Zsolt Szakonyi

Presented by: BAMOU Fatima Zahra

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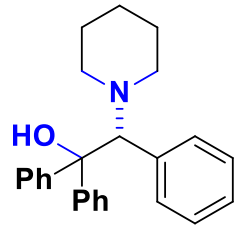
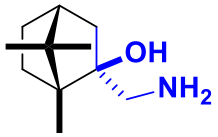
# INTRODUCTION

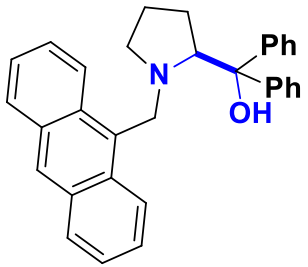


S. Rodrí guez-Escrich *et* al.
*J. Org. Chem*. **2008**, *73*, 5343.

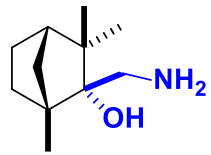


V. Dimitrov *et* al. *Tetrahedron Asymmetry* **2001**, *12*, 1325.

**Enantioselective addition of diethylzinc to aldehydes**



M. Barry *et* al. *Org.Lett.* **2011**,*13, 1902* .



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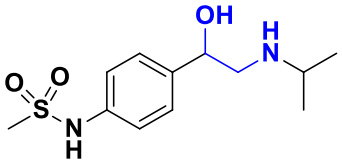
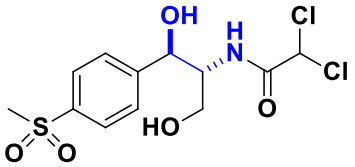
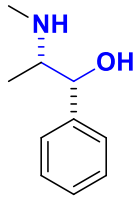


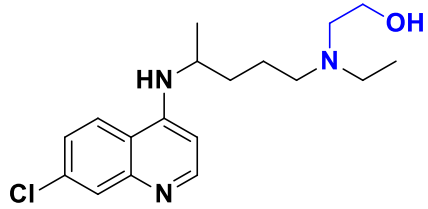
Sotalol
**( Beta blocker )**



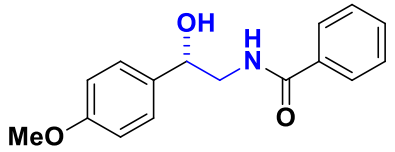
Thiamphenicol
**( Antibiotic )**



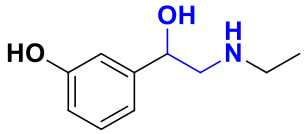
Ephedrine
**( Sympathomimetic agent )**



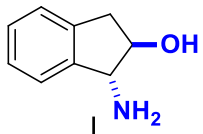
Hydroxychloroquine
**( Treatement of Coronavirus )**

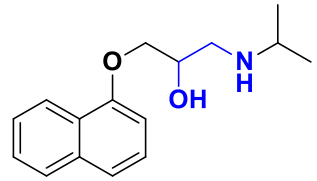


(+)-tembamide
**( Antiviral natural product )**



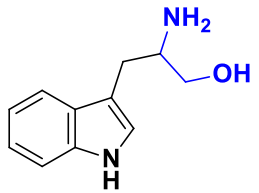
Etilefrine
**( antihypotensive )**

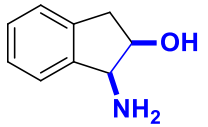




Propranolol
**( Beta blocker )**

**Aldol reaction catalysts**



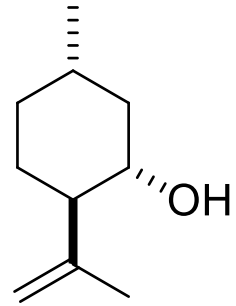


J. Schrittwieser *et* al. *Green Chem.* **2013**, *15*, 3319.

T. Katherine *et* al. *Antimicrob. Agents. Chemother.* **2006**, *50*, 640.

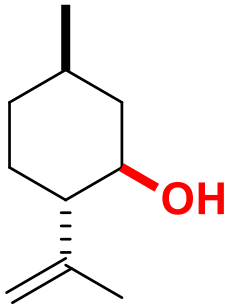
C. Arróniz *et* al. *Org. Biomol. Chem.* **2011**, 9, 5079.

# Aim




**(+)-Isopulegol**
synthetically from citronellal

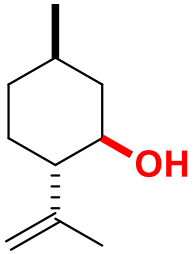
1 ml ≈ 100€ (Merck Co.)



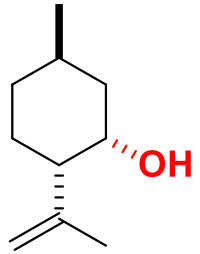

**(-)-Isopulegol (natural)**

1 kg ≈ 100€ (Merck Co.)

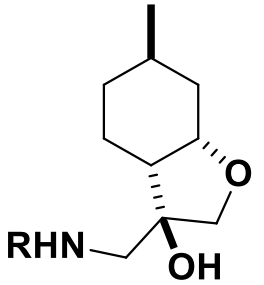
Mentha pulegium

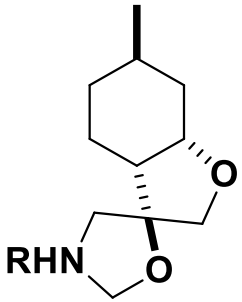



**(-)-Isopulegol**

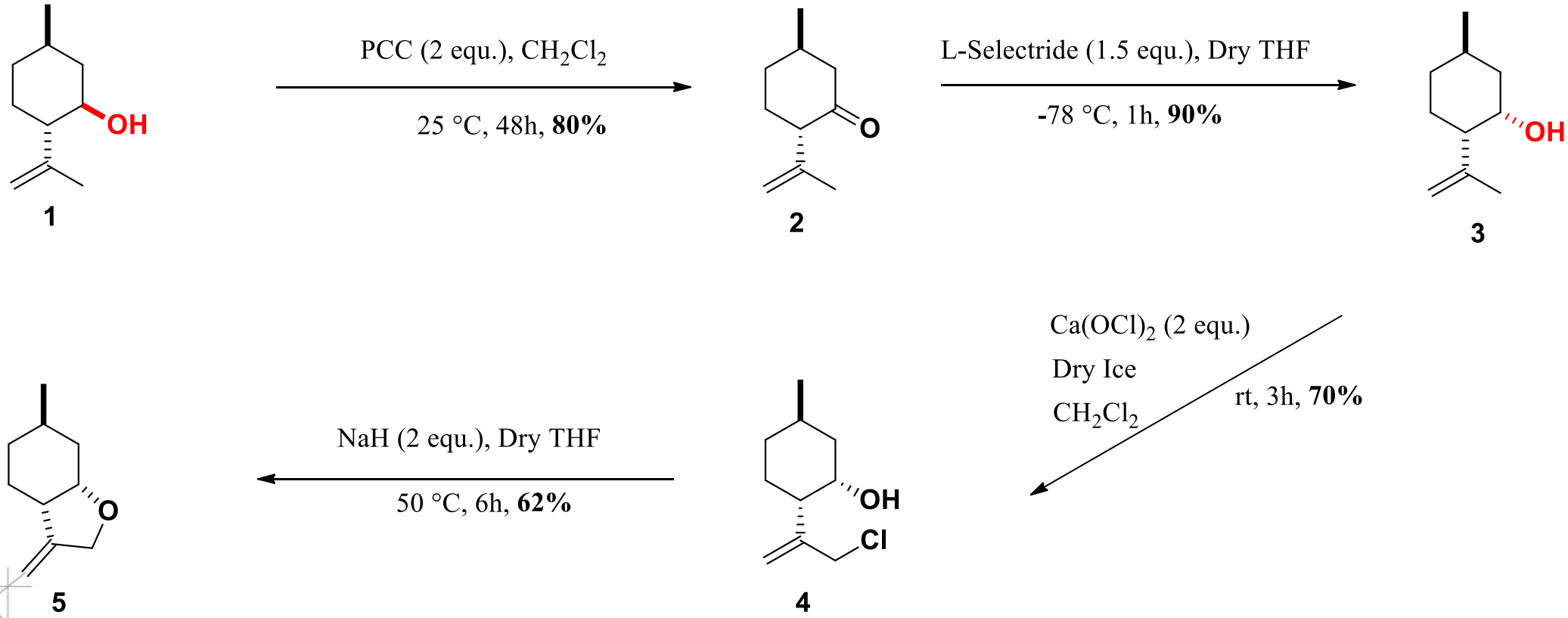



**(+)-Neoisopulegol**



# Synthesis of exo-methylene-substituted perhydrobenzofurane derivative :



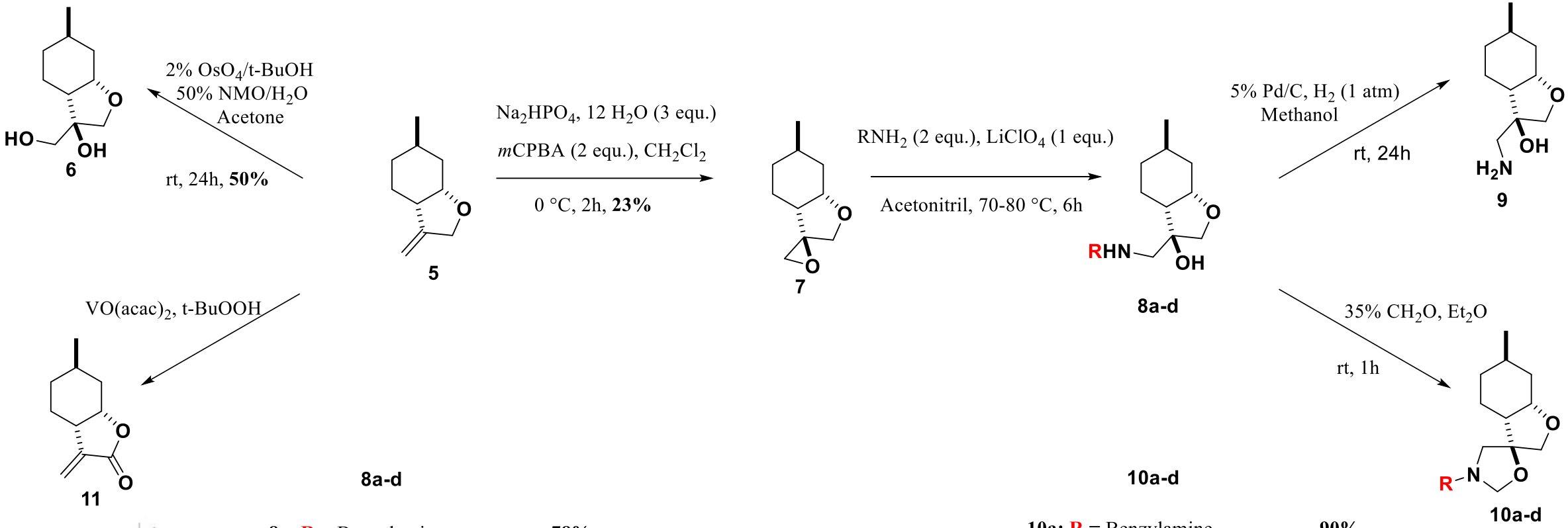


W. Engel *et* al *Food Chem.* **2003**, *51*, 6589.

D. Friedrich *et* al *Tetrahedron.* **1988**, *44*, 1369.

T. Brocksom *et* al *Synth. Commun.* **1988**, *18*, 1403.

# Synthesis of 1,2-aminoalcohols and spirooxazolidines :




**8a-d**

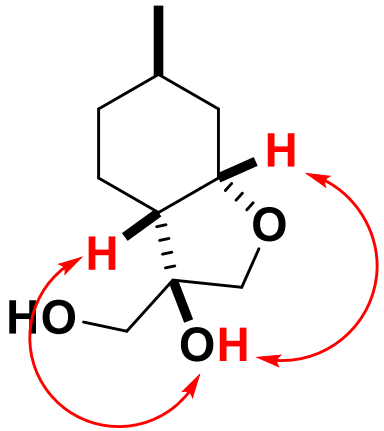
| | | |
|---|---|---|
| **8a:** | **R** = Benzylamine | **78%** |
| **8b:** | **R** = Isopropylamine | **83%** |
| **8c:** | **R** = (*S*)-Methylbenzylamine | **75%** |
| **8d:** | **R** = (*R*)-Methylbenzylamine | **65%** |

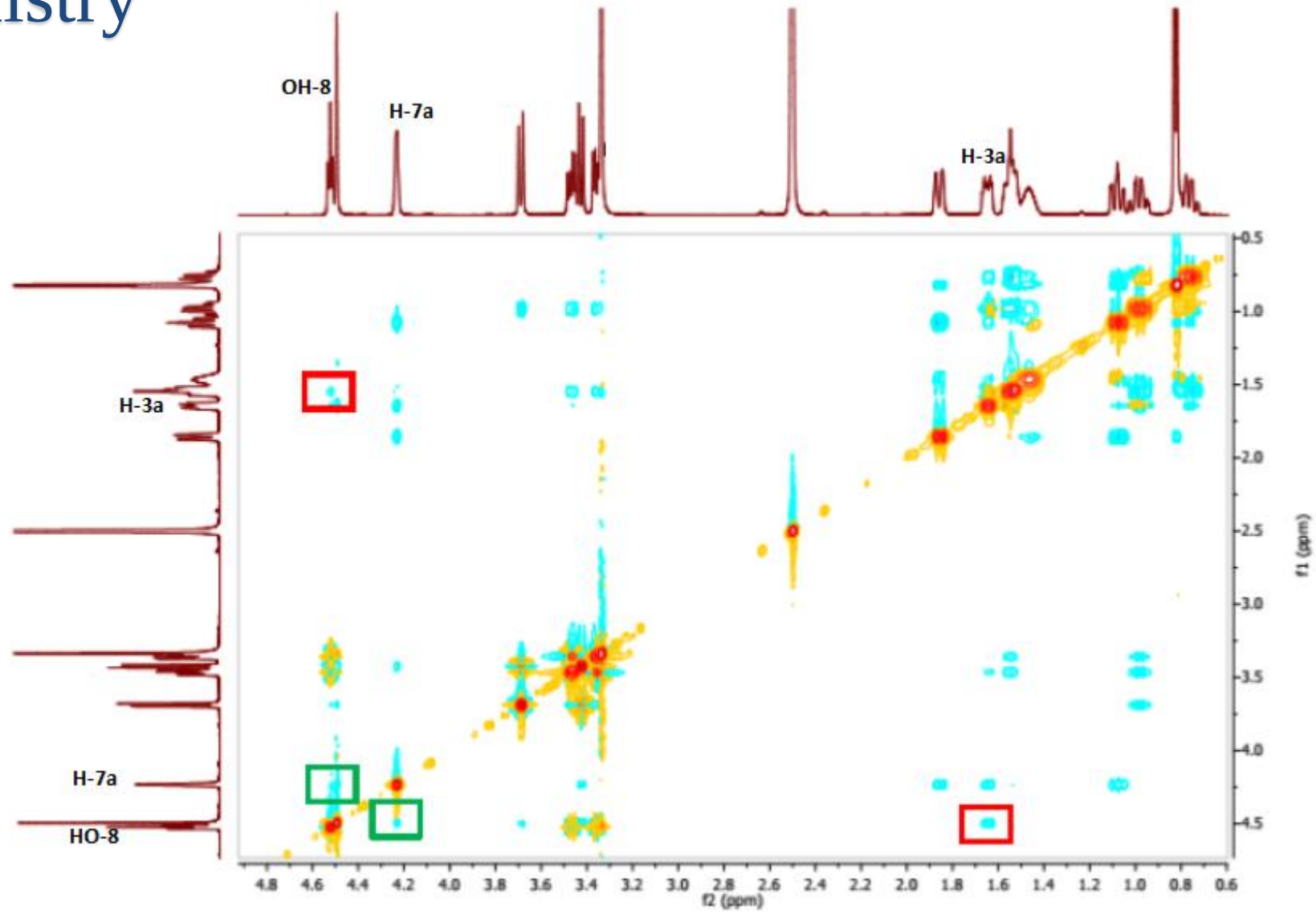
**10a-d**

| | | |
|---|---|---|
| **10a:** | **R** = Benzylamine | **90%** |
| **10b:** | **R** = Isopropylamine | **95%** |
| **10c:** | **R** = (*S*)-Methylbenzylamine | **95%** |
| **10d:** | **R** = (*R*)-Methylbenzylamine | **50%** |

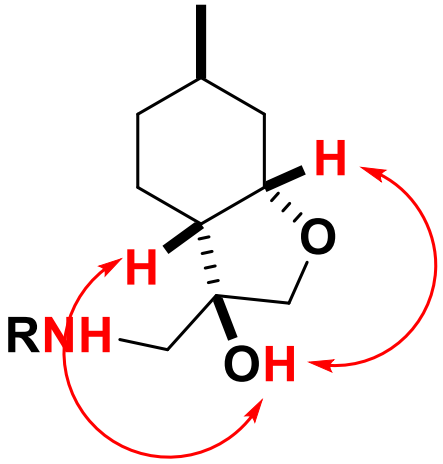
T. Brocksom et al *Synth. Commun*. **1988**, 18, 1403

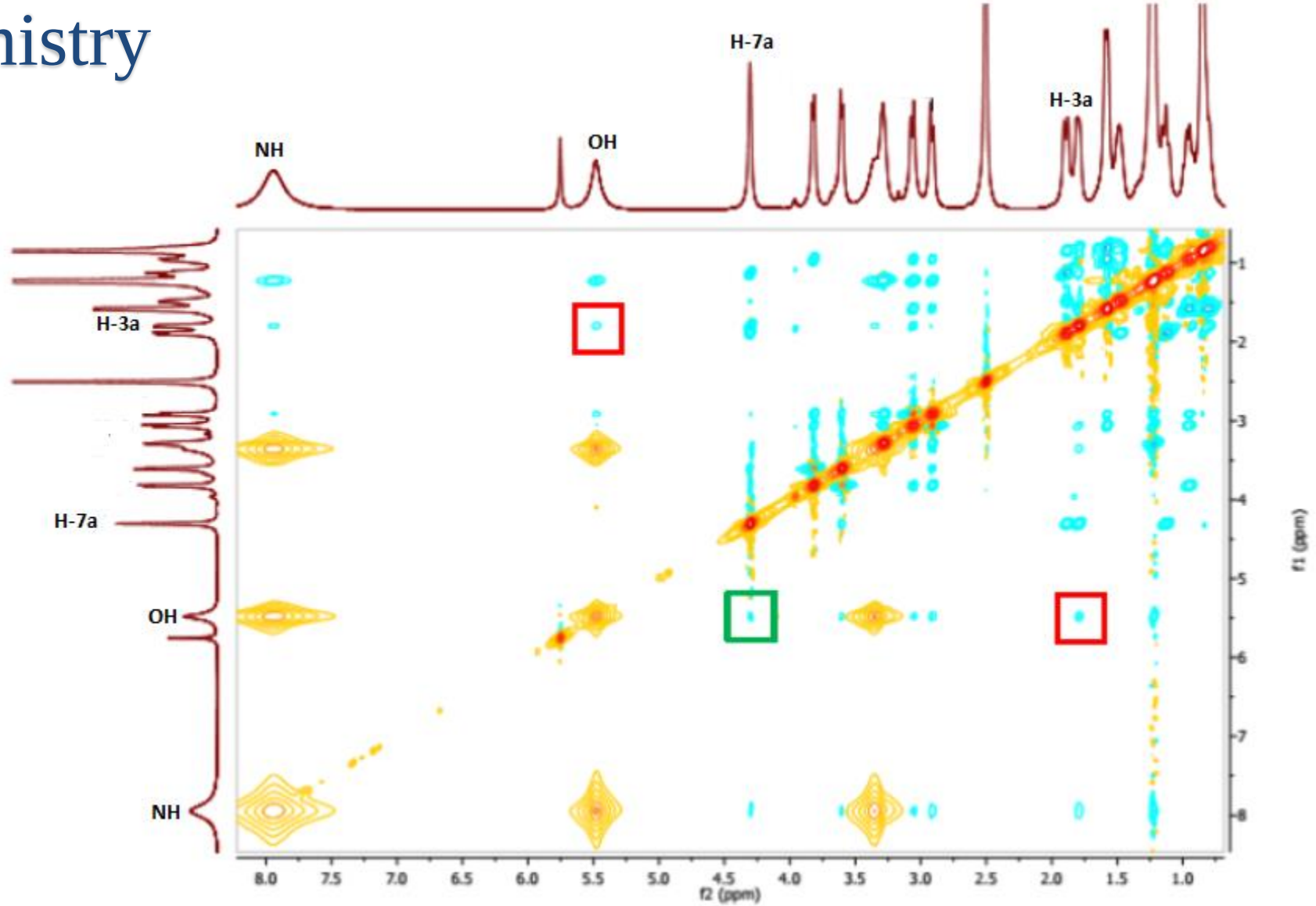
# Stereochemistry



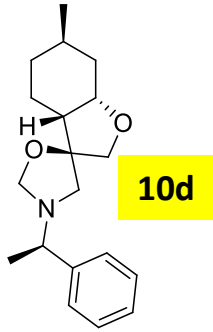
# Stereochemistry



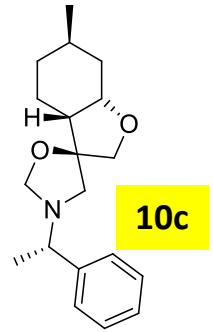



# Antimicrobial activities of the synthesized compounds :

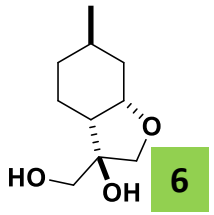
| | | Inhibitory effect (%) ± RSD (%) | | | | | |
|---|---|---|---|---|---|---|---|
| | | Yeast | | Gram-negative | | Gram-positive | |
| **Analogue** | Conc. (µg/mL) | C. albicans | C. krusei | E. coli | P. aeruginosa | B. subtilis | S. aureus |
| **6** | 10 | – | **36.5±8.4** | – | – | – | – |
| | 100 | – | **58.4±14.4** | – | – | 21.7±6.05 | – |
| **8d** | 10 | – | – | 8.7±3.15 | 7.5±1.54 | – | – |
| | 100 | – | – | 20.0±2.81 | 8.7±0.49 | – | 7.1±4.3 |
| **8c** | 10 | – | – | – | – | 19.0±2.61 | – |
| | 100 | – | – | 17.1±4.94 | 5.3±4.31 | 31.9±2.74 | – |
| **8a** | 10 | – | – | 16.7±6.68 | 9.9±1.8 | – | – |
| | 100 | – | – | 21.0±5.05 | 31.6±1.73 | 9.8±11.2 | 13.8±1.73 |
| **8b** | 10 | – | – | 3.7±1.68 | – | – | – |
| | 100 | – | – | 4.3±10.71 | 2.3±5.93 | 10.5±10.12 | – |
| **9** | 10 | – | 3.7±0.04 | – | – | – | – |
| | 100 | – | 16.0±14.5 | – | – | – | – |
| **10d** | 10 | – | – | **15.3±4.35** | – | – | 9.2±7.75 |
| | 100 | – | – | **26.2±4.06** | 1.8±6.28 | – | 20.2±8.92 |
| **10c** | 10 | – | – | **17.1±8.19** | – | – | – |
| | 100 | – | – | **27.7±8.54** | 7.0±4.62 | – | 3.9±3.39 |
| **10a** | 10 | – | – | 14.6±4.38 | 4.1±7.70 | – | 12.6±0.57 |
| | 100 | – | – | 25.3±2.99 | 16.8±5.69 | – | 14.0±3.68 |
| **10b** | 10 | – | – | 5.1±7.92 | – | – | – |
| | 100 | – | – | 14.8±4.87 | – | 1.5±11.4 | – |




**10d**

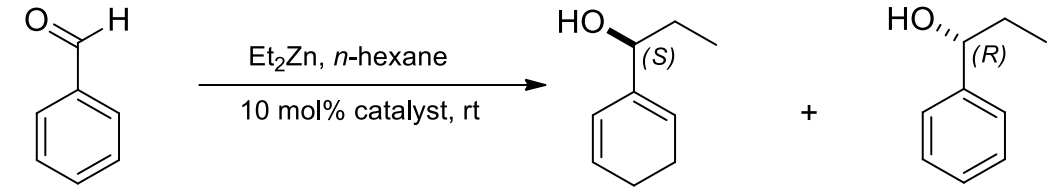



**10c**

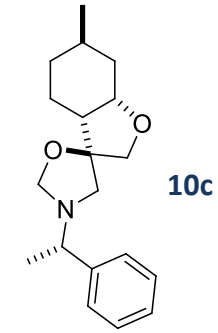


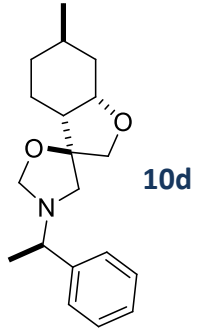

**6**

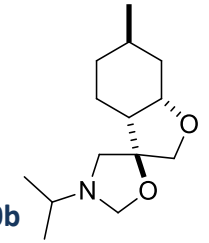
# Catalytic Addition of Diethylzinc to Benzaldehyde :

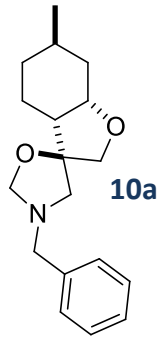


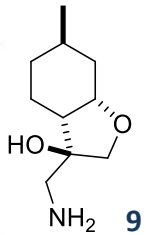

| Entry | Compounds | Yield (%) | ee (%) | Configuration |
|---|---|---|---|---|
| 1 | 8d | 86 | 8 | (R) |
| **2** | **8c** | **90** | **39** | **(S)** |
| 3 | 8a | 89 | 11 | (S) |
| 4 | 8b | 93 | 4 | (S) |
| 5 | 9 | 95 | 7 | (S) |
| 6 | 10d | 88 | 11 | (R) |
| 7 | 10c | 90 | 3 | (R) |
| 8 | 10a | 82 | 6 | (R) |
| 9 | 10b | 80 | 7 | (R) |

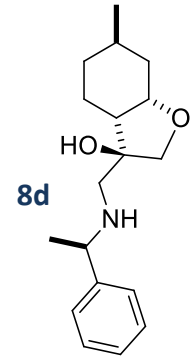


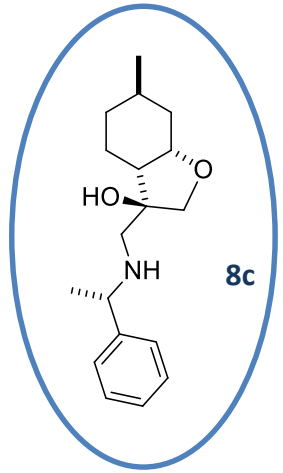



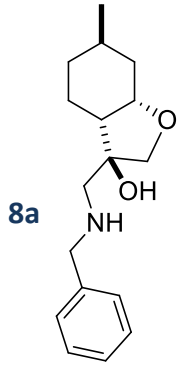



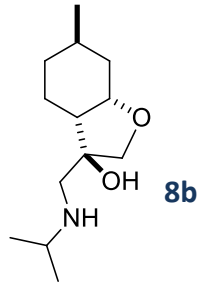



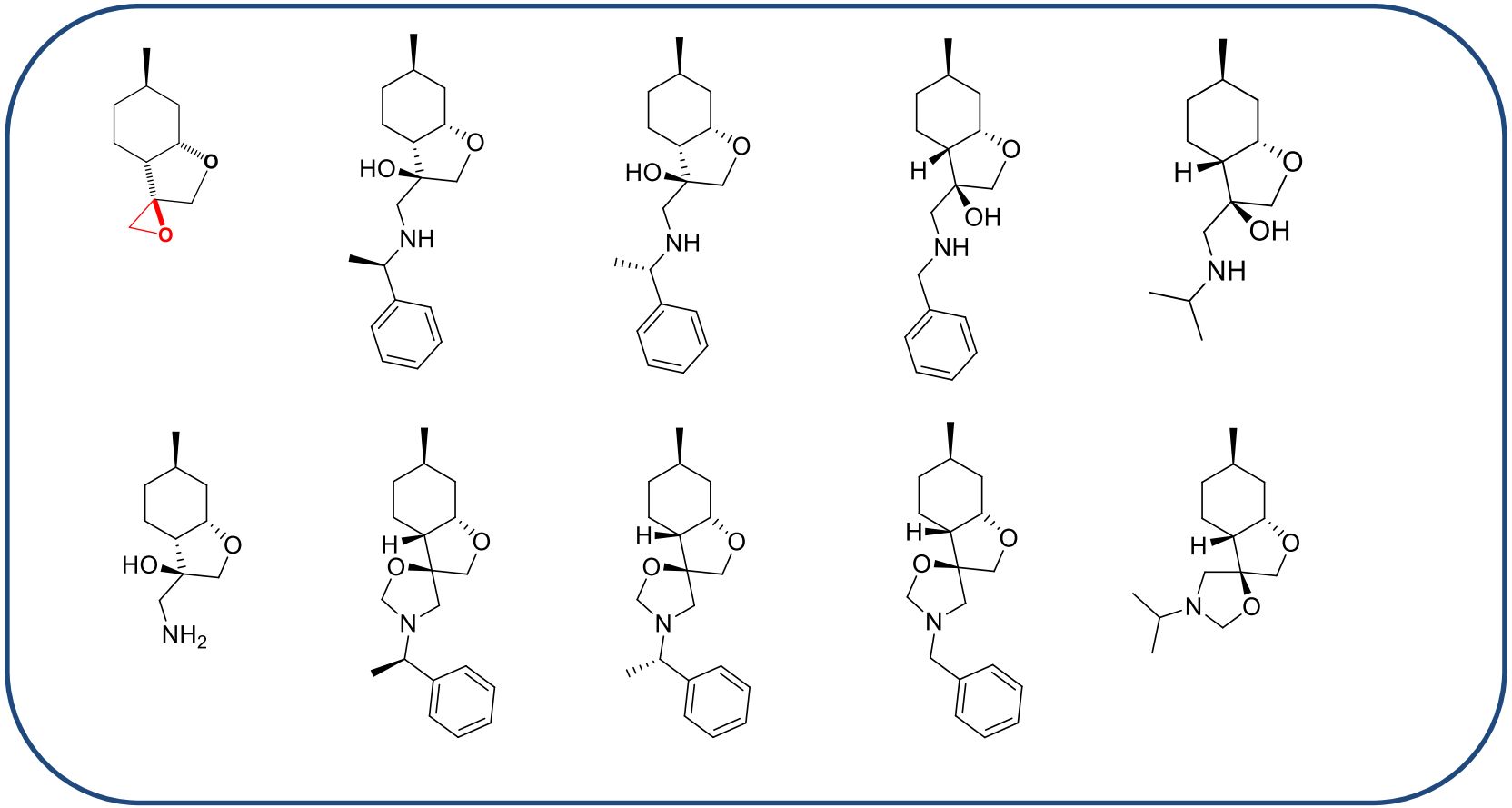



# SUMMARY

- Synthesis of new epoxide derivative
- Synthesis of 1,2-aminoalcohols with octahydrobezofuran core library,
- Synthesis of spiroxazolidines.



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# *Thank you for your attention!*

**BAMOU Fatima Zahra**

**INSTITUTE OF PHARMACEUTICAL CHEMISTRY, University of Szeged**

**EU-funded Hungarian grant GINOP-2.3.2-15-2016-00014**