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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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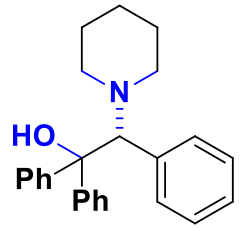
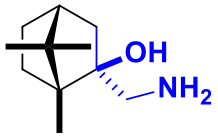
INTRODUCTION

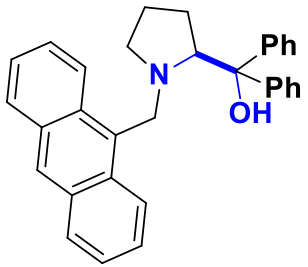


S. Rodrí guez-Escrich *et* al.
J. Org. Chem. **2008**, *73*, 5343.

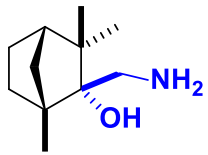


V. Dimitrov *et* al. *Tetrahedron Asymmetry* **2001**, *12*, 1325.

Enantioselective addition of diethylzinc to aldehydes



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



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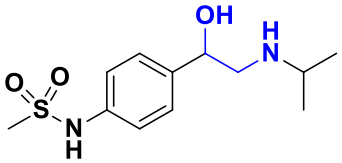
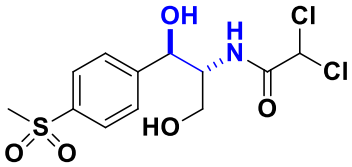
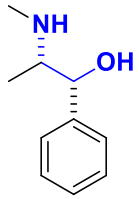


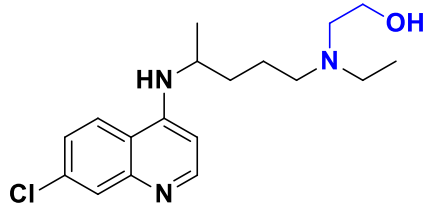
Sotalol
(Beta blocker)



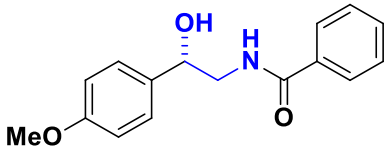
Thiamphenicol
(Antibiotic)



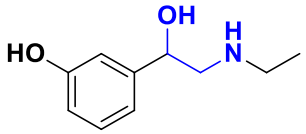
Ephedrine
(Sympathomimetic agent)



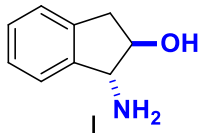
Hydroxychloroquine
(Treatement of Coronavirus)

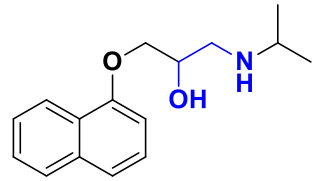


(+)-tembamide
(Antiviral natural product)



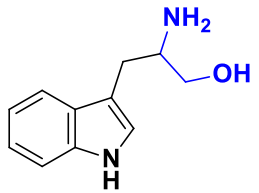
Etilefrine
(antihypotensive)

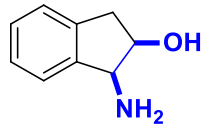




Propranolol
(Beta blocker)

Aldol reaction catalysts





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

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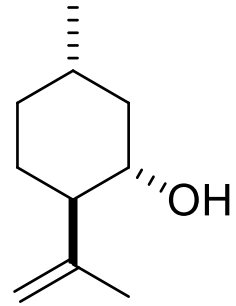
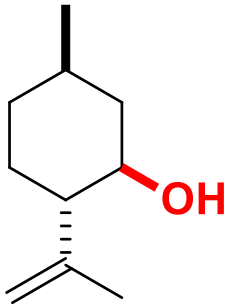
Aim



(+)-Isopulegol
synthetically from citronellal

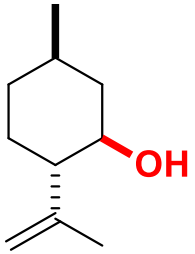
1 ml ≈ 100€ (Merck Co.)



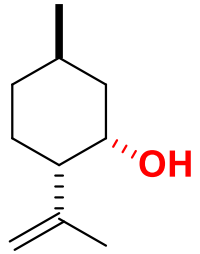
(-)-Isopulegol (natural)

1 kg ≈ 100€ (Merck Co.)

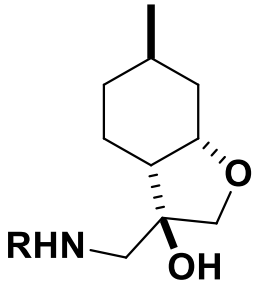
Mentha pulegium

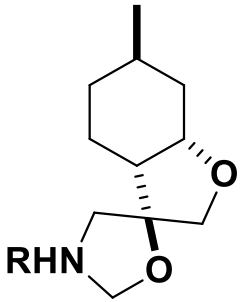


(-)-Isopulegol

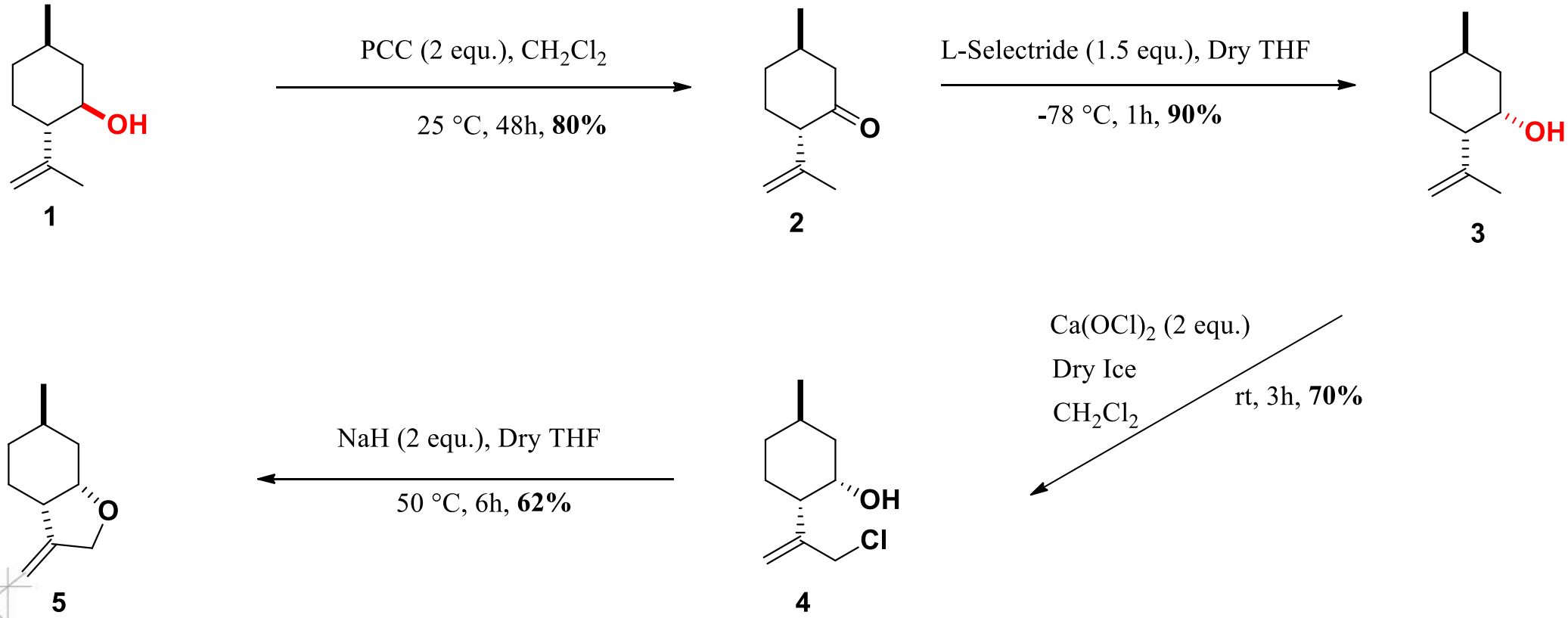


(+)-Neoisopulegol





Synthesis of exo-methylene-substituted perhydrobenzofurane derivative :



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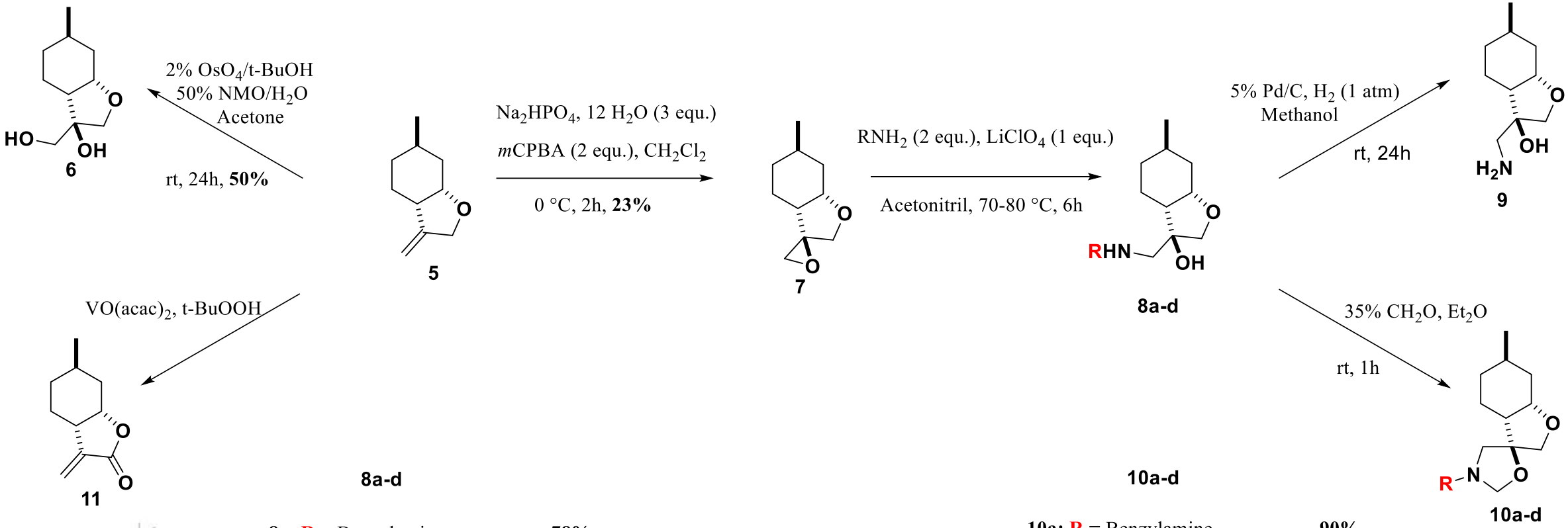
T. Brocksom *et* al *Synth. Commun.* **1988**, *18*, 1403.

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%**

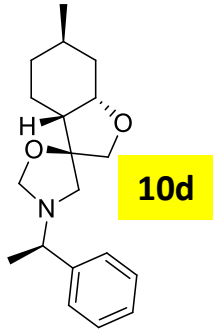
10a-d

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

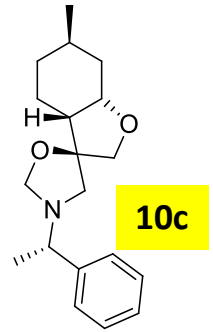
T. Brocksom et al *Synth. Commun*. **1988**, 18, 1403

Antimicrobial activities of the synthesized compounds :

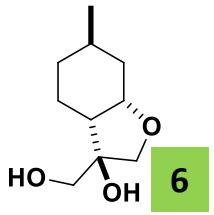
		Inhibitory effect (%) ± RSD (%)					
		Yeast		Gram-negative		Gram-positive	
Analogue	Conc. (µg/mL)	C. albicans	C. krusei	E. coli	P. aeruginosa	B. subtilis	S. aureus
6	10	–	**36.5±8.4**	–	–	–	–
	100	–	**58.4±14.4**	–	–	21.7±6.05	–
8d	10	–	–	8.7±3.15	7.5±1.54	–	–
	100	–	–	20.0±2.81	8.7±0.49	–	7.1±4.3
8c	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

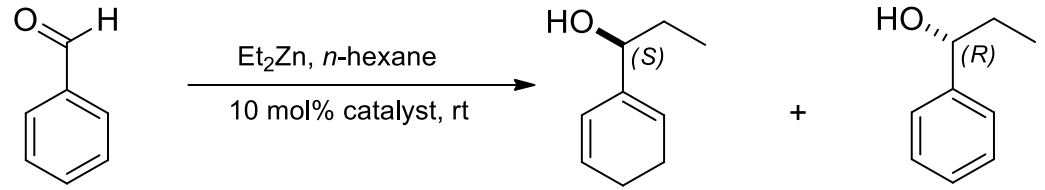


10c

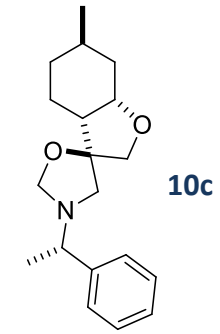


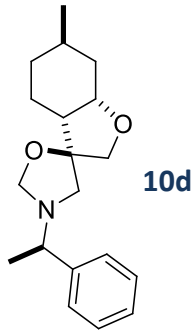
6

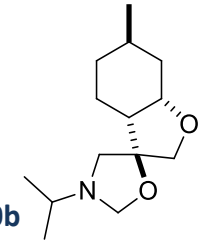
Catalytic Addition of Diethylzinc to Benzaldehyde :

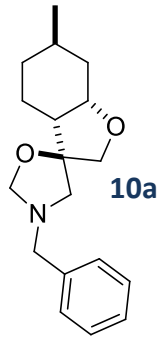


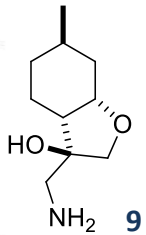
Entry	Compounds	Yield (%)	ee (%)	Configuration
1	8d	86	8	(R)
2	**8c**	**90**	**39**	**(S)**
3	8a	89	11	(S)
4	8b	93	4	(S)
5	9	95	7	(S)
6	10d	88	11	(R)
7	10c	90	3	(R)
8	10a	82	6	(R)
9	10b	80	7	(R)

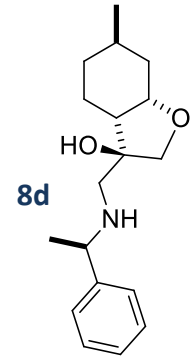


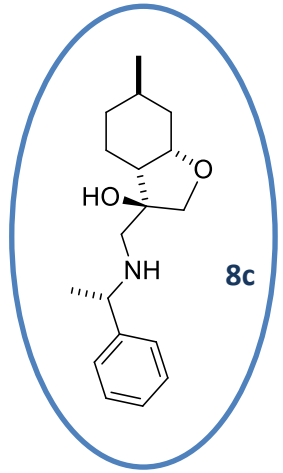


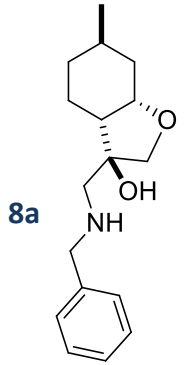


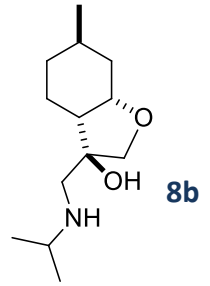




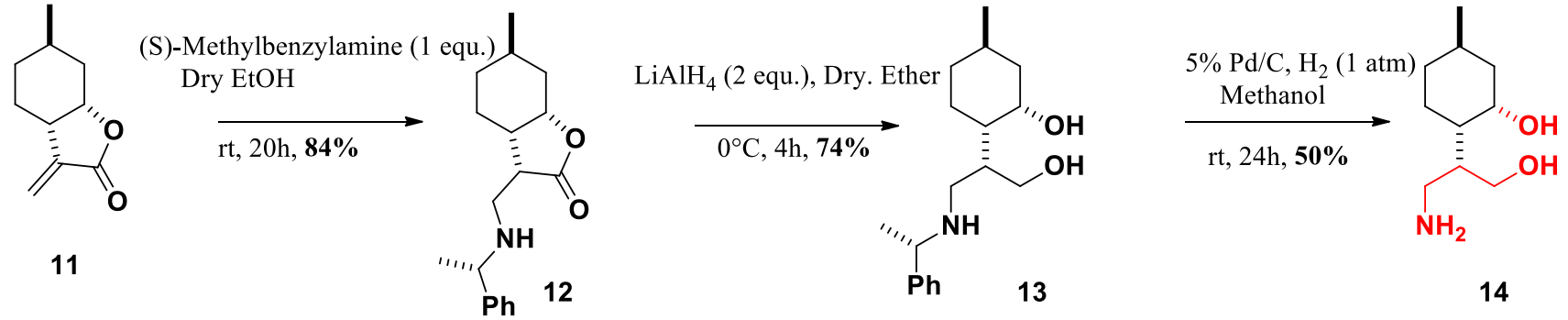


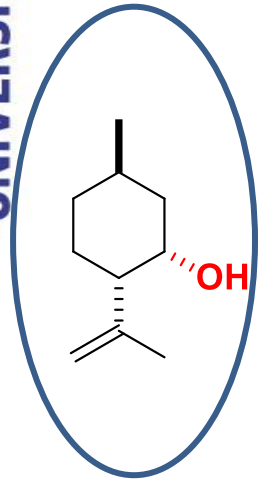


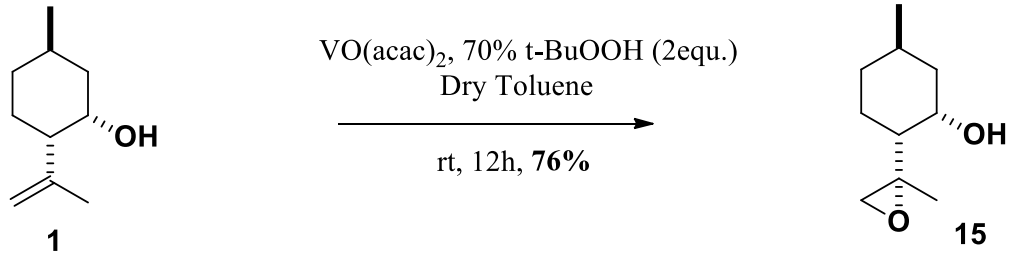


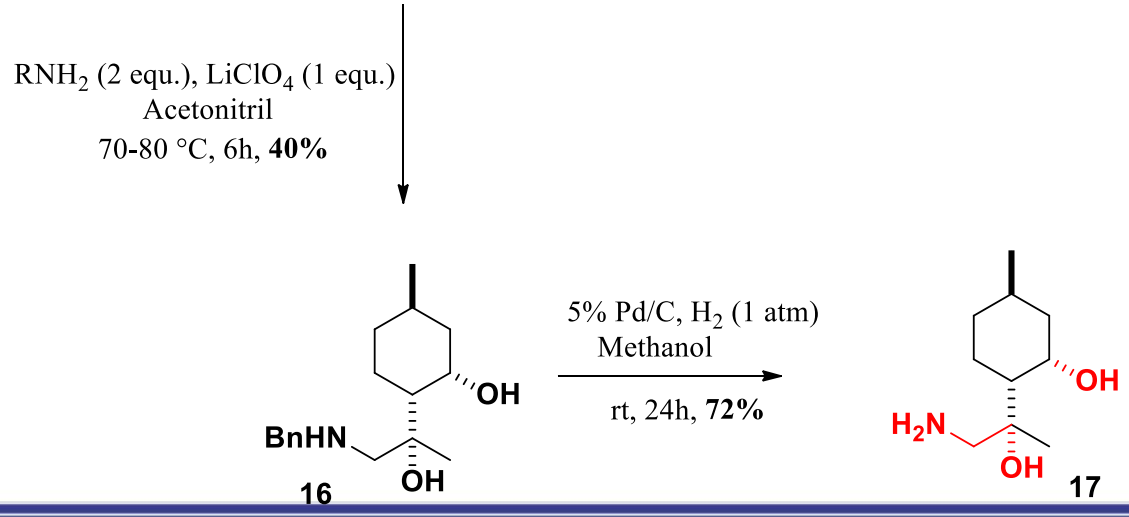


Preparation of Starting Materials

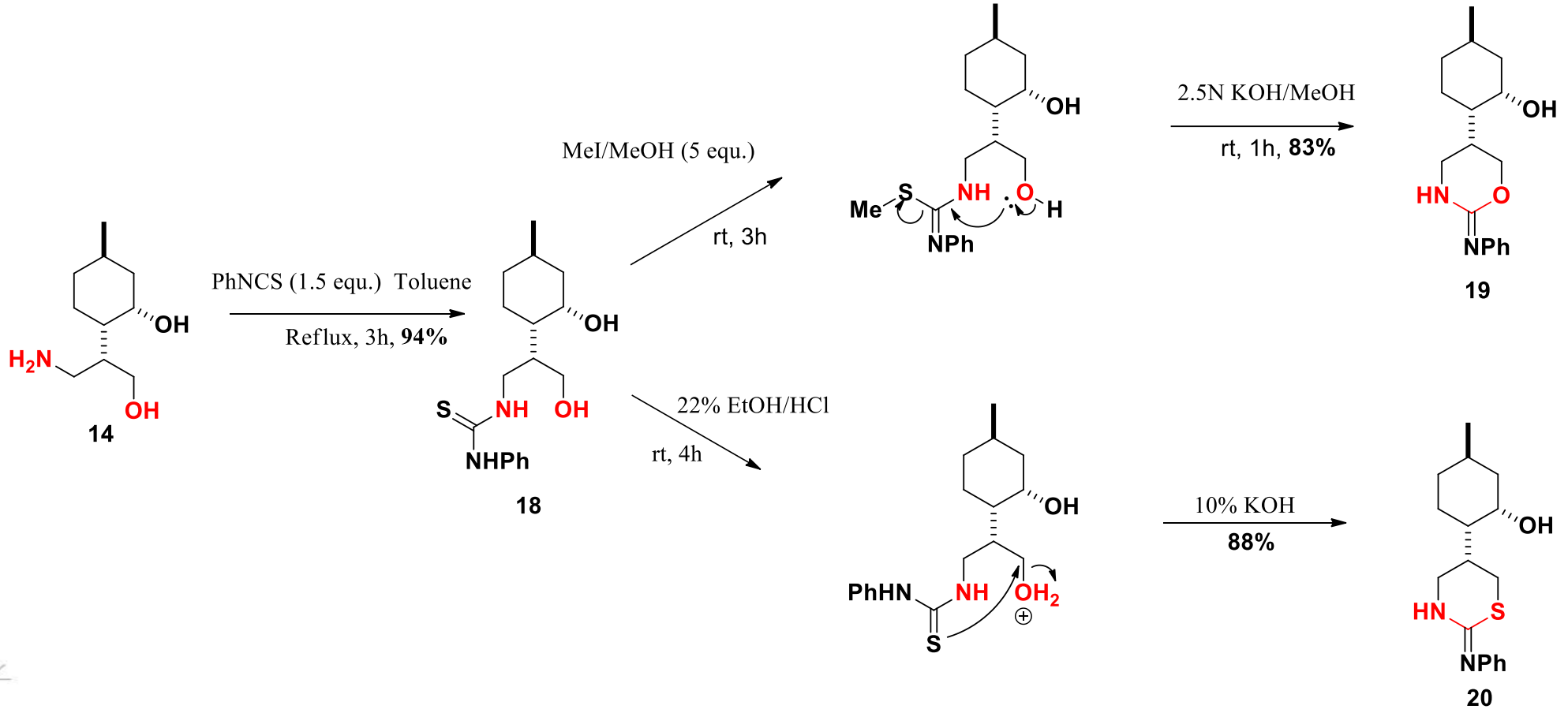








Preparation of Thiocarbamides, Thiazines and oxazines derivatives



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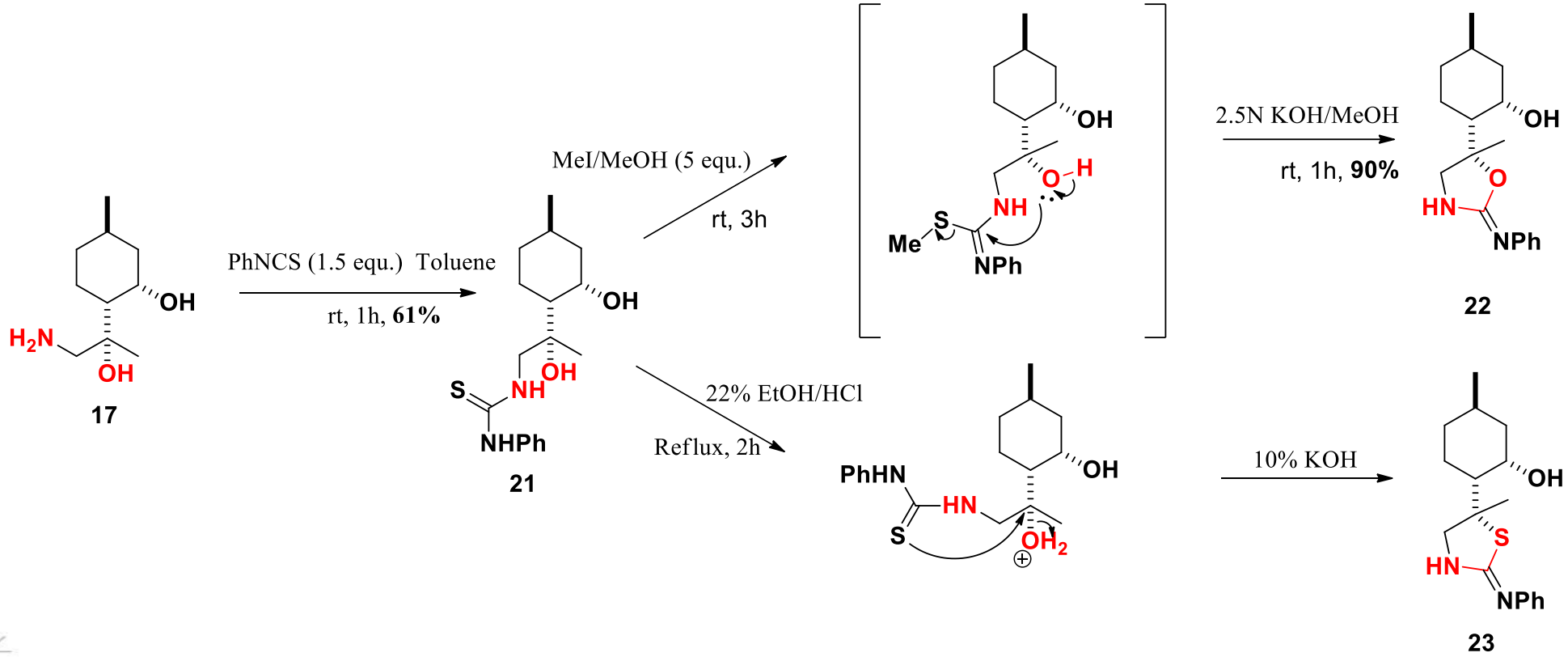

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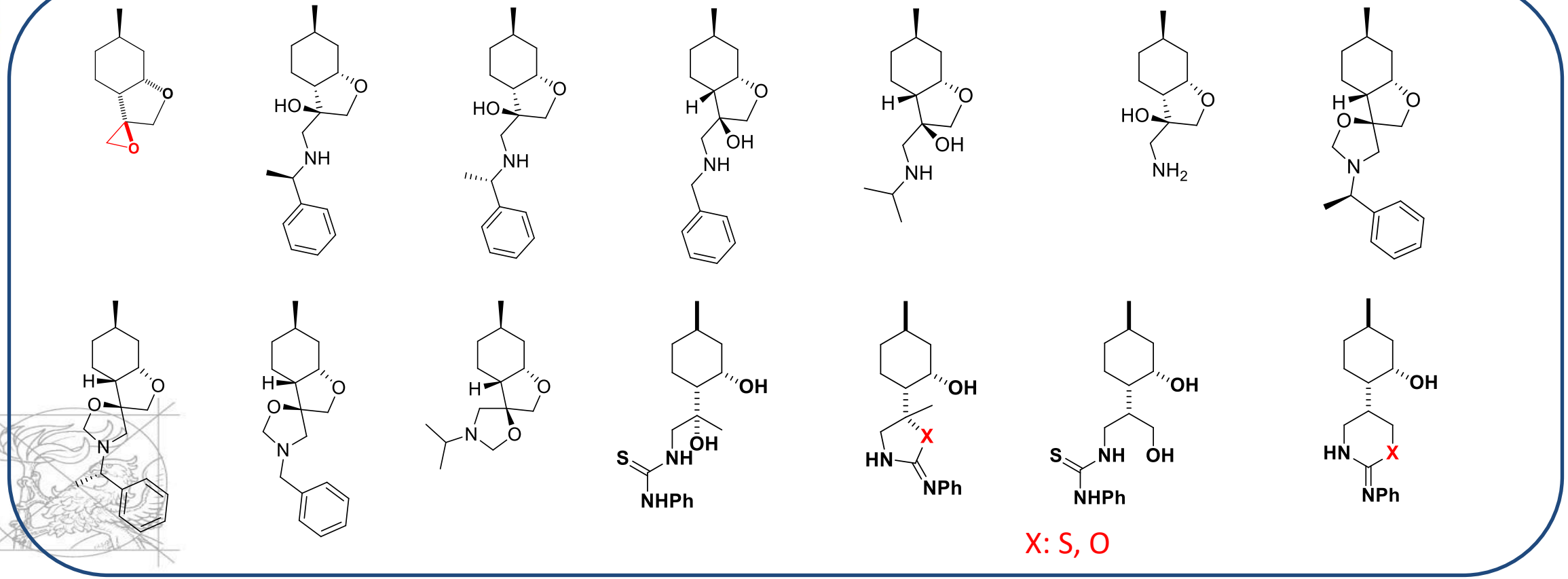
SUMMARY

- Synthesis of new epoxide derivative
- Synthesis of 1,2-aminoalcohols with octahydrobezofuran core library,
- Synthesis of spiroxazolidines.
- Synthesis of 2-imino-oxazolidines, thiazolidines, 1,3-oxazines and thiazines



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Thank you for your attention!

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