SYNTHESIS, SPECTROSCOPIC STUDIES AND ANTIFUNGAL ACTIVITY OF 1,10-DI(3-HYDROXYMETHYLPYRIDINIUM)DECANE DIBROMIDE

Anna Komasa[1], Piotr Barczyński[1], Patrycja Kwaśniewska-Sip[2], Grzegorz Cofta[2], Bartłomiej Mazela[2]

[1]Faculty of Chemistry, Adam Mickiewicz University, Umultowska 89b, 61614 Poznan, Poland

[2] Poznan University of Life Sciences, Institute of Wood Chemical Technology, Wojska Polskiego 28, PL-60637 Poznan, Poland

Joint Conference: COST Action FP 1303 &DURAWOOD Project 30-31 August 2016, Poznan

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RESEARCH AREA

Derivatives of

- **Imidazoles (betaines and complexes with mineral acides)**
- **Bispyridinium quaternary salts**

Prof. Piotr Barczyński
Dr Anna Komasa
Mgr Łukasz Czekański

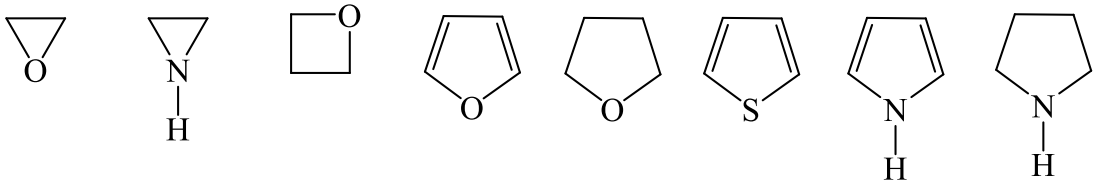
Adam Mickiewicz University in Poznań

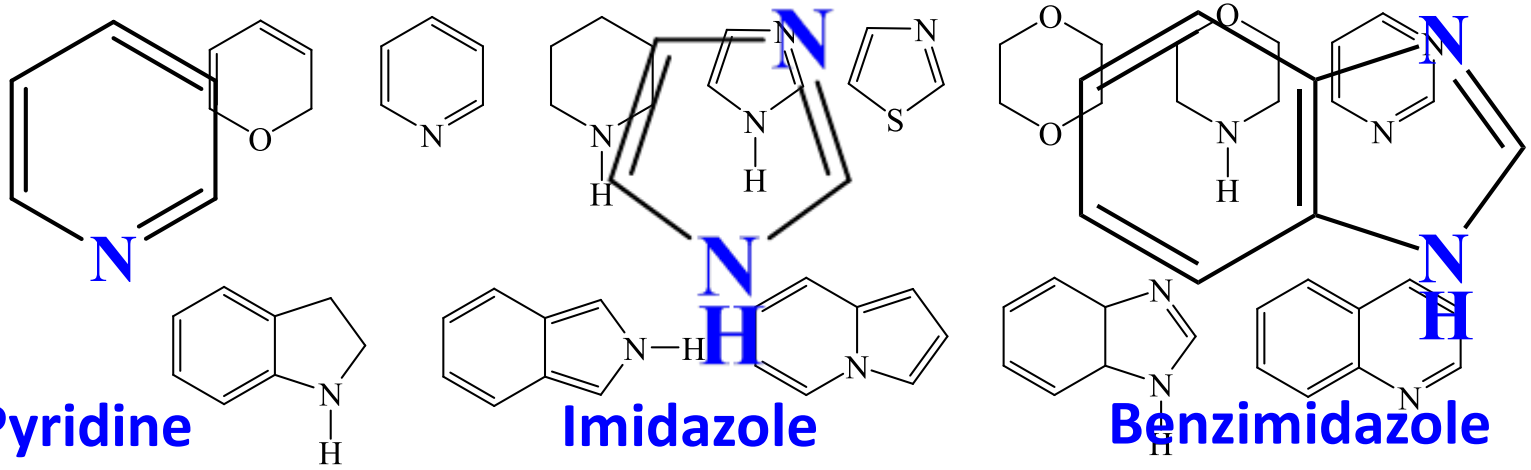
Fungicide activites of synthesised compounds

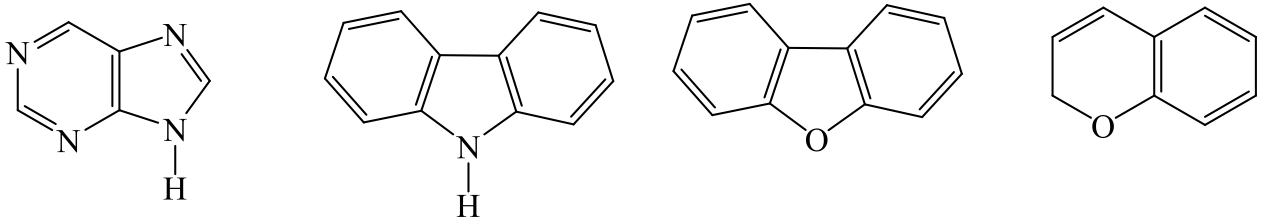
Dr hab. Grzegorz Cofta
Mgr Patrycja Kwaśniwska-Sip

Poznań University of Life Sciences

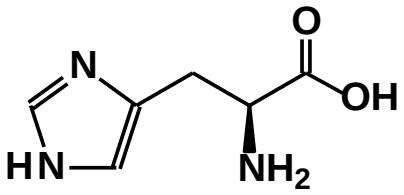
HETEROCYCLIC COMPOUNDS







BIOACTIVE MOLECULES



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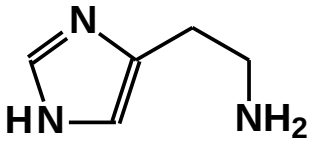

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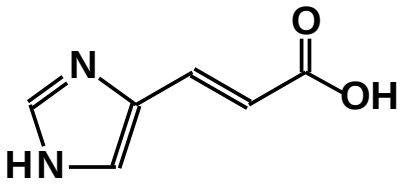
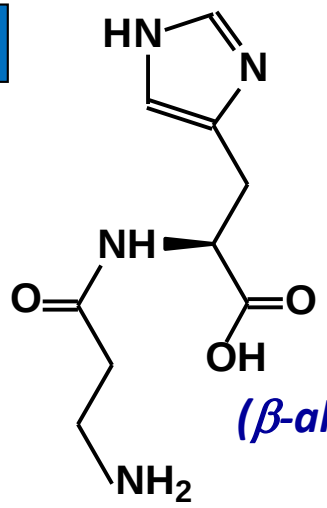
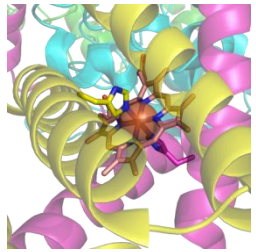


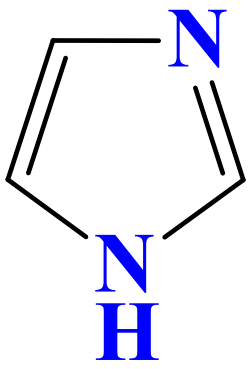
UROCANIC ACID



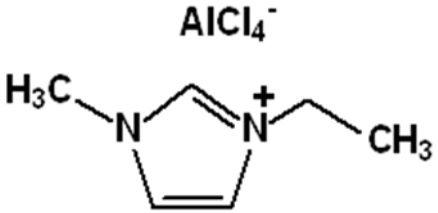
CARNOSINE

(β-alanyl-L-histidine)

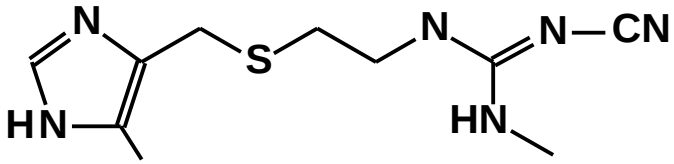




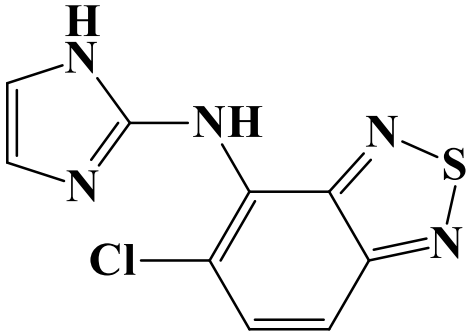
IONIC LIQUIDS



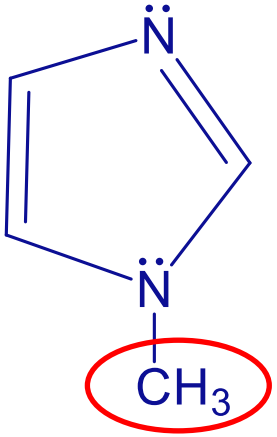
DRUGS



CIMETIDINE

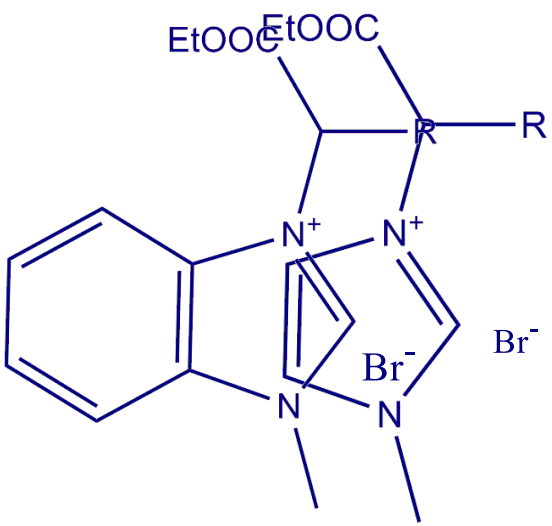


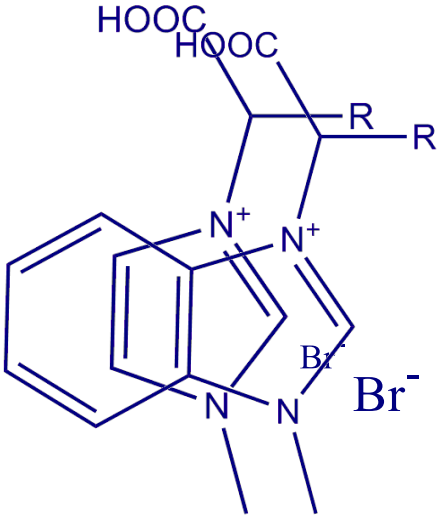
TIZANIDYNE

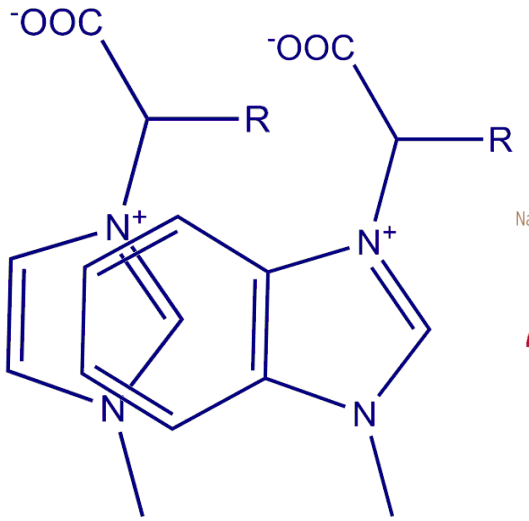


1-methylimidazole

3-(1-carboxyalkyl)-1-methybenzimidazolium inner salts and their hydrobromides



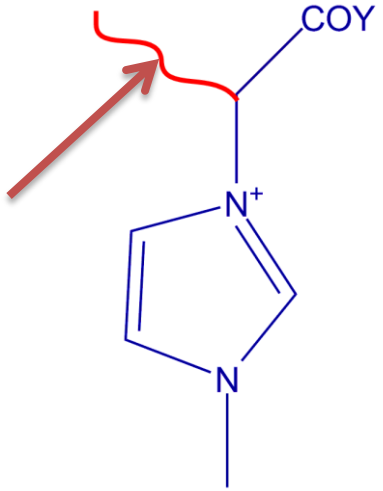




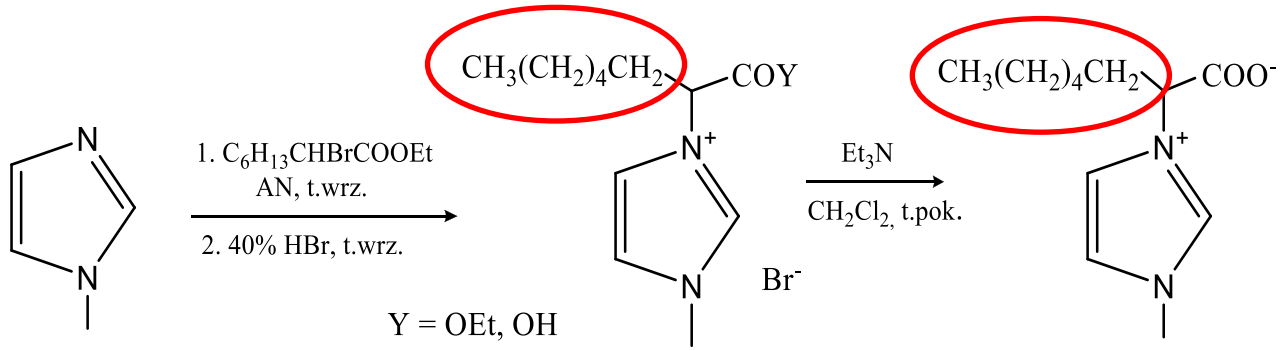
R = H, CH_3, CH_2CH_3

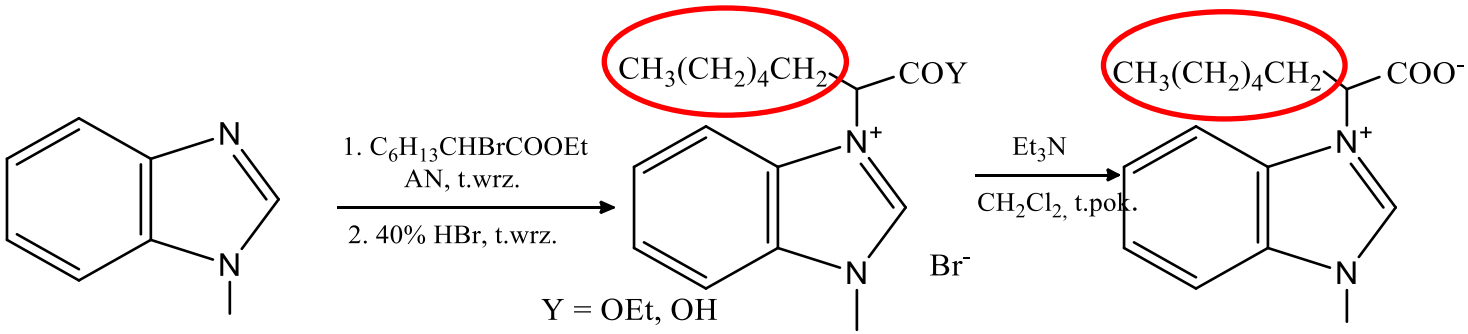
R = H, CH_3, CH_2CH_3

MODYFICATION BY ALKYL CHAIN ELONGATION

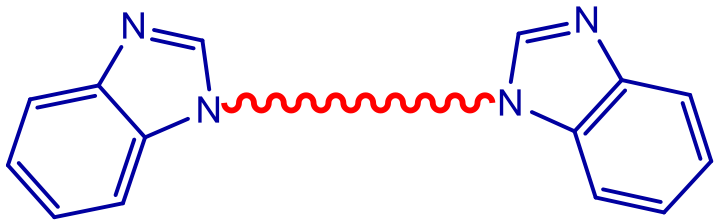


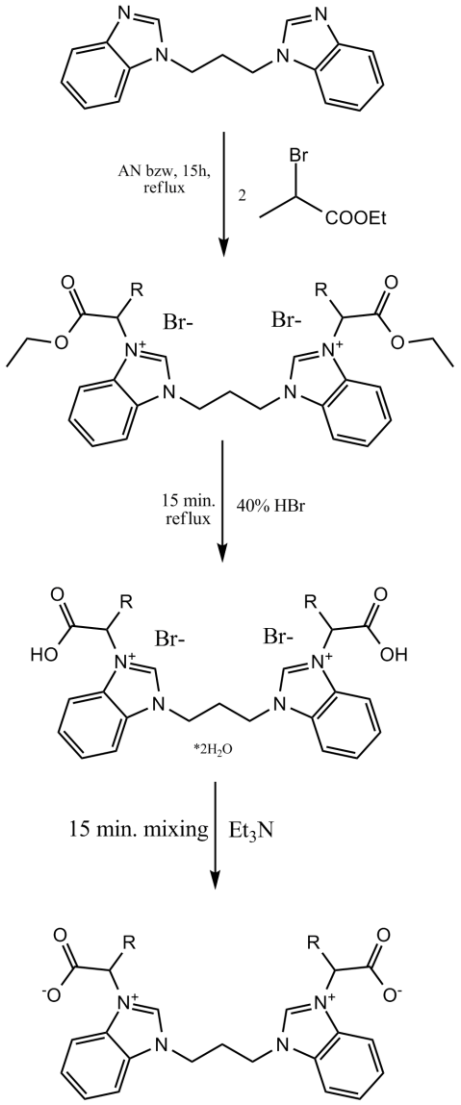
Y=OEt, OH





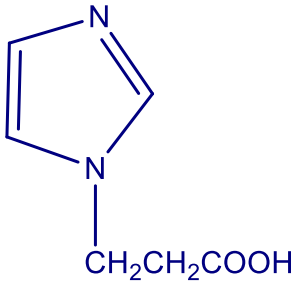
MODYFICATION
SYNTHESIS DIMERS OF BENZIMIDAZOLE

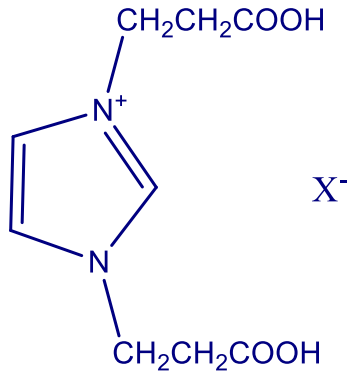


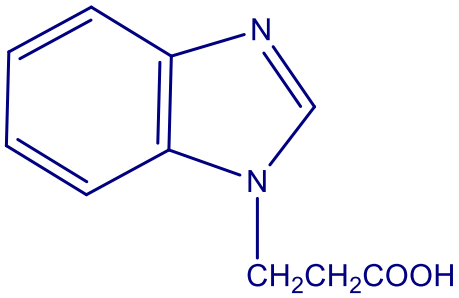


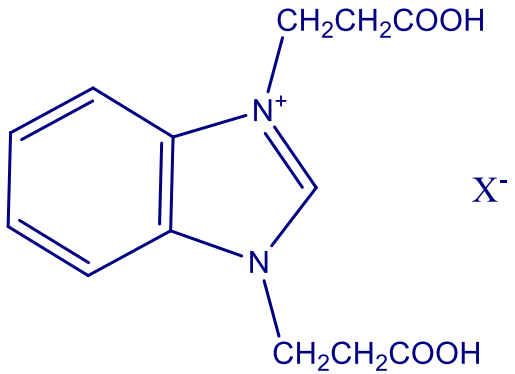
R=H, CH_3

MODYFICATION
carboxyethyl derivatives of imidazole and benzimidazole





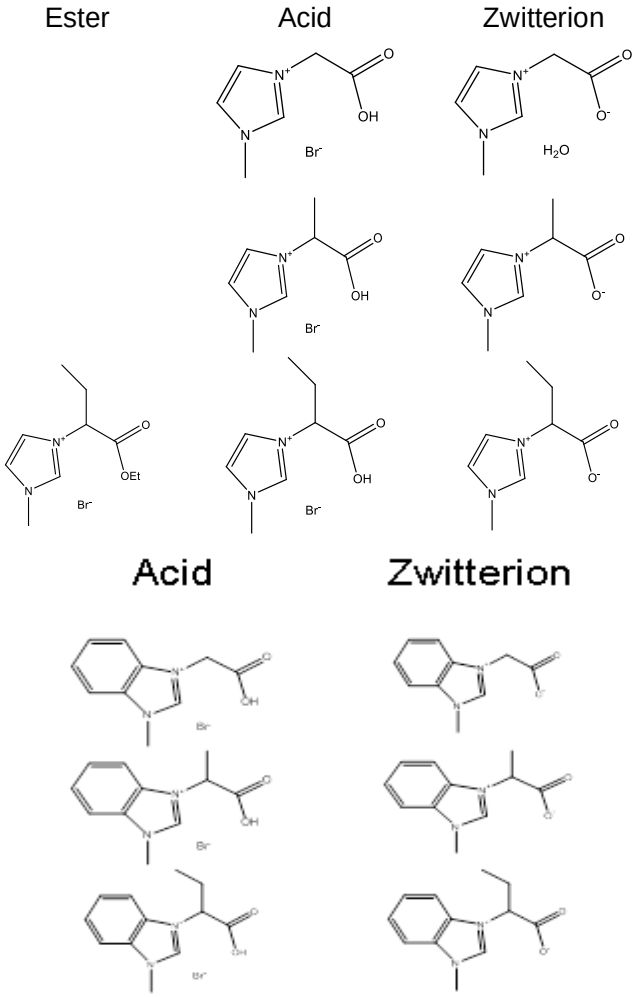


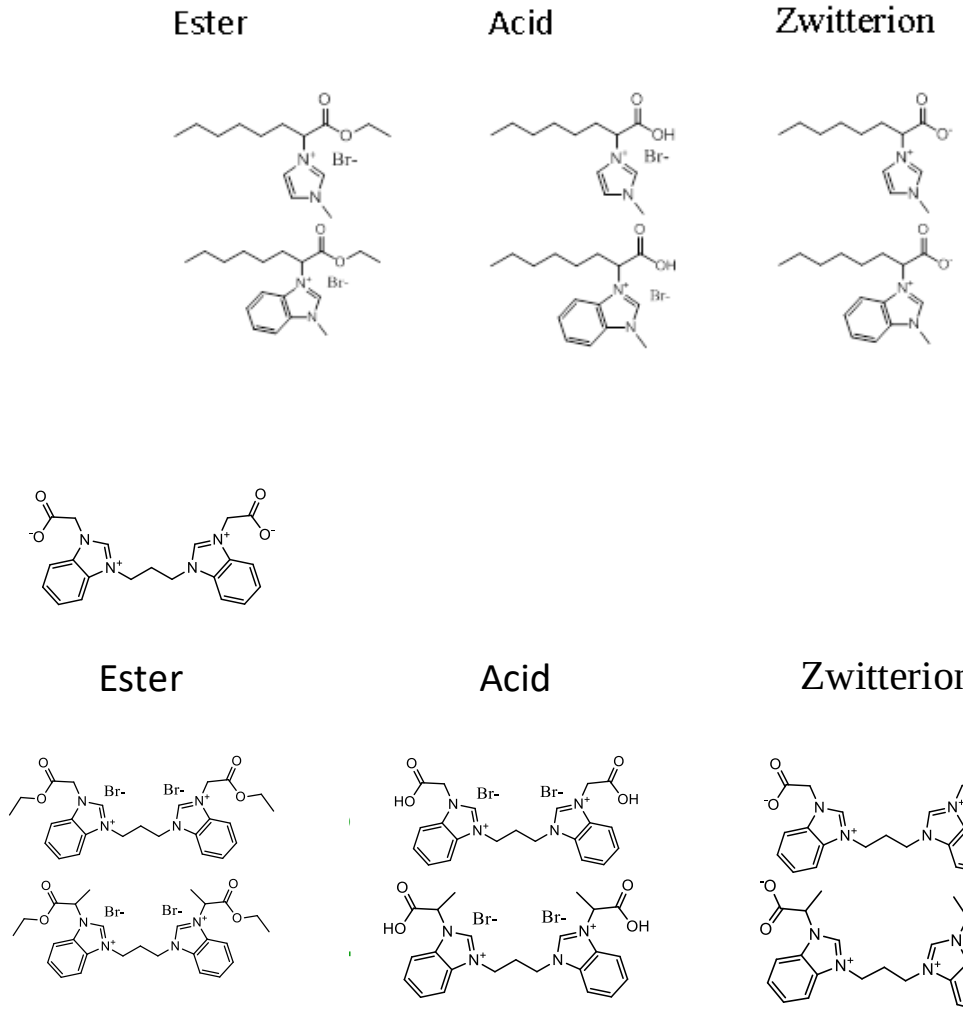


$X^- = Br^- Cl^-, ClO_4^-, BF_4^-$

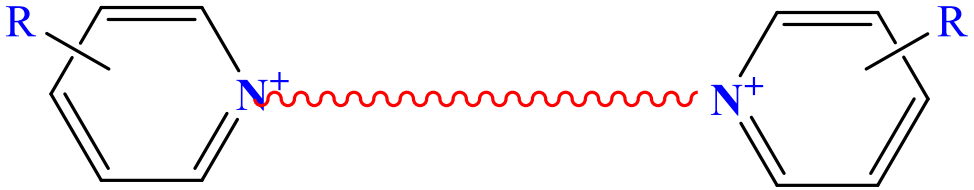
Carboxyalkyl derivatives of imidazole and benzimidazole

40 compounds (New compounds, commercialy unavalable)

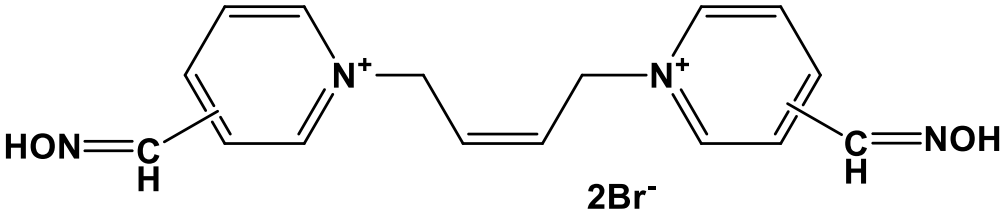




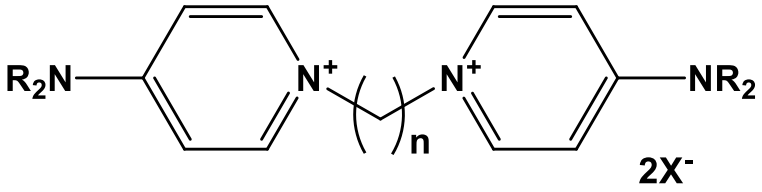
BISQUATERNARY PYRIDINIUM SALTS



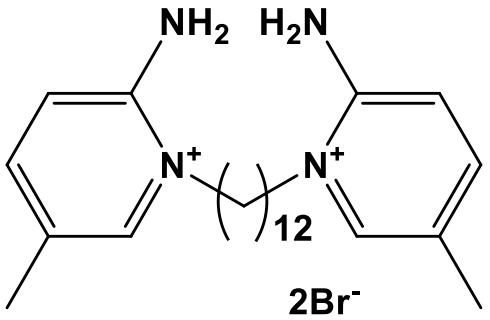
Acetylocholinesterase inhibitiors



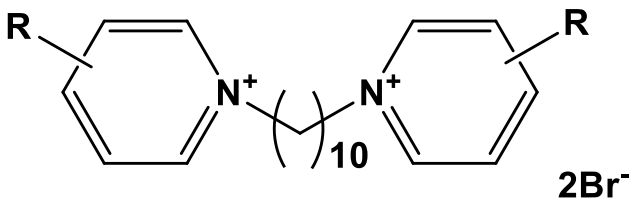
Antymicrobial activity



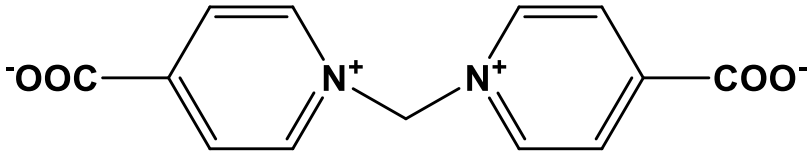
Antymalarial activity

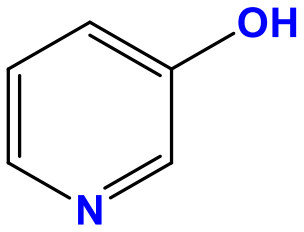


Antifungal activity

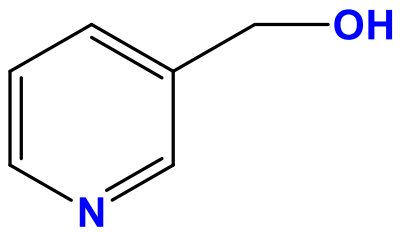


Ligands



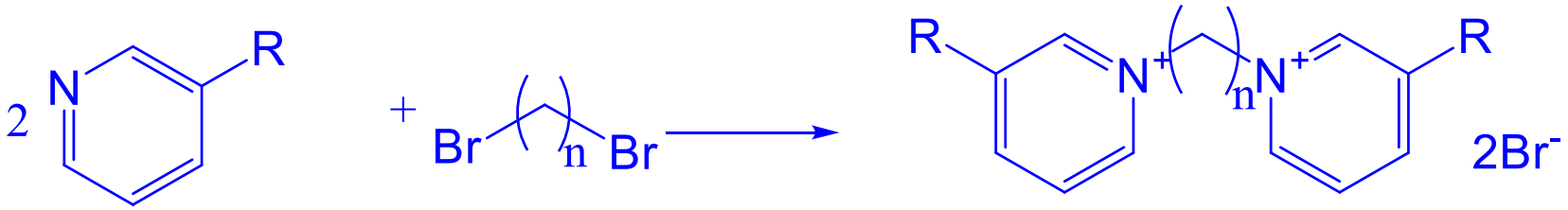


3-hydroxypyridine



3-hydroxymethylpyridine

Synthesis dimers of 3-hydrox- and 3-hydroxymethylpyridine



n=2, 3, 4, 5, 6, 8, 10

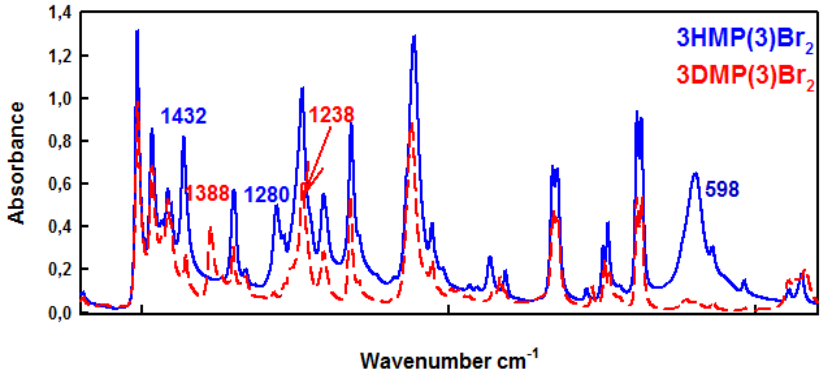
R: OH
CH_2OH

14 compounds

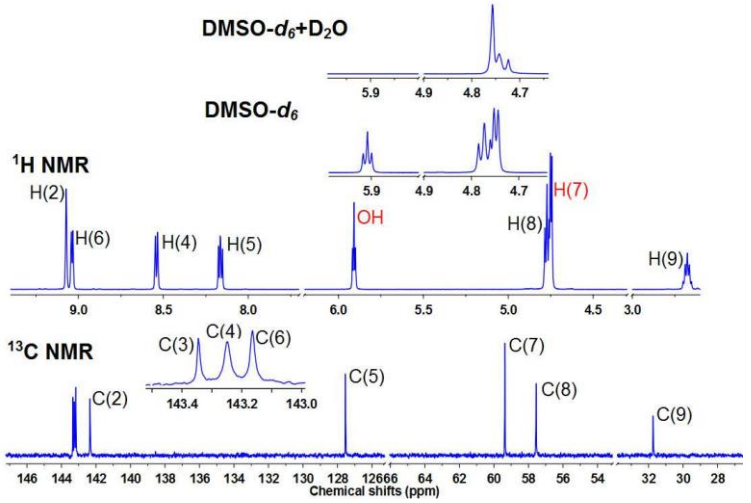
Characterisation of synthesised compouds

- **Elemental analysis**
- **Spectroscopic analysis**

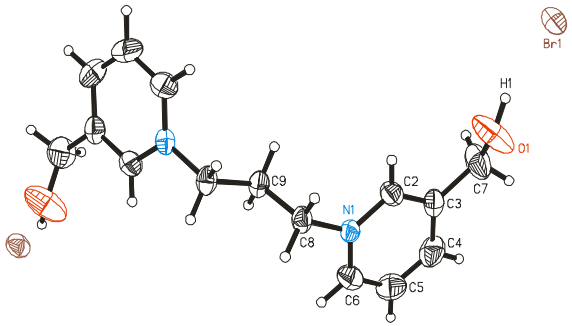
IR/Raman



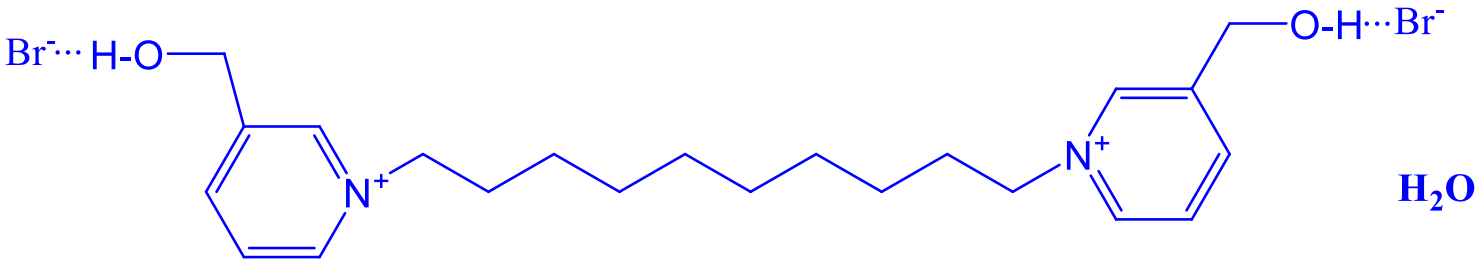
^{1}H and ^{13}C NMR



- **X-ray analysis**

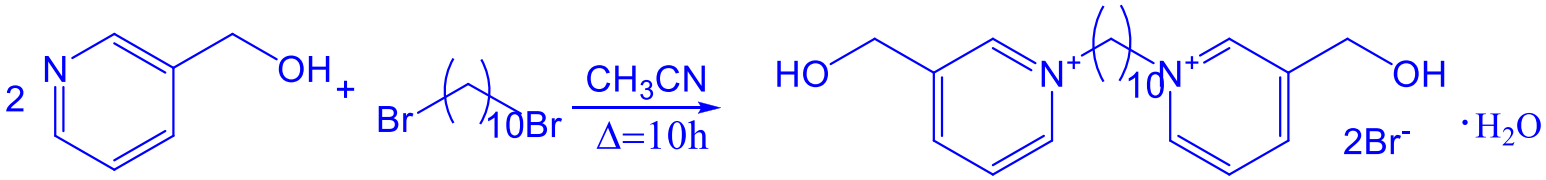


1,10-di(3-hydroxymethylpyridinium)decane dibromide



3HMP(10)Br_2 (AK17)

Synthesis



3HMP **3HMP(10)Br_2 (AK17)**

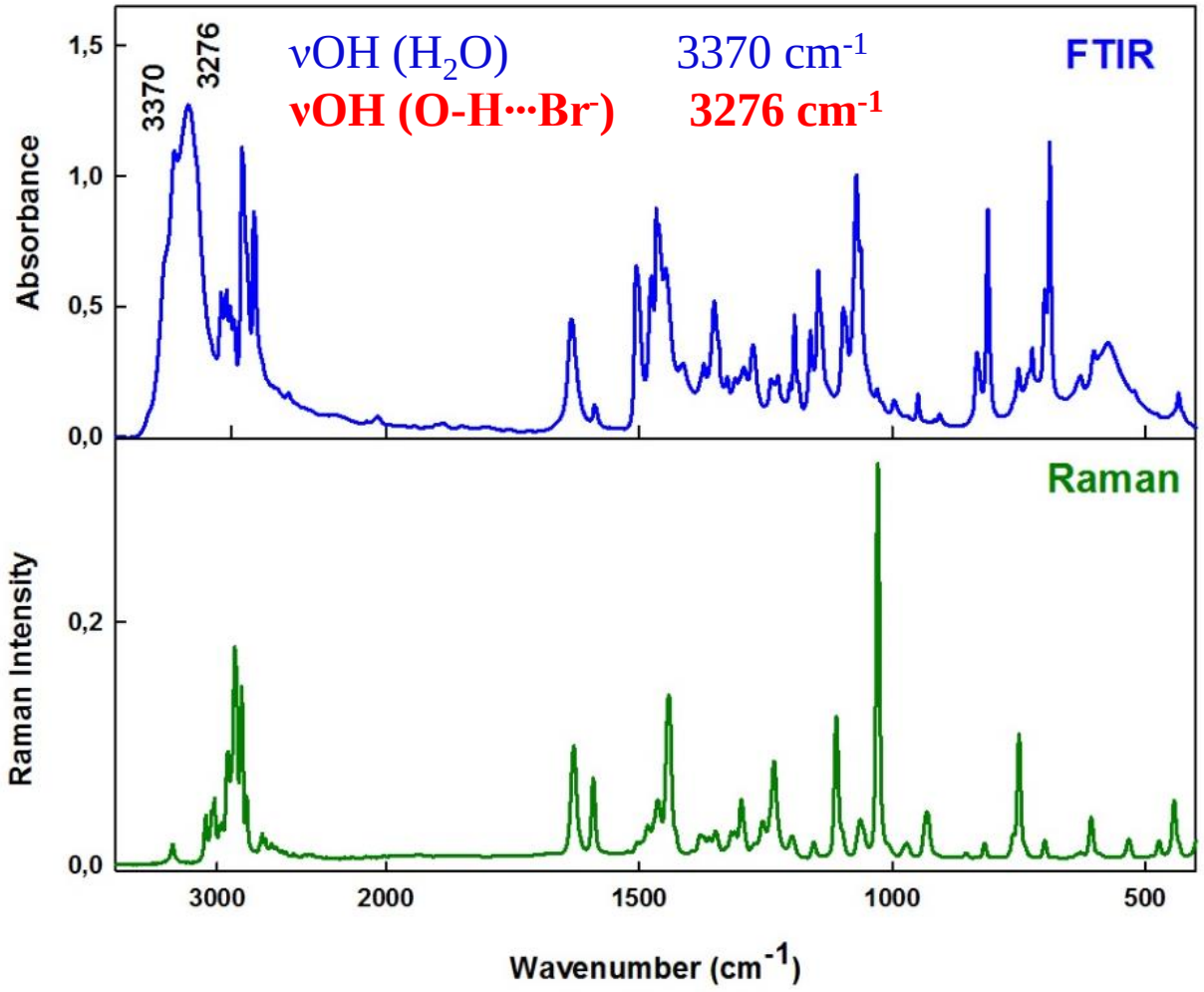
Yield 92.8 %, m.p. 113 °C

Elemental analysis for $C_{22}H_{34}Br_2N_2O_2 \cdot H_2O$:

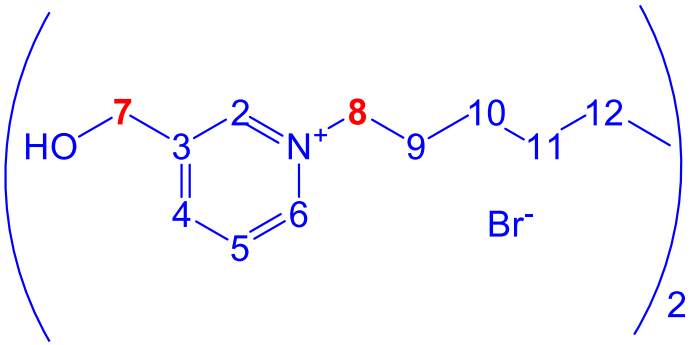
	Calc.	Exp.	Diff.
%C	49.27	49.21	0.06
%H	6.77	6.44	0.33
%N	5.22	5.08	0.14

Infrared/Raman spectra

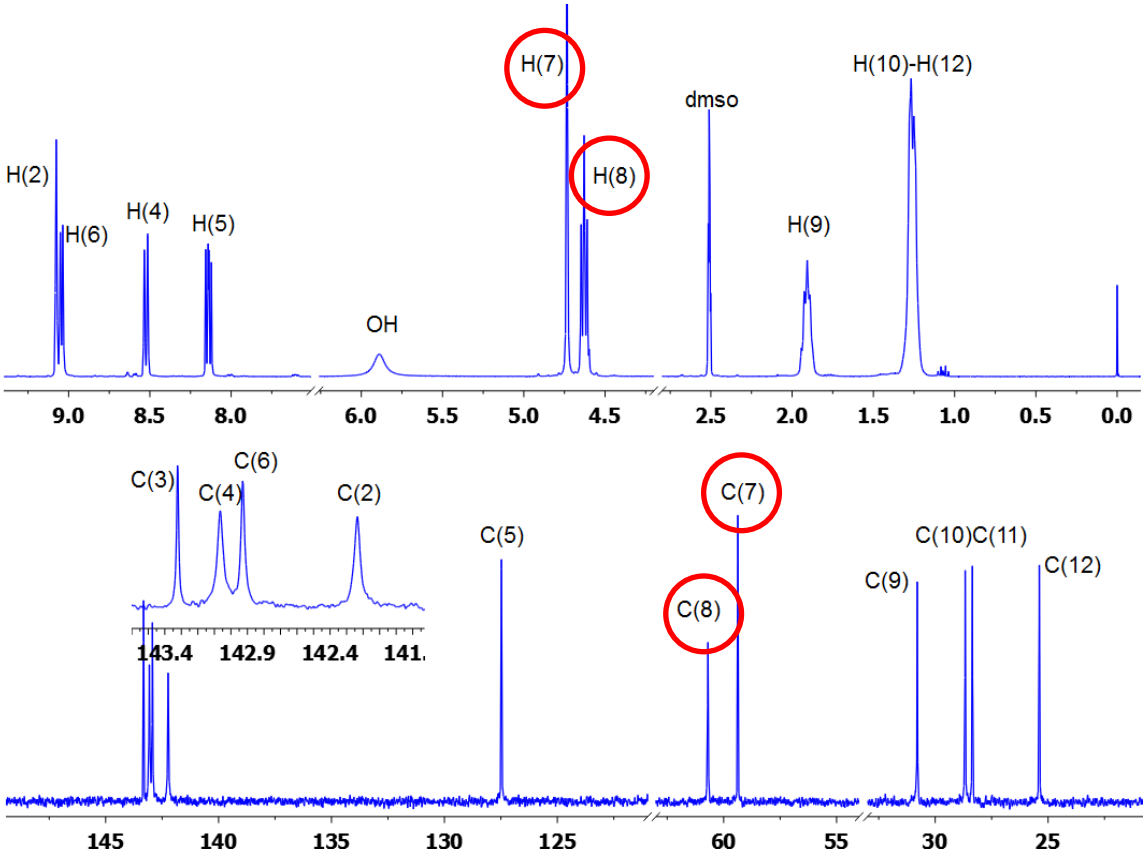
Spectroscopic analysis supported by quantum-chemical calculations



^{1}H and ^{13}C NMR



AK17



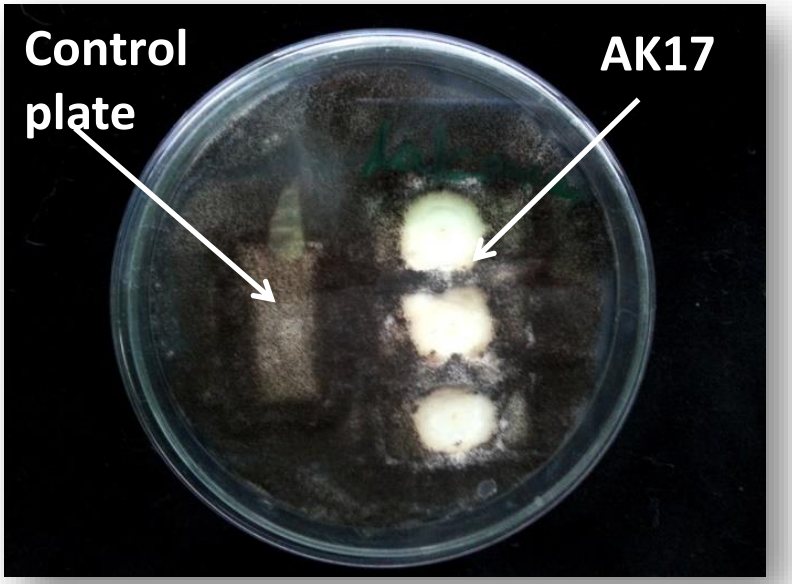
ANTIFUNGAL PROPERTIES

BIOAUTOGRAPHY-TLC

- *Aspergillus niger* van Tiegen ATCC 6275 (BAM 4)

- Scale of intensity mycelium growth:

0 - no growth
1 - growth of hyphae without spores
2 - sporulation mycelium



ANTIFUNGAL PROPERTIES (*Aspergillus niger*)

BIOAUTOGRAPHY-TLC

	index of *mycelium* growth in the next day of test					
Symbol	24h	48h	72h	Day 4	Day 5	Day 7
3HMP(2)Br_2	1	2	2	2	2	2
3HMP(3)Br_2	1	2	2	2	2	2
3HMP(4)Br_2	1	2	2	2	2	2
3HMP(5)Br_2	1	2	2	2	2	2
3HMP(6)Br_2	1	2	2	2	2	2
3HMP(8)Br_2	1	2	2	2	2	2
3HMP(10)Br_2 (AK17)	0	0	0	0	0	0
Control	1	2	2	2	2	2

0 – no growth

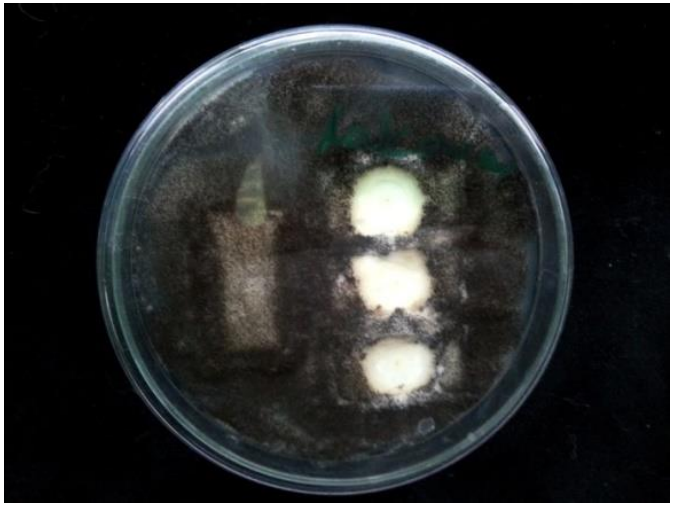
1 – growth of hyphae without spores

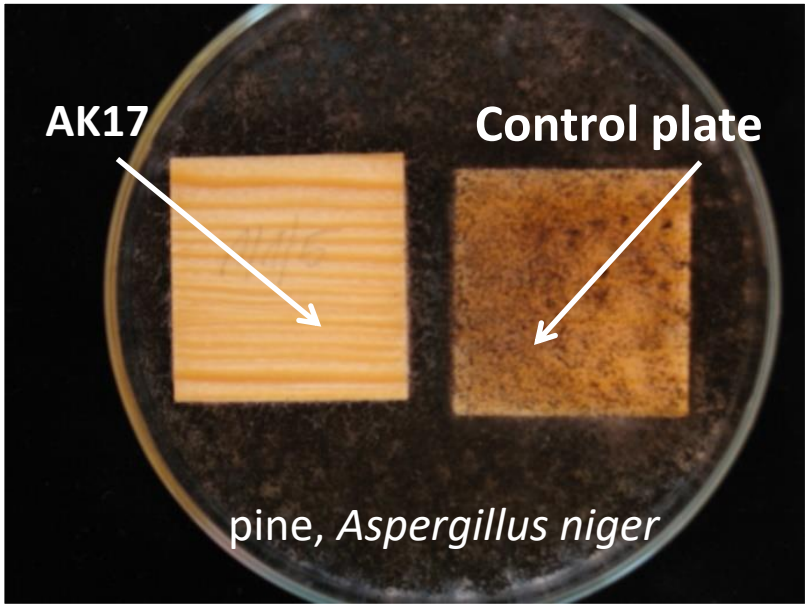
2 - sporulation mycelium

Minimum inhibitory concentration (MIC) for 3HMP(10)Br_2 is equal to 1%.

ANTIFUNGAL PROPERTIES

THE NEXT STEP OF TEST





ISO 846 pine, *Aspergillus niger*
EN-839 pine, *Coniophora puteana*,
beech *Corolius versicolor*

The growth of mycelium of *A. niger* on the surface of pine wood

Retension AK17	The average value of moulds overgrowing index after 3 weeks of exposure							
	4 days		1 week		2 weeks		3 weeks	
	Treated	Control	Treated	Control	Treated	Control	Treated	Control
4,1g/m^2	**0,75**	3	**1**	3,5	**2**	4	**2,5**	5
2,05g/m^2	**0,5**	3	**1**	3,5	**2**	4	**3**	5

Assessement of fungal growth (acc. ISO-846)

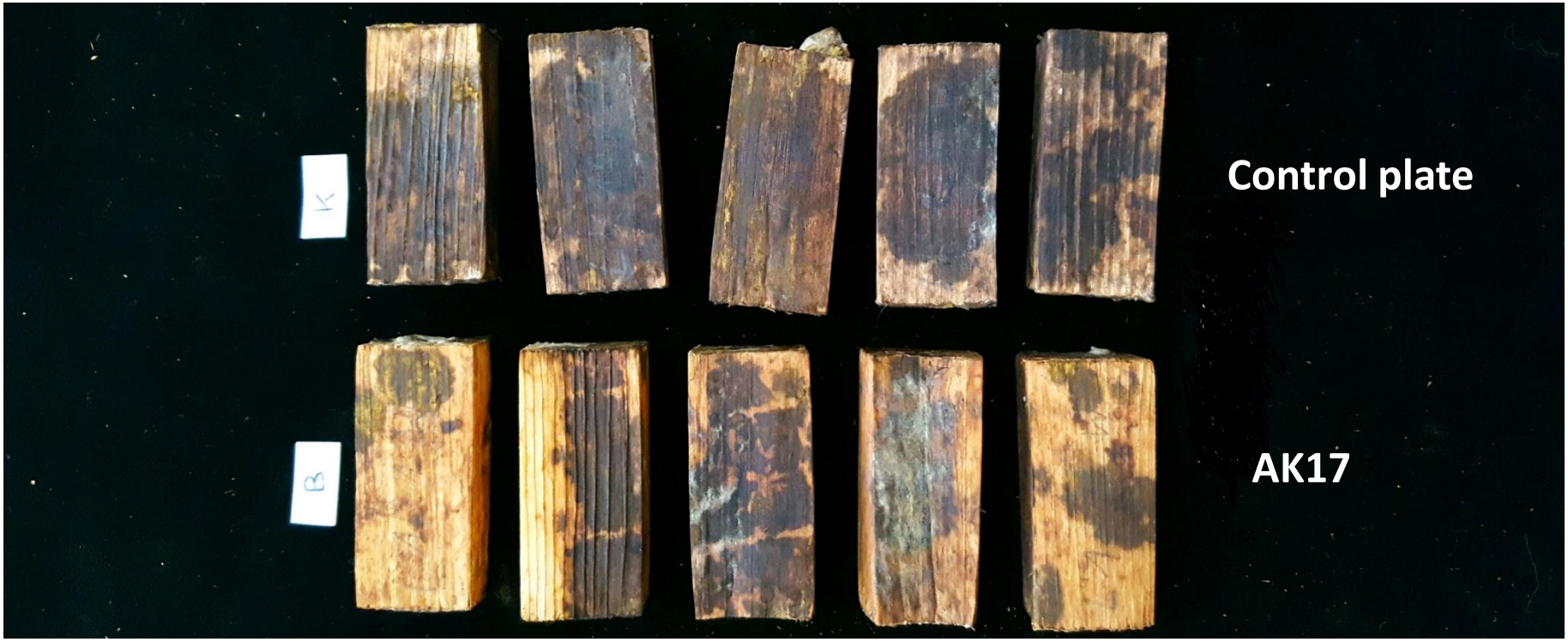
Intensity of growth	Evaluation
0	No growth apparent under the microscope.
1	No growth visible to the naked eye, but clearly visible under the microscope.
2	Growth visible to the naked eye, covering up to 25% of the test surface.
3	Growth visible to the naked eye, covering up to 50% of the test surface.
4	Considerable growth, covering more than 50% of the test surface.
5	Heavy growth, covering the entire test surface.

The results of the mycological tests against *Coniophora puteana* (pine wood)

Active Ingredients	Unleaching						
	Concentration	Medium	Retention	Weight loss treated samples (RSD)	Moistured treated samples (RSD)	Weight loss untreated samples (RSD)	Moisture untreated samples (RSD)
	[%]		[g/m^2]	[%]	[%]	[%]	[%]
AK17 + WAB	16	W	40,8	33,7 (1,7)	36,7 (1,7)	46,0 (6,0)	43,3 (2,5)
WAB	0,5	W	36,9	38,7 (6,7)	40,2 (2,8)	42,6 (6,6)	40,5 (2,5)
	Leaching						
AK17	16	W	44,1	32,5 (4,1)	39,5 (6,2)	35,4 (4,5)	41,2 (1,6)
WAB	0,5	W	27,7	63,1 (6,5)	38,7 (1,5)	38,7 (3,0)	36,1 (6,5)

RSD – relative standard deviation
WAB – water resin

The results of the mycological tests against *Coniophora puteana* (pine wood)



The results of the mycological tests against *Coriolus versicolor* (beech wood)

Active Ingredients	Unleaching						
	Concentration	Medium	Retention	Weight loss treated samples (RSD)	Moistured treated samples (RSD)	Weight loss untreated samples (RSD)	Moisture untreated samples (RSD)
	[%]		[g/m^2]	[%]	[%]	[%]	[%]
AK17 WAB	1 6	W	24.0	22.7 (3.2)	47.7 (2,9)	28.6 (2.4)	45.2 (4.2)
WAB	0,5	W	22.5	37.6 (7.1)	47,3 (6.6)	38.3 (5.9)	47,5 (2.8)
	Leaching						
AK17 WAB	1 6	W	26.8	23.8 (3.1)	47.9 (3.3)	30.2 (3.4)	49.2 (3.0)
WAB	0,5	W	22.5	37.6 (7.1)	47.3 (6.6)	23.6 (1.8)	47.0 (2.2)

RSD – relative standard deviation
WAB – water resin

Conclusions

- **AK 17 exhibit fungistatic properties against *Aspergillus Niger***

- **AK17 does not protect wood from *Coriolus versicolor* and *Coniophora puteana***

Thank you for cooperation

Prof. Bartłomiej Mazela

Prof. Piotr Barczyński
inż. Maria Bartkowiak
Dr Magdalena Broda
Dr hab. Grzegorz Cofta
PhD student mgr Łukasz Czekański
PhD student mgr Patrycja Kwaśniewska –Sip
Dr Lone Ross Gobakken
Dr Wojciech Grześkowiak
PhD student mgr Waldemar Perdoch
Dr hab. Anna Przybył
Mgr inż. Anna Szulc

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Thank you for your attention

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