

Dr. Alexander Pauli  
Fürther Str. 13  
90513 Zirndorf  
a.pauli@reviewscience.com

# A.Pauli

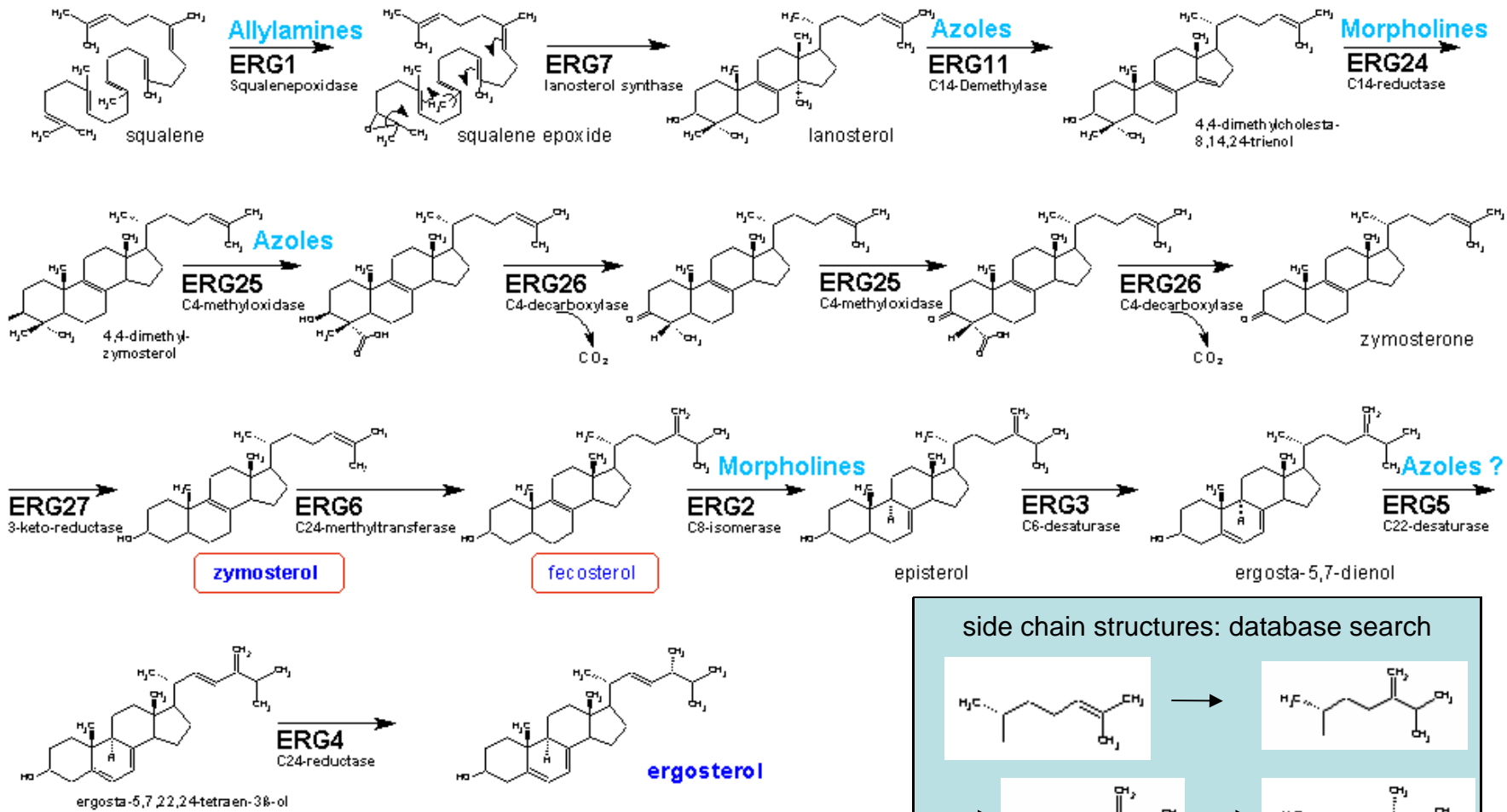
## Hawaii Presentation

### PacifiChem 2005

- - - Part Ergosterol - - -



**Ergosterol biosynthesis - the "post squalene pathway"**




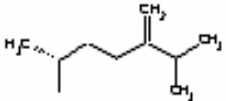
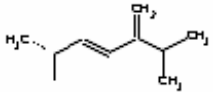
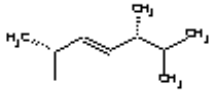
side chain structures: database search

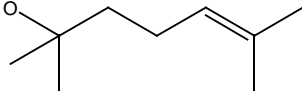
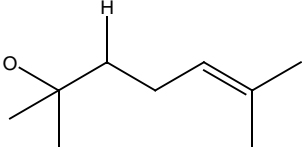
The diagram shows four side chain structures of ergosterol in a 2x2 grid, connected by arrows, illustrating a database search process:

- Top-left: CC(C)C=CC(C)C
- Top-right: CC(C)C=CC(C)C(C)C
- Bottom-left: CC(C)C=CC(C)C(C)C
- Bottom-right: CC(C)C=CC(C)C(C)C

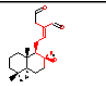
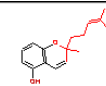
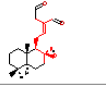
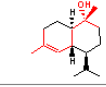
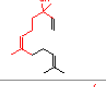
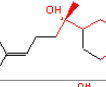
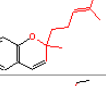
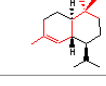
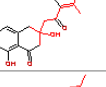
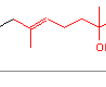
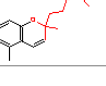
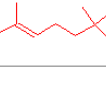
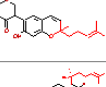
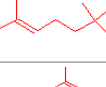
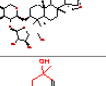
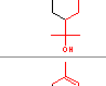
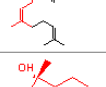
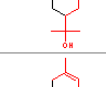
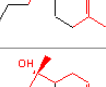
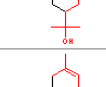
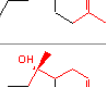
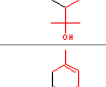
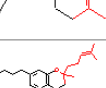
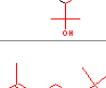
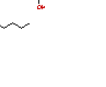

Modified scheme, original:  
 Veen, M., Lang, C. Appl. Microbiol.  
 Biotechnol. 63, 635-46 (2003)

# Mycosterol side chains: Fungi, *Candida* hits in AmicBase

	<b>1231</b>
	<b>489</b>
	<b>40</b>
	<b>98</b>

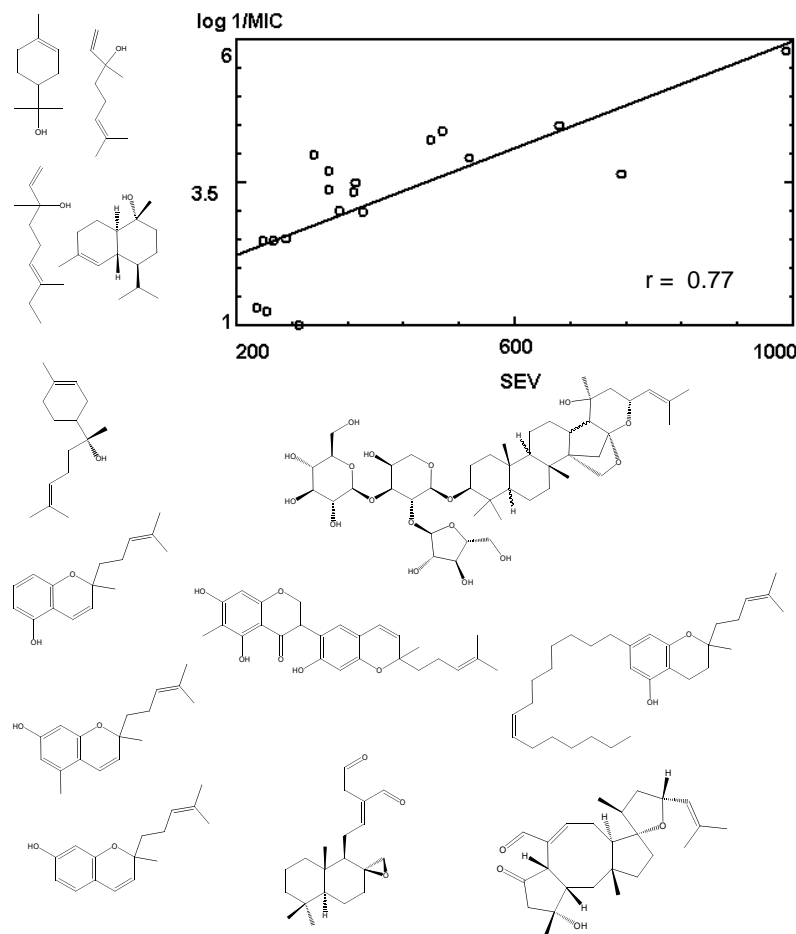
	<b>307</b>
 20-DMH = 20-2,6-dimethylhept-5-ene	<b>226</b>
Serial or agar dilution tests only	<b>156</b>
<i>Candida albicans</i> only	<b>97</b>

# Selected 2O-DMH compounds sorted by activity

	MIC 12.5		<i>Candida albicans</i>	AJ 4409	trans-8beta(17)-Epoxy-12		MIC 100		<i>Candida albicans</i>	ATCC 10231	2-Methyl-2-(4-methyl-pent-2-en-1-yl)-5-hydroxy-3,6-dihydro-2H-pyridin-4-one
	12.5		<i>Candida albicans</i>	NHL 4019	trans-8beta(17)-Epoxy-12		225		<i>Candida albicans</i>		alpha-Cadinol
	24	in mixture with 50% Pinene	<i>Candida albicans</i>		Nerolidol		500		<i>Candida albicans</i>		alpha-Bisabolol
	25		<i>Candida albicans</i>	ATCC 10231	2-Methyl-2-(4-methyl-pent-2-en-1-yl)-5-hydroxy-3,6-dihydro-2H-pyridin-4-one		500		<i>Candida albicans</i>		alpha-Cadinol
	40		<i>Candida albicans</i>		3,6,8-Trihydroxy-3-(3,5-dimethylbut-2-enyl)-7-oxo-2,4-dihydro-2H-pyridin-4-one		500		<i>Candida albicans</i>		Ethyl linalool
	50		<i>Candida albicans</i>	ATCC 10231	2,5-Dimethyl-2-(4-methyl-pent-2-en-1-yl)-5-hydroxy-3,6-dihydro-2H-pyridin-4-one		500		<i>Candida albicans</i>	I	Linalool
	50	MIC: 50 - 100 ppm	<i>Candida albicans</i>	IA-1007	Desmodianone A		500		<i>Candida albicans</i>		Linalool
	50		<i>Candida albicans</i>		Jujubogenin 3-O-alpha-L-arabinofuranoside		500		<i>Candida albicans</i>	II	alpha-Terpineol
	70	in mixture with 50% Eugenol	<i>Candida albicans</i>		Nerolidol		930		<i>Candida albicans</i>	KEM H5	alpha-Terpineol
	100	at room temperature	<i>Candida albicans</i>	2929	alpha-Bisabolol		1000		<i>Candida albicans</i>	I	alpha-Terpineol
	100		<i>Candida albicans</i>		alpha-Bisabolol		1000		<i>Candida albicans</i>		alpha-Terpineol
	100	fungistatic activity	<i>Candida albicans</i>		alpha-Bisabolol		1000		<i>Candida albicans</i>	PCM 1409 FZH	alpha-Terpineol
	100		<i>Candida albicans</i>	ATCC 10231	2-Methyl-2-(4-methyl-pent-2-en-1-yl)-5-hydroxy-3,6-dihydro-2H-pyridin-4-one		1000		<i>Candida albicans</i>	II	Linalool

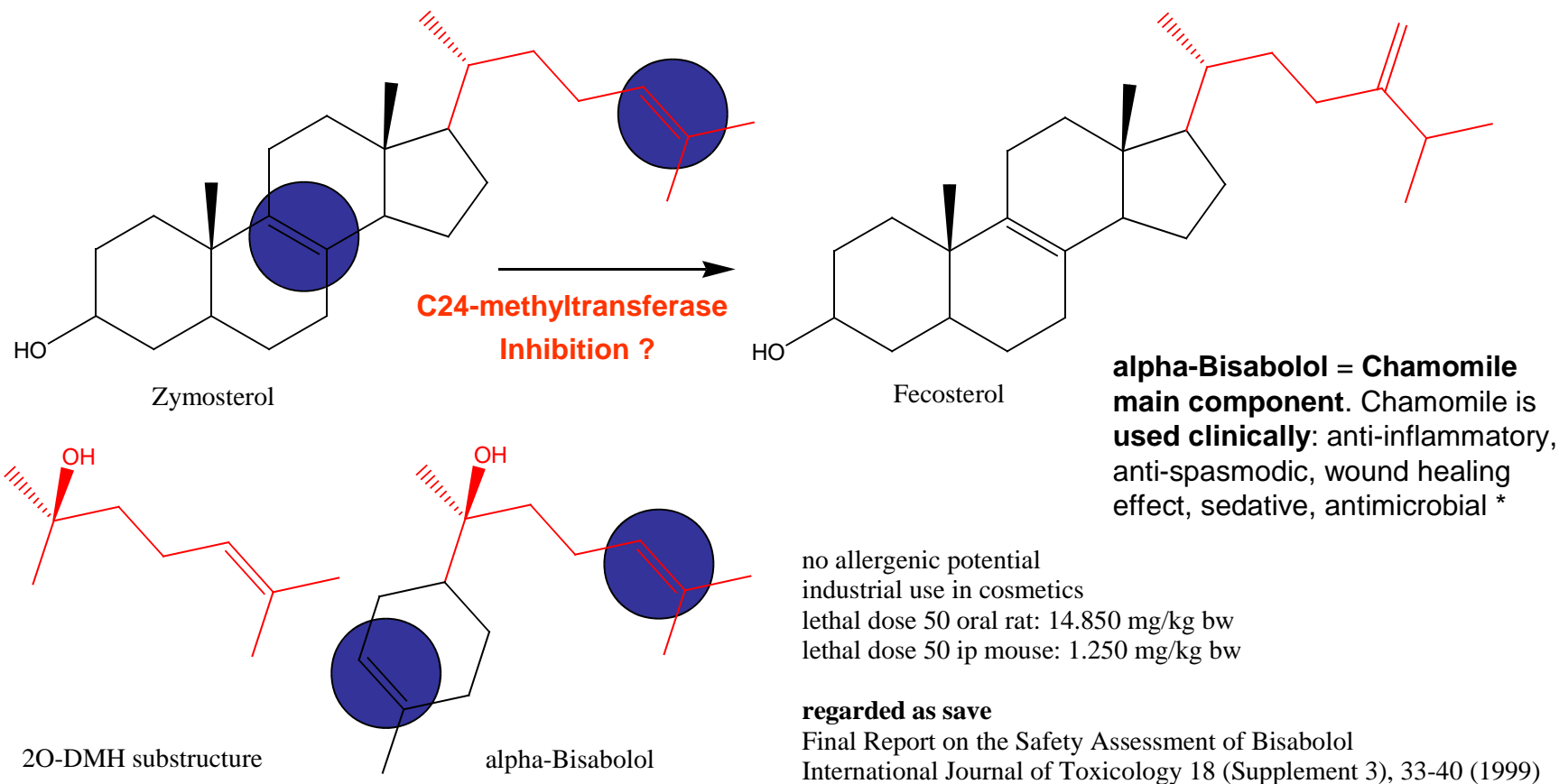
# Relationship between molecular volume and anticandidal activity of 2O-DMH compounds

Compound names	MIC in mg/L	SEV in Å <sup>3</sup>	log 1/MIC
Antifungal US 5702929	1	989.266	5.81
Ophiobolin A	12.50	662.842	4.50
trans-8b(17)Epoxy-12-labdene-15,16-dial	12.50	495.317	4.41
Cannabichromene III	25	310.502	3.99
Desmodianone A	50	534.202	3.94
Nerolidol (+ 50% pinene)	70	370.413	3.50
Cannabichromene II	50	332.037	3.71
Jujubogenin glykosid (aglycon only)	100	478.357	4.25
Cannabichromene IV	100	752.939	3.66
Cannabichromene I	100	332.274	3.39
alpha-Bisabolol	100	367.719	3.35
alpha-Cadinol	225	381.239	2.99
Smeathxanthone B	312.5	347.293	3.01
Ethyl linalool	500	270.755	2.52
Linalool	500	253.133	2.49
alpha-Terpineol	500	237.436	2.49
Hydroxycarvone	8000	228.531	1.32
Sobrerol	9500	242.624	1.25
Linalyl acetate	19300	289.184	1.01



SEV = Connolly Solvent-Excluded Volume

# A new type of fungal inhibitors ?



\* Heinz Schilcher et al.: Wirkungsweise und Anwendungsformen der Kamillenblüten, BMV Berliner Medizinische Verlagsanstalt GmbH Berlin 2004