Synthesis of linalool and limonene sensitizing hydroperoxides

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Methods to prepare hydroperoxides

Autoxidation of unsaturated compounds

General mechanism

Initiation $RH \longrightarrow R^{\bullet}$

Propagation $R^{\bullet} + {}^3O_2 \rightleftharpoons ROO^{\bullet}$ fast

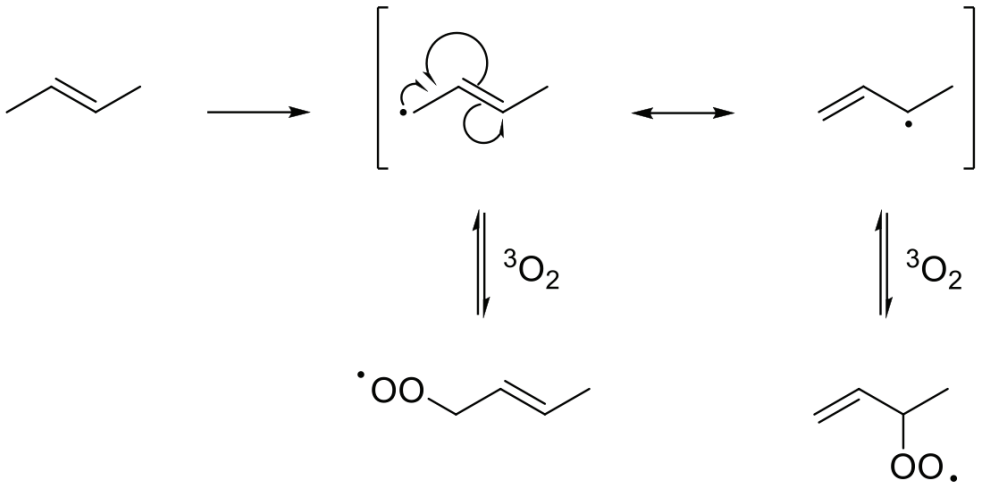
$ROO^{\bullet} + RH \longrightarrow ROOH + R^{\bullet}$ slow

Termination $2\ R^{\bullet} \longrightarrow$

$R^{\bullet} + ROO^{\bullet} \longrightarrow$ } non-radical products

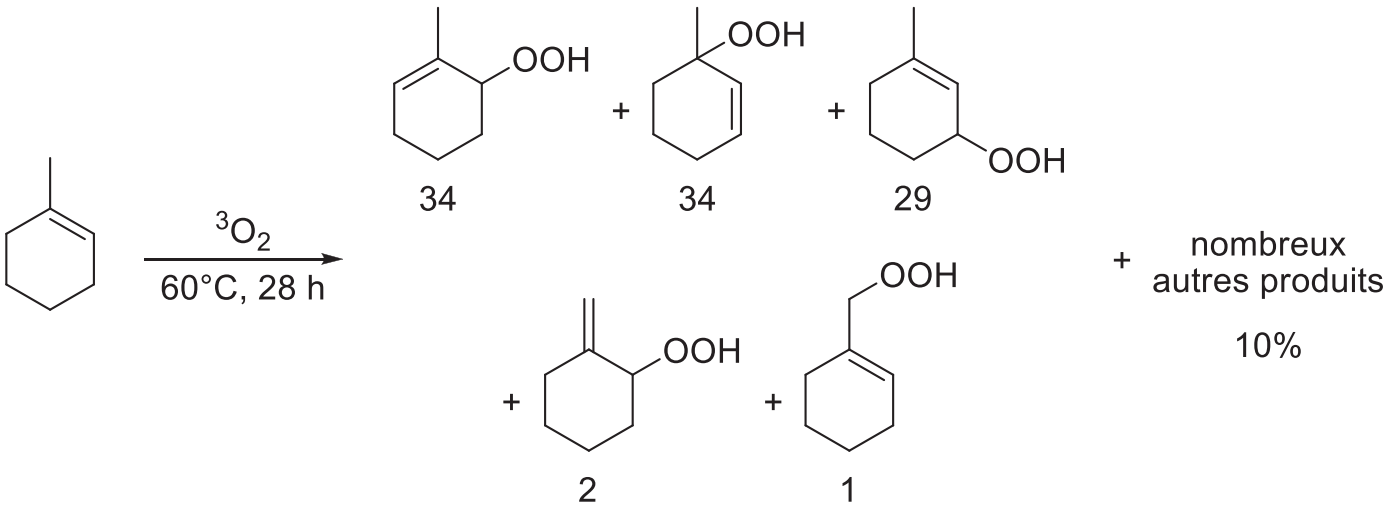
$2\ ROO^{\bullet} \longrightarrow$

For unsaturated compounds



Methods to prepare hydroperoxides

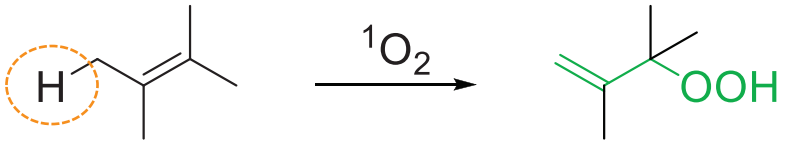
Non-selective, multitude of oxidation products …



Courtneidge JL, Bush M. *J Chem Soc, Chem Comm* 1989, 17,1227

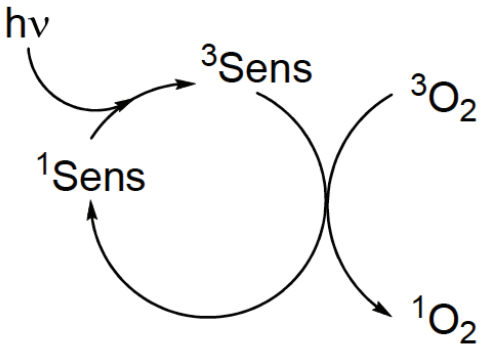
Methods to prepare hydroperoxides

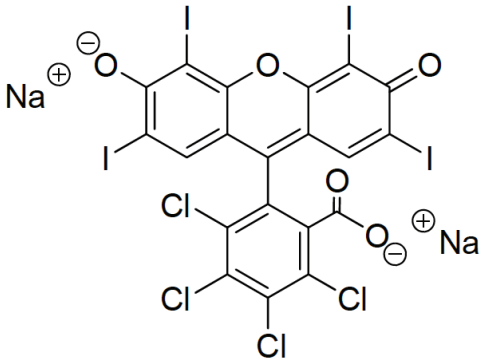
Singlet oxygen ene reaction – Schenck reaction



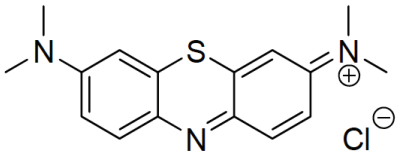
production of singlet oxygen

Photochemical methods : mostly employed





Bengal Rose



Methylene Blue

Methods to prepare hydroperoxides

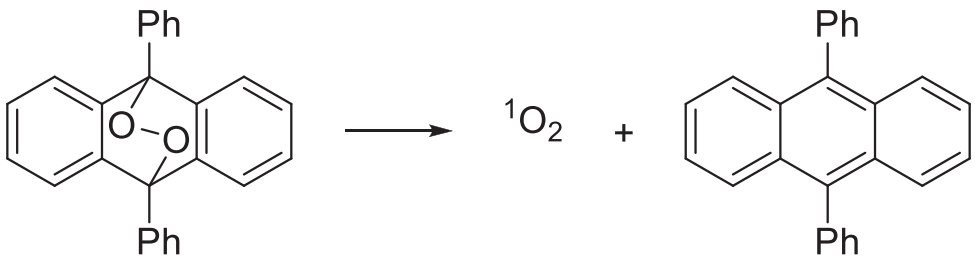
Singlet oxygen ene reaction – Schenck reaction

Chemical methods:

$H_2O_2 + NaOCl \longrightarrow {}^1O_2 + H_2O + NaCl$

$(PhO)_3PO_3 \longrightarrow {}^1O_2 + (PhO)_3PO$

$MoO_6^{2-} \longrightarrow {}^1O_2 + MoO_4^{2-}$

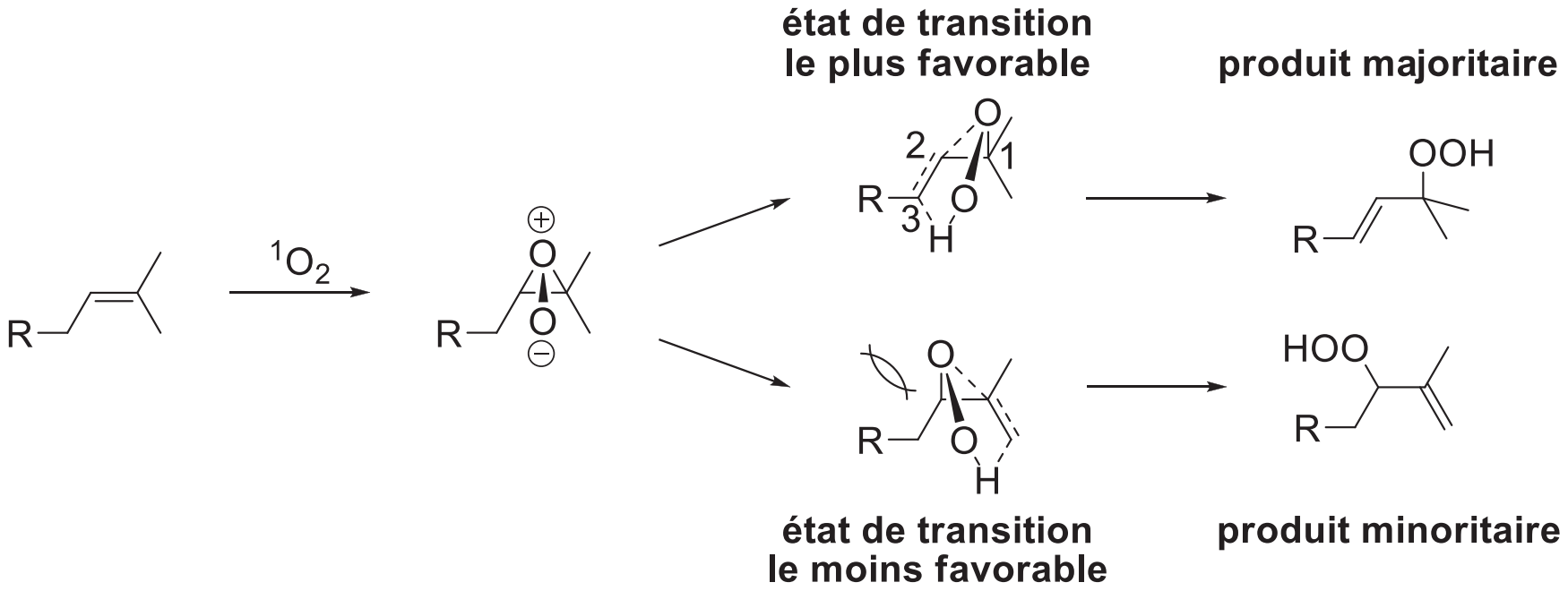


peroxomolybdates intermediates

Methods to prepare hydroperoxides

Schenck reaction on trisubstituted olefins

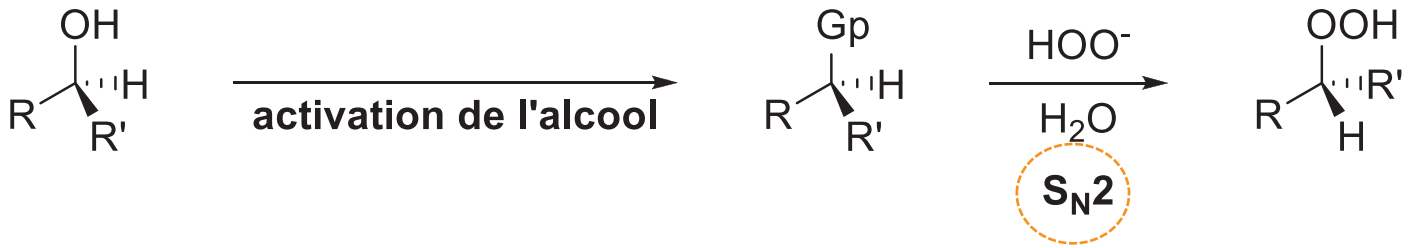
regioselectivity and stereoselectivity

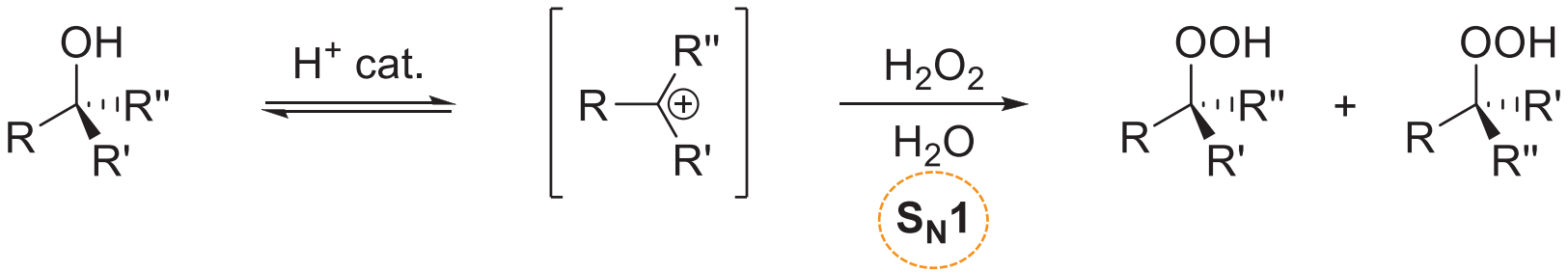


Stratakis M, Orfanopoulos M, *Tetrahedron* 2000, 56, 1595

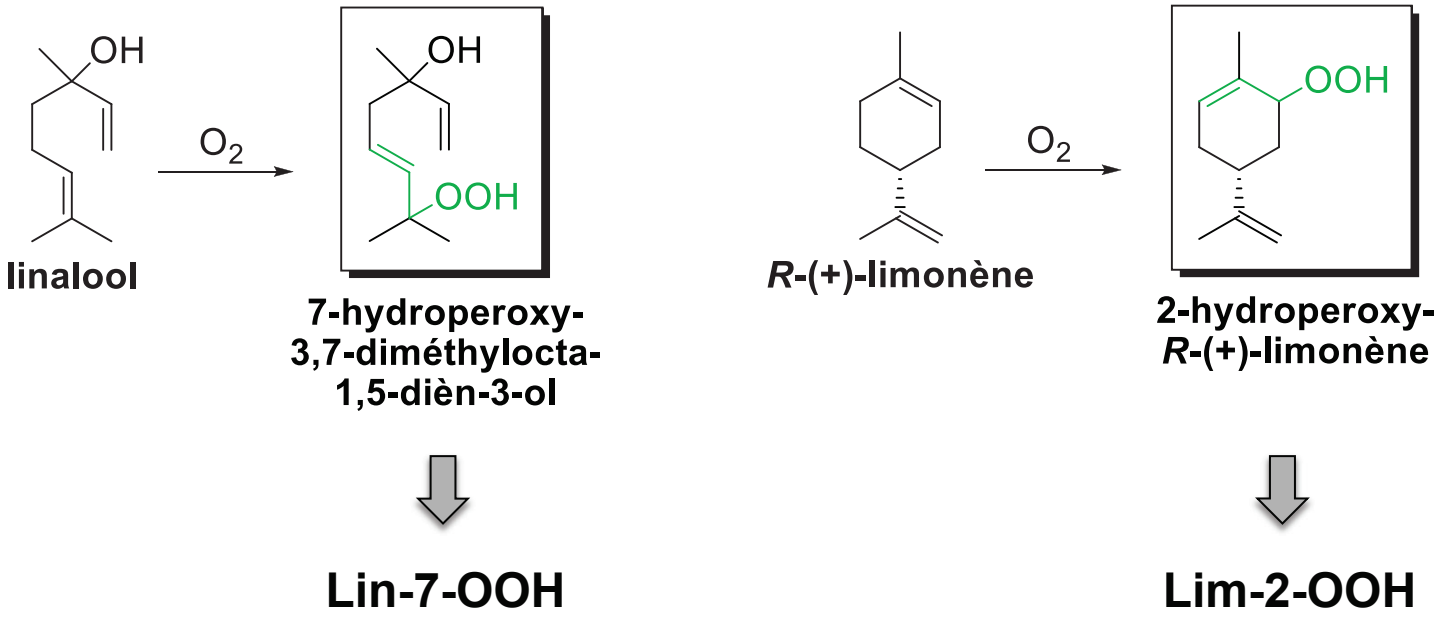
Methods to prepare hydroperoxides

Nucleophilic substitution on allylic alcohols





Hydroperoxides of our concern



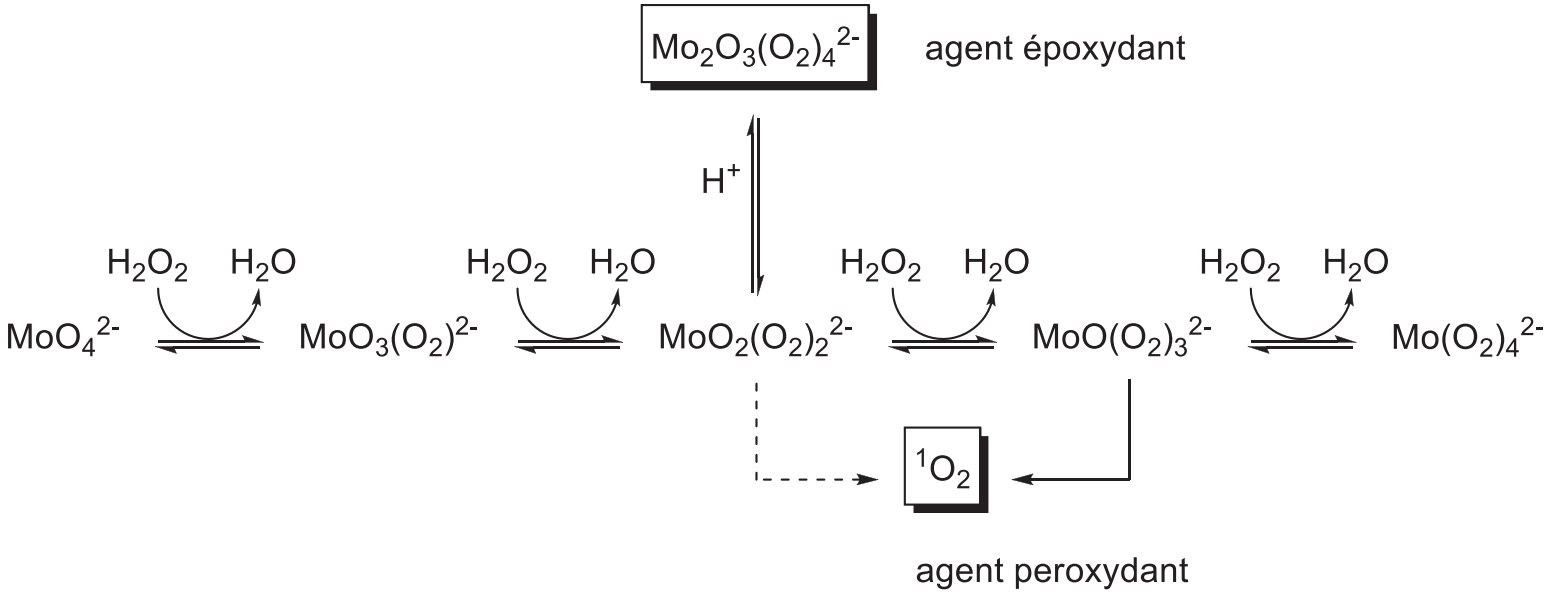
Synthesis of Lin-7-OOH

Schenck reaction on trisubstituted olefin

Experimental conditions : obtention of $^1O_2$

$$2\ H_2O_2 \xrightarrow[\text{pH 9-12}]{MoO_4^{2-}\ \text{cat.}} {}^1O_2 + 2\ H_2O$$

100%

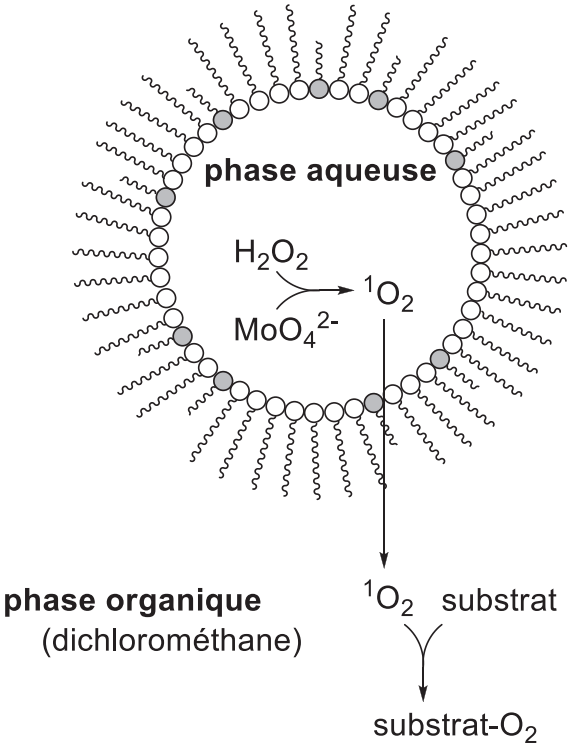


Aubry J-M *et al.*, *Tetrahedron* 2006, 62, 10753

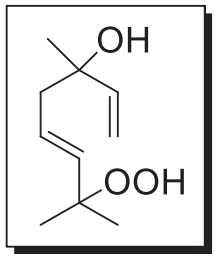
Synthesis of Lin-7-OOH

Schenck reaction on trisubstituted olefin

Experimental conditions : microemulsion



H_2O_2, MoO_4^{2-} cat.
microémulsion, t.a.
réaction de Schenck
80%



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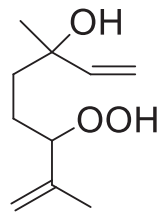
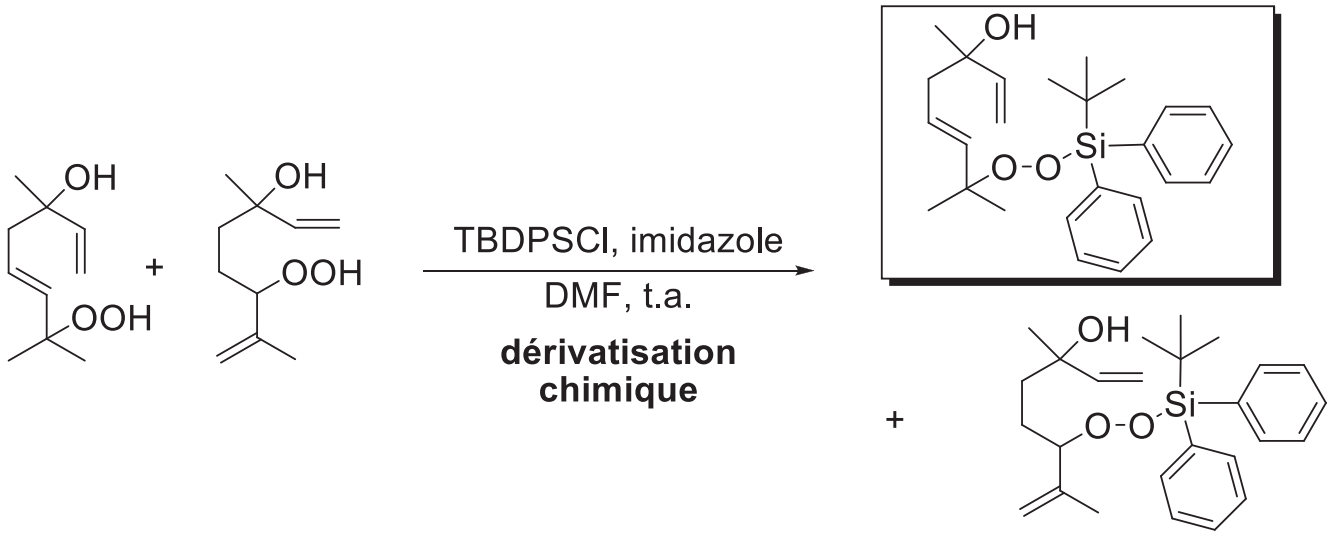


32% **48%**

rapport 4:6

Synthesis of Lin-7-OOH

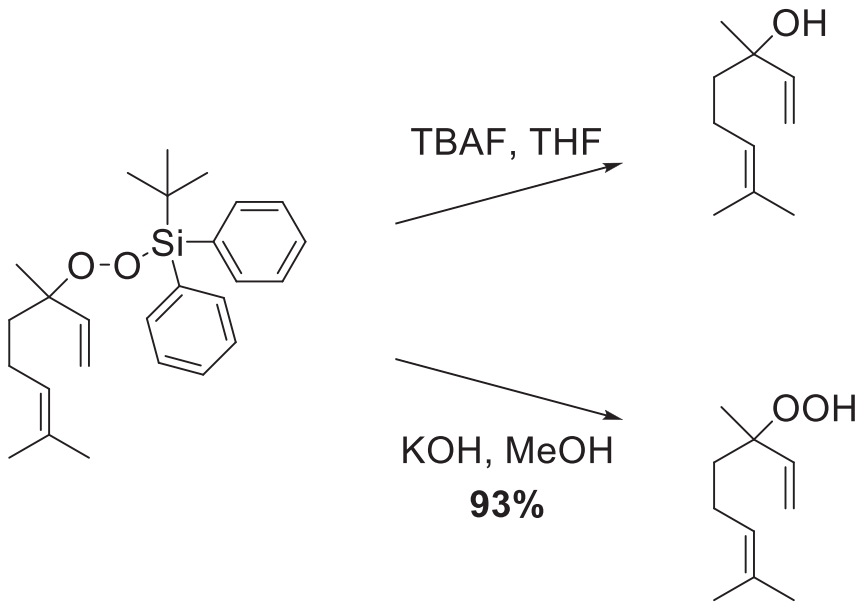
Chemical derivatization (silylization) of the hydroperoxides

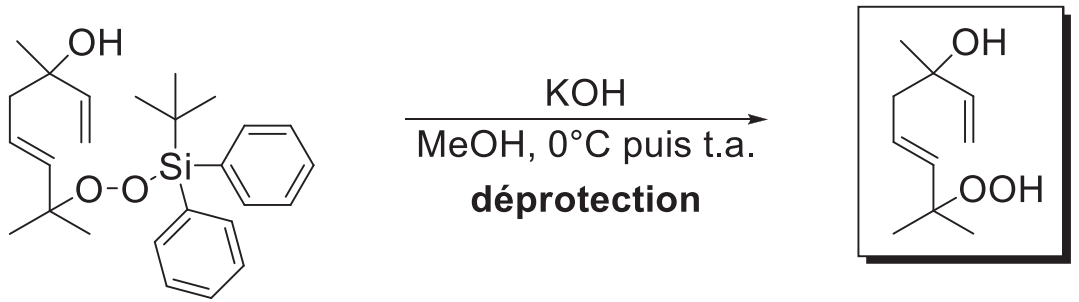


Mixture of hydroperoxides	TBDPSCl	Imidazole	DMF	
391 mg	1,2 éq.	2 éq.	8,5 mL	Two isomers protected
200 mg	1,2 éq.	2 éq.	8,5 mL	One single isomer protected

Synthesis of Lin-7-OOH

Deprotection of the peroxysilane





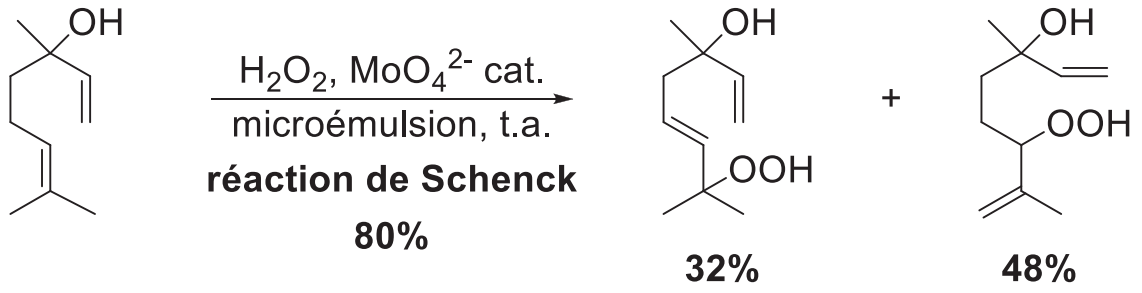
Synthesis of Lin-7-OOH

Derivatization/Deprotection optimization

Weight mixture hydroperoxides	Concentration mixture hydroperoxides	Reaction time	Yield on the last two steps
200 mg	0,13 mol.L^{-1}	2 days	13%
200 mg	0,11 mol.L^{-1}	10 days	61%
200 mg	0,14 mol.L^{-1}	10 days	59%
200 mg	0,21 mol.L^{-1}	10 days	96%
1 g	0,21 mol.L^{-1}	10 days	9%

Synthesis of Lin-7-OOH

Summary

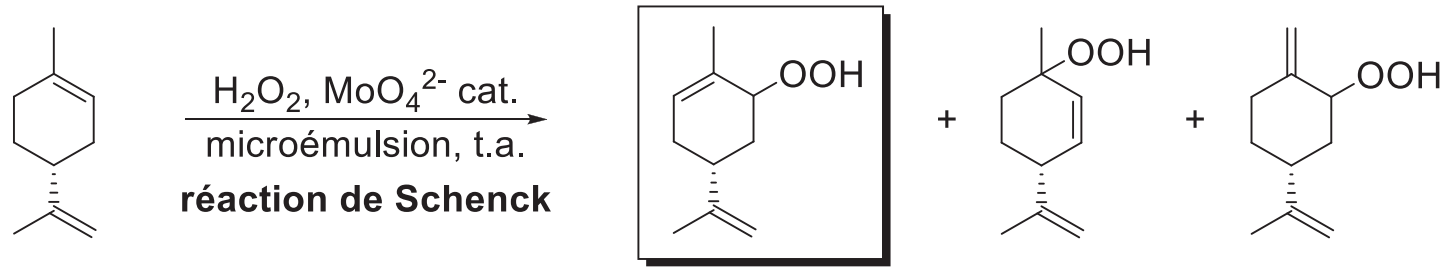


Kao D *et al.*, *J Org Chem,* 2011, 76, 6188

Synthesis of Lim-2-OOH

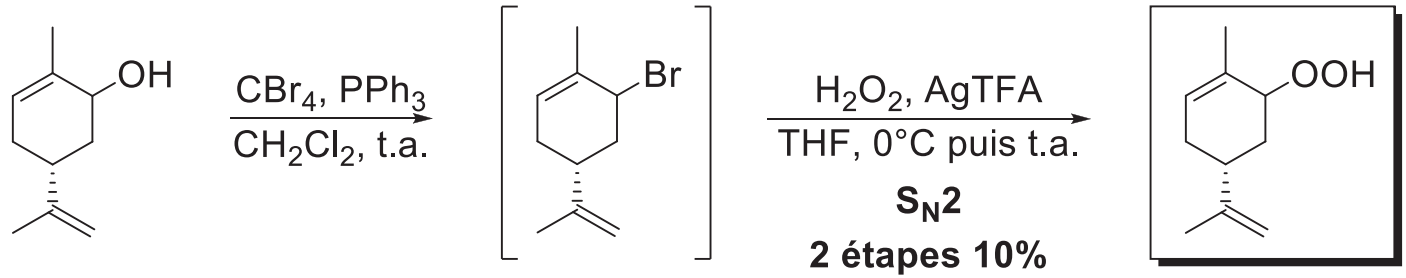
First tests

Schenck reaction



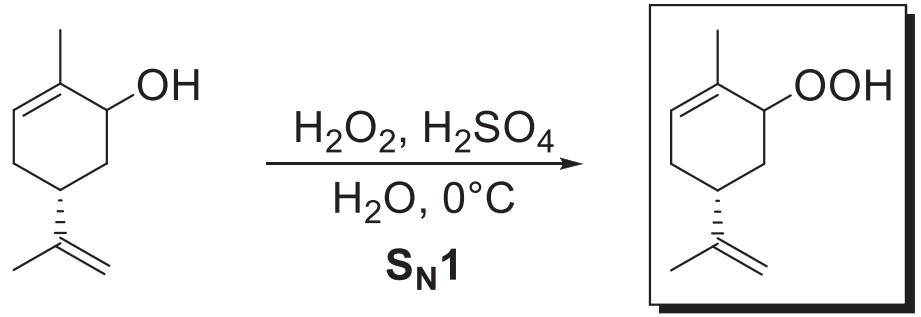
produit minoritaire

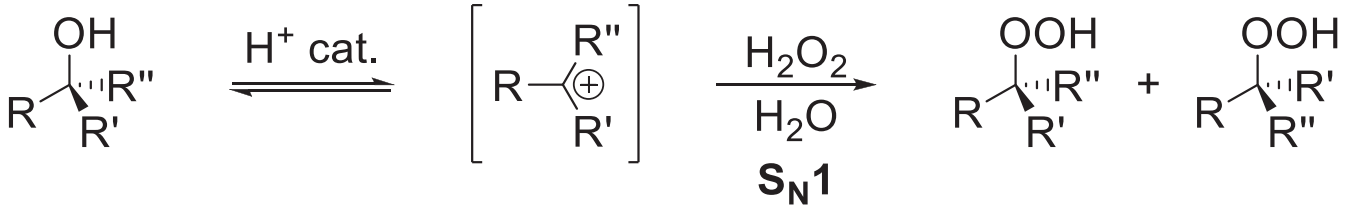
S_N2 nucleophilic substitution



Synthesis of Lim-2-OOH

S_N1 nucleophilic substitution





Kao D *et al.*, *J Org Chem,* 2011, 76, 6188