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Epoxidation of allylic alcohols in aqueous solutions of non surfactant amphiphilic sugars

Cécile Denis,[a] Khalid Misbahi,[a] Abdelali Kerbal,[b] Vincent Ferrières[a] and Daniel Plusquellec*[a]

[a] *Ecole Nationale Supérieure de Chimie de Rennes, Synthèses et Activations de Biomolécules, CNRS UMR 6052, Institut de Chimie de Rennes, Avenue du Général Leclerc F-35700. Rennes, France. E-mail: daniel.plusquellec@ensc-rennes.fr; Fax: (+33 0) 2 99 87 13 98; Tel: (+33 0) 2 99 87 13 01*
[b] *Laboratoire de Chimie Organique, Faculté des Sciences, Dhar Elmehrez, Fès, Morocco*

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A variety of cyclic and acyclic allylic alcohols undergo efficient chemo-, regio- and/or stereoselective epoxidations in neutral aqueous solutions of amphiphilic carbohydrates (sucrose, L-arabinose, methyl or ethyl β-D-fructopyranoside) by using dilute hydrogen peroxide in the presence of molybdic or tungstic salts.

Epoxides are versatile building blocks for organic synthesis, because the epoxide group can be readily opened to produce vicinal functionalities. Chemo-, regio-, diastereo- and enantioselective processes have therefore been developed over the last decades for the synthesis of oxiranes.[1] Traditionally, the conversion of an alkene into an epoxide is performed by using peroxycarboxylic acids or *tert*-butyl hydroperoxide in conjunction with transition metal catalysts in organic solvents.[1] Nevertheless the need for reducing the amounts of toxic waste from chemical processes requires the use of environmentally friendly solvents and reagents. In this context, intensive efforts have been developed in the field of organic synthesis in water.[2,3] In this communication, we report a novel and very simple route for epoxidation of allylic alcohols by aqueous hydrogen peroxide[4] in the presence of molybdic or tungstic salts[5] in neutral aqueous solutions of non surfactant amphiphilic carbohydrates.

Reactions were carried out in water solutions of selected carbohydrates, *e.g.* sucrose **1**, α-L-arabinopyranose **2** and methyl or ethyl β-D-fructopyranoside **3a**,**b** (Fig. 1). Recent reinvestigation of sucrose conformation in water reveals the existence of an interresidue water-bridge.[6] This conformation resembles that found in the crystal[7] and in polar aprotic solvents.[8] Applying the Oxford Molecular MAD program[9] to that conformation of sucrose revealed the outside section of the fructose moiety to be hydrophobic in type.[10]

The composition of an equilibrated mixture of L-arabinose **2** in water greatly favours pyranoses (60% α, 35% β) over furanoses (3% α, 2% β) at 25 °C.[11] In the most abundant α-pyranose form, L-arabinose **2α** is characterised by an arrangement of hydroxy, methine and methylene groups which divides the molecule into hydrophobic and hydrophilic surfaces. This expectation is clearly corroborated by computation of the hydrophilicity potential. Moreover, we have synthesised methyl and ethyl β-D-fructopyranosides **3a** and **3b**, respectively, according to a procedure recently developed in our laboratory.[12]

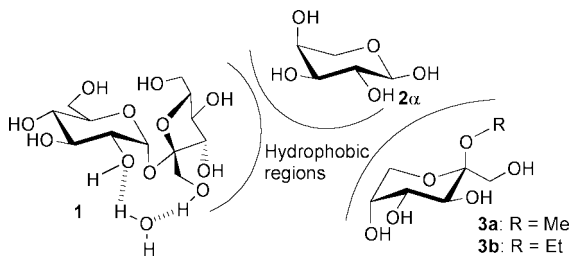

Fig. 1 Structure and hydrophobic areas of amphiphilic carbohydrates **1**–**3**.

Carbohydrates **1**–**3a**,**b** display therefore facial amphiphilicity and apolar organic compounds are expected to interact in aqueous media with the hydrophobic regions of these sugars in order to minimise unfavourable interactions with water. Aqueous solutions of amphiphilic carbohydrates are therefore expected i) to enhance the solubility of allylic alcohols and ii) to localise and to orientate the organic substrates.

Epoxidations of allylic alcohols (Fig. 2, 1 mmol) were performed with 30% hydrogen peroxide (10 mmol) in the presence of molybdic acid or sodium tungstate (0.1 mmol) in aqueous buffered solutions (20 mL, pH7, phosphate buffer)

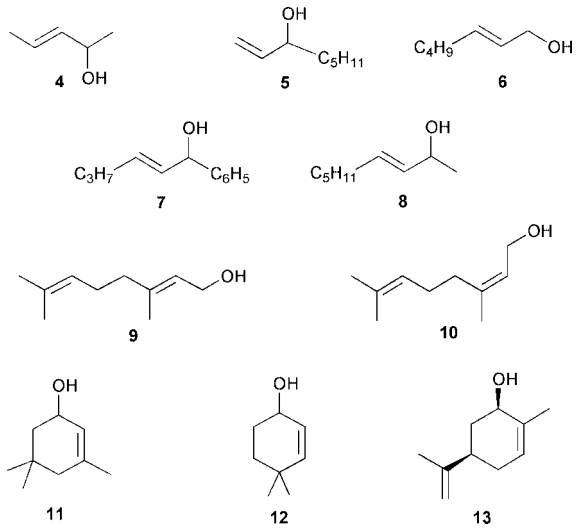

Fig. 2 Selected allylic alcohols **4**–**13**.

containing 20 mmol (molar solutions) of sugar additives. Indeed epoxidations were therefore carried out in dilute ~2% aqueous hydrogen peroxide. The reactions were stirred for 12–72 h (Table 1) at +2 °C and the products were then easily extracted with diethyl ether and their purity was determined by capillary GLC analysis. To compare our system with previously described aqueous solutions of surfactants,[13] some epoxidations were carried out under the same conditions without any amphiphilic carbohydrate.

Results of the epoxidation of a number of acyclic and cyclic allylic alcohols are reported in Table 1. Simple allylic alcohols **4**–**8** (entries 1–6) afforded the corresponding epoxides in high conversion yields when reactions were performed in the presence of carbohydrates **1** or **2**. It is noteworthy that no enone formation was observed[14] (see for example entry 2) and that conversion of the less reactive terminal olefin **5**[1] was dramatically enhanced in the presence of sucrose additive (entries 2, 3). Moreover, under the present conditions, no triol, resulting from oxirane opening, could be detected.

In order to extend our investigation on the regioselectivity of the reaction, geraniol **9** and nerol **10** were chosen as typical polyolefinic substrates that are sparingly soluble in pure water

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Table 1 Epoxidation of allylic alcohols with H_2O_2–metal catalyst in aqueous neutral solutions of glycosidic additives at + 2 °C

Entry	Alcohol	Additive	Metal catalyst	Reaction time (h)	Conversion (%)	Epoxide : ketone ratio	Isolated yield (%)
1	**4**	**1**	Mo^{+6}	24	100	>99 : 1	75
2	**5**	**1**	Mo^{+6}	72	78	>99 : 1[a]	72
3	**5**	—	Mo^{+6}	72	30	>99 : 1	28
4	**6**	**1**	W^{+6}	24	100	95 : 5	83
5	**7**	**1**	Mo^{+6}	72	92	>99 : 1	83
6	**8**	**2**	Mo^{+6}	72	97	>99 : 1	88
7	**9**	**1**	Mo^{+6}	48	94	>99 : 1	92
8	**10**	**1**	Mo^{+6}	48	98	>99 : 1	92
9	**11**	**2**	Mo^{+6}	24	97	90 : 10	80
10	**11**	**3a**	W^{+6}	48	100	97 : 3	86
11	**11**	**3b**	W^{+6}	48	100	97 : 3	85
12[b]	**11**	**3b**	W^{+6}	48	100	98 : 2	84
13	**12**	**1**	W^{+6}	72	100	83 : 17	80
14	**13**	**2**	Mo^{+6}	24	70	87 : 13	66
15	**13**	—	Mo^{+6}	48	72	60 : 40	68
16	**13**	**3a**	Mo^{+6}	24	70	85 : 15	67

[a] Oxirane oxidation in CH_2Cl_2 gave 51 : 49.[14b] [b] Recycled aqueous solution from entry 11.

but highly soluble in 1 M sucrose solutions. A site-selective epoxidation occurred at the least electron-rich allylic double bond and pure 2,3-epoxy-geraniol and -nerol were isolated in high yields (entries 7, 8). Unfortunately, epoxidation of geraniol **9** in the presence of sucrose gave 2,3-epoxygeraniol with modest enantioselectivity (ee = 10% determined by polarimetry). Our results obtained in neutral media therefore compare favourably with previous work performed with peracids in strongly alkaline media[13] or with transition metal catalysed epoxidations in organic solvents.[15,16]

Oxidations of six-membered cyclic substrates (Table 1, entries 9–15) indicated that enone formation competed with epoxidation. The ratio of oxirane to ketone showed a pronounced dependence on both substrates and reaction conditions as exemplified by entries 14 and 15. The best chemoselectivities were attained by using tungsten(VI) catalyst in the presence of sugar additives. Moreover, it is important to mention that solutions containing fructosides and catalyst could be recycled for further experiments without loss of conversion yield, chemoselectivity and stereoselectivity (entry 12).

The results presented here suggest OH-assisted epoxidation of allylic alcohols, presumably related to the formation of an intermediate in which the olefinic alcohol is most likely coordinated to the metal *via* the hydroxy group. Such an intermediate was previously suggested for tungsten catalysed epoxidations in protic media.[16,17] The next step was therefore to ascertain whether sugar–substrate and/or intermediate interactions were strong enough to promote stereodiscrimination in the epoxidation reaction. Some significant results for the epoxidation of representative cyclic and acyclic allylic alcohols are listed in Table 2. The data indicate that acyclic alcohols **4–8** gave mixtures of *erythro/threo* epoxides. Nevertheless, epoxidation in glycosidic aqueous media generates stereoselectively *erythro* enriched epoxy alcohols. This outcome is the same as for metal catalysed systems in organic solvents but is opposite to that obtained using peroxyacids in organic media.[16]

Table 2 Diastereoselective epoxidations of allylic alcohols in aqueous neutral solutions of carbohydrates **1–3**

Entry	Substrate	Additive	Metal catalyst	dr[a] *erythro* : *threo* (*cis* : *trans*)	mCPBA or analogues (lit.)
1	**4**	**1**	Mo^{+6}	68 : 32	30 : 70[13]
2	**5**	**1**	Mo^{+6}	68 : 32	38 : 62[14]
3	**8**	**1**	Mo^{+6}	62 : 38	36 : 64[14]
4	**11**	**2**	Mo^{+6}	(99 : 1)	(95 : 5)[18]
	11	**3a** or **3b**	W^{+6}	(>99 : 1)	(95 : 5)[18]
5	**12**	**1**	W^{+6}	(95 : 5)	
6	**12**	**3a** or **3b**	W^{+6}	(>99 : 1)	
7	**13**	**2**	Mo^{+6}	(94 : 6)	(90 : 10)
8	**13**	—	Mo^{+6}	(89 : 11)	

[a] dr: diastereoisomeric ratio were determined by GLC. *erythro/threo* refers to acyclic substrates whereas *cis/trans* to cyclic products.

In the case of cyclohex-2-enols **11–13** the epoxidation was highly stereoselective when compared with the results obtained by a peracid epoxidation (Table 2). In particular, allylic alcohols **11–12** gave exclusively the product where epoxide and OH functions are *cis* to each other when the reactions were performed in aqueous solutions of D-fructose derivatives **3a** or **3b** in the presence of Mo^{+6} or W^{+6} catalyst. Once again, comparison of *cis* : *trans* ratio underlines the role played by arabinose as additive (entries 7 and 8).

The predictable sense of the addition to cyclic olefins can be rationalised by means of a model where hydrophobic interactions are probably involved between the most hydrophobic face of the cyclic alcohol and that of sugar additive. These interactions may account for the enhanced stereoselective hydroxy directed epoxidation of cyclic allylic alcohols observed herein.

In conclusion, it was shown that dilute hydrogen peroxide together with molybdenum(VI) or tungsten(VI) salts is an efficient system for the chemo-, regio- and stereoselective epoxidation of allylic alcohols in aqueous solutions of carbohydrates characterised by a facial amphiphilicity.

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