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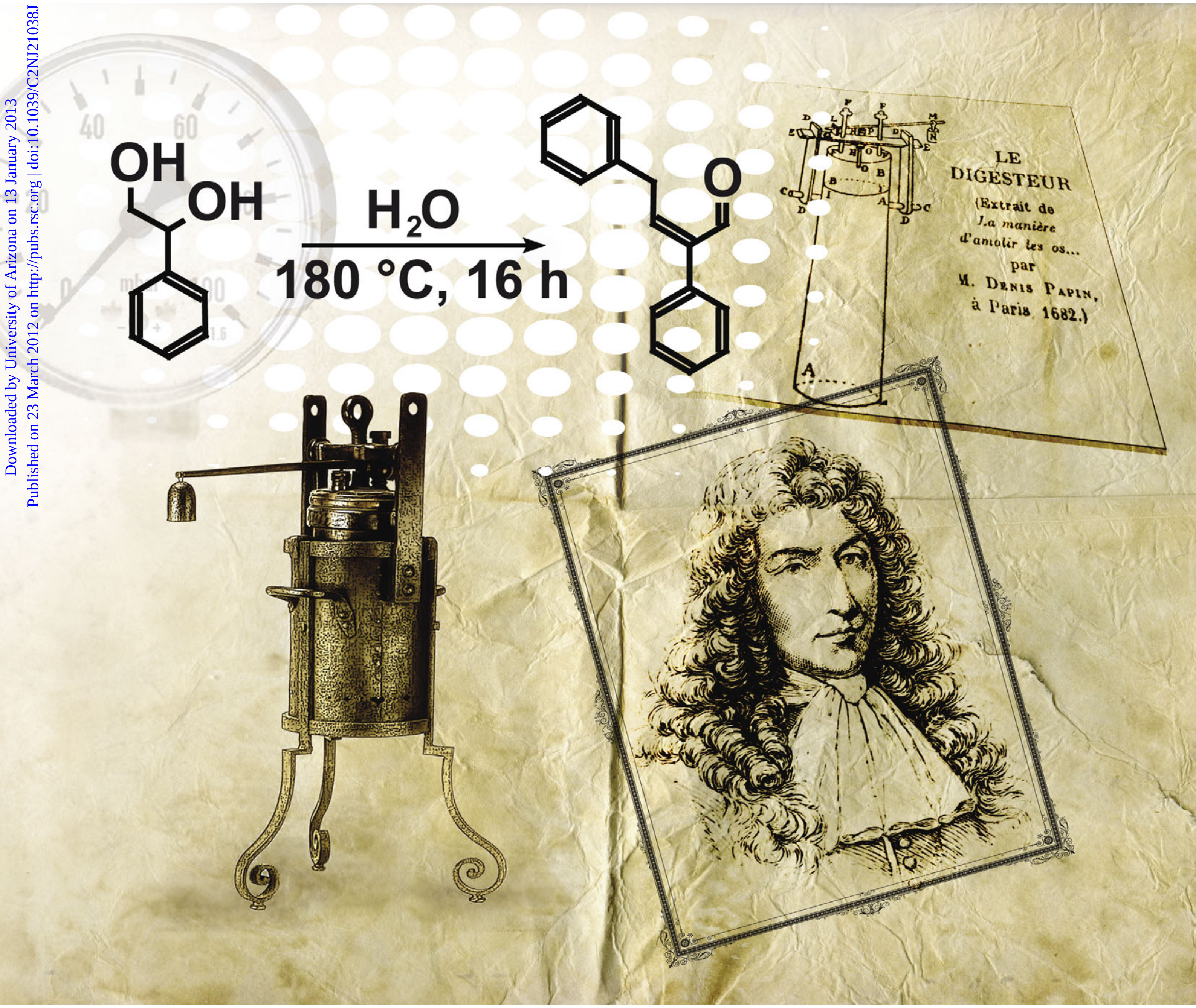

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PAPER

Organic reactivity of alcohols in superheated aqueous salt solutions: an overview†

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The low dielectric constant and high self-dissociation constant of water in a temperature range between 150 and 250 °C make it a very appealing solvent for synthesis. Surprisingly, while organic chemistry in water at low temperature or around its critical point has been investigated in detail, very little seems to be known about the behaviour of organic molecules under hydrothermal conditions. The present work thus aims at shading some light on this field. As a start, we decided to investigate the reactions in which alcohols can undergo in water in the above-mentioned temperature range. Knowing that very strong salt effects on organic reactions have already been observed in super critical water, the impact of salt on the outcome of our tests was also investigated in detail.

A Introduction

The search for greener solvents is one of the key issues for achieving more sustainable chemical processes.[1] This purpose renewed a long time interest for water as a reaction medium for organic synthesis. Actually, the properties of (liquid) water are strongly impacted by temperature. This explains why researchers differentiate between two domains of working conditions, namely: (i) "standard" water at normal pressure between 0 and 100 °C and (ii) supercritical water (SCW) (the critical point of water lying at 374 °C and 218 bars). Water under normal conditions, on the one hand, is well known to most people and chemists, in particular. It is able to solubilise numerous very polar species, hydrogen bond donors or acceptors and most ionic species. What is also well known to chemists is that a majority of organic compounds are not soluble in water between 0 and 100 °C (which explains a recurring controversy on the question whether organic reactions featuring water as their solvent are actually occurring "in" water or "in the presence of" water).[2] Super critical water, on the other hand, is a very good solvent for organic molecules (alkanes are, for example, infinitely soluble in SCW) and could thus appear as an ideal reaction medium for many organic reactions. Actually numerous review articles are summarising the works undertaken on this topic.[3] Unfortunately, SCW is only obtained under harsh (and thus at some point expensive) conditions. It also imposes high requirements on the used reaction vessels. All these features restrict the industrial applicability of SCW.

The intermediate range between "normal" and supercritical water is often referred to as sub-critical, superheated (SHW), hot compressed water (HCW) or hydrothermal water (HTW).[4] Notwithstanding the advantages or drawbacks of these labels, we decided, for convenience, to employ the terms "super-heated water" and "hydrothermal conditions" equivalently in this work. In the hydrothermal domain, the physicochemical properties of water are evolving rapidly and minor temperature changes have dramatic effects (as can be seen in Fig. 1 adapted from ref. 5). Around 250 °C the dielectric constant of water is already very low (which makes it a good solvent for apolar species), its self-dissociation constant reaches a maximum, while the corresponding autogenic pressure does not exceed 40 bars. The corrosion behaviour of water at this temperature is known and it is possible to deal with them industrially (see the working conditions of numerous power plants).

These working conditions are familiar to most material scientists. Indeed, materials as important as zeolites,[6] oxide nanoparticles[7] or mesoporous oxides[8] are often synthesized under hydrothermal conditions. More recently even hybrid or purely organic materials have been successfully synthesised under such conditions, as can be exemplified by metal organic frameworks[9] or hydrothermal carbon.[10] Despite these achievements and the above-mentioned advantages, super-heated water still is unfamiliar to organic chemists (except some pioneering works by Kopetzki *et al.*[11] and contributions from the own group).[12] The aim of the present work was to start paving the way to a real use of hydrothermal conditions in organic synthesis.

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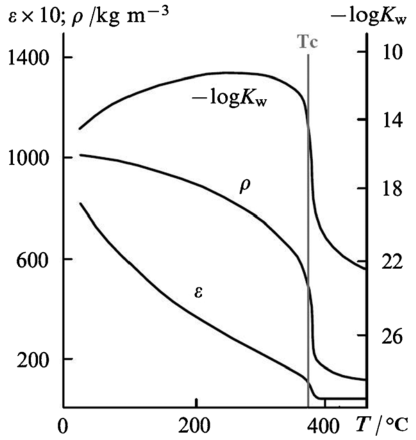


Fig. 1 Evolution of the dielectric constant (ε), the density (ρ) and self-dissociation constant (k_w) of water with temperature. Reprinted from ref. 5 by permission of Turpion Ltd.

As most alcohols are hydrotropic molecules we thought that it is convenient to start our investigation with this family of molecules. In addition, biomass, which is very rich in hydroxylated molecules, will, in a foreseeable future, more and more be used as a feedstock for the chemical industry.[13] But existing chemical plants have been designed to deal with molecules issuing from oil processing (such as alkanes and alkenes), which have a very low content of heteroelements. It thus is of great importance to find sustainable ways to convert biomass derivatives into molecules, with which the chemical industry can deal. We also decided, knowing that salts strongly impact the properties of near critical water (see for example ref. 14), to investigate how very simple salts impacted the reactivity of our alcohols.

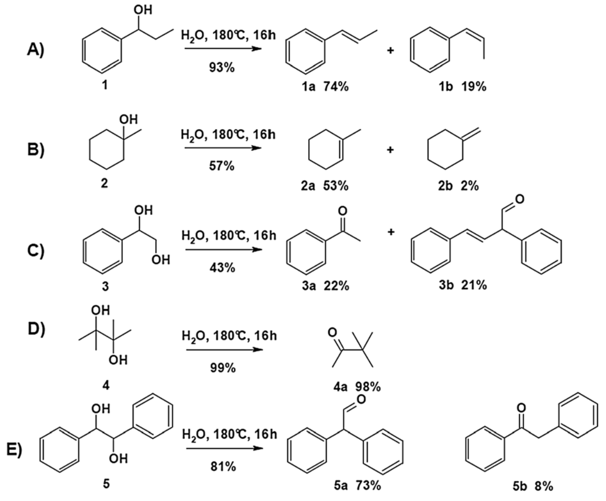
B Results and discussion

1 Screening of the reactivity of various alcohols in super heated water

At first, we wanted to screen the behaviour of various (activated) alcohols in aqueous solutions, just to get access to a mapping of possible organic reactions in this medium. We thus heated up 5 mmol of phenylpropanol and 200 mg of some other alcohols in 10 ml of aqueous medium to 180 °C for 16 h under autogeneous pressure. In preliminary runs, simple alcohols, like heptanol, failed to undergo any reaction in high yields even at higher temperatures (see Table S1 in the ESI†). We thus selected a range of activated alcohols: 1-phenylethanol **1** as a secondary alcohol (which, in addition, is activated by its aromatic ring), 1-methylcyclohexan-1-ol alcohol **2** as a tertiary, phenylethan-1,2-diol **3** as a simple diol, pinacol **4** and *meso*-hydrobenzoin **5** as two diols known to undergo pinacolic rearrangements. The results of these reactions are displayed in Scheme 1.

These results led us to the following observations:

(i) Despite the fact that most tested alcohols are sensitive to oxidation, no detectable amount of oxidation product was formed. This is a fundamental difference between superheated and supercritical water, where radical reactions (and thus oxidations) can be strongly favoured.[15]



Scheme 1 Reaction of various alcohols in water at 180 °C.

(ii) In all cases, the tested alcohols underwent (at least in a first step) a foreseeable dehydration reaction in moderate to high yields. This is consistent with the fact that the self-dissociation constant of water is already very high at 180 °C. Indeed, these dehydration reactions can be promoted by protons, which is the reason why they usually are run in strongly acidic media.[16]

(iii) In a second step, some of the dehydration products or intermediates underwent further transformations. Pinacol **4** and *meso*-hydrobenzoin **5** for example yielded the expected pinacolic rearrangements (**4a** and **5a** in, respectively, 98 and 73%). 1-Phenylethan-1,2-diol yielded 1-phenylethanone (which is a tautomer of the expected enolic dehydration product) but part of it condensed to a dimer through an aldol reaction. This opens the perspective of more complex multistep reactions in superheated water.

2 Screening of the impact of salts on the reactivity of various alcohols in super heated water

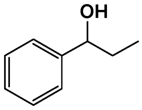
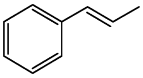
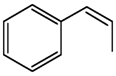
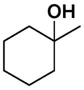
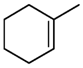
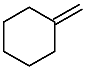
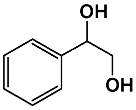
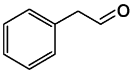
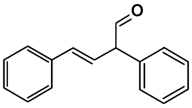
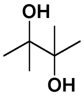
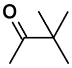
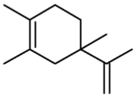
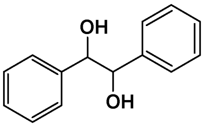
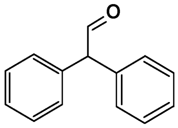
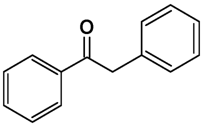
As previously mentioned, we also were interested in determining how strongly the presence of salts would impact the outcome of the reactions; we thus not only used pure (MiliQ) water as a solvent but also a 1 M NaCl solution and a 1 M Na_2SO_4 solution. Sodium chloride was selected because it probably is the most abundant salt on earth (sea water being basically a 0.5 M NaCl solution) and sodium sulfate because its impact on organic reactions in water is already documented.[11a] The results of these tests are displayed in Table 1. The previously described results in pure water are also reported there, for comparison purpose.

Here again the obtained results lead to some observations:

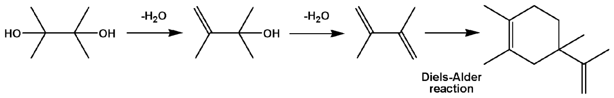
(i) Compared to pure water, the addition of NaCl resulted in increased conversions (The conversion of phenylethandiol increased from 43 to 93%, see Table 1, entries **7** and **8**), while the addition of Na_2SO_4, in most cases, drastically reduced the conversion rates (see again for phenylethandiol Table 1, entry **9**, a conversion reduced to 2%).

(ii) In the cases where secondary reactions are observed, these reactions are also promoted by the addition of sodium chloride. In the case of phenylethandiol the previously observed aldol condensation product is formed with 64% yield. In a series of tests at 200 °C (see ESI†, Table S1) pinacol

Table 1 Comparative investigation of the effect of salt on the transformation of various alcohols under hydrothermal conditions[a]

Entry	Substrate	Solvent	Conversion[b] (%)	Product 1[c] (%)	Product 2[c] (%)	Selectivity for the major product[d] (%)
						
1		H_2O	82	75	7	91
2		1 M NaCl	96	88	8	92
3		1 M Na_2SO_4	43	39	4	91
						
4		H_2O	57	53	2	93
5		1 M NaCl	71	70	1	99
6		1 M Na_2SO_4	77	62	15	81
						
7		H_2O	43	22	21	53
8		1 M NaCl	93	29	64	69
9		1 M Na_2SO_4	2	1	0	—
						
10		H_2O	99	98	0	99
11		1 M NaCl	98	98	0	100
12		1 M NaCl[e]	98	32	54	55
13		1 M N_2SO_4	33	32	0	97
						
14		H_2O	81	73	8	90
15		1 M NaCl	100	89	11	89
16		1 M NaCl[e]	100	96	4	96
17		1 M Na_2SO_4	8	7	1	—

[a] For these reactions, 5 mmol of phenyl ethanol or 200 mg of the desired alcohol were added to 10 ml of solvent and heated to 180 °C for 16 h. [b] Conversions were determined by GC-FID with an internal standard as the ratio between consumed and initial amounts of substrate. [c] The product yields were also determined by GC-FID as the molar ratio between the detected amount of product and the initial amount of substrate. [d] Selectivities were calculated as the ratio between the formed amount of product and the consumed amount of substrate. [e] Reactions run at 200 °C.



Scheme 2 Mechanism of the dehydration/Diels–Alder reaction of pinacol.

not only yielded the rearrangement product, but also a more complex Diels–Alder condensation product displayed in Scheme 2.

(iii) The selectivities remained good (*i.e.* a limited number of products was obtained). It is worth noticing that no intermolecular dehydration (be it a Friedel–Crafts reaction or the formation of an ether) could be detected even at higher alcohol concentration (see Table S2 in the ESI†).

3 Investigation of salt effects on the dehydration of 1-phenylpropan-1-ol

The above-described promoting, respectively, blocking effects of NaCl and Na_2SO_4 are relatively surprising. We thus decided to study these salts effects in more detail on one model reaction: the dehydration of 1-phenylpropan-1-ol (Scheme 1A).

3.1 The effect of sodium chloride. First we investigated the influence of NaCl concentration on this reaction at 180 °C for 16 hours. The results are displayed in Fig. 2. As previously observed, pure super heated water is able to give a reasonable conversion, but that conversion is improved by adding even an "inert" salt. At moderate salt concentrations an increase of the conversion was seen, which leveled into a plateau, and then

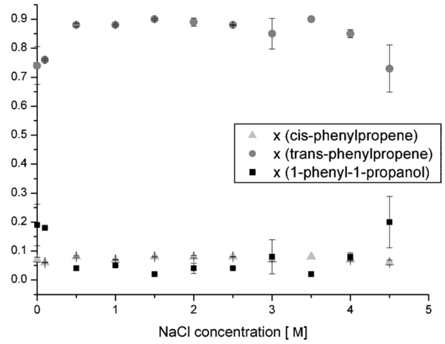


Fig. 2 Influence of the NaCl concentration on the dehydration of 1-phenyl-1-propanol at 180 °C after 16 hours.

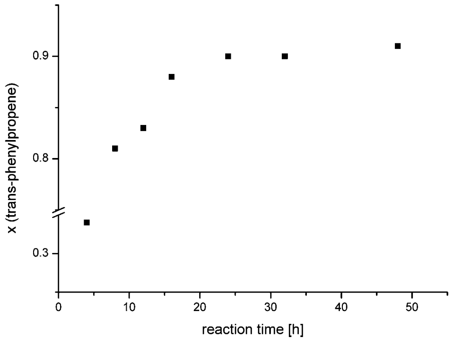


Fig. 4 Time dependence of the 1-phenylpropene yield in a 1 M NaCl solution at 180 °C.

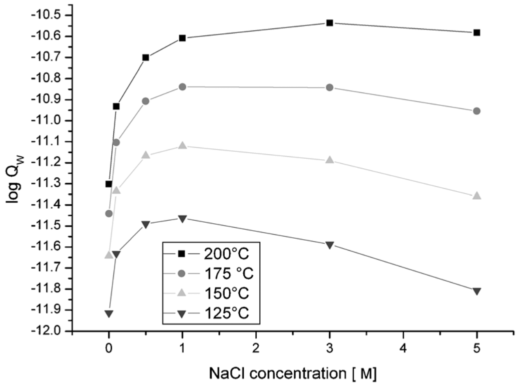


Fig. 3 Dependence of the water dissociation constant on temperature and NaCl concentration. Adapted from ref. 18.

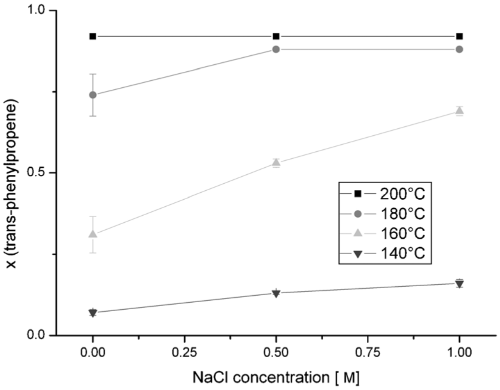


Fig. 5 *Trans*-phenylpropene yield after 16 hours as a function of the temperature of the reaction and the NaCl concentration.

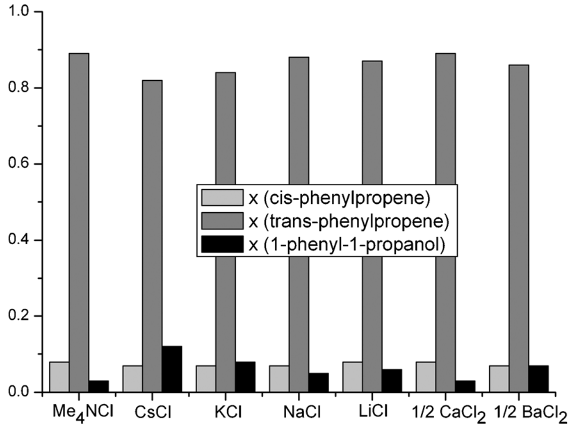


Fig. 6 Molar fraction of *trans*-phenylpropene after dehydration at 1 M chloride concentration and 180 °C reaction temperature, with variations of the cation.

dropped again. Torry *et al.* observed a similar phenomenon when investigating the rate of hydrolysis of dibenzyl ether and benzyl phenyl amine in near-critical aqueous NaCl.[17] The initial acceleration of the reaction was assigned to an initial increase of the polarity of the solvent favouring the polar transition state of the reaction. This may apply to our case. The authors attributed the decrease of the reaction rate at higher salt concentration to a decrease in water availability for the reaction. This may be reasonable in their case, but seems less plausible in ours (where on the contrary water is generated). Another, more plausible, interpretation draws on the *in situ* proton concentration. According to Busey and Mesmer,[18] the water dissociation constant not only varies with temperature but also with NaCl concentration (Fig. 3), showing a broad maximum between 1 M (molar) and 3 M ionic strength ($-\log K_w$ reaching 10.8 at 1 M and 175 °C). This provides an increased proton concentration in this range and, thus, an accelerated dehydration reaction.

In a second step, we tested the time dependence of the yield of *trans*-phenylpropene at 180 °C at constant salt concentration. The results we obtained are displayed in Fig. 4. As can be seen, the equilibrium is almost attained after 16 h.

The influence of temperature on the outcome of the reaction was also tested at different salt concentrations. Fig. 5 shows the yield of 1-phenylpropene after 16 hours as a function of temperature and salt concentration. At 200 °C the reaction proceeds so fast that no effect of the salt could be observed. On the opposite at 140 °C the reaction is so slow that the salt effect is smoothed out. At intermediate temperatures a strong yield increase is observed which is consistent with the data reported in Table 1.

3.2 Cation variation. In the following series of tests, we intended to investigate the action of a broad range of salts on the dehydration of 1-phenylpropan-1-ol (still at 1 M anion concentration, 180 °C for 16 h). Fig. 6 displays the results obtained when chloride was kept as an anion and the cations

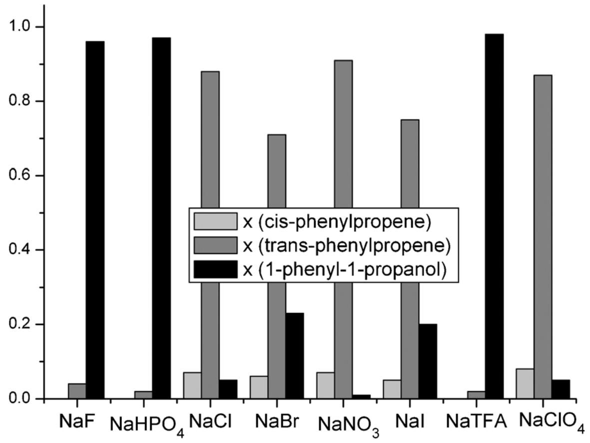


Fig. 7 Molar fraction of *trans*-phenylpropene after dehydration at 1 M salt concentration, with variations of the anion.

were varied. As can be seen, cation variation had only little impact on the 1-phenylpropene yield (between 85 and 95% of alkenes are obtained as long as chlorine is the anion), at least for the examples presented here. This is somewhat unusual as catalytic behaviour is very often ascribed to the cations and more specifically to metals and their incomplete coordination sphere. But in our case, as the observed reactions of our alcohols are usually proton catalysed, these observations just indicate that the employed cations neither directly interfere in the reactions nor impact the *in situ* proton concentration.

3.3 Anion variation. Fig. 7 displays the results obtained when sodium was used as the cation and the anions were varied. As was to be expected, drawing on the results reported in Table 1, the nature of the anions had a pronounced impact on the phenylpropene yield. Interestingly, anions classically assumed to feature some activity (*e.g.* fluoride, phosphate, trifluoroacetate) show almost no conversion, while the highest conversion is found for nitrate. The observations at hand allow us to exclude that the anion effects on the reaction rate can be ordered according to a classical Hofmeister series,[19] *i.e.* the influence of the anion on water structuration is not the driving force of the reaction. In contrast, ordering the anions according to their basicity (*via* the pK_a of the corresponding acids, Fig. 8) seems to be more conclusive. All anions, which are the conjugated base of strong acids (like HCl, HNO_3 or H_2SO_4), favoured the dehydration reaction, while the anions, which are the conjugated base of weak acids, slowed the dehydration reaction down. This leads us again to the conclusion that the amount of free protons in the aqueous medium at 180 °C is the main reason for changes in the *trans*-phenylpropene yield. Anyhow, we cannot exclude additional chemical effects of the anions on the reaction as the data still show minor variations within the group of acidic and basic anions.

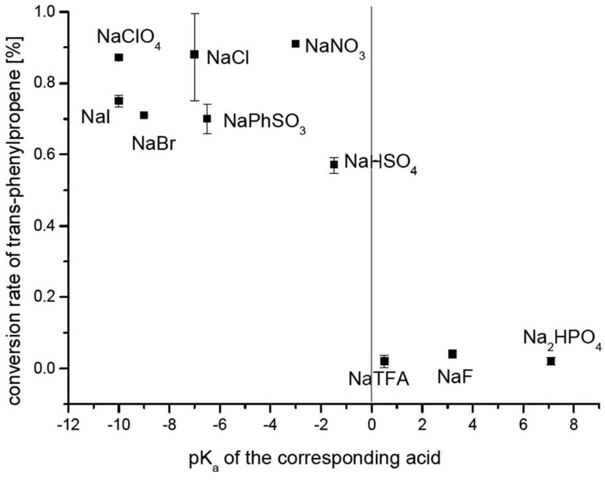


Fig. 8 Conversion ratio of 1-phenyl-1-propanol to *trans*-phenylpropene *vs.* basicity of the added salt anion.

C Conclusion

The aim of this paper was to investigate both the reactivity of alcohols under hydrothermal conditions and the impact of simple salts on this reactivity. The first screening test shows that alcohols and their reaction products can undergo a broad range of reactions including:

- dehydration
- tautomerism
- pinacol rearrangement
- dehydrative ringclosure (see Table S1, ESI†, norborneol)
- aldol condensation
- Diels–Alder reactions

While the reactions directly related to dehydration were not big surprises, the C–C bond forming reactions were unexpected and are of great synthetic interest. Interestingly, despite the numerous possible reactions under hydrothermal conditions, the chemoselectivity of our tests remained relatively high. These preliminary results thus open the path for further investigations of specific reactions in superheated water.

The screening of the impact of simple salts on the outcome of a model dehydration reaction shows that some families of salts promoted the tested organic reactions in the medium while other slowed them down. The exact mechanism of these effects is still to be understood. A putative interpretation of our results can be that all the tested salts had a positive impact on water dissociation at high temperature (as evidenced by Busey and Mesmer on NaCl)[18] but that anions corresponding to weak acids were partially protonated in the medium thus reducing the availability of protons in the medium, and slowing down the reactions. Such an interpretation has two main consequences:

- It must be possible to control the outcome and/or selectivity of organic reactions in superheated water just by selecting the right simple salt (which could be of interest to tune the outcome of hydrothermal carbonisation reactions).
- It should be also possible to promote OH^- catalysed reactions by using the above-mentioned blocking salts. Unfortunately, very few organic reactions are catalysed by bases only and, with the exception of the above-mentioned works of Kopetzki *et al.*, when such reactions are at hand, their reactants are often sensible to hydrolysis (consider the typical base catalysed example of the Knoevenagel condensation of benzaldehyde with malononitrile: the first reactant can undergo a Cannizzaro reaction and the nitrile group can hydrolyse to carboxylic acids).

Both aspects are, thus, still under investigation.

Experimental section

The experiments were done in stainless steel autoclaves with PTFE inlets and an inner volume of 21 mL. The pressure during the reaction is the autogeneous pressure of the solution at reaction temperature. Reaction mixtures consisted of 10 mL Millipore water, an inorganic salt, and 5 mmol 1-phenylpropanol, or 200 mg of a different alcohol. After sixteen hours standard reaction time the autoclaves were cooled down to room temperature, and then the reaction mixture was extracted three times with 5 mL diethyl ether each time. From the extracts GC-MS and GC-FID analysis were done, usually with toluene as internal standard. For the test reaction the response factor was determined by reference standards, subjected to the same extraction procedure. FID peak areas during the alcohol screening were evaluated using the response factor prediction model from Jorgensen, refined by Kàllai.[20]

Notes and references

1 M. Poliakoff, J. M. Fitzpatrick, T. R. Farren and P. T. Anastas, *Science*, 2002, **297**, 807.

2 Y. Hayashi, *Angew. Chem.*, 2006, **118**, 8281.

3 (*a*) P. E. Savage, *Chem. Rev.*, 1999, **99**, 603; (*b*) A. R. Katritzky, D. A. Nichols, M. Siskin, R. Murugan and M. Balasubramanian, *Chem. Rev.*, 2001, **101**, 837; (*c*) M. Siskin and R. Kaminsky, *Chem. Rev.*, 2001, **101**, 825; (*d*) M. Wanatabe, T. Sato, H. Inomata, R. L. Smith, K. Arai, A. Ktuse and E. Dinjus, *Chem. Rev.*, 2004, **104**, 5803; (*e*) S. A. Nolen, C. L. Liotta, C. A. Eckert and R. Gläser, *Green Chem.*, 2003, **5**, 663; (*f*) A. Kruse and E. Dinjus, *J. Supercrit. Fluids*, 2007, **39**, 362.

4 P. E. Savage, *J. Supercrit. Fluids*, 2009, **47**, 407.

5 A. A. Galkin and V. V. Lunin, *Usp. Khim.*, 2005, **74**, 24.

6 (*a*) C. S. Cundy and P. A. Cox, *Chem. Rev.*, 2003, **103**, 663; (*b*) C. S. Cundy and P. A. Cox, *Microporous Mesoporous Mater.*, 2005, **82**, 1.

7 (*a*) M. Henry, J. P. Jolivet and J. Livage, *Struct. Bonding*, 1992, **77**, 153; (*b*) B. L. Cushing, V. L. Kolesnichenko and C. J. O'Connor, *Chem. Rev.*, 2004, **104**, 3893.

8 (*a*) A. Taguchi and F. Schuth, *Microporous Mesoporous Mater.*, 2005, **77**, 1; (*b*) A. Corma, *Chem. Rev.*, 1997, **97**, 2373.

9 (*a*) G. Ferey, *Chem. Mater.*, 2001, **13**, 3084; (*b*) G. Ferey, *Chem. Soc. Rev.*, 2008, **37**, 191.

10 M. M. Titirici, A. Thomas and M. Antonietti, *Adv. Funct. Mater.*, 2007, **17**, 1010.

11 (*a*) D. Kopetzki and M. Antonietti, *Green Chem.*, 2010, **12**, 656; (*b*) D. Kopetzki and M. Antonietti, *New J. Chem.*, 2011, **35**, 1787.

12 B. Smutek, W. Kunz and F. Goettmann, *C. R. Chim.*, 2012, **15**, 96.

13 (*a*) J. N. Chelda, G. W. Huber and J. A. Dumesic, *Angew. Chem., Int. Ed.*, 2007, **46**, 7164; (*b*) A. Corma, S. Iborra and A. Velty, *Chem. Rev.*, 2007, **107**, 2411; (*c*) P. Mäki-Arvela, B. Holmbom, T. Salmi and D. Y. Murzin, *Catal. Rev. Sci. Eng.*, 2007, **49**, 197; (*d*) T. Werpy and G. Petersen, *Top Value Added Chemicals from Biomass: Volume 1—Results of Screening for Potential Candidates from Sugars and Synthesis Gas*, National Renewable Energy Laboratory, 2004.

14 (*a*) L. P. M. De Leo, H. L. Bianchi and R. Fernandez-Prini, *J. Chem. Thermodyn.*, 2005, **37**, 499; (*b*) A. G. Dickson, D. J. Wesolowski, D. A. Palmer and R. E. Mesmer, *J. Phys. Chem.*, 1990, **94**, 7978.

15 M. J. Antal, A. Brittain, C. Dealmeida, S. Ramayya and J. C. Roy, *ACS Symp. Ser.*, 1987, **329**, 77.

16 A. Chenede, N. AbdRahman and I. Fleming, *Tetrahedron Lett.*, 1997, **38**, 2381.

17 J. Penninger, R. Kersten and H. Baur, *J. Supercrit. Fluids*, 2000, **17**, 215.

18 R. Busey and R. Mesmer, *J. Chem. Eng. Data*, 1978, **23**, 175.

19 (*a*) M. Chaplin, *Water Structure and Science*, http://www1.lsbu.ac.uk/water, accessed 06.12.2009; (*b*) W. Kunz, J. Henle and B. Ninham, *Curr. Opin. Colloid Interface Sci.*, 2004, **9**, 19; (*c*) H. Wang, J. Wang, S. Zhang and X. Xuan, *J. Phys. Chem. B*, 2008, **9**, 19.

20 (*a*) A. D. Jorgensen, K. C. Picel and V. C. Stamoudis, *Anal. Chem.*, 1990, **62**, 683; (*b*) M. Kàllai, Z. Veres and J. Balla, *Chromatographia*, 2001, **54**, 511.