Aquathermolysis: Reactions of Organic Compounds with Superheated Water

ALAN R. KATRITZKY* AND STEVEN M. ALLIN

Center for Heterocyclic Compounds, Department of Chemistry, University of Florida, Gainesville, Florida 32611-7022

MICHAEL SISKIN*

Products Research Division, Exxon Research and Engineering Company, 1900 E. Linden Avenue, Linden, New Jersey 07036

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I. Preliminaries

1. Introduction. In this Account, we will emphasize that organic molecules undergo a wide range of chemistry in neutral superheated water. Counter to what is traditionally taught in organic chemistry courses, no acids, bases, or catalysts need to be added. In this chemistry, water participates as a catalyst, reactant, and solvent. For example, polyethylene terephthalate (plastic soda bottles), polyurethanes, and other polymers are cleaved to their starting materials at 300 °C. Diaryl ethers cleave rapidly, Diels–Alder reaction selectivities are dramatically enhanced, and several types of deuteration reactions are effected in pure superheated deuterium oxide. Such reactions, and many others, are facilitated by changes in the chemical and physical properties of water as temperature increases. These changes make the solvent properties of water (density, dielectric constant) at high temperature similar to those of polar organic solvents at room temperature, thus facilitating reactions with organic compounds in an environmentally friendly medium. An increase in the dissociation constant by 3 orders of magnitude allows water at >200 °C to act as an acid, base, or acid–base bicatalyst without the need for costly and cumbersome neutralization and catalyst regeneration steps.

In addition, transformations of organic compounds in superheated water are of significant interest in (a) better understanding of the formation pathways of the world's petroleum resources, most of which has been formed in hot aqueous environments under pressure, (b) discovering methods for upgrading fossil fuel resources to remove sulfur and nitrogen, and their impact on pollution of the atmosphere, by aqueous treatments rather than expensive hydrogenation, and (c) possible applications in treating various wastes ranging from household and industrial refuse to chemical warfare agents.

When our collaborative project between the University of Florida and the Exxon Research and Engineering Co. started in 1985, published work on the chemical reactions of organic molecules in aqueous environments was sparse and fragmentary. Our work over the past 10 years has been published in over 30 joint papers which have covered the reactions of a wide range of aliphatic, carbocyclic, and heterocyclic compounds and some of their most important substituted derivatives and identifies many novel reaction products and pathways. With the exception of an overview of the geochemical and technological implications,[1] no review of this work has appeared. Moreover, most of our papers have been published in the ACS journal *Energy & Fuels* which is unfamiliar to many organic chemists. This Account reviews our work from the point of view of the organic chemistry involved.

Reactions of organic compounds with pure water at high temperatures, both sub- and supercritical, have been studied by others, with especially significant contributions made by the groups of Klein,[2] Houser,[3] Penninger,[4] and Clark.[5] Recent reviews of this field have appeared by Savage,[6] Lubineau,[7] Li,[8] and Breslow.[9] Supercritical water in the presence of oxygen has been studied extensively for the disposal

Alan R. Katritzky (born 1928, London, U.K.) is Kenan Professor of Chemistry and Director of the Institute for Heterocyclic Compounds at the University of Florida. A light-hearted account of his life appeared in *J. Heterocycl. Chem.* **1994**, *31*, 569–602, and an overview of his scientific work in *Heterocycles* **1994**, *37*, 3–130. He is actively engaged in research and teaching, editing, industrial consulting, international travel, and windsurfing.

Steven M. Allin obtained a B.Sc. from the University of Liverpool, England, in 1990. In 1993 he was awarded a Ph.D. for studies carried out under the auspices of Dr. Philip Bulman Page. He worked (1993–95) as a postdoctoral research associate with Professor Alan R. Katritzky at the University of Florida, where he has conducted research in areas as diverse as aquathermolysis, heterocyclic methodology, and asymmetric synthesis. In March 1995 he was appointed as Lecturer in Organic Chemistry at the University of Huddersfield, England.

Michael Siskin was born in Brooklyn, NY, in 1943. He obtained a B.S. degree in chemistry from Brooklyn College in 1965 and in 1968 received a Ph.D. in organic chemistry from the University of Pennsylvania. Following postdoctoral research at Harvard University, he joined the Corporate Research Laboratory of Exxon Research and Engineering Co. His research has covered the areas of strong acid catalysis of hydrocarbons, coal and oil shale kerogen structural characterization and maturation studies, and most recently, the chemical, geochemical, and technological aspects of the reactivity of organic compounds in superheated water.

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of hazardous waste.[10,11] The present account concentrates on our results; a full overview of the field, in which our studies are placed in the context of the whole body of work, is in preparation and will be submitted in due course to *Chemical Reviews*.

2. Objectives. The initial objective of our studies was to uncover the general pattern of reactivity toward high-temperature water of the common, naturally occurring ring systems and functional groups. Structural types, e.g., acid anhydrides, acid halides, etc., expected to be reactive at low temperatures were not included. We planned to provide a science base to aid understanding of the geological formation of fossil fuel resources and the generation of petroleum from these sources. Such a science base would also allow experiments designed to modify fuel feedstocks to be carried out more efficiently. Later in our investigations, we began to study some compound classes analogous to those occurring in the more important chemical warfare agents. Our approach could be described as focusing on relatively small groups of related compounds, wherein information obtained from one compound would be of general value in interpreting reactions of other members of the group.

High-temperature water under autogenic pressure provides a significantly more favorable reaction medium for nonpolar compounds than does water up to its boiling temperature. At 300 °C, water exhibits a density and polarity similar to those of acetone at room temperature.[12] The dielectric constant of water drops rapidly with temperature, and at 300 °C has fallen from 80 (at 20 °C) to 2.[13] This means that, as the water temperature is increased, the solubility of organic compounds increases much more than expected for the natural effect of temperature. Furthermore, the negative logarithmic ionic product of water at 250 °C is 11, and of deuterium oxide is 12, as compared to 14 and 15, respectively, at 20 °C.[13,14] This means that water becomes both a stronger acid and a stronger base as the temperature increases. Therefore, in addition to the natural increase in kinetic rates with temperature, both acid and base catalyses by water are enhanced at higher temperatures.

Our standard procedure is carried out in a stainless steel tubing bomb made up of a Swagelok cap and plug. No significant effects on the reactions by the metal surfaces have been observed in liquid water.[15] Analysis by inductively coupled plasma emission spectroscopy (ICPES) of deuterium oxide after a 10-day exposure at 300 °C and of the reactor contents following reactions failed to indicate any significant amounts of metallic components.[16] Controls in sealed quartz tubes and sapphire NMR tubes were run. Heat was supplied by a fluidized sand bath with temperatures controlled to ±2 °C. Reactions were usually carried out between 250 and 460 °C; as the critical temperature of water is 374 °C, our experiments were both sub- and supercritical. Only differences in rate, not in pathway, were observed in going from sub- to supercritical water, except in a few cases involving elimination of organic sulfur and hydrogenation of aromatic N-containing heterocycles when carbon monoxide was present.[17,18] Products were analyzed by GC−MS. Because of the impracticality of obtaining standards for all the products, we paid particular attention to developing a method for calculating response factors from the structure.[19,20] In many cases, an internal standard of heptane or biphenyl was used. Full details of our experimental techniques are given in refs 21−23. Product identification was carried out by MS. Detailed interpretations of the MS fragmentation patterns of compounds not available, or whose spectra were not available in a database or from an alternative source, are included in the supplementary material of our publications.

In addition to carrying out the reactions in pure water, we also made comparisons under other conditions. In almost all cases, this has included heating for the same time period in cyclohexane solvent, in order to differentiate aqueous from purely thermal reactions. Cyclohexane was chosen because of its nonpolar character and because it seemed likely to give rise itself to a fairly small number of side products for which the structures should be easy to deduce. Reactions in aqueous formic acid provide a convenient means to consider the technically important result of heating under reducing conditions with water and carbon monoxide. The use of sodium formate has allowed the probable effects of ion exchange of alkali metals in the form of metal carboxylates, as found in fuel sources, to be studied in combination with an aqueous carbon monoxide treatment. We also frequently used sodium bisulfite (because of the common occurrence of sulfur) and phosphoric acid (to study the effects on rate and mechanism using a thermally stable acid) and pyridine, calcium carbonate, or sodium carbonate to study the effects of base. This Account, however, focuses primarily on the high conversion chemical reactivity of organic compounds in pure superheated water rather than on the alternative pathways of thermal reactions.

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II. Cleavage/Hydrolysis Reactions

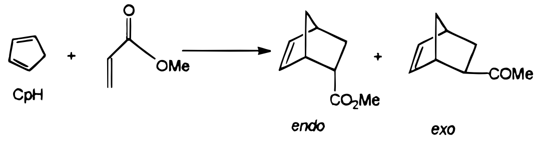
1. Neutral Reactions. Rapid and clean ring cleavage of 2,5-dimethylfuran in pure deuterium oxide at 250 °C yielded 2,5-hexanedione quantitatively and irreversibly within 30 min:[16] 2,5-hexanedione underwent no ring closure at this temperature in 1 h. These reaction conditions are in contrast to those reported in a mechanistic study of this reaction, in which a 0.1M DCl solution at 70 °C was required to cleave the ring.[24] Dibenzofuran[25] and 2-hydroxydibenzofuran[26] proved to be stable to aquathermolysis even at 460 °C.

Acetals and ketals are highly reactive to neutral aquathermolysis, undergoing in nearly all cases 100% hydrolysis within 30 min at 205−250 °C without side or secondary reactions.[16] Greater than 90% deprotection of cyclopentanone ethylene ketal and 1,4-cyclohexanedione bis(ethylene ketal) was achieved at 250 °C. Equal reactivities to pure water were determined for benzaldehyde and tolualdehyde diethyl acetals at 186 and 250 °C resulting, during 30 min of reaction, in 91−94% and 100% conversion, respectively. Hydrolysis of benzaldehyde diethyl acetal went to completion overnight at room temperature but decreased to 33% in the presence of basic barium oxide at 80 °C over 45 min. At 254 °C, quantitative hydrolysis of this acetal in aqueous KOH at acetal:base molar ratios as low as 1:0.25 (72.5 mM in KOH) was followed by a Cannizarro disproportionation, as indicated by the formation of benzyl alcohol, benzoic acid, and, via subsequent decarboxylation of the acid, small amounts of benzene. Formation of Cannizarro products of benzaldehyde in the presence of a much weaker base, pyridine, was reported previously.[27] Tsao and Houser suggested the possibility of a Cannizarro reaction of this aldehyde catalyzed by ammonia in supercritical water, but product distributions indicate the involvement of radical pathways.[28]

Diacetone D-glucose (0.31 M) and 1,6-anhydro-β-D-glucose (0.30 M) were converted quantitatively at 205 °C to predominantly D-glucose and traces of another glucose isomer.[16] Under the same conditions in the presence of 1 equiv of KOH (0.29 M), 1,6-anhydro-β-D-glucose was unreactive and only the exocyclic, 5,6-acetone moiety of diacetone D-glucose was cleaved. Cellulose is rapidly converted to soluble species with relatively high glucose yield in pure water near its critical temperature.[29] In a semibatch or flow reactor, 100% conversion of cellulose was achieved in 1 h or less (15 s at 400 °C). Parallel thermal transformations of the glucose product take place to form fructose, 1,6-anhydro-D-glucose, erythrose, glycolaldehyde, glyceraldehyde, dehydroxyacetone, pyruvaldehyde, and acids.

Quantitative rearrangements of pinacol, 1,1′-dihydroxy-1,1′-bicyclopentyl, and 1,1′-dihydroxy-1,1′-bicyclohexyl[30] to the corresponding ketones, with negligible alkene formation, occurred in deuterium oxide in 60 min at 275 °C.[16] The efficiency of aquathermolysis is very much in evidence here, considering that quantitative formation of pinacolone from pinacol via a classical method requires boiling in 25% H_2SO_4 for 3 h.[31] The formation of pinacolone via rearrangement of pinacol in pure superheated deuterium oxide was quantitative and not reversible; no deuterium incorporation into the *tert*-butyl methyl groups was observed.[32] Thus, the *tert*-butyl resonance served as an internal standard in the measurements of the rates of deuterium incorporation at the α-methyl position by ^{1}H NMR. At 225 °C and 370 psia of (autogenic) pressure this appears to follow the classical pathways elucidated under classical acid- or base-catalyzed conditions at conventional temperatures. Pseudo-first-order kinetics suggest that the reaction proceeds via classical enolization with an observed first-order rate constant of 8.8×10^{-3} min^{-1}.

Scheme 1. Effect of Polar Solvents on the Rate and Selectivity of the Diels−Alder Reaction[35]



Solvent	ε	endo/exo
isooctane	2	2.3
butanol	17	5
water	78	7.4
formamide	109	6.7
N-methyl acetamide	183	4.7

The use of water as the solvent for the Diels−Alder reaction gives higher endo selectivity in comparison with organic solvents (Scheme 1).[33,34] This effect is general and illustrates the role of the high cohesive energy density of water in these phenomena. The Diels−Alder reaction has a negative activation volume (ca. −30 cm^3 mol^{-1}), and between the two possible transition states, the endo state is more compact (as supported by increasing endoselectivity as a function of external pressure). It has been established that the polarity alone was not the cause of either the endoselectivity or the rate enhancement, since more polar solvents such as formamide or *N*-methylacetamide do not promote these trends (Scheme 1).[35]

The acceleration of the Diels−Alder reaction in water has been explained by the suggestion that water brings together the two nonpolar organic substrates via the hydrophobic effect, which is the tendency of nonpolar species to aggregate in water solution so as

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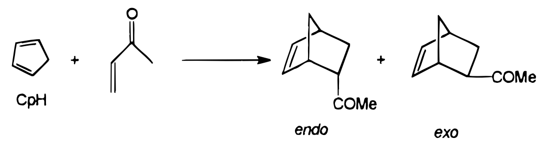
Scheme 2. Influence of the Hydrophobic Effect on the Aqueous Diels–Alder Reaction[9,33]

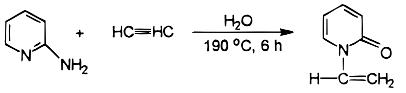


Solvent	$10^5k_2(M^{-1}S^{-1})$	Solvent	Endo/Exo
isooctane	5.94	cyclopentadiene	3.85
MeOH	75.5	EtOH	8.5
H_2O	4400	0.15 M CpH in H_2O	21.4
H_2O + 4.86 M LiCl	10800	0.007 M CpH in H_2O	22.5
H_2O + 4.86 M $(NH_2)_3CCl$	4300		
β-cyclodextrin (10mM)	10900		
α-cyclodextrin (10mM)	2610		

to decrease the hydrocarbon–water interfacial area Scheme 2).[9] This effect is the principal force determining the secondary and tertiary structures of proteins and nucleic acids and the binding of substrates to receptors. Certain agents that decrease hydrocarbon solubility in water, such as LiCl, will favor the aggregation of the nonpolar species and increase the hydrophobic effect, while others that increase hydrocarbon solubility lead to a decrease of the hydrophobic effect. Breslow has studied the influence of the hydrophobic effect on the aqueous Diels–Alder reactions in detail.[36,37] Schneider has reported a quantitative correlation between solvophobicity and rate enhancement of aqueous Diels–Alder reactions.[38,39]

2. Autocatalytic Cleavage/Hydrolysis Reactions. The products formed in the reactions described above are not expected to significantly alter the reaction environment. This is not the case, however, in the hydrolysis of esters, wherein the formation of soluble carboxylic acids creates the potential for autocatalysis. Autocatalytic approaches have been used to form (i) glycols by hydrolysis of the corresponding acetic acid diesters at 50–80 °C,[40] (ii) formic acid from methyl formate at 90–140 °C,[41] and (iii) glycerine by hydrolysis of glycerol triacetate with water at 180–245 °C.[42] In other studies[43] modeling kerogen reactivity, decyl decanoate was readily hydrolyzed in water at 250 °C in an ionic reaction that was further catalyzed by brine (10% NaCl) and calcium montmorillonite. Evstratova et al.[44] hydrated 2,6-dicyanopyridine stepwise to the diamide in boiling water in a reaction that is acid- and base-catalyzed. Norton[45] described a hydrolytic process for making aromatic carboxylic acids from nitriles at 200–300 °C in a process where no catalyst is added directly, but the aqueous solution from earlier hydrolyses is used in order to take advantage of autocatalysis by ammonia formed during the hydrolysis of the amide intermediate.

Benzonitriles, pyridinecarbonitriles, benzamides, and pyridinecarboxamides are almost unaffected by thermolysis but are rapidly hydrolyzed in water at 250 °C to the corresponding ammonium carboxylates (the nitriles via the amides). The ammonia formed autocatalyzes these hydrolyses and the subsequent decarboxylations.[46] Interestingly, 2-aminopyridine reacts with acetylene in water at 190 °C in 6 h to form *N*-vinyl-2-pyridone (75%) (eq 1).[47] The reaction does not take place through hydrolysis to the amide because 2-pyridone is not vinylated, and without acetylene present, 2-aminopyridine is stable. Phenylacetylene undergoes hydration in water at 250 °C for 5 days.[48]



(1)

In water, carboxylic acids lose CO_2 quite readily from the 2- or 4-position of a pyridine ring,[49,50] less easily from the pyridine 3-position,[21] with difficulty when directly attached to benzene,[27] but more easily from $PhCH_2CO_2H$.[51] This pattern is readily understandable because it follows the stability of the carbanion remaining after CO_2 loss from the acid anion. The substituents CH_2OH and CHO can also be lost from pyridine rings as HCHO and HCO_2H, respectively; again the mechanism probably involves the expulsion of Ar^- from the anion $ArCH_2O^-$ or $ArCH(OH)O^-$.

Interconversions among CO_2H, CHO, CH_2OH, and CH_3 substituents and their loss by ring-C scission in water set up a series of oxidation–reduction reactions between these substituents when they are directly attached to a benzene[27] or pyridine ring.[21,49,50] Thus, CH_2OH substituents can disproportionate to CHO and CH_3 and, similarly, CHO substituents to CO_2H and CH_2OH. Hydride ion transfer from RCH_2O^- or $RCH(OH)O^-$ is probably involved. In such sequences, the parent RH compound and methyl derivative both behave as sinks. Added oxidizing or reducing agents such as formaldehyde and formic acid shift the oxidation–reduction reactions in the expected direction.

Aldol-type C–C bond formations involving substituent carbon atoms rely on the formation of a carbanionic center α to the ring, and usually need base catalysis (Scheme 3). The phenyl group does not afford much activation, and reactions of this type are rarely observed in benzenes containing CH_3 or CH_2OH substituents.[27] The corresponding 3-substituted pyridines are more reactive and form various products containing two pyridine rings. The initial step is

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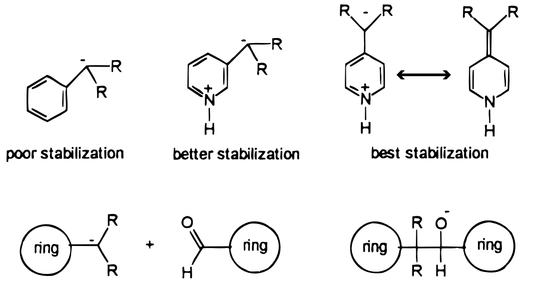
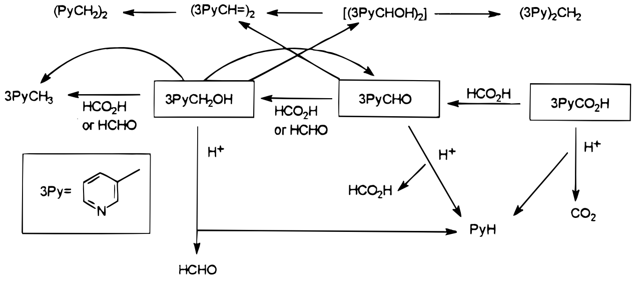
Scheme 3. C−C Bond Formation in a Generalized Aldol Reaction (R = H or OH)



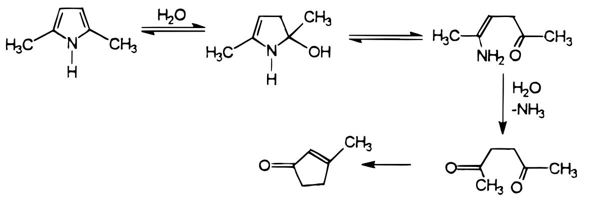
Scheme 4. Overall Reaction Pathway for 3-Substituted Pyridines[21]



probably reaction of the aldehyde with the alcohol and/or methyl derivative (Scheme 4).[21] Parallel decomposition reactions of the pyridine acid, alcohol, and aldehyde in water generate molecules of carbon dioxide, formic acid, and formaldehyde, respectively, which are water-soluble and potential reagents in acid catalysis and hydride transfer reductions (Scheme 4). Therefore, in addition to the reduction mechanism leading to 3-picoline in Scheme 4, several types of condensation reactions and synergisms take place among the 3-pyridyl derivatives (Scheme 4).

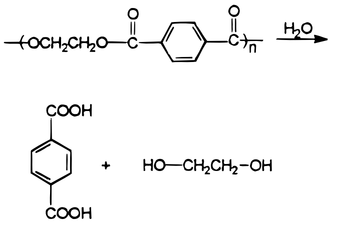
Such C−C bond forming becomes very favorable in the 4-pyridine series, and a host of products arise from the elaboration of initial aldol-type products.[50] The product slate for 2-substituted pyridines is even more complex.[49]

An interesting variation of Aldol chemistry involves reaction of 2,5-dimethylpyrrole in water at 250 °C for 5 days which forms 3-methylcyclopent-2-en-1-one (65%) via ring opening to hexanedione (reversal of synthetic route), followed by loss of ammonia and intramolecular aldol condensation (eq 2).[52]



(2)

Hydrolysis reactions have been used to effect desired chemical changes in synthetic polymers in a manner similar to that of reactions observed for lower molecular weight molecules which are soluble. Mandoke[53] described a simple approach for the neutral hydrolytic decomposition of condensation polymers such as polyethylene terephthalate (soda bottles) (eq 3), nylon 6 and 66, other synthetic fibers, and polycarbonates in water at 200−300 °C. Similarly, polyurethane foams can be hydrolyzed to reusable diamines and glycols (Eq 4).[54] Polyacrylonitrile (PAN) is hydrolyzed at 250−300 °C to low molecular weight water soluble oligomeric products, with ammonia generated instead of the toxic hydrogen cyanide formed by thermolysis.[55]



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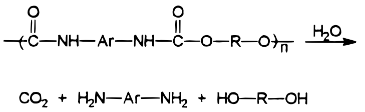
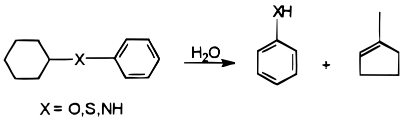


(4)

Thermally stable methyl 1-naphthoate is quantitatively hydrolyzed after 2 h and 5.5 day treatments at 343 and 250 °C, respectively.[25] Naphthanoic acid is the major product at 250 °C, but its decarboxylation led predominantly to the formation of naphthalene during a 2 h conversion at 343 °C, a reaction catalyzed by the generated carbonic acid. Examinations of methyl benzoate and its 4-chloro, 4-methyl, and 4-methoxy derivatives revealed up to 50% hydrolysis within 30 min at 250 °C,[16] but no evidence of decarboxylation. Partial cleavage of the *p*-methoxy group is assumed to be caused by the increased acidity of the medium resulting from carboxylic acid formation, since no ether was observed for α-ethyl-4-methoxybenzyl alcohol in neutral water under otherwise more extreme conditions (277 °C, 75 min). In a reaction typical of *β*-keto esters, ethyl acetoacetate underwent complete conversion to acetone, ethanol, and CO_2 (not analyzed) in 30 min at 250 °C.[16] Under similar conditions, *tert*-butyl acetate decomposed to a bright red, highly insoluble mixture of unidentified products resulting from polymerization of isobutylene;[56] methyl trimethylacetate was unreactive.

Cyclohexyl-X-phenyl compounds with oxygen, sulfur, and nitrogen links were shown to be relatively unreactive thermally but readily cleaved in water at 250 °C to form methylcyclopentene together with phenol, thiophenol, or aniline, respectively (Eq 5).[57]



(5)

Ionic reactions of these types are enhanced in 10% NaCl and in the presence of an acidic clay but are

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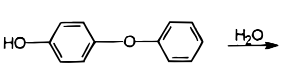
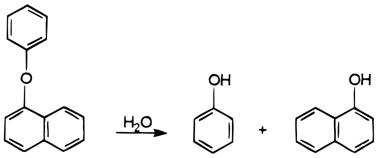
depressed by basic calcium carbonate. This evidence supports an acid-catalyzed carbocation mechanism for this system in water at high temperature. Although an acyclic diaryl ether (diphenyl ether) and a cyclic diaryl ether (dibenzofuran) were unreactive under both aqueous and thermal conditions, an activated diaryl ether (4-phenoxyphenol) was cleaved in water to form phenol (eq 6).[25] Penninger and Kolmschate treated 2-methoxynaphthalene with supercritical water at 390 °C for 1.5 h to give 2-naphthol and methanol as the main reaction products.[4] Benzyl aryl ethers were also much more susceptible to cleavage under aqueous than thermal conditions at 250 °C. Klein reported that phenethyl phenyl ether formed phenol and styrene as the primary products after 1 h at 400 °C and dibenzyl ether yielded benzyl alcohol, toluene, and benzaldehyde after treatment in water at 374 °C for 1 h.[58]



(6)

Thermally stable 1-phenoxynaphthalene is cleaved in water at 315 °C after 3 days to phenol and 1-naphthol (95% conversion) (eq 7) and is thus significantly more reactive than diphenyl ether.[59] In aqueous sodium formate reduction of 1-naphthol to naphthalene and dihydronaphthalenes occurs. 9-Phenoxyphenanthrene similarly yields phenol and 9-hydroxyphenanthrene (eq 8) and is more reactive than its 1-phenoxy isomer.[60] Interestingly, the rate of hydrolysis of such diaryl ethers is affected dramatically by additives such as NaCl, LiCl, KBr, and Na_2SO_4.[61] The conversion of 1-phenoxynaphthalene in water alone at 315 °C after 72 h was 94.6%; on reaction of this substrate with a 1% aqueous solution of each of the above salts, the conversion was reduced to 7.4%, 4.8%, 3.8%, and 0%, respectively. These results strongly suggest that, at high temperatures, alkali metal halides and sodium sulfate behave as salts of strong bases and weak acids and reduce the hydrogen ion activity of the solutions, in agreement with previous indications.[61]



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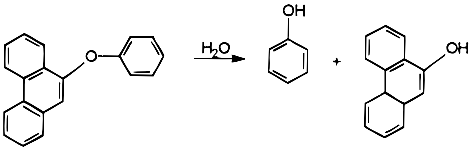
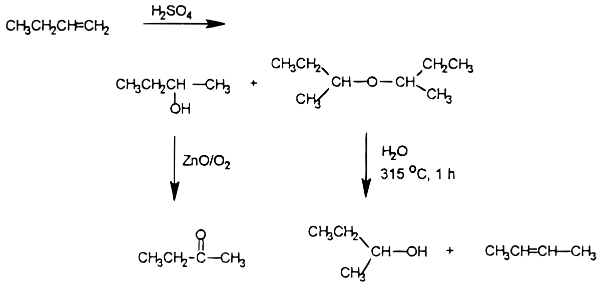


(8)

Chemical reactions carried out in hot water have the potential to provide a cleaner, safer environment than reactions in hydrocarbon solvent media. In addition, water acting as a catalyst or reagent could minimize, or possibly eliminate, the need for catalyst synthesis, recycle, regeneration, and disposal. Such application to the recycle of condensation polymers including plastics, synthetic fibers, and polycarbonates is attractive.[53,54] Another potential application is the use of hot water treatment to upgrade low-value byproducts. A demonstrated example occurs in the hydration of propylene with sulfuric acid to form isopropyl alcohol with thermally stable diisopropyl ether as a byproduct. Hydrous cleavage of this ether at 315 °C for 30 min readily forms essentially equimolar amounts of the desired product (isopropyl alcohol) and recyclable propylene.[62] Di-*sec*-butyl ether, a byproduct in the hydration of butylene to *sec*-butyl alcohol in the methyl ethyl ketone (MEK) process, can similarly be converted to the alcohol in hot water[62] (eqs 9 and 10). The aldol condensation byproduct of MEK production, a C_8-unsaturated ketone, is quantitatively reversed to MEK by hydration followed by retro-aldol cleavage.[63]



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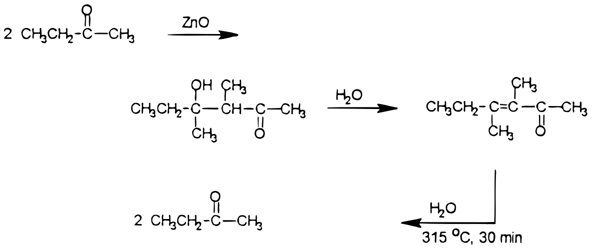

(10)

More recently, the potential detoxification of several organophosphorus and organoarsenic compounds, chosen as analogs of military nerve gases, has been investigated under neutral aquathermolysis conditions at temperatures up to 460 °C.[64] At higher temperatures (350 °C), the organophosphorus compounds were highly reactive in 1 h and completely converted to simpler products that did not contain the P residue. ^{31}P NMR indicates phosphorus is largely lost as phosphoric acid. The hydrolysis of triphenyl phosphate is highlighted in eq 11. Similarly, diethyl (1-naphthylmethyl)phosphonate is hydrolyzed largely to 1-methylnaphthalene (eq 12).

At 200 °C in water, organoarsenic compounds such as 4-arsanilic acid and 4-aminoarsine are hydrolyzed to aniline and other non-arsenic-containing compounds. 5,10-Dihydro-10-ethylarsazine is hydrolyzed largely to a series of diphenylamine derivatives, and

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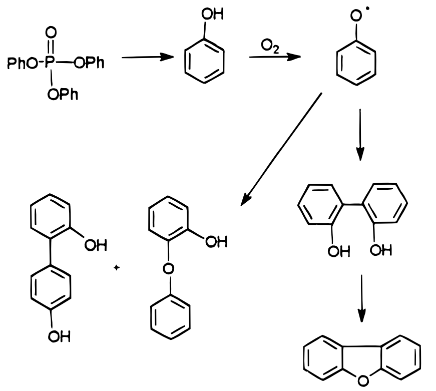

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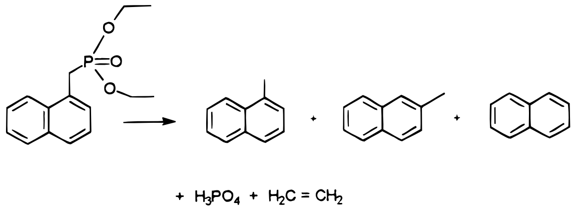
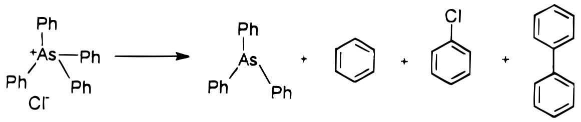


(12)

tetraphenylarsonium chloride is hydrolyzed to triphenylarsine and simple, non-arsenic-containing compounds (eq 13).[64]



(13)

3. Hydrogen Exchange Reactions. When the ring cleavage reaction of 2,5-dimethylfuran was conducted in deuterium oxide,[65] extensive deuteration of the methyl and methylene groups of the product, 2,5-hexanedione, was observed; the same result was detected by ^1H and ^{13}C NMR when this dione was the initial reagent. Thus, it became evident that this medium was suitable for $^1H/^2H$ exchange.[16] These exchange reactions afforded a means to study organic transformations in a reaction environment undergoing minimal changes; for example, no products are formed that have properties or reactivities significantly different from those of the initial reagents. Also, no changes occur in reaction mechanisms, volume, vapor pressure, or the dielectric or dissociation constants of deuterium oxide because of the formation of ionic products and potential catalysts or cosolvents.

Deuterium oxide treatment of methyl (300 °C, 93 h), isopropyl, and neopentyl alcohol (200 °C, 30 min, and 300 °C, 60 min, respectively) did not induce any exchange of CH hydrogens; the same negative results were obtained in experiments with ethylene glycol (300 °C, 60 min) and pentaerythritol (250 °C, 60 min).[16] Hydrogen exchange was achieved rapidly and nearly quantitatively in the α and α' (where applicable) positions of ketone carbonyl groups. Table 1 lists the extents and sites of deuteration observed in selected ketones. In all cases, the operating enol–keto tautomerism led exclusively to hydrogen exchange; no aldol products were observed.

Table 1. Hydrogen/Deuterium Exchange in Ketones

compd	% D (position)	reaction conditions temp (°C)	reaction conditions time (min)
pinacolone[a]	100 (α-CH_3)	277	60
acetone	97 (α,α'-CH_3)	200	60
cyclopentanone[b]	100 (α,α'-CH_2)	225	30
1,4-cyclohexanedione	100 (α,α'-CH_2)	225	30
acetophenone	>88 (α-CH_3)	250	60
deoxybenzoin[c]	99 (α-CH_2)	250	30

[a] Exchange observed in the rearrangement product of pinacol. [b] Exchange observed in the hydrolysis product of the corresponding ethylene ketal. [c] $PhCH_2COPh$.

Examination of hydrogen exchange in CH acids revealed fluorene (100% D incorporation at C9) to be a stronger acid in deuterium oxide than triphenylmethane (no D incorporation) under equal reaction conditions of 1 h at 300 °C. This order in acidity corresponds to that established by Bordwell in DMSO;[66] it also agrees with results obtained in methanolic sodium methoxide by Streitwieser and coworkers, which reported pK_{HB} values of 22.6 and 23.0 for fluorene[67,68] and 31.5 for triphenylmethane.[69] An upper limit of pK_{HB} of 40 for H/D exchange in water at 200–300 °C is indicated. The basicity of D_2O at 300 °C proved insufficient to abstract methyl hydrogens of toluene, which has a reported pK_{HB} of 40.9.[70]

Interestingly, in deuterium oxide, the acidity of acetone (Table 1) may exceed that of fluorene, whereas pK_{HB} values in DMSO of approximately 20 for the hydrocarbon and 26 for acetone[67] indicate lower acidity of acetone in this organic medium. Additional stability gained by hydrogen bonding and solvation—attainable for acetone in water but not in DMSO and for fluorene in neither medium—may contribute to this apparent reversal of acidities. The increased acid/base character of hot water and the decrease in its dielectric constant could therefore expand acidity determinations of acids with H acceptor/donor capacity in aqueous solutions to higher pK_{HB} ranges than those accessible under traditional conditions.

III. Elimination Reactions

α-Ethyl-4-methoxy- and *d,l*-4-chloro-α-propylbenzyl alcohol (0.50 M) underwent nearly quantitative elimination reactions in pure liquid water at 277 °C within 75 min.[16] Only a trace, less than 1%, of an unidentified side product was formed in each case. Neither cleavage of the para substituents nor polymerization of the products was detected by ^1H or ^{13}C NMR of chloroform extracts of the two-phase product mixtures. Conversion of a related benzyl alcohol derivative, α-phenethanol, to a slate of compounds via intermediacy of the α-phenethyl cation occurred.[48]

Cyclohexanol and methylcyclohexanol derivatives underwent exclusively dehydration in deuterium oxide at 250–300 °C.[16] A 60 min treatment of cyclohexanol in water at 300 °C led to a 33% conversion solely to cyclohexene; during 18 h at 278 °C an 85% yield of the cycloalkene was obtained. The acid-catalyzed conversion was enhanced when sulfuric or hydrochloric acid (0.02 wt %, 5 mM at room temperature) was added.

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[65] The ion product of D_2O is approximately 1 order of magnitude larger than that of H_2O at equal temperature; e.g., at 250 °C, $-\log K(H_2O) = 11$ and $-\log K(D_2O) = 12$. See: Perrin, D. D. *Ionization Constants of Inorganic Acids and Bases in Aqueous Solutions,* 2nd ed.; IUPAC Data Series 29; Pergamon: New York, 1982.

[66] Personal communication.

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cis- and *trans*-2-Methylcyclohexanol underwent elimination to 1-methylcyclohexene in low yield, but with 100% selectivity during a 60 min, 300 °C treatment with pure water. An 18 h reaction of the *trans* isomer at 270 °C, however, yielded a mixture of methylcyclohexenes that were clearly the products of dehydration/hydration equilibria, at a total conversion of approximately 70%. The predominant product was identified by NMR and GC to be 1-methylcyclohexene (>70% relative to other isomers). Similar results were obtained for *cis*-2-methylcyclohexanol; however, even greater 1-methylcyclohexene formation was observed relative to double-bond migration products.[16]

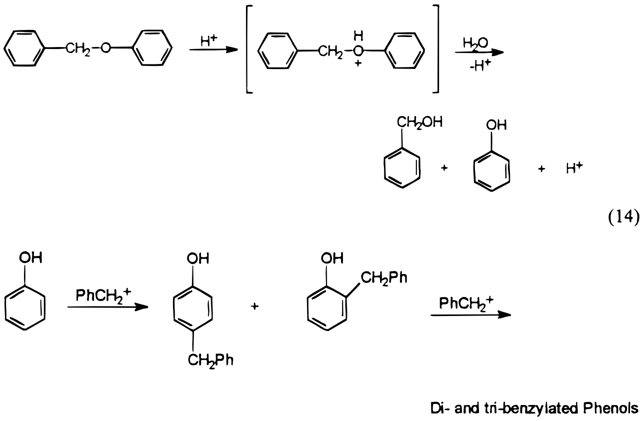
Dehydration of neopentyl alcohol or pentaerythritol, concomitant with the required carbon-bond migration, did not take place in 60 min at 250−300 °C. None of the alcohols studied underwent dehydration to ethers to any observable degree.[16]

Poly(vinyl chloride) (PVC) undergoes ~90% dehydrochlorination in water at 315 °C for 1 h.[71] Chlorobutyl rubber is dehydrohalogenated (~60%) and depolymerized in superheated water at 350 °C for 1 h.[72]

IV. Condensation Reactions

1. Formation of Ethers and Esters by C−O Bond Formation. Unexpectedly, in addition to C−O bond cleavages, C−O bond formations occur quite readily in aqueous solution just as they do in cyclohexane. Thus, 2-phenylethanol and benzyl alcohol both give equilibria with considerable proportions of the corresponding ethers formed by dehydration.[27,51] Esters are also formed, as well as hydrolyzed, quite readily in aqueous solution. Thus, heating benzyl and phenethyl alcohol in aqueous acetic acid gives significant amounts of benzyl acetate ($PhCH_2OCOCH_3$) and phenethyl acetate ($PhCH_2CH_2OCOCH_3$), respectively.[27] Heating PhCHO with HCHO gives some $PhCO_2Me$ via hydride transfer to intermediates $PhCO_2H$ and MeOH.[27] 4-$PyCH_2OH$ gives some 4-$PyCO_2Me$; here some CH_2O is liberated, and hydride transfer provides the required 4-$PyCO_2H$ and MeOH.[50]

2. Formation of C−C Bonds at Ring Carbon Atoms by CH_2OH Substituents. Reactions of this type generally involve the ring carbon atom behaving as a nucleophile and being attacked by a C electrophile. The ring carbon atoms of pyridine are strongly deactivated toward electrophilic attack and do not show such reactions in aquathermolysis. By contrast, these reactions are very common for benzenes, and the aquathermolysis of benzyl alcohol results in a highly complex set of products[27] based on the fundamental carbocation reaction type $PhCH_2OH_2^+ + ArH \rightarrow ArCH_2Ph$. Substitution generally occurs ortho and para to the existing substituent, and multiple reactions are common. The overall concept, while complex, is well illustrated by the reaction pathway for benzyl phenyl ether (eq 14).



(14)

V. Conclusions

This Account emphasizes the reactivity of organic molecules in hot water. In addition to biological processes, where aqueous chemistry predominates and is catalyzed by enzymes, petroleum formation is a major arena in nature where aqueous chemistry is observed. In this chemistry, water participates as catalyst, reactant, and solvent. While the geochemical aspects served as a foundation for understanding the aqueous chemistry described, the implications for a wide variety of other organic chemical transformations and technological applications are potentially large, and they are just beginning to emerge. The ability of water to carry out condensation, cleavage, and hydrolysis reactions and to effect selective ionic chemistry (not accessible thermally) is largely due to changes in its chemical and physical properties, which become more compatible with the reactions of organics as the temperature is increased, because the solvent properties of water at 250−350 °C approach those of polar organic solvents at room temperature. Water can act as an acidic or basic catalyst, and its reactivity is often reinforced by autocatalysis from water soluble reaction products. Additional positive aspects of the use of aqueous chemistry are its simplicity, low cost, and favorable environmental impact. An understanding of aqueous organic chemistry may lead to potential applications in areas as diverse as recycling of plastics, the synthesis of chemicals, and detoxification of chemical warfare agents.

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(72) Saleh, R. Y.; Siskin, M.; Knudsen, G. A. U.S. Patent 5,283,318, Feb 1, 1994.