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Deuterium NMR spectroscopy is a versatile and economical tool for monitoring reaction kinetics in ionic liquids†

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Time-resolved ^2H NMR spectroscopy is used to monitor the progress of and gain kinetic information for a variety of reactions in different ionic media.

Ionic liquids are used as reaction media for various types of organic and organometallic transformations. These media hold many advantages, such as high thermal stability and negligible volatility, over conventional molecular solvents.[1] These liquids are easily prepared, are recyclable, and allow for the easy separation of products from a reaction mixture. There is much interest in using ionic liquids as solvents for homogeneous transition metal-catalyzed industrial processes, since the inefficient separation of costly catalysts from products leads to increased costs and the risk of introducing reactive species into the surroundings.[2] Spectrophotometric kinetic studies have been conducted on reactions in these media;[3,4] however, due to the low availability and high cost of perdeuteriated ionic liquids there are currently no reports of kinetic studies that utilize NMR spectroscopy. An alternative method to conduct NMR kinetic studies in these media is to use proteated ionic liquids and employ ^2H NMR to monitor the conversion of deuteriated reactants over time. We report herein on the use of ^2H NMR spectroscopy, a versatile and economical method, in monitoring reaction progress in ionic media.

NMR spectroscopy has been used to gain insight into the nature of species present in room temperature chloroaluminate melts.[5–7] For example, Zawodzinski and Osteryoung employed ^1H, ^2H, and ^{17}O NMR to study the equilibria between HCl, Cl^-, and HCl_2^-, as well as the water content in these media.[5,6]

McMath and co-workers reported one facile ring deuteriation of imidazole and mono- and dialkylimidazolium cations with D_2O and catalytic amounts of Pd/C.[8] In order to prepare dialkylimidazolium cations with perdeuteriated *N*-alkyl groups suitable for use as ^1H NMR solvents, the use of expensive perdeuteriated alkylating agents is required. Furthermore, in order to obtain high ($>97\%$) levels of incorporation of deuterium into the ring positions, two successive treatments with D_2O and Pd/C are necessary.

In our work, ^2H NMR is used to monitor the progress of several fundamental organic reactions in different proteated ionic liquids.‡Using deuteriated reactants, one is able to directly and quantitatively monitor the conversion of reactants to products in real time. The initial concentration of the deuteriated starting materials is approximately 50 mM in each case and an external standard is present as a reference for chemical shifts and integrations.

We illustrate the high utility of this technique in several important chemical transformations. The first reaction is the methyltrioxorhenium (MTO)-catalyzed dihydroxylation of $[D_8]$styrene by aqueous hydrogen peroxide,[9] which is an environmentally friendly oxidant since its only reaction by-product is water.[10] $[D_8]$Styrene is a viable reactant and is commercially available. This transformation was carried out in the ionic liquid *N*-ethylpyridinium tetrafluoroborate ($[Et\text{-}Py]BF_4$). In the first experiment, a tenfold molar excess of H_2O_2 is used, and its concentration (0.5 M) is such that under steady-state conditions the major rhenium peroxo species is $(CH_3)Re(O)_2(\eta^2\text{-}O_2)$.[11] A smooth conversion of reactant (R) to product (P) over the course of 1 h at room temperature is observed, with the rapid formation of a deuteriated intermediate (I) species at $\delta = 4.3$ ppm that remains in nearly constant concentration over the course of the reaction (Fig. 1). ^2H resonances for the alkyl portion of the product appear at $\delta = 5.0$ ppm (α) and 4.1 ppm (β); the ratio of integrations ($\alpha:\beta$) is 1:2 throughout the reaction.

When this reaction is conducted with a higher concentration of H_2O_2 (5.0 M), the conversion proceeds at nearly the same rate; however, the presence of another steady-state intermediate with a different chemical shift ($\delta = 5.3$ ppm) is observed *via* ^2H NMR (Fig. S1, ESI†). The aliphatic ^2H resonances of the product, $[D_8]$styrene-1,2-diol, are present at the same δ values as in the previous reaction. At the latter concentration of H_2O_2, the major rhenium species is $(CH_3)Re(O)(\eta^2\text{-}O_2)_2$.[11] After 24 h at ambient temperature, neither of these intermediate species is present, as their ^2H signals vanish.

In the epoxidation of $[D_8]$styrene‡ with urea hydrogen peroxide (UHP), an anhydrous source of hydrogen peroxide, these intermediates are absent and a quantitative yield of racemic $[D_8]$styrene oxide is obtained (Fig. S2, ESI†). Similarly, no such intermediates are present when $[D_{10}]$cyclohexene is epoxidized with UHP (Fig. S3, ESI†). Furthermore, when $[D_{10}]$cyclohexene is dihydroxylated with aqueous H_2O_2/MTO in ionic media, a steady-state intermediate is again observed at

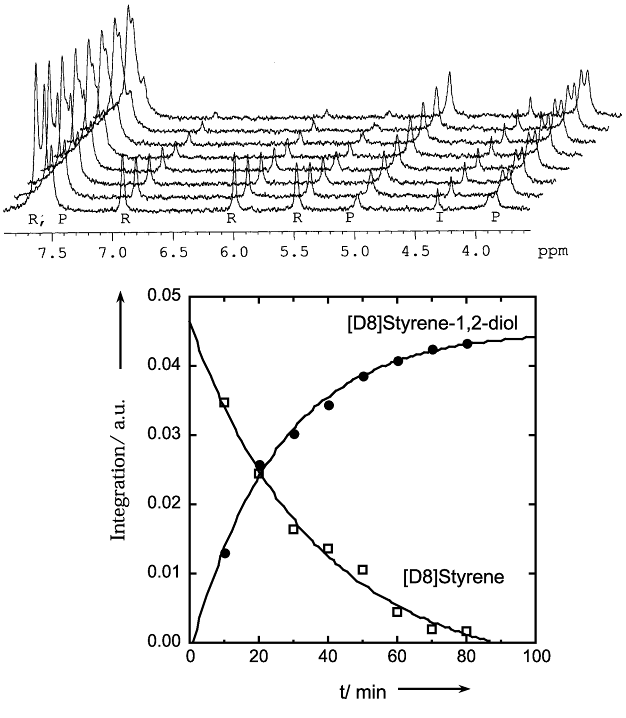

Fig. 1 $[D_8]$Styrene dihydroxylation, 0.5 M H_2O_2.

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† Electronic supplementary information (ESI) available: Figs. S1–6: NMR stack plots and kinetic traces. See http://www.rsc.org/suppdata/cc/b1/b108864e/

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δ = 4.3 ppm throughout the course of the reaction (Fig. S4, ESI†). Based on these observations, we conclude that these steady-state intermediates are the η^2-diolato complexes of the predominant Re(VII) peroxo species in the reaction mixtures. Since the major rhenium-containing species is dependent on the concentration of H_2O_2,[12] different intermediates are observed at different concentrations of H_2O_2.

Using commercially available deuteriated substrates, we also examined several other fundamental organic transformations in ionic media (Table 1). These reactions are a testimony to the various types of reactions and substrates that can be monitored in ionic media using ^{2}H NMR. Although each of these reactions proceeds to completion using stoichiometric amounts of reactants, we used a large excess of one reactant in order to conduct these reactions under pseudo-first order conditions. Two reactions were conducted in different ionic liquids to probe the dependency of rate on the nature of the solvent (entries 3, 4 and 7, 8)—in these cases there is no appreciable difference in rate when the reactions are conducted in two structurally different ionic liquids. Here we also show how ^{2}H NMR can be used to easily monitor reactions in various ionic liquids.

There are many advantages to using this technique. This method is highly cost efficient, since only a small amount of deuteriated starting material is required for any given experiment. There are many types of commercially available perdeuteriated compounds that can be used as reactants (^{1}H NMR solvents are good examples). Most importantly, there is no need to prepare relatively large amounts of various costly perdeuteriated ionic liquids. Since the extent of protium incorporation in proteated ionic liquids is naturally high (99%), no residual solvent peaks are observed in the ^{2}H spectra. It is therefore possible to easily conduct NMR kinetic experiments in a variety of easily prepared ionic liquids. Using this method it is possible to detect reaction intermediates that are undetectable using other forms of spectroscopy or are not present in reactions carried out in molecular solvents.

This technique allows a variety of chemical transformations to be studied in ionic media, since many types of organic molecules can be regioselectively deuteriated using conventional, economical H/D exchange processes. Examples include carbonyl compounds, alkenes,[13,14] terminal alkynes,[15] and cyclopentadiene.[16] Only one reactant need be deuteriated, and deuteriation is required only in positions that experience a change during the course of a reaction. Given that certain reactions exhibit significant kinetic (H/D) isotope effects, caution must be employed in applying quantitative kinetic data to reactions involving the analogous proteated substrates. Nonetheless, by conducting reactions in structurally different ionic liquids, the effects of solvent–solute interactions, such as hydrogen bonding, Lewis acid–base, ionic, and ion–dipole, on reaction rates, yields, and selectivities can be investigated. These studies are currently in progress.

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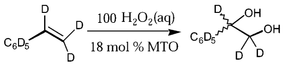
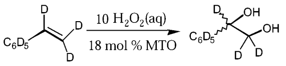
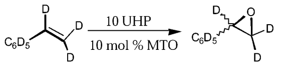
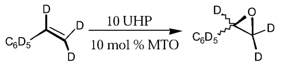
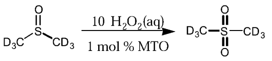
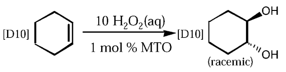
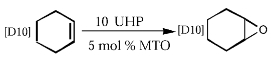
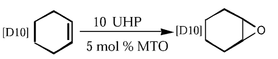
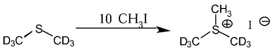
Table 1 Reactions monitored *via* ^{2}H NMR in ionic media

Entry	Reaction[a]	Solvent[b]	$k_{obs}/[Re]_T/$ $M^{-1}\ s^{-1}$
1		[EtPy]BF$_4$	0.20 ± 0.02
2		[EtPy]BF$_4$	0.090 ± 0.02
3		[Emim]BF$_4$	0.034 ± 0.004
4		[BuPy]BF$_4$	0.040 ± 0.008
5		[Emim]BF$_4$	2.600 ± 0.003
6		[Emim]BF$_4$	1.750 ± 0.006
7		[Emim]BF$_4$	0.20 ± 0.01
8		[BuPy]BF$_4$	0.23 ± 0.02
9		[Emim]BF$_4$	3.000 ± 0.002[c]

[a] Although these reactions proceed to completion using stoichiometric amounts of reactants, a large excess of one reactant is used here to ensure pseudo-first order conditions. UHP = Urea hydrogen peroxide complex, MTO = methyltrioxorhenium(VII). [b] [Emim]BF$_4$ = 1-ethyl-3-methylimidazolium tetrafluoroborate, [BuPy]BF$_4$ = *N*-(n-butyl)pyridinium tetrafluoroborate. [c] Since this is not a catalytic reaction, the reported rate constant is given by $k_{obs}/[CH_3I]$.

Notes and references

‡ *A typical experimental procedure*: ([D$_8$]Styrene epoxidation). An NMR tube was charged with [Emim]BF$_4$ (0.5 mL), UHP (47 mg), and 125 μL of a 0.040 M MTO stock solution in CH_3CN. After 10 min, an external standard of CD_3CN in C_6H_6 (30% v/v, δ = 1.55 ppm) was added, along with [D$_8$]styrene (6 μL). The contents of the tube were mixed well, and ^{2}H NMR spectra were subsequently collected every 5 min on a Brüker Avance 500 MHz (^{1}H) spectrometer.

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