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^{79}Br NMR spectroscopy as a practical tool for kinetic analysis

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^{79}Br NMR spectroscopy has been used to monitor a series of reactions in which the bromide ion is produced, including the Menschutkin reaction of pyridine with a range of substituted benzyl bromides and a Heck coupling process. In cases where the process could also be monitored using ^{1}H NMR spectroscopy, the kinetic analyses using heteronuclear magnetic resonance spectroscopy were shown to be completely consistent. Both the utility of the process in following reactions which may be difficult to analyse using other techniques and the practical limitations associated with solvent choice are discussed. Copyright © 2009 John Wiley & Sons, Ltd.

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Keywords: NMR; ^{79}Br; ^{1}H; kinetic analysis; Menschutkin reaction

Introduction

NMR spectroscopy offers a particularly powerful tool for following the progress of chemical reactions, not least because it allows continuous monitoring of the process without the need to sample a reaction mixture but also because the precision and accuracy of quantitative NMR spectroscopy have been shown to rival chromatographic methods such as HPLC and GC.[1] However, the commonly examined nuclei, such as ^{1}H, may not always be appropriate to follow a given reaction, often as a result of components of the reaction mixture contributing signals that obscure the signal of interest. This is particularly problematic when solvents which are NMR silent (such as deuterated solvents for ^{1}H NMR spectroscopy) are either not available or are prohibitively expensive.[2] While methods have been developed to overcome the problem of overlapping resonances, such as single-scan 2D methods,[3] the presence of heteroatoms in the systems offers another alternative.

The principal advantage of heteronuclear magnetic resonance spectroscopy over ^{1}H NMR spectroscopy is the reduction in the number of signals in a spectrum. This has been exploited for following the kinetics of various processes using nuclei with spin number, I, having a value of 1/2 including ^{15}N,[4] ^{19}F,[5] ^{29}Si,[6] and ^{31}P.[7] However not all reaction mixtures to be examined contain these nuclei, hence other nuclei need to be considered.

Quadrupolar nuclei, those with $I > 1/2$, are generally harder to study than those with $I = 1/2$ due to their dominant quadrupolar relaxation characteristics and the fact that they often have poor sensitivity due to low natural abundance and magnetogyric ratio.[8] However, both these factors do not eliminate such nuclei from consideration as line broadening is less of an issue in spectra with few signals, or even one in some cases, and the rapid relaxation times allow a large number of scans to be accumulated in a given time, overcoming the inherently low sensitivity. We have previously reported the use of ^{17}O NMR spectroscopy to quantify oxygenated additives in fuels[9] and the utility of ^{35}Cl NMR spectroscopy to monitor a solvolysis process in mixtures of methanol and an ionic liquid.[10,11] Herein we report an extension of this latter approach which uses ^{79}Br NMR spectroscopy.

The linewidth of signals in a ^{79}Br NMR spectrum, as for all quadrupolar nuclei, is markedly dependent on the environment of the nucleus; a symmetrical electronic distribution around the bromine centre results in, effectively, zero field gradient and hence relatively sharp signals while quadrupolar relaxation (and hence line broadening) is more significant in cases where the nucleus is in an asymmetric environment.[8] Given our previous experience with ^{35}Cl,[10,11] it was anticipated that organobromine compounds would not give rise to an observable signal, with bromide ion producing the only signal observed in the ^{79}Br NMR spectrum. The methods used below are based on the fact that the NMR signal is proportional to the number of nuclei present and hence the concentration of the sample. Thus the amount of the bromide ion evolved during the process can be readily determined.

The ^{79}Br nucleus might be considered the slightly less favourable of the bromine nuclei for NMR studies, as while it is the slightly dominant isotope, it has the lower sensitivity and the signals have larger linewidth.[12] However, in determining if bromine NMR spectroscopy is useful for following the progress of a reaction neither of these relatively small differences is particularly significant, since only one signal is likely to be observed. Further, the reactions examined involve generating a bromide ion in the presence of one of the range of cations and the effect of a cation on the ^{79}Br NMR signal of bromide has been well-described.[13] Finally, the resonance frequency of ^{79}Br is similar to that of ^{13}C and thus it can be observed on a ^{13}C channel without the need for

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a broadband probe.[12] The arguments presented here, however, might equally well be seen as demonstrating the practical utility and limitations of the use of ^{81}Br NMR spectroscopy in following chemical kinetics; to date neither of these nuclei has been used to follow the progress of the reaction. (The use of ^{81}Br NMR spectroscopy in mechanistic elucidation to identify bromide ion as a product has been reported.[14] Conceptually, such a method might be extended to follow reaction kinetics as outlined here.)

It is worth noting that throughout the work presented here, conditions such as reagent concentration and temperature reflect those that are typical for a given process. While increasing the concentration of species under consideration might increase the signal to noise ratio of the spectra obtained and changing the temperature might reduce the linewidth of a signal, it is following the reaction progress under typical conditions which is required for this technique to be practically useful.

The reactions chosen for examination in this study are summarised in Schemes 1–5 below and represent a range of organic processes in which bromide is generated. The Menschutkin reaction of each of the substituted benzyl bromides **1a–e** with pyridine **2** to give the corresponding benzylpyridinium bromides **3a–e** (Scheme 1) is representative of the substitution process in which bromide is produced.[15] It also offers the advantages of being readily followed using ^{1}H NMR spectroscopy and that variation of the substituent on the bromides **1a–e** allows tuning of the rate of the reaction in order to test the scope of this spectroscopic method. The elimination of hydrogen bromide from the dibromide **4** to give the ester bromides **5** and **6** (Scheme 2)[16] and the conversion of the dibromoketone **7** to the corresponding chalcone **8** (Scheme 3)[17] are examples of elimination processes. The palladium catalysed coupling of the bromotoluene **9** and the acetal **10** (Scheme 4)[18] is an example of the Heck reaction, a process widely used in synthetic organic chemistry and can be difficult to follow using ^{1}H NMR spectroscopy.[19] Finally, the solvolysis of the bromide **12** (Scheme 5) was considered as it is a further example of the substitution process and it cannot be followed using ^{1}H NMR spectroscopy due to overlapping of signals corresponding to the starting material **12** and the product **13**.[10,20]

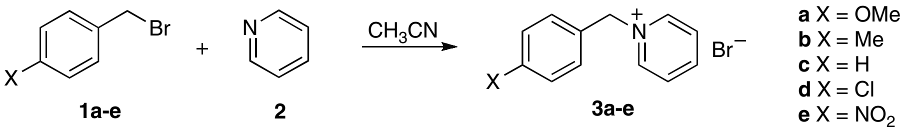
Experimental

The benzyl bromides **1a–e** were either commercially available or prepared from commercially available starting materials using literature methods.[21] The dibromides **4** and **7** were prepared by modification of literature procedure[22] through the addition of bromine to ethyl *trans*-cinnamate and the chalcone **8**, respectively. The alkyl bromide **12** was prepared through modification of literature procedure,[20] from the corresponding alcohol **12** and phosphorus tribromide and identified using the key resonance in the ^{13}C NMR spectrum at δ_C 74.6. Ethanol was distilled from sodium ethoxide and acetone was purified using silver nitrate.[23] All other reagents were used as received.

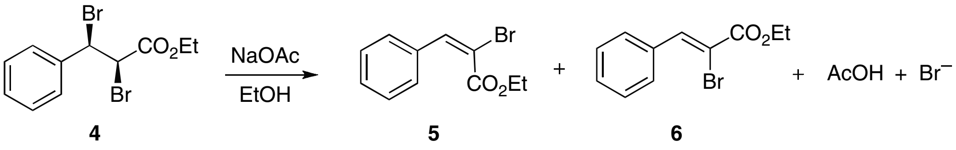
^{1}H NMR and ^{79}Br NMR spectra were either recorded on a Bruker DMX 500 Avance spectrometer (500 MHz, ^{1}H; 125.3 MHz, ^{79}Br) or on a Bruker DPX spectrometer (300.17 MHz, ^{1}H; 75.19 MHz, ^{79}Br) using *ca* 0.8 ml of either sample or reaction mixture in a 5-mm NMR tube. Spectra were referenced externally against TMS (^{1}H; δ_H 0) and 0.05-mol l^{-1} sodium bromide in deuterium oxide (^{79}Br; δ_{Br} 0). Typical instrument parameters used for ^{79}Br NMR spectroscopy were $p90 = 13\ \mu s$ (−4.0 dB), $AQ = 20$ ms, $d_1 = 1$ ms and 5000 scans. Line broadening was set at 0.2 Hz and integration was done manually due to a slight change in the chemical shift of signal due to the bromide ion as the reactions proceeded and the bromide ion concentration increased.

Kinetic analyses of the Menschutkin reactions were carried out in acetonitrile containing the appropriate benzyl bromide **1** (*ca* 0.05 mol l^{-1}) and pyridine **2** (0.50 mol l^{-1}) at 298 K. In each case the reaction was followed using both ^{1}H and ^{79}Br NMR spectroscopies until more than 90% of the starting material was consumed. Spectra were taken at regular intervals during the reaction and the extent of reaction calculated through integration of the signals corresponding to benzyl protons in the starting materials **1a–e** (*ca* δ_H 4.5) and the products **3a–e** (*ca* δ_H 5.8), and the bromide ion (*ca* δ_{Br} 75). (At least 20 of each type of spectrum were obtained for each kinetic run.) From this information, the pseudo-first-order rate constant for the reaction of each of the species **1a–e** under these conditions was calculated.

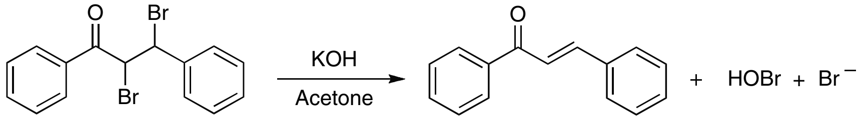
The elimination of hydrogen bromide from the dibromide **4** at 343 K was followed by monitoring the reaction mixture [dibromide **4** (*ca* 20 mg), sodium acetate (*ca* 30 mg) in d6-ethanol (1.0 ml)] using both ^{1}H and ^{79}Br NMR spectroscopies until more than 90% of the starting material was consumed. Spectra were taken at intervals during the reaction and the extent of reaction calculated through integration of the signals corresponding to the bromoalkyl protons in the starting material **4** (*ca* δ_H 4.9, 5.4) and the bromoethylene proton in the product **6** (*ca* δ_H 8.2). (At least 20 of each type of spectrum were obtained for each kinetic run.) From this information, pseudo-first-order rate constants for the reaction under these conditions were calculated. No signal corresponding to the bromide ion was observed in the ^{79}Br NMR spectra.



Scheme 1. The Menschutkin reaction between the benzyl bromides **1a–e** and pyridine **2**.[15]



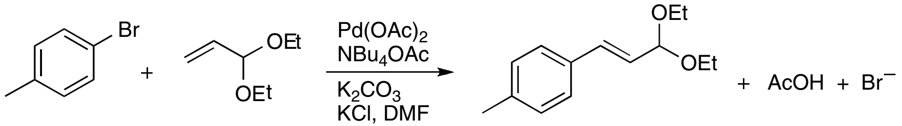
Scheme 2. The elimination of hydrogen bromide from *erythro*-ethyl cinnamate dibromide **4**.[16]



7

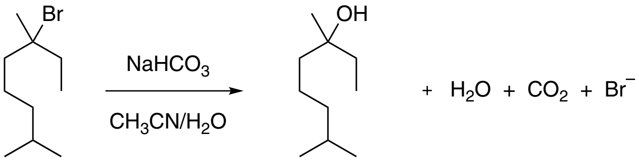
8

Scheme 3. Treatment of the dibromide **7** yields the chalcone **8**.[17]



9 **10** **11**

Scheme 4. Heck reaction of 4-bromotoluene **9** with acrolein diethyl acetal **10**.[18]



12 **13**

Scheme 5. Solvolysis of the tertiary alkyl bromide **12**.[20]

The formation of the chalcone **8** from the dibromide **7** [*ca* 25 mg, dissolved in a d_6-acetone solution of potassium hydroxide (0.36 mol l^{-1}, 1.0 ml)] at 298 K was monitored using both ^{1}H and ^{79}Br NMR spectroscopies until more than 90% of the starting material was consumed. Spectra were taken at intervals during the reaction and the extent of reaction calculated through integration of the signals corresponding to the bromoalkyl protons in the starting material **7** (*ca* δ_H 5.6, 5.8) and the bromide ion (*ca* δ_{Br} 53).

Reaction mixtures for the Heck coupling process were prepared by dissolving 4-bromotoluene **9** (*ca* 45 mg), acrolein diethyl acetal **10** (*ca* 100 mg), palladium acetate (*ca* 40 µg, added through addition of *ca* 2 mg ml^{-1} solution), potassium carbonate (*ca* 50 mg), potassium chloride (*ca* 20 mg) and tetrabutylammonium acetate (*ca* 150 mg). The coupling reaction was monitored at 343 K using both ^{1}H and ^{79}Br NMR spectroscopies until more than 90% of the starting material was consumed. Spectra were taken at intervals during the reaction and the extent of reaction calculated through integration of the signals corresponding to the acetal proton of the product **11** (*ca* δ_H 5.3) and the bromide ion (*ca* δ_{Br} 97). At least 20 of each type of spectrum were obtained for each kinetic run.

For the solvolysis of the bromide **12**, reaction mixtures were prepared by adding 3-bromo-3,7-dimethyloctane **12** (165.9 mg, 0.75 mmol) to a mixture of saturated $NaHCO_3$ solution, acetonitrile and acetonitrile-d_3 (1.2 ml, ratio 0.65:0.29:0.06). The production of bromide ion was monitored at 298 K using ^{79}Br NMR spectroscopy until no further production of bromide ion was evidenced (*ca* δ_{Br} 97).

Results and Discussion

Initial studies of the salts **3a–e** from the Menschutkin reaction were conducted to evaluate whether these salts would give reasonable ^{79}Br NMR spectra. Interestingly, the line broadening of the signal due to the bromide ion was observed to change on modification of the cation. There was a general, though not completely consistent, trend of increasing linewidth with increasing electron-donating nature of the substituent on the phenyl ring. It is unlikely that this is due to changes in ion-pairing in solution both because increasing electron donation to the cationic centre is anticipated to result in a decrease in ion-pairing and hence a decrease in line broadening but also because previous studies[13] have demonstrated that ion-pairing is of limited importance in these systems. It is more likely that changing the electronic nature of the substituent alters the solvent–anion interactions; this will be touched on below.

Table 1. Pseudo-first-order rate constants for the reactions described in Scheme 1, as monitored using either ^{1}H or ^{79}Br NMR spectroscopy. Rates are the average of at least three kinetic runs and reported uncertainties represent two standard deviations from the mean

Substrate	k_{obs}/s^{-1} – ^{1}H	k_{obs}/s^{-1} – ^{79}Br
1a	$(2.2 \pm 0.1) \times 10^{-3}$	$(2.3 \pm 0.3) \times 10^{-3}$
1b	$(6.9 \pm 0.4) \times 10^{-4}$	$(6.2 \pm 0.6) \times 10^{-4}$
1c	$(3.7 \pm 0.2) \times 10^{-4}$	$(3.7 \pm 0.1) \times 10^{-4}$
1d	$(3.4 \pm 0.2) \times 10^{-4}$	$(3.3 \pm 0.3) \times 10^{-4}$
1e	$(2.2 \pm 0.1) \times 10^{-4}$	$(2.2 \pm 0.1) \times 10^{-4}$

The reaction of each of the bromides **1a–e** with pyridine was monitored using both ^{1}H and ^{79}Br NMR spectroscopies (an example of the latter is shown in Fig. 1) by interleaving data acquisition and thus the method was directly evaluated. The rate constants for these reactions were calculated using each set of spectroscopic data and the values are summarised in Table 1. The first key feature is the reproducibility of the kinetic data, with the uncertainties in the rate constants being *ca* 10% at most. However, more importantly, the rate constants determined using either ^{1}H or ^{79}Br NMR spectroscopy for each of the substrates **1a–e** were the same within uncertainty. This indicates that this ^{79}Br NMR spectroscopic method can be used to accurately measure rates of reaction in these systems. Further, these results demonstrate that sufficiently accurate ^{79}Br NMR spectra to determine rate constants could be obtained for reactions with half-lives as short as 7 min (as was the case for the bromide **1a**).

The elimination of hydrogen bromide from the dibromide **4** could be readily followed using ^{1}H NMR spectroscopy and pseudo-first-order rate constants for the process obtained. However, under the conditions of the experiment, no signals were observed in the

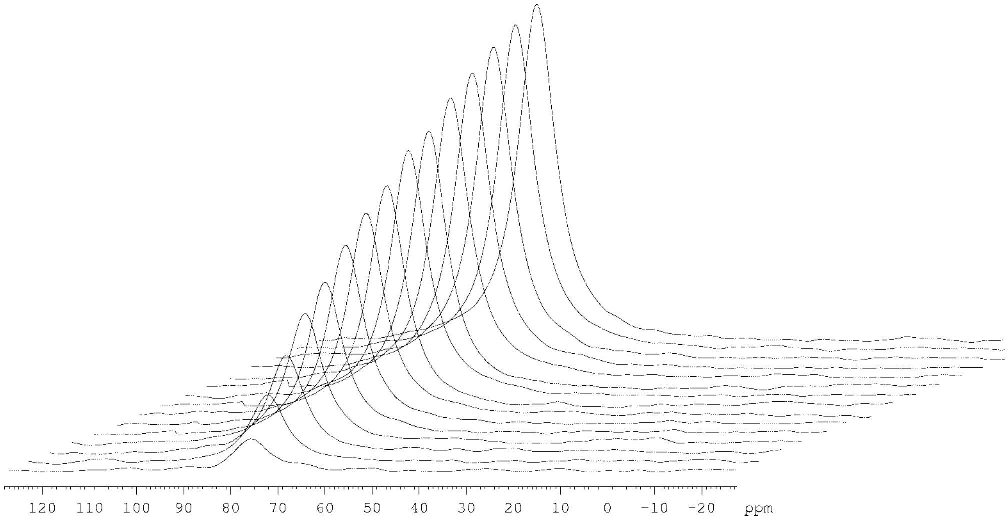


Figure 1. Stacked plots of ^{79}Br NMR spectra for a Menschutkin reaction of the bromide **1b** with pyridine at 298 K. The first spectrum was that acquired after 145 s and each subsequent spectrum occurs in increments of 217 s. The signal corresponds to bromide anion.

^{79}Br NMR spectrum. Previously, line broadening in such spectra has been observed on going from aqueous to alcoholic solvents,[24] though in this case it demonstrates a limitation of the process in terms of solvent choice when attempting to obtain spectra of dilute solutions in short time frames.

A brief survey of some common solvents demonstrated that under these conditions (*ca* 0.05 mol l^{-1} bromide, 5000 scans) signals were observed in the ^{79}Br NMR spectra for acetonitrile, acetone, N,N-dimethylformamide (DMF) and water while no signals were observed for methanol, ethanol and isopropanol. It is clear by considering viscosity values for these solvents[25] that viscosity alone cannot account for the lack of an observable signal. Studies on the linewidth of the signal due to the bromide ion in methanol/water systems, which we have reproduced below under our conditions (Fig. 2), have attributed the change to a combination of the viscosity and the dielectric constant of the medium.[24] It is perhaps useful to consider this at the molecular level, and the effect of the solvent on the symmetry of the electronic distribution (and hence field gradient) about the bromine atom. In systems where the symmetry is preserved, such as acetonitrile,[14] a signal is observed. In systems where hydrogen bonding to the bromide ion occurs, contributions from the ion–solvent and solvent–solvent interactions are significant. If these two interactions cancel one another out, as is the case in water,[14,26] the result is spherical symmetry and a signal is observed. If they do not, as is the case for methanol where the solvent–solvent interactions are notably different,[14,27] an asymmetric bromide environment results in significant line broadening. Irrespective, these results demonstrate that as a practical tool for chemical kinetics, ^{79}Br NMR spectroscopy is not appropriate for reactions in which alcohols are used as the solvent, unless in a small proportion.

The reaction of the cinnamate dibromide **4** was also attempted using d_6-acetone as a solvent and replacing the sodium acetate with an acetone soluble base, tetrabutylammonium acetate. The signal due to the bromide ion in ^{79}Br NMR spectra could be readily observed, however the reaction had gone to completion prior to the acquisition of the first spectrum. As such, investigations were discontinued and the elimination of bromine from the chalcone dibromide **7** was considered. At 298 K in d_6-acetone, this process was readily followed using ^{79}Br NMR spectroscopy, however other components of the reaction mixture obscured signals in the ^{1}H NMR spectra due to the starting material and the product. As such, ^{79}Br NMR spectroscopy represents a practical method of following this process though it is worth noting that under the conditions used, the half-life of the process (*ca* 8 min) is at the limit of that which can be practically followed using ^{79}Br NMR spectroscopy.

Next considered was the Heck coupling of reagents **9** and **10**. This type of reaction might be considered typical of those for which ^{79}Br NMR spectroscopy might be useful as the reaction mixture contains many components, resulting in complex ^{1}H NMR spectra that are not readily integrated. This is demonstrated in Figs 3 and 4, which illustrate the relative precision of the two techniques in these cases. While in this case, the signal due to the acetal proton on the coupled product **11** can be identified, it is not readily integrated due to the presence of large nearby signals. The result is Fig. 3, which clearly shows sigmoidal character but a significant degree of scatter in the observed data. The same problems are not present in the ^{79}Br NMR spectra and, as such, the same sigmoidal shape is observed but with substantially greater precision.

The final reaction considered was the solvolysis of the bromide **12** to the corresponding alcohol **13**. The starting material **12** and the product **13** have significant overlapping resonances in the ^{1}H NMR spectrum which, along with the presence of protonated solvent, makes following the reaction impossible using this method (Figure S1, Supporting Information). (We have previously examined using ^{35}Cl NMR spectroscopy for following reactions of the corresponding chloride for similar reasons.)[10,11] However, when the reaction was followed using ^{79}Br NMR spectroscopy, the production of the bromide ion could be readily observed without interference of other signals (Figure S2, Supporting Information) demonstrating that this method can be used for systems in which ^{1}H NMR spectroscopy is inappropriate. It is worth noting that the nature of the base is significant here as, when triethylamine was used, no signal corresponding to the bromide was observed despite being detected using other methods (such as addition of silver(I)). It is thought that this is due to interaction of the bromide with the protonated triethylamine, introducing asymmetry about the bromide atom and hence significant signal broadening.

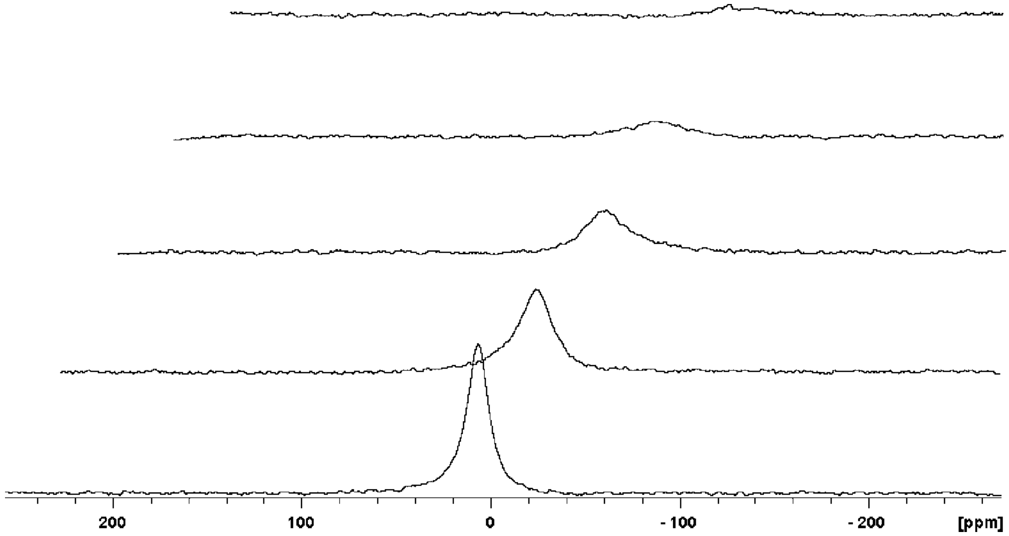


Figure 2. Stacked plots of ^{79}Br NMR spectra for solutions containing *ca* 0.05 mol l^{-1} sodium bromide at 298 K. The first spectrum is taken in 10% v/v methanol in water and each subsequent spectrum has the amount of methanol increased by 10%.

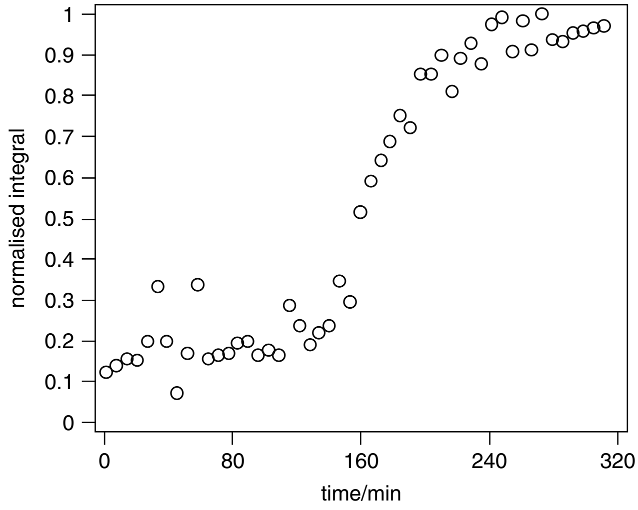


Figure 3. Graph of the integral corresponding to the appearance of the ^{1}H NMR signal at δ_H 5.25 of the reaction of 4-bromotoluene **9** and acrolein diethyl acetal **10** with 5 mmol l^{-1} palladium (II) acetate at 343 K.

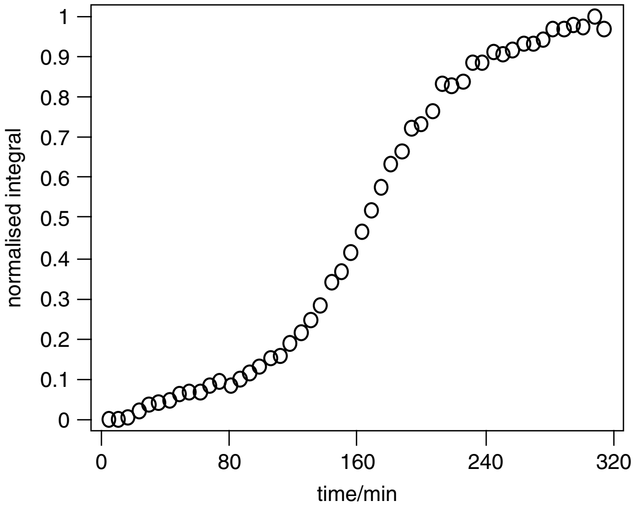


Figure 4. Graph of the integral corresponding to the appearance of the ^{79}Br NMR signal at δ_{Br} 97 of the reaction of 4-bromotoluene **9** and acrolein diethyl acetal **10** with 5 mmol l^{-1} palladium (II) acetate at 343 K.

Conclusions

The results described demonstrate that ^{79}Br NMR spectroscopy can be readily used to follow processes in which a bromide ion is generated. These can range from simple first order processes to more complicated systems and in the case of the former rate constants calculated using this and other spectroscopic techniques are in good agreement. Some limitations in terms of the choice of solvent have been shown, based on line broadening of the bromide signal, however the overall utility has been demonstrated by considering reactions that cannot be readily analysed using conventional NMR techniques. It is anticipated that a range of processes in which bromide ions are generated might now be easily monitored.

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Supporting information

Supporting information may be found in the online version of this article.

References

[1] R. J. Wells, J. M. Hook, D. B. Hibbert, T. S. Al-Deen, *J. Agric. Food. Chem.* **2002**, *50*, 3366.

[2] For example it is difficult to obtain deuterated ionic liquids see C. Hardacre, J. D. Holbrey, S. E. J. McMath, *J. Chem. Soc. Chem. Commun.* **2001**, 367.

[3] M. Gal, M. Mishkovsky, L. Frydman, *J. Am. Chem. Soc.* **2006**, *128*, 951.

[4] M. Roy, P. A. Jennings, *J. Mol. Biol.* **2003**, *328*, 693.

[5] (a) J. M. Salvino, E. Orton, N. V. Kumar, P. Krolikowski, M. J. Drew, *J. Comb. Chem.* **2000**, *2*, 8; (b) M. Mogemark, J. Kihlberg, M. Elofsson, *Org. Lett.* **2001**, *3*, 1463; (c) P. V. Yushmanov, I. Furo, P. Stilbs, *Colloids Surf., A* **2006**, *291*, 59.

[6] (a) J. C. Pouxviel, J. P. Boilot, J. C. Beloeil, J. Y. Lallemand, *J. Non-Cryst. Solids* **1987**, *89*, 345; (b) R. Liu, Y. Xu, D. Wu, Y. Sun, H. Gao, H. Yuan, F. Deng, *J. Non-Cryst. Solids* **2004**, *343*, 61.

[7] (a) Z. Yao, F. A. Cotton, H. Chen, *Inorg. Chem.* **1994**, *33*, 4255; (b) A. Spyros, A. Philippidis, P. Dais, *J. Agric. Food Chem.* **2004**, *52*, 157.

[8] C. G. Tsanaktsidis, P. Gerothanassis, *Concepts Magn. Reson.* **1996**, *8*, 63.

[9] J. M. Hook, D. G. Lonnon, *Anal. Chem.* **2003**, *75*, 4659.

[10] B. Y. W. Man, J. M. Hook, J. B. Harper, *Tetrahedron Lett.* **2005**, *46*, 7641.

[11] H. M. Yau, S. A. Barnes, J. M. Hook, T. G. A. Youngs, A. K. Croft, J. B. Harper, *Chem. Commun.* **2008**, 3576.

[12] B. Lindman, S. Forsén, *Chlorine, Bromine and Iodine NMR: Physico-chemical and Biological Applications*, Springer-Verlag: New York, **1976**.

[13] (a) B. Lindman, S. Forsén, E. Forslind, *J. Phys. Chem.* **1968**, *72*, 2805; (b) B. Lindman, H. Wennerstrom, S. Forsén, *J. Phys. Chem.* **1970**, *74*, 754.

[14] R. R. Pappalardo, J. M. Martinez, E. S. Marcos, R. Ayala, *J. Phys. Chem. A* **2000**, *104*, 2799.

[15] P. Haberfield, A. Nudelman, A. Bloom, R. Romm, H. Ginsberg, *J. Org. Chem.* **1971**, *36*, 1792.

[16] C. C. Tung, A. J. Speziale, *J. Org. Chem.* **1963**, *85*, 1353.

[17] C. L. Bickel, *J. Am. Chem. Soc.* **1950**, *72*, 349.

[18] G. Fabrizi, S. Cacchi, G. Battistuzzi, *Org. Lett.* **2003**, *5*, 777.

[19] I. P. Beletskaya, A. V. Cheprakov, *Chem. Rev.* **2000**, *100*, 3009.

[20] P. Müller, J. C. Rossier, *J. Chem. Soc., Perkin Trans. 2.* **2000**, 2232.

[21] T. Yokoyama, G. R. Wiley, S. I. Miller, *J. Org. Chem.* **1969**, *34*, 1859.

[22] (a) S. D. Sharma, S. Kanwar, S. Rajpoot, *J. Heterocycl. Chem.* **2006**, *43*, 11; (b) C. Kashima, M. Shimizu, T. Tajima. *Heterocycles* **1981**, *15*, 961.

[23] W. L. F. Amarego, *Purification of Laboratory Chemicals* (5th edn), Butterworth-Heinemann: Boston, **2003**.

[24] R. E. Richards, B. A. Yorke, *Mol. Phys.* **1983**, *6*, 289.

[25] T. W. Swaddle, M. Matsumoto, *Inorg. Chem.* **2004**, *43*, 2724.

[26] (a) S. Raugei, M. L. Klein, *J. Chem. Phys.* **2002**, *116*, 196; (b) R. R. Pappalardo, P. J. Merkling, J. M. Martinez, E. S. Marcos, R. Ayala. *J. Chem. Phys.* **2003**, *119*, 6647.

[27] (a) C. Faralli, M. Pagliai, G. Cardini, V. Schettino, *J. Phys. Chem. B* **2006**, *110*, 14923; (b) P. D'Angelo, A. DiNola, M. Mangoni, N. V. Pavel, *J. Chem. Phys.* **1996**, *104*, 1779.