Probing "microwave effects" using Raman spectroscopy

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The use of *in situ* Raman spectroscopy is reported as a tool for probing the effects of microwave irradiation on molecules. Our results show no evidence for localized superheating, an often-cited specific microwave effect. While the microwave energy may interact with the polar molecules more so than with non-polar ones, the conversion of electromagnetic energy into kinetic energy is slower than conversion of kinetic energy into thermal energy. As a result, more polar molecules are not at a temperature greater than that of the bulk.

Introduction

The use of microwave heating offers a versatile approach to synthetic organic chemistry; a key advantage over conventional heating being the fact that reaction times can often be dramatically reduced.[1] This, in turn, may sometimes result in higher conversions to the desired products since side product formation or loss of catalyst activity partly associated with extended reaction times can be mitigated.[2] While preparative chemists have been quick to embrace the technology there is debate in the literature as to exactly how reaction rates are so greatly accelerated. Indeed, there have been reports in the literature suggesting that different product distributions and yields can be obtained if certain chemical transformations are carried out at the same measured reaction temperature using microwave as opposed to conventional heating.[3] These observations could be explained simply as the result of a rate acceleration in a microwave field that cannot be achieved or duplicated by conventional heating but is still temperature-related in origin. As such, these are defined as specific microwave effects.[2a] Alternatively, the differences between conventional and microwave heating could be explained in terms of non-thermal effects, *i.e.* effects resulting from direct interaction of the electric component of the microwave irradiation with specific molecules in a reaction medium.

An example of specific microwave effects is the ability to superheat solvents to above their boiling points at atmospheric pressure under microwave irradiation. This is a known phenomenon and it can be attenuated with adequate stirring or addition of nucleation additives.[4] Another example of specific microwave effects is the ability of microwave energy to be preferentially absorbed by highly polar substrates. This phenomenon has been exploited to heat reactions under microwave irradiation when carried out in poorly absorbing solvents by using ionic additives such as ionic liquids or tetrabutylammonium bromide[5] or by adding highly microwave-absorbing silicon carbide plugs.[6]

Strouse and co-workers claim to have recently demonstrated a specific microwave effect when utilizing microwave irradiation to synthesize CdSe and CdTe nanomaterials in the non-polar hydrocarbon solvents heptane, octane, and decane.[7] They speculate that the precursor substrates are able to selectively absorb the microwave irradiation, leading to more uniform morphologies of the resulting nanomaterials compared to conventional heating methods. Similarly, specific microwave effects claim to have been demonstrated in enzyme-catalyzed transformations. Copty and co-workers invoke selective heating of green fluorescent protein by microwave irradiation, leading to denaturing of the enzyme and hence an increase in fluorescence that is not consistent with the observed changes in bulk temperature.[8] Similarly, Deiters and co-workers claim to observe an increase in reactivity in three of the four hyperthermophilic enzymes they investigated at bulk temperatures far below their optimal activity window when the reactions were carried out under microwave irradiation.[9] It is important to note, however, that this phenomenon is most likely very dependent upon the particular enzyme as other studies have found no difference in enzymatic activity whether heated with microwave irradiation or when using conventional heating.[10] Indeed, the microwave mediated selective heating at the point of reaction seems to be the exception rather than the rule, existing in only very specific instances or highly manipulated protocols.

Unlike specific microwave effects, "non-thermal" microwave effects cannot be rationalized in terms of either thermal/kinetic or specific microwave effects. There are numerous examples reported in the literature and proponents suggest that when the reaction is performed solvent free or in a non-polar medium, the presence of the electric field generated by the microwave leads to orientation effects of dipolar molecules or intermediates and hence changes the pre-exponential factor (A) or the activation energy terms in the Arrhenius equation. Additionally, in the case of polar reaction mechanisms where the relative polarity of the reaction is enhanced from the ground state to the transition state, it is claimed that acceleration due to an increase in microwave absorbance of the intermediate could occur.[11] When non-thermal microwave effects are discussed, they are generally invoked as a result of comparison of the outcome of microwave and conventionally heated experiments. However, a major flaw in this argument is that the comparisons are most likely not at isothermal operation. Kappe and co-workers have performed detailed studies of a number of reactions in which non-thermal effects have previously been invoked.[12,13] They find that when meticulous attention is paid

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to ensure that the reactions are run under isothermal conditions identical product yields and distributions are obtained under both microwave and conventional heating. Similarly, a kinetic investigation into the intramolecular Newman–Kwart rearrangement by Moseley and co-workers illustrated identical rates of reaction and hence activation energies and rate constants regardless of whether the reaction was carried out under microwave irradiation or heated conventionally.[14]

In our laboratory we have employed a Raman spectrometer interfaced with a commercial scientific microwave apparatus to probe a number of organic reactions.[15,16] This equipment offers a powerful methodology for generating kinetic data rapidly and reliably.[17] Building on our experience and the results obtained using this experimental set-up we have turned to Raman spectroscopy as a tool for probing potential microwave effects and present our findings here.

Experimental section

Unless otherwise noted, materials were obtained from commercial sources and used without further purification. Reactions were conducted using a previously-reported apparatus comprising a monomode microwave unit (CEM Discover® S-Class) interfaced with a Raman spectrometer (Enwave Optronics).[15,16,17] All reactions were performed in an open-vessel set up at atmospheric pressure in a 50-mL borosilicate glass long-necked round-bottom flask equipped with a reflux condenser. When monitoring $Cr(CO)_3(\eta^6\text{-}C_6H_5OMe)$, the solution was refluxed under a nitrogen atmosphere. The contents of the reactions vessels were stirred in all cases by means of an electromagnetic stirring mechanism located below the floor of the microwave cavity with a Teflon-coated magnetic stir bar in the reaction vessel. Additionally, all investigations carried out at reflux also employed boiling chips. Temperature and power profiles were monitored using commercially available software provided by the microwave manufacturer.

Results and discussion

Raman spectroscopy is a second-order spectroscopic technique where the electronic component of the incident light first interacts with the electron cloud of a molecule.[18] As a consequence, the molecule will be excited from the ground state to a virtual energy state. If a second photon then encounters the molecule in the virtual state, it has the ability to impart some of its energy to activate a resonant vibrational frequency. Hence, the photon returns to the detector lower in energy and longer in wavelength than the incident photon, this being termed a Stokes shift. Raman spectroscopy has a unique temperature dependence where the intensity for the Stokes shift is inversely related to temperature by the Boltzmann distribution given in eqn (1).

$$\frac{I_{\text{anti-Strokes}}}{I_{\text{Strokes}}} = \frac{(v_0 + v_j)^4}{(v_0 - v_j)^4} e^{\left(\frac{-hv_j}{kT}\right)} \qquad (1)$$

Where I = signal intensity, v_0 = laser frequency, and v_j = Raman shift. As temperature increases there are fewer molecules in the ground vibrational state leading to a concomitant loss of signal intensity. The intensity of the Stokes shift can thus act as a monitor for temperature. As an example, a plot of intensity as a function of temperature for a signal arising at 1599 cm^{-1} from a solution of benzaldehyde in hexane is shown in Fig. 1. Increasing the temperature by just 10 °C has a significant effect on the signal intensity.

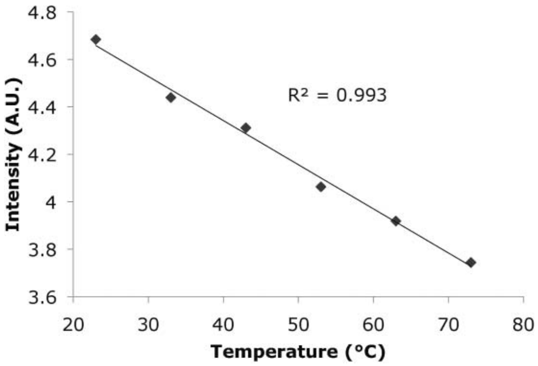
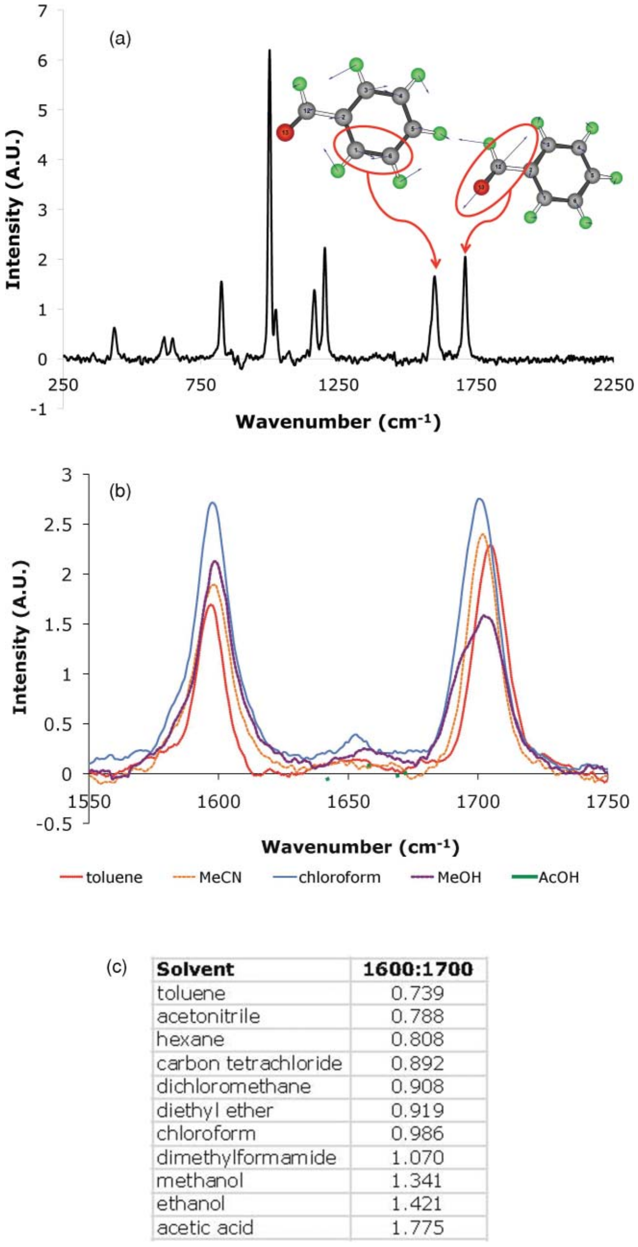


Fig. 1 A plot of Raman signal intensity at 1600 cm^{-1} *vs.* temperature for a 0.80 M solution of benzaldehyde in hexane.

In theory, when performing a reaction using microwave heating, if some molecules are being heated to temperatures exceeding the observed bulk temperature (specific microwave effects), the Raman spectrum should bear this out with a change in signal intensity that is a function of the applied power of the microwave field. Additionally, since Raman spectroscopy has its origins in the polarizability of a molecule, if microwaves can distort the electron cloud of a molecule or couple selectively to a more polar region of a molecule (non-thermal microwave effects), it may be an ideal technique for investigating this phenomenon. This distortion of the electron cloud is clearly seen when examining the Raman spectrum of benzaldehyde in a range of solvents. Non-polar bonds (*e.g.* C=C bonds) when in a polar environment are more easily polarized by the incident irradiation of the Raman laser than when in a non-polar solvent. Conversely, bonds that exhibit a significant dipole moment (*e.g.* C=O bonds) exhibit the opposite phenomenon. These polar bonds are more polarized by the polar solvent, thus becoming less polarizable by the incident light of the laser, ultimately resulting in a loss of signal strength for polar bonds in polar solvents. An overlay of the spectra of 0.40 M solutions of benzaldehyde in a number of solvents is shown in Fig. 2 together with relative ratios of the peak heights for the signals arising at ~1600 cm^{-1} (C=C double bond stretch) and ~1700 cm^{-1} (C=O double bond stretch) for a more extensive range of solvents. As the polarity of the solvent increases the signal at ~1600 cm^{-1} generally becomes more intense and the signal at ~1700 cm^{-1} generally becomes less intense.

Seeing the variation of intensity in the Raman spectra of benzaldehyde in various solvents, we then sought to explore whether microwave irradiation has a similar impact upon the polarizability of a molecule and whether the microwave irradiation could selectively heat one portion of a molecule at the expense of another. We chose a solution of benzaldehyde in hexane as our solvent since hexane has a very low dielectric constant and thus is almost microwave transparent (tan δ, 2.45 GHz, 20 °C = 0.020).[1b] As a result we would expect to exacerbate any effects from selective heating of benzaldehyde molecules. In order



Solvent	1600:1700
toluene	0.739
acetonitrile	0.788
hexane	0.808
carbon tetrachloride	0.892
dichloromethane	0.908
diethyl ether	0.919
chloroform	0.986
dimethylformamide	1.070
methanol	1.341
ethanol	1.421
acetic acid	1.775

Fig. 2 (A) Raman spectrum of benzaldehyde in the region 250–2250 cm^{-1}; Inset: Calculated stretching modes at approximately 1600 cm^{-1} and 1700 cm^{-1}, for benzaldehyde (B3LYP/6–31G(d)). (B) An overlay of the spectra of 0.40 M solutions of benzaldehyde in a number of solvents. (C) Relative ratios of the peak heights for the signals arising at ~1600 cm^{-1} and ~1700 cm^{-1} for a more extensive range of solvents.

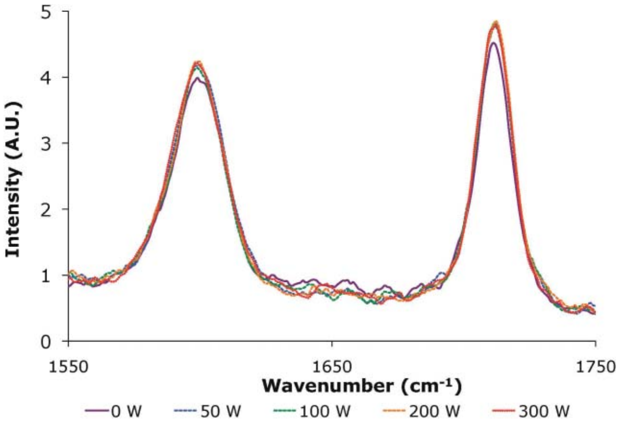


Fig. 3 Raman spectra in the region 1550–1750 cm^{-1} for a refluxing solution of benzaldehyde (0.80 M) in hexane while under microwave irradiation as a function of input microwave power.

to work under isothermal conditions, we performed our trials in an open-vessel set-up at reflux temperature, with nucleation additives and stirring of the solution constantly. This allowed us to maintain a constant bulk temperature while varying the applied microwave power from 0–300 W. The results are shown in Fig. 3.

Looking at the spectra, there is no detectable variation in peak heights or peak ratios as a function of microwave power. At all times the temperature was measured to be 72 °C using an external IR probe. The slight decrease in signal strength at 0 W is due to the cessation of reflux, and hence slightly more dilute concentration of the benzaldehyde under no irradiation. More telling than absolute intensities, however, is the observation that the relative intensities of the peaks do not change as a function of input microwave power. Our data indicate that: (a) the benzaldehyde molecules are always at the same temperature as the bulk solution, (b) there are no signs that microwave irradiation is able to polarize benzaldehyde molecules, and (c) there is no selective coupling of the microwave irradiation with a polar region of benzaldehyde over a non-polar region. This suggests that while the microwave energy may interact with the more polar benzaldehyde molecules more so than with the non-polar hexane solvent, the conversion of electromagnetic energy into kinetic energy is slower than conversion of kinetic energy into thermal energy. This is contrary to previous speculation that heating reactions under microwave irradiation leads to an artificially high population of energetically excited molecules.[19] As a result, our data indicate that the benzaldehyde molecules are not at a temperature greater than that of the bulk; *i.e.* there is not any localized superheating.[20] Instead, the benzaldehyde molecules effectively heat the solvent around them.

To show the generality of our observation we next recorded the Raman spectrum of chlorobenzene in hexane as a function of input microwave power under isothermal operation. Chlorobenzene, like benzaldehyde, contains both polar (C–Cl) and non-polar (C=C) moieties. Again we find no variation in Raman spectrum as the input microwave power is varied (Fig. 4).

Metal-catalyzed reactions facilitated using microwave heating have been the subject of significant research activity.[21] In addition metal complexes would be expected to be highly microwave absorbing and thus could be prime candidates for exhibiting microwave effects. As a result, we decided to turn our attention to probing the effects of microwave irradiation on a transition metal complex. We chose the η^6-arene complex $Cr(CO)_3(\eta^6\text{-}C_6H_5OMe)$, **1**, as our candidate since it is readily prepared from chromium hexacarbonyl and anisole and has a characteristic Raman spectrum. We again wanted to perform our reaction under isothermal conditions at reflux and wanted to ensure that at the temperature we performed our trials there was no decomposition or ligand-substitution reactions of **1**. Chromium arene complexes are readily soluble in ethers and, with a boiling point of 69 °C, diisopropyl ether seemed an excellent candidate as solvent. Using

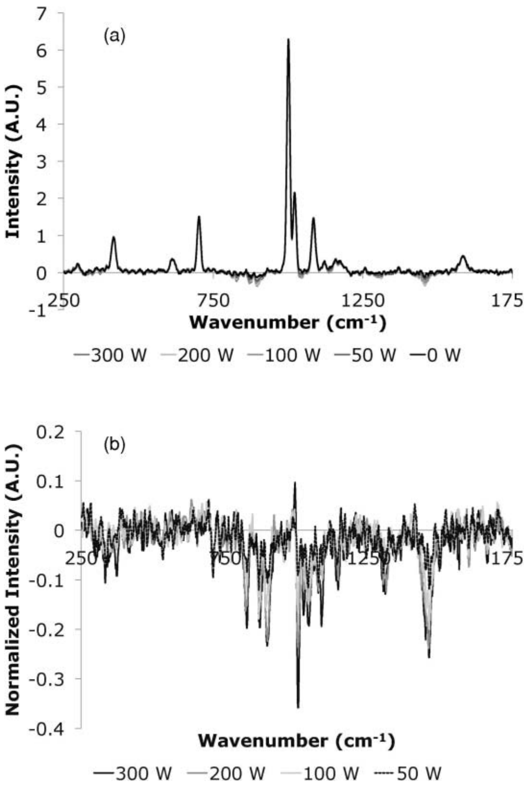


Fig. 4 (A) Raman spectrum in the region 250–1750 cm^{-1} for a refluxing solution of chlorobenzene in hexane while under microwave irradiation. (B) The spectrum at 0 W is subtracted from spectra at different microwave powers showing clearly the fact that there is no variation in signal intensity as a function of input microwave power.

a 0.04 M solution, we again performed trials at a range of applied microwave powers, monitoring using the *in situ* Raman spectrometer. We focused our attention on a signal at 987 cm^{-1} due to the a_{1g}-symmetric ring "breathing" stretch of the anisole ring and at 1900 cm^{-1} due to the CO triple bond stretch of the carbonyl ligands. Our results are shown in Fig. 5

We find no significant variation in intensity of these signals as the input microwave power is varied. This is despite the fact that the solution of **1** in diisopropyl ether is significantly microwave absorbing. Indeed, we were only able to perform the study up to an input microwave power of 100 W before the reflux became too vigorous.

Conclusion

In summary, we have used *in situ* Raman spectroscopy as a tool for probing the effects of microwave irradiation on molecules. Raman monitoring has the advantage of allowing us to probe reaction mixtures on a microscopic level in real time. The results from our studies presented here suggest that the local temperature at a molecular level is no higher than the bulk temperature of the reaction mixture. While the microwave energy may interact with the polar molecules more so than with non-polar ones, the conversion of electromagnetic energy into kinetic energy is slower than conversion of kinetic energy into thermal energy. As a result, the more polar molecules are not at a temperature greater than that of the bulk; *i.e.* there is not any localized superheating. Instead, the polar molecules effectively heat the reaction mixture around them.

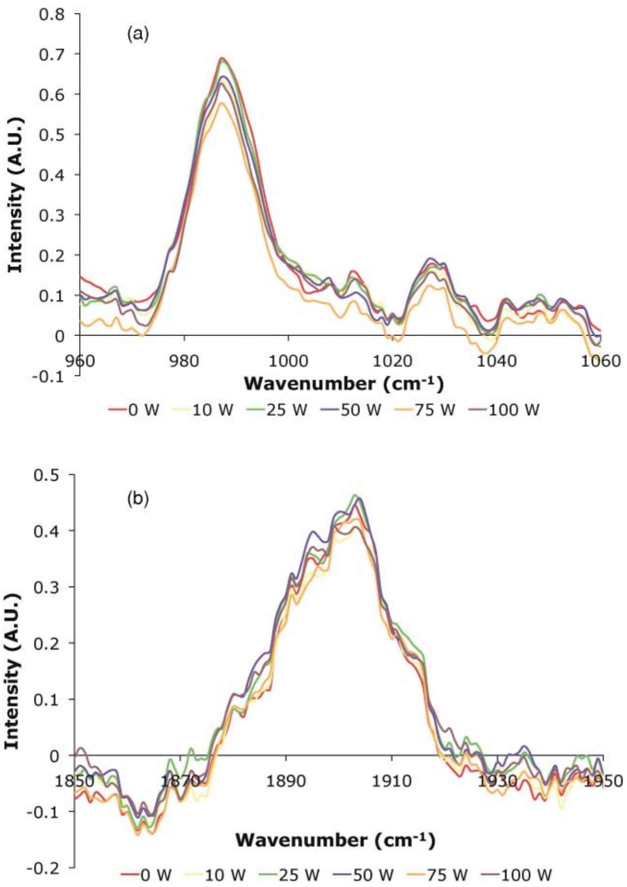


Fig. 5 Raman spectra in the region (A) 960–1060 cm^{-1} and (B) 1850–1950 cm^{-1} for a refluxing solution of $Cr(CO)_3(\eta^6\text{-}C_6H_5OMe)$ (0.05 M) in diisopropyl ether while under microwave irradiation.

Acknowledgements

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