Reducing the NMR line widths of quadrupole nuclei by employing supercritical solvents

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An outline of the use of supercritical solvents in NMR spectroscopy is given, with emphasis on instrumentation and applications. Especially the advantages of the low viscosity of supercritical solvents, resulting in appreciable reductions of the line widths of NMR resonances of quadrupole nuclei ($I > 1/2$), are discussed. The main focus of the review is on the development of transition metal and ^{14}N NMR spectroscopy, to aid the analysis of transition metal complexes. The choices of the supercritical solvent and ligand modifications are discussed in the context of solubility and reduction of the line width.

1 Introduction

Nuclear magnetic resonance in solution plays a key role in chemical research for structural analysis and characterisation of compounds and mixtures of compounds. The introduction of high field high resolution Fourier transform spectrometers has extended the application of NMR to nuclei with low natural abundance and low resonance frequencies (low gyromagnetic ratio γ) for structure elucidation. Magnetic resonance spectroscopy of these nuclei is particularly difficult due to the inherently low sensitivity and problems associated with the low resonance frequencies, such as long relaxation times (T_1 up to minutes *e.g.* ^{103}Rh)[1] and hardware problems often referred to as probe ringing or acoustic ringing resulting in distorted baselines.[2] The introduction of high field spectrometers, multipulse sequences and inverse heteronuclear detection schemes[3] has greatly enhanced the sensitivity with which low γ, low natural abundance nuclei can be measured (*e.g.* ^{27}Al, ^{103}Rh, ^{57}Fe).[1] Employing inverse correlation spectroscopy insensitive nuclei can be measured with sensitivities close to that of protons.

The use of transition metal NMR in organometallic chemistry has greatly increased the knowledge of the relation between chemical shift and structure in coordination complexes and can help in solving structures and elucidating reaction mechanisms.[4] As the chemical shift range of transition metals can be up to several ten thousand ppm and small structural changes in a complex bring about relatively large changes in the transition metal chemical shift, transition metal NMR is a very sensitive analytical tool. However the number of transition metals for which NMR has successfully been employed is limited. Upon inspection of the nuclear properties of the elements one finds that approximately 75% of the nuclei involved have a nuclear spin $I > 1/2$ which characterises these nuclei by their electric quadrupole moment in addition to their magnetic dipole moment. The anisotropic charge distribution of the nucleus, the nuclear electric quadrupole moment, has a very strong interaction with the electric field gradient of the molecule, which is schematically shown in Fig. 1. The interaction of the electric field gradient, caused by the asymmetry of the molecule, with the quadrupole of the nucleus is characterised by the nuclear quadrupole coupling constant χ.[5] The quadrupolar interaction causes rapid reorientation of the magnetic dipole moment of the nucleus as it is coupled to the electric quadrupole moment. The quadrupolar interaction causes (extremely) fast relaxation of quadrupole nuclei resulting in broad resonance lines varying

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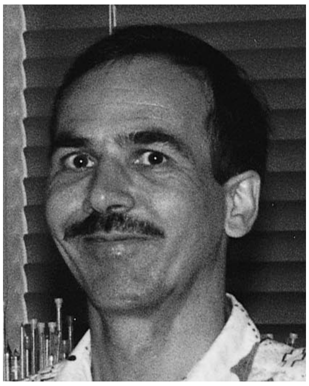

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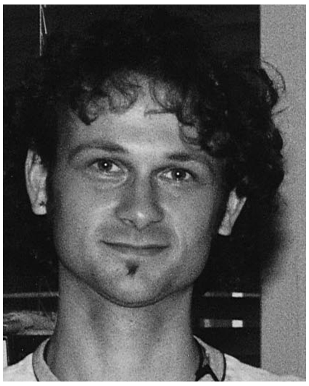

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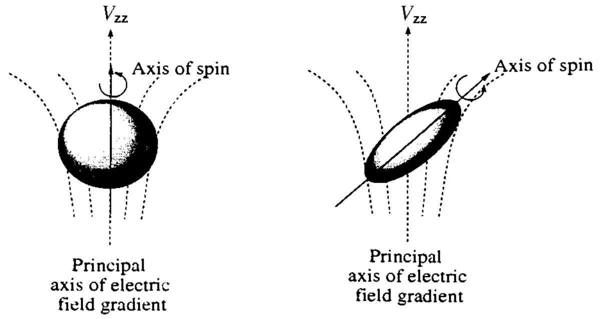

Fig. 1 The interaction of the electric field gradient with the anisotropic charge distribution of a nucleus with $I > 1/2$ causes reorientation of the nucleus (right). The electric field gradient does not interact with the isotropic charge distribution of a nucleus with $I = 1/2$ (left).

from several Hz to several kHz,[5] as follows from the indeterminacy principle of Heisenberg ($\Delta E \times \Delta t \geqslant h/2\pi$).

Due to the short relaxation times of quadrupole nuclei, correlation spectroscopy as developed for the detection of nuclei with low γ and low natural abundance is inappropriate in most cases. Correlation spectroscopy is based on the correlation of insensitive nuclei to more sensitive nuclei *via* scalar couplings.[3] As the correlation is brought about in evolution times proportional to $1/nJ$ (where n is an integer and J the scalar coupling) these techniques cannot generally be used for the detection of quadrupole nuclei as the magnetisation of the quadrupolar nucleus has in most cases decayed before sufficient magnetisation has been transferred to the more sensitive nucleus. The few exceptions are the quadrupole nuclei with a small quadrupole moment (*e.g.* ^{2}H, ^{6}Li) or nuclei arranged in a symmetric environment (*e.g.* ^{53}Cr in $Cr(CO)_6$ and ^{61}Ni in $(P(t\text{-}Bu)_3)Ni(CO)_3)$[1] resulting in small values of χ.

In order to render NMR spectroscopy of quadrupolar nuclei in solution feasible, a different approach has to be taken. In eqn. (1) the relaxation of a nucleus with $I > 1/2$ is given,[5] where I

$$\Delta\nu_{\frac{1}{2}} = \frac{1}{\pi T_1} = \frac{1}{\pi T_2} = \frac{3\pi}{10}\left(\frac{2I+3}{I^2(2I-1)}\right)\left(1+\frac{\eta_s}{3}\right)(\chi)^2\tau_c \qquad (1)$$

denotes the nuclear spin, η_s is the asymmetry parameter of the complex, χ is the nuclear quadrupole coupling constant and τ_c is the rotational correlation time of the molecule in solution. Nuclei with a higher nuclear spin will thus show narrower resonance lines as will nuclei in complexes with higher symmetry (low η_s and low χ). Changes in the asymmetry parameter will only result in small changes in the relaxation rates as $0 \leqslant \eta_s \leqslant 1$, this parameter is therefore frequently omitted. For a given nucleus in a given compound, all parameters except for τ_c are fixed. The rotational correlation time τ_c is a measure of the tumbling speed of a molecule in solution, it is the time it takes a molecule to rotate through an angle of one radian. Hence short correlation times imply fast molecular motion. The correlation time τ_c depends on the temperature and the bulk viscosity (η_v) of the solvent according to the Stokes–Einstein–Debye approximation, see eqn. (2).[5,6]

$$\tau_c = A\frac{\eta_v}{kT} + \tau_0 \qquad (2)$$

From eqn. (1) it can be seen that the line width of quadrupole nuclei is inversely proportional to T_1 and T_2. Decrease of τ_c, hence increase of T_1 will thus lead to a decrease of the line width of quadrupole nuclei, which facilitates detection of overlapping signals, scalar couplings and increases the signal to noise ratio. This is well known from resolved couplings in *e.g.* ^{1}H-NMR spectra of amines where the 1:1:1 triplet of $-NH_2$ is resolved when increasing the temperature. A reduction of the line width of a resonance broadened by quadrupolar relaxation can thus be accomplished by either increasing the temperature of the solution or by decreasing the bulk viscosity of the solvent. The latter is demonstrated by measuring the line width of a quadrupolar nucleus in acetone (η_v = 0.316 cP; T = 25 °C),[7] which will show a (theoretical) line width reduced to about a third of the line width in pyridine (η_v = 0.974 cP; T = 20 °C).[7]

As supercritical (sc) solvents have bulk viscosities an order of magnitude lower[8] (η_v(sc CO_2, 31 °C; 73.8 bar) = 0.032 cP, η_v(benzene at 30 °C) = 0.564 cP)[7] than classic organic solvents, supercritical solvents appear to be the solvents of choice for the reduction of line widths of quadrupole nuclei, and a theoretical reduction of an order of magnitude should be possible.

The use of supercritical fluids in NMR spectroscopy has been demonstrated by Jonas *et al.*[9,10] for self-diffusion experiments in supercritical ethane and water. It was found that the diffusion coefficients decrease with increasing density of the supercritical fluid, as a result of higher bulk viscosity. Later, small organic molecules and transition metal complexes have been measured in high pressure NMR probes.[11,12] Large reduction factors $F_{1/2}$ ($F_{1/2}$ = ratio of line width under normal conditions to line width in supercritical solution) were found for ^{14}N and ^{33}S resonances in supercritical solutions containing nitro compounds[13] and heterocycles containing nitrogen and sulfur.[12] The line widths were compared to those of the pure samples and acetone solutions, the reduction factor $F_{1/2}$ was found to vary from 2.5 up to 11.

The first example in which supercritical solvents have been employed in pressurised NMR tubes for the reduction of quadrupolar broadened resonance lines involved gases (N_2O, NH_3) dissolved in supercritical CO_2 and supercritical ethylene as shown in Fig. 2.[14] For these molecules, gaseous at ambient temperature and pressure, slight improvements in the resolution of their ^{14}N and ^{17}O resonances were observed at temperatures close to the critical temperatures of the solvents employed. The improvements were only modest as the rotational correlation times of the molecules do not change tremendously compared to a solution in organic solvents (hexane) or supercritical solutions, since dissolved gases already have low τ_c due to their small moment of inertia and small molecular volume.

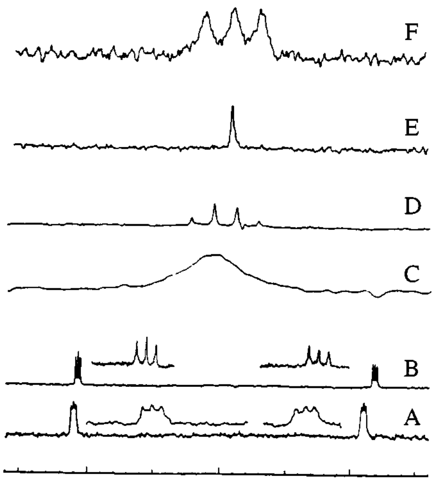

Fig. 2 A, ^{14}N spectrum of hexane saturated with nitrous oxide at 1 atm, 28 °C; B, ^{14}N spectrum of supercritical nitrous oxide at 40 °C; C, ^{14}N spectrum of 7 M aqueous NH_3; D, ^{14}N spectrum of 0.5 M NH_3 in supercritical ethene at 28 °C; E, ^{17}O spectrum of subcritical carbon dioxide at 28 °C; F, ^{17}O spectrum of subcritical nitrous oxide. Reproduced with permission from *J. Am. Chem. Soc.*, 1985, **107**, 3733; © 1985 American Chemical Society.

2 Supercritical solvents

The supercritical state of a compound (or of a mixture of compounds) is characterised by the critical pressure (P_c) and critical temperature (T_c) above which compression of the fluid does not lead to condensation.[8] No phase boundary from gas to liquid is crossed, as can be seen from the *ρPT*-diagram of CO_2 in Fig. 3. The supercritical state combines fluid like densities with gas like viscosities. Close to the critical point small changes in the temperature and pressure cause large changes in the properties of the supercritical fluid, especially the density and the viscosity change dramatically in this region. The properties of supercritical fluids can thus be 'tuned' between certain limits simply by varying temperature and pressure of the solvent. Upon passing the critical point, the bulk viscosity drops steeply and the density at the critical point is approximately half that of the liquefied gas. Especially the low viscosity is of great importance in the study of molecular motions and in the application of supercritical fluids in NMR studies on quadrupole nuclei (eqns. (1) and (2)).

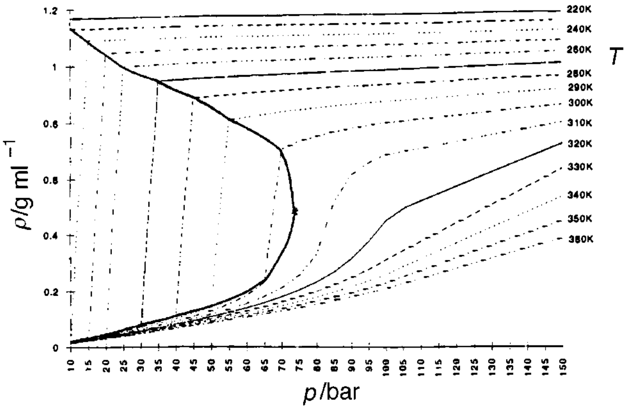

Fig. 3 *ρPT*-diagram of CO_2. Data taken from *International Thermodynamic Tables of the Fluid State*, Vol. 3, *Carbon dioxide*, Ed. S. Angus, Butterworths, London, 1976.

In Table 1 several substances with their critical data are given.[7] It is clear that a wide range of critical temperatures and pressures is possible and it is not easy to quantify the factors which are important in determining the critical constants. The effect of polarisability and dipole moment on the critical temperature becomes somewhat clearer from Table 2 in which the critical points of a series of halogenated methanes are given. Going from CH_4 to CF_4 to CCl_4 it can be seen that the critical temperature increases dramatically whereas the critical pressure for these three compounds is about 40 bar. The increase of the polarisability[15] from H < F << Cl (CH_4: α = 2.60 Å^3; CF_4: α = 2.85 Å^3; CCl_4: α = 10.5 Å^3, where α is the polarisability) results in an increased intermolecular interaction raising the critical temperature. The same applies for the series $ClCF_3$ < Cl_2CF_2 < Cl_3CF where the dipole moment of the molecules is approximately constant whereas the critical temperature increases from 28.9 °C to 198.1 °C. In the series CH_4, FCH_3, F_2CH_2, F_3CH (CH_4: α = 2.60 Å^3; FCH_3: α = 2.61 Å^3; F_2CH_2: α = 2.73 Å^3; F_3CH: α = 2.80 Å^3) the increase of the dipole moment results in an increase of the critical temperature CH_4 < FCH_3 < F_3CH < F_2CH_2 from −82.6 °C to 78.5 °C whereas the pressure increases only by 12.8 bar from 46.0 bar to 58.8 bar. This demonstrates that the polarisability of a solvent molecule is of great importance in determining the critical temperature, whereas the critical pressures of this class of compounds lie in a rather narrow range (37.4–66.8 bar). Unfortunately, polarisable solvents are generally good solvents for organic and organometallic compounds (Cl_2CH_2, Cl_3CH) but have intrinsically high critical temperatures (see Table 2).

Table 1 Selected compounds with their critical temperature (T_c), critical pressure (P_c), critical molar volume (V_c) and dipole moment (μ)

Compound	T_c/°C	P_c/bar	V_c/cm^3 mol^{-1}	μ/Debye
H_2	−240.2	12.9	65	0
N_2	−146.9	33.9	90	0
Ethylene	9.2	50.4	131	0
Xe	16.6	58.4	118	0
CO_2	31.0	73.8	94	0
SF_6	45.5	37.7	199	0
H_2S	100.1	89.4	99	0.97 ± 0.01
Me_3N	159.6	40.9	254	0.61 ± 0.01
CS_2	278.9	79.0	173	0
H_2O	374.0	220.6	56	1.85 ± 0.01

Table 2 Homologous series of freons with their critical temperature (T_c), critical pressure (P_c), critical molar volume (V_c) and dipole moment (μ)

Compound	T_c/°C	P_c/bar	V_c/cm^3 mol^{-1}	μ/Debye
CH_4	−82.6	46.0	99	0
CF_4	−45.6	37.4	140	0
CCl_4	283.5	45.2	276	0
H_3CF	44.7	58.8	113	1.85 ± 0.01
H_2CF_2	78.5	58.3	121	1.97 ± 0.01
HCF_3	26.2	48.6	133	1.65 ± 0.01
$ClCF_3$	28.9	38.7	180	0.50 ± 0.01
Cl_2CF_2	111.8	41.4	217	0.51 ± 0.05
Cl_3CF	198.1	44.1	248	0.45 ± 0.05
$ClCH_3$	143.1	66.8	139	1.87 ± 0.01
Cl_2CH_2	236.9	61.0		1.60 ± 0.03
Cl_3CH	263.3	54.7	239	1.01 ± 0.02

For application as a low viscosity solvent in NMR experiments, to reduce quadrupolar broadened lines, a supercritical fluid should meet several criteria: the viscosity should be considerably lower than classical organic solvents and the critical temperature and pressure should be within reasonable limits to ensure relatively easy handling and routine operation. Importantly, the solvent should solubilise a wide variety of organic and organometallic compounds preferably in concentrations up to 0.1 M and it should be inert. It is virtually impossible to find a supercritical solvent which meets all these demands. For high solubility a polar and polarisable solvent would be required, but generally solvents meeting this requirement have (extremely) high critical temperatures, which for many solute compounds of interest will exceed their decomposition temperature. Furthermore NMR experiments at high temperatures will require the use of high temperature probes. The first solvent of choice is CO_2 as it is non-toxic, it has low T_c and P_c, it is relatively inert (transition metals complexes containing CO_2 are known[16]), readily available, and it is polarisable[15] (CO_2: α = 2.63 Å^3), but also CHF_3, $ClCF_3$, H_2CF_2 seem to have promising features as supercritical solvents for application to NMR of quadrupole nuclei. It is known[11–14, 17–21] that several apolar and volatile organic and organometallic complexes dissolve reasonably well in supercritical CO_2, but the solubility of polar non-volatile organic and organometallic compounds in CO_2 is limited. Organic solvents may have to be added as modifiers to increase the solubility in supercritical fluids, or other supercritical solvents (*e.g.* halogenated hydrocarbons) may have to be used. Alternatively, derivatives of compounds of interest with higher solubility in supercritical fluids have to be used as model compounds.

3 Instrumentation

Note: When performing experiments under high pressures one should always take appropriate safety measures, the person working with high pressure tubes may never be directly exposed to a pressurised cell. Pressurising and handling of the high pressure cell should under all conditions be done in a protective polycarbonate vessel.[22] The individual scientist should verify that newly designed high pressure equipment used meets the necessary safety requirements.

For NMR experiments in supercritical fluids it is of vital importance to have proper equipment to measure a wide variety of nuclei in pressurised sample containers. Equipment for the study of reactions involving gas–liquid interfaces is readily available in several laboratories (reviewed in refs. 22 and 23) and can easily be adapted for NMR studies in supercritical fluids. Two types of high pressure NMR systems have been developed, the high pressure *probes* and the high pressure *cells* which are shown in Fig. 4a and b, respectively.[11,24] Recent developments in high pressure probes employ toroid cavity detectors[25] with which high temperatures and pressures are possible. Conveniently the RF field gradients can be used for imaging and measurements of diffusion rates.

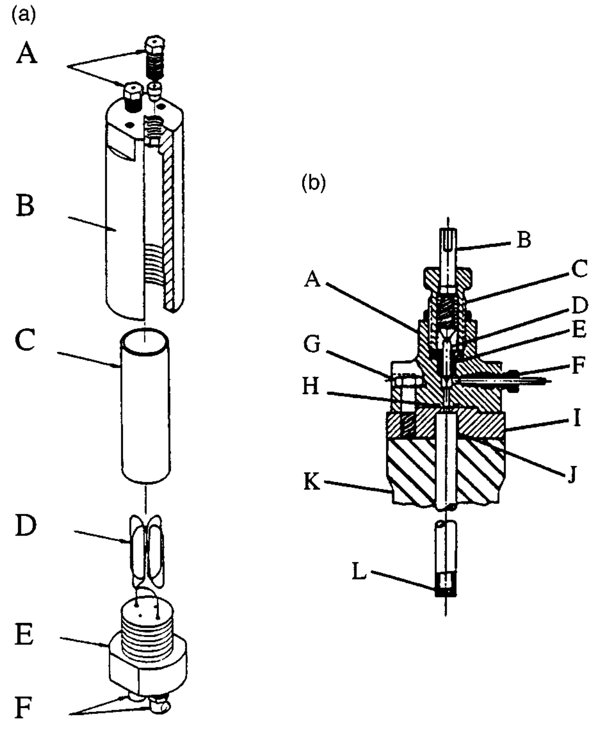

Fig. 4 (a) A, Gas connections; B, reactor body (1 1/8' od); C, glass liner; D, toroid coil; E, bottom plug; F, RF feedthroughs. Reproduced with permission from *J. Magn. Reson.*, 1989, **85**, 150; © 1989 Academic Press, Inc. (b) Ti alloy valve and sapphire tube assembly: A, valve body; B, valve stem drive handle; C, stem drive and packing gland; D, non-rotating stem; E, packing assembly; F, gas inlet port for 1/16-inch tubing; G, assembly screw (total of four); H, Viton O-ring seal; I, tube mounting flange; J, epoxy sealant; K, spinner turbine; L, sapphire tube. Reproduced with permission from *J. Magn. Reson.*, 1985, **63**, 388; © 1985 Academic Press, Inc.

The most convenient systems for multinuclear applications are the high pressure cells, these can be operated in commercial 5 or 10 mm probes retaining the full multinuclear capabilities of the spectrometer. Typically, sapphire tubes are employed with brass or titanium valves as these materials are non-magnetic and light[23,24] enabling operation of the spectrometer in the spinning mode. Importantly, Ti/Al/V (90/6/4) has the same coefficient of thermal expansion as sapphire enabling variable temperature experiments over a wide temperature range. Thick walled glass NMR tubes have been used,[14] however these have proven insufficiently reliable for an extended period of time at higher temperatures and pressures.

Recently a new type of high pressure NMR cell has been developed[26] in which a glass capillary is folded in a commercial 5 mm glass NMR tube. Pressures up to several kbar are possible with the capillary cell, but the small amount of compounds which can be introduced in the coils poses a severe limitation to the detection of insensitive nuclei. A great advantage of this cell is the safe operation up to extremely high pressures considering the high ratio of wall thickness to vessel diameter. Importantly, in case of rupture of the capillary only a small volume of the supercritical fluid expands, implying no danger to the experimentalist, nor the instrument.

A system based on the sapphire tubes which is also capable of varying pressure and temperature independently has been designed by Grant *et al.*[27] The high pressure cell is devised such that only the part which resides in the thermostated coils contains a gaseous or supercritical sample. This design avoids temperature gradients which might occur in the NMR tube and thus limits convection in the tube as a result (estimates of the temperature gradient in the tube vary from 4 °C to 9 °C).[28] The system is connected to pressurising equipment *via* a capillary, unfortunately filling and depressurising of the cell is a rather time consuming process (4 h for all high pressure compartments to equilibrate to atmospheric pressure).

Recently, we have developed a high pressure NMR cell[29] which is based on the high pressure NMR cell designed by Roe,[24] modified with a 10 mm od, 8 mm id sapphire tube.[22] Fitted into a newly designed titanium pressure head, a titanium high pressure sensor enables the continuous measurement of the pressure in the cell during the NMR experiment. This modification is of vital importance to continuously determine the state of the (supercritical) solution[8] at all stages of an NMR experiment. A schematic representation of this modified high pressure cell is shown in Fig. 5. An electrical signal proportional to the pressure is transmitted *via* a copper wire through the magnet bore and the final recording is accurate to ±0.05 bar (between 1 and 350 bar). The great advantage of this system is its flexibility as no high pressure equipment is needed in the NMR laboratory besides the cell itself, a polycarbonate safety vessel and a pressure readout.

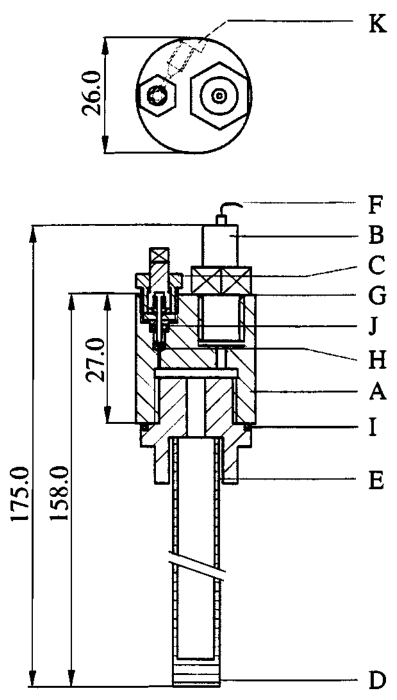

Fig. 5 A, Titanium valve assembly; B, titanium pressure sensor; C, needle valve; D, sapphire tube; E, glue clearance; F, copper wire; G, Viton O-ring; H, Vespel O-ring; I, Teflon O-ring; J, Viton O-ring; K, gas inlet.

4 Small organic molecules in supercritical solvents

In Fig. 6a and b the ^{17}O chemical shift changes of CO_2 at natural abundance are shown upon heating a sample of liquid CO_2 from below the critical temperature to well above T_c, the densities of the resulting supercritical samples are 0.61 g ml^{-1} and 0.40 g ml^{-1}, respectively. We found that the reduction of the density of the CO_2(l) sample results in a chemical shift change of the

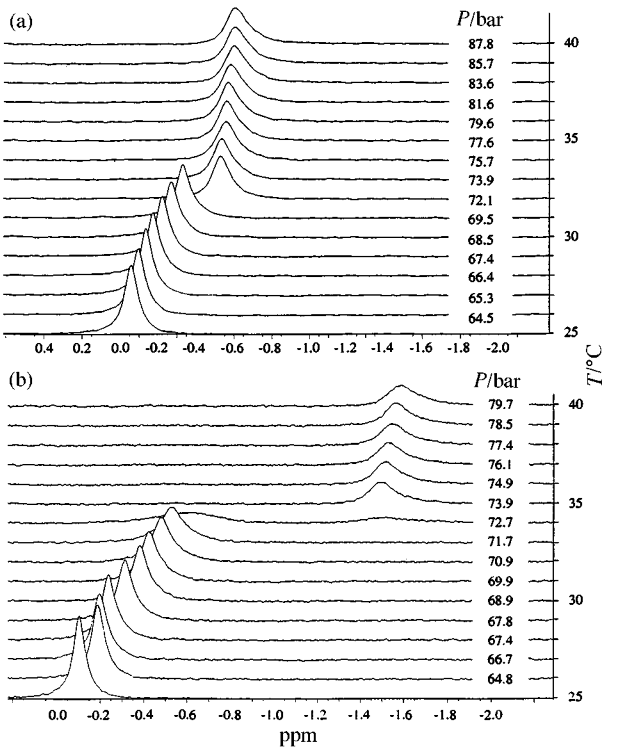

Fig. 6 The chemical shift changes of the ^{17}O resonance of CO_2 at natural abundance as measured in the new sapphire high pressure cell, (a) density 0.61 g ml^{-1}, (b) 0.40 g ml^{-1}.

^{17}O resonance to lower ppm value.[29] The chemical shift change is best seen close to the critical point as the changes in density with small temperature changes are most pronounced in this region, see Fig. 3. At densities just above the supercritical density (ρ_c) the change in chemical shift of the ^{17}O resonance is -1 ppm. For densities below ρ_c, also a significant change in the chemical shift of the ^{17}O of about -1.5 ppm occurs between 33–35 °C. In such cases we observe near 34 °C two signals, which are attributed to the coexistence of two phases in the region of the tube between the coils. The chemical shift changes are not observed in a tube which is completely filled with liquid CO_2 as the density of the supercritical phase is equal to the initial liquid density. From these experiments it is clear that the ^{17}O chemical shift of CO_2 can be used as a monitor, to indicate whether the supercritical state has been reached in this particular setup. The phenomenon is most pronounced close to and below the critical density.[29]

In a solvent such as benzene, even at 75 °C, the ^{14}N signals of a mixture of NEt_3 and NPr_3 are not resolved due to the dominant quadrupolar relaxation mechanism. In supercritical CO_2, the quadrupolar relaxation rate is reduced due to the decrease of the bulk viscosity upon passing the critical point, as discussed. Hence, reduced rotational correlation times lead to an increase of the T_1 of the quadrupolar nuclei, resulting in an appreciable reduction of the line width. This can be seen in Fig. 7 from the increased resolution of the ^{14}N spectrum at 45 °C and 82 bar of a mixture of Me_3N (‡), Et_3N (†), Pr_3N (*).[29] It can be seen that the signal to noise ratio decreases due to the decrease of the amount of material between the RF coils as the supercritical fluid spreads the amine mixture throughout the whole cell. The ^{17}O resonance of the CO_2 of the amine solution is shown next to the ^{14}N spectrum. The traces (*T*: 40–45 °C; *P*: 76–82 bar) where the chemical shift of the ^{17}O resonance changes coincide with the traces where the resolution in the ^{14}N spectrum increases. This indicates that the previously discussed dependence of the ^{17}O chemical shift of CO_2 on the state of the solvent is indeed reliable.

The theoretical reduction expected from the difference in viscosity of the supercritical solvent compared to organic solvents was, however, not met in the aforementioned cases. A lower limit for τ_c can be attributed to the 'free rotor' limit of the molecules under investigation. As the τ_c in gases is determined by the moment of inertia,[6] additional interactions from the denser supercritical solvent (the local density augmentation, the clustering of solvent molecules around the solute[29–31]) will add to the rotational correlation time. Hence, resonance lines in solution will be broad compared to gaseous samples, and solvents with higher solvent–solute interactions (van der Waals, H-bonding, Coulomb, π-stacking) will show broader lines compared to solvents with a low solvent–solute interaction.

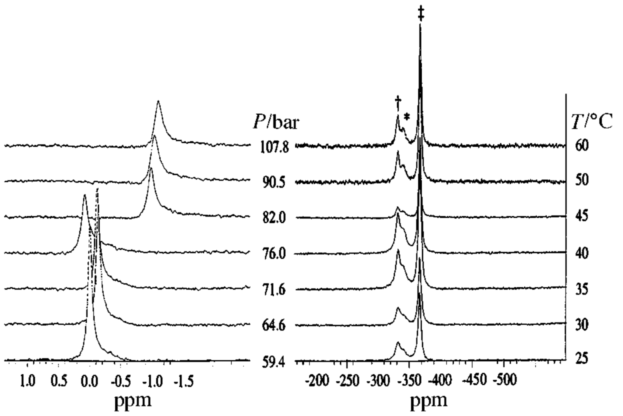

Fig. 7 The ^{17}O (left) and $^{14}N\{^1H\}$ (right) resonances of a mixture of three amines in CO_2 (*d* = 0.56 g ml^{-1}) upon heating the solution from room temperature to well above the critical point. Me_3N (‡), Et_3N (†), Pr_3N (*).

Jonas *et al.* pointed out that the major problem in employing supercritical solvents for reducing line widths of quadrupolar broadened lines is the right balance between signal intensity determined by the concentration of the solution and the reduction of the line width. For good solubility a high density of the supercritical solvent would be needed, which implies a higher viscosity of the solvent resulting in less reduction of the line width. This follows from the reduced diffusion rates found for the self diffusion in supercritical water and ethene at higher supercritical densities.[9,10] This effect has been demonstrated for nitrobenzene in supercritical ethene by Evilia *et al.*[13] and for methyl manganese pentacarbonyl in supercritical ethene by Jonas *et al.*[12]

5 Solubility in supercritical solvents

Especially for high molecular weight, non-volatile compounds with strong intermolecular interactions (*e.g.* van der Waals, π-stacking, Coulomb and H-bonding) the solubility in supercritical solvents may be very poor. This may be overcome by two main approaches, the right choice of solvent to increase solubility or the modification of compounds (synthesis of derivatives, *e.g.* branched alkyl or fluorocarbon tails, to obtain model compounds for the study in supercritical solvents). Possible solutions to the solubility problem will be briefly discussed.

Only if the factors affecting the solubility of chemical compounds in supercritical media are well understood, will we be able to employ NMR on quadrupole nuclei in supercritical solvents to its full extent as a method which can be (routinely) applied as an analytical tool. Very little quantitative data are available concerning the solubility and phase behavior of organic and organometallic compounds dissolved in supercritical solvents, and the studies performed are limited almost exclusively to sc CO_2 solutions. Volatile compounds (gases) dissolve very well in supercritical media,[14] *e.g.* the concentration of dihydrogen in sc CO_2 can be up to 12 M while in n-heptane saturated with H_2 the concentration is 1.8 M.[11] The real challenge lies in solubilising non-volatile polar molecules. One of the few detailed NMR studies concerning the solubility of an organic compound was performed by Jonas *et al.*[32] The solubility of naphthalene in near and supercritical CO_2 was studied between 50 and 58.5 °C and from 120 to 500 bar and was found to vary from 0.06 M (at 58.5 °C and 120 bar) to 1.18 M (at 58.5 °C and 500 bar) due to the increase of the density of the CO_2 at higher pressures. Generally only small amounts of transition metal complexes dissolve in supercritical CO_2. Recent studies concerned with the extraction of heavy metals as a waste processing method[17,33] showed concentrations in the order of 10^{-7}–10^{-5} M with one exception of 0.1 M.[17] Although concentrations in the order of 10^{-7}–10^{-5} M are sufficient for the photochemical synthesis of complexes with weakly coordinating molecules (*e.g.* C_2H_4[18]) the concentrations are orders of magnitude too low for NMR spectroscopy on inherently insensitive quadrupole nuclei.

The use of fluorinated ligands has proven successful for the application of transition metal catalysis in supercritical CO_2. The introduction of a lipophilic fluorinated anion ($[B(3,5\text{-}(CF_3)_2C_6H_4)_4]^-$, ($BAr_f$)) in the rhodium catalysed hydrogenation of prochiral α-enamides resulted in increased solubility and also showed increased enantiomeric excess compared to organic solvents.[19] Ligands designed for catalysis in supercritical CO_2 generally consist of triphenylphosphine based ligands, modified with 'ponytails' of fluorinated alkyl chains.[20] This type of ligand is known from catalysis in biphasic systems in which a compound with 'ponytails' dissolves in perfluoroalkanes but not in the hydrocarbon phase whereas the products do dissolve in the hydrocarbon phase.[34] Heating the system will cause mixing of the perfluorinated phase and organic phase for catalysis, which will separate again upon cooling. As the introduction of perfluoroalkanes in existing ligands has proven successful in catalysis in supercritical CO_2 it might prove to be a successful approach for NMR in supercritical fluids on transition metal complexes.

6 Transition metal complexes in supercritical solvents

Only a few examples are known where transition metal NMR on quadrupole nuclei in supercritical solvents has successfully been applied. The first example was given by Jonas *et al.*, who measured the ^{55}Mn resonance of $MeMn(CO)_5$ in supercritical ethene.[12] The ^{55}Mn line width at half height decreased from 1620 Hz in acetone at room temperature to 280 Hz in supercritical ethene (P = 60 bar, T = 62 °C), a reduction by a factor of $F_{1/2} = 5.8$. The use of supercritical ethene might prove to be a problem as a solvent for transition metal complexes as ethene is known to coordinate strongly to various transition metals and to substitute other ligands. Supercritical ethene has successfully been used for the photochemical synthesis of labile ethene complexes, which was studied by *in situ* NMR employing the fused silica capillary NMR cell.[18] The pressure dependence of the ^{55}Mn shift for several cyclopentadienyl manganese carbonyl complexes has been described by Waugh and Lawless; the ^{55}Mn resonance frequency was found to shift to lower frequency upon raising the pressure of a solution in supercritical xenon.[35] These changes were attributed to the changes in bulk susceptibility of the xenon at higher densities. In the same review the observation of the β-N of the complex $CpMn(CO)_2N_2$[35] in supercritical xenon is presented, this is the only known ^{14}N resonance of a transition metal complex.

Rathke *et al.* measured several transition metal nuclei in a high pressure probe. ^{55}Mn NMR of $Mn_2(CO)_{10}$ was measured as well as ^{187}Re NMR of $Re_2(CO)_{10}$. For the ^{187}Re resonance a line width of 7.2 kHz was observed, but no signal could be observed in $CDCl_3$, clearly demonstrating the advantage of supercritical fluids for the detection of quadrupolar transition metal nuclei.[36] For ^{59}Co, the resonance of $Co_2(CO)_8$ was obtained in supercritical CO_2; a line width at half height of 30.0 kHz was observed in benzene-d_6 at 25 °C and of 5.1 kHz in supercritical CO_2 at 32 °C, corresponding to a reduction factor of $F_{1/2} = 6$.[11] A reaction studied by ^{59}Co NMR by Rathke *et al.* was the cobalt catalysed hydroformylation of propylene in supercritical CO_2 where the reduction of the ^{59}Co line width made it possible to observe the various species present in the supercritical solution. This elegantly demonstrates the advantages of sc CO_2, a high concentration of H_2 and a low viscosity enabling the detection of an intermediate in the cobalt catalysed hydroformylation. Especially the possibility to observe the $(CO)_5CoC(O)CH_2CH_2CH_3$ resonance in supercritical CO_2 underscores the importance of the application of supercritical fluids, see Fig. 8.

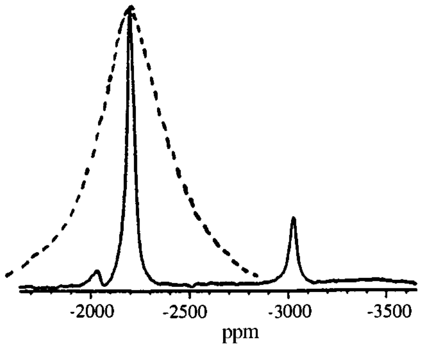

Fig. 8 ^{59}Co NMR spectrum of catalytic intermediates during the hydroformylation of propene at 80 °C in supercritical CO_2 (solid line), and the ^{59}Co resonance of $Co_2(CO)_{10}$ in benzene-d_6 (dashed line). Adapted with permission from *Organometallics*, 1991, **10**, 1350; © 1991 American Chemical Society.

The advantage of the application of supercritical solvents for the detection of quadrupolar transition metals has recently also been demonstrated for ^{53}Cr.[29] In our investigation, the ^{53}Cr NMR of a solution (0.05 M) of $(CO)_5Cr{=}C(NH_2)(Ph)$ in CO_2(sc) + 5% acetone-d_6 results in a ^{53}Cr line width of 430 Hz ± 5 Hz (T = 323 K, 14 h measuring time). Importantly, at the same sample concentration no signal could be obtained in acetone-d_6 after 14 hours. A concentrated sample of 0.4 M in acetone-d_6 had a line width of $\Delta\nu_{1/2} = 1150$ Hz. Although not many results have so far been published, our experience thus far underscores the aptness of the methodology for measuring NMR of quadrupolar transition metals at relatively low concentrations in supercritical solvents. Although primary nitrogens are known to form carbamates in the presence of CO_2 no changes in the ^{53}Cr chemical shift could be observed.

Recently, the ligand displacement of cycloocta-1,5-diene by ethene in (cycloocta-1,5-diene)dimethylplatinum in supercritical ethene was studied by ^1H-NMR, by Yonker *et al.*[21] up to pressures of 200 bar. In the same publication, the ^{19}F chemical shift dependence of $La(fod)_3$ and $Pr(fod)_3$-d_{27} (fod = 6,6,7,7,8,8,8-heptafluoro-2,2-dimethyloctane-3,5-dione) in a binary system of CO_2 and methanol up to 1 kbar was described. Later, they studied the photolysis of $CpMn(CO)_3$ and $MeCpMn(CO)_2$ in supercritical ethene by proton NMR and were able to observe the formation of ethene substituted complexes.[18]

7 Future perspective

So far only a limited number of NMR studies have been performed involving transition metal complexes in supercritical fluids and even less concerning the reduction of quadrupolar broadened resonance lines in NMR spectra. Especially the problems associated with the solubility of organic and organometallic compounds in supercritical fluids pose a substantial problem for the routine application of supercritical solvents in NMR spectroscopy. As the interest in catalysis in supercritical fluids (and CO_2 in particular) grows, there is a concomitant rapid development in ligand design aimed at increasing the solubility of a wide variety of polar metal complexes in supercritical fluids. These ligands will certainly be employed in NMR studies on quadrupolar transition metals of (model) compounds. For the development of routine applications of NMR in supercritical solvents (for the reduction of line widths of quadrupole nuclei and monitoring of reactions) the sapphire cells are invaluable tools as these systems can be employed in any spectrometer retaining the full RF capabilities as well as gradient selection. New solvents will be tested and applied, for which the delicate balance between a good solubility of various compounds and a low critical temperature is the main concern.

The use of supercritical solvents for NMR studies of transition metal compounds will expand to less accessible transition metal nuclei by common NMR techniques (*e.g.* ^{99}Ru, $^{47/49}$Ti, ^{53}Cr, ^{61}Ni, ^{91}Zr). Therefore, the use of supercritical fluids may develop into a useful analytical tool for future work in organometallic chemistry.

8 Conclusions

Catalysis and NMR in supercritical solvents are rapidly expanding research topics. The use of low viscosity solvents in the reduction of quadrupolar broadened resonance lines of organic and organometallic compounds has been shown to result in appreciable reductions of line widths in NMR spectra of a variety of quadrupole nuclei. Line widths are generally reduced by a factor of three to six but reductions by a factor of 11 or more are possible depending on the ratio of the bulk viscosity of the classic solvent and the applied supercritical solvent and the temperature. The application of supercritical solvents makes it possible to observe resonances of nuclei which are too broad under normal conditions (^{187}Re) or at low concentrations (^{53}Cr). The possibility to distinguish various species in a catalytic reaction mixture by means of ^{59}Co NMR, or in a mixture of amines by ^{14}N NMR demonstrates the power of the technique. With the growing interest in chemistry in supercritical solvents and the need for detailed studies of transition metal complexes by means of transition metal NMR, the development of HP-NMR equipment and ligands will continue. The use of NMR techniques in supercritical solvents may become an additional, valuable tool for studies in organometallic and coordination chemistry.

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