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# Effect of fluorine substitution, pressure and temperature on the tautomeric equilibria of acetylacetonate $\beta$-diketones

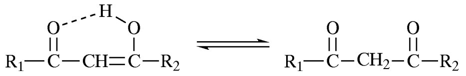
**S. L. Wallen,[a] C. R. Yonker,[a] C. L. Phelps[b] and C. M. Wai[b]**

[a] *Chemical Sciences Department, Pacific Northwest National Laboratory,† Richland, WA 99352, USA*

[b] *Department of Chemistry, University of Idaho, Moscow, ID 83843, USA*

The equilibrium between the keto and enol tautomers of acetylacetone, trifluoroacetylacetone and hexafluoroacetylacetone in the neat liquid state and dissolved in supercritical fluid carbon dioxide have been studied, as a function of pressure and temperature, by $^1H$ NMR. This allows determination of the thermodynamic parameters, $\Delta H$ and $\Delta S$, for the keto–enol equilibrium. The observed trends are well correlated with extraction results for this class of compounds.

Fundamental experiments concerning solvation dynamics and fluid structure in supercritical fluids will inevitably lead to a wider range of applications of supercritical fluid technology and will continue to offer challenges to theoreticians involved in condensed matter research. The application of fluids to the extraction and purification of metals has recently been shown to be a viable alternative to typical liquid-solvent-based systems.[1–6] Achieving solubility of the metal chelating agent in the supercritical fluid is imperative to further development of a fluid based metal extraction strategy. Two of us initially discovered that fluorination of a ligand could enhance the solubility of a ligand in supercritical $CO_2$ by several orders of magnitude.[1,6] Several extraction methods for the complexation of metals, including lanthanides and actinides, in supercritical $CO_2$ were subsequently developed.[2–5] Two ligands successfully used in these studies were the fluorinated $\beta$-diketones trifluoroacetylacetone (TFA: $R_1 = CH_3$; $R_2 = CF_3$) and hexafluoroacetylacetone (HFA: $R_1 = R_2 = CF_3$) which have chelating properties similar to acetylacetone (ACAC: $R_1 = R_2 = CH_3$) but higher solubility in $CO_2$. It has been proposed that the formation of an enolate anion will accelerate formation of the metal chelate.[5] Therefore, the equilibrium between the enol and keto forms of the $\beta$-diketones,



$$R_1\text{—}\overset{\text{O}\cdots\text{H}}{\overset{\|}{\text{C}}}\text{—CH=}\overset{\text{O}}{\overset{|}{\text{C}}}\text{—}R_2 \rightleftharpoons R_1\text{—}\overset{\text{O}}{\overset{\|}{\text{C}}}\text{—CH}_2\text{—}\overset{\text{O}}{\overset{\|}{\text{C}}}\text{—}R_2 \qquad \text{(I)}$$

should play an important role in metal complexation.

Several researchers have examined the thermodynamic properties of ACAC including enthalpy, $\Delta H$, and entropy, $\Delta S$, for the equilibrium in eqn. (1) as neat liquids,[7–13] gaseous ACAC[13] and in a variety of solvents.[7,10,11,14] There has also been a low-pressure study of the equilibrium for neat liquid ACAC.[15] The pressure and temperature dependence of this equilibrium has not been thoroughly examined in relation to the extraction efficiencies. Furthermore, a comparison of the thermodynamic parameters has not made between the non-fluorinated, the trifluorinated and the hexafluorinated ligands in either the neat liquids or in supercritical fluid solutions. The goal of the present work is to determine the effects of pressure and temperature on the keto–enol tautomerization in ACAC, TFA and HFA in the neat liquid state and dissolved in supercritical fluid $CO_2$. Characterization of the differences in the equilibria between these molecules is an important first step in understanding the role of this equilibrium in supercritical fluid solutions and the underlying chemistry which can influence extraction efficiencies.

## Experimental

ACAC, TFA and HFA were purchased from the Aldrich Chemical Company, with the respective purity of each being >99%, 98% and 99%. The supercritical fluid chromatography grade $CO_2$ was purchased from Scott Specialty Gases. All compounds were used without further purification and were loaded directly into 100 μm id, 360 μm od fused-silica capillary tubing (Polymicro Technologies, Inc.). In the $CO_2$ mixtures, saturated solutions of the $\beta$-diketones were used in the studies.

All $^1H$ NMR measurements were made on a Varian (VXR-300) pulsed 300 MHz spectrometer with a 7.04 superconducting magnet. All results presented here are based on the Fourier transforms of free-induction decays (FID) after single 45° pulses with the following acquisition parameters: spectral width 12 500 Hz, acquisition time 1.2 s, the Fourier number 16k and relaxation delay 1.0 s. Each FID was the result of 128–1024 co-added scans, depending on the signal-to-noise ratio. The high-pressure fused-silica capillary NMR cell used to contain the sample and its components has been described previously in recent literature.[16,17] Pressure was measured using a calibrated electronic transducer (Precise Sensors, Inc.) with a precision of ±0.7 bar. Temperature was controlled to ±0.2 °C using the air-bath controller on the NMR spectrometer and was calibrated using a reference thermocouple. The keto–enol tautomerization was studied at temperatures ranging from 27 to 166 °C and pressures ranging from 75 to 2590 bar. Spectra were acquired in an unlocked mode with no sample spinning. All chemical shifts are referenced to a removable chloroform–tetramethylsilane standard contained in a sealed capillary tube at 25.0 °C.

Conversion between the tautomers described in eqn. (I) occurs on an appropriate timescale such that individual signals of the $^1H$ resonances for both the enol and keto tautomers can be observed using NMR and the equilibrium can be followed through determination of $K_{EQ}$

$$K_{EQ} = \frac{[\text{keto}]}{[\text{enol}]} \qquad (1)$$

The enol and keto concentrations are obtained by integrating the enol vinyl proton, —CH=, and the keto methylene, $—CH_2—$, resonances with the integrated area of the latter resonance divided by two in order to account for the differing

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† Operated by Battelle Memorial Institute.

numbers of protons in the respective resonances. The integrations were taken over ranges of ±30–100 Hz from the centre of the peaks. These ranges were chosen to reflect the linewidths at the different thermodynamic states which ranged between 1.7 and 5.6 Hz. The same range was used on each of the keto/enol peaks at each thermodynamic state. All reported thermodynamic variables have been determined based on a least-squares regression of the data at several pressures in the absence of a pressure dependence. The uncertainties reported for these variables are determined from the standard deviations of the slope and the intercept of each regression.

## Results

### ACAC

Typical low- and high-pressure $^1H$ NMR spectra of ACAC are given in Fig. 1A–C which correspond to temperatures and pressures of 27.3 °C and 74.8 bar, 27.3 °C and 2588.4 bar and 144.4 °C and 2588.4 bar, respectively. The resonances investigated for the enol form at these conditions are the hydroxy proton (—OH) observed at 16.14, 15.96 and 15.65 ppm, the vinyl proton (—CH=) located at 6.07, 5.92 and 6.24 ppm and the methyl protons ($—CH_3$) located at 2.52, 2.36 and 2.68 ppm, respectively. The resonances investigated for the keto tautomer under these conditions are the methylene resonance ($—CH_2—$) appearing at 4.15, 4.01 and 4.29 ppm and the methyl resonance appearing at 2.68, 2.53 and 2.85 ppm, respectively. An increase in pressure at constant temperature results in a more shielded nucleus. This is illustrated for ACAC in Fig. 1A and B. A comparison of these spectra shows shifts to lower frequency (higher field) with an increase in pressure at constant temperature. An increase in temperature at constant pressure results in a less shielded nucleus for all protons with the exception of the —OH, which is generally more shielded with increases in temperature. This is illustrated in Fig. 1B and C in which the increase in temperature results in shifts to lower field.

The enol content of neat ACAC at 27.3 °C and 75 bar is 74%. This result agrees well with the data in previous publications.[7–15] An earlier NMR investigation of the keto–enol equilibrium in pure ACAC by von Joanne and Heidberg indicated that it is possible to shift the equilibrium toward the more polar keto form as pressure is increased at constant temperature or as temperature is increased at constant pressure.[15] Fig. 2 is a van't Hoff plot for pure ACAC at pressures of 74.8, 1075.8 and 2588.4 bar. We should stress that, contrary to the previous study of ACAC over a much lower pressure range,[15] an increase in pressure does not increase the population of the keto tautomer relative to the enol form, within the experimental uncertainty (Fig. 1A and B). However, an increase in temperature does result in an increase in the keto tautomer as shown in Fig. 1B and C. The values of $\Delta H$, 2.80 ± 0.08 kcal $mol^{-1}$ and $\Delta S$, 7.2 ± 0.2 cal $mol^{-1}$ $K^{-1}$, are constant at pressures of 74.8, 1075.8 and 2588.4 bar. The present results agree with previously reported values for neat ACAC with $\Delta H = 2.8$, 2.81 and 2.83 kcal $mol^{-1}$ and $\Delta S = 6.4$, 6.39 and 6.49 cal $mol^{-1}$ $K^{-1}$ in ref. 9, 13 and 15, respectively. Without a change in the keto–enol equilibrium with pressure, the reaction volume, $\Delta\bar{V}$, could not be determined, however, using our experimental uncertainty and eqn. (2) it is possible to calculate an upper bound on $\Delta\bar{V}$ for the equilibrium in eqn. (1). The value calculated is $\Delta\bar{V} < |-1.8|$ $cm^3$ $mol^{-1}$ at 27.3 °C, which represents the smallest $\Delta\bar{V}$ we could observe with NMR.

NMR spectra for saturated solutions of ACAC dissolved in $CO_2$ were similar to the spectra of the neat liquid, with the exception of small solvent shifts which are generally observed upon dilution. The van't Hoff plots for this supercritical fluid solution at several pressures are given in Fig. 3. The data acquired at 1039 bar and below are all plotted as open

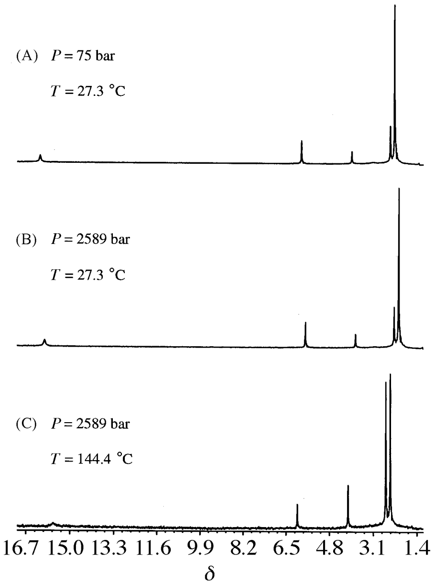

**Fig. 1** Typical $^1H$ NMR spectra of ACAC at A, 27.3 °C and 74.8 bar; B, 27.3 °C and 2588.4 bar and C, 144.4 °C and 2588.4 bar. The enol resonances are the hydroxy proton (—OH) observed at 16.14, 15.96 and 15.65 ppm, the vinyl proton (—CH=) at 6.07, 5.92 and 6.24 ppm and the methyl protons ($—CH_3$) at 2.52, 2.36 and 2.68 ppm in A, B and C, respectively. The keto resonances are the methylene resonance ($—CH_2—$) appearing at 4.15, 4.01 and 4.29 ppm and the methyl resonance appearing at 2.68, 2.53 and 2.85 ppm in A, B and C, respectively.

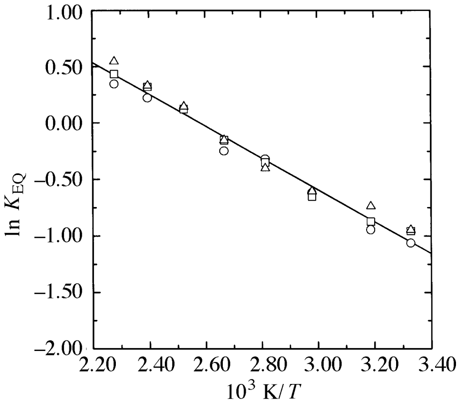

**Fig. 2** Van't Hoff plots for ACAC at pressures of (○) 74.8, (□) 1075.8 and (△) 2588.4 bar

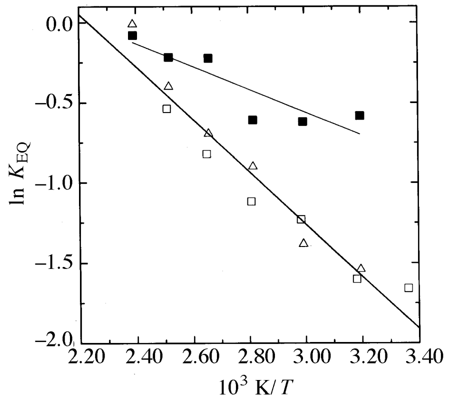

**Fig. 3** Van't Hoff plots for ACAC dissolved in supercritical $CO_2$ at pressures of (□) 167, (△) 1039 and (■) 2168 bar. The solid lines represents the least-squares regressions of data from the three lowest pressures and the high pressure, regressed separately.

symbols while the data for 2168 bar are presented as filled symbols. The lower-pressure data are regressed together separately from the 2168 bar data. The values of $\Delta H$ and $\Delta S$ from this regression are $3.2 \pm 0.3$ kcal mol$^{-1}$ and $7.2 \pm 0.8$ cal mol$^{-1}$ K$^{-1}$, respectively. There is a large difference in the higher-pressure data relative to the lower-pressure data as shown in Fig. 3. The data at 2168 bar clearly lie outside the confidence limits determined by the lower-pressure experiments. Regression of this data at 2168 bar yields $\Delta H$ and $\Delta S$ values of $1.4 \pm 0.4$ kcal mol$^{-1}$ and $3.1 \pm 1.0$ cal mol$^{-1}$ K$^{-1}$, respectively. Since there is not a continuous change in the van't Hoff plots as a function of pressure it is not possible to calculate $\Delta \bar{V}$ for this supercritical fluid solution, however, the sign of $\Delta \bar{V}$ can be determined by comparing the low-pressure data sets and the high-pressure data, which indicate that $\Delta \bar{V} < 0$.

### Trifluoroacetylacetone

It is well known that fluorination of ACAC drastically changes the keto–enol equilibrium towards the enol. For TFA under ambient conditions we determined that the enol content is 96%. This result agrees well with the data in previous publications.[9–11] Fig. 4 is a van't Hoff plot for pure TFA at pressures of 76.4, 1076.0 and 2568.9 bar. As in the non-fluorinated ACAC, an increase in temperature increases the keto tautomer population relative to the enol population while an increase in pressure, up to 2569 bar, does not change the keto–enol equilibrium within the experimental uncertainty. The values of $\Delta H$, $3.7 \pm 0.1$ kcal mol$^{-1}$, and $\Delta S$, $5.1 \pm 0.4$ cal mol$^{-1}$ K$^{-1}$, are independent of pressure, within the experimental uncertainty. Once again, $\Delta \bar{V}$ could not be determined.

NMR spectra for saturated solutions of TFA dissolved in $CO_2$ were similar to the spectra of the neat liquid with the exception that, at higher pressures, the keto $-CH_2-$ peak broadens considerably as a function of temperature and a new peak appears *ca.* 1 ppm downfield from the keto $-CH_2-$ at increased pressures. This behaviour was reproducible and, therefore, van't Hoff plots of the higher-pressure data are not presented for $CO_2$ solutions of TFA. Fig. 5 is a van't Hoff plot for this supercritical fluid solution at a pressure of 179 bar. The upper temperature limit was determined by the broadening of the keto $-CH_2-$ band which was undetectable above the background at temperatures greater than 125 °C. The values of $\Delta H$ and $\Delta S$ from this regression are $4.5 \pm 0.5$ kcal mol$^{-1}$ and $5.5 \pm 1.4$ cal mol$^{-1}$ K$^{-1}$, respectively.

### Hexafluoroacetylacetone

Complete fluorination of the methyl groups led to this $\beta$-diketone being 100% in the enol state at 26.1 °C and atmospheric pressure, within the detection limits of the NMR technique. Increases in temperature to 164.4 °C and pressure to 2253 bar are unable to shift the equilibrium toward the keto tautomer and, therefore, it is not possible to give a van't Hoff plot or determine any thermodynamic parameters for this compound. Moreover, the supercritical fluid solution in $CO_2$ was exclusively in the enol form under all pressure and temperature conditions examined.

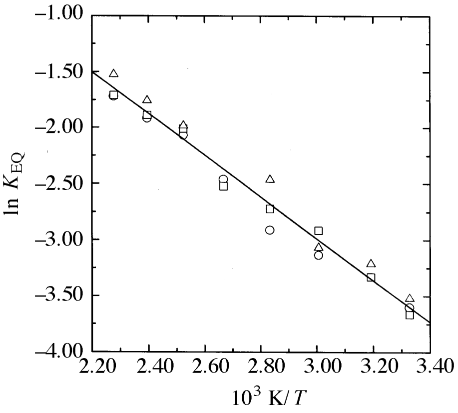

**Fig. 4** Van't Hoff plots for trifluoroacetylacetone at pressures of (○) 76.4, (□) 1076.0 and (△) 2568.9 bar. The solid line represents the least-squares regression of data from all three pressures.

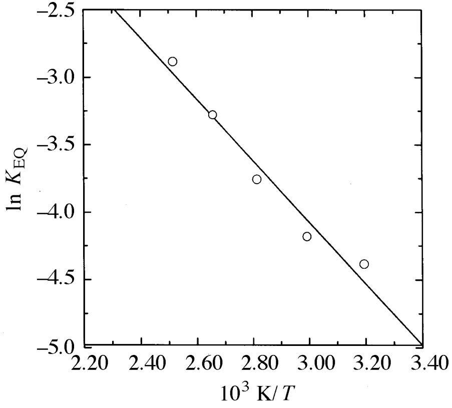

**Fig. 5** Van't Hoff plot for trifluoroacetylacetone dissolved in supercritical $CO_2$ at a pressure of (○) 179 bar

## Discussion

The results presented above show the dramatic effect that the degree of fluorination can have on the stability of the enol tautomer in $\beta$-diketones. The $\Delta H$ values indicate that the enol tautomer is enthalpically favoured in both ACAC and TFA. The latter compound has a greater enthalpy difference between the keto and enol forms than the former in both the neat liquid and in the supercritical $CO_2$ fluid solution state. The primary reason for this is the electron-withdrawing fluorine substituents which further stabilize the enol form through enhanced electron delocalization in the intramolecular resonance-assisted hydrogen bond (RAHB).[13,18,19] The complete enolization and the inability of increasing temperature to shift the equilibrium in the fully fluorinated HFA also point to the magnitude of this enol stabilization due to the electron-withdrawing fluorine substituents.

Another finding in this study is the non-response of the keto–enol equilibrium, in all three neat systems, to pressure. This was especially surprising in the case of ACAC, in which it has been previously reported that a pressure increase of 350 bar had caused a shift in the equilibrium equal to a 2% increase of the keto tautomer population relative to the enol tautomer.[15] If this trend with increasing pressure were continued up to 2500 bar one should observe an increase of *ca.* 9% in the keto tautomer relative to the enol tautomer. This large change should be easily observed using NMR. However, as shown in Fig. 1, there is no effect of pressure on the keto–enol equilibrium for pure ACAC within the experimental uncertainty. The calculated molecular volume of the enol and keto tautomers implies that the former is in fact 3.0 cm$^3$ mol$^{-1}$ less.[13] This difference in the molal volume does not take into consideration the difference between cyclic and straight-chain forms of the enol, which suggest that the enthalpically stable intramolecular hydrogen-bonded enol possesses an excluded volume relative to the straight-chain form. This excluded volume was invoked to explain the pressure dependence of the keto–enol equilibrium in ethyl acetoacetate.[20] However, in the present study, the results indicate that no volumetric preference with pressure is observed between the keto and enol tautomers for neat ACAC, TFA and HFA, indicating that any excluded volume due to cyclization of the enol form is not significantly different from the excluded volume of the keto form.

The results for the supercritical fluid solutions are qualitatively the same as those for the pure liquids with the keto population increasing as temperature is increased. For ACAC $\Delta H$ increases by *ca.* 0.4 kcal mol$^{-1}$ relative to the neat liquid at the lower pressures investigated, while at the higher-pressure of 2168 bar $\Delta H$ decreases by *ca.* 1.4 kcal mol$^{-1}$. The primary difference in the higher-pressure system is the increased density relative to the lower-pressure systems. Also, as the temperature is increased the density changes for this higher-pressure system are not as great as those of the lower-pressure systems. These facts and the results suggest that molecular packing does play a role, however, from the present study only a hint of this is observed. The only analysable data for a $CO_2$–TFA solution indicate that the $\Delta H$ increases by 0.8 kcal mol$^{-1}$ relative to the neat liquid. The disappearance of the keto $-CH_2-$ with increased temperature and increased pressure, as well as the appearance of a new peak in this region, suggests that an exchange process is occurring. Two forms of the enol (*cis* and *trans*) form of TFA are certainly possible, however, based on the present experimental effort we cannot definitively address this issue. Further investigations are of interest.

The supercritical fluid solution data imply that the enol form is more energetically stable, relative to the keto form, than in the neat liquids. This is expected since $CO_2$ is a more non-polar solvent relative to the pure $\beta$-diketones, which would result in a shift of the keto–enol equilibrium toward the more non-polar form of the $\beta$-diketone (*i.e.* enol). Quadrupolar interactions of $CO_2$ with the solute are much weaker and would be secondary considerations in determining the concentrations of non-polar and polar species in the supercritical fluid solutions.

The results also show that the entropy of the keto tautomers is greater than that of the enol tautomers in both ACAC and TFA. This is in agreement with the previous atmospheric-pressure study of ACAC.[10–13] TFA has a stronger intramolecular hydrogen bond than ACAC and the experimental difference in the values of $\Delta S$ for ACAC and TFA can be rationalized on the basis of the differing hydrogen-bond strength of the enol in the two compounds and the resulting reduced torsional motion of TFA relative to ACAC. In the supercritical fluid solutions for both low-pressure ACAC and TFA the $\Delta S$ values are the same as the pure liquids, within the experimental uncertainty.

## Conclusions

The stability of the enol tautomer increases with the degree of fluorination. The earlier reported effect of pressure shifting the equilibrium toward the keto tautomer in ACAC is not observed. It was seen that the keto tautomers have a greater entropy than the enol tautomers in both neat ACAC and TFA and in the supercritical fluid solutions. Based on the assumption that the formation of an enolate anion results in metal chelate formation and stability, the present results imply that changes in pressure within the 'normal' extraction range would not drastically change extraction efficiencies. However, changes in temperature should affect the extraction efficiency and the lowest possible temperature should be used to optimize metal extractions with the $\beta$-diketones, ACAC and TFA. Among the three metal chelating agents, the extraction efficiencies are expected to decrease in the series HFA > TFA > ACAC.

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## References

1 K. E. Laintz, C. M. Wai, C. R. Yonker and R. D. Smith, *J. Supercrit. Fluids*, 1991, **4**, 194.
2 K. E. Laintz, C. M. Wai, C. R. Yonker and R. D. Smith, *Anal. Chem.*, 1992, **64**, 2875.
3 Y. Lin, R. D. Brauer, K. E. Laintz and C. M. Wai, *Anal. Chem.*, 1993, **65**, 2549.
4 Y. Lin, C. M. Wai, F. M. Jean and R. D. Brauer, *Environ. Sci. Technol.*, 1994, **28**, 1190.
5 Y. Lin and C. M. Wai, *Anal. Chem.*, 1994, **66**, 1971.
6 K. E. Laintz, J. J. Yu and C. M. Wai, *Anal. Chem.*, 1992, **64**, 311.
7 H. S. Jarrett, M. S. Sadler and J. N. Shoolery, *J. Chem. Phys.*, 1953, **21**, 2092.
8 L. W. Reeves, *Can. J. Chem.*, 1957, **35**, 1351.
9 J. L. Burdett and M. T. Rogers, *J. Am. Chem. Soc.*, 1964, **86**, 2105.
10 J. L. Burdett and M. T. Rogers, *J. Phys. Chem.*, 1966, **70**, 939.
11 G. Allen and R. A. Dwek, *J. Chem. Soc. London B*, 1966, 161.
12 J. N. Spencer, E. S. Holmboe, M. R. Kirshenbaum, D. W. Firth and P. B. Pinto, *Can. J. Chem.*, 1982, **60**, 1178.
13 M. M. Folkendt, B. E. Weiss-Lopez, P. Chauvel Jr. and N. S. True, *J. Phys. Chem.*, 1985, **89**, 3347.
14 M. T. Rogers and J. L. Burdett, *Can. J. Chem.*, 1965, **43**, 1516.
15 J. von Joanne and J. Heidberg, *J. Magn. Reson.*, 1972, **7**, 1.
16 D. M. Pfund, T. S. Zemanian, J. C. Linehan, J. L. Fulton and C. R. Yonker, *J. Phys. Chem.*, 1994, **98**, 11846.
17 C. R. Yonker, T. S. Zemanian, S. L. Wallen, J. C. Linehan and J. A. Franz, *J. Magn. Reson. A*, 1995, **113**, 102.
18 G. Gilli, F. Bellucci, V. Ferretti and V. Bertolasi, *J. Am. Chem. Soc.*, 1989, **111**, 1023.
19 V. Bertolasi, P. Gilli, V. Ferretti and G. Gilli, *J. Am. Chem. Soc.*, 1989, **113**, 4917.
20 W. J. Le Noble, *J. Am. Chem. Soc.*, 1960, **82**, 5253.

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