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A High-Precision Carbon-13 Shift Thermometer for the Temperature Range 100–300 K

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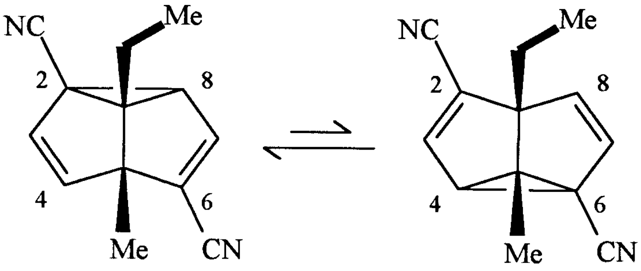
The first carbon-13 shift thermometer for the temperature range of 100–300 K is based on the very rapid equilibration of a pair of semibullvalene valence tautomers. The temperature dependence of the equilibrium constant is reflected in strongly temperature-dependent shift differences $\Delta\delta$ between averaged signals, e.g., $d(\Delta\delta)/dT = 0.051$ ppm K^{-1} at 300, 0.087 ppm K^{-1} at 200, and 0.175 ppm K^{-1} at 110 K for the quaternary carbon atoms C2 and C6. At 37 temperatures T, which were measured with calibrated platinum resistance thermometers, shift differences $\Delta\delta$ were taken from nondecoupled carbon-13 spectra recorded from solutions of 1 in mixtures of chlorodifluoromethane and deuterated dimethyl ether without spinning. The least-squares fit of these $\Delta\delta$ vs T data to a polynomial equation of the fourth degree (Eq. [5], $r^2 = 0.9999$) allows the calculation of temperatures from measured shift differences with a standard deviation of 0.46 K and an estimated error of about 1 K. The heating effects of WALTZ-16 decoupling and the influence of solvents on $\Delta\delta$ are investigated. A comparison with existing NMR thermometers demonstrates the superior performance of the new carbon-13 shift thermometer with respect to precision and the accessible temperature range. © 1998 Academic Press

Key Words: **NMR thermometer; low-temperature carbon-13 spectroscopy; WALTZ-16 decoupling; semibullvalenes; Cope rearrangement.**

INTRODUCTION

The development of modern, sophisticated, high-field NMR spectrometers has solved several of the pernicious problems that troubled variable-temperature magnetic resonance spectroscopy in earlier days (*1–3*), e.g., insufficient temperature stability of the probe (*4, 5*), heating effects by high-power heteronuclear decoupling (*6–8*), and temperature gradients in the sample (*9, 10*). At the same time, the lower temperature limit accessible to commercially available spectrometers has been extended down to temperatures as far as about 100 K, thus allowing the study of chemical exchange involving very low barriers. While it has long been recognized (*2, 3, 10–12*) that uncertainty in the sample temperature is a major source of error in the determination of activation parameters, to the best of our knowledge, no NMR thermometer for very low temperatures exists, let alone high-precision calibration samples that match the temperature stability and accuracy of a modern high-quality temperature controller. Therefore, very low sample temperatures have to be measured directly with the help of a calibrated thermocouple or a platinum resistance thermometer inserted into either the sample of interest itself or a very similar tube that may substitute for the sample. The practical realization of such direct measurements raises certain technical difficulties that render them inconvenient, particularly in routine experiments. Therefore, it is desirable to have a precise and accurate secondary temperature standard for the range of 100–200 K. The first such standard is described here.

Most NMR thermometers so far reported are based on the temperature dependence of chemical shifts. Strongly temperature-dependent chemical shifts in carbon-13 spectra have been reported for certain substituted semibullvalenes that exist as a pair of different valence tautomers equilibrating rapidly on the NMR time scale by nondegenerate Cope rearrangements (*13–15*) e.g., **1a** and **1b.** Based on the following considerations, it should be possible to design semibullvalenes of this type that could serve as secondary standards at very low temperatures.



1a **1b**

The averaged chemical shift δ_i of a rapidly exchanging carbon C_i is given by

$$\delta_i = \delta_{ia}p_a + \delta_{ib}(1 - p_a), \qquad [1]$$

where δ_{ia} and δ_{ib} are the chemical shifts in the absence of exchange and p_a the mole fraction of the valence tautomer **1a**

(*11*). From the expression for the equilibrium constant $K = (1 - p_a)/p_a$, it follows that

$$\delta_i = \frac{\delta_{ia} + K\delta_{ib}}{1 + K}, \qquad [2]$$

and the equilibrium-dependent shift difference $\Delta\delta$ is then given by

$$\Delta\delta = \delta_6 - \delta_2 = \frac{K(\delta_{6b} - \delta_{2b}) + \delta_{6a} - \delta_{2a}}{1 + K}. \qquad [3]$$

Equation [3] defines the necessary criteria for effective secondary temperature standards. First, it is evident that the difference $\Delta\delta$ between the averaged shifts δ_6 and δ_2 of two carbon atoms, i.e., C6 and C2, which are both exchanged between cyclopropyl and vinyl positions of **1a** and **1b,** exhibits a particularly large temperature dependence because of the enormous shift differences between these positions in the absence of exchange, viz., $\delta_{6a} - \delta_{2a}$ and $\delta_{6b} - \delta_{2b}$. The same is true for the pair C4 and C8, of course. In other words, in the case of semibullvalenes, the temperature dependence, inherent in K, is not merely reflected in $\Delta\delta$ but magnified considerably by the size of the shift differences in the absence of exchange.

Secondly, Eq. [3] shows that the values of K must be in the intermediate range. Extreme positions of equilibria, viz., $K \gg 1$ and $K \ll 1$, lead to very small measurable temperature dependence of $\Delta\delta$. The same is true if the degeneracy is only very slightly disturbed, e.g., by isotopic substitution. This results in K values very close to 1 and very similar values for the shift differences in the absence of exchange (*16–19*).

Although several nondegenerate semibullvalenes meet these requirements for large temperature dependence of carbon-13 shifts (*13–15*), most of them still possess barriers to exchange which are too high, resulting in line broadening and the emerging of the spectra of the nonrearranging valence tautomers at temperatures well above 100 K. The known accelerating effect of suitably placed cyano groups on the degenerate Cope rearrangement of semibullvalene (*20*) has led us to conceive the pair of valence tautomers **1** ($\triangleq$ **1a** and **1b**), which is also useful in another context (*21*). It is a stable, crystalline material (m.p. 111–112°C) which can be synthesized in seven steps from commercially available precursors on a scale of several grams and handled without special precautions (*21, 22*). Furthermore, it is stable in solutions of common organic solvents and sufficiently soluble in mixtures of chlorodifluoromethane and deuterated dimethyl ether, which are appropriate for low-temperature NMR spectroscopy. The valence tautomer **1a** is somewhat favored over **1b.** Small samples are available on request from the first author.

RESULTS

For the study of **1** at low temperatures, we employed mixtures of chlorodifluoromethane and perdeuterated dimethyl ether (ca. 3:1 to 4:1) as solvents in order to provide for both fluorine and deuterium lock, though the latter becomes rather unsatisfactory at these temperatures ($<$ca. 130 K), because the high viscosity of the solvent gives rise to very broad deuterium resonances. Because the spectrometers used in the present study unfortunately lacked a fluorine lock, the carbon-13 spectra had to be recorded with a weak lock signal at temperatures below 130 K. Saturated solutions of **1** were prepared by vacuum line techniques and kept in sealed 5 mm tubes.

The shift difference $\Delta\delta$ between the signals of the quaternary carbon atoms C6 and C2 of **1** increases by no less than 20 ppm on lowering the temperature from 301 to 104 K. Line broadening due to the slowing down of the chemical exchange is noticeable but not deleterious below 135 K. Only at 104 K was the precise determination of $\Delta\delta$ precluded by the large linewidth. The signals of the protonated carbon atoms C4 and C8 of **1** behave similarly, except that at low temperatures, the signal of C4 is obscured by solvent signals and that of C8 disappears in the noise (Fig. 1). These results suggested that a sensitive secondary standard for very low temperatures might be based on the difference $\Delta\delta$ of the averaged shifts of C6 and C2 of **1.**

Calibration of the new NMR thermometer was performed with two different samples (A and B) and NMR spectrometers, and in two different laboratories. Their results show excellent agreement. All experimental data $\Delta\delta$ and T_{Pt} are listed in Table 1 together with the temperatures T_{calc} calculated from $\Delta\delta$ with the help of Eq. [5], which represents the least squares fit of the data to the most appropriate of five different equations $T = f(\Delta\delta)$ (see later discussion).

The widely used thermocouples possess only a poor sensitivity, e.g., 40 μV/K for a copper–constantan thermocouple, whereas the 100 ohm platinum resistor, driven by 1 mA of current, has a sensitivity of 400 μV/K (*5, 23*). Hence, the latter was employed as primary temperature standard in both calibration experiments. Calibration of sample A was carried out with a calibrated platinum resistance thermometer assembly whose resistor was inserted into a 5 mm sample tube containing a mixture of pentane and 2-methylbutane (1:3). The resistance was measured with a high-precision digital multimeter and converted to temperature with the help of a constant factor, which was part of the calibration report. The output of a platinum resistance thermometer is somewhat altered when it is in the presence of a strong magnetic field. For example, a typical platinum resistor has an error ($\Delta T/T$) of 0.08% at 300 K (0.24 K) and 0.65% at 110 K (0.72 K) in a magnetic field of 15 T that parallels the long axis of the resistor (*24*).

Carbon-13 spectra at 27 different temperatures in the range between 301 and 104 K were taken on a Bruker DMX 600 spectrometer from the thermally equilibrated sample A without

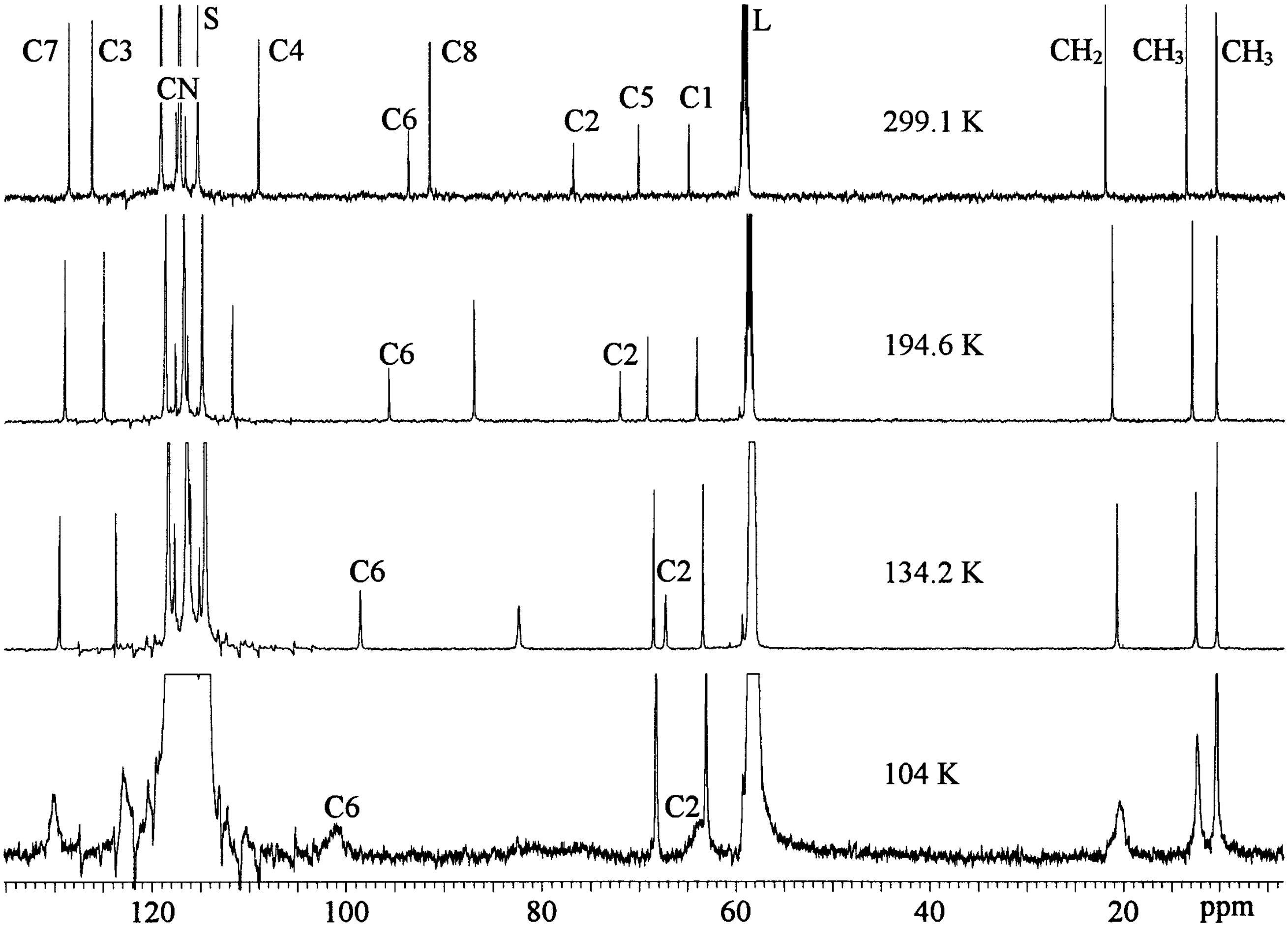


FIG. 1. 151 MHz carbon-13 spectra recorded for a solution of the rapidly equilibrating valence tautomers **1a** and **1b** in chlorodifluoromethane (S)/perdeuterated dimethyl ether (L) (4:1) at various temperatures. The numbers refer to the predominating valence tautomer **1a.** Chemical shifts are calibrated with the high-field methyl signal (δ = 10.617 ppm relative TMS at 304.1 K), which was taken as temperature-independent.

proton decoupling and without spinning of the tube. Before and after recording of each spectrum, the sample was replaced with the tube containing the platinum resistance thermometer. Temperatures were read off when they remained constant within 0.04 K, which took about 10–15 min. Both values agreed within 0.1 K in most cases. At five temperatures, differences between 0.1 and 0.2 K and, at four temperatures, differences between 0.2 and 0.3 K were observed. Average temperatures, T_{Pt}, are listed in Table 1. A conservative estimate of the error in T_{Pt} is 0.3 K at 300 K and 0.8 K at 110 K.

Calibration with sample B was performed as described for sample A at 10 different temperatures in the range between 290 and 108 K, except that the proton-coupled carbon-13 spectra were recorded on a Bruker AMX 500 spectrometer and the temperatures were measured with a platinum resistance thermometer which was inserted in a 5 mm tube filled with silicon oil.

As the temperatures of the samples were measured in the absence of a decoupling field, the peak separations $\Delta\delta$ were taken from proton-coupled carbon-13 spectra. Thus, any heating effects which might be caused by proton decoupling were excluded. The signals of C2 and C6 in a nondecoupled carbon-13 spectrum with a particularly high signal-to-noise ratio, which was recorded for a saturated solution of **1** in deuterodichloromethane at 300.1 K, are narrow, complex, symmetrical multiplets. While the center of the multiplet of C6 is indicated by a sharp line, the center of the multiplet of C2 is readily recognized from a very narrow valley between two lines. At low temperatures, recording of such spectra was impossible because of lower solubility, lower resolution due to the inadequacy of the deuterium lock, and the need to perform the measurements within reasonable periods of time. Therefore, spectra were recorded during the temperature calibration from less concentrated solutions in chlorodifluoromethane–perdeuterated dimethyl ether and hence had a poorer signal-to-noise ratio. A different method for the recognition of the centers of the multiplets was therefore required. Toward this end, each FID was multiplied with an exponential function having a

TABLE 1

Shift Differences $\Delta\delta = \delta_6 - \delta_2$ in Nondecoupled Carbon-13 Spectra Recorded from Solutions of the Rapidly Equilibrating Valence Tautomers 1a and 1b, Measured Temperatures T_{Pt}, Temperatures T_{calc} Calculated from $\Delta\delta$ with Eq. [5], and Deviations $\Delta T = T_{\mathrm{calc}} - T_{\mathrm{Pt}}$[a]

Control setting	$\Delta\delta$	T_{Pt}	T_{calc}	ΔT	$\Delta\delta\{^1\mathrm{H}\}$	$T\{^1H\}$	$\Delta T\{^1H\}$
Bruker DMX 600, sample A[b]							
300.0	16.785	300.9	300.5	−0.4			
290.0	17.368	288.2	288.1	−0.1			
280.0	17.844	278.1	278.5	0.4			
270.0	18.363	268.0	268.7	0.7			
260.0	18.933	258.0	258.5	0.5			
250.0	19.528	248.0	248.5	0.5			
240.0	20.178	237.8	238.3	0.5			
230.0	20.905	227.6	227.7	0.2			
220.0	21.717	217.0	216.8	−0.2			
210.0	22.597	206.2	206.0	−0.2			
200.0	23.553	195.8	195.3	−0.5			
190.0	24.536	185.5	185.2	−0.3			
180.0	25.666	175.0	174.7	−0.3			
175.0	26.247	169.6	169.7	0.0			
170.0	26.876	163.8	164.5	0.6			
165.0	27.453	158.9	159.9	1.0	27.409	160.2	0.3
160.0	28.240	154.2	154.0	−0.2	28.179	154.4	0.4
155.0	28.810	149.9	149.9	0.0			
150.0	29.491	145.1	145.2	0.1			
145.0	30.275	140.0	140.1	0.1			
140.0	31.132	134.7	134.7	0.0	31.048	135.2	0.5
135.0	32.057	129.3	129.3	−0.1	31.949	129.9	0.6
130.0	32.988	124.1	124.1	0.0	32.819	125.0	0.9
125.0	34.203	118.7	117.8	−0.8	33.894	119.4	1.6
120.0	35.123	113.6	113.5	−0.1	34.954	114.3	0.8
115.0	36.167	108.7	109.1	0.3	35.958	109.9	0.8
110.0[c]	36.87	103.8	106.5	2.8			
Bruker AMX 500, sample B[d]							
	17.326	289.6	289.0	−0.6			
	18.403	269.0	267.9	−1.1			
	19.586	247.9	247.6	−0.3			
	20.978	226.9	226.7	−0.2			
	22.559	206.4	206.5	0.1			
	24.331	187.5	187.2	−0.3			
	26.526	168.0	167.3	−0.7			
	29.138	147.9	147.6	−0.3			
	32.415	127.2	127.2	0.0			
	36.437	108.1	108.0	−0.1			
Heating effect of WALTZ-16 decoupling between 200 and 300 K (Bruker DMX 600, sample A[b])							
	16.627		304.0		16.622	304.1	0.1
	19.699		245.8		19.691	245.9	0.1
	22.276		209.9		22.267	210.0	0.1
	22.892		202.6		22.877	202.8	0.2

[a] The influence of proton decoupling with the WALTZ-16 sequence on the temperature of the samples, $\Delta T\{^1\mathrm{H}\} = T\{^1\mathrm{H}\} - T_{\mathrm{calc}}$, was determined from $\Delta\delta\{^1\mathrm{H}\}$ by calculation of the temperature $T\{^1\mathrm{H}\}$ with Eq. [5]. Shift differences are given in ppm, and temperatures in kelvins.

[b] Saturated solution of **1** in chlorodifluoromethane–perdeuterated dimethyl ether (ca. 3:1, v/v).

[c] Not used for the least-squares fit affording Eq. [5].

[d] Saturated solution of **1** in chlorodifluoromethane–perdeuterated dimethyl ether (ca. 4:1, v/v).

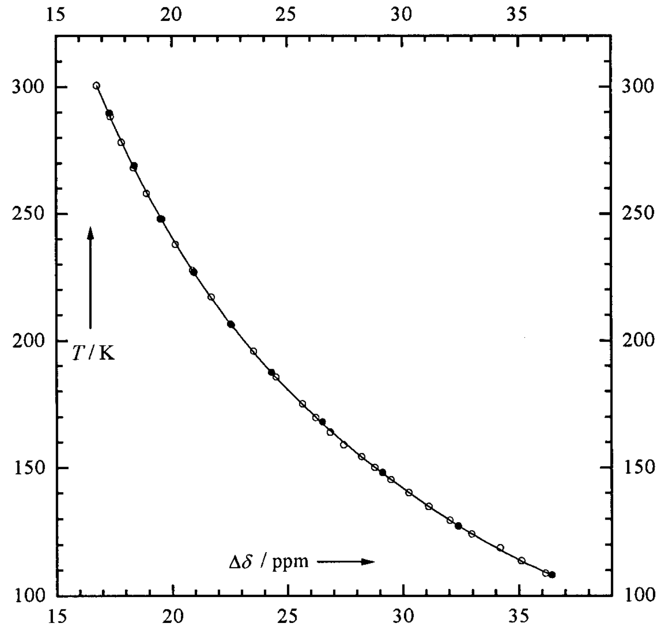


FIG. 2. Temperature dependence of the carbon-13 chemical shift difference $\Delta\delta = \delta_6 - \delta_2$ of the carbon atoms C6 and C2 of the valence tautomers **1a** and **1b** in the limit of fast exchange. The data points are taken from Table 1; hollow circles stem from sample A, filled circles from sample B. The curve was calculated with Eq. [5].

line-broadening factor of 3.0 Hz. Credence was lent to this procedure by a comparison of the results obtained when the peak distance $\Delta\delta$ in the spectrum from the saturated solution in deuterodichloromethane was measured after transformation of the FID without ($\Delta\delta = 15.1181$ ppm) and with line broadening ($\Delta\delta = 15.1192$ ppm). The difference between the results of the two methods, 0.0011 ppm, compares to the order of magnitude of the digital resolution (0.00054 ppm/point) and would translate into an error in the temperature of 0.03 K at 300.1 K.

In view of the large temperature range investigated and the complicated relationship Eq. [3] between $\Delta\delta$ and the equilibrium constant K, in which the equilibrium-driven part of the temperature dependence of $\Delta\delta$ is rooted, a simple equation $T = f(\Delta\delta)$ cannot be anticipated. In fact, neglecting the inherent temperature dependence of carbon-13 chemical shifts, which is typically about 0.004 to about 0.02 ppm/K (*9, 10*), Eq. [4] can be derived from the temperature dependence of K, viz. $K = \exp(-\Delta H/RT + \Delta S/R)$:

$$T = \frac{-\Delta H}{R[\ln(\delta_{6a} - \delta_{2a} - \Delta\delta) - \ln(\Delta\delta - \delta_{6b} + \delta_{2b})] - \Delta S}. \qquad [4]$$

Equation [4], which describes an approximate[1] theoretical relationship between T and $\Delta\delta$, contains no fewer than four unknown parameters. In order to find a practical and accurate mathematical relationship between T and $\Delta\delta$, we fitted the experimental data of Table 1 with the least-squares method to five different equations $T = f(\Delta\delta)$, viz., an exponential equation $T = a \exp[b(\Delta\delta/\mathrm{ppm})]$, a potential equation $T = a(\Delta\delta/\mathrm{ppm})^b$, and polynomial equations of the second, third, and fourth degree. While the fits to the first three equations gave unacceptable results, a polynomial equation of the third degree reproduced the experimental data with reasonable accuracy, i.e., a standard deviation $\sigma = 0.77$ K and a square of the correlation coefficient $r^2 = 0.9998$ (*25*). A significantly better result was achieved by the fit of the data to a polynomial equation of the fourth degree, which resulted in the parameters given in Eq. [5]:

$$\begin{aligned} T_{\mathrm{calc}} = {} & 1289.606 - 115.707(\Delta\delta/\mathrm{ppm}) \\ & + 4.7751(\Delta\delta/\mathrm{ppm})^2 - 0.095446(\Delta\delta/\mathrm{ppm})^3 \\ & + 7.4432{*}10^{-4}(\Delta\delta/\mathrm{ppm})^4 \quad (\mathrm{K}). \end{aligned} \qquad [5]$$

The standard deviation for Eq. [5] is $\sigma = 0.46$ K, the square of the correlation coefficient $r^2 = 0.9999$, and the standard error (or expected error) $(\sigma^2/n)^{1/2} = 0.08$ K (*25*), where n is the number of values. The experimental data and the curve $T = f(\Delta\delta$, calculated according to Eq. [5], are displayed in Fig. 2.

Heating effects in carbon-13 spectroscopy, caused by proton noise decoupling at high frequencies (270 MHz), have been studied by Led and Petersen and were found within the uncertainty of their temperature determination in neat solvents, viz., pentane, *tert*-butyl alcohol, and water (*26*). Heating effects of WALTZ-16 decoupling at 400 MHz in biological samples have been reported (*27*). With a secondary standard for very low temperatures at hand, we tested the influence of WALTZ-16 decoupling at 600 MHz in that temperature range. Toward this end, carbon-13 spectra with WALTZ-16 decoupling were recorded at 12 different temperatures between 304 and 109 K, after the spectra had been taken under exactly the same conditions but without decoupling. Peak separations $\Delta\delta\{^1\mathrm{H}\}$ obtained in this way were converted into temperatures $T\{^1\mathrm{H}\}$ with the help of Eq. [5]. The heating effect by WALTZ-16

TABLE 2

Peak Separations $\Delta\delta\{^1\mathrm{H}\} = \delta_6 - \delta_2$ [ppm] in WALTZ-16 Decoupled Carbon-13 Spectra Recorded for Solutions of 1 (23 mg) in Some Solvents (0.7 ml) at 301.0 K

Solvent	$\Delta\delta\{^1\mathrm{H}\}$
Chlorodifluoromethane, [D_6]dimethyl ether[a]	16.808
[D_3]Methanol	16.213
[D_3]Acetonitrile	16.141
[D_2]Dichloromethane	15.179
[D_8]Toluene	14.585

[a] Sample A; see Table 1.

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[1] In reality, ΔH is probably *not* independent of the temperature over a range of 200 K.

decoupling is then given by $\Delta T\{^1H\} = T\{^1H\} - T_{\text{calc}}$. The data listed in Table 1 show that under the experimental conditions used in the present study, WALTZ-16 decoupling heats the sample by 0.1–0.2 K in the temperature range between 200 and 300 K. Below 200 K, the heating effect increases to about 1 K in the lower limit of the temperature range considered.

The solvent dependence of the shift difference $\Delta\delta$ of **1** was briefly investigated at a constant temperature of 301 K. The shift differences obtained from solutions of **1** in five different solvents are listed in Table 2. A cursory inspection of the data shows that the influence of the solvents is too large to allow use of **1** as secondary standard in solvents other than the one employed in this study, unless such solutions have been calibrated with a primary temperature standard.

Finally, we compared the new carbon-13 shift thermometer **1** with Van Geet's classical secondary standard methanol, which is the most common proton shift thermometer for temperatures between 175 and 330 K, although somewhat different parameters have been reported for the quadratic equation relating the temperature to the peak separation (*28, 29*). Peak separations in nondecoupled carbon-13 spectra, recorded from a nonspinning sample of **1** (sample A) on two different spectrometers (Bruker DMX 600, Bruker AC 200), were converted into temperatures $T_{(\mathbf{1})}$ with Eq. [5], while peak separations $\Delta\delta$ in proton spectra that were taken from a methanol calibration sample at the same spectrometers and under exactly the same conditions (nitrogen flow, nonspinning samples, setting of the temperature controller), were used to calculate temperatures T_{methanol} with the help of Van Geet's equation Eq. [6] (*28*).

$$T_{\text{methanol}} = 403.0 - 29.46(\Delta\delta/\text{ppm}) - 23.832(\Delta\delta/\text{ppm})^2 \quad (\text{K}) \qquad [6]$$

$$T_{\text{methanol}} = -2.17 + 1.007T_{(\mathbf{1})} \quad (\text{K}) \qquad [7]$$

The values $T_{(\mathbf{1})}$ and T_{methanol} are depicted in Fig. 3. The 45° line drawn corresponds to perfect agreement, of course. Satisfactory agreement is found above 195 K as shown by the correlation expressed by Eq. [7] ($r^2 = 0.9998$, standard deviation $\sigma = 0.73$ K, standard error $[\sigma^2/n]^{1/2} = 0.23$ K). Only at 187 and 188 K—temperatures which are close to the limit of the applicability of the methanol standard—do both values differ by 2 K.

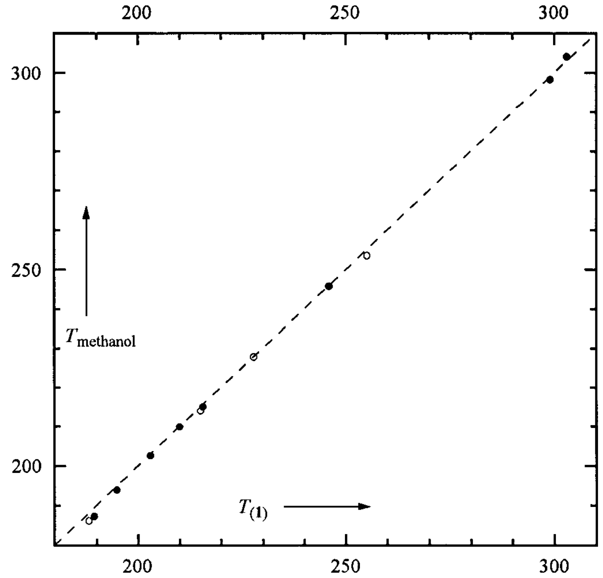

FIG. 3. Comparison of Van Geet's standard methanol (T_{methanol}) with **1** $T_{(\mathbf{1})}$) on two different spectrometers. Hollow circles stem from spectra recorded with a Bruker AC 200, filled circles from spectra recorded with a Bruker DMX 600 spectrometer. The 45° line corresponds to perfect agreement.

DISCUSSION

The carbon-13 shift thermometer described in this study is the first to be used to measure temperatures from room temperature down to about 100 K. The lower limit, which is due to early exchange broadening associated with the high frequency (151 MHz) of the spectrometer employed, should be at even lower temperatures for spectrometers that operate at lower frequencies. This becomes evident from a consideration of the well-known relationship between the rate constant of exchange, the exchange broadening, and the peak separation [Hz] in the absence of exchange (*11*). Both of our spectrometers were equipped only with a deuterium lock, which is not very satisfactory at very low temperatures (<130 K). Hence, use of a fluorine lock may provide even more accurate data in this temperature range.

The performance of the new NMR thermometer compares very favorably with those of the existing low-temperature NMR thermometers, which are compiled in Table 3 for comparison. Most of them are restricted to temperatures above about 180 K or higher, except the multinuclear shift thermometer by Bornais and Brownstein (entries 2 and 3) for which, however, only a limited number of calibration data have been reported. Furthermore, only the temperature dependence of the fluorine peak separation exhibits an acceptable sensitivity (*31*). The sensitivity of the new carbon-13 shift thermometer, expressed by the slope $d(\Delta\delta)/dT$ at 200 K, is surpassed only by the sensitive temperature dependence of the ytterbium-induced pseudo-contact shift exploited by Schneider, Freitag, and Schommer (*32*) (entry 4). It is gratifying that, in the particularly interesting range of very low temperatures, the sensitivity of the new shift thermometer still increases up to a value of 0.175 ppm K^{-1} at 110 K. The precision of the measurements rivals that of the most precise NMR shift thermometers described so far (entries 6, 9). On the basis of the standard deviation of the calibration curve (0.46 K, Eq. [5], Fig. 2) and the error of platinum resistance thermometers in strong magnetic fields (see previous discussion), an error of ≤1 K can be estimated. An equilibrium-driven temperature dependence of chemical shifts may also be observed in proton spectra of **1,** of course. ^{1}H, ^{1}H coupling and the inherent smaller sensitivity,

TABLE 3

Referencing of Low Temperatures (<273 K) Based on Variations of Chemical Shifts (Entries 1–10) and Linewidths (Entry 11) in NMR Spectra of More Common Nuclei

	Composition of the NMR thermometer	Temperature (K)	Nucleus	$d(\Delta\delta)/dT$[a] (ppm/K)	Error (K)	Ref.
1	Methanol	175–330	^{1}H	0.007	0.8[b]	(*28–30*)
2[c]	Dichlorofluoromethane, hexafluorobenzene, toluene	128–301	^{1}H	0.0012	[d]	(*31*)
			^{19}F	0.0115		
3[e]	Dichlorofluoromethane, hexafluorobenzene, [D$_8$]toluene	138–301	^{1}H	0.0008	[d]	(*31*)
		138–301	^{19}F	0.0111		
		138–301	^{13}C	0.0044		
4	Acetone, TMS, [D$_6$]acetone, carbon disulfide, trichlorofluoromethane, Yb(fod)$_3$	204–313	^{1}H	0.088	1.5	(*32*)
		204–313	^{13}C	0.240	1.5	
5	Acetone, carbon tetrachloride	190–360	^{13}C	0.019	1.1[f]	(*26*)
6	Iodomethane, TMS	214–274	^{13}C	0.035	0.35[g] 0.12[h]	(*33*)
7	[D$_4$]Methanol	185–297	^{2}H	0.007	[i]	(*34, 35*)
8	1,1-Dichloro-2,2-difluoroethene, trichlorofluoromethane, tetrachloro-1,2-difluoroethane	179–262	^{19}F	0.009	[i]	(*36*)
9	Triphenylphosphine, triphenylphosphine oxide, [D$_8$]toluene	183–343	^{31}P	0.032	0.47[g] 0.34[j]	(*37*)
10	**1,** chlorodifluoromethane, [D$_6$]dimethyl ether	108–301	^{13}C	0.087	0.46[g] 0.08[h]	This work
11	Furfural, [D$_8$]tetrahydrofuran	203–283	^{13}C		1[f]	(*38*)

[a] Sensitivity at 200 K.

[b] RMS error of the least-squares fit of the T–$\Delta\delta$ data.

[c] Peak separation method.

[d] Only 9 calibration data are tabulated for the entire temperature range.

[e] Absolute frequency method.

[f] Estimated uncertainty.

[g] Standard deviation σ of the least-squares fit of the T vs $\Delta\delta$ data.

[h] Standard error (expected error) $(\sigma^2/n)^{1/2}$.

[i] Not reported.

[j] Mean deviation.

however, give rise to less satisfactory results. The multinuclear probe heads and the temperature stability of the control units, common among the modern generation of high-field spectrometers, also allow the use of the new carbon-13 shift thermometer for the temperature calibration of spectra of other nuclei.

CONCLUSION

At temperatures above 180 K, the low temperature carbon-13 shift thermometers disclosed in this study may perhaps not substitute the well-established shift thermometers such as Van Geet's methanol sample (*28–30*) or the triphenylphosphine/triphenylphosphine oxide thermometer (*37*), although the new thermometer has superior performance in that temperature range. The reason for this is that the latter are currently more readily available and are honored by long tradition. At temperatures below 180 K, however, the new thermometer will provide improved accuracy and reproducibility in variable temperature NMR studies of rates and equilibria involving very low energy barriers.

EXPERIMENTAL

Instrumentation. A Bruker DMX 600 spectrometer was used, equipped with a temperature control assembly B-VT-2000 (display and control unit BTO-2000-E) and a probe head heater BMT 05. The cooling system consisted of two connected 25 l containers filled with liquid nitrogen. The gas flow was generated in the first container by an electrical heating coil, the heating power of which was regulated with the control unit. In the calibration experiment between 170 and 300 K, we employed 35% of the maximum heating power. Between 110 and 165 K, 40% was used. The cooling gas passed through a copper coil immersed in the liquid nitrogen of the second container before it was heated to the desired temperature at the probe head. A Bruker AMX 500 spectrometer was also used, equipped with a temperature control unit B-VT-2000. The probe head heater was for MAS probe heads. In addition, a Bruker AC 200 spectrometer was used, equipped with a Bruker variable temperature unit B-VT-1000.

Temperature measurement. Temperature measurements were carried out with a 20.3 mm long 2 mm diameter platinum resistor (Pt-102-77L, serial no. P1814) by Lake Shore Cryotronics, Inc., 64 East Walnut Street, Westerville, Ohio 43081-2399, USA, connected by an insulated 10 m long Four Lead, Quad-Twist wire (SMOD-4-QT32-10m) to a temperature transmitter (231P-230). The assembly was calibrated by the manufacturer between 77 and 325 K (±0.020 K at 100 K and ±0.035 K at 300 K). The calibration curve was loaded in a PROM at the factory (calibration report no. 282605). The current, which is linearly dependent on the temperature at the outlet of the temperature transmitter, was measured with a digital multimeter (Goldstar DM-441B, 4 $\frac{1}{2}$ digit) by LG Precision Co., Ltd., 133, Gongdan, Gumi shi Gyeongsanbuk Do, 730-030, South Korea (sensitivity 1 digit/10^{-3} mA, corresponding to 1 digit/0.016 K) and converted to temperature by multiplication by the constant factor 16.250 K/mA supplied by Lake Shore Cryotronics. The platinum resistor was placed at the height of the receiver coil in a high-precision 5 mm sample tube (Varian, 507-PP) filled with a mixture of pentane and 2-methylbutane (1:3, ca. 0.5 ml = 5 cm height), and was supported by a 3 mm PTFE insert. The 10 m wire, which connected the platinum resistor and the temperature transmitter, was protected by tubing made from silicon rubber.

Calibration of sample A on the Bruker DMX 600 spectrometer. When the specific control setting and the value displayed at the temperature control unit agreed within 0.1 K, the tube containing the platinum resistor was allowed to equilibrate thermally for 15 min. Already after about 10 min, the temperature, determined with the platinum resistor, remained constant within 0.04 K. The tube with the platinum resistor was exchanged for sample A, which was also allowed to equilibrate thermally for 15 min. At each temperature, changes of the frequencies of the proton and carbon-13 channels and in the impedance of the receiver circuit, which were caused by the variation of the temperature, were carefully compensated before recording the spectrum. A nondecoupled carbon-13 spectrum was recorded followed by a WALTZ-16 decoupled spectrum at certain temperatures (Table 4). Thereafter, the temperature was measured again with the platinum resistor as described. All spectra were recorded without spinning of the sample.

TABLE 4

Chemical Shifts in WALTZ-16 Decoupled Carbon-13 Spectra Recorded for a Saturated Solution of 1 in Chlorodifluoromethane–Perdeuterated Dimethyl Ether (ca. 3:1, v/v) at 304.1 K, 187.6 K, and 109.9 K[a]

Temperature	304.1	187.6	109.9 K
C1	54.686	53.857	53.223
C2	66.786	61.395	54.538
C3	115.994	114.652	112.896
C4	98.729	101.758	[b]
C5	59.913	58.955	58.313
C6	83.409	85.694	90.487
C7	118.309	118.788	119.830
C8	81.436	76.411	[c]
2-CN	*106.350*	*106.228*	[b]
6-CN	*107.342*	*107.513*	[b]
5-CH_3	3.155	2.520	2.011
$\mathit{CH_2}CH_3$	11.613	10.921	10.275
$CH_2\mathit{CH_3}$	0.000	0.000	0.000

[a] Chemical shifts are relative to that of the methyl group of the ethyl group at 304.1 K (δ = 10.617 ppm relative TMS). Chemical shifts that are printed *in italics* may be exchanged.

[b] Hidden under the signals of chlorodifluoromethane.

[c] The signal is very broad because of slow exchange.

A total of 250 transients were acquired with 30° pulses, a delay time of 5 s, a sweep width of 21,185 Hz, and 65,536 complex data points. Zero filling up to 262,144 data points and multiplication by an exponential function with a line-broadening factor of 3.0 Hz was performed before the FID was transformed. The WALTZ-16 decoupled spectra were recorded under the same conditions using 30° pulses and a delay of 5 s. Their FIDs were multiplied by an exponential function with a line-broadening factor of 1.2 Hz.

Calibration of sample B on the Bruker AMX 500 spectrometer. Calibration was performed as described for the DMX 600 spectrometer. Nondecoupled carbon-13 spectra were recorded without spinning. In the temperature range of 147.9–289.6 K, a total of 256 transients were acquired with 75° pulses, a delay time of 3 s, and a sweep width of 25,000 Hz. At 127.2 and 108.1 K, 512 and 2048 transients, respectively, were employed.

*Comparison of the secondary standards methanol and **1** (see Fig. 3).* Nondecoupled carbon-13 spectra were taken for **1** with 3000 transients on the Bruker AC 200 and with 250 transients on the Bruker DMX 600 spectrometer with sample A. The spectra were recorded under the same conditions as used in the calibration of sample A. Temperatures were calculated with Eq. [5]. Proton spectra were recorded for a standard methanol sample by Varian with one pulse, a sweep width of 8992.8 Hz, and 65,536 complex data points (DMX 600) or a sweep width of 2998.9 Hz and 32,768 complex data points (AC 200). No line-broadening factor was used. Temperatures were calculated with Van Geet's equation [6]. All spectra were recorded without spinning of the sample.

Solvent dependence of the shift difference $\Delta\delta$. WALTZ-16 decoupled carbon-13 spectra were recorded for solutions of **1** in various solvents on the Bruker DMX 600 spectrometer at 301.0 K as described in the calibration of sample A. The temperature was measured with sample A after each spectrum.

Preparation of the calibration samples. A high-precision 5 mm tube (Varian 507-PP), charged with **1** (40 mg), was attached to a vacuum line with a standard glass joint, evacuated to 10^{-2} bar, and cooled with liquid nitrogen. Perdeuterated dimethyl ether was transferred from a steel cylinder into the tube to give about 0.2 ml of a solid (height 1.5 cm). Subsequently, chlorodifluoromethane was transferred from a steel cylinder into the tube to produce a total height of the solid of 6–7 cm (0.8–1 ml). The tube was evacuated to 10^{-2} bar and sealed with a torch. The solid solvent mixture was allowed to thaw *very slowly* to afford saturated solutions of **1.**

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REFERENCES

1. F. A. L. Anet, Variable temperature ^{13}C NMR, *in* "Topics in Carbon-13 NMR Spectroscopy" (G. C. Levy, Ed.), Vol. 3, pp. 79–83, Wiley-Interscience, New York (1980).
2. M. L. Martin, G. J. Martin, and J.-J. Delpuech, "Practical NMR Spectroscopy," pp. 330–345, Heyden, London (1980).
3. J. Sandström, "Dynamic NMR Spectroscopy," Academic Press, London (1982).
4. R. L. Vold and R. R. Vold, *J. Magn. Reson.* **55,** 78–87 (1983).
5. T. C. Farrar, E. Sidky, and J. D. Decatur, *J. Magn. Reson.* **86,** 605–612 (1990).
6. A. J. Shaka, J. Keeler, T. Frenkiel, and R. Freeman, *J. Magn. Reson.* **52,** 335–338 (1983).
7. A. J. Shaka, J. Keeler, and R. Freeman, *J. Magn. Reson.* **53,** 313–340 (1983).
8. A. Allerhand, R. E. Addleman, D. Osman, and M. Dohrenwend, *J. Magn. Reson.* **65,** 361–363 (1985).
9. A. Allerhand, R. E. Addleman, and D. Osman, *J. Am. Chem. Soc.* **107,** 5809–5810 (1985).
10. S. R. Maple and A. Allerhand, *J. Magn. Reson.* **66,** 168–171 (1986).
11. A. Allerhand, H. S. Gutowsky, J. Jonas, and R. A. Meinzer, *J. Am. Chem. Soc.* **88,** 3185–3194 (1966).
12. R. R. Shoup, E. D. Becker, and M. L. McNeel, *J. Phys. Chem.* **76,** 71–78 (1972).
13. H. Quast, Y. Görlach, E.-M. Peters, K. Peters, H. G. von Schnering, L. M. Jackman, G. Ibar, and A. J. Freyer, *Chem. Ber.* **119,** 1801–1835 (1986).
14. R. Gompper, M. L. Schwarzensteiner, and H.-U. Wagner, *Tetrahedron Lett.* **26,** 611–614 (1985).
15. R. V. Williams, V. R. Gadgil, K. Chauhan, D. van der Helm, M. B. Hossein, L. M. Jackman, and E. Fernandes, *J. Am. Chem. Soc.* **118,** 4208–4209 (1996).
16. R. Askani, H.-O. Kalinowski, and B. Weuste, *Org. Magn. Reson.* **18,** 176–177 (1982).
17. H.-O. Kalinowski, *Nachr. Chem. Tech. Lab.* **32,** 874–881 (1984).
18. R. Askani, H.-O. Kalinowski, and B. Weuste, *Tetrahedron Lett.* **25,** 2321–2324 (1984).
19. H. U. Siehl, *Adv. Phys. Org. Chem.* **23,** 63–163 (1987).
20. H. Quast, J. Christ, E.-M. Peters, K. Peters, and H. G. von Schnering, *Chem. Ber.* **118,** 1154–1175 (1985).
21. M. Dohle, J. Manz, G. K. Paramonov, and H. Quast, *Chem. Phys.* **197,** 91–97 (1995).
22. A. Witzel, *Dissertation,* University of Würzburg (1994).
23. J. V. Nicholas and D. R. White, "Traceable Temperatures," chapter 6 and 7, DSIR Science Information Division, Wellington, New Zealand (1982).
24. B. L. Brandt, L. G. Rubin, and H. H. Sample, *Rev. Sci. Instrum.* **59,** 642–645 (1988).
25. L. Sachs, "Angewandte Statistik," 7th ed., Springer, Berlin (1992).
26. J. L. Led and S. B. Petersen, *J. Magn. Reson.* **32,** 1–17 (1978).
27. W. A. Bubb, K. Kirk, and P. W. Kuchel, *J. Magn. Reson.* **77,** 363–368 (1988).
28. A. L. Van Geet, *Anal. Chem.* **42,** 679–680 (1970).
29. D. S. Raiford, C. L. Fisk, and E. D. Becker, *Anal. Chem.* **51,** 2050–2051 (1979).
30. C. Ammann, P. Meier, and A. E. Merbach, *J. Magn. Reson.* **46,** 319–321 (1982).
31. J. Bornais and S. Brownstein, *J. Magn. Reson.* **29,** 207–211 (1978).
32. H. J. Schneider, W. Freitag, and M. Schommer, *J. Magn. Reson.* **18,** 393–395 (1975).
33. D. W. Vidrine and P. E. Peterson, *Anal. Chem.* **48,** 1301–1303 (1976).
34. E. W. Hansen, *Anal. Chem.* **57,** 2993–2994 (1985).
35. K. Roth, *Magn. Reson. Chem.* **25,** 429–431 (1987).
36. R. A. Newmark and R. E. Graves, *J. Phys. Chem.* **72,** 4299–4303 (1968).
37. F. L. Dickert and S. W. Hellmann, *Anal. Chem.* **52,** 996–998 (1980).
38. S. Combrisson and T. Prange, *J. Magn. Reson.* **19,** 108–110 (1975).