Relax with TEMPO: A Paramagnetic Relaxation Agent Useful also for Silicon-29 NMR Spectroscopy

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Summary: TEMPO enhances longitudinal relaxation rates of silicon compounds significantly (e.g., enhancement by a factor of 150 for Si(OEt)$_4$) while tolerating a wide range of reactive functionalities making it a favorable alternative to other relaxation enhancers for ^{29}Si NMR spectroscopy.

Silicon compounds are important bulk and specialty chemicals with an estimated global production volume exceeding 400 megatons/year.[1] The composition and structural assignment of silicon species frequently involves ^{29}Si NMR spectroscopy.[2] ^{29}Si is a spin ½ nucleus with a natural relative abundance of 4.7% which is higher than that of ^{13}C. Unfortunately, its low magnetogyric ratio, a negative NOE, and rather long relaxation times can be factors limiting sensitivity.[2–4] One simple way to overcome this issue is to use concentrated solutions to improve the signal-to-noise ratio. Furthermore, the presence of hydrogen or fluorine atoms in the vicinity ($|J|>0$) of the observed silicon nuclei allows the use of INEPT techniques to improve sensitivity by transfer of magnetization from the more sensitive nuclei (^{1}H, ^{19}F) to the insensitive ^{29}Si.[3,5,6] If no hydrogen/fluorine atoms are present, acquisition times can be quite long especially for sparingly soluble compounds. Usually compounds bearing few or no protons close to the silicon atom in addition have very long longitudinal relaxation times, which can amount to several minutes and therefore require excessive spectrometer usage.[7–9]

Generally, the sensitivity of the spin-relaxation behavior toward paramagnetic substances can shorten acquisition times significantly.[8,10–12] However, only a few paramagnetic agents like Cr(acac)$_3$, Fe(acac)$_3$, or other transition metal complexes are commonly used in ^{29}Si NMR spectroscopy.[2,8] These substances influence mainly longitudinal relaxation (T_1), while the transverse relaxation mechanism remains almost unaffected.[8,11] Disadvantages of these metal complexes are their limited solubility, potential interactions with the sample, environmental aspects (e.g., Cr(acac)$_3$), and difficulties to recover the sample. The stable organic nitroxy-radical 2,2,6,6-tetramethylpiperidine-*N*-oxyl (TEMPO) has been known for some years as a relaxation enhancer in ^{13}C and ^{15}N spectroscopy, and nowadays it is a very important tool for the analysis of proteins and biomolecules.[13–18] Moreover, TEMPO is well soluble in a wide range of solvents. Therefore, we were interested to investigate the influence of TEMPO on relaxation rates of a variety of silicon compounds with different functionalities.

For an efficient relaxation enhancer, it is very important that the paramagnetic molecule is chemically inert toward the observed compound, to avoid problems concerning chemical stability and the assignment of shifted signals. We tested the suitability of the organic radical TEMPO for this purpose employing some basic silicon compounds that vary in functionality and steric protection, namely, Si(CH$_3$)$_4$, **1**, SiCl$_4$, **2**, Si(OEt)$_4$, **3**, the sterically demanding *tert*-butyltrichlorosilane, **4**, and the even more crowded silanetriol 2,6-Mes$_2$C$_6$H$_3$-Si(OH)$_3$,[19] **5** (Mes = 2,4,6-trimethylphenyl).

The extent to which the unpaired spin of an electron interacts with the nucleus under study is dependent on several parameters (e.g., the correlation time of the unpaired electron τ_s, the gyromagnetic constants of the electron, γ_s, and the observed nucleus, γ_I, the larmor frequency of the electron ω_s, and the observed nucleus, ω_I).[11] The connection of these terms can be expressed by the relaxivity r, which is directly proportional to the (macroscopic) relaxation rate R.[11] The concentration dependence in solution can be formulated according to eq 1, where T_1^0 is the relaxation time of the pure sample.

$$R = 1/T_1 = 1/T_1^0 + r[M] \quad (1)$$

The T_1^0 values for the compounds in the absence of a relaxation enhancer have been redetermined by us as a reference to eliminate alterations in the relaxation behavior owing to different instrumentation or sample handling (e.g., paramagnetic O_2 content). Longitudinal relaxation times were determined using the inverse gated inversion–recovery pulse sequence (5

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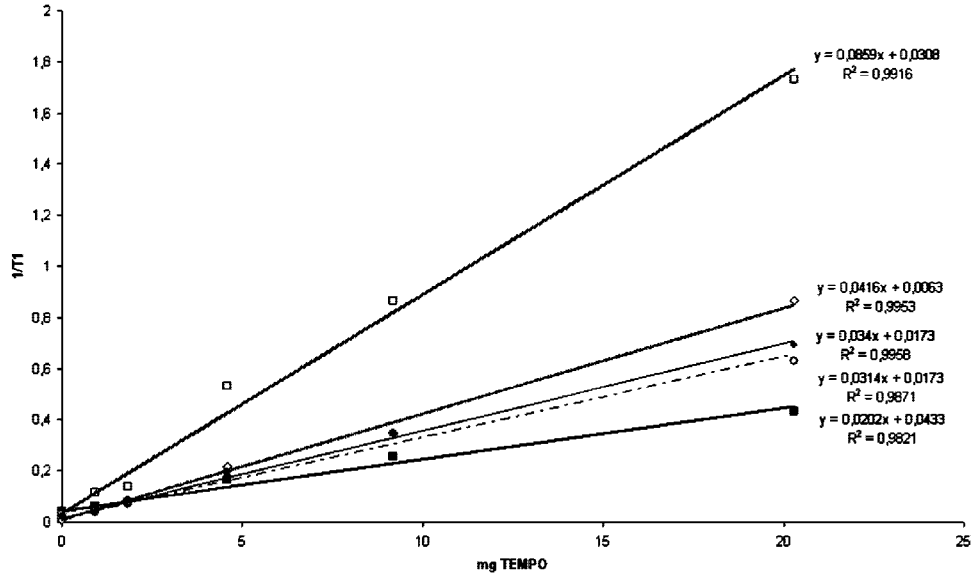

Figure 1. $1/T_1$ plotted as a function of the concentration of TEMPO according to eq 1. ■, TMS; □, $Mes_2C_6H_3Si(OH)_3$; ◇, $Si(OEt)_4$; •, $SiCl_4$; ○, $^tBuSiCl_3$.

Table 1. Longitudinal Relaxation Time T_1 [s] of Compounds 1–5 in the Presence of TEMPO at Different Concentrations[a]

TEMPO [mg/sample]	TEMPO [mol/l]	TMS[b] **1**	$SiCl_4$[b] **2**	$Si(OEt)_4$[b] **3**	$^tBuSiCl_3$[b] **4**	$Mes_2C_6H_3Si(OH)_3$[c] **5**
0.0	0.000	23.1 (1.1)	43.3 (12)	158.7 (2.4)	57.7 (6.0)	32.5 (1.2)
0.9	0.012	15.4 (1.2)	26.0 (12)	21.6 (3.5)	24.5 (6.1)	8.7 (1.4)
1.8	0.024	12.7 (1.2)	10.8 (16)	13.0 (3.5)	14.4 (7.1)	7.2 (2.0)
4.6	0.059	6.1 (1.2)	5.0 (16)	4.6 (4.2)	5.0 (7.2)	1.9 (2.0)
9.2	0.118	3.9 (1.4)	2.9 (16)	2.9 (5.0)	2.9 (7.4)	1.1 (2.1)
20.5	0.262	2.3 (1.5)	1.4 (19)	1.2 (5.5)	1.6 (13.8)	0.6 (2.5)

[a] Values in parentheses are half-line widths in Hz. Estimated errors of T_1: <5%. [b] 60% in C_6D_6. [c] 60% in d_8-THF.

$\times T_1 - 180° - t - 90°$-detection). The values obtained are in good agreement with literature values where available.[9,20] The T_1 values (298 K) found for $Si(CH_3)_4$ (23 s) and $Si(OEt)_4$ (159 s) are slightly longer than those previously reported (19 and 140 s)[21,22] which can be explained by concentration differences, different solvents, and a more efficient removal of dissolved oxygen using the freeze–thaw method.[2] The T_1 value found for $SiCl_4$ is 0.7 s shorter (43.3 s) than those reported in the literature (44 s).[20]

In all cases where protons are close to the silicon [($^2J_{SiH}$, (**1**), (**5**)) two bonds between hydrogens and silicon] relaxation times are significantly shorter than for substances where hydrogens are further away ($^3J_{SiH}$, (**3**), (**4**)), which can be explained by more effective dipolar relaxation and longer correlation times.[10,12] The longest longitudinal relaxation time was found for $Si(OEt)_4$ (159 s), the shortest for TMS (23 s).

In a second step, we investigated the relaxation behavior of compounds **1**–**5** by treating all samples with the same volume (100 μL) of stock solutions containing TEMPO in different concentrations ranging from 9.2 to 203 mg/mL of C_6D_6. All substances **1**–**5** showed a significant enhancement of the relaxation rate even in the presence of small amounts of TEMPO. At a concentration of 20.5 mg of TEMPO per NMR sample, **1** exhibits the longest relaxation time of all investigated compounds (2.3 s). At this concentration, $Si(OEt)_4$ exhibits a relaxation time of 1.2 s, which means that the acquisition time of a ^{29}Si NMR spectrum is reduced by a factor of 150 compared to the sample without TEMPO. Since the S/N ration is proportional to the square root of the number of scans, an S/N-enhancement of ~12 is achieved. The improved relaxation behavior is not limited to the quite high concentrations used by us to save spectrometer time. Also, for concentrations ten times lower than those listed in Table 1, we found similar values for all samples we measured (e.g., TMS (6%) with 20.2 mg of TEMPO per sample gave a T_1 of 1.5 s).

All compounds showed only a slight shift of the signals even at higher TEMPO concentration assuming that there is no direct interaction between the observed silicon center and the nitroxy radical. In the case of **4**, the largest signal shift (from 17.7 to 18.5 ppm) can be found; for all other compounds investigated by us, the shift differences are substantially smaller with values below 0.4 ppm. Furthermore, no significant line broadening was noticed suggesting that the transverse relaxation mechanism is only marginally affected by TEMPO.[11] An exception is $SiCl_4$ for which half-line widths are generally larger owing to $^{29}Si-^{35}Cl$ interaction.[23] For the other compounds, again **4** is affected more by line broadening than the other ones we selected. The observed half-line widths range from 1.2 Hz ((**1**), no TEMPO) to 14 Hz ((**4**), 20.5 mg of TEMPO) and are listed in Table 1. At combinations of low sample concentrations with high TEMPO concentrations, however, larger adverse effects can be observed. For instance, terphenyl derivative **5** at a concentration of 0.153 mol/L shows a low field signal shift of up to 3 ppm, in case the molar concentration of TEMPO substantially exceeds that of the silicon compound (molar ratio

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Si/TEMPO = 0.6). For such extreme concentration scenarios, also the ^{1}H NMR spectra show a line broadening. In the above-mentioned example, the carbon-bound protons show line widths of ca. 20–25 Hz while the OH protons are even broader with ca. 70 Hz. The stronger shifting behavior of compound **5** can be explained by its tendency to form hydrogen bonds with TEMPO which for related compounds has been reported to cause similar effects.[24] In contrast, at higher molar ratios of Si/TEMPO, e.g., ranging between 6 and 130 (referring to the values listed in Table 1), also compound **5** shows only slight signal shifting of up to ± 0.2 ppm.

A significant point in the use of TEMPO as a relaxation enhancer is its chemical reactivity toward the sample to be measured. For highly sensitive compounds such as silylenes, West et al. already reported that a conversion to the disiloxane via silanone intermediates takes place.[25] From our investigations, all compounds used except $SiCl_4$ proved to be chemically inert toward TEMPO. $SiCl_4$ reacts at least in traces with the nitroxy-radical probably under formation of Si−O bonds.

As we could show, TEMPO can enhance longitudinal relaxation rates of silicon compounds with different functionalities significantly. In the case of $Si(OEt)_4$, an enhancement by a factor of 150 was achieved. Especially for compounds with moderately reactive functionalities (e.g., **1**, **3**) or sterically shielded organosilicon compounds (e.g., **4**, **5**), TEMPO is a favorable alternative to other relaxation enhancers like $Cr(acac)_3$. Half-line widths are not significantly broadened, and chemical shifts do not change essentially. Further advantages include the low cost (25 g costs about $36)[26] and good solubility in a wide range of organic solvents. In principle, sample and relaxation enhancer recovery should also be possible if desired, owing to the low sublimation point of TEMPO (30 °C at p = 0.1 mbar). For very sensitive compounds, however, TEMPO seems less suitable because (partial) reactions of the sample with TEMPO might proceed.

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Experimental

^{29}Si NMR spectra were recorded on a Bruker AMX 360 with a standard 5 mm narrow bore heteronuclear probe at a frequency of 71.522 MHz using a 90° high-power-pulse width of 5.8 μs. T_1 values were determined using the inversion–recovery method ($5 \times T_1$−180°−t−90°-FID). All manipulations including NMR sample preparation were performed under strict exclusion of oxygen and moisture under an inert atmosphere of argon using standard Schlenk techniques. Deuterated solvents were dried over CaH_2 and freshly distilled prior to use. TMS, $SiCl_4$, *tert*-butyltrichlorosilane, and $Si(OEt)_4$ were purchased from Sigma and distilled prior to use. 2,6-$Mes_2C_6H_3Si(OH)_3$ was prepared according to a literature procedure.[19] Liquid samples were degassed three times using the freeze–thaw method. Solid samples were evacuated and vented by argon (three times). Samples without any relaxation enhancers were dissolved in C_6D_6 or d_8-THF (60 wt %). Samples for relaxation enhancement contain 300 μL (liquid samples) or 300 mg (solid samples) of the pure compound, 100 μL of C_6D_6 or d_8-THF, and 100 μL of stock solutions containing 9.2 to 203 mg of TEMPO/mL of C_6D_6. All measurements were performed using standard 5 mm NMR tubes charged with 0.5 mL of sample solution. Routinely, samples have been referenced externally, and the shift values obtained showed no deviation to internally referenced samples with a sealed capillary insert, as was checked for several randomly selected samples.

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