Ligand Exchange Processes in Tetraalkoxytelluranes

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Alkoxy groups in acyclic tetraalkoxytelluranes interchange quickly on the NMR time scale at room temperature, both intramolecularly (axial/equatorial positional interconversion) and intermolecularly (the reaction between telluranes and free alcohols). In the latter case, no thermodynamic preference is found for the binding of simple primary or secondary alcohols, but *tert*-butyl alcohol is significantly less favored as a ligand. The ^{125}Te NMR signals for $Te(OEt)_4$ and $Te(O^iPr)_4$ are shown to be broad and very solvent- and concentration-dependent, probably due to associative processes in solution. In contrast, cyclic telluranes such as $Te(OCH_2CH_2O)_2$ and $Te(OCMe_2CMe_2O)_2$ are thermodynamically favored and give sharper ^{125}Te lines. For the latter substance, three ligand reorganization processes were defined and measured by NMR line-shape analysis: (a) a low-barrier ($\Delta G^\ddagger$ = 7.0 kcal/mol) axial/equatorial interchange (such as a Berry pseudorotation) that still leaves two distinct methyl signals in the spectrum; (b) a high-barrier ($\Delta G^\ddagger$ = 20.9 kcal/mol) mechanism that averages all the methyl groups in the molecule to one line; (c) an acid-catalyzed process, probably involving tellurium inversion, that has the same result as process b.

Introduction

A few years ago it was found in our laboratory that some organotellurium compounds have immunomodulatory activity *in vitro* and *in vivo*;[1] specifically, ammonium trichloro(dioxyethylene-*O,O'*)tellurate (AS-101) is now undergoing clinical trial in cancer and AIDS patients. In connection with this project, we became interested in the structure and NMR properties of tetraalkoxytelluranes. In 1981 Denney *et al.*[2] (the only study on this subject) provided ^{1}H, ^{13}C, and ^{125}Te NMR data and discussed ligand reorganization in the title compounds and their selenium analogs. In this paper we present new data concerning ligand exchange processes in tetraalkoxytelluranes.

Results and Discussion

Acyclic Tetraalkoxytelluranes. The ^{1}H and ^{13}C NMR spectra of tetraethoxy- (**1**) and tetraisopropoxytellurane (**2**) show one set of signals for the alkyl groups. Since these compounds are expected to have a trigonal bipyramid (TBP) structure with two equatorial and two axial alkoxy groups,[3,4] the ligands must be exchanging position at a rate which is fast with respect to the NMR time scale, at room temperature.

We performed a series of ^{1}H NMR experiments in which we added varying amounts of alcohols (methanol, ethanol, 2-propanol, *tert*-butyl alcohol, and benzyl alcohol) to solutions of **1** and **2** in $CDCl_3$ or C_6D_6. The result for the $Te(OEt)_4$/EtOH system is shown in Figure 1. Only one set of ethyl group signals is seen in every spectrum, while the oxymethylene signal is shielded with the addition of ethanol (the methyl group is also shielded, but less so). A plot of δ *vs* the fraction of noncoordinated alkoxy groups (Figure 2a) gives a straight line which extrapolates approximately to the chemical shift of pure ethanol in the same solvent. This is what would be expected for fast exchange between the ethoxy groups of the tellurane and the free alcohol.

We get a very similar result for $Te(OEt)_4$/MeOH, with both types of alkoxy group signals being shielded with increasing amounts of added methanol. The good fit to a straight line in Figure 2b (virtually the same as in Figure 2a) indicates that the equilibrium constant between species with a bound methoxy and ethoxy group is close to **1**; i.e., there is no significant preference for binding either of these moieties to tellurium. This is also the case for all the other combinations we tried, except for those involving *tert*-butyl alcohol (e.g. Figure 2c), where the bulky tertiary group prefers to remain as a free alcohol.

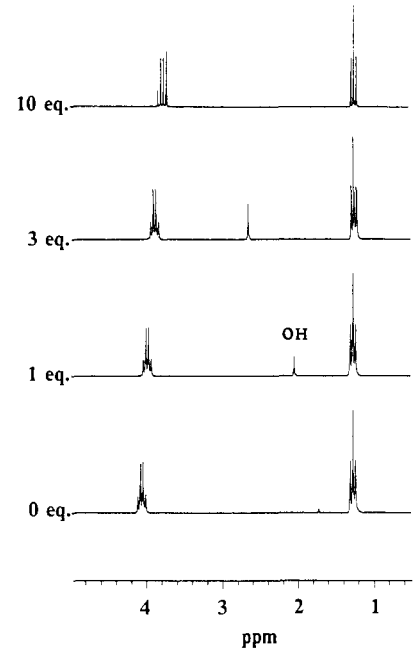

Figure 1. ^{1}H NMR spectra of a 0.22 M solution of $Te(OEt)_4$ in $CDCl_3$, to which were added increasing amounts (values on the left, in equivalents) of EtOH.

^{125}Te NMR Studies. The 94.7 MHz ^{125}Te NMR spectra of **1** and **2** in $CDCl_3$ and acetone-d_6 gave unexpectedly broad lines; for *ca.* 0.1 M solutions, these were several hundred hertz wide. Increasing the concentration caused both significant upfield shifts and line narrowing. Figure 3 summarizes the results for $CDCl_3$ (acetone solutions gave similar chemical shifts and line widths). In contrast, C_6D_6 as a solvent results in much sharper signals and a weaker concentration dependence (see Figure 3).[5]

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(1) Albeck, M.; Tamari, T.; Sredni, B. *Synthesis* **1989**, 635.
(2) Denney, D. B.; Denney, D. Z.; Hammond, P. J.; Hsu, Y. F. *J. Am. Chem. Soc.* **1981**, *103*, 2340.
(3) Holmes, R. R. *Acc. Chem. Res.* **1979**, *12*, 257.
(4) Day, R. O.; Holmes, R. R. *Inorg. Chem.* **1981**, *20*, 3071.

(5) Measurements of the depression of the melting point of benzene as a function of the concentration of dissolved $Te(OEt)_4$ or $Te(O^iPr)_4$, up to 1 M, show that these telluranes are essentially monomeric under these conditions.

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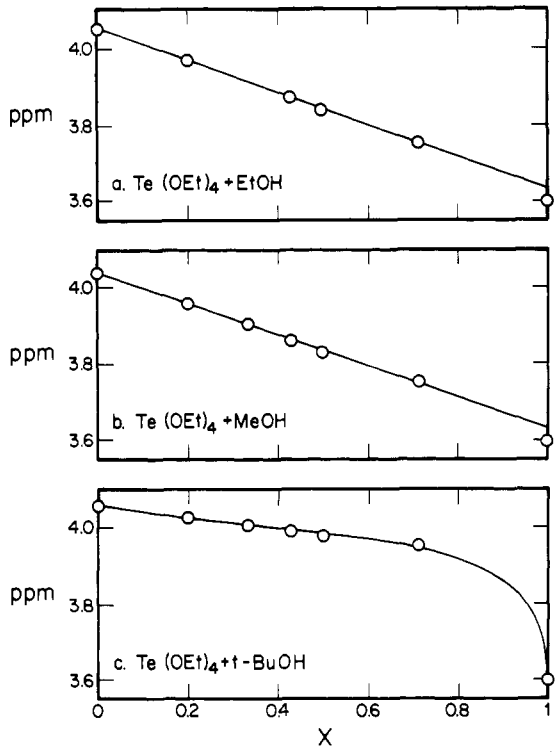


Figure 2. ^{1}H chemical shifts of the oxymethylene of $Te(OEt)_4$ as a function of the amount of added free alcohol. δ's are plotted *vs* X, the molar fraction of alkoxy groups not bound to Te (e.g. $X = 0.5$ indicates that the ratio $Te(OEt)_4$:ROH = 1:4). The points for $X = 1$ correspond to the chemical shift for EtOH in the same solvent.

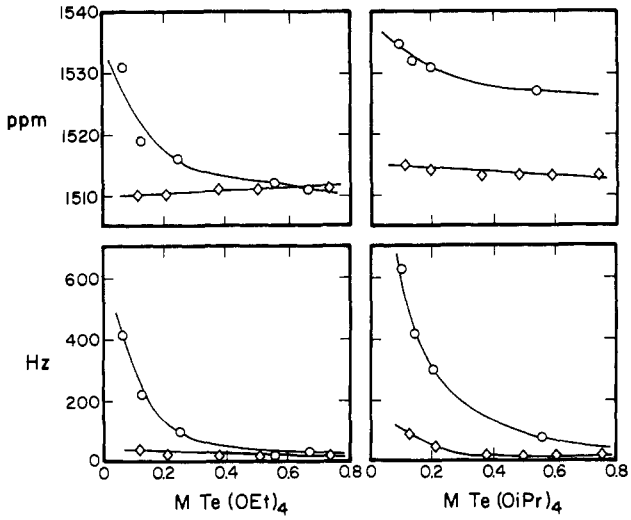


Figure 3. ^{125}Te chemical shifts (top) and line widths ($\nu_{1/2}$, bottom) for $Te(OEt)_4$ and $Te(O^iPr)_4$ as a function of concentration. Circles and diamonds refer to $CDCl_3$ and C_6D_6 solutions, respectively.

The most likely explanation for the strong concentration and solvent dependence of the ^{125}Te NMR parameters is some type of associative process in solution (the wide ^{125}Te chemical shift range makes this nucleus very sensitive to such phenomena). In fact, the few known X-ray structures of tetraoxytelluranes show that in the solid these substances exist as polymeric chains in which an axial oxygen coordinates with the tellurium atom of the next monomer unit.[4,6] The most extreme case may be that of $Te(OMe)_4$, which is so insoluble that we could not even detect ^{1}H NMR signals. The small size of the ligands probably enables the formation of a very stable polymeric crystalline lattice. The contrast between this high-melting, virtually insoluble solid, and

(6) Lindqvist, O. *Acta Chem. Scand.* **1967**, *21*, 1473.

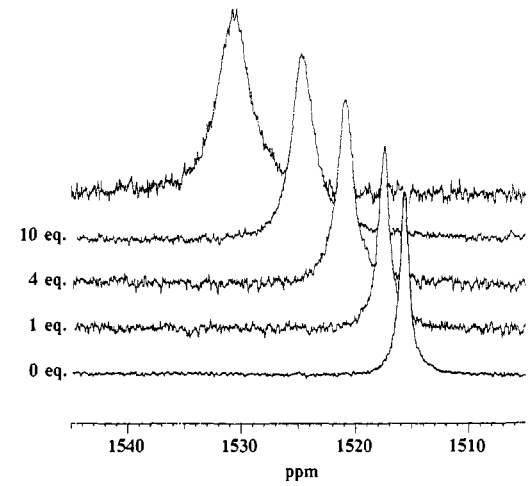
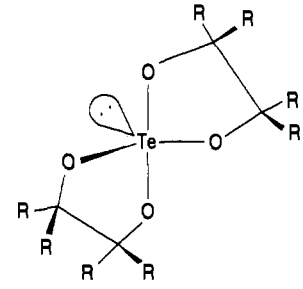


Figure 4. Bottom traces: ^{125}Te NMR spectra of a 0.25 M solution of $Te(OEt)_4$ in $CDCl_3$, to which were added increasing amounts (values on the left, in equivalents) of ^{i}PrOH. Top trace: ^{125}Te NMR spectrum of a 0.21 M solution of $Te(O^iPr)_4$ in $CDCl_3$.

1 and **2**, distillable liquids which readily dissolve in nonpolar organic solvents, could not be starker.

The ligand exchange phenomenon described in the previous section is apparent also in the ^{125}Te NMR spectra. As can be seen in Figure 4, addition of 2-propanol to a $CDCl_3$ solution of $Te(OEt)_4$ causes a downfield shift and broadening of the Te signal, which can be seen to extrapolate to the spectrum of $Te(O^iPr)_4$, taken at a similar concentration. In contrast, when a diol such as ethylene glycol is added to a tetraalkoxytellurane, e.g. **2**, 2 equiv of the diol (which can displace four 2-propanol molecules) results in a sharp line that no longer significantly changes if an excess of glycol is added. This result indicates that the reaction goes to completion; i.e., the equilibrium strongly favors cyclic telluranes such as **3**. It is known that complexes of P, S, and Se in which the central atom is part of a five-membered ring are relatively highly stable.[3] The present study shows that this conclusion is valid also for a fourth-row element in spite of the difference in the size of the central atom.

We used the exchange reaction described in the previous paragraph, preparatively, to obtain the telluranes derived from ethylene glycol (**3a**) and pinacol (**3b**); as expected, their ^{125}Te as well as ^{1}H NMR spectra are not affected by the addition of simple alcohols to the NMR solutions. The solubility/ligand size correlation mentioned above applies for the cyclic telluranes as well; while **3b** (mp 128 °C) readily dissolves in $CDCl_3$ and other nonpolar solvents, **3a** (mp > 210 °C dec) only dissolved appreciably in DMSO-d_6.



3a, R = H
3b, R = CH_3

Intramolecular Ligand Exchange. As is the case for acyclic tetraalkoxytelluranes, ligand reorganization for the cyclic derivatives **3a** and **3b** is fast with respect to the NMR time scale at room temperature, at which these compounds give only one sharp ^{13}C line for the oxygenated carbon (a CH_2 or a C, respectively).

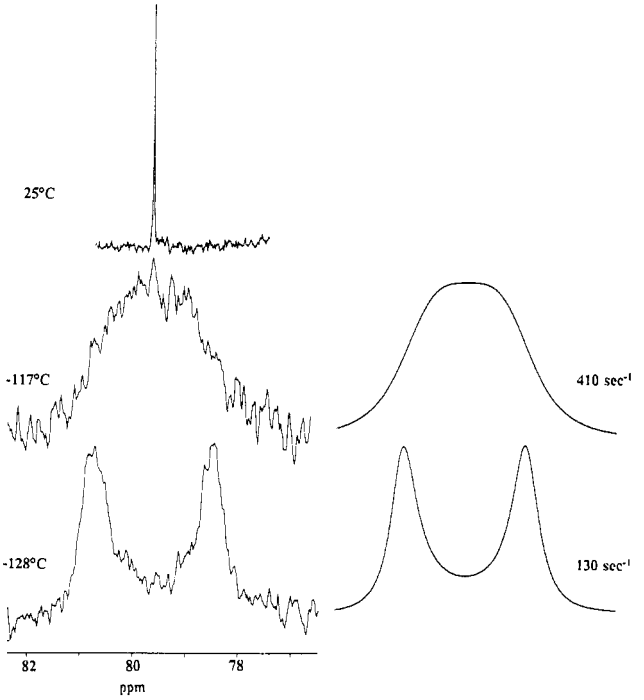


Figure 5. ^{13}C NMR spectra of the oxycarbon region of **3b**, as a function of the temperature (on the left), and calculated line shapes (on the right, for the rate constants indicated).

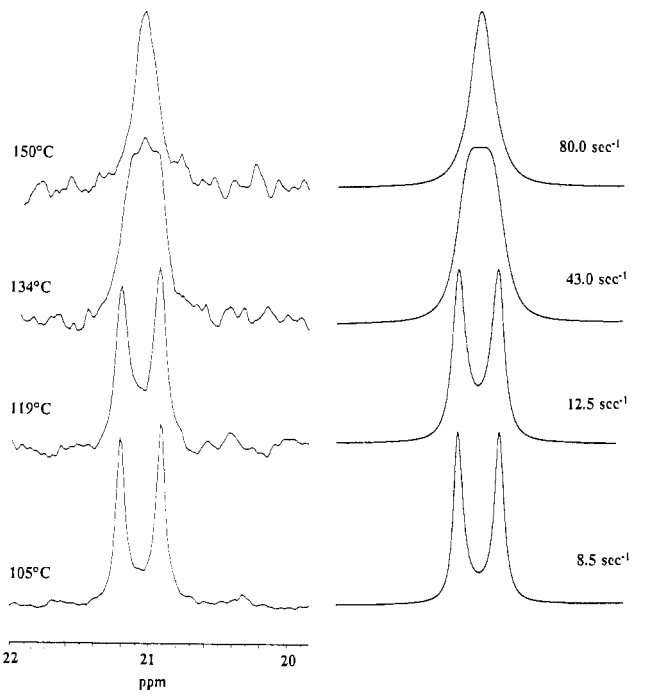


Figure 6. ^{13}C NMR spectra of the methyl region of **3b**, as a function of the temperature (on the left), and calculated line shapes (on the right, for the rate constants indicated).

Table I. Kinetic Parameters for Ligand Exchange Reactions in **3b**

T, °C	k, s^{-1}	$\Delta G^{\ddagger}$, kcal·mol^{-1}
	(a) Low-Energy Process[a]	
−127.7	130	6.9
−117.1	410	7.1
	(b) High-Energy Process[b]	
104.6	8.5	20.5
118.6	12.5	21.0
133.6	43	20.9
149.8	80	21.2

[a] In 2:1 CF_2Cl_2 + toluene-d_8. [b] In C_6D_5Br.

At very low temperatures, however, we observed two signals of the same intensity for the quaternary carbon of pinacol derivative **3b**. Lineshape analysis (Figure 5 and Table Ia) allows us to determine that the barrier for ligand interconversion is 7.0 ± 0.1 kcal/mol. This seems to be the first reported measurement of such a process in alkoxytelluranes; it is also the lowest known barrier among group 16 analogs. For the corresponding selenurane[2] and for the CF_3-equivalent sulfurane,[7] $\Delta G^{\ddagger}$ values of *ca.* 8 and 7.5 kcal/mol, respectively, are documented in the literature. Similar processes for group 15 central atoms (e.g. phosphoranes and arsoranes) are usually too fast to be measured by NMR.[3]

We may interpret the scrambling of the axial and equatorial ligands as a Berry pseudorotation (BPR) in which the equatorial electron pair serves as a pivot. The transition state of this reaction is a tetragonal pyramid with an axial electron pair; as a consequence, the identity of the axial and equatorial substituents in the original TBP is lost. While this will result in averaging of the oxycarbons, it will not, however, completely average the R groups in structure **3**, since residues *cis* and *trans* relative to the electron pair, respectively, do not interchange. Full coalescence requires a distinct mechanism, e.g. a BPR in which one of the equatorial alkoxy groups serves as a pivot. This process will produce a conformer with one diequatorial ring as an intermediate; a second BPR step would quickly restore the original structure. A repetition of the sequence with the other equatorial group as a pivot would finally lead to complete scrambling of magnetization among all the possible equivalent sites.[8]

The experimental evidence is consistent with the two processes described in the previous paragraph or symmetry-equivalent transformations. We already mentioned the low-barrier mechanism that scrambles the axial and equatorial ligands. At room temperature, this is fast with respect to the NMR time scale, but the methyl groups of **3b** or the hydrogens of **3a** still give two separate signals in the ^1H and/or ^{13}C spectra. By heating a C_6D_5Br solution of **3b**, however, we did observe the coalescence of the two methyl signals in the ^1H and ^{13}C NMR spectra into one line (Figure 6). The $\Delta G^{\ddagger}$ value obtained from line-fitting of the ^{13}C line shapes (Table Ib) is 20.9 ± 0.2 kcal/mol for the 100–150 °C temperature range. Fitting of the ^1H line shapes is less precise since the two methyl signals can be seen by resolution enhancement techniques to be quartets ($^4J_{HH}$ = 0.5 Hz). Similarly, the ^1H NMR spectrum of a DMSO-d_6 solution of **3a** simplifies on heating, from two broad humps at room temperature to a singlet, with T_C = *ca.* 60 °C. It is very difficult, however, to get quantitative estimates of $\Delta G^{\ddagger}$ due to the complexity of the NMR spin system ($AA'BB' \rightarrow A_4$) as well as because it is impossible to be sure of the dryness of this exceedingly hygroscopic solvent (*vide infra*).

While we know of no previous report of such a process for tetracoordinated group 16 elements, its equivalent is well-known for pentacoordinated group 15 complexes. For instance, for the analogs of **3b**, $PH(OCMe_2CMe_2O)_2$ and $AsCH_3(OCMe_2CMe_2O)_2$, the energies of activation are 18.4[9] and 21.8[10] kcal/mol, respectively.

Acid-Catalyzed Exchange. The thermal mechanism described in the previous paragraphs is not the only process which will completely average all the methyl groups in **3b**. One can envisage

(7) Astrologes, G. W.; Martin, J. C. *J. Am. Chem. Soc.* **1976**, *98*, 2895.

(8) We cannot exclude the possibility of methyl scrambling through direct Te–O bond fission followed by Te inversion and reattachment (*vide infra*). However, while Te–C bond breakage is well documented and leads to disproportionation, we know of no precedent for its existence in the case of oxygen substituents: Barton, D. H. R.; Glover, S. A.; Ley, S. V. *J. Chem. Soc., Chem. Commun.* **1977**, 266. Oae, S.; Uchida, Y. *Acc. Chem. Res.* **1991**, *24*, 202.

(9) Houalla, D.; Wolf, R.; Gagnaire, D.; Robert, J. B. *J. Chem. Soc., Chem. Commun.* **1969**, 443.

(10) Casey, J. P.; Mislow, K. *J. Chem. Soc., Chem. Commun.* **1970**, 1410.

protonation of one of the oxygens of the tellurane followed by Te–O bond cleavage to an intermediate with a positively charged tellurium. Inversion followed by ring closure and deprotonation will also lead to overall methyl averaging.[11] In order to explore this possibility, measured amounts of a solution of CF_3CO_2H in $CHCl_3$ were added to **3b** in $CDCl_3$ at 24 °C. This caused broadening and eventually coalescence of the methyl peaks. The rate constants from line fitting were roughly proportional to the amount of added acid, with coalescence ($k_{obs} = ca.\ 50\ s^{-1}$) occurring when a total of 0.016 equiv of acid had been introduced. In order to establish that the measured reaction rate constants (Table Ib) had not been affected by traces of acid or water, we performed a control experiment in which (diethylamino)trimethylsilane, an acid and water scavenger,[2] was added to our **3b**/C_6D_5Br sample. The NMR line shapes, at the temperatures measured previously, remained unchanged.

It is interesting to note that the acid-catalyzed process seems to be much more facile in the tetraalkoxyselenuranes. Under normal conditions, the trace amount of water present in $CDCl_3$ is sufficient, as found by Denney,[2] to catalyze this reaction. In contrast, in the tellurane system, much higher temperatures[12] or a much stronger acid are required to induce such a process at a measurable rate.

Experimental Section

Most NMR spectra were recorded on a Bruker AM-300 instrument, at 300.1 (^{1}H), 75.5 (^{13}C), or 94.7 MHz (^{125}Te), respectively. For ^{1}H and ^{13}C, chemical shifts are referred to internal TMS. For ^{125}Te, a spectrum of 0.42 M Ph_2Te in $CDCl_3$ was obtained and the tellurium line taken as 688 ppm (neat Me_2Te = 0 ppm).[13] This frequency was maintained as an external reference. Some ^{1}H NMR experiments were performed at 200.1 MHz on a Bruker AC-200 instrument. Probe temperatures were measured with a calibrated Eurotherm 840/T digital thermometer connected to a thermocouple which was introduced into a solvent-filled NMR tube. Readings are estimated to be correct up to ±0.5 °C. NMR line shapes were derived from a program written by R. E. D. McClung, University of Alberta, Edmonton, Alberta, Canada T6J 2G2 (the program does a full density matrix calculation and allows for any number of interchanging species). $\Delta G^{\ddagger}$ values were obtained *via* the Eyring equation, assuming a transmission coefficient = 1. The acid-catalyzed methyl exchange experiment for **3b** was performed with a 0.016 M solution of the tellurane in $CDCl_3$ to which measured amounts of a 0.013 M solution of CF_3CO_2H in $CHCl_3$ were added.

Mass spectra were obtained on a Finnigan 4021 instrument. All fragments containing Te show a typical isotope pattern; in the following, we report the m/z value (% relative intensity) for those including only the most abundant, highest atomic weight isotope, ^{130}Te.

Materials. All alcohols and solvents were dried prior to use. A freshly opened bottle of $TeCl_4$ (Merck) was used without any other treatment.

Tetraethoxytellurane (1) was prepared by the method of Denney *et al.*,[2] except that the difficult step of filtration of NaCl was substituted by centrifugation. ^{1}H NMR ($CDCl_3$): δ 1.26 (t, J = 7 Hz, 12 H), 4.03 (q, J = 7 Hz, 8 H). ^{13}C NMR ($CDCl_3$): δ 18.50 (CH_3), 59.36 (CH_2). ^{125}Te NMR (0.56 M, $CDCl_3$): 1512 ppm ($\nu_{1/2}$ = 17 Hz). MS (CI, CH_4): 265 [100%, $Te(OEt)_3^+$], 236 [55%, $TeO(OEt)_2^+$], 207 [10%, TeO_2OEt^+]. Anal. Calcd for $C_8H_{20}O_4Te$: C, 31.21; H, 6.54; O, 20.78; Te, 41.44. Found: C, 30.81; H, 6.32; O, 20.42; Te, 41.05.

Tetraisopropoxytellurane (2) was prepared by the method of Merothra and Mathur,[14] with the addition of a centrifugation step. ^{1}H NMR ($CDCl_3$): δ 1.23 (d, J = 6.5 Hz, 24 H), 4.56 (septet, J = 6.5 Hz, 4 H). ^{13}C NMR ($CDCl_3$): δ 26.12 (CH_3), 65.95 (CH). ^{125}Te NMR (0.56 M, $CDCl_3$): 1229 ppm ($\nu_{1/2}$ = 68 Hz). MS (CI, CH_4): 307 [100%, $Te(OPr)_3^+$], 265 [20%, $TeOH(OPr)_2^+$], 223 [21%, $Te(OH)_2OPr^+$], 181 [22%, $Te(OH)_3^+$].

Tetramethoxytellurane was prepared by the procedure of Denney *et al.*,[2] (*vide supra*). MS (CI, NH_3): 477 [100%, $Te_2(OMe)_7^+$], 431 [18%, $Te_2O(OMe)_5^+$], 223 [65%, $Te(OMe)_3^+$].

1,4,6,9-Tetraoxa-5-telluraspiro[4,4]nonane (3a). A 0.45-g sample of **2** (1.37 mmol) was added with stirring to 0.17 g (2.74 mmol) of ethylene glycol. The reaction was exothermic, and a precipitate of **3a** formed immediately. Vacuum drying provided 0.34 g of **3a** (99% yield), which was pure by NMR and elemental analysis. ^{1}H NMR (DMSO-d_6): δ 3.79 (br, 4 H), 3.93 (br, 4 H). ^{13}C NMR (DMSO-d_6): δ 63.97 (CH_2). ^{125}Te NMR (0.20 M, DMSO-d_6): 1698 ppm ($\nu_{1/2}$ = 12 Hz). MS (CI, NH_3): 268 [28%, MNH_4^+], 251 [100%, MH^+]. MS (EI): 220 [14%, $(M\text{-}CH_2O)^+$], 190 [100%, $Te(C_2H_4O_2)^+$], 160 [10%, $Te(CH_2O)^+$], 130 [17%, Te^+]. Anal. Calcd for $C_4H_8O_4Te$: C, 19.38; H, 3.23; O, 25.84; Te, 51.15. Found: C, 19.20; H, 2.99; O, 26.19; Te, 51.81.

2,2,3,3,7,7,8,8-Octamethyl-1,4,6,9-tetraoxa-5-telluraspiro[4,4]nonane (3b). The procedure used for **3a** was repeated with 0.52 g (1.42 mmol) of **2** and 0.33 g (2.84 mmol) of pinacol. Yield: 0.51 g (99%). ^{1}H NMR ($CDCl_3$): δ 1.21 (s, 12 H), 1.28 (s, 12 H). ^{13}C NMR ($CDCl_3$): δ 25.36 (CH_3), 25.53 (CH_3), 80.03 (C). ^{125}Te NMR (0.23 M, C_6D_6): 1504 ppm ($\nu_{1/2}$ = 3 Hz). MS (EI): 363 [93%, MH^+], 347 [29%, $(M - CH_3)^+$], 263 [14%, $TeOH(C_6H_{12}O_2)^+$], 246 [100%, $Te(C_6H_{12}O_2)^+$]. Anal. Calcd for $C_{12}H_{24}O_4Te$: C, 40.05; H, 6.72; O, 17.78; Te, 35.45. Found: C, 39.94; H, 6.68; O, 17.78; Te, 35.20. **3a** and **3b** may be similarly prepared from **1** and the appropriate glycols.

(11) A review has brought to our attention a report in the literature [Kuhn, N.; Schumann, H.; Zauder, E. *J. Organomet. Chem.* **1987**, *327*, 17] on the measurement of the kinetics of inversion about the S atom of Me_2SFe moieties and their Se analogs. These authors were unable, however, to obtain $\Delta G^{\ddagger}$ values for Te derivatives (T_c > 100 °C).

(12) A sample of **3b** which was allowed to stand for several days showed a much lower coalescence temperature (*ca.* 100 °C; compare to Figure 6), presumably due to absorbed water. Addition of Et_2NSiMe_3 restored the original line shape.

(13) Luthra, N. P.; Odom, J. D. *The Chemistry of Organic Selenium and Tellurium Compounds*; Patai, S., Rappoport, Z., Ed.; Wiley: Chichester, England, 1986; Chapter 6.

(14) Merothra, R. C.; Mathur, S. N. *J. Indian Chem. Soc.* **1965**, *42*, 1.