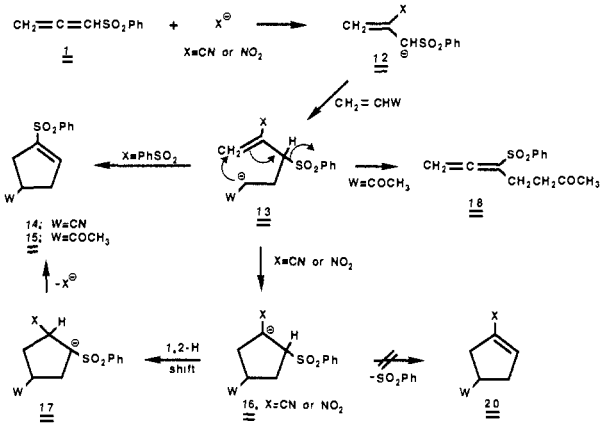
Scheme IV



the abnormal adduct **9** as the major product (60%)[10] (see Scheme III). This is perfectly compatible with the reaction sequence outlined in Scheme II. An additional piece of data which supports the SN'_2 sequence was obtained by carrying out the reaction of bis(phenylsulfonyl)methane with 3-(phenylsulfonyl)-buta-1,2-diene in the presence of sodium benzenesulfinate. The major product isolated here corresponded to structure **10**.[11] The formation of **10** is readily explained in terms of an attack of anion **7** onto the methylene carbon of the initially formed disulfone **11**.

Considering the great utility of vinyl sulfones in organic synthesis,[12] we sought to develop an annulation strategy for cyclopentenyl sulfone formation which involves treating (phenylsulfonyl)allene with an activated olefin in the presence of a nucleophilic reagent (see Scheme IV). In this approach, generation of carbanion **12** by reaction of the nucleophile with **1** is followed by a cyclization-elimination sequence[2] to provide the five-membered ring. Indeed, when allene **1**, acrylonitrile, and sodium benzenesulfinate (trace) are stirred in THF at ambient temperature, cycloadduct **14**[13] was isolated in 73% yield. Similar results were obtained when sodium cyanide or sodium nitrite were used as catalysts. Addition of these reagents to the allene generates a cyclized intermediate (i.e., **16**) which undergoes a 1,2-proton shift to give **17** prior to sulfinate ejection. A subsequent elimination of cyanide (or nitrite) ion generates the observed product (Scheme IV).

A similar set of reactions takes place when methyl vinyl ketone was used as the trapping agent.[14] Addition of sodium nitrite to **1** and MVK gave **15** in 75% yield in addition to allene **18** (8% yield).[15] The formation of **18** involves intramolecular proton transfer of the hydrogen adjacent to the sulfonyl group to the enolate oxygen followed by loss of sulfinate.

The high efficiency of this novel five-membered ring-forming process, coupled with the simplicity of the procedure, promises to provide an efficient route to a variety of cyclopentenyl-substituted sulfones. We are continuing to explore the scope and mechanistic details of this novel annulation reaction and will report additional findings at a later date.

Acknowledgment. We thank the National Science Foundation for generous support of this work.

(10) **9**: NMR ($CDCl_3$, 300 MHz) δ 2.83 (d, 2 H, J = 7.6 Hz), 3.69 (s, 6 H), 3.83 (t, 1 H, J = 7.6 Hz), 5.83 (s, 1 H), 6.41 (s, 1 H), and 7.5-7.8 (m, 5 H).

(11) **10**: NMR ($CDCl_3$, 300 MHz) δ 2.04 (d, 3 H, J = 7.2 Hz), 3.23 (d, 2 H, J = 6.4 Hz), 5.85 (t, 1 H, J = 6.4 Hz), δ 7.20 (q, 1 H, J = 7.2 Hz), and 7.4-7.8 (m, 15 H).

(12) Magnus, P. D. *Tetrahedron* **1977**, *33*, 2019.

(13) **14**: NMR ($CDCl_3$, 300 MHz) δ 2.80-3.1 (m, 4 H), 3.30 (p, 1 H, J = 6.9 Hz), 6.68 (s, 1 H), and 7.5-7.9 (m, 5 H).

(14) The cycloaddition proceeded smoothly with use of ethyl (or phenyl) vinyl ketone. Reaction with acrolein or methyl acrylate, on the other hand, led to polymer. Further work is currently underway so as to ascertain the scope and generality of the reaction.

(15) **15**: NMR ($CDCl_3$, 300 MHz) δ 2.10 (s, 3 H), 2.65-2.90 (m, 4 H), 3.40 (p, 1 H, J = 7.6 Hz), 6.63 (s, 1 H), and 7.5-7.9 (m, 5 H). **18**: NMR ($CDCl_3$, 300 MHz) δ 2.08 (s, 3 H), 2.44-2.50 (m, 2 H), 2.62 (t, 2 H, J = 7.1 Hz), 5.35 (t, 2 H, J = 3.3 Hz) and 7.5-7.9 (m, 5 H).

First Simultaneous Observation of the ^{133}Cs NMR from Cs^+, Cs^-, and Cs^+e^- in a Metal Solution

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There is much current interest in the preparation and study of solutions of alkali metals in nonaqueous solvents containing either crown ethers or cryptands.[1] The observation of nuclear magnetic resonance (NMR) signals from all the alkali anions (except lithium) in these systems has provided detailed information about these intriguing species.[2-8] By comparison, in these metal solutions, the characterization of species based on either the alkali metal cation (M^+) or the electron-cation species (M^+e^-) has been largely neglected. Here we report the first NMR observation of all three cesium species, Cs^+, Cs^+e^-, and Cs^-, present in the same metal solution.

No ^{133}Cs NMR signals could be detected from solutions of cesium metal in the pure crown ether solvents, 12-crown-4 (12C4) and 15-crown-5 (15C5), even though the optical spectra of these blue solutions reveal the presence of the Cs ions.[9,10] The failure to observe such NMR signals suggests that they are broadened beyond detection either by chemical exchange processes or by a highly efficient relaxation mechanism. Unfortunately, these two liquid crown ethers have only a very narrow temperature range because of their relatively high freezing points (>260 K). However, as illustrated by Dye,[1] the accessible liquid temperature range can be increased by the addition of a cosolvent such as tetrahydrofuran (THF).

Figure 1 shows ^{133}Cs NMR spectra at 193 K for three saturated cesium metal solutions containing different proportions of the liquid crown ethers 12C4 and 15C5, in THF. Solutions which contain low crown ether content (<5% v/v), Figure 1 (parts a and b), yield spectra which consist of either two or three signals. The signals at chemical shifts (δ, see caption to Figure 1) of -300 and -280 ppm for 12C4 and 15C5 solutions, respectively, can be assigned[2] to the cesium anion (Cs^-). For the cesium-THF solution containing 5% 12C4 (Figure 1a) there are two additional signals, having chemical shifts of +1.9 and +65.9 ppm, which we assign to cation-based species. The signal at +1.9 ppm is assigned to the species ($Cs^+(12C4)_2$) consisting of a Cs^+ ion complexed by two 12C4 molecules. This assignment is unambiguous because signals having similar chemical shifts (δ = -4 ppm) and line widths ($\Delta\nu_{1/2}$, approximately 50 Hz) are observed from solutions of cesium halides (CsX; X = Cl, Br, I) in neat liquid 12C4. There are two compelling reasons for assigning the broader signal located at +65.9 ppm to the paramagnetic complex $Cs^+(12C4)_2e^-$. First, the NMR signal from the solid electride $Cs^+(12C4)_2e^-$, whose crystal structure has been characterized, occurs at almost the identical chemical shift.[11] Secondly, the shift difference between the $Cs^+(12C4)_2$ and $Cs^+(12C4)_2e^-$ signals is a Knight shift

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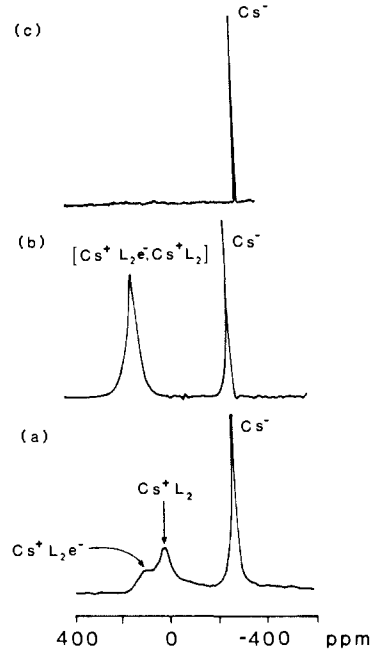

Figure 1. ^{133}Cs NMR spectra (52.485 MHz) at 193 K of cesium–metal solutions in (a) 5% v/v 12C4/THF, (b) 5% v/v 15C5/THF, and (c) 20% v/v 12C4/THF solvent mixtures. Spectra (a) and (b) have 500 Hz exponential broadening. Chemical shifts are measured relative to an infinitely dilute solution of CsCl in D_2O. A negative chemical shift corresponds to an increase in the nuclear shielding.

$(\Delta H/H)$ which originates from the Fermi contact interaction with the unpaired electron. This shift difference is given by [12]

$$\frac{\Delta H}{H} = -\frac{g_e\beta_e}{g_n\beta_n}\frac{A}{4kT} \quad (1)$$

where A is the metal hyperfine coupling constant and g_e and g_n are the electronic and nuclear g factors, whilst β_e and β_n are the Bohr and nuclear magneton. By using this equation, it is predicted from the observed Knight shift of 64 ppm, that A is 20 000 Hz. In the liquid state, one expects to observe a single NMR signal from the species $Cs^+(12C4)_2e^-$ if T_{1e}^{-1}, the inverse of the electron spin-lattice relaxation time, is much greater than A. If the nuclear relaxation of ^{133}Cs in $Cs^+(12C4)_2e^-$ is dominated by the modulation of the hyperfine coupling by the electron spin-lattice relaxation, the width of the NMR signal is given by[13]

$$\Delta\nu_{1/2}(\text{Hz}) = \pi A^2 T_{1e} \quad (2)$$

Our experimentally derived value for T_{1e} of 3×10^{-8} s at 190 K for this solution, when combined with the above A value of 20 000 Hz, predicts from eq 2 that the width of the NMR signal from $Cs^+(12C4)_2e^-$ is 38 Hz. The contribution to the observed line width arising from other processes, such as quadrupolar relaxation, can be expected to be similar to those occurring for the diamagnetic species $Cs^+(12C4)_2$. It is found experimentally that the NMR line width of $Cs^+(12C4)_2e^-$ is some 30 Hz greater than that of the $Cs^+(12C4)_2$ signal. The close similarity between this experimental result with the width calculated above provides compelling evidence for the assignment.

Upon raising the temperature, the signals from $Cs^+(12C4)_2e^-$ and $Cs^+(12C4)_2$ broaden rapidly and finally coalesce to form a single broad line at 200 K. The averaging of these two NMR signals we ascribe to the equilibrium

$$Cs^+(12C4)_2 + e^- \rightleftarrows Cs^+(12C4)_2e^- \quad (3)$$

At higher temperatures the signal broadens very rapidly to become unobservable. The failure of the averaged signal to sharpen with increase in temperature arises from an extremely efficient nuclear spin relaxation mechanism, whose rate increases very rapidly with temperature. The physical origins of this relaxation mechanism will be described in detail elsewhere. The dynamic processes responsible for broadening the Cs^+-based species can also be enhanced by the addition of further 12C4 to the mixed solvent system. Thus the nuclear relaxation processes responsible for the failure to observe cation-based signals in the 5% v/v 12C4 solution at high temperatures are also the cause of the absence of similar signals in the system containing 20% v/v 12C4 (Figure 1c), even at the lowest temperatures.

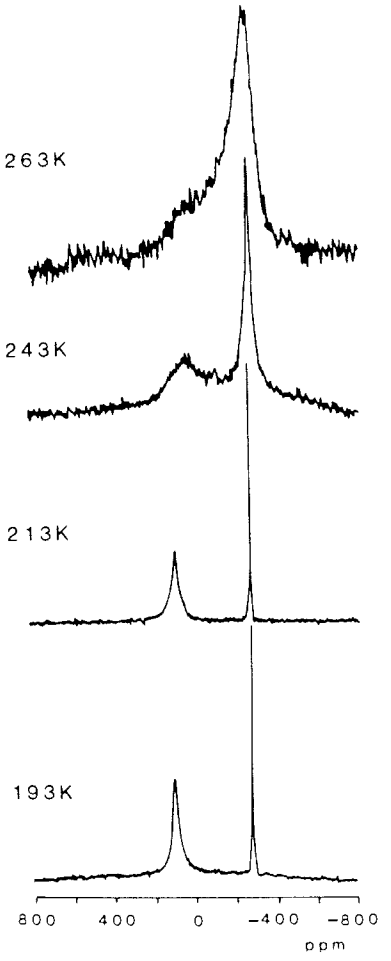

Figure 2. Temperature dependence of ^{133}Cs NMR spectra of cesium–metal solution in 5% v/v 15C5/THF solvent mixtures.

The ^{133}Cs NMR spectra at various temperatures from a solution of Cs metal in a 5% v/v mixture of 15C5 and THF are shown in Figure 2. In the lowest temperature spectrum, the signal at $\delta = +109$ ppm can be assigned largely, if not entirely, to the species $Cs^+(15C5)_2e^-$, because this shift is very similar to that measured for the solid electride $Cs^+(15C5)_2e^-$.[12] If this signal does not arise entirely from this paramagnetic species but rather represents a time average of signals from both $Cs^+(15C5)_2e^-$ and $Cs^+(15C5)_2$, then the observed shift suggests that the equilibrium analogous to eq 3 is well over to the right for the heavier ionophore. The spectrum at 193 K shows that the cation signal at $\delta = +109$ ppm has an integrated area x ($x > 5$) times greater than that of the Cs^- signal at $\delta = -280$ ppm. Hence the contributions to the widths of these peaks arising from lifetime limitation in the classic two-site exchange process would be in the ratio $1:x$. Therefore, the major contribution to the width of the cation signal at this temperature cannot arise from direct exchange between the cation-based species and the Cs^- ion. On increasing the temperature, the cation signal broadens much more rapidly than the anion signal. If this broadening were to arise from the direct exchange process, the anion signal would have to broaden at a rate x times greater than the cation signal. This is not observed experimentally. Indeed,

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at 213 K the anion signal has almost the same width as that at 193 K, whilst the cation signal has broadened by some 50%. Hence the broadening of both cation and anion peaks over the entire temperature range shows that this broadening does not arise from a classic two-site exchange process.

Solutions which contain mixed alkali metals CsM (M = Na, K, and Rb) in crown ether (L)-THF solvent mixtures show ^{133}Cs NMR spectra which consist of only a single NMR line due to the complex cation $Cs^+(L)_2$. Furthermore, ^{23}Na, ^{39}K, ^{85}Rb, and ^{87}Rb NMR studies of the same solutions show the presence of the Na^-, K^-, and Rb^- ions. This clearly reflects the greater thermodynamic stability, in these solutions, of each species $Cs^+(L)_2M^-$ compared with $M^+(L)_2Cs^-$. The temperature dependences of the NMR characteristics (δ, $\Delta\nu_{1/2}$) of the Cs^+ signals in these mixed-metal solutions are consistent with the assignment to $Cs^+(L)_2$. Increasing the temperature leads to a substantial increase in the line width of the cation signal, coupled with a very small diamagnetic shift and decrease in the spin-lattice relaxation rates. For example, the $Cs^+(12C4)_2$ NMR signal observed from CsNa solutions in a 12C4/THF solvent mixture has δ = -22.4 ppm, $\Delta\nu_{1/2}$ = 95 Hz, and T_{1n} = 8 ms at 198 K changing to δ = -26.4 ppm, $\Delta\nu_{1/2}$ = 720 Hz, and T_{1n} = 34.5 ms at 243 K. No signal could be detected above 250 K. The decrease in the cesium nuclear spin-lattice relaxation rate at higher temperatures is consistent with quadrupolar relaxation for the cation-based signal in the system. However, the substantial increase in the line width suggests the presence of exchange processes. Clearly, direct exchange between Cs^- and, for example, Na^+ is ruled out in these mixed-metal solutions.

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The Characterization of Abasic Sites in DNA Heteroduplexes by Site Specific Labeling with ^{13}C

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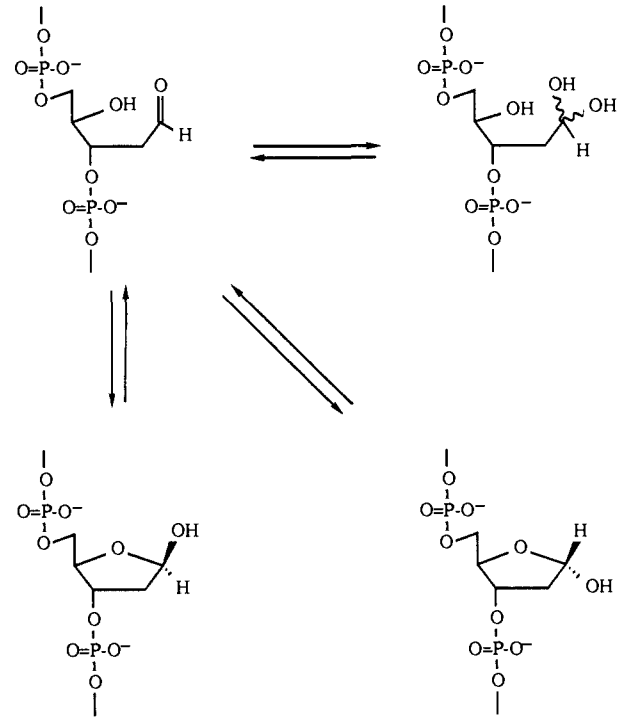
Damage to a base in DNA duplexes is followed by either chemical or enzyme-catalyzed hydrolysis of the N-glycosidic bond to yield a baseless site.[2,3] For example, the spontaneous hydrolysis of the 4-amino group of cytosine to yield uracil occurs at a genetically significant rate. Since this lesion is mutagenic, the cells of all organisms contain the enzyme uracil-DNA glycosylase which hydrolyzes the N-glycosidic bonds of deoxyuridine residues to release uracil. The resulting mixture of open chain aldehyde and hydrate and cyclic hemiacetals (Scheme I) is termed an abasic site. The abasic site is then repaired by the action of several additional enzymes. Despite the intermediacy of abasic sites in the repair of damaged DNA and their reported mutagenicity during transcription,[4,5] no detailed information is available about their structure, and controversy exists regarding the chemical reactivity of such sites.[6,7] We have prepared heptameric heteroduplexes containing a single abasic site (with each of the four bases opposite the abasic site) in which the 1- and 3-carbons of the abasic site are labeled with ^{13}C, thereby enabling direct observation of the ^{13}C resonances associated with the aldehydic carbon of the abasic site.

Scheme I



The synthesis of d(GCGUGCG) in which the deoxyuridine moiety is labeled in its 1'- and 3'-carbons with ^{13}C was previously described;[8] the unlabeled single strand and the four "complementary" single strands d(CGCNCGC), where N = A, G, T, and C (designated the A, G, T, and C strands), were prepared with phosphoramidite chemistry by using an automated DNA synthesizer. The strands were judged homogeneous by HPLC and ^1H NMR spectroscopy at 400 MHz.

Single strands containing the abasic site were obtained by incubation of the deoxyuridine containing strands with sufficient uracil-DNA glycosylase from *Escherichia coli*[9-11] to give complete reaction in approximately 12 h as assessed by HPLC and ^1H NMR spectroscopy.[12] Equal amounts of the abasic strand (designated the D strand for *d*eoxyribose) and each of the four complementary stands were mixed to generate the heteroduplexes studied by NMR spectroscopy.

^1H NMR spectra (at 400 MHz) of the imino region and of the aromatic and anomeric region of mixtures of strands using unlabeled U strand were recorded to assess whether duplex formation

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(12) The incubations were carried out at room temperature in a solution of 10 mM sodium cacodylate, pH 7.0, containing 0.1 M NaCl and 0.1 mM EDTA in D_2O to allow monitoring of the reaction by ^1H NMR spectroscopy; the concentration of the deoxyuridine containing single strand was 1 to 2 mM. The same buffer was used for the NMR studies.

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