Table I. Vibrational Assignments for CF_2=NX

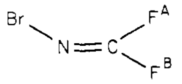
	CF_2=NF[a]		CF_2=NCl		CF_2=NBr[c]	
	IR	Raman	IR[b]	Raman[c]	IR	Raman
C=N	1740.3 s	1733 m, p	1728 vs	1731 m, p	1742R vs[e] 1732P	1731 w, p
CF_2(as)	1385.5 s	1388 vw, p	1322 s	1322 vw, p	1305R vs[e] 1293P	1305 vw, p
NX	1021.2 s	1013 w, p	771 m	777 vs, p	726R m[e] 718P	727 s, p
CF_2(s)	932.9 s	932 vvs, p	981 s	989 m, p	981R 976Q s 972P	981 w, p
δ-CF_2	640	644 vs, p	598 w	598 s, p	578 w	587 m, p
ρ-CF_2	520.0 w	522 s, p	465 w	465 vs, p	391 w	390 vs, p
δ-NX	285.7 w	291 w, p	228 m[c,d]	237 m, p	200?[f]	199 m, p
β-CF_2	643.2 m	649 m, dp	658 m	659 m, dp	673R 665Q m 657P	663 w, dp
tors	302.5 w	306 m, dp	234 m[c,d]	245 sh, dp?	213 vw[g]	225 vs, dp?

[a] Reference 12. [b] Reference 11. [c] This work. IR taken on a Perkin-Elmer 1430 Data System using a 10-cm cell fitted with CsI windows. Raman spectra were taken on a Spex 1403 Ramalog Double Spectrometer with a Scamp data system. Samples were contained in a low-temperature liquid cell; excitation was by the 514.5 nm line of an argon ion laser (CF_2=NCl, 400 mW; CF_2=NBr, 100 mW). [d] Two overlapping bands. [e] Q branches clearly evident but not readily resolved. [f] Low-wavenumber limit of instrumentation was 200 cm^{-1}. Comparison of background and sample spectrum indicates presence of a medium absorption just below 200 cm^{-1}. [g] Presence of a weak band at 300 torr is clearly evident. At higher pressures, attack of CF_2=NBr on the CsI windows is rapid.

flask is then evacuated and cooled to -196 °C, and Br_2 (4.8 mmol) and FC≡N (3.5 mmol) are added by vacuum transfer. The reactor is then warmed to 22 °C in a water bath while agitating the contents by shaking. Reaction is rapid near 22 °C, and after 1 h, the volatile materials are pumped through a series of cold traps yielding (mmol) CF_3NBr_2 (-75 °C, 1.3) CF_2=NBr (-111 °C, 1.3), and small amounts of FC≡N and C_2F_5Br (-196 °C), the latter present as an impurity in the starting FC≡N.

N-Bromodifluoromethanimine is a pale yellow gas (bp 14.5 °C, $\log P(\text{torr}) = 6.5472 - (642.38/T) - (118655/T^2)$, $\Delta H_{\text{vap}} = 6.71$ kcal/mol, $\Delta S_{\text{vap}} = 23.3$ eu), which freezes to a pale yellow solid (mp -93 to -92 °C). A UV-vis spectrum (210-780 nm) of the gas at 5 torr (10 cm) exhibits an intense absorption at 240 nm ($\epsilon_{\max}$ 651 M^{-1} cm^{-1}) with a weak shoulder near 340 nm. At 20 torr, absorption begins at 600 nm. Under the same conditions, CF_2=NCl shows evidence of strong absorption below 210 nm.

The mass spectrum of CF_2=NBr exhibits intense molecular ions in both EI (100%) and CI (100%) at 143/145 and 144/146, respectively. A vapor-density molecular weight determination gave a value of 144 (calcd 143.923). The ^{19}F NMR (1% in



80:20:1/CCl_4:$CDCl_3$:$CFCl_3$) gave the expected AB spin system with A -31.3, B -54.3, and $^2J_{AB} = 68$ Hz.

The infrared (g) and Raman (l) spectra allow a good assignment of the fundamental vibrational modes in CF_2=NBr based on C_s symmetry. These assignments were easily made by comparison with the spectra of CF_2=NF and CF_2=NCl.[11,12] For CF_2=NCl, previous assignments based on only a partial infrared spectrum must be revised in view of Raman data obtained in this work. The assignments for the compounds are compared in Table I by using the description previously given for CF_2=NF.[12] Within the resolution limit of our instrument, the band contours for CF_2=NBr appear to be nearly identical with those of CF_2=NF. For both CF_2=NBr and CF_2=NCl, the assignment of the torsional frequency is tentative. Neither molecule exhibits a distinct Raman band for this mode. However, very weak features at a somewhat higher frequency than δ-NX are evident in the spectra. In the case of CF_2=NF, the torsion is the second least intense Raman band, and this provides support for the assignments in CF_2=NCl and CF_2=NBr. Taken together, the assignments in Table I provide very reasonable values for the three compounds.

The chemistry of CF_2=NBr is under active investigation and will be reported separately. Other reactions of FC≡N suggested by this work are also being explored.

Acknowledgment. Financial support of this research by the U.S. Army Research Office (DAAG29-83-K0173) and the National Science Foundation (CHE-8217217) is gratefully acknowledged.

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Testing for Symmetry in Neighboring Group Participation in Carbocation Formation. An Insight into Double-Bond Participation via Trifluoromethyl Group Substitution

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As part of our extensive studies of neighboring group participation in carbocation formation, we have made use of two tests for the nature of the interaction of a neighboring group in the stabilization of an incipient carbocation. One of these tests[1] has become known as the "tool of increasing electron demand" and has been extensively used.[2,3] The other involved changing the substituents on the neighboring group to enhance its electron density and hence its ability to act as a neighboring group.[4] This test has not been widely used because the observed rate differences

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(2) For a detailed discussion, see: Brown, H. C. "The Nonclassical Ion Problem"; Plenum Press: New York, 1977; pp 101, 163-175.

(3) For a recent leading reference, see: Olah, G. A.; Prakash, G. K. S.; Farnum, D. G.; Clausen, T. P. *J. Org. Chem.* **1983**, *48*, 2146.

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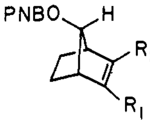
Table I. Rates of Solvolysis of Derivatives of *anti*-7-Hydroxybicyclo[2.2.1]hept-2-ene in 2,2,2-Trifluoroethanol Buffered with 2,6-Lutidine

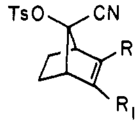
compd	temp (±0.02), °C	rate, s^{-1}	$\Delta H^{\ddagger}$, kcal/mol	$\Delta S^{\ddagger}$, eu	k_{rel}(25 °C)
3	−20.00	$(8.95 \pm 0.04) \times 10^{-4}$	16.68 ± 0.17	−6.27 ± 0.67	
3	−10.00	$(3.28 \pm 0.04) \times 10^{-3}$			
3	25.00[a]	1.55×10^{-1}			1.4×10^{12}
4	85.00	$(4.35 \pm 0.04) \times 10^{-5}$	19.06 ± 0.32	−25.60 ± 0.85	
4	100.00	$(1.41 \pm 0.01) \times 10^{-4}$			
4	115.00	$(3.73 \pm 0.03) \times 10^{-4}$			
4	25.00[a]	1.66×10^{-7}			1.5×10^{6}
6	−10.00	$(2.69 \pm 0.03) \times 10^{-4}$	19.85 ± 0.28	0.85 ± 1.00	
6	5.00	$(2.41 \pm 0.01) \times 10^{-3}$			
6	20.00	$(1.45 \pm 0.04) \times 10^{-2}$			
6	25.00[a]	2.65×10^{-2}			
5	25.00[b]	1.09×10^{-13}			1
7	85.00	$(1.56 \pm 0.01) \times 10^{-5}$	23.37 ± 0.21	−15.60 ± 0.56	
7	100.00	$(6.34 \pm 0.01) \times 10^{-5}$			
7	115.00	$(2.15 \pm 0.02) \times 10^{-4}$			
7	25.00[a]	1.74×10^{-8}			

[a] Extrapolated from other temperatures. [b] $k_5 = k_7(k_4/k_6)$.

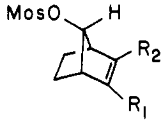
in solvolysis reactions were relatively small. For instance, the relative rates of solvolysis of **1a**, **1b**, and **1c** were 1, 9.5, and 153,



1a, $R_1 = R_2 = H$
b, $R_1 = H$; $R_2 = CH_3$
c, $R_1 = R_2 = CH_3$



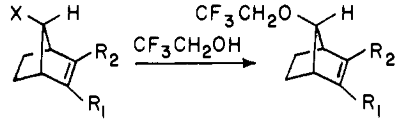
2a, $R_1 = R_2 = H$
b, $R_1 = H$; $R_2 = CH_3$
c, $R_1 = R_2 = CH_3$



3, $R_1 = R_2 = H$
4, $R_1 = H$; $R_2 = CF_3$
5, $R_1 = R_2 = CF_3$

respectively, at 25 °C.[4,5] While these relative rate factors were small, they were sufficient to demonstrate the symmetrical nature of the transition state involved in the ionization of **1a–c**. More recently, we showed that these relative rate factors could be magnified to 1, 86, and 3976 for **2a**, **2b**, and **2c**, respectively, when we destabilized the incipient cationic center through inclusion of an electron-withdrawing group at the site of ionization.[5] We now wish to report that the usefulness of this test for symmetry can be dramatically improved through a new approach, which involves progressive destabilization of the developing delocalized cation through electron withdrawal from the neighboring group. We believe this is amply demonstrated by the relative rate factors observed for the solvolysis of **3–5**.[6-8]

Table I lists the rate data for the solvolyses of **3–7** in anhydrous 2,2,2-trifluoroethanol buffered with 2,6-lutidine. As can be seen from Table I, the relative rates of solvolysis of **3**, **4**, and **5** are 10^{12}, 10^{6}, and 1! *The magnitude of these rate differences illustrates the dramatic effect that can be achieved by electron withdrawal from a neighboring group in a solvolysis reaction.* In addition, the fact that each trifluoromethyl group decreases the rate of ionization by 10^{6} provides overwhelming evidence that the interactions of the double bonds of **3–5** with the incipient carbocation involve symmetrical (nonclassical) transition states, rather than pairs of rapidly equilibrating (classical) cations.[4,11]

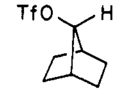


3, X = OMos; $R_1 = R_2 = H$
4, X = OMos; $R_1 = H$; $R_2 = CF_3$
7, X = OTf; $R_1 = R_2 = CF_3$

14, $R_1 = R_2 = H$
15, $R_1 = H$; $R_2 = CF_3$
16, $R_1 = R_2 = CF_3$

Product studies showed that **3**, **4**, and **7** gave **14**, **15**, and **16** in 94%, 100%, and 100% yields, respectively.[12] The structure of each product was established through a combination of ^1H and ^{13}C NMR analysis and a comparison of these spectra with those of **10** and **13**, whose stereochemistry at C7 had been established via a lanthanide-shift study. Due to the electron-withdrawing nature of the trifluoroethyl group, lanthanide-shift studies could not be used to establish the stereochemistry at C7 of the products. However, decoupling experiments at 300 MHz showed that the proton at C7 was W-form coupled[13] to the endo protons at C5 and C6 (i.e., 0.9 Hz for **16** and 0.6 Hz for **13**).

The fact that **7** solvolyzed with retention of stereochemistry was of particular significance because it indicated, along with the cumulative rate factors, that double-bond participation was occurring even for the slowest of the three systems. Even more interesting is the fact that **7** solvolyzes 17 times slower than the saturated parent system **17** ($k_{17} = 2.90 \times 10^{-7}$ at 25 °C in anhydrous 2,2,2-trifluoroethanol[14]). This would appear to add some



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(6) The rate factors were compared as 4-methoxybenzenesulfonates in order to be able to compare **3–5** with only one extrapolation of leaving group. As shown in Table I, the monotrifluoromethyl derivative was run both as the 4-methoxybenzenesulfonate (mosylate; Mos; **4**) and as the trifluoromethanesulfonate (triflate; Tf; **6**) in order to obtain the mosylate/triflate rate ratio. This was necessary in order to calculate the rate for **5** from that of the corresponding triflate **7** ($k_4/k_6 = k_{Mos}/k_{Tf} = 6.26$ *me 10^{-6}).

(7) Satisfactory elemental analyses and/or exact mass molecular weights were obtained on all new compounds, except for **6**, which was too unstable at room temperature. All compounds discussed gave spectral data consistent with the assigned structures.

(8) The syntheses of 4 and **6** utilized the free radical addition of trifluoromethyl iodide to *anti*-7-*tert*-butoxybicyclo[2.2.1]hept-2-ene[9] to give *anti*-7-*tert*-butoxy-2-iodo-3-(trifluoromethyl)bicyclo[2.2.1]heptane (**8**; 62% yield). Treatment of **8** with potassium *tert*-butoxide afforded dehydrohalogenation to produce *anti*-7-*tert*-butoxy-2-(trifluoromethyl)bicyclo[2.2.1]-hept-2-ene (**9**; 91% yield), which on treatment with 4 N hydrochloric acid gave *anti*-7-hydroxy-2-(trifluoromethyl)bicyclo[2.2.1]hept-2-ene (**10**; 61% yield). The conversion of **10** into 4 and **6** occurred in 59% and 48% yields, respectively. The synthesis of **7** involved the addition of 1,1,1,4,4,4-hexafluorobut-2-yne to dimethylfulvene to yield 7-(1-methylethylidene)-2,3-bis(trifluoromethyl)bicyclo[2.2.1]hepta-2,5-diene (**11**; 55%).[10] Selective reduction of the C5–C6 double bond of **11** over platinum oxide afforded 7-(1-methylethylidene)-2,3-bis(trifluoromethyl)bicyclo[2.2.1]hept-2-ene (**12**; 88%). Ozonolysis of **12** followed by a sodium borohydride reductive workup gave *anti*-7-hydroxy-2,3-bis(trifluoromethyl)bicyclo[2.2.1]hept-2-ene (**13**; 56%). Reaction of **13** with trifluoromethanesulfonic anhydride gave 45% of **7**, mp 30.5–31.0 °C.

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(11) The difference in mechanistic implications between a cumulative effect (x^2:x:1) and a statistical effect (2x:x:1) of substituents on a neighboring group has been previously discussed in detail.[4,5]

(12) These yields were determined by vapor-phase chromatographic analysis vs. an internal standard. Isolated yields were 82%, 84% and 76% for **14**, **15**, and **16**, respectively.

(13) For a discussion of this W-form coupling, see: Meinwald, J.; Meinwald, Y. C.; Baker, T. N., III *J. Am. Chem. Soc.* **1964**, *86*, 4074.

credence to Winstein's original suggestion[15] that the saturated parent system, **17**, underwent ionization with some anchimeric assistance.

Acknowledgment. We are indebted to the National Science Foundation for Grant CHE81-14772, which supported this investigation, and to Dr. W. H. Campbell for his assistance in obtaining high-field NMR data.

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NMR Characterization of DNA: Assignment of Major Groove Sugar Protons of the λ-Phage Operator Site O_L1 by Two-Dimensional NOE and *J*-Correlated Spectra

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The 17 base-pair DNA operator site O_L1 is recognized by the *c*I and Cro repressors of bacteriophage λ and thus provides a model system for specific protein–DNA recognition.[1] The solution structure and dynamics of this oligonucleotide are being studied by two-dimensional correlated (COSY) and Overhauser (NOESY) proton NMR methods.[2-4] We and others have recently proposed a sequential assignment strategy for oligomers of B DNA.[5-8] This strategy is extended here to include the major groove sugar protons H3′ and H4′ and is illustrated by the assignment of these protons in the oligonucleotide O_L1. The H3′ and H4′ protons are of particular interest because they lie on the outer surface of the double helix and may be involved in ligand binding.

The essential element in this and other DNA assignment strategies[5-8] is that the DNA double helix, unlike some RNAs (e.g., tRNA) and proteins, is a two-dimensional polymer with a characteristic structure. Protons distant in the primary sequence are also spatially separated, and it is possible to predict which proton NOE's are expected to be nonnegligible.[9] Each strand of the B DNA double helix in D_2O solution is found to constitute an independent cross-relaxation network of base and sugar protons. Each deoxyribose sugar contributes to this network a distinct set of spins exhibiting strong mutual cross-relaxation, but only weak interaction with the protons of other sugars. Because DNA is a two-dimensional polymer containing a string of largely independent spin reservoirs, spin diffusion can be an aid rather than a hindrance to sequential assignment.[10]

The H1′ and H2′–H2″ sugar protons and the base protons in the major groove of the O_L1 DNA double helix have been assigned previously by a sequential method.[7,11,12] The assignments of these protons can be used to assign the H3′ and H4′ protons. The H3′ protons may be identified by indirect nuclear Overhauser effects (NOE's) from the base protons and also from the H1′ and H2′–H2″ sugar protons. The assignment of these sugar protons to the same sugar is confirmed by a chain of *J* connectivities from H1′ to H2′ and then from H2′ to H3′ observed in the COSY experiment. The H4′ protons may be identified by NOE's from the H1′ protons; weak indirect effects are sometimes also observed from the base protons. Where resolved, the *J* connectivity between the H3′ and H4′ protons verifies the consistency of these two sets of assignments.[13]

O_L1 is an asymmetric duplex of 17 base pairs with sequence

$$5'\ T_1A_2C_3C_4A_5C_6T_7G_8G_9C_{10}G_{11}G_{12}T_{13}G_{14}A_{15}T_{16}A_{17}\ 3'$$

$$3'\ A_1T_2G_3G_4T_5G_6A_7C_8C_9G_{10}C_{11}C_{12}A_{13}C_{14}T_{15}A_{16}T_{17}\ 5'$$

where for convenience we have numbered the base pairs from left to right; i.e., T_1 is the first (5′) base of the upper strand, A_1 the last (3′) base of the lower strand. There are eight AT and nine GC base pairs. The variety of magnetic environments makes possible the resolution of many of the individual base and sugar protons. Figure 1 shows a region of the NOESY spectrum containing cross-peaks between thymidine H6 protons and H3′ protons. Each of the thymidine H6 protons in this region cross-relaxes with two H3′ protons: a strong NOE with H3′ of its own sugar and a weaker NOE with that of its 5′ neighbor.[14] Thus, the sequential assignments of the base protons can be extended to assign the H3′ resonances of their sugar.

Figure 2 shows a region of the NOESY spectrum containing strong cross-peaks between the H1′ and H4′ sugar resonances. Since the H1′ resonance at 5.758 ppm has been assigned to T_{16},[7] its cross-relaxation with an H4′ at 4.04 ppm identifies this resonance as H4′ of the same sugar from the distance relations in the B DNA duplex. Cross-peaks a–h are identified similarly, and their assignments are given in the figure caption. Several trends are

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(9) Interproton distances were calculated from hydrogen coordinates inferred from the heavy-atom coordinates given in: Arnott, S.; Cambell-Smith, P.; Chandra Sekharan, P. "CRC Handbook of Biochemistry, of Nucleic Acids", Chemical Rubber Co.: Cleveland, 1976; Vol. II, p 411. In addition, interproton distances were calculated from the single-crystal B-DNA structures: Dickerson, R. E.; Drew, H. R. *J. Mol. Biol.* **1981**, *149*, 761. Although somewhat different, these distances are consistent with the magnetic model of DNA presented here. The calculations were done with the assistance of Dr. Bernard R. Brooks.

(10) A major groove base proton, such as a pyrimidine H6, may relax with its own or 5′-flanking sugar. The closest neighbor of H6 among its own sugar protons is H2′ (1.94 Å in standard B DNA). At short mixing times (<100 ms) this direct NOE predominates. Spin diffusion among protons of the same sugar observed at longer mixing times gives rise to indirect effects between such a base proton and H1′, H2″, H3′, and H4′. Similarly, a base proton gains magnetic access to the 5′-flanking set of sugar protons via H2″ (2.55 Å from an H6) and H1′ (2.96 Å from H6), from which spin diffusion may occur involving H2′, H3′, and H4′.

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(13) The COSY experiment, which identifies *J*-connected spin systems, provide a stringent consistency check for the assignment of the sugar protons. Resonances assigned to the same sugar must exhibit the appropriate pattern of *J* connectivities. The H2′ of T_{16}, for example, is connected to an H3′ resonance at 4.69 ppm, which was assigned above to the same sugar. The H3′ of T_{16} is connected to an H4′ resonance at 4.04 ppm, which was also assigned above to that sugar (data not shown).

(14) For example, the thymidine H6 resonance at 6.984 ppm, assigned to T_{13} by the sequential method,[7] cross-relaxes with its own H3′ at 4.74 ppm and, to a lesser extent, with the H3′ of G_{12} at 4.79 ppm. Similarly, the H8 proton of G_{12} at 7.512 ppm cross-relaxes with its own H3′ at 4.79 ppm and, to a lesser extent, with the H3′ of G_{11} at 4.85 ppm (data not shown).