Partisil M9 10/50 column, 50% EtOAc/hexanes, 4.0 mL/min). The elution order was as follows: vinylallene **5a**, then the *ZZ* isomer **7a** (less polar isomer A), followed by *ZE* isomer **8a** (more polar isomer B). The ratio of *ZZ* isomer **7a** to *ZE* isomer **8a** varied from 84:16 to 78:22 over the temperature range.

Rates of Thermal [1,5] Sigmatropic Rearrangement of 1-[3′,3′-Dideuterio-6′,6′-dimethyl-2′-(trideuteriomethyl)-1′-cyclohexen-1′-yl]-4,4-dimethyl-3-(diphenylphosphinoyl)-1,2-pentadiene (5b). The general procedure for the kinetic studies was followed by integrating the proton resonances (^{1}H NMR, benzene-d_6) of the *gem*-dimethyl groups corresponding to the starting material and the rearranged products. These appear at 0.67 and 0.79 ppm for the starting vinylallene **5b**, 0.48 ppm for the *ZZ* isomer **7b**, and 1.06 ppm for the *ZE* isomer **8b**.

For spectral characterization of the individual rearranged triene products, samples from the kinetic runs were combined and concentrated and then the residue was subjected to HPLC purification (Whatman Partisil M9 10/50 column, 50% EtOAc/hexanes, 4 mL/min). The elution order was as follows: vinylallene **5b**, then the *ZZ* isomer **7b** (less polar isomer A) and the *ZE* isomer **8b** (more polar isomer B). The ratio of *ZZ* isomer **7b** to *ZE* isomer **8b** varied from 83:17 to 79:21 over the temperature range.

Thermolysis of the Rearranged Products. Control Experiments. (2-(1′)*Z*,2′*Z*,4′*Z*)-1,1-Dimethyl-2-[5′-(diphenylphosphinoyl)-3′,6′,6′-trimethyl-2′,4′-heptadienylidene]-3-methylenecyclohexane (9). A sample of *ZZZ*-tetraene **9a** was subjected to the same conditions as in the kinetic studies. The sample was heated at 90 °C and the reaction was followed by ^{1}H NMR. After 13.5 h, a mixture of *ZZZ*-tetraene **9a** (~76%), *ZZE*-tetraene **10a** (~14%), and a third component (~10%) identical by ^{1}H NMR with the starting dienallene **6a** was observed. To fully characterize the compounds obtained in this control thermolysis experiment, the same experiment was conducted on a semipreparative scale. The *ZZZ*-tetraene **9a** (240 mg) was heated (90 °C, benzene as solvent, sealed tube) as in the ^{1}H NMR experiment, and after 20 h, the solvent was removed and the residue was purified by HPLC (Dynamax Macro column, 40% EtOAc/hexanes, 8 mL/min). The fraction containing a mixture of *ZZE*-tetraene **10a** and allene **6a** was concentrated and reinjected onto the HPLC (Whatman Partisil M9 10/50 column, 50% EtOAc/hexanes, 4 mL/min). A sample was obtained which proved to be spectroscopically (^{1}H NMR, IR) identical with the starting allene **6a**.

(2(1′)*Z*,2′*Z*,4′*E*)-1,1-Dimethyl-2-[5′-(diphenylphosphinoyl)-3′,6′,6′-trimethyl-2′,4′-heptadienylidene)-3-methylenecyclohexane (10a). A sample of *ZZE*-tetraene **10a** was subjected to the same conditions as in the kinetic studies. After 20 h at 90 °C, no change was observed in the ^{1}H NMR spectrum of the sample. The *ZZE*-tetraene **10a** proved to be thermally stable even after 20 h at 160 °C.

(2(1′)*Z*,2′*E*)-1,1-Dimethyl-3-methylene-2-[4′,4′-dimethyl-3′-(diphenylphosphinoyl)-2′-pentenylidene]cyclohexane (8a). A sample of *ZE*-triene **8a** was heated at 100 °C under the same conditions as in the kinetic studies. After 1.5 h, a new set of signals corresponding to the *ZZ* isomer **7a** was observed. No changes other than the formation of *ZZ* isomer **7a** were apparent over a 10-h period as determined by ^{1}H NMR (ratio *ZE*/*ZZ*, 91:9).

(2(1′)*Z*,2′*Z*)-1,1-Dimethyl-3-methylene-2-[4′,4′-dimethyl-3′-(diphenylphosphinoyl)-2′-pentenylidene]cyclohexane (7a). A sample of *ZZ*-triene **7a** was subjected to the same conditions as in the kinetic studies. No change was apparent in the ^{1}H NMR spectrum after 1.5 h at 100 °C. After 1.5 h, a small amount of *ZE* isomer **8a** was observed. The thermolysis was followed for 5.5 h, and no species other than the two components (ratio *ZZ*/*ZE*, 90:10) were observed during this period of time.

Thermolysis of Allene 6a. Preparation of (2(1′)*Z*,2′*Z*,4′*Z*)-9a (Isomer A) and (2(1′)*Z*,2′*Z*,4′*E*)-1,1-Dimethyl-2-[5′-(diphenylphosphinoyl)-3′,6′,6′-trimethyl-2′,4′-heptadienylidene]-3-methylenecyclohexane (10a; Isomer B). Allene 6a (30 mg) was dissolved in benzene (15 mL) and heated under a nitrogen atmosphere for 27 h. The solvent was evaporated under reduced pressure, and HPLC purification of the resulting residue (Whatman Partisil column, 40% EtOAc/SSB) led to separation of two geometrically isomeric tetraenes. The less polar compound 9a (isomer A, characterized as the 4′*Z* compound) was obtained as the minor isomer (11 mg, 37%) and the more polar compound **10a** (isomer B, identified as the 4′*E* compound) as the major isomer (17 mg, 57%) (total yield, 94%). A trace of the starting allene was also recovered (eluted third).

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Supplementary Material Available: Spectral and kinetic data for **5a,b-10a,b** and **12** (10 pages). Ordering information is given on any current masthead page.

Synthesis of (Sulfodifluoromethyl)phosphonic Acid

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Abstract: (Sulfodifluoromethyl)phosphonic acid, $(HO)_2P(O)CF_2SO_3H$, has been synthesized for the first time. This mixed phosphonic–sulfonic acid was prepared from $(C_2H_5O)_2P(O)CF_2SO_3Na$, which had been synthesized via oxidation of the corresponding sulfinate salt, $(C_2H_5O)_2P(O)CF_2SO_2Na$. The sulfinate salt was prepared from $(C_2H_5O)_2P(O)CF_2X$ (X = Br, I) and $[(C_2H_5O)_2P(O)CF_2SO_2]_2Cd$ precursors.

The incorporation of fluorine into organic compounds has a significant effect on the acidity of the resultant molecule. When the initial substrate is an acid, such as a carboxylic, sulfonic, or phosphonic acid, the acidity is increased several orders of magnitude, and the perfluorinated acid analogues are some of the strongest organic acids known. Acids, such as trifluoroacetic acid and triflic acid, have also become important products of commerce, and derivatives of the longer chain analogues are utilized industrially as surfactants and fabric treatment agents. Although not investigated as extensively as the carboxylic or sulfonic acids, the perfluoroalkanephosphonic acids have recently attracted attention as biological chelating agents[2] and electrolytes.[3]

Mixed analogues, such as $HO_2CCF_2SO_3H$ and $(HO)_2P(O)CF_2COOH$ have also been prepared.[4] However, the parent phosphonic–sulfonic acid analogue, $(HO)_2P(O)CF_2SO_3H$, has thus

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far eluded the synthetic chemist. Since we anticipated that this unknown mixed acid would also exhibit interesting electrolyte and chelating properties, we have investigated synthetic routes to this acid, and a successful route to this compound is outlined below.

Results and Discussion

The synthetic route to this mixed phosphonic–sulfonic acid involves the preparation of its precursors $(RO)_2P(O)CF_2SO_2Na$ (I) and $(RO)_2P(O)CF_2SO_3Na$ (II) from commercially available materials. Three alternate routes were utilized for the preparation of I (R = C_2H_5, Ia; *i*-C_3H_7, Ib). However, chlorination of I with

$$(C_2H_5O)_3P + CF_2Br_2 \rightarrow$$

$$(C_2H_5O)_2P(O)CF_2Br \xrightarrow[NaHCO_3,\ 100\ °C]{Na_2S_2O_4} \underset{75\%}{Ia^{5-7}} \quad (1)$$

$$(C_2H_5O)_2P(O)CF_2ZnX + I_2 \rightarrow$$

$$(C_2H_5O)_2P(O)CF_2I \xrightarrow[80\ °C]{Na_2SO_3} \underset{85\%}{Ia^{7,8}} \quad (2)$$

$$(i\text{-}C_3H_7O)_2P(O)CF_2ZnX + I_2 \rightarrow$$

$$(i\text{-}C_3H_7O)_2P(O)CF_2I \xrightarrow[NaHCO_3,\ 50\ °C]{Na_2S_2O_4} \underset{70\%}{Ib^{7,8}}$$

$$(RO)_2P(O)CF_2CdX + SO_2 \rightarrow$$
$$R = C_2H_5,\ i\text{-}C_3H_7$$

$$[(RO)_2P(O)CF_2SO_2]_2Cd \xrightarrow[25\ °C]{NaOH} \underset{90\%}{Ib^{9}} \quad (3)$$

chlorine gas to the sulfonyl halide occurred in very low yield, and the subsequent reaction with sodium hydroxide gave a very complex mixture. Therefore, the sulfinate was converted to the corresponding sulfonate by using 30% hydrogen peroxide.

$$I + H_2O_2 \rightarrow \underset{56\text{–}80\%}{(RO)_2P(O)CF_2SO_3Na\ (II)}$$

or $$[(i\text{-}C_3H_7O)_2P(O)CF_2SO_2]_2Cd + H_2O_2 \rightarrow \underset{63\%}{[(i\text{-}C_3H_7O)_2P(O)CF_2SO_3]_2Cd}$$

It is difficult to remove the inorganic starting materials completely from I, especially when $Na_2S_2O_4$ is the sulfur reagent. Therefore, the reaction with hydrogen peroxide was usually performed with the impure compound. The inorganic impurities (e.g., $Na_2S_2O_4$, NaBr, NaF) were removed after the sulfinate was converted to the corresponding sulfonate by concentrating and cooling the solution that contained II.

Treatment of II with concentrated hydrochloric acid[10] gave rise to $(HO)_2P(O)CF_2SO_3Na$ (III). III was repeatedly extracted with anhydrous CH_3CN to insure complete removal of solid impurities.

$$II + HCl_{aq} \xrightarrow{80\text{–}120\ °C} \underset{79\text{–}85\%}{(HO)_2P(O)CF_2SO_3Na\ (III)}$$

The aqueous solution of III was passed through a strongly acid resin—Amberlite IR-120. Crude $(HO)_2P(O)CF_2SO_3H$ was obtained after evaporation under reduced pressure at 100–120 °C. Finally, the crude aqueous acid solution was treated with charcoal and dried under reduced pressure to yield a white solid. The acid is stable in water to at least 150 °C.

$$III \xrightarrow[resin]{acid} \underset{\sim 76\%}{(HO)_2P(O)CF_2SO_3H\ (IV)}$$

An aqueous solution of $(C_2H_5O)_2P(O)CF_2SO_3Na$ was passed through the acid resin in a similar way to give $(C_2H_5O)_2P(O)CF_2SO_3H$ in good yield.

$$II \xrightarrow[resin]{acid} \underset{\sim 93\%}{(C_2H_5O)_2P(O)CF_2SO_3H\ (V)}$$

Titration of an aqueous solution of $(HO)_2P(O)CF_2SO_3H$ (IV) with sodium hydroxide (0.0508 N) gave rise to two inflection points—one for 2 equiv (the sulfonic acid proton and one phosphonic acid proton) and one for 1 equiv (the second phosphonic acid proton) of the acid. The total titre gives 95% of a tribasic acid based on an anhydrous molecular weight of 212 g/mol.

When the acid is dissolved in isopropyl alcohol and titrated with a toluene/methanol solution of tetrabutylammonium hydroxide (TBAH, 0.0392 N), two equivalence points are observed at approximately equal volumes of titrant. Addition of a slight excess (~10%) of TBAH after the second inflection point was followed by the addition of 10 mL (~15%) of H_2O. When the electrode had stabilized, the titration with TBAH was continued to a third inflection point. A plot of voltage versus volume is given in Figure 1. The three acid protons are easily resolved by this combination of nonaqueous/aqueous titration.

In summary, a successful route to the parent mixed phosphonic–sulfonic acid (IV) has been developed from readily available precursors. Future work will detail applications and synthetic ability of this acid as well as extensions to homologous acids of the type $(HO)_2P(O)(CF_2)nSO_3H$ ($n > 1$).

Experimental Section

Materials. Literature methods were used to prepare $(C_2H_5O)_2P(O)CF_2Br$,[5,6] $(RO)_2P(O)CF_2I$ (R = C_2H_5, *i*-C_3H_7),[8] and $(RO)_2P(O)CF_2CdX$ (R = C_2H_5, *i*-C_3H_7).[9] The other chemicals were obtained as follows: $Na_2S_2O_4$, CH_3CN, and HCl (Merck); $NaHCO_3$ and H_2O_2 (30%) (J. T. Baker); charcoal (activated "Norit" SGII) (MCB).

General Procedures. ^{19}F NMR spectra were obtained on a JEOL FX-90Q Fourier transform NMR spectrometer operating at 84.26 MHz. Chloroform-*d*, D_2O, CD_3CN, or DMSO-d_6 were used as solvent with $CFCl_3$ as external reference. ^{31}P NMR spectra were obtained at an operating frequency of 36.20 MHz with H_3PO_4 as an external reference. ^1H NMR spectra were recorded at 89.56 MHz. Mass spectra were recorded with a VG 7070HS mass spectrometer with FAB at 3.9, 4.8, or 10 V. Elemental analyses were performed by Beller Mikroanalytisches Laboratorium, Göttingen, Federal Republic of Germany.

Preparation of $[(RO)_2P(O)CF_2SO_2]_2Cd$. To a dry, three-necked, 100-mL flask fitted with a reflux condenser were successively added acid-washed Cd powder (6.2 g, 55 mmol), dry DMF (50 mL), and $(i\text{-}C_3H_7O)_2P(O)CF_2Br$ (14.8 g, 50 mmol). The mixture was stirred for 2 h (initial exotherm), after which the greenish solution of $(i\text{-}C_3H_7O)_2P(O)CF_2CdBr$ was filtered off from the excess Cd, via a Schlenk filter funnel under N_2 pressure, into another 100-mL flask. This flask was then fitted with a Dewar condenser filled with dry ice and isopropyl alcohol, and excess SO_2 gas was introduced. The mixture was stirred for 15 min, during which time the solution turned yellow. The solvent and excess SO_2 were then removed under vacuum. The residual paste was washed with water (15 mL) and filtered. The solid was recrystallized from hot isopropyl alcohol after filtration to remove an insoluble orange residue. The aqueous solution was allowed to stand overnight, filtered to remove precipitated inorganic matter, and evaporated to near dryness, and the resulting solid was also recrystallized from isopropyl alcohol. The white powdery product was washed with ether and dried under vacuum. The combined yield was 7.25 g (43%). The analogous compound $[(C_2H_5O)_2P(O)CF_2SO_2]_2Cd$ was similarly prepared from $(C_2H_5O)_2P(O)CF_2Br$, Cd, 1,4-dioxane, and SO_2 and recrystallized from ethanol in 62% yield.

For $[(i\text{-}C_3H_7O)_2P(O)CF_2SO_2]_2Cd$: mp 128 °C; ^{19}F NMR (DMSO-d_6) ϕ −118.3 d ($J_{F\text{-}P}$ = 93 Hz); $^{31}P\{H\}$ (DMSO-d_6) δ 4.74 t; $^{13}C\{H\}$ (D_2O) δ 121.8 td ($J_{C\text{-}P}$ = 191 Hz, $J_{C\text{-}F}$ = 309 Hz), 78.7 d ($J_{PO\text{-}C}$ = 7.3 Hz), 25.6 d ($J_{PO\text{-}CC}$ = 6.6 Hz); ^{113}Cd (D_2O, MeOH) 65.6 s (relative to external $CdSO_4$). Anal. Calcd for $C_{14}H_{28}F_4P_2S_2O_{10}Cd$: C, 25.06; H, 4.21; P, 9.23; S, 9.56. Found: C, 24.98; H, 5.63; P, 9.22; S, 9.69.

For $[(C_2H_5O)_2P(O)CF_2SO_2]_2Cd$: mp 156 °C, ^{19}F NMR (EtOH) ϕ −116 d ($J_{F\text{-}P}$ = 93 Hz); $^{31}P\{H\}$ (DMSO-d_6) δ 7.5 t; $^{13}C\{H\}$ NMR (D_2O) δ 122.3 td ($J_{C\text{-}P}$ = 185 Hz; $J_{C\text{-}F}$ = 309 Hz), 68.1 d ($J_{PO\text{-}C}$ = 7.1 Hz), 18.1 d ($J_{PO\text{-}CC}$ = 5 Hz); ^{113}Cd (D_2O) w 65.6 s (relative to external $CdSO_4$). Anal. Calcd for $C_{10}H_{20}F_4P_2S_2O_{10}Cd$: C, 19.53; H, 3.27; F, 12.36; P, 10.07; S, 10.48. Found: C, 19.32; H, 3.12; F, 12.30; P, 9.48; S, 10.54.

Preparation of $[(i\text{-}C_3H_7O)_2P(O)CF_2SO_3]_2Cd$. $[(i\text{-}C_3H_7O)_2P(O)CF_2SO_2]_2Cd$ (5.03 g, 7.5 mmol) was suspended in water (10 mL) in a 25-mL flask. The mixture was cooled with rapid stirring in an ice water

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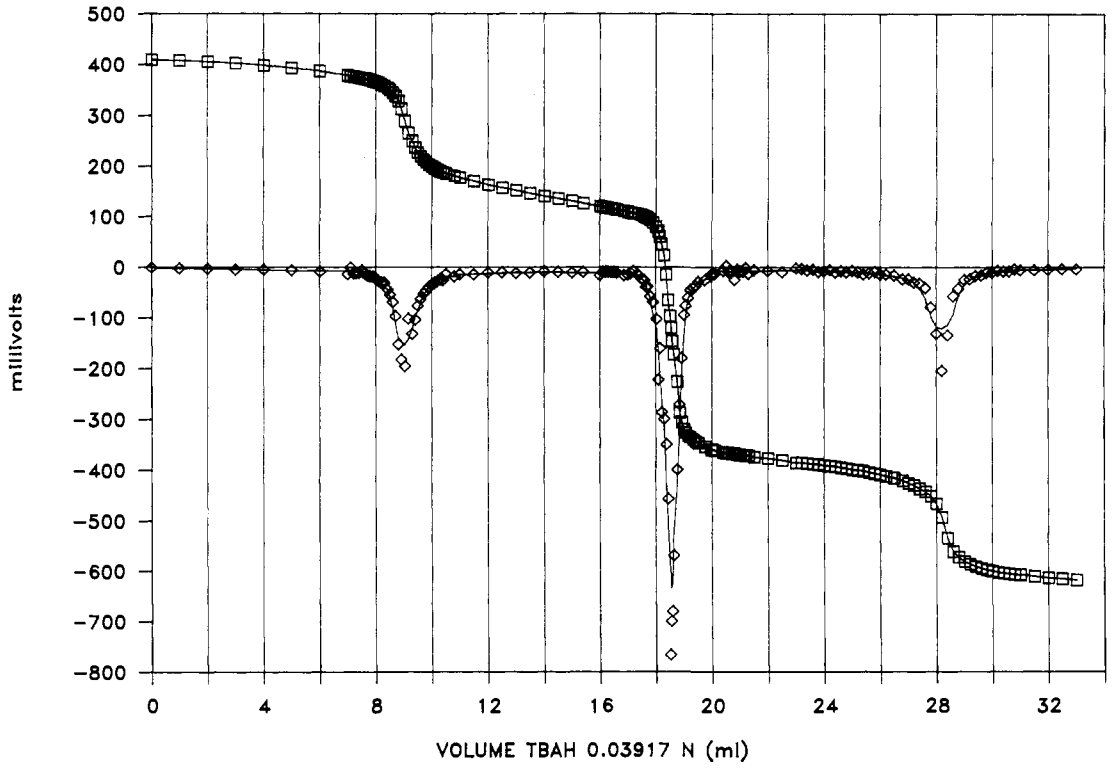

Figure 1. Titration of (sulfodifluoromethyl)phosphonic acid in isopropyl-alcohol water solution: (□) titration curve, (◇) derivative curve raw data. Extrapolated equivalence points are 9.16, 9.37, and 9.65 mL of tetra-*N*-butylammonium hydroxide (TBAH).

bath, and 50% H_2O_2 (1.7 mL) was added slowly dropwise. The mixture was allowed to warm up to room temperature and stirred overnight, during which time the solid almost completely dissolved. The solution was filtered and concentrated to dryness on a rotary evaporator. The residual solid was washed with a little acetone and with ether and dried under vacuum. The yield was 3.32 g (63%): ^{19}F NMR (DMSO-d_6) ϕ −109.2 d (J_{P-F} = 93 Hz); $^{31}P\{H\}$ (DMSO-d_6) δ 2.2 t; ^{113}Cd (D_2O) δ 77.6 s (relative to external $CdSO_4$).

Preparation of $(C_2H_5O)_2P(O)CF_2SO_3Na$. In a 125-mL, three-necked, round-bottomed flask were placed 13.89 g (79.8 mmol) of $Na_2S_2O_4$, 6.7 g (79.8 mmol) of $NaHCO_3$, 10.64 g (39.9 mmol) of $(C_2H_5O)_2P(O)CF_2Br$,[5,6] 25 mL of water, and 15 mL of CH_3CN. Under a stream of nitrogen the contents were stirred vigorously at 80 °C for 12 h. The reaction mixture was filtered. The filtrate was evaporated to dryness under reduced pressure to give a white residue that was washed with chloroform and petroleum ether. Finally, the solid was dried under vacuum at 80 °C for 4 h to give crude $(C_2H_5O)_2P(O)CF_2SO_2Na$: ^{19}F NMR spectrum (D_2O) ϕ −125.8 d (J_{F-P} = 83.3 Hz); $^{31}P\{H\}$ (D_2O) δ 2.67 t; ^1H (D_2O) δ 1.33 t (3 H, J_{H-H} = 7.08 Hz), 4.09 q (1 H), 4.17 q (1 H) (J_{H-P} = 7.35 Hz); MS (FAB, solvent H_2O) (*m/e*, species, %) 291, $M^+ + H_2O - 1$, 1.5; 205, $M^+ - C_2H_5OH - Na$, 15.3; 187, $M^+ - SO_2Na$, 2.62; 149, $(C_2H_5O)_2P(O)C^+$, 5.43; 143, $C_2H_6O_2PCF_2^+$, 1.11; 137, $(C_2H_5O)_2P(O)^+$, 7.51; 115, $H_2O_2PCF_2^+$, 19.1; 109, $C_2H_6O_3P^+$, 13.3; 105, $SO_2Na{\cdot}H_2O^+$, 5.73; 65, $PO_2H_2^+$, 100; 63, PO_2^+, 32.1.

The crude $(C_2H_5O)_2P(O)CF_2SO_2Na$ and 14 mL of water were placed into a 50-mL flask. Then hydrogen peroxide (30%) (molar ratio: $(C_2H_5O)_2P(O)CF_2SO_2Na/H_2O_2$ = 1:1.75) was added at 0 °C. The mixture was stirred at room temperature for 4 h and was filtered. After concentrating and cooling, the inorganic solid impurities were removed by filtration. The filtrate was evaporated under reduced pressure to give a crude product that was washed with chloroform and petroleum ether and was filtered to give a white solid. It was dried under reduced pressure at 80 °C for 4 h to yield 6.51 g of $(C_2H_5O)_2P(O)CF_2SO_3Na$ (yield 56.3%): ^{19}F NMR spectrum (D_2O) ϕ −110.1 d (J_{F-P} = 78.6 Hz); $^{31}P\{H\}$ (D_2O) δ 0.36 t; ^1H (D_2O) δ 1.34 t (3 H, J_{H-H} = 7.28 Hz); 4.13 q (1 H), 4.21 q (1 H) (J_{H-P} = 7.56 Hz); MS (FAB, solvent H_2O) (*m/e*, species, %) 307, $M^+ + H_2O - 1$, 27.6; 267, $M^+ - Na$, 0.84; 235, $(C_2H_5O)_2P(O)CF_2SO^+$, 1.78; 219, $(C_2H_5O)_2P(O)CF_2S^+$, 1.05; 1.87, $M^+ - SO_3Na$, 4.94; 165, $M^+ + H_2O - C_2H_6O_2PCF_2$, 22.3; 149, $(C_2H_5O)_2P(O)C^+$, 18.1; 143, $C_2H_6O_2PCF_2^+$, 4.17; 137, $(C_2H_5O)_2P(O)^+$, 19.9; 121, $SO_3Na{\cdot}H_2O^+$, 1.40; 115, $H_2O_2PCF_2^+$, 56.8; 109, $C_2H_6O_3P^+$, 23.1; 103, SO_3Na^+, 1.59; 65, $PO_2H_2^+$, 100; 63, PO_2^+, 58.1.

Preparation of $(C_2H_5O)_2P(O)CF_2SO_2Na$ from $(C_2H_5O)_2P(O)CF_2I$ and Na_2SO_3. To a two-necked, 100-mL flask fitted with a reflux condenser were added 1,4-dioxane (8 mL), water (25 mL), Na_2SO_3 (25.3 g, 200 mmol), and $(C_2H_5O)_2P(O)CF_2I$ (15.7 g, 50 mmol). The mixture was heated in an oil bath at 80–85 °C for 10 h. It was then cooled to room temperature, the solvents were evaporated off on a rotary evaporator, and the residue was washed with acetone and dried. The yield was 85% by ^{19}F NMR: ^{19}F NMR (D_2O) ϕ −122.8 d (J_{P-F} = 83 Hz); $^{31}P\{H\}$ (D_2O) δ 2.7 t.

Preparation of $(i\text{-}C_3H_7O)_2P(O)CF_2SO_2Na$ from $[(i\text{-}C_3H_7O)_2P(O)CF_2SO_2]_2Cd$ and NaOH. $[(i\text{-}C_3H_7O)_2P(O)CF_2SO_2]_2Cd$ (33.5 g, 50 mmol) was dissolved in water (200 mL), and NaOH pellets were added to the solution until the pH was slightly basic (ca. 8). The precipitated $Cd(OH)_2$ was filtered off, and the solution was concentrated to dryness on a rotary evaporator, giving the product. The yield was 27.3 g (90%).

Preparation of $(i\text{-}C_3H_7O)_2P(O)CF_2SO_2Na$ from $(i\text{-}C_3H_7O)_2P(O)CF_2I$ and $Na_2S_2O_4$. To a 100-mL, three-necked flask fitted with a reflux condenser were successively added water (10 mL), acetonitrile (10 mL), $NaHCO_3$ (3.4 g), and $Na_2S_2O_4$ (7.0 g). The mixture was stirred rapidly, and $(i\text{-}C_3H_7O)_2P(O)CF_2I$ (6.85 g, 20 mmol) was added by syringe. The mixture was then warmed very gently in an oil bath until the temperature reached 50 °C and maintained at that temperature for 4 h. The mixture was then heated to boiling and filtered hot. The residual solid was extracted thrice with 10–15-mL portions of boiling acetonitrile/water (9:1), also filtered hot. The combined filtrates were evaporated to dryness in a rotary evaporator to give the crude product, which was recrystallized from water, with concentration, two crops of the product being obtained from the mother liquor. The combined solids were washed with acetone and ether and dried under vacuum. The yield was 4.2 g (70%): ^{19}F NMR (DMSO-d_6) ϕ −121.3 d (J_{F-P} = 92 Hz); $^{31}P\{H\}$ (D_2O) δ 3.7 t.

Preparation of $(i\text{-}C_3H_7O)_2P(O)CF_2SO_3Na$. $(i\text{-}C_3H_7O)_2P(O)CF_2SO_2Na$ (2.72 g, 9 mmol) was stirred with 30% H_2O_2 for 30 min at room temperature and then concentrated to dryness on a rotary evaporator to give the product. The yield was 2.73 g (89%): ^{19}F NMR (D_2O) ϕ −110.0 d (J_{P-F} = 81 Hz); $^{31}P\{H\}$ (D_2O) δ −0.5 t.

Preparation of $(HO)_2P(O)CF_2SO_3Na$. A mixture of $(C_2H_5O)_2P(O)CF_2SO_3Na$ (5.72 g, 19.7 mmol) and hydrochloric acid (12 N, 11.7 g) was stirred vigorously at 120 °C for 10 h, and the reaction mixture was filtered. The filtrate was evaporated to dryness under vacuum to obtain a crude product that was taken up in CH_3CN. A small quantity of solid was removed by filtration. After removal of the solvent under vacuum, a transparent viscous liquid was obtained. This process was repeated twice to insure complete removal of solid impurities. The product was taken up in water, and methylene chloride was added. The mixture was stirred vigorously for 1 h. The water phase was collected and evaporated at reduced pressure at 60–80 °c to yield 3.64 g (78.9%) of a white solid $(HO)_2P(O)CF_2SO_3Na$: ^{19}F NMR spectrum (DMSO-d_6) ϕ −111.84 d (J_{F-P} = 87.9 Hz); $^{31}P\{H\}$ (DMSO-d_6) δ 0.85 t; ^1H

(DMSO-d_6) δ 9.37 s; MS (FAB, solvent 3-nitrobenzyl alcohol) (m/e, species, %) 301, $M^+ + 3Na^+ - 2$, 40.02; 279, $M^+ + 2Na^+ - 1$, 17.49; 257, $M^+ + Na^+$, 34.59; 235, $M^+ + 1$, 9.67; 153, $CF_2SO_3Na^+$, 2.55; 149, $M^+ + H_2O - SO_3Na$, 100; 103, SO_3Na^+, 1.43; 79, PO_3^+, 13.18; 65, $PO_2H_2^+$ 20.76; 64, PO_2H^+, 8.97; 63, PO_2^+, 39.35.

Preparation of $(HO)_2P(O)CF_2SO_3Na$. (i-$C_3H_7O)_2P(O)CF_2SO_3Na$ (2.54 g, 8 mmol) and concentrated HCl (20 mL) were heated together with stirring for 6 h at 80 °C in a 50-mL boiling flask fitted with a reflux condenser. The mixture was then concentrated to dryness on a rotary evaporator to give the product. The yield was 1.6 g (85%): ^{19}F NMR (D_2O) ϕ -110.5 d (J_{P-F} = 81 Hz); $^{31}P\{H\}$ (D_2O) δ -0.1 t; $^{13}C\{H\}$ (D_2O) δ 120.5 td (J_{P-C} = 179 Hz, J_{F-C} = 295 Hz).

Preparation of $(HO)_2P(O)CF_2SO_2OH$. An aqueous solution of $(HO)_2P(O)CF_2SO_3Na$ (3.48 g, 14.9 mmol) was passed through an Amberlite IR-120 ion-exchange resin (strongly acidic gel-type resin). The volume of the aqueous acid was reduced, and then the crude product was evaporated at reduced pressure at 100-120 °C. The product was dissolved in water, and charcoal (0.3 g) was added. The mixture was stirred at 50-60 °C for 2 h. After the charcoal was removed, the filtrate was evaporated at reduced pressure at 100 °C for 4 h to yield 2.4 g (75.9%) of a white solid, $(HO)_2P(O)CF_2SO_3H$. The solid melts at 76-78 °C. The acid is very hygroscopic: ^{19}F NMR spectrum (DMSO-d_6) ϕ -110.9 d (J_{F-P} = 92.7 Hz); $^{31}P\{H\}$ (DMSO-d_6) δ 0.85 t; ^1H (DMSO-d_6) δ 12.5 s; MS (Cl^+) (m/e, species, %) 213, $M^+ + 1$, 0.62; 149, $M^+ + 1 - PO_2H$, 2.86; 131, $M^+ - (HO)_2P(O)$ or $M^+ - SO_3H$, 0.30; 111, HO_3PCF^+, 9.20; 91, PO_3C^+, 2.03; 81, $(HO)_2P(O)^+$, or SO_3H^+, 2.21; 79, PO_3^+, 2.66; 65, $PO_2H_2^+$, 100; 64, PO_2H^+, 1.66; 59, POC^+, 35.65. Anal. Calcd for $CH_3F_2O_6PS$: C, 5.66; H, 1.41; F, 17.92; S, 15.12. Found: C, 5.77; H, 1.77; F, 17.90; S, 15.04.

Preparation of $(C_2H_5O)_2P(O)CF_2SO_3H$. An aqueous solution of $(C_2H_5O)_2P(O)CF_2SO_3Na$ (4.08 g, 14.1 mmol) was passed through an Amberlite IR-120 ion-exchange resin (strongly acidic gel-type resin). The volume of the aqueous acid was reduced, and then the crude product was evaporated at reduced pressure to yield 3.52 g (93.1%) of a viscous liquid $(C_2H_5O)_2P(O)CF_2SO_3H$: ^{19}F NMR spectrum (DMSO-d_6) ϕ -109.81 d (J_{F-P} = 87.9 Hz); $^{31}P\{H\}$ (DMSO-d_6) δ 1.21 t; ^1H (DMSO-d_6) δ 1.11 t (3 H, J_{H-H} = 6.96 Hz), 4.03 q (1 H), 3.95 q (1 H) (J_{H-P} = 7.14 Hz), δ 10.31 s; MS (EI^+) (m/e, species, %) 269, M + 1, 0.42; 137, $M^+ - CF_2SO_3H$, 8.40; 132, $M^+ + 1 - P(O)(OC_2H_5)_2$, 53.8; 121, $^+P(OC_2H_5)_2$, 9.42; 109, $C_2H_6O_3P^+$, 68.7; 81, SO_3H^+, 100; 65, $PO_2H_2^+$, 91.28; 64, PO_2H^+, 50.33.

Titration. Titration of the acid (IV) was monitored utilizing an Orion Model 701A digital Ionalyzer and Corning combination pH electrode. Sodium hydroxide was standardized with primary standard potassium acid phthalate. Tetrabutylammonium hydroxide in toluene/methanol solution was prepared from tetrabutylammonium iodide[11] and standardized against primary standard benzoic acid in dimethyl formamide.

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Registry No. Ia, 118576-78-6; Ib, 118576-80-0; IIa, 118576-79-7; IIb, 118576-81-1; II (R = H), 118576-82-2; $(C_2H_5O)_2P(O)CF_2Br$, 65094-22-6; $(C_2H_5O)_2P(O)CF_2I$, 80077-69-6; (i-$C_3H_7O)_2P(O)CF_2I$, 118576-72-0; (i-$C_3H_7O)_2P(O)CF_2Br$, 65094-24-8; (i-$C_3H_7O)_2P(O)CF_2CdBr$, 118576-83-3; $[(C_2H_5O)_2P(O)CF_2SO_2]_2Cd$, 118576-76-4; $[(i\text{-}C_3H_7O)_2P(O)CF_2SO_2]_2Cd$, 118576-75-3; $[(i\text{-}C_3H_7O)_2P(O)CF_2SO_3]_2Cd$, 118576-77-5; $(HO)_2P(O)CF_2SO_2OH$, 118576-73-1; $(C_2H_5O)_2P(O)CF_2SO_3H$, 118576-74-2.

(11) USP/NF XX(XV) 1980, 1113. United States Pharmacopeial Convention.

The Nitrogen Inversion Barrier of 7-Methyl-7-azabicyclo[2.2.1]heptane and the "Bicyclic Effect"

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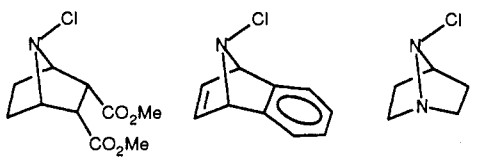
Abstract: The free energy of activation for nitrogen inversion of the title compound was determined to be 13.77 (4) kcal/mol at 25 °C in $CDCl_3$ by dynamic ^{13}C NMR and that for the 7-ethyl compound to be 13.17 (4) kcal/mol under the same conditions. The change in α(av) (the average of the three bond angles at nitrogen) during nitrogen inversion is used to assist comparison of inversion barriers for amines with different substituents attached. Comparison with literature data and AM1 calculations indicate that the barrier increase for 7-methyl-7-azabicyclo[2.2.1]heptane N inversion relative to an α-unbranched monocyclic compound of the same pyramidality at nitrogen is on the order of 3.5 kcal/mol, while the less strained 1-bridge-azabicyclo[3.3.1]nonyl and -[3.2.1]octyl systems show barrier increases of about 1.5 kcal/mol. This represents an estimate of the size of Lehn's "bicyclic effect".

7-Azabicyclo[2.2.1]heptane (7-azanorbornane) derivatives have especially high nitrogen inversion barriers. Lehn[1] reported a dynamic ^1H NMR $\Delta G^{\ddagger}_i$ of 21 (1) kcal/mol at 140 (10) °C for chloroamine **1**, and Rautenstrauch[2] determined a 23.5 kcal/mol barrier at 23 °C for **2** by direct equilibration. CNC bond angle restriction clearly causes higher nitrogen inversion barriers,[1,3] and restriction of the $C_1N_7C_4$ angle by the bicyclic ring system is a factor causing the high $\Delta G^{\ddagger}_i$ values observed. Lehn suggested[4] that there is also an unexplained "bicyclic effect" raising nitrogen inversion barriers in 7-azanorbornane derivatives, because their inversion barriers are substantially higher than might be expected from the CNC angle imposed by the bicyclic framework. For example, Lambert and co-workers[5] observed $\Delta G^{\ddagger}_i$ of ca. 13.4 kcal/mol at -20 °C for *N*-chloroazetidine, which has a smaller endocyclic CNC angle imposed by its four-membered ring than that of 7-azanorbornane derivatives. More recently, Malpass and



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