ponification, affording the respective carboxylates.

The preparation of the pyrimidine moiety of bleomycin serves to verify the revised structure proposed[20] for this portion of the antibiotic. The syntheses of each of the components of bleomycin have now been described, suggesting the feasibility of a total synthesis of the antibiotic, as well as structurally related species of utility in defining its mechanism of action.

Acknowledgment. We thank Professor David G. Lynn for a helpful discussion during the course of this work and Mark Levin for assistance with the assignment of absolute configurations. This investigation was supported by research Grant CA-27603 from the National Cancer Institute, National Institutes of Health, Department of Health, Education and Welfare.

(20) Takita, T.; Muraoka, Y.; Nakatani, T.; Fujii, A.; Umezawa, Y.; Naganawa, H.; Umezawa, H. *J. Antibiot. (Tokyo)* **1978**, *31*, 801.

(21) National Cancer Institute Postdoctoral Trainee, 1978-1979; National Cancer Institute Postdoctoral Fellow, 1979-1980.

(22) Alfred P. Sloan Fellow, 1975-1979; NIH Research Career Development Awardee, 1975-1980.

Heihachiro Arai, William K. Hagmann,[21] H. Suguna Sidney M. Hecht*[22]

Departments of Chemistry and Biology
University of Virginia
Charlottesville, Virginia 22901
Department of Chemistry
Massachusetts Institute of Technology
Cambridge, Massachusetts 02139

Received May 28, 1980

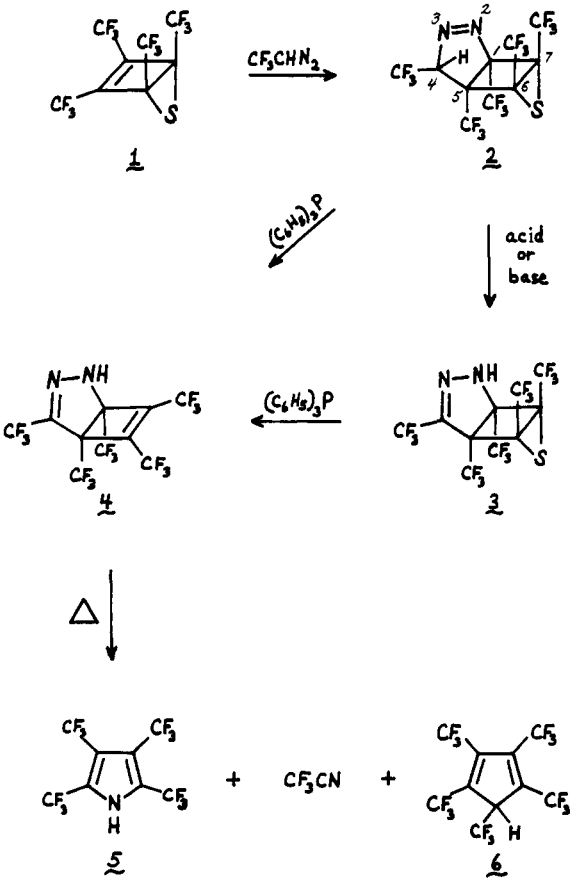
5*H*-Perfluoropentamethylcyclopentadiene, an Extraordinary Carbon Acid

Sir:

We report the synthesis of the title compound, a carbon acid which exceeds nitric acid in strength despite its lack of conjugating substituents.

2,2,2-Trifluorodiazoethane was added at room temperature to perfluorotetramethyl Dewar thiophene (**1**)[1] to yield azothiirane **2** (75%),[2] mp 53.5-54.5 °C (Scheme I). **2** had the following spectral data: IR (CCl_4) 3019 (C-H) cm^{-1}; mass spectrum (MS), *m/e* 466 (parent), 69 (base, CF_3); UV (cyclohexane) λ_{max} 330 (ϵ 233), 270 (135), 235 nm (1230); ^{19}F NMR[3,4] ($CDCl_3$) δ 56.92 (A, C_6), 60.08 (B, C_5), 60.16 (C, C_7), 64.37 (D, C_4), 67.64 (E, C_1); $J_{AB} \simeq 3.0$, $J_{AC} \simeq 4.7$, $J_{BD} \simeq 16.4$, $J_{BE} \simeq 6.1$, $J_{CE} \simeq 2.7$, $J_{DH} = 7.0$, $J_{DE} \simeq 1.2$, $J_{AH} = 1$ Hz. From a set of four stereoisomeric possibilities, only configuration **2** was formed. Both candidates having a syn framework are inconsistent with the NMR data, and the C_4 epimer of **2** can be ruled out on the basis that nonbonded repulsions between the C_4 and C_7 trifluoromethyl groups would be severe. Though subtler, the origin of the preference for anti stereochemistry[5] is also presumed to be steric.

Scheme I



Surprisingly, attempts to contract the pyrazoline ring of **2** by elimination of nitrogen led to complex mixtures when carried out photochemically, and to an acyclic product[7] when performed thermally.[8] Desulfurization of **2** with triphenylphosphine was essentially instantaneous. The remarkable facility of this process is apparent from the following list of other reagents, each of which effected desulfurization at room temperature: phosphorus trichloride, zinc dust, sodium iodide, sodium benzenesulfinate, pyridine, acetone, and benzophenone. No matter how mild the conditions chosen for the reaction, however, a second transformation invariably accompanied the loss of sulfur, namely, prototropic rearrangement to the hydrazone tautomer **4**: mp 45-47 °C; IR (vapor) 3450 (N-H), 1704 (C=C), 1593 (C=N) cm^{-1}; UV (cyclohexane) λ_{max} 242 (ϵ 2500), λ_{sh} 263 nm; MS, *m/e* 434 (parent), 69 (base); ^{19}F NMR ($CDCl_3$) δ 62.48 (A, C_7), 62.93 (B, C_6), 63.65 (C, C_4), 67.02 (D, C_5), 72.38 (E, C_1); $J_{AB} \simeq 6$, $J_{AE} \simeq 3.2$, $J_{BC} \simeq 6$, $J_{BD} \simeq 4$-5, $J_{CD} \simeq 7$, $J_{DE} \simeq 10.8$ Hz.[2]

Gentle treatment with acid or base (even acetic acid or pyridine) brought about tautomerization of **2** without desulfurization, giving **3**, which was transformed in turn into **4** by triphenylphosphine. **3** had the following spectral properties: IR (neat) 3463 and 3395 (N-H), 1607 (C=N) cm^{-1}; MS, *m/e* 466 (parent), 69 (base); ^{19}F NMR ($CDCl_3$) δ 59.07 (A, C_7), 60.77 (B, C_4), 62.50 (C, C_5), 63.47 (D, C_6), 71.80 (E, C_1); $J_{AD} \simeq 5.5$, $J_{AE} \simeq 2.8$, $J_{BC} \simeq 8$,

(1) (a) Kobayashi, Y.; Kumadaki, I.; Ohsawa, A.; Sekine, Y.; Mochizuki, H. *Chem. Pharm. Bull.* **1975**, *23*, 2773. (b) Wiebe, H. A.; Braslavsky, S.; Heicklen, J. *Can. J. Chem.* **1972**, *50*, 2721.

(2) Satisfactory analytical data (±0.3%) were obtained.

(3) All ^{19}F NMR chemical shifts are reported in ppm upfield from internal Freon 11 ($CFCl_3$).

(4) NMR spectra were analyzed with the help of spin-decoupling and spectral simulation techniques. ^{19}F NMR assignments and deductions regarding structure or configuration based on ^{19}F NMR depended upon a powerful generalization which we have tested on many compounds without finding an exception. This rule states that a F-F coupling constant greater than ~1 Hz between nongeminal CF_3 groups indicates the existence of van der Waals overlap of the coupled atoms, and that the larger the observed coupling the greater is the overlap.

(5) Anti stereochemistry has also been found in the Diels-Alder addition of **1** to furans: Kikutani, N.; Iitaka, Y.; Kobayashi, Y.; Kumadaki, I.; Ohsawa, A.; Sekine, Y. *Acta Crystallogr., Sect. B* **1975**, *B31*, 1478. Kobayashi, Y.; Kumadaki, I.; Ohsawa, A.; Sekine, Y. *Tetrahedron Lett.* **1974**, 2841. See also ref 1a. In other cycloadditions of **1**, anti stereochemistry has been assumed: Kobayashi, Y.; Kumadaki, I.; Ohsawa, A.; Sekine, Y.; Ando, A. *J. Chem. Soc., Perkin Trans. 1* **1977**, 2355. Also see ref 6.

(6) Kobayashi, Y.; Ando, A.; Kumadaki, I. *J. Chem. Soc., Chem. Commun.* **1978**, 509. Kobayashi, Y.; Kumadaki, I.; Ohsawa, A.; Ando, A. *J. Am. Chem. Soc.* **1977**, *99*, 7350.

(7) Laganis, E. D.; Lemal, D. M. *J. Am. Chem. Soc.*, following paper in this issue.

(8) In contrast, adducts of **1** with azides (triazoline analogues of **2**) smoothly ring contract upon UV irradiation (ref 6).

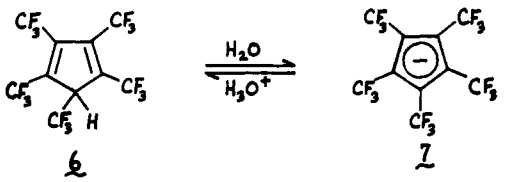
0002-7863/80/1502-6633$01.00/0

$J_{BD} \simeq 6$, $J_{CD} \simeq 3$, $J_{CE} = 6.7$ Hz. Azothiirane **2** is easily handled and can be stored for long periods or even heated without suffering tautomerization; thus, the extreme prototropic lability of its desulfurization product provides a sharp contrast. Models indicate that the proton in **2** is well shielded by the trifluoromethyl group at C_6, and the existence of "through-space" H-F coupling between them corroborates their proximity. Removal of sulfur requires rehybridization at C_6 and C_7, with concomitant exposure of the proton.[9]

Pyrazoline **4** was heated in the presence of mild bases in the hope of establishing rapid equilibrium with its elusive azo tautomer under conditions where the latter would extrude nitrogen.[10] This tactic was successful, but for reasons discussed in the accompanying communication[7] neither the desired cyclopentadiene nor its bicyclic isomer was obtained.

High-temperature flash pyrolysis (~600 °C) in a Vycor flow system at low pressure transformed **4** into a mixture whose dominant components were trifluoroacetonitrile[11] and perfluorotetramethylpyrrole (**5**)[12] (Scheme I). **5**: mp 40.5-41.5 °C; IR (vapor) 3487 (N-H), 1612 and 1474 (ring stretching) cm^{-1}; MS, *m/e* 339 (parent), 69 (base); ^{19}F NMR ($CDCl_3$) δ 56.63, 59.76 (nearly symmetrical multiplets of equal intensity).[13] The mixture also contained the desired 5*H*-perfluoropentamethylcyclopentadiene **6**, which was isolated in 11% yield[14] by GLC trapping. Diene **6** is a volatile liquid which attacks even silylated glass containers. It has the following data: IR (vapor) 2977 (C-H), 1664 (C=C) cm^{-1}; MS, *m/e* 406 (parent), 69 (base); ^{19}F NMR ($CDCl_3$) multiplets at δ 57.05 (C_1, C_4), 59.94 (C_5), 60.75 (C_2, C_3).[15]

Freely soluble in water, **6** ionized to give perfluoropentamethylcyclopentadienide ion **7**, whose ^{19}F NMR spectrum comprised a sharp singlet. Strong acidification with concentrated



6 7

sulfuric acid resulted in attenuation of the singlet and development of the 2:1:2 pattern of multiplets characteristic of the cyclopentadiene.[16] The resonance for the anion was 8.46 ppm *downfield* from the lowest field diene signal.[17] Based on cyanocarbon acids, Boyd's H_- acidity function[18] should be well-suited for determination of the pK_a of the new fluorocarbon acid. Measurement of the relative concentration of diene and its conjugate base as a function of sulfuric acid concentration and application of the H_- function established that the pK_a of **6** is ≤ -2.[19] Since the pK_a of cyclopentadiene itself is 16,[20] the five trifluoromethyl groups of **6** are responsible for an increase in acidity of at least 18 orders of magnitude. 1,2,3,4,5-Pentacyanocyclopentadiene, the strongest carbon acid known, is far more powerful yet ($pK_a < -11$),[21] but we are unaware of any carbon acid without conjugating substituents which approaches the acidity of **6**.[22]

The remarkable ability of perfluroalkyl groups to enhance the acidity of weak carbon acids is evident in the contrast in the pK_a values of methane (~68-70)[23] and tris(trifluoromethyl)methane (~21).[24] The present work demonstrates that their potency persists even into the realm of strong acids. In contrast, fluorine itself reveals a chameleon-like character, powerfully stabilizing methide ion (pK_a of fluoroform, 30.5[24]), yet destabilizing through electron repulsion lower energy anions such as those derived from fluorene[25] and nitromethanes.[26]

Acknowledgment. We thank Howard Hutchins for valuable assistance with NMR measurements and the National Science Foundation for generous financial support.

(9) It is conceivable, of course, that tautomerization actually occurs on the desulfurization pathway, via internal attack on the proton by an intermediate carbanion.

(10) We thank Professor Armin de Meijere (University of Hamburg) for suggesting this approach. For a review, see: Müller, E. *Methoden Org. Chem. (Houben-Weyl)* **1971**, *4*, Part 3, 42-89.

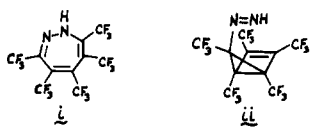
(11) Identified by its infrared spectrum: Edgell, W. F.; Potter, R. M. *J. Chem. Phys.* **1956**, *24*, 80.

(12) Kobayashi, Y.; Kumadaki, I.; Hansawa, Y. *Yuki Gosei Kagaku Kyokaishi* **1979**, *37*, 183.

(13) The yield of pyrrole is optimal (62% after purifcation) at lower pyrolysis temperatures (~530 °C).

(14) This experiment was successfully performed on several occasions, but on others, miniscule amounts of the cyclopentadiene were obtained. It is apparent that surface effects play a crucial role in this pyrolysis.

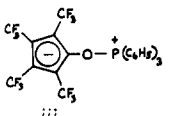
(15) The mechanisms for formation of pyrrole **5** plus trifluoroacetonitrile on the one hand and cyclopentadiene **6** plus nitrogen on the other have not been established. It is likely that ring opening of **4** to the diazepine i led via recyclization/fragmentation to the first pair of products while a Cope-like rearrangement of **4** to the bicyclic diimide ii produced the second pair.



i ii

(16) This behavior provided the basis for an alternative method for isolating the diene from the pyrolysis products of **4**, namely, by extraction from an organic solvent into a small volume of water followed by acidification with a large excess of concentrated sulfuric acid.

(17) This result underlines the fact that paramagnetic contributions to ^{19}F shielding can easily overshadow charge density considerations. A close analogue of **7** is the zwitterion iii, whose ^{19}F NMR spectrum is centered 5.23 ppm below the lowest field signal of diene **6** (both in $CDCl_3$): Roundhill, D. M.; Wilkinson, G. *J. Org. Chem.* **1970**, *35*, 3561.



iii

(18) Boyd, R. H. *J. Am. Chem. Soc.* **1961**, *83*, 4288.

(19) This pK_a value is an upper limit because of the low solubility of **6** in aqueous sulfuric acid. Our measurements may have overestimated the amount of diene actually dissolved.

(20) Streitwieser, A., Jr.; Nelson, L. L. *J. Am. Chem. Soc.* **1976**, *98*, 2188.

(21) Webster, O. W. *J. Am. Chem. Soc.* **1966**, *88*, 3046.

(22) For a general discussion of carbon acids, see: Reutov, O. A.; Beletskaya, I. P.; Butin, K. P. "CH-Acids", Pergamon Press: Oxford, 1978.

(23) Breslow, R.; Grant, J. L. *J. Am. Chem. Soc.* **1977**, *99*, 7745.

(24) Streitwieser, A., Jr.; Holtz, D.; Ziegler, G. R.; Stoffer, J. O.; Brokaw, M. L.; Guibe, F. *J. Am. Chem. Soc.* **1976**, *98*, 5229.

(25) Streitwieser, A.; Mares, F. *J. Am. Chem. Soc.* **1968**, *90*, 2444.

(26) Adolph, H. G.; Kamlet, M. J. *J. Am. Chem. Soc.* **1966**, *88*, 4761.

(27) Goodyear Fellow, 1978-1979. This report is based on the Ph.D. Dissertation of E.D.L., Dartmouth College, 1979.

Evan D. Laganis,[27] David M. Lemal*
Department of Chemistry, Dartmouth College
Hanover, New Hampshire 03755

Received February 26, 1980

Stereospecific 1,3-Dipolar Cycloelimination in Strained Pyrazolines

Sir:

Described herein is a family of closely related, stereocontrolled cycloeliminations, each of which yields a different type of ultimate product. These reactions illustrate part of the spectrum of synthetic possibilities inherent in the four-carbon homologation of diazo compounds whose prototype is shown in eq 1.[1-3]

(1)

