was more pronounced. Dilution of the trap with an inert solvent (perfluorohexane) enhanced this further. The results are shown in Table I. Automerization is not fast enough to provide for complete scrambling of the label [25:50:25 for positions 1(6), 2(5,7,8), and 3(4), respectively] before the reactive intermediates are destroyed in effectively irreversible reactions. The data, however, fit very well a statistical analysis correlating label distribution with the ratio of rate of automerization (K_a) to rate of irreversible removal of the carbene (K_r).[8]

Our findings provide unambiguous proof for automerization of homocubylidene and its corollary that the homocubene-to-homocubylidene rearrangement is indeed reversible. As the energy difference between 9-phenyl-1(9)-homocubene (**1**) and 1-phenylhomocubylidene (**2**) is less than that between the desphenyl pair,[6,9] it is economic to assume similar conclusions for this system.

Acknowledgment. This work was supported by the National Institutes of Health (GM 36436) and the Office of Naval Research. ONR provided in addition funding for the Varian VXR-400 NMR spectrometer essential to the project. R.B.A. acknowledges fellowship support from the NIH Pharmacological Sciences Training Program at The Univesity of Chicago (GM 07151-14). We are most grateful to Professor Martin Saunders of Yale for his statistical analysis of the label-scrambling process.

(8) Saunders, M., private communication.
(9) Reference 1; footnote 12.

Hydrocarbon Oxidation by Antimony Pentafluoride

Jean-Christophe Culmann and Jean Sommer*

UA CNRS 469, Dêpartement de Chimie
Universitê Louis Pasteur. 1. rue Blaise Pascal
F-67000 Strasbourg, France

Received November 21, 1989

Acid-catalyzed hydrocarbon conversion processes such as isomerization, alkylation, and cracking are industrial transformations of high economic importance. The common key step in these reactions is the formation of the reactive trivalent carbocations. Whereas a consensus has been reached on the nature of this intermediate species, the mode of its formation remains controversial despite the important contributions of mechanistic and structural studies facilitated by the use of superacid solutions as pioneered by Olah and his group.[1]

In this work, we report experimental proof of the direct oxidation of isobutane by antimony pentafluoride to the *tert*-butyl cation. The presence of a proton trap shows that the proton is not essential for this ionization process.

When isobutane (13.4 mmol) is mixed at −80 °C with excess SbF_5 (65 mmol) in SO_2ClF (70 mmol) at −80 °C and the temperature is raised to −30 °C, a stoichiometric volume of hydrogen gas (6.5 mmol) can be collected over a period of 1 h. The quantitative transformation of isobutane into the *tert*-butyl ion is shown by ^1H NMR spectra of the starting and resulting solutions. The reduction of SbF_5 to SbF_3 is evidenced by RX analysis of the white precipitate that occurs during the reaction, which can be written as

$$2\,i\text{-}C_4H_{10} + SbF_5 \rightarrow 2\,t\text{-}C_4^+ + 2F^- + SbF_3 + H_2 \quad (1)$$

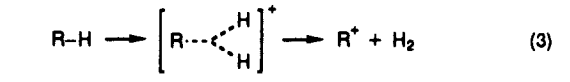
In fact, SbF_5 in SO_2ClF is a polymeric chain and the fluoride ions will be complexed and form polymeric $Sb_nF_{5n+1}^-$ ions[2] (n = 4 or 5).

When under the same experimental conditions excess acetone (molar ratio 3:1 to isobutane) is dissolved in the SbF_5–SO_2ClF solution before isobutane addition, only traces of hydrogen are detected, whereas the ^1H NMR spectrum shows the complete ionization of isobutane to the *tert*-butyl ion and the formation of the corresponding amount of protonated acetone (COH^+ signal at 13.5 ppm).

The ionization reaction of isobutane can thus be written as

$$i\text{-}C_4H_{10} + 3SbF_5 + (CH_3)_2CO \rightarrow t\text{-}C_4H_9^+ + (CH_3)_2COH^+ + 2SbF_6^- + SbF_3 \quad (2)$$

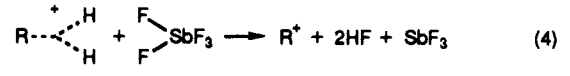
In fact, as shown by the ^1H chemical shift of the methyl groups of acetone (δ = 3.0 ppm) and in accord with the literature on $SbCl_5$ adducts,[3] the ketone is not a free base in the presence of SbF_5 but complexed by the Lewis acid at the start. The immediate appearance of the COH^+ signal during the ionization process of isobutane shows, however, that the affinity for the proton is much higher. Since the early observations of alkane ionization in superacid solutions reported by Olah and his group,[4] a large number of attempts have been made to establish the mechanism of the ionization step. The first mechanism as proposed by Olah[5] is based on the σ-donor ability of the C–H and C–C bonds. The ionization step occurs after protonation of the alkane via a three-center two-electron bond intermediate with formation of hydrogen:



(3)

This pathway has been strongly supported by experiment[6] as well as theory[7] and thermodynamics.[8] The potential acidity diagrams (Pourbaix type) of the lower alkanes plotted vs the H^+/H_2 system as shown by Devynck[9] can be very useful to illustrate the acidity domain in which this reaction will take place. However, whereas the stoichiometric production of hydrogen could be demonstrated in various systems, this was not always the case, and the deficiency in H_2 was related to the concomitant reduction of SbF_5.[10-12] For this reason, controversial propositions have been made in which SbF_5 was the main oxidant.

As SbF_5 is not reduced by H_2 under the usual experimental conditions, two different mechanistic pathways have been proposed implying the participation of the Lewis acid in the ionization process: (1) reduction of SbF_5 by the protonated alkane (reaction 4), which is a way to attribute the reduction of SbF_5 to an activated



(4)

form of hydrogen as proposed by Olah[11] and later by Ledford;[12] and (2) reduction of SbF_5 after formation of an antimony hydride obtained by hydride abstraction from the alkane (reactions 5–7).

$$R\text{-}H + SbF_5 \rightarrow HSbF_5^- + R^+ \quad (5)$$

$$HSbF_5^- + 2SbF_5 \rightarrow SbF_6^- + SbF_3 + HSbF_6 \quad (6)$$

$$HSbF_5^- + HSbF_6 \rightarrow H_2 + SbF_5 + SbF_6^- \quad (7)$$

(1) (a) Olah, G. A.; Schleyer, P. v. R. In *Carbonium Ions*; Wiley: New York, 1976. (b) Olah, G. A.; Prakash, S. K.; Sommer, J. In *Superacids*; Wiley: New York, 1985.
(2) Dean, P. A. W.; Gillespie, R. J. *J. Am. Chem. Soc.* **1969**, *91*, 7260-7264.
(3) Kessler, J. E.; Knight, C. T. G.; Merbach, A. E. *Inorg. Chim. Acta* **1986**, *115*, 75-83, 85-89.
(4) (a) Olah, G. A.; Lukas, J. *J. Am. Chem. Soc.* **1967**, *89*, 2227-2228. (b) Olah, G. A.; Lukas, J. *J. Am. Chem. Soc.* **1967**, *89*, 4739-4744. (c) Olah, G. A.; Klopman, G.; Schlosberg, R. H. *J. Am. Chem. Soc.* **1969**, *91*, 3261-3268.
(5) Olah, G. A. In *Carbocations and Electrophilic Reactions*; Verlag Chemie Wiley: 1974.
(6) (a) Bonifay, R.; Torck, B.; Hellin, M. *Bull. Soc. Chim. Fr.* **1977**, *11/12*, 1057-1065. (b) Bonifay, R.; Torck, B.; Hellin, M. *Bull. Soc. Chim. Fr.* **1977**, *9/10*, 808-814.
(7) Lathan, W. A.; Hehre, W. J.; Pople, J. A. *Tetrahedron Lett.* **1970**, 2699-2701.
(8) Larsen, J. W. *J. Am. Chem. Soc.* **1977**, *99*, 4379-4383.
(9) Fabre, P.-L.; Devynck, J.; Tremillon, B. *Chem. Rev.* **1982**, *82*, 591-614.
(10) Kirchen, R. P.; Sorensen, T. S.; Wagstaff, K.; Walker, A. M. *Tetrahedron Lett.* **1986**, *42*, 1063-1070.
(11) (a) Olah, G. A.; Halpern, Y.; Shen, J.; Mo, Y. K. *J. Am. Chem. Soc.* **1971**, *93*, 1251. (b) Olah, G. A.; Halpern, Y.; Shen, J.; Mo, Y. K. *J. Am. Chem. Soc.* **1973**, *95*, 4960-4970.
(12) Ledford, T. H. *J. Org. Chem.* **1979**, *44*, 23-25.

0002-7863/90/1512-4057$02.50/0

This hypothesis was consistent with the fact that ^1H NMR did not reveal any peak for acid protons. On the other hand, until this work, due to the difficulty of purifying SbF_5, no experimental proof was available to exclude the participation of residual protons when the neat Lewis acid was used. In this case, the protolytic cleavage of the C-H bond could occur at a much faster rate in an autocatalytic way via reaction 4.

In our experiments, the simultaneous production of the protons and the carbocation in the presence of SbF_5 throws considerable doubt on both proposed reduction mechanisms.

In itself, the postulated direct hydride abstraction is not very plausible as already indicated by Olah, because a very strong C-H bond would be heterolytically cleaved to form the weak Sb-H bond. On top of this, the existence of a metal hydride, even as a short-lived intermediate, in the presence of strong electrophiles (such as the proton that is formed, the proton on the carbonyl, and the activated carbonyl group) without chemical reaction seems an unacceptable hypothesis. Unfortunately, this concept of hydride abstraction from saturated alkanes by Lewis acids has already found its way into the literature with extension to aluminum halides.[13]

Our experiments with acetone exclude also the hypothesis of the reduction of SbF_5 by the protonated alkane. In the presence of acetone, the protons are quantitatively trapped by the carbonyl group, no hydrogen is formed, and no protons are available for alkane protonation. Nevertheless, the formation of the ion and reduction of SbF_5 are verified. When deuterated isobutane (2-deuterio-2-methylpropane) was used as starting material in the presence of acetone, the quantitative formation of $(CH_3)_2COD^+$ could be followed by ^2H NMR. This experiment again proves that the proton is formed during the oxidation step of the hydrocarbon.

In 1976, Larsen[8] applied classical thermodynamics to the various superacid-catalyzed hydrocarbon oxidation processes proposed in the literature and found that the direct oxidation of isobutane by SbF_5 (reaction 1) should not occur because the reaction was strongly endothermic. In light of our results, this prediction seems puzzling, as in the same paper it was shown that SbF_5 was able to oxidize hydrogen and further that protons were

$$SbF_5 + H_2 \rightarrow SbF_3 + 2HF \qquad -33 \text{ kcal}$$

able to oxidize isobutane. This contradiction is probably due to the lack of data concerning the solvation enthalpy of the various species in superacid solution.

That SbF_5 itself was the oxidant has also been suggested earlier by Herlem[13] by comparison with HSO_3F-containing systems where the formation of SO_2 during the ionization process could be measured.

Formally the oxidoreduction process is best represented as

$$SbF_5 + 2e^- \rightarrow SbF_3 + 2F^-$$

$$RH - 2e^- \rightarrow R^+ + H^+$$

The excess SbF_5 accepts the fluoride ions to form polymeric anions, which are the well-known low-nucleophilic counterions in superacid media, whereas the proton will attack rapidly the strongest base present in the system. In the presence of acetone, it will be trapped by the carbonyl group and no hydrogen is formed. In the absence of acetone, the strongest base is the alkane and the protolytic ionization process will occur via protonation of the tertiary C-H bond in accord with the σ-bond reactivity sequence proposed by Olah,[11] tertiary C-H $\gg$ C-C > secondary C-H $\gg$ primary C-H, and the stoichiometric amount of hydrogen (based on isobutane) will be recovered; the differentiation between Lewis and Brønsted acid cannot be established.

Acknowledgment. We thank NORSOLOR (subsidiary company of ORKEM) for financial support.

Registry No. *i*-C_4H_{10}, 75-28-5; SBF_5, 7783-70-2.

(13) (a) Marcewski, M. *J. Chem. Soc., Faraday Trans. 1* **1986**, *82*, 1687-1701. (b) Marcewski, M. *Bull. Soc. Chim. Fr.* **1986**, 750-755.
(14) (a) Herlem, M. *Pure Appl. Chem.* **1977**, *49*, 107-113. (b) Thiebault, A.; Herlem, M. *J. Electroanal. Chem.* **1977**, *85*, 107-116.

Iron(II)-Bleomycin-Mediated Reduction of O_2 to Water: An ^{17}O Nuclear Magnetic Resonance Study

John R. Barr, Reuel B. Van Atta, Anand Natrajan, and Sidney M. Hecht*

Departments of Chemistry and Biology
University of Virginia, Charlottesville, Virginia 22901

Gijs A. van der Marel and Jacques H. van Boom

Department of Organic Chemistry, University of Leiden
Leiden, The Netherlands

Received December 29, 1989

The bleomycins (BLMs) are antitumor agents believed to exert their therapeutic effects via DNA degradation.[1] Bleomycin-mediated DNA degradation requires O_2 and a redox-active metal ion such as Fe, Cu, or Mn.[2,3] Extensive mechanistic studies of DNA degradation have established two sets of products and suggested that both form by initial abstraction of the C-4′ H from deoxyribose.[3,4]

Although the formation of activated Fe·BLM involves the reduction of oxygenated Fe(II)·BLM,[5] much less is known about the stoichiometry of O_2 consumption or the fate of the O atoms when BLM is activated in the presence or absence of DNA. To characterize O_2 participation in greater detail, we have employed ^{17}O NMR spectroscopy[6] to monitor product formation concomitant with $^{17}O_2$ consumption by Fe(II)·BLM in the presence and absence of DNA.

Admixture of equimolar quantities of Fe(II) and BLM in oxygenated solution has been shown to afford equal amounts of Fe(III)·BLM and an activated Fe·BLM[3b,4f,5] believed to contain a reactive, coordinated oxygen.[3,5] In the absence of DNA, the activated species decays within minutes to Fe(III)·BLM,[5a-c] presumably with concomitant formation of H_2O. Formulation of the catalytic cycle as a $4e^-$ reduction of O_2 to H_2O, consistent with other metal-catalyzed O_2 reductions,[7] is supported by O_2 consumption data[5b] and the $2e^-$ titration of activated Fe·BLM to Fe(III)·BLM with I^- or thio-NADH.[8] The low natural abundance

(1) (a) Hecht, S. M. In *Bleomycin: Chemical, Biochemical and Biological Aspects*; Hecht, S. M., Ed.; Springer-Verlag: New York, 1979; p 1 ff; (b) Umezawa, H. In *Medicinal Chemistry Series: Anticancer Agents Based on Natural Products Models*; Cassady, J. M., Douros, J. D., Eds.; Academic: New York, 1980; Vol. XVI, p 148 ff.
(2) (a) Sausville, E. A.; Peisach, J.; Horwitz, S. B. *Biochem. Biophys. Res. Commun.* **1976**, *73*, 814. (b) Sausville, E. A.; Peisach, J.; Horwitz, S. B. *Biochemistry* **1978**, *17*, 2740.
(3) (a) Hecht, S. M. *Fed. Proc., Fed. Am. Soc. Exp. Biol.* **1986**, *45*, 2784. (b) Hecht, S. M. *Acc. Chem. Res.* **1986**, *19*, 383. (c) Stubbe, J.; Kozarich, J. W. *Chem. Rev.* **1987**, *87*, 1107.
(4) (a) Burger, R. M.; Berkowitz, A. R.; Peisach, J.; Horwitz, S. B. *J. Biol. Chem.* **1980**, *255*, 11832. (b) Giloni, L.; Takeshita, M.; Johnson, F.; Iden, C.; Grollman, A. P. *J. Biol. Chem.* **1981**, *256*, 8608. (c) Wu, J. C.; Kozarich, J. W.; Stubbe, J. *J. Biol. Chem.* **1983**, *258*, 4694. (d) Murugesan, N.; Xu, C.; Ehrenfeld, G. M.; Sugiyama, H.; Kilkuskie, R. E.; Rodriguez, L. O.; Chang, L.-H.; Hecht, S. M. *Biochemistry* **1985**, *24*, 5735. (e) Sugiyama, H.; Xu, C.; Murugesan, N.; Hecht, S. M. *J. Am. Chem. Soc.* **1985**, *107*, 4104. (f) Sugiyama, H.; Kilkuskie, R. E.; Hecht, S. M.; van der Marel, G.; van Boom, J. H. *J. Am. Chem. Soc.* **1985**, *107*, 7765. (g) Wu, J. C.; Kozarich, J. W.; Stubbe, J. *Biochemistry* **1985**, *24*, 7562. (h) Wu, J. C.; Stubbe, J.; Kozarich, J. W. *Biochemistry* **1985** *24*, 7569. (i) Rabow, L.; Stubbe, J.; Kozarich, J. W.; Gerlt, J. A. *J. Am. Chem. Soc.* **1986**, *108*, 7130. (j) Sugiyama, H.; Xu, C.; Murugesan, N.; Hecht, S. M.; van der Marel, G. A.; van Boom, J. H. *Biochemistry* **1988**, *27*, 58.
(5) (a) Burger, R. M.; Horwitz, S. B.; Peisach, J.; Wittenberg, J. B. *J. Biol. Chem.* **1979**, *254*, 12299. (b) Kuramochi, H.; Takahashi, K.; Takita, T.; Umezawa, H. *J. Antibiot.* **1981**, *34*, 576. (c) Burger, R. M.; Peisach, J.; Horwitz, S. B. *J. Biol. Chem.* **1981**, *256*, 11636. (d) Van Atta, R. B.; Long, E. C.; Hecht, S. M.; van der Marel, G. A.; van Boom, J. H. *J. Am. Chem. Soc.* **1989**, *111*, 2722.
(6) Kintizinger, J. P. *NMR Newly Accessible Nucl.* **1983**, *2*, 79.
(7) (a) Caughey, W. S.; Wallace, W. J.; Volpe, T. A.; Yoshikawa, S. In *The Enzymes*; Boyer, P., Ed.; Academic Press: New York, 1976; Vol. 13, pp 299-344. (b) Durand, R. R., Jr.; Bencosme, C. S.; Collman, J. P.; Anson, F. C. *J. Am. Chem. Soc.* **1983**, *105*, 2710. (c) Forshey, P. A.; Kuwana, T. *Inorg. Chem.* **1983**, *22*, 699. (d) Collman, J. P.; Kim, K. *J. Am. Chem. Soc.* **1986**, *108*, 7847.
(8) Burger, R. M.; Blanchard, J. S.; Horwitz, S. B.; Peisach, J. *J. Biol. Chem.* **1985**, *260*, 15406.

0002-7863/90/1512-4058$02.50/0