

Selective Electrophilic Activation of Alkanes

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Saturated hydrocarbons are the main components of natural gas and raw oil. They play a key role in the world economy as the number one source of energy, especially for heating and transportation. These fossil fuels are the outcome of a 600-million-year-old geological transformation of organic sediments, and considering the yearly consumption, following an optimistic forecast, the supply should last for only 40 years. The chemical industry, however, to meet its demand for carbon-containing feedstock, takes less than a 10% share of this raw material. The rest (90%) is burned mainly for energy supply.

This situation is alarming and should be of concern not only to chemists (Figure 1).

One major drawback for the direct use of alkanes as chemicals is their chemical inertness toward most of the usual reagents. For this reason, costly, large-scale refinery operations such as catalytic reforming and vapocacking are needed, which necessitate the use of noble metal catalysts and/or high temperature to activate the strong C-H and C-C bonds and yield the primary chemical building blocks such as ethylene, propylene, butadiene, benzene, toluene, and xylene.

In response to the challenge to use more economically a larger share of alkanes, an increasing number of research groups are working on the activation functionalization processes of the saturated hydrocarbon C-H bond. The goal is to overcome smoothly and selectively the chemical inertness of the starting (paraffinic) material. A book and special issue¹ have been published recently on this subject.

Alkanes and Superacids

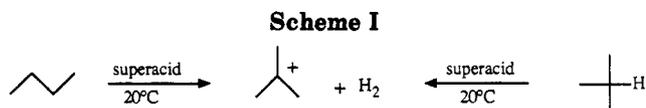
Despite earlier observations, it is accepted that the first clear evidence of the reactivity of alkanes under mild temperature and pressure has been reported

Jean Sommer was born in Strasbourg, France, on March 12, 1937, and graduated from the Ecole Nationale Supérieure de Chimie de Strasbourg in 1960. After his doctorate on Friedel-Crafts reactions at the Faculté des Sciences of Strasbourg, he joined Olah's group at Case Western Reserve University in Cleveland as a postdoctoral fellow. Back in Strasbourg he started a research group at the Louis Pasteur University as assistant professor in 1972. Head of the Chemistry Department from 1985 to 1988, he is an associate fellow at the Loker Hydrocarbon Institute at USC, where he stayed in 1978 and 1983. His research interests are focused on mechanistic studies concerning alkane activation processes by liquid and solid superacids.

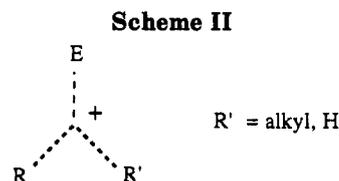
Jozef Bukala was born in Kujawki, Poland, on September 11, 1939. He received a M.Sc. degree in chemical organic technology from Technical University of Szczecin, Poland, in 1963 and a Ph.D. in chemistry from the same university in 1972. After postdoctoral work with George Olah at Case Western Reserve University in 1974, he was adjunct professor at the Technical University of Szczecin. After a sabbatical stay from 1983 to 1986 at Loker Hydrocarbon Research Institute at USC as visiting professor, he returned to Poland to join the Air Pollution Control Design Office "PROAT" in Szczecin as a senior scientist. His current interests are related to hydrocarbon reactions in liquid and on solid superacids.

independently by Olah and Lukas as well as by Hogeveen and co-workers using superacidic media.²

When *n*-butane or isobutane was reacted with HSO₃F-SbF₅ or HF-SbF₅ at room temperature, the *tert*-butyl cation was formed with evolution of hydrogen gas (Scheme I).



Pioneering this field, Olah recognized soon the scope of this reaction and ascribed it to the so-called σ -basicity of alkanes³ (i.e., the σ -bonded electron pair of the C-C and C-H bonds). He pointed out that the single bond was able to share its electron pair with an electrophile and form a two-electron-three-center bonded intermediate or transition state (Scheme II).



This concept was found to be extremely useful, extending the structural variety of carbocations from the classical sp²-hybridized ions to the hypercoordinated ions (including protonated alkanes).⁴ Using superacid solutions and Olah's technique, many research groups were able to observe spectroscopically a variety of these reaction intermediates.⁵

On the other hand, this concept was also very practical for depicting the reaction intermediates in protolysis, alkylolysis, electrophilic substitution, and hydrogen/deuterium exchange reactions on alkanes, and recently a review on two-electron C-H-C bonds in organic chemistry has appeared in this journal.⁶

However, in the industrial applications of such reactions, a major problem is the lack of selectivity, due to the general inertness of the starting molecule and the very high reactivity of the cationic reaction

(1) (a) Hill, C. L. *Activation and Functionalization of Alkanes*; Wiley-Interscience: New York, 1989. (b) *Alkane, Activation and Functionalization* (Special Issue). *New J. Chem.* 1989, 645-793.

(2) (a) Bloch, H. S.; Pines, H.; Schmerling, L. *J. Am. Chem. Soc.* 1946, 68, 153. (b) Hogeveen, H.; Bickel, G. F. *J. Chem. Soc., Chem. Commun.* 1967, 635. (c) Olah, G. A.; Lukas, J. *J. Am. Chem. Soc.* 1967, 89, 4739.

(3) Olah, G. A. *Angew. Chem., Int. Ed. Engl.* 1973, 12, 173.

(4) Olah, G. A.; Prakash, G. K. S.; Williams, R. E.; Field, L. D.; Wade, K. *Hypercarbon Chemistry*; Wiley-Interscience: New York, 1987.

(5) Olah, G. A.; Prakash, G. K. S.; Sommer, J. *Superacids*; Wiley-Interscience: New York, 1985.

(6) (a) McMurry, J. E.; Lectka, T. *Acc. Chem. Res.* 1992, 25, 47. (b) McMurry, J. E.; Lectka, T. *J. Am. Chem. Soc.* 1990, 112, 869.

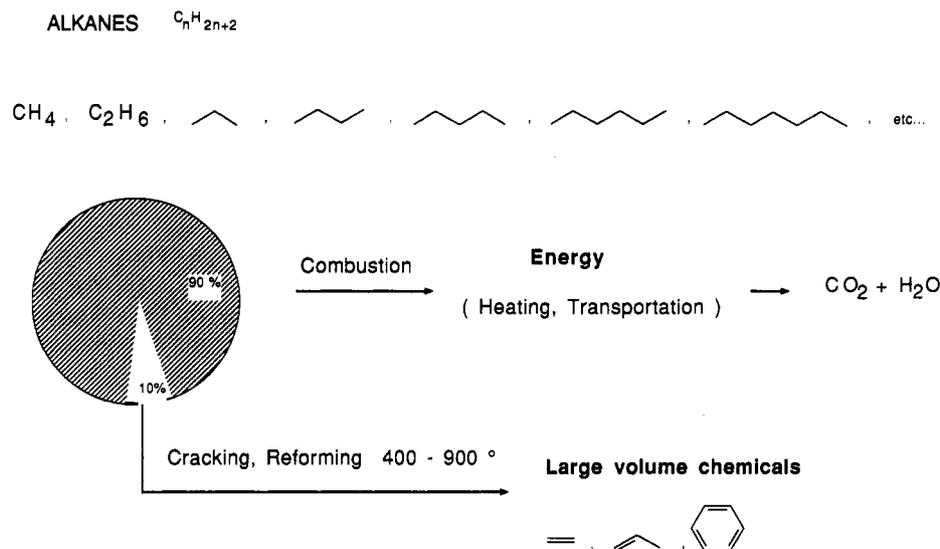


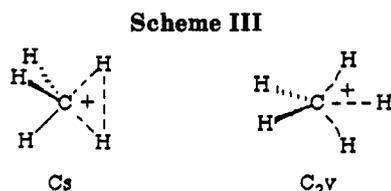
Figure 1.

intermediates, leading to cracking and rearrangement of the carbon skeleton.

In this Account we intend to illustrate the factors governing the selectivity in electrophilic activation of alkanes by comparing the three competitive activation pathways which take place in HF-SbF₅ superacid solution: protolysis, hydride abstraction, and oxidation by SbF₅. Propane and isobutane are used as model compounds, and the reactions are run in the presence of excess carbon monoxide. Thus the initially formed unstable carbocations react rapidly with CO and yield the much more stable oxocarbenium ions, which can be quenched in excess ethanol-sodium hydrogen carbonate. GC analysis of the resulting esters and of the hydrocarbons in the gas phase allows a full material balance over the acid and neutral phases.

Protonation of Alkanes

The first spectroscopic observation of a protonated alkane was made in the gas phase during relatively high pressure ion-molecule reaction studies by mass spectroscopy.^{7a} The methonium ion (CH₅)⁺ was produced by reacting methane with the proton produced in the spectrometer. The structure of this ion has been extensively studied by ab initio theoretical calculations, and the C_s symmetry has been found the most stable.^{7b} Recently, more refined calculations find no difference with the C_{2v} structure^{7c} (Scheme III).



With alkanes having a larger number of carbon atoms, competitive protonation can occur on primary, secondary, and tertiary C-H bonds as well as on various C-C bonds. Despite a large amount of experimental

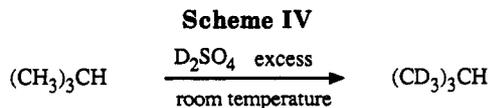
(7) (a) Field, F. H.; Munson, M. S. B. *J. Am. Chem. Soc.* **1965**, *87*, 3289. (b) Raghavachari, K.; Whitesides, R. A.; Pople, J. A.; Schleyer, P. v. R. *J. Am. Chem. Soc.* **1981**, *103*, 5649. (c) Schleyer, P. v. R.; Carneiro, J. W. de M. *J. Comput. Chem.* **1992**, *13*, 997.

data supporting the occurrence of protonated alkanes in liquid and in solid-superacid-catalyzed reactions, the proof of their formation as reaction intermediates when alkanes react with superacids in the condensed state is based only on product distribution.

The following competing reactions can be observed: (1) protium/deuterium isotope exchange; (2) protolysis of C-H bonds; (3) protolysis of C-C bonds; (4) activation of the alkane by hydride transfer; and (5) direct oxidation by SbF₅.

We will illustrate here which parameters control the selectivity of the activation process.

C-H Bond Protolysis and the Protium/Deuterium Exchange Reaction. (We follow in this text the IUPAC recommendation for nomenclature of hydrogen atoms or ions and use the specific names pertaining to the specific isotope.³¹ In the literature the expression hydrogen/deuterium exchange has been most generally used up to now.) Hydrogen exchange, which may occur in competition with CH bond protolysis, can be observed only if the alkane or the acid is isotopically labeled. Isotope exchange taking place between hydrogen atoms of isoparaffins (paraffins possessing tertiary carbon atoms) and the hydrogens of sulfuric acid had already been reported in the 1930s by Ingold and co-workers⁸ using sulfuric acid-d₂. A more detailed study in the 1950s by Stevenson and co-workers⁹ showed that all hydrogens on carbon atoms adjacent to the tertiary carbon atom exchanged rapidly with sulfuric acid whereas invariably the hydrogen on the tertiary carbon was recovered unexchanged. For isobutane, for example, see Scheme IV. This was



rationalized as an ionic chain reaction, via tertiary carbocationic intermediates in which the protium/

(8) Ingold, C. K.; Raisin, C. G.; Wilson, C. L. *J. Chem. Soc., Chem. Commun.* **1936**, 1643.

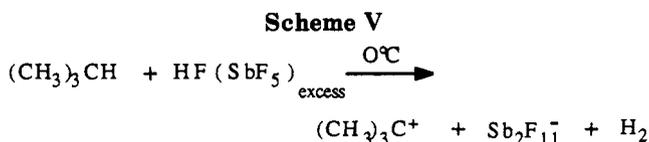
(9) (a) Otvos, J. W.; Stevenson, D. P.; Wagner, C. D.; Beck, O. *J. Am. Chem. Soc.* **1951**, *73*, 5741. (b) Stevenson, D. P.; Wagner, C. D.; Beck, O.; Otvos, J. W. *J. Am. Chem. Soc.* **1952**, *74*, 3269.

deuterium exchange probably takes place via elimination and reversible olefin deuteration.

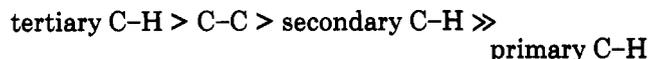
In the first years of superacid chemistry, both Hogeveen¹⁰ and Olah¹¹ observed deuterium \rightarrow protium exchange on deuterated methane treated with HF-SbF₅ or HSO₃F-SbF₅ superacid mixtures under mild conditions of temperature and pressure. In this case olefin formation could not be considered, and the exchange mechanism was suggested to take place via protonated methane as a transition state or intermediate of C_s type geometry (see Scheme III).

Dedeuteration of isobutane-d₂ in HF-SbF₅ was observed to be much faster than ion formation via hydride abstraction.¹² On the other hand, Olah and his group reported also a significant exchange but only of the tertiary hydrogen when isobutane was treated with deuterated superacids at low temperature (-78 °C) and atmospheric pressure.¹³ Believing that the rates of the protonation exchange process should be fundamentally related to the σ -basicity of the C-H bonds as defined by Olah, we reinvestigated the hydrogen exchange problem under our experimental conditions.

When a mixture of isobutane and nitrogen (1:1 molar ratio) was bubbled at atmospheric pressure through a HF-SbF₅ solution (4:1 molar ratio), during 1 h at 0 °C, 20% of the alkane was converted into the *tert*-butyl cation and a stoichiometric amount of hydrogen was recovered.¹⁴ This is a clear example of a selective C-H bond protolysis as less than 1.5% methane and propane could be detected (Scheme V). The observed selectivity



is due mainly to the structural effect of the protolysis reaction as pointed out by Olah¹³ in the early 1970s:

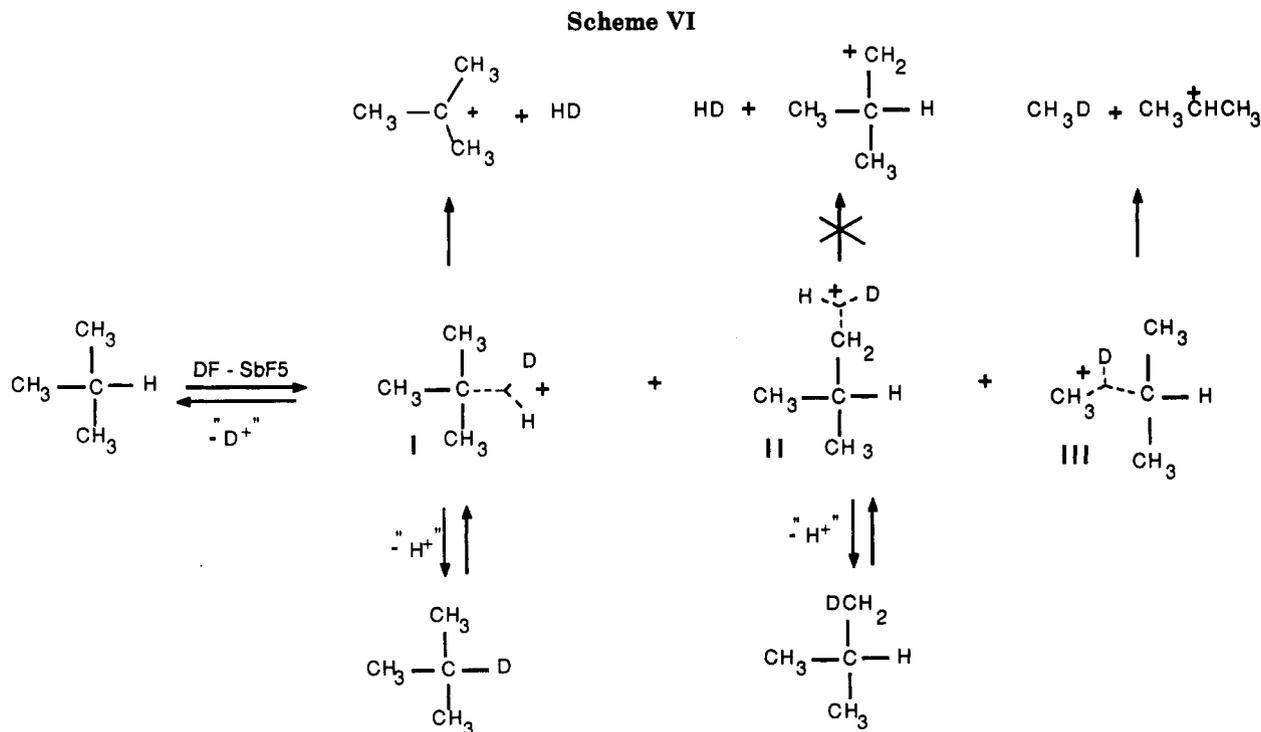


When HF was replaced by DF, carbon monoxide was added to the hydrocarbon stream (RH:CO, 1:3 molar ratio) in order to inhibit the formation of isobutane from the *tert*-butyl cation by protide transfer. ¹H and ²H NMR analyses of the recovered isobutane show a significant exchange on the alkane. Both the methine and the methyl hydrons were exchanged for deuterium to the extent of 13% per atom.

These results are rationalized as depicted in Scheme VI. The protonation takes place on both primary and tertiary C-H bonds at comparable rates, yielding carbocationic intermediates I and II. Species I can either lose H-D and form the stable *tert*-butyl ion or exchange the tertiary hydron for deuterium. Species II by loss of H-D would lead to a very energetic primary carbocation, and for this reason ionization does not take place. Species III can only cleave, forming CH₃D and the secondary isopropyl cation at a rate which is much lower than the rate of formation of *tert*-butyl cation from I.

The deuteration of *propane* by DF-SbF₅ also has been studied¹⁵ in the presence of carbon monoxide to avoid side reactions. The results show that primary and secondary hydrons exchange also at comparable rates: 15% of the methyl hydrons and 15% of the methylene hydrons were exchanged for deuterium when propane was bubbled through a DF-SbF₅ solution as described above for isobutane.

Under the same experimental conditions, methane and ethane also exchange the primary hydrons for



(10) Hogeveen, H.; Gaasbeck, C. J. *Recl. Trav. Chim. Pays-Bas* 1968, 87, 319.

(11) Olah, S. A.; Schlosberg, R. H. *J. Am. Chem. Soc.* 1968, 90, 2726.

(12) Hogeveen, H.; Gaasbeck, C. J.; Bickel, A. F. *Recl. Trav. Chim. Pays-Bas* 1969, 88, 703.

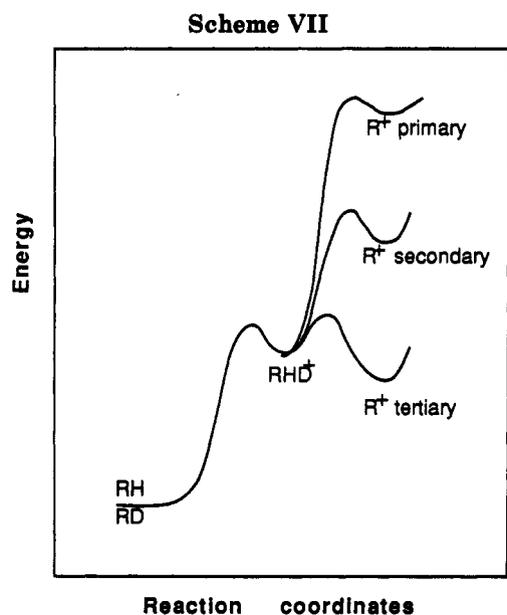
(13) Olah, G. A.; Halpern, Y.; Shen, J.; Mo, Y. K. *J. Am. Chem. Soc.* 1971, 93, 1251.

(14) Sommer, J.; Bukala, J.; Rouba, S.; Graff, R.; Ahlberg, P. *J. Am. Chem. Soc.* 1992, 114, 5884.

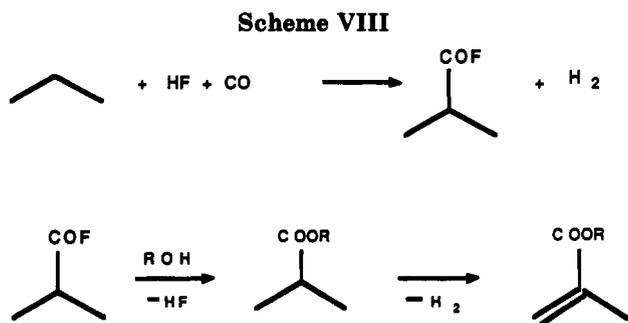
(15) Sommer, J.; Bukala, J. Unpublished data.

deuterium but need longer contact times. It is clear in all these cases that the exchange mechanism is different from the one taking place in less acidic media such as H_2SO_4 in which only the hydrons adjacent to a tertiary carbon exchange for deuterium.

The important point to notice is that all C-H bonds behave as σ -bases independently of further reactivity of the protonated alkane. A small difference in basicity does not lead to a significant difference in the protonation exchange rates. In our view these results indicate clearly that the protonated alkane is an intermediate step on the way to protolytic ionization. Once formed in the superacid medium, the C-H protonated alkane can either exchange H for D or continue on the reaction path depending on the energy available (Scheme VII).



C-C Bond Protolysis and Selective Activation via Hydride Abstraction. In comparison with the selective protolytic activation of isobutane, the case of propane is a better illustration of the competitive pathways an alkane can undergo in superacid media. On the other hand, propane is a potential starting material for the synthesis of methacrylic esters via isobutyric acid, a source of high-quality polymeric material (Scheme VIII).



As depicted in Scheme IX, four competing reaction pathways can be considered: (1) protolytic cleavage of a primary C-H bond (energetically very disfavored); (2) protolytic cleavage of a secondary C-H bond (giving

the thermodynamically most stable ion); and (3) protolytic cleavage of one of the C-C bonds (kinetically favored) yielding either (a) methane or (b) ethane.

Trapping the intermediate ions quantitatively with CO helped us to establish the relative importance of these pathways. When a propane-carbon monoxide mixture ($\text{CO}:\text{C}_3$ molar ratio = 3) was bubbled during 1 h through the $\text{HF}-\text{SbF}_5$ solution (4:1 molar ratio) in a Kel-F reactor, the NMR spectrum of the resulting solution showed only two ions: the isopropylloxocarbenium ion (IPOC) and the ethylloxocarbenium ion (ETOC) in a 2:3 relative ratio. The amount of hydrogen produced was negligible in comparison with the amount of isopropylloxocarbenium ions formed in the superacid solution (the ratio of C-H/C-C bond protolysis is of the order of 1:70 at 0 °C). On the other hand, besides unreacted propane, methane and ethane were found in the gas phase ($\text{CH}_4 > \text{C}_2\text{H}_6 \gg \text{H}_2$).

Further, when our experiments were carried out with a variable $\text{CO}:\text{C}_3$ ratio, the influence of this ratio on the selective production of the isopropylloxocarbenium became apparent (Figure 2).

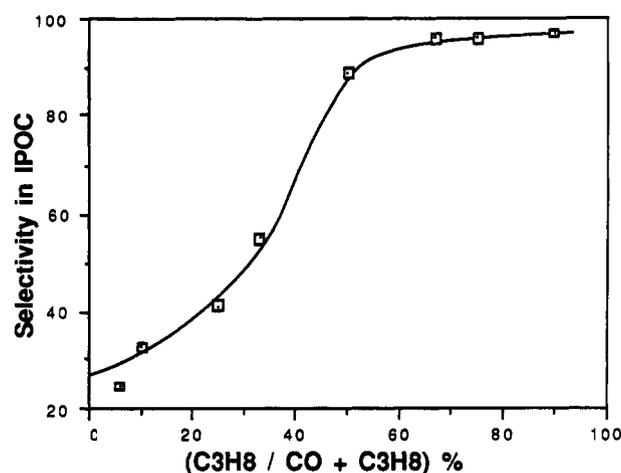


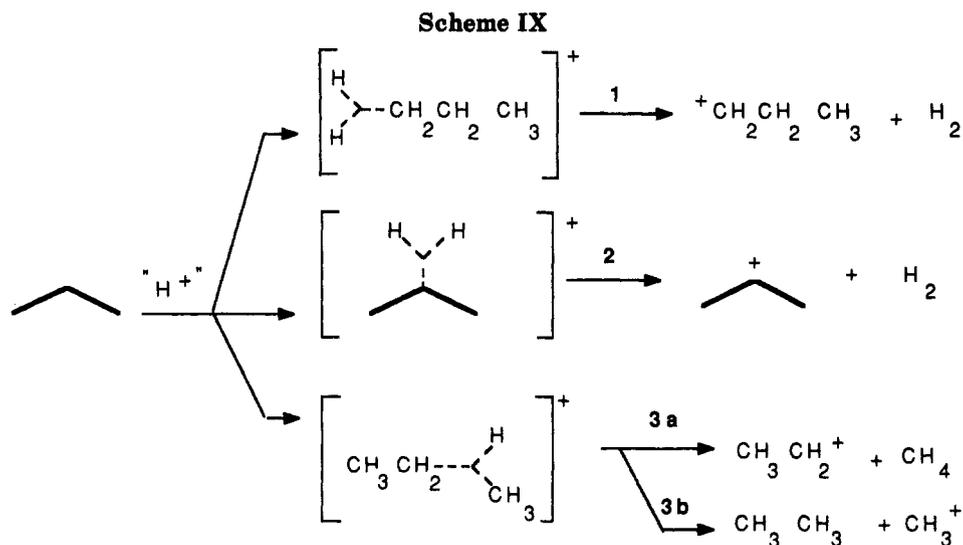
Figure 2.

At high $\text{CO}:\text{C}_3$ ratios, the product distribution is in accord with preferential protolytic C-C bond cleavage followed by carbonylation of the ethyl cation (path a, Scheme X). However, when the $\text{CO}:\text{C}_3$ ratio is below unity, the ethyl cation rapidly abstracts a hydride from available propane (path b), and the resulting more stable isopropyl cation reacts with carbon monoxide. Ethane and methane are then produced in equivalent amounts. Under these conditions the selective carbonylation of 1 mol of propane is achieved at the expense of 1 mol of propane sacrificed to produce the ethyl cation and methane.¹⁷

These results illustrate well the early conclusions by Olah and his group: the initial protolytic cleavage of the C-C bond in the small alkanes, forming lower alkanes and reactive carbocations, results in hydride abstraction by these ions from the starting alkanes.¹⁶ Due to the relative bulkiness of these ions compared with the superacidic proton, the less hindered C-H bond is preferred. Under these conditions, with alkanes having no tertiary hydrogen, the protolytic activation via C-H bond protolysis becomes negligible as shown

(16) Olah, G. A.; Halpern, Y.; Shen, J.; Mo, Y. K. *J. Am. Chem. Soc.* 1973, 95, 4960.

(17) Delavrenne, S.; Simon, S.; Fauconet, M.; Sommer, J. J. *Am. Chem. Soc.* 1989, 111, 383.



by the trace amount of H_2 in the gas phase after reaction. In the presence of excess carbon monoxide, the initial ions obtained by cleavage of the C-C bond are trapped as oxocarbenium ions. In the absence of carbon monoxide the product selectivity is governed by the reactivity of those ions formed by C-C bond cleavage and able to activate the alkane by hydride abstraction.

Selective Activation via Hydride Abstraction by Other "Super" Electrophiles. Hydride Abstraction by Halogen Cations or Halocarbonyl Cations. During our studies on propane carbonylation, we noticed accidentally that the presence of catalytic amounts of bromide ion induced a drastic change in selectivity in favor of secondary C-H bond activation.¹⁷ Moreover, the conversion of propane into isopropyl-oxocarbenium ion was also remarkably enhanced. The same results could be achieved by addition of small amounts of bromine (Figure 3). The effect of adding iodine was much smaller, and addition of chlorine had no effect at all.

A careful analysis of the product distribution showed that under these conditions a selectivity of 99% in IPOC could be obtained and only negligible amounts of methane and ethane are produced. (No hydrogen was detected.)

The intriguing point was not the high selectivity, which could be ascribed to steric requirements hindering electrophilic attack on the C-C bond, but the absence

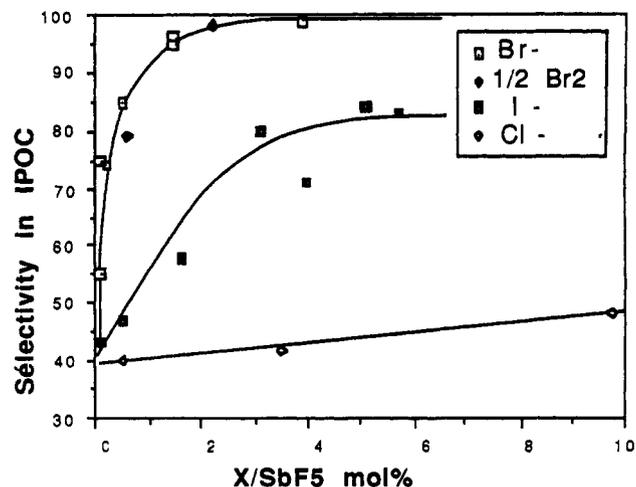
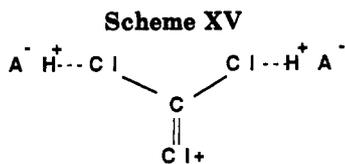


Figure 3.

of protolytic C-C bond cleavage in the presence of a large excess of superacidic protons under these conditions. These results were rationalized as follows: the bromide ion or bromine is oxidized in situ (by antimony pentafluoride) into positive halogen cations having a powerful hydride-abstraction ability; the rate of hydride abstraction is much faster than the competitive protolysis of the C-C bond (Scheme XI).

Despite the fact that no experimental evidence has been brought for the existence of monatomic ions, the



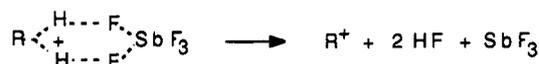
ion²⁶ (NO₂H²⁺) in superacid-catalyzed nitration led Olah to suggest calling these species "super-electrophiles" (electrophiles activated by protosolvation in superacid media).

The selectivity is here again ascribed to the high hydride-transfer rates from the alkane to the super-electrophile in comparison with the rates of C-C and C-H bond protolysis occurring under the same conditions.

Alkane Oxidation by SbF₅. Since the early observations of alkane ionization in superacid solution, the reaction mechanism via C-H bond protolysis has been a subject of controversy because the amount of hydrogen produced was not stoichiometric and depended on the alkane, the acid, and reaction conditions. The deficiency in hydrogen was related to the concomitant reduction of SbF₅, and controversial propositions have been made for the reduction mechanism of the Lewis acid.

As hydrogen does not reduce SbF₅ under the usual experimental conditions, two pathways have been proposed implying the participation of the Lewis acid in the alkane ionization process: (1) reduction of SbF₅ after formation of an antimony hydride obtained via hydride abstraction from the alkane²⁷ and (2) reduction of SbF₅ by the protonated alkane (Scheme XVI), which

Scheme XVI



is a way to attribute the reduction of SbF₅ to an activated form of hydrogen ("nascent hydrogen").²⁸ In hypothesis 1, the postulated hydride abstraction from the strong C-H bond to form the very weak SbH bond is not very plausible, but hypothesis 2 was difficult to disprove because of the experimental difficulty to remove residual protons from neat SbF₅. The use of a proton trap helped us solve this problem²⁹ by comparing the two following experiments: (i) Isobutane was mixed at low temperature (<-30 °C) with SbF₅ in SO₂ClF solution, and a stoichiometric amount of hydrogen was collected. (ii) Under the same experimental conditions, excess acetone was added before addition of isobutane (molar ratio, 3:1 acetone:isobutane). No hydrogen was produced, and the ¹H NMR spectrum showed the complete ionization of isobutane to the *tert*-butyl ion and the corresponding amount of protonated acetone.

These reactions can be written as depicted in Scheme XVII. The oxidation of the alkane occurs selectively

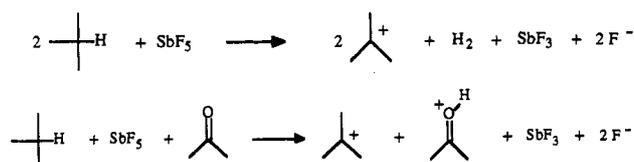
(26) Olah, G. A.; Rasul, G.; Aniszfeld, R.; Prakash, G. K. S. *J. Am. Chem. Soc.* 1992, 114, 5608.

(27) Lukas, J.; Kramer, P.; Kouwenhoven, A. *Recl. Trav. Chim. Pays-Bas* 1973, 92, 44.

(28) Ledford, T. H. *J. Org. Chem.* 1979, 44, 23.

(29) Culmann, J. C.; Sommer, J. *J. Am. Chem. Soc.* 1990, 112, 4057.

Scheme XVII



on the tertiary C-H bond and generates an equivalent amount of protons and *tert*-butyl cation. Formally the oxidoreduction process is best represented as depicted in (Scheme XVIII).

Scheme XVIII



In the presence of acetone, the proton generated by the oxidation process is trapped by the carbonyl group and no hydrogen is formed. In the absence of acetone, the proton will attack the strongest base present, i.e. the alkane, on the tertiary C-H bond, in agreement with the σ -bond reactivity sequence, and protolytic ionization of the alkane does occur.

The relative amount of H₂ produced by the protolytic cleavage and by direct oxidation is in a ratio of 2:1. This explains why in many cases the stoichiometric amount of hydrogen was not found.

The direct oxidation of the alkane by SbF₅ occurs also as a competitive activation during the carbonylation reaction of propane described above, and the relative importance of this activation step can be measured by a careful analysis of the product balance.¹⁹ We have also shown that this activation is regioselective, for when propane is carbonylated in the presence of SbF₅ alone, the exclusive formation of the isobutyryl cation can be observed by ¹H NMR of the resulting solution.³⁰

Here again the selectivity is ascribed to an oxidoreductive step which depends on regeneration of the superacid solution.

Conclusion

Protonated alkanes are "bona fide" reaction intermediates in superacid-catalyzed protolysis. Protonation occurs on all C-C and C-H σ -bonds independently of the further reactivity of the protonated alkane as confirmed by using ²H-labeled superacids. The protonated alkane either deprotonates or undergoes protolytic cleavage depending on the energy profile of the reaction. The use of carbon monoxide as trapping agent for the reactive carbocations inhibits the competitive side reactions that usually occur.

Direct and selective C-H bond protolysis is limited to tertiary alkanes whereas linear alkanes undergo less selective C-C bond cleavage. However, the use of super-electrophiles such as halogen cations or halocarbenium ions, which act as strong hydride acceptors, allows regioselective activation of linear alkanes on secondary C-H bonds. Unfortunately, the generation of these highly reactive species is obtained at the expense of the stoichiometric complexation or reduction of antimony pentafluoride.

(30) Fauconet, M. Unpublished results from the Doctorate Thesis of Michel Fauconet submitted to Université Louis Pasteur, November 1987.

(31) Bunnett, J. F.; Jones, R. A. Y. *Pure Appl. Chem.* 1988, 60, 1115.