

Some New Synthetic Reagents and Reactions

GEORGE A. OLAH

Department of Chemistry and Hydrocarbon Research Institute, University of Southern California, Los Angeles, California 90007

Received September 20, 1979 (Revised Manuscript Received May 12, 1980)

Our work in synthetic chemistry is directed toward the development of new synthetic reagents and reactions, as well as improvement of basic (unit) reactions. These are of importance since they form the building blocks for all synthesis, including those of natural products or other complex target molecules.

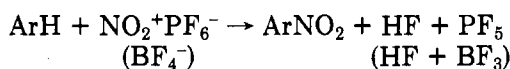
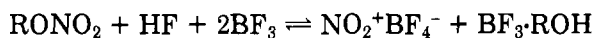
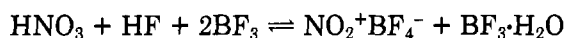
It is impossible in a short review even to attempt to give the background of such a broad field. Thus I will only give an account of our recent work and results relating to the development of a series of new synthetic reagents and reactions. The reader is reminded of the large diversity of existing methods, to which ours, we hope, made some useful contributions. The scope of this account, which is based on a recent lecture covering some of our work, does not allow credit to the many fine contributions in the field, for which I can only apologize and refer to the literature.

Nitronium and Nitronium Salts and Related Reagents

As Nitrating Agents. There are several inherent difficulties associated with the conventional electrophilic nitration¹ of aromatic compounds using mixtures of sulfuric and nitric acids. In particular, the water formed as the reaction proceeds dilutes the acid and therefore reduces its strength. Secondly the strong oxidizing ability of the mineral acids makes it unsuitable to nitrate many acid-sensitive compounds. The disposal of the spent acid also poses a significant environmental problem.

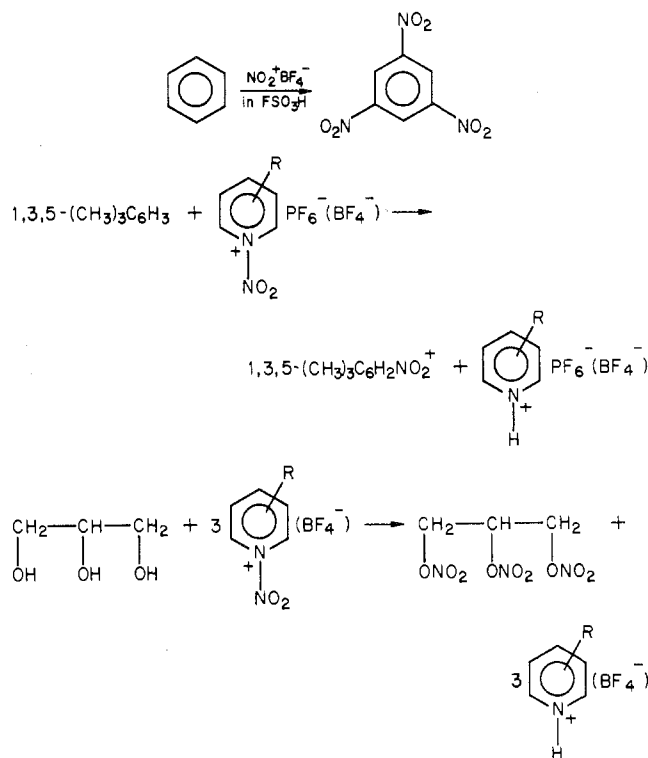
In order to overcome these difficulties we developed nitronium salts (such as $\text{NO}_2^+\text{BF}_4^-$ and $\text{NO}_2^+\text{PF}_6^-$) and related reagents as efficient nitrating agents.

Stable nitronium salts which are readily prepared from nitric acid (or nitrates) with HF and BF_3 (and other Lewis acids such as PF_5 , SbF_5 , etc.) nitrate² aromatics in organic solvents generally with close to quantitative yield. As HF and PF_5 (or BF_3) can be easily recovered and recycled, the method can be considered as a nitric acid nitration using a superacid catalyst.



George A. Olah is Distinguished Professor of Chemistry and Scientific Co-Director of the Hydrocarbon Research Institute at the University of Southern California, Los Angeles. He was born and educated in Hungary and migrated to Canada in 1957 and to the United States in 1964. He was Professor of Chemistry at Case Western Reserve University before moving to Southern California in 1977. His research interests are in mechanistic and synthetic chemistry, hydrocarbon chemistry, study of reactive intermediates, and biological alkylating agents. This Account is based on his Award lecture for the ACS Award for Creative Work in Synthetic Organic Chemistry, given before the Joint ACS-CSF Meeting in Honolulu, April 1979.

The powerful nature of nitronium salts as nitrating agents is demonstrated in their ability to affect even trinitration³ of benzene to trinitrobenzene. Nitronium salts enable nitration of every conceivable nitratable aromatic substrate. It is regrettable that mechanistic studies (still controversial in some aspects) until now overshadowed the obvious broad preparative utility of the nitronium salt reagents. More selective nitronium ions such as *N*-nitropyridinium salts, which are readily prepared^{4a,b} from the corresponding pyridine and nitronium salts, act as convenient transfer nitrating agents. Transfer nitrations are applicable to C-nitrations as well as to a variety of heteroatom nitrations. For example, they allow safe, acid-free preparation of alkyl nitrates and polynitrates from alcohols^{4c} (polyols) in nearly quantitative yield.



Electrophilic nitration of olefins can also be carried out⁵ with nitronium salts in pyridinium polyhydrogen

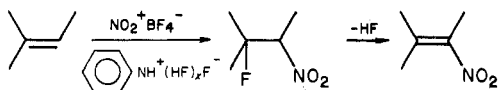
(1) Hoggett, J. A.; Moodie, R. B.; Penton, J. R.; Schofield, K. "Nitration and Aromatic Reactivity"; Cambridge University Press: Cambridge; 1971.

(2) (a) Olah, G. A.; Kuhn, S. J.; Flood, S. H. *J. Am. Chem. Soc.* **1961**, *83*, 4581. (b) Olah, G. A.; Kuhn, S. J. *Ibid.* **1962**, *84*, 3684. (c) Olah, G. A.; Kuhn, S. J.; Flood, S. H.; Evans, J. C. *Ibid.* **1962**, *84*, 3687.

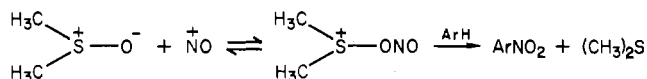
(3) Olah, G. A.; Lin, H. C. *Synthesis* **1974**, 444.

(4) (a) Olah, G. A.; Olah, J. A.; Overchuk, N. A. *J. Org. Chem.* **1965**, *30*, 3373. (b) Cupas, C. A.; Pearson, R. L. *J. Am. Chem. Soc.* **1968**, *90*, 4742. (c) Olah, G. A.; Narang, S. C.; Pearson, R. L.; Cupas, C. A. **1978**, *Synthesis*, 452. (d) Olah, G. A.; Narang, S. C.; Pearson, R. L.; Cupas, C. A. *J. Am. Chem. Soc.*, in press.

fluoride solution (which also acts as solvent) to give high yields of nitrofluorinated alkanes. In the presence of added halide ions (iodide, bromide, chloride) the related haloalkanes are formed, and these can be dehydrohalogenated to the corresponding nitroalkenes.

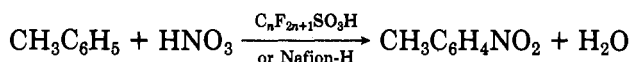
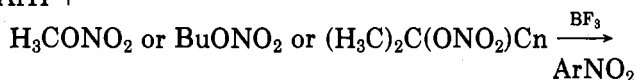


Unexpectedly, we have also found^{6a} nitrosonium salts in Me₂SO to be nitrating agents. The S-nitro to S-nitronium ion transformation was directly observed by ¹³C and ¹⁵N NMR spectroscopy.^{6b}



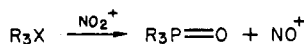
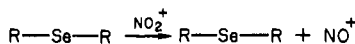
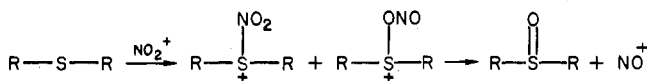
With BF₃ as catalyst, alkyl nitrates such as MeONO₂⁷ and BuONO₂ or acetone cyanohydrin nitrate⁸ (Me₂C(CN)ONO₂) were found to be efficient selective nitrating agents. Nitrations with alkyl nitrates were also carried out by using superacidic solid perfluorinated sulfonic acid catalyst (including Nafion-H, to be discussed subsequently) instead of liquid protic or Friedel-Crafts Lewis acid catalysts. Further the azeotropic nitration of aromatics with nitric acid was also developed over these superacid catalysts.⁸

ArH +



Water formed is continuously azeotroped off by excess of the aromatic substrate, thus preventing the dilution of acid and allowing maximum utilization of the nitric acid (although some of the acid distills over with the azeotrope).

As Oxidizing Agents. Until recently the nitronium ion was recognized only as a nitrating agent. In our work, it was found^{6b} to possess significant ambident reactivity and thus capable of acting as an oxidizing agent. Dialkyl (aryl) sulfides, triarylsulfines, and triarylstibines react with nitronium salts to give the corresponding oxides.



X = P, As, or Sb, R = alkyl, aryl

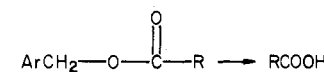
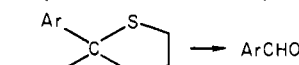
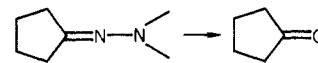
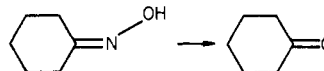
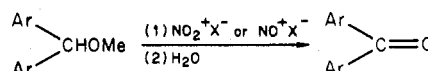
Stable nitronium (NO₂⁺) and related nitrosonium (NO⁺) salts, particularly with PF₆⁻ and BF₄⁻ counterions, can act as mild, selective oxidative cleavage

(5) Olah, G. A.; Nojima, M. *Synthesis* 1973, 785.
(6) (a) Olah, G. A.; Lin, H. C.; Olah, J. A.; Narang, S. C. *Proc. Natl. Acad. Sci. U.S.A.* 1978, 75, 1045. (b) Olah, G. A.; Gupta, B. G. B.; Narang, S. C. *J. Am. Chem. Soc.* 1979, 101, 5317.

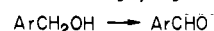
(7) (a) Olah, G. A.; Lin, H. C. *Synthesis* 1973, 489. (b) Olah, G. A.; Lin, H. C. *J. Am. Chem. Soc.* 1974, 96, 2892.

(8) (a) Olah, G. A.; Narang, S. C. *Synthesis* 1973, 690. (b) Olah, G. A.; Malhotra, R.; Narang, S. C. *J. Org. Chem.* 1978, 43, 4628. (c) Narang, S. C.; Thompson, M. J. *Aust. J. Chem.* 1978, 31, 1839.

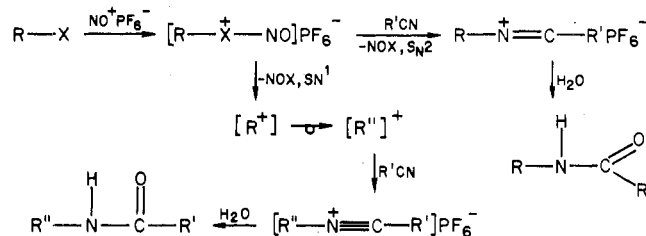
reagents⁹ for a wide variety of functional groups. The following examples illustrate the utility of these methods.



R = alkyl, aryl



NO⁺ Salt-Initiated Electrophilic Reactions. NO⁺ salts also find useful applications as initiators for various electrophilic reactions, including a Ritter-type reaction.^{10a} We have found that nitrosonium salts act as mild initiators for the condensation of alkyl or arylalkyl halides with nitriles.^{10b}



R = alkyl, aralkyl

X = F, Cl, Br, I

R' = CH₃, C₂H₅, C₃H₇, C₆H₅, C₆H₄CH₂

Halogenating Agents

Pyridine-Hydrogen Fluoride Reagent (Pyridinium Poly(hydrogen fluoride)). Anhydrous hydrogen fluoride is the most commonly used industrial fluorinating agent. However, due to its low boiling point (20 °C) and corrosive nature, reactions must be usually carried out in special pressure equipment. Efforts have been made in the past¹¹⁻¹⁵ to effect fluorinations at atmospheric pressure by complexing HF with various nonbonded electron donors such as THF, amines, etc. However, none of these complexes were studied in detail or gained wider use.

Our interest in the fluorination of organic compounds prompted us to examine several complexes of HF and

(9) (a) Olah, G. A.; Ho, T. L. *Synthesis* 1976, 609. (b) *Ibid.* 1976, 610. (c) *J. Org. Chem.* 1977, 42, 3097. (d) Ho, T. L.; Olah, G. A. *Synthesis* 1977, 418. (e) Olah, G. A.; Narang, S. C.; Salem, G. F.; Gupta, B. G. B. *Ibid.* 1979, 273.

(10) (a) Krimen, L. I.; Cota, D. J. *Org. React. (N.Y.)* 1969, 17, 213. (b) Olah, G. A.; Gupta, B. G. B.; Narang, S. C. *Synthesis* 1979, 274.

(11) (a) Aranda, G.; Jullien, J.; Martin, J. A. *Bull. Soc. Chim. Fr.* 1965, 1890. (b) *Ibid.* 1966, 2850.

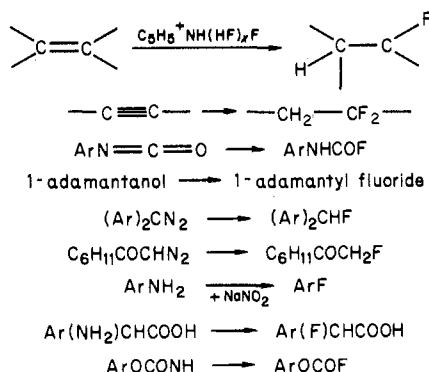
(12) (a) French Patent 1370827; *Chem. Abstr.* 1965, 62, P2721h. (b) Balicheva, T. G.; Borodin, P. M.; Pologikh, I. V. *Yad. Magn. Rezonans* 1969, 49. (c) Hecht, S. S.; Rothman, E. S. *J. Org. Chem.* 1973, 38, 395.

(13) French Patent FR 1374591; *Chem. Abstr.* 1965, 62, P9212a.

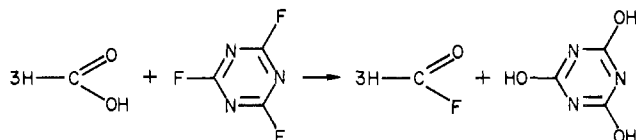
(14) van der Akken, M.; Jellinek, F. *Recl. Trav. Chim. Pays-Bas* 1967, 86, 275.

(15) (a) Thomas, R. K. *Proc. R. Soc. London, Ser. A*, 1971, 322, 137. (b) Politanski, S. F.; Ivanyk, G. D.; Sarancha, V. N.; Shevchuk, V. U. *Zh. Org. Khim.* 1974, 10, 693.

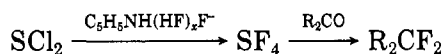
amines in detail. We have found that a stable liquid complex of HF and pyridine (70:30 by weight), $C_5H_5NH^+(HF)_x F^-$, has a relatively low vapor pressure up to 60 °C.^{16b} This permits^{16a-j,17} a wide variety of synthetically useful fluorination reactions to be carried out at atmospheric pressure in polyolefin laboratory equipment. Some representative fluorination reactions with pyridinium poly(hydrogen fluoride) are shown below.



Cyanuric Fluoride. During our studies on fluorinating agents, we found that cyanuric fluoride is a convenient fluorinating agent.¹⁸ Carboxylic acids, including formic acid, are easily converted into their acyl fluorides. This method gives a 40% yield of the elusive formyl fluoride and 80–90% yields of the higher homologue acyl fluorides.



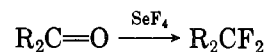
In Situ Sulfur Tetrafluoride Reagent. Sulfur tetrafluoride, developed by Smith, is a fluorinating agent of broad utility,¹⁹ particularly suitable for converting carbonyl compounds into geminal difluorides. However, the low boiling point of SF_4 usually necessitates work at superatmospheric pressure. To overcome these difficulties, in the course of our work, we have found¹⁷ that pyridinium poly(hydrogen fluoride) is a very suitable reagent for transforming inexpensive sulfur dichloride into sulfur tetrafluoride.



Since sulfur tetrafluoride is quite soluble in pyridinium poly(hydrogen fluoride), fluorinations with SF_4 can be effectively carried out in this solution. Thus in many cases, the reagent generated in situ can be directly used for fluorinations.

Selenium Tetrafluoride. In our efforts to overcome the necessity of using pressure equipment for fluorinations, we have found selenium tetrafluoride to be a simple alternative reagent to sulfur tetrafluoride.²⁰

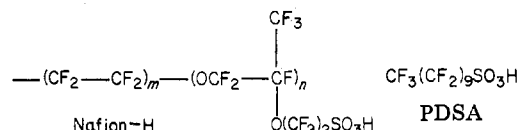
Selenium tetrafluoride, SeF_4 , which has an atmospheric boiling point of 106 °C, is a very effective fluorinating agent of broad scope. Fluorination of ketones, aldehydes, etc., generally proceeds in high yield, frequently even higher than those with SF_4 . However, selenium compounds are generally toxic and must be handled with great care.



Friedel-Crafts and Related Acid-Catalyzed Reactions

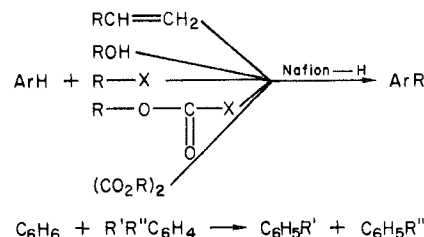
Alkylation and Acylation over Solid Superacid Catalysts. In Friedel-Crafts alkylations using aluminum chloride or related metal halide catalysts, generally complex mixtures of products are formed due to polyalkylation, isomerization, and transalkylation processes. The reactions are accompanied by extensive complex formations necessitating the use of large amounts of the catalyst (red oils).²¹

The use of high-acidity solid acid catalysts is gaining popularity because they minimize side reactions resulting in clean heterogeneous reaction mixtures without the usual messy workup problems. Conventional solid acid catalysts such as the sulfonated polystyrene resins are of limited utility, and chalcogenides like silica-alumina require high temperatures. We have found²² a series of solid or supported perfluorinated alkanesulfonic acids capable of effecting a wide variety of Friedel-Crafts type reactions. These perfluorinated acids include the acid form of Du Pont's commercially available Nafion ion membrane resin (Nafion-H) and the longer chain (C_6 to C_{18}) perfluorinated alkanesulfonic acids, representative of which is perfluorodecanesulfonic acid (PDSA).



If needed, the acidity of these solid acids can be further increased by complexing with higher valency metal fluorides, such as SbF_5 , TaF_5 , and NbF_5 .²³

Alkylation of aromatics with olefins, alkyl halides, alcohols (including methyl alcohol), esters, and other alkylating agents readily occurs over these catalysts.²⁴ Transalkylation of aromatics with di- or polyalkylbenzenes can also be carried out with equal ease.²⁵



(20) Olah, G. A.; Nojima, M.; Kerekes, I. *J. Am. Chem. Soc.* **1974**, *96*, 925.

(21) Olah, G. A. "Friedel-Crafts Chemistry", Wiley-Interscience, New York, 1973.

(22) Olah, G. A.; Messina, G.; Bukala, J.; Olah, J. A.; Mateescu, G. D. Abstracts, 1st Chemical Congress of the North American Continent, Mexico City, Dec 1975, Paper PHSC153.

(23) Olah, G. A.; Kaspi, J. *J. Org. Chem.* **1977**, *42*, 3046.

(24) (a) Kaspi, J.; Montgomery, D. D.; and Olah, G. A. *J. Org. Chem.* **1978**, *43*, 3147. (b) Olah, G. A.; Meidar, D. *Nouv. J. Chim.* **1979**, *3*, 269.

(c) Kaspi, J.; Olah, G. A. *J. Org. Chem.* **1978**, *43*, 3142. (d) Olah, G. A.; Malhotra, R.; Meidar, D.; Olah, J. A.; Narang, S. C. *J. Catal.*, in press.

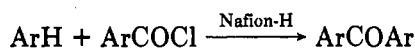
(16) (a) See ref 5. (b) Olah, G. A.; Nojima, M. *Synthesis* **1973**, 783. (c) Olah, G. A.; Nojima, M.; Kerekes, I. *Ibid.* **1973**, 779. (d) *Ibid.* **1973**, 780. (e) Olah, G. A.; Nojima, M. *Ibid.* **1973**, 786. (f) Olah, G. A.; Welch, J. *Ibid.* **1974**, 652. (g) *Ibid.* **1974**, 653. (h) *Ibid.* **1974**, 654. (i) *Ibid.* **1974**, 896. (j) Olah, G. A.; Welch, J. *J. Am. Chem. Soc.* **1975**, *97*, 208. (k) Olah, G. A.; Welch, J.; Vankar, Y. D.; Nojima, M.; Kerekes, I.; Olah, J. A. *J. Org. Chem.* **1979**, *44*, 3872.

(17) Olah, G. A.; Bruce, M. R.; Welch, J. *Inorg. Chem.* **1977**, *16*, 2637.

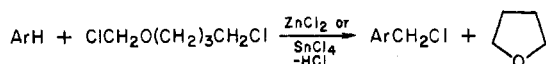
(18) Olah, G. A.; Nojima, M.; Kerekes, I. *Synthesis* **1973**, 487.

(19) Smith, W. C. *Angew. Chem., Int. Ed. Engl.* **1962**, *1*, 467.

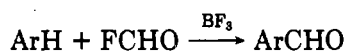
Not only alkylations but various other reactions²⁶ including acylations, sulfonylations, and halogenations are effectively catalyzed. Interestingly, attempted acylation with acetyl chloride gives preferentially ketene under the reaction conditions.²⁶



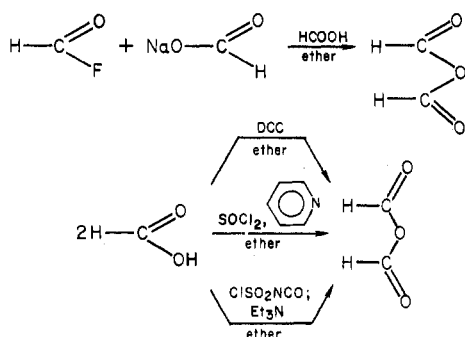
New Chloromethylating Agents. In the course of our work on chloromethylation we have developed new chloromethylating agents of decreased volatility which greatly reduce health hazards. 1-Chloro-4-chloromethoxybutane is a particularly effective²⁷ reagent as it reacts via oxygen participation, forming tetrahydrofuran as the byproduct. This complexes the acid catalyst and decreases secondary side reactions (e.g., formation of diarylmethanes).



Formylation with Formyl Fluoride and Formic Anhydride. Formyl fluoride, the only stable acyl halide of formic acid, reacts with aromatics in the presence of boron trifluoride catalyst to yield aldehydes.²⁸ Improved preparations of formyl fluoride, such as the discussed use of cyanuric fluoride or the reaction of benzoyl fluoride with sodium formate, allowed the extension of the utility of the reaction.



Formyl fluoride was also used in the preparation of the elusive formic anhydride.²⁹ Formic anhydride was further prepared by three different dehydration methods.



It should be noted that chlorosulfonyl isocyanate (CSI) was found to be a good dehydrating agent not only for formic acid but also in such reactions as the conversion of aldoximes and amides into nitriles.^{30a} It also activates dimethyl sulfoxide as an extremely mild oxidizing agent for converting alcohols into carbonyl compounds.^{30b}

Onium Ion and Carbocation Salt Reagents

Dialkylhalonium Salts. The well-known Meerwein³¹ trialkyloxonium tetrafluoroborate and hexa-

(25) (a) Olah, G. A.; Kaspi, J. *Nouv. J. Chim.* 1978, 2, 581. (b) *Ibid.* 1978, 2, 585.

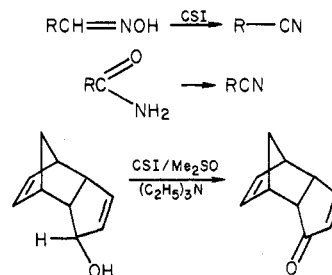
(26) Olah, G. A.; Malhotra, R.; Narang, S. C.; Olah, J. A. *Synthesis* 1978, 672.

(27) (a) Olah, G. A.; Beal, D. A.; Yu, S. H.; Olah, J. A. *Synthesis* 1974, 560. (b) Olah, G. A.; Beal, D. A.; Olah, J. A. *J. Org. Chem.* 1976, 41, 1627.

(28) Olah, G. A.; Kuhn, S. J. *J. Am. Chem. Soc.* 1960, 82, 2380.

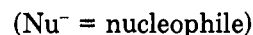
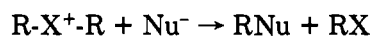
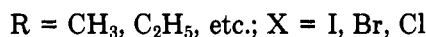
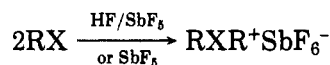
(29) Olah, G. A.; Vankar, Y. D.; Arvanaghi, M.; Sommer, J. *Angew. Chem.* 1979, 18, 614.

(30) (a) Olah, G. A.; Vankar, Y. D.; Garcia-Luna, A. *Synthesis* 1979, 227. (b) Olah, G. A.; Vankar, Y. D.; Arvanaghi, M. *Ibid.* 1980, 141.

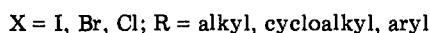
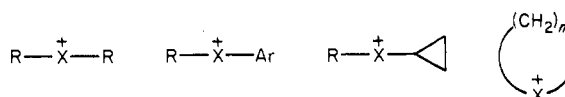


chloroantimonate salts (as well as the hexafluorophosphate salts used in our work³²) are widely used as transfer alkylating agents. However, they lack selectivity, as the onium oxygen atom cannot be substituted by sulfur, selenium, or tellurium, because these onium ions show very little reactivity.

Dialkylhalonium salts are very effective alkylating agents. The salts such as dimethylbromonium and dimethyliodonium fluoroantimonates can be readily prepared from excess alkyl halide with antimony pentafluoride or fluoroantimonic acid and isolated as stable solids. The less stable chloronium salt can be obtained in solution. As the nature of the halogen atom can be readily varied, from I⁺ to Br⁺ to Cl⁺, the use of halonium ions provides useful selectivity in their alkylation reactions.³³



A great variety of various other halonium ions were also prepared, not only in our laboratory but also by Petersen and other investigators, including alkyl-, cycloalkyl-, and arylhalonium ions, and their alkylating ability was studied.^{33,34}



Carbocation Salts. On the basis of our methods developed for preparing solutions of stable carbocations in superacidic media, we were recently successful in isolating a series of stable crystalline carbocations by evaporation of solvent SO₂, SO₂ClF, or SO₂F₂ or by addition of Freon-type solvents.³⁵ Typically, isolated carbocation fluoroantimonate salts include such tertiary ions as the *tert*-butyl and adamantyl cation,³⁶ but also stabilized secondary ions such as the norbornyl cation.

(31) (a) Meerwein, H. *Org. Synth.* 1966, 46, 120. (b) Meerwein, H.; Battenberg, E.; Gold, H.; Pfeil, E.; Willfang, G. *J. Prakt. Chem.* 1940, [2] 154, 83.

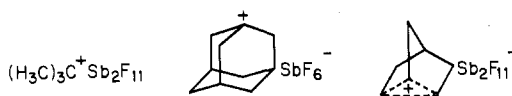
(32) (a) Olah, G. A.; Svoboda, J. *J. Synthesis* 1973, 52. (b) Olah, G. A.; Olah, J. A.; Svoboda, J. *J. Ibid.* 1973, 490.

(33) (a) Olah, G. A.; Svoboda, J. *J. Synthesis* 1973, 203. (b) Olah, G. A.; Mo, Y. K. *J. Am. Chem. Soc.* 1974, 96, 3560. (c) Olah, G. A. "Halonium Ion"; Wiley-Interscience: New York, 1975, and references given therein.

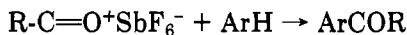
(34) Olah, G. A.; Prakash, G. K. S.; Bruce, M. R. *J. Am. Chem. Soc.* 1979, 101, 6463.

(35) (a) Olah, G. A. *Angew. Chem.* 1973, 85, 183. (b) *Aldrichim. Acta* 1973, 6, 7.

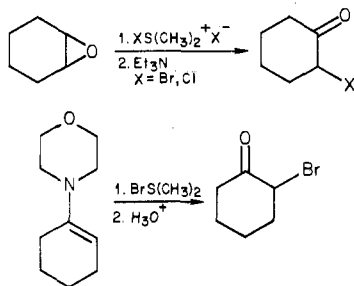
(36) Olah, G. A.; Svoboda, J. J.; Ku, A. T. *Synthesis* 1973, 492.



Isolated acylium salts, as well as similarly isolated sulfonyl halide-antimony pentafluoride complexes, are effective acylating and sulfonylating agents,³⁷ respectively.



Miscellaneous Onium Ion Reagents. Bromodimethylsulfonium bromide (crystalline solid, decomposes at 80 °C), prepared³⁸ by reacting dimethyl sulfide and bromine, is a convenient source of electrophilic bromine. We have found the reagent very useful in the cleavage of thioketals.^{39a} Oxidation of thiols^{39b} readily gives disulfides. Epoxides, upon treatment with bromo-(BDMS) or chlorodimethylsulfonium chloride in the presence of triethylamine, are readily converted into α -bromo and α -chloro ketones respectively. Enamines also react with BDMS to give α -bromo ketones.^{39c}

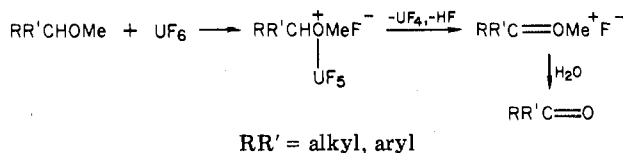


Oxidizing and Oxygenating Agents

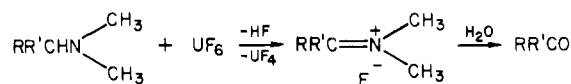
Higher Valency Metal Fluorides. In the course of our studies we have investigated a series of higher valency metal fluorides such as UF_6 , WF_6 , IF_5 , MoF_6 , and CoF_3 as oxidizing agents. In spite of the ready availability of uranium hexafluoride depleted of fissionable ^{235}U , the study of the reactions of UF_6 with organic compounds remained virtually unexplored. The highly covalent nature of UF_6 makes it particularly suitable for reactions⁴⁰ in nonaqueous solvents. Stable solutions of UF_6 in chlorofluorocarbons (Freons) or chlorohydrocarbons (methylene chloride or chloroform) can be conveniently used in the usual glass apparatus.

Ethers undergo oxidative cleavage⁴⁰ with UF_6 to form carbonyl compounds and alcohols. Furthermore, the direction of cleavage is predictable and thus the utility of ethers (such as benzyl or benzhydryl) as protecting groups of alcohols can be broadened. The cleavage of methyl ethers also takes place in high yields and is regioselective. Trapping experiments with phenyllithium suggest the intermediacy of methoxycarbenium ions in the reaction.

Benzyl and benzhydryl ethers are cleaved to the corresponding alcohols and benzaldehyde or benzophenone, respectively. Benzylic alcohols are further

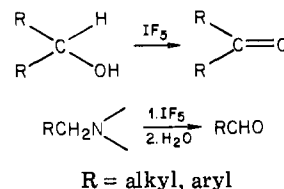


readily oxidized to the corresponding carbonyl compounds. Oxidative cleavage of protected carbonyl compounds such as tosylhydrazones and N,N -dimethylhydrazones takes place with ease upon aqueous quenching of the initially formed UF_6 adducts. N,N -Dimethylalkyl- (cycloalkyl-) amines are also oxidized by UF_6 , yielding the corresponding carbonyl compounds upon aqueous workup.



Tungsten hexafluoride, WF_6 , similar to uranium hexafluoride, has been found⁴¹ to be a convenient oxidizing agent. Typically, N,N -dimethylhydrazones and tosylhydrazones are cleaved to the carbonyl compounds under mild conditions. WF_6 is easily handled, does not attack glass, and is readily soluble in a variety of solvents including chloroform and 1,1,2-trichlorotrifluoroethane (Freon 113).

Iodine pentafluoride, IF_5 , is also⁴² a versatile oxidizing agent capable of oxidizing a variety of functional groups such as alkyl iodides, tertiary amines, alkyl methyl ethers, and alcohols. Although it has been previously reported that reactions with iodine pentafluoride are difficult to control, we have found that its solution in 1,1,2-trichlorotrifluoroethane is easy to handle.



Similarly we have found^{43a} that molybdenum hexafluoride oxidatively cleaves dimethylhydrazones and tosylhydrazones in tetrahydrofuran solution in high yield under moderate conditions.

In certain cases cobalt trifluoride has also been found⁴⁴ to be a suitable reagent for the oxidative cleavage of hydrazones and oximes to their parent carbonyl compounds. This reagent is also relatively easy to handle and shows significant selectivity, giving the highest yields with N,N -diethylhydrazones.

Ozonium and Peroxonium Ion Reagents. During the course of our work on the utility of superacids, we have found that hydrogen peroxide and ozone protonate readily to give the reactive electrophilic oxygenating agents, $\text{H}_2\text{O}^+ - \text{OH}$ and $\text{O}=\text{O}^+ - \text{OH}$, respectively.

Protonated ozone (ozonium ion)⁴⁵ (O_3H^+) upon reaction with a tertiary alkane such as isobutane gives a very unstable trioxide, which immediately undergoes

(37) (a) Olah, G. A.; Lin, H. C. *Synthesis* 1974, 342. (b) Olah, G. A.; Lin, H. C.; Germain, A. *Ibid.* 1974, 895.

(38) Furukang, N.; Inoue, T.; Aida, T.; Oae, S. *J. Chem. Soc., Chem. Commun.* 1973, 212.

(39) (a) Olah, G. A.; Vankar, Y. D.; Arvanaghi, M.; Prakash, G. K. S. *Synthesis* 1979, 720. (b) Olah, G. A.; Arvanaghi, M.; Vankar, Y. D. *Ibid.* 1979, 721. (c) Olah, G. A.; Vankar, Y. D.; Arvanaghi, M. *Tetrahedron Lett.* 1979, 3653.

(40) (a) Olah, G. A.; Welch, J.; Ho, T. L. *J. Am. Chem. Soc.* 1976, 98, 6717. (b) Olah, G. A.; Welch, J. *Ibid.* 1978, 100, 5396.

(41) Olah, G. A.; Welch, J. *Synthesis* 1976, 809.

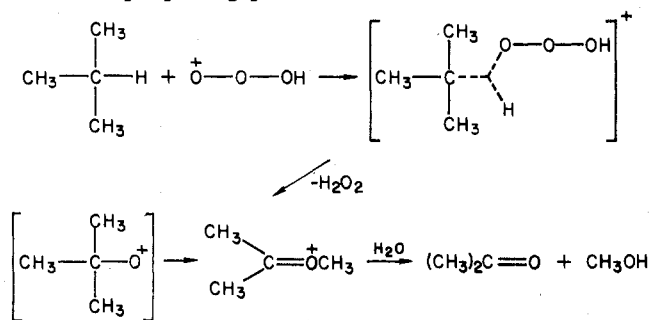
(42) Olah, G. A.; Welch, J. *Synthesis* 1971, 419.

(43) (a) Olah, G. A.; Welch, J.; Prakash, G. K. S.; Ho, T. L. *Synthesis* 1976, 808. (b) Olah, G. A.; Arvanaghi, M.; Prakash, G. K. S. *Ibid.* 1980, 220.

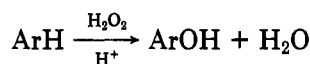
(44) Olah, G. A.; Welch, J.; Henninger, M. *Synthesis* 1977, 308.

(45) (a) Olah, G. A.; Yoneda, N.; Parker, D. G. *J. Am. Chem. Soc.* 1976, 98, 2251. (b) *Ibid.* 1976, 98, 5261. (c) Olah, G. A.; Yoneda, N.; Ohnishi, R. *Ibid.* 1976, 98, 7341. (d) Olah, G. A.; Parker, D. G.; Yoneda, N. *Angew. Chem.* 1978, 17, 909.

cleavage-rearrangement, to yield acetone and methyl alcohol. The reaction can be considered as the aliphatic equivalent of the well-known cumene hydroperoxide route for preparing phenol and acetone.

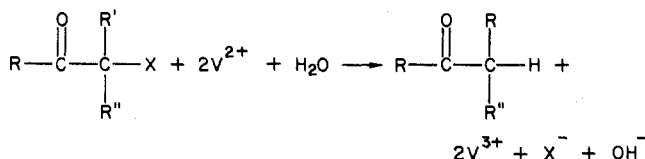


Aromatic hydrocarbons such as benzene and alkyl-benzenes are also readily hydroxylated to phenols with hydrogen peroxide in superacidic media with high selectivity.⁴⁶ As the phenolic products are protonated in the media, they are thus protected from further oxidation.

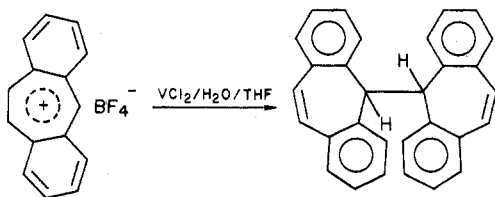


Reducing Agents

Low Valency Metal Ions. Our interest in metal ion reagents led us to investigate the vanadium(II) ion, a very useful reducing agent.⁴⁷ Generally the reductions are carried out in tetrahydrofuran solution. The reduction of α -halo ketones to the parent ketones proceeds in high yields.



Benzils and quinones are also readily reduced to benzoin and hydroquinones, respectively, even at room temperature. Aryl azides are reduced to the corresponding amines at room temperature. Vanadium(II) ion also cleaves semipolar heteroxygen bonds. For example, sulfoxides are reduced to the corresponding sulfides in good yields. Another interesting reaction with vanadium(II) ion is the facile reductive dimerization of tropylium salts.

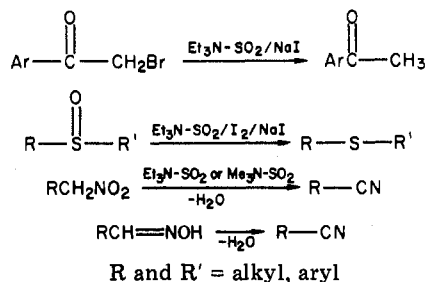


Vanadium(II) ion reductions can also be carried out in nonaqueous media and are of interest because nonacidic conditions can be employed and difficulties of limited substrate solubility can be eliminated. Thus we have found that the coupling of benzylic and allylic halides and debromination of *vic*-dibromides proceed

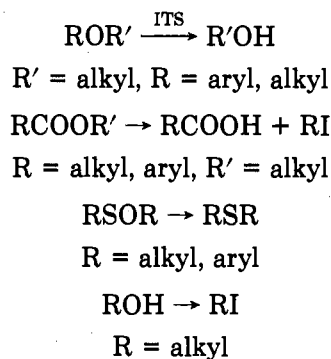
smoothly in tetrahydrofuran solutions. The vanadium(II) species is conveniently generated in situ by the lithium aluminum hydride reduction of vanadium(III) chloride in anhydrous tetrahydrofuran.

Besides the vanadium(II) ion, low-valent titanium and molybdenum ions are also useful reducing agents. Thus molybdenum(III) reagent, prepared by treating molybdenyl chloride (MoOCl_3) with zinc dust in tetrahydrofuran solution, reduces⁴⁷ sulfoxides to sulfides at room temperature in excellent yields. Oximes too are reductively cleaved⁴³ to the corresponding carbonyl compounds in high yields.

Trimethyl- (Ethyl-) amine-Sulfur Dioxide Reagents. Sulfur dioxide due to its low boiling point (-10°C) and obnoxious nature gained little use as a reagent in organic synthesis. To overcome these difficulties we have recently studied⁴⁸ various stable complexes of sulfur dioxide with different tertiary amines. This led to the findings that trimethylamine-sulfur dioxide, a white solid crystalline complex (mp 77°C), and triethylamine-sulfur dioxide, a liquid complex stable at room temperature, are convenient substitutes for sulfur dioxide. These complexes can be readily utilized in various synthetic reactions.⁴⁸ They are particularly suitable reducing and also dehydrating agents in the presence of sodium iodide.



Iodotrimethylsilane and Related "Hard-Soft" Reagents. The use of iodotrimethylsilane (ITS)^{49,50} and its in situ generated analogues (studied independently also by Jung)⁵¹ give excellent results in mild, neutral nonaqueous cleavage-hydrolysis reactions, deoxygenations, oxidations, halogenations, and the like. Illustrative are the following reactions.



(48) (a) Olah, G. A.; Vankar, Y. D. *Synthesis* 1978, 702. (b) Olah, G. A.; Vankar, Y. D.; Gupta, B. G. B. *Ibid.* 1979, 36. (c) Olah, G. A.; Vankar, Y. D.; Fung, A. P. *Ibid.* 1979, 59. (d) Olah, G. A.; Vankar, Y. D.; Arvanaghi, M. *Ibid.* 1979, 984.

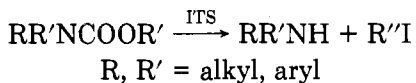
(49) Ho, T. L.; Olah, G. A. *Angew. Chem.* 1976, 15, 774.

(50) (a) Olah, G. A.; Ho, T. L. *Synthesis* 1977, 417. (b) Olah, G. A.; Ho, T. L. *Proc. Natl. Acad. Sci. U.S.A.* 1978, 75, 4. (c) Olah, G. A.; Gupta, B. G. B.; Narang, S. C. *Synthesis* 1977, 583.

(51) (a) Jung, M. E.; Andrus, W. A.; Ornstein, P. L. *Tetrahedron Lett.* 1977, 4175 and references cited therein. (b) Jung, M. E.; Muzarek, M. A.; Lim, R. M. *Synthesis* 1978, 588.

(46) Olah, G. A.; Ohnishi, R. *J. Org. Chem.* 1978, 43, 865.

(47) (a) Ho, T. L.; Olah, G. A. *Synthesis* 1976, 807. (b) *Ibid.* 1976, 815. (c) Ho, T. L.; Henninger, M.; Olah, G. A. *Synthesis* 1976, 815. (d) Olah, G. A.; Prakash, G. K. S.; Ho, T. L. *Synthesis* 1976, 810. (e) Olah, G. A.; Ho, T. L. *Synthesis* 1976, 798. (f) Ho, T. L.; Olah, G. A. *Synthesis* 1977, 170.



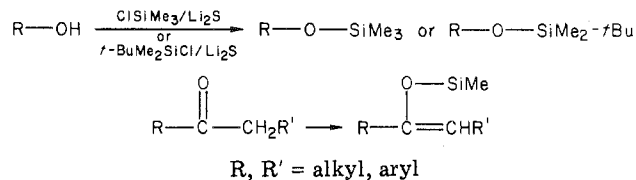
Since iodotrimethylsilane is of limited stability (light sensitive) and expensive, our efforts led to the development of methods utilizing its in situ generation to carry out the above-mentioned reactions.^{52,53} In our work, reactions of phenyltrimethylsilane with iodine, or chlorotrimethylsilane with sodium iodide in acetonitrile, and of hexamethyldisilane with iodine have been found to be convenient and inexpensive alternatives for $\text{ISi}(\text{CH}_3)_3$.

We have also found^{53b} that chlorotrimethylsilane with lithium sulfide converts alcohols and ketones to silyl

(52) (a) Olah, G. A.; Narang, S. C.; Gupta, B. G. B.; Malhotra, R. *Synthesis* 1979, 61. (b) Olah, G. A.; Narang, S. C.; Gupta, B. G. B.; Malhotra, R. *J. Org. Chem.* 1979, 44, 1247. (c) Olah, G. A.; Gupta, B. G. B.; Narang, S. C.; Malhotra, R. *Ibid.* 1979, 44, 4272. (d) Olah, G. A.; Narang, S. C.; Gupta, B. G. B.; Malhotra, R. *Angew. Chem., Int. Ed. Engl.* 1979, 8, 612.

(53) Morita, T.; Okamoto, Y.; Sakurai, H. *J. Chem. Soc., Chem. Commun.* 1978, 874.

ethers and enol silyl ethers, respectively, at room temperature. A special advantage of this method is that synthetically important TBDMS ethers can also be prepared more readily than by other conventional methods.



Support of our work by the National Science Foundation, the National Institutes of Health, the U.S. Army Office of Research, and the Hydrocarbon Research Institute of the University of Southern California is gratefully acknowledged. Our results to a great degree are the merit of my talented and enthusiastic co-workers, with whom I was fortunate to have been associated and whose names are cited in the references. Dr. Yashwant D. Vankar and Dr. Sunya G. K. Prakash are thanked for their help in preparing this Account.