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Selective replacement of hydrogen at a saturated carbon atom under the action of oxidising agents

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ABSTRACT. Data have been correlated for the heterolytic substitution reaction of hydrogen atoms in saturated hydrocarbons and also in some ethers and esters under the action of oxidising agents, viz. halogens, nitronium salts, halogen fluorides and ozone. Alternative schemes of electrophilic and nucleophilic substitution of hydrogen at an sp^3-hybrid carbon atom are considered.

The bibliography contains 79 references.

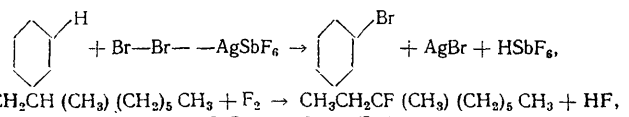
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I. Introduction

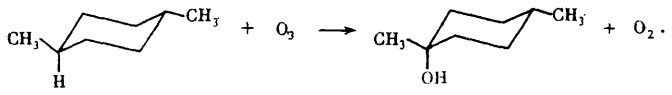
It was shown recently that halogen atoms in alkyl halides are selectively substituted by other functional groups under the action of various oxidising agents with the formation of extremely valuable final products. Proof has been presented of the fact that all these reactions are linked by a general mechanism and may be considered as oxidative nucleophilic substitutions of halogen at a saturated carbon atom.[1]

In recent years it has been reported that similar oxidising agents are capable of selectively replacing hydrogen atoms (mainly at tertiary carbon atoms or α-hydrogen atoms in ethers). Typical examples of such reactions are:



$$CH_3CH_2CH(CH_3)(CH_2)_5CH_3 + F_2 \rightarrow CH_3CH_2CF(CH_3)(CH_2)_5CH_3 + HF,$$

$$(CH_3)_2CHCO_2R_F + BrF_3 \rightarrow (CH_3)_2CFCO_2R_F + HF + Br_2,$$



Many investigators of these reactions have considered the development of preparative methods of 'functionalising' organic compounds by replacement of hydrogen at a saturated carbon atom to be an extremely promising direction and the selection of conditions at which the yield of substitution product reaches 50–60% to be a great success. Since low temperature non-radical oxidative substitution processes for hydrogen atoms are a very important type of chemical conversion of organic compounds and are seemingly fairly widely distributed in nature, it seemed expedient to us just now to correlate all the available information on such processes. We are confident that analysis of such data will permit formulation of a fairly objective representation of the overall rules of oxidative substitution of hydrogen atoms and planning of routes for further investigation of the problem.

Table 1. Halogenation of alkanes by molecular halogen in the presence of Lewis acids in CH_2Cl_2.[9,10]

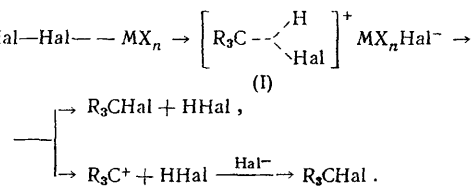
No.	Alkane	Halogen	Lewis acid	Molar ratio Hal:Lewis acid:alkane	Temp. °C (time, min)	Reaction products (yield[a], %)
1	Isobutane	Cl_2	$AlCl_3$[b]	1:0.1:1	25 (960)	over 20 products[c]
2	Isobutane	Cl_2	$AgSbF_6$	0.5:0.1:1	−15 (10)	t-butyl chloride (7)
3	Isobutane	Br	$AgSbF_6$	0.5:0.1:1	−15 (10)	isobutyl bromide (84) t-butyl bromide (11) 2,3-dibromoisobutane (6)
4	Cyclohexane	Cl_2	$AgSbF_6$	0.5:0.1:1	15 (10)	cyclohexyl chloride (5)
5	Cyclohexane	Br_2	$AgSbF_6$	0.5:0.1:1	25 (15)	cyclohexyl bromide (27)
6	Norbornane	Cl_2	$AlCl_3$	1:0.1:1	25 (960)	*exo*-2-chloronorbornane (17) *endo*-2-chloronorbornane (8) 7-chloronorbornane (4)
7	Norbornane	Br_2	$AgSbF_6$	0.5:0.1:1	25 (15)	*exo*-2-bromonorbornane (71) *endo*-2-bromonorbornane (12) 7-bromonorbornane (12)
8	Adamantane	Cl_2	$AlCl_3$	1:0.1:1	25 (1260)	1-chloroadamantane (63) 2-chloroadamantane (3)
9	Adamantane	Cl_2	$AgSbF_6$	0.5–0.1:1	−45 (5)	1-chloroadamantane (62) 2-chloroadamantane (1) 1-hydroxyadamantane (36)

[a] In the case of $AlCl_3$ catalyst the yield is given on Cl_2 taken, in the case of $AgSbF_6$ on catalyst.
[b] Reactions were carried out without solvent.
[c] t-Butyl chloride and isobutyl chloride were absent from the products.

The numerous reactions for the oxidation of hydrocarbons by transition metal salts and by chromic and manganic acids are not considered in the review. The ample material on this type of side-chain oxidation of alkylaromatic compounds is correlated in a review paper[2] and in a monograph.[3] Preparative possibilities and proposed mechanisms of oxidation of saturated hydrocarbons by chromic acid and by transition metal salts have been described.[4–7]

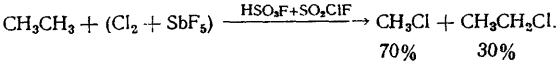
II. Reactions of saturated hydrocarbons with Hal_2–Lewis acid (Hal = Br, Cl) systems and other oxidising agents

The first attempts to effect the preparative replacement of hydrogen atoms at a saturated carbon atom by electrophilic oxidising agents under conditions excluding the possibility of free radical reactions were undertaken by G Olah in the seventies.[8–10] It was shown that Cl_2 and Br_2 in the presence of SbF_5, $AlCl_3$ and $AgSbF_6$ were able to interact at low temperature in the dark with saturated hydrocarbons to form alkyl halides (Table 1). He proposed that positively polarised halogen effected a frontal electrophilic attack on the C–H bond forming a pentacoordinate carbenium ion (I) which may then be converted into an alkyl halide by two routes: first, by ejection of a proton and formation of a bond between the carbon atom and the attacking halogen atom or second, by transfer of a hydride ion to the oxidising agent with subsequent capture of the resulting carbocation by halide anion.

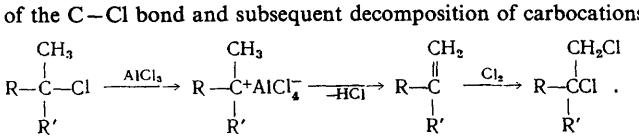


(I)

The use of antimony pentafluoride, the most powerful chlorination catalyst, in chlorination reactions led not only to hydrogen atom replacement (chlorination) but also to cleavage of a σ C–C bond in the alkane (chlorolysis). Thus the reaction of ethane in the Cl–SbF_5 system at room temperature gave methyl chloride and ethyl chloride in the ratio 70:30

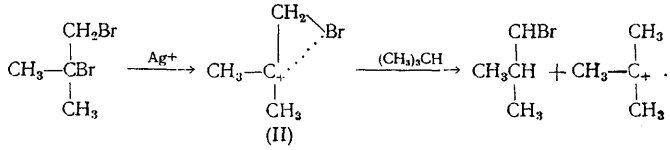


In the presence of the weaker catalysts $AlCl_3$ and $AgSbF_6$ no chlorolysis was observed. All types of σ C–H bonds (primary, secondary, tertiary) were chlorinated on catalysis by aluminium chloride, in addition the resulting alkyl halides were converted into products of further chlorination as a result of the ease of heterolysis of the C–Cl bond and subsequent decomposition of carbocations.



Thus isobutane gave more than 20 products in the presence of $AlCl_3$ (Table 1, compound No. 1). Since the elimination of a proton and double bond formation at a bridgehead is impossible for norbornane and adamantane, the chlorination of these compounds gave appreciable quantities of the corresponding monochlorides (Table 1, compounds No. 6, 8).

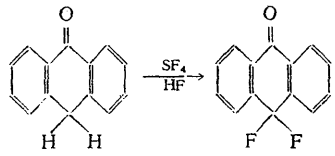
The Hal_2–$AgSbF_6$ systems possess even lower electrophilicity and correspondingly greater selectivity towards the C–H bond. Only isoalkanes and cyclic hydrocarbons (see Table 1) react in these systems at low temperature. In the presence of $AgSbF_6$, alkyl chlorides are less inclined to further conversion than with aluminium chloride. Thus only t-butyl chloride is formed from isobutane (Table 1, No. 2). In contrast to chlorination the bromination of isobutane gave isobutyl bromide, t-butyl bromide and 2,3-dibromobutane (Table 1, No. 3). The fact that the main bromination product of isobutane is not t-butyl bromide but isobutyl bromide is explained by transfer of a hydride ion from isobutane to the carbocation (II) which was formed by heterolysis of the tertiary C–Br bond in 2,3-dibromobutane:



(II)

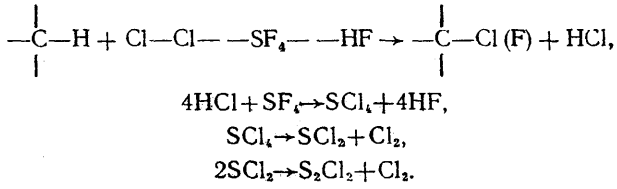
This was confirmed by special experiments on the bromination of a mixture of 2,3-dibromobutane and isobutane in the presence of $AgSbF_6$.

Interesting communications have appeared recently on the influence of small additions of Cl_2 on the ability of SF_4–HF systems to replace hydrogen at a saturated carbon atom by fluorine.[11,12] It was known previously that these systems replace hydrogen atoms in anthrone and adamantane by fluorine at moderate temperatures (60–70 °C):[13,14]

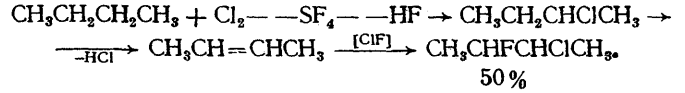


85%

It was shown[11] that after careful purification from traces of Cl_2 and SCl_2 (the initial product in SF_4 synthesis) sulphur tetrafluoride was unable to replace hydrogen in adamantane. Consequently it was concluded that Cl_2 was a necessary component of this system but the effectiveness of the action of traces of sulphur chlorides is linked with the generation of molecular chlorine in this system by the reaction sequence:[12]



On introducing large quantities of chlorine into the SF_4–HF system (molar component ratios 2:1:5 respectively) it was possible to effect substitution of hydrogen in n-butane even at 20 °C. The following reaction sequence was proposed to explain the observed facts:[12,15]

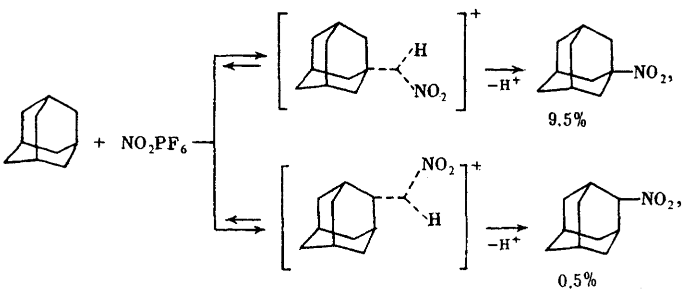


50%

However such an explanation is unconvincing since it is not very likely that dehydrochlorination of 2-chlorobutane may occur under these conditions. It is possible that alkenes are formed by loss of a proton from the intermediate carbenium ion resulting in transfer of hydride ion to the oxidising agent.

$$CH_3CH_2CH_2CH_3 + Cl_2 - -SF_4 - -HF \rightarrow [CH_3CH_2\overset{+}{C}HCH_3] \rightarrow$$
$$\xrightarrow[-HCl]{} CH_3CH{=}CHCH_3 \xrightarrow{[ClF]} CH_3CHFCHClCH_3.$$

Oxidative replacement of hydrogen atoms in alkanes may be effected by various systems containing the nitronium cations.[16–19] On reaction of nitronium hexafluorophosphate with saturated hydrocarbons in an aprotic solvent at 25 °C nitroalkanes are formed although fission of σ C–C bonds has also been observed in addition to replacement of hydrogen atoms.[16] The yield of nitroalkanes in these reactions is extemely low, in the case of acyclic compounds the yield of products did not exceed 2–5%. The best result was obtained in the reaction of adamantane when 1- and 2-nitroadamantanes were isolated in 10% total yield.



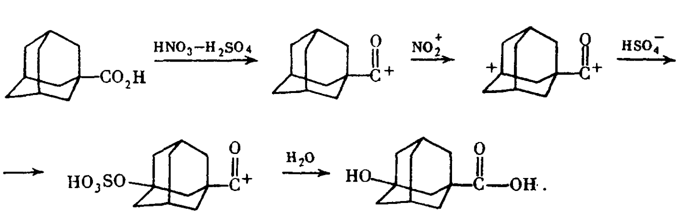
In the authors' opinion the main obstacle to achieving preparative yields is the high basicity of the solvent, containing atoms with unshared electron pairs, in comparison with the basicity of the σ C–H bond. A mixture of concentrated nitric and sulphuric acids may be used in place of nitronium salts in nitration reactions.[16] On nitrating isobutane with this mixture the following set of products was obtained: CH_3NO_2 (28%), $CH_3CH_2NO_2$ (5%), $(CH_3)_2CHNO_2$ (1%), $(CH_3)_3CNO_2$ (66%).

However carrying out the reaction in a mixture of strong acids was complicated by protolytic cleavage of the secondary and tertiary nitroalkanes.

$$(CH_3)_3CNO_2 \overset{H+}{\rightleftarrows} (CH_3)_3CNO_2H^+ \rightarrow (CH_3)_3C^+ + HNO_2.$$

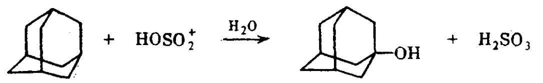
The interaction of 1-nitro-2,2-dimethylpropane with benzene and toluene in the presence of strong acids led only to the t-butyl derivatives of benzene and toluene.

On reacting 1-adamantanecarboxylic acid with a mixture of nitric and sulphuric acids no nitro derivatives were detected but 3-hydroxy-1-adamantanecarboxylic acid was obtained in high yield.[17] The authors proposed a reaction scheme including removal of the hydride ion by the nitronium cation with subsequent capture of the resulting carbocation by the hydrogen sulphate anion.



Analogous replacement of a hydrogen atom occurred on reaction of adamantane with 90–100% nitric acid and mixtures of it with acetic anhydride[18,19] or a mixture of 96–98% sulphuric acid with trifluoroacetic anhydride.[20] Thus on reacting adamantane with 90% HNO_3 the nitrate of 1-hydroxyadamantane was obtained in 50–65% yield.[18] It was proposed that in a $H_2SO_4/(CF_3CO)_2O$ mixture the active species is the $HOSO_2^+$ cation.[20] SO_2 is separated in the oxidation process.

$$H_2SO_4 + (CF_3CO)_2O \rightleftarrows HOSO_2^+ + CF_3CO_2^- + CF_3CO_2H\ ,$$



$$H_2SO_3 \longrightarrow SO_2 + H_2O\ .$$

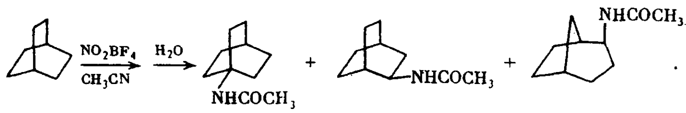
Evidently the oxidation of hydrocarbons by concentrated sulphuric acid occurs in a similar manner:[7]

$$RH + H_2SO_4 \rightarrow [R^+HSO_4^-] + SO_2 + H_2O.$$

On oxidation of adamantane with nitronium salts the magnitude of the kinetic isotope effect was 1.86,[21] of isobutane with a mixture of nitric and sulphuric acids 2,[22] and of 1,3,5-trimethyladamantane 4.4.[18] The kinetics of the oxidation of adamantane, and its derivatives substituted in the angular positions, by nitric acid in methylene chloride solution have been investigated.[23] It was established that the rate constants were linked linearly to the rate constants for solvolysis of the corresponding bromo derivatives and to the Taft induction constants. This is also in agreement with a mechanism including as limiting stage the removal of a hydride ion by the oxidising agent with the formation of the adamantyl cation. Evidence in favour of the mechanism involving the formation of carbenium ions was obtained not only in the oxidation of adamantane but also of other saturated organic compounds.[21,24] Thus on oxidation of 2-methylbutane with nitronium fluoroborate in acetonitrile at room temperature 2-acetamido-2-methyl-3-nitrobutane was obtained in good yield. Since this compound is also obtained by the addition of nitronium fluoroborate to trimethylethylene in acetonitrile medium the reaction sequence depicted in the scheme may be the sole explanation:

$$(CH_3)_2CHCH_2CH_3 \xrightarrow{NO_2BF_4} (CH_3)_2\overset{+}{C}CH_2CH_3 \xrightarrow[-H+]{}$$
$$\rightarrow (CH_3)_2C{=}CHCH_3 \xrightarrow[CH_3CN]{NO_2BF_4} (CH_3)_2\underset{^+N\equiv CCH_3}{\underset{|}{C}}CHNO_2CH_3 \xrightarrow{H_2O}$$
$$\rightarrow (CH_3)_2\underset{NHCOCH_3}{\underset{|}{C}}CHNO_2CH_3.$$

The interaction of bicyclo[2.2.2]octane with nitronium fluoroborate led to the formation of a mixture of acetamides (III–V) in 73% total yield.



(III), 65% (IV), 22% (V), 13%

The ratio of unrearranged acetamide (IV) to rearranged amide (V) was close to 2:1 as in the solvolysis of bicyclo[2.2.2]octyl bromobenzenesulphonate.[25] On oxidation of adamantane under

these conditions N-(1-adamantyl)acetamide (88%) was obtained. Norbornane gave exclusively N-(*exo*-2-norbornyl)acetamide (78%). The ease of transfer of hydride ions from adamantane, bicyclo[2.2.2]octane and norbornane was in direct relation to the stability of the corresponding carbenium ions.[26] Proof of the fact that nitro derivatives are not formed as intermediates on reaction of alkanes with nitronium fluoroborate in acetonitrile was the inertness of 2-methyl-2-nitropropane and 1-nitroadamantane towards the reagent at 25 °C.[21]

Trifluoroacetyl nitrate formed *in situ* in the reaction of ammonium nitrate and trifluoroacetic anhydride is also an efficient oxidising agent for saturated hydrocarbons:[24]

$$NH_4NO_3 + (CF_3CO)_2O \rightleftarrows CF_3CO_2NO_2 + CF_3CO_2NH_4.$$

Oxidation was carried out in trifluoroacetic acid medium at 25–40 °C. It was proposed that the active electrophile in this system was protonated trifluoroacetyl nitrate $[CF_3CO_2NO_2H]^+$. Under these conditions cyclooctyl trifluoroacetate was obtained in good yield (50%) from cyclooctane and also *exo*-2-trifluoroacetoxynorbornane (52%) and *exo*-2-norbornyl nitrate (23%) from norbornane.

III. Heterolytic oxidation of ethers

The α-hydrogen atoms of amyl ethers are replaced significantly more readily than hydrogen atoms in alkanes since the ether oxygen atom facilitates both the radical and ionic replacement of α-hydrogen atoms while stabilising the resulting free radical or carbocation intermediate.[27] Oxidation proceeds according to a free radical or ionic mechanism depending on the type of oxidising agent and on the conditions of carrying out the reaction. The classical oxidation reaction of ethers by atmospheric oxygen has been well studied and its free radical mechanism is not in doubt. On UV irradiation and also at elevated or room temperatures many alkyl ethers interact energetically with elementary chlorine by a free radical mechanism.[27,28] However dark low-temperature halogenation of ethers evidently proceeds according to a heterolytic mechanism and leads to replacement of hydrogen atoms by chlorine exclusively at the position α to the alkoxy group.[28–30] α-Chloroethyl ether (42%) and α,α′-dichlorodiethyl ether (57%) are obtained as a result of the chlorination of diethyl ether at –20 to –30 °C. But even at –5 to +5 °C more extensive chlorination occurs principally at the β-position.[28]

Due to the fact that the alkoxy group effectively stabilises carbenium ions, attack by the oxidising agent at the σ-bond of the α-hydrogen atoms leads to transfer of hydride ion to the oxidising agent with the formation of resonance-stabilised carbocation (VI):[27,29]

$$Hal{-}Hal + H{-}\underset{|}{\overset{|}{C}}{-}OR \rightarrow Hal^- + $$

$$+ HalH + \left[\underset{|}{\overset{|}{C}}{=}\overset{+}{O}R \;\; (VI)\right] \xrightarrow{Hal^-} Hal{-}\underset{|}{\overset{|}{C}}{-}OR,$$

Hal=Cl, Br.

Probably other oxidising agents may react under milder conditions with ethers by the same mechanism. Chlorine monofluoride is a reagent for which all descriptions of reaction with organic compounds bear a clearly marked heterolytic character.[12] At low temperature in HF medium it readily replaces an α-hydrogen atom in the ethyl group of 1-chloro-2,2-difluoro-3-oxapentane:[30]

$$CH_2ClCF_2OCH_2CH_3 + ClF \rightarrow CH_2ClCF_2OCHFCH_3.$$

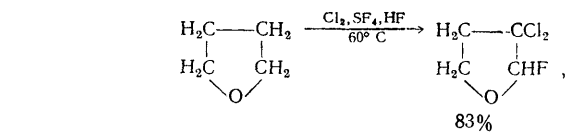
Bromine trifluoride at room temperature in the absence of solvent replaces a hydrogen atom in the methyl group of ether (VII) and an α-hydrogen atom in the ethyl group of compound (VIII):[31]

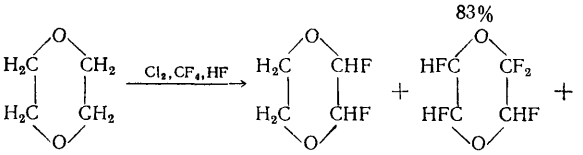
$$\underset{(VII)}{(CF_3)_2CHCF_2OCH_3} \xrightarrow[20°C]{BrF_3} \underset{48\%}{(CF_3)_2CHCF_2OCH_2F},$$

$$\underset{(VIII)}{(CF_3)_2CHCF_2OCH_2CH_3} \xrightarrow{BrF_3} \underset{74\%}{(CF_3)_2CHCF_2OCHFCH_3}.$$

Since the electron-donating ability of the oxygen atom is strongly reduced in a polyhalogenated alkoxy group, the ionic and radical halogenation of ethers of type (VII, VIII) proceeds with difficulty. Thus radical chlorination of similar compounds occurs only on UV irradiation. The use of such powerful electrophilic oxidising agents as ClF and BrF_3 permits heterolytic replacement of α-hydrogen atoms. The system Cl_2-SF_4-HF effectively fluorinates ethers at moderate temperatures.[6,10,14] In this way more extensive halogenation occurs, viz. replacement of β-hydrogen atoms predominantly by chlorine:

$$CH_3CH_2OCH_2CH_3 \xrightarrow[50°C]{Cl_2,SF_4,HF} \underset{89\%}{CCl_3CHFOCH_2CH_3},$$

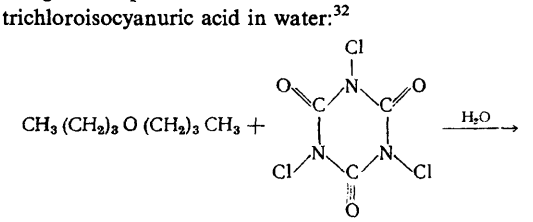




$+ CF_3CHFOCH_2CH_2F.$

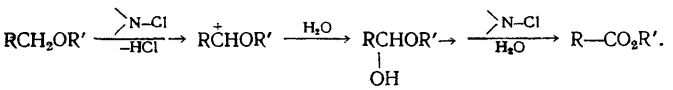
These reactions probably occur by the initial oxidative replacement of α-hydrogen atoms by fluorine according to a heterolytic mechanism analogous to that presented above. However as a result of the extreme instability of α-fluoroethers[28] the products of mild monofluorination are not isolated. Under more forcing conditions further fluorination and chlorination of the α-fluoroethers occur. The polyhalogenated ethers obtained in this way are then completely stable since the nucleophilic replacement of α-fluoro atoms occurs with more difficulty as a result of the electron-accepting influence of the vicinal halogens.

One further interesting example of the selective replacement of α-hydrogen atoms in ethers under the action of oxidising agents containing electropositive chlorine is the reaction of dibutyl ether with trichloroisocyanuric acid in water:[32]

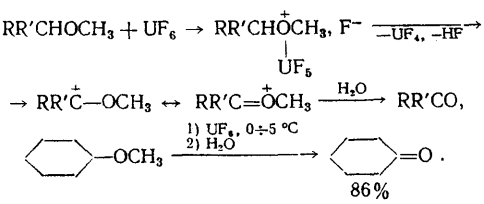


$\rightarrow CH_3(CH_2)_2CO_2(CH_2)_3CH_3.$

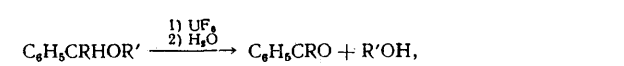
This reaction may be represented as follows:



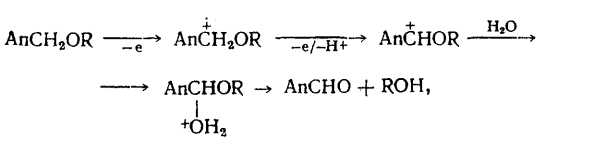
Uranium hexafluoride has been proposed for the selective oxidation of ethers and certain other organic compounds.[33] Carbonyl compounds and alcohols are formed as a result of the oxidation of unsymmetrical ethers. In the case of methyl ethers the reaction proceeds regioselectively. The authors put forward a scheme assuming initial attack of uranium hexafluoride at the oxygen atom:



Aromatic compounds and aliphatic alcohols are formed on oxidation of alkyl benzyl ethers and benzhydryl ethers:

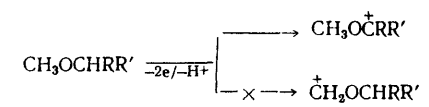


It is interesting that extremely similar results were obtained on electrochemical oxidation of alkyl benzyl ethers.[34,35] An especially good yield (74 to 98%) was observed in the case of *p*-methoxybenzyl ethers. A mechanism was proposed for these reactions.[36]



An = anisyl.

By electrochemical oxidation of ethers it is possible to obtain orthoesters, acetates of hemiacetals or acetals which are readily hydrolysed in aqueous acidic medium and give the corresponding aldehydes in good yield.[34,37,38] The regioselectivity on electrochemical oxidation is the same as on oxidation by uranium hexafluoride and is determined by the ability of substituents at the reaction centre to stabilise the positive charge formed by elimination of the α-hydrogen atom:



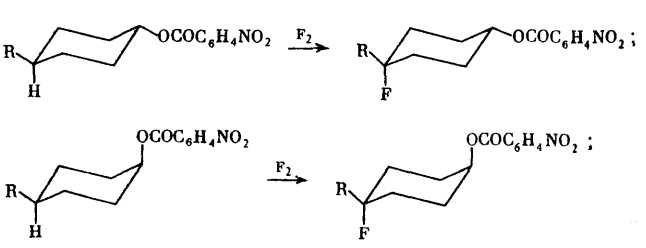
Consequently the hydrogen atoms of CH_3 groups are not affected during oxidation of mixed alkyl methyl ethers. For the same reason selective replacement of benzylic hydrogen atoms occurs for alkyl benzyl ethers having no electron-accepting substituents in the aromatic ring.[33,38]

IV. Selective fluorination of organic compounds containing tertiary and secondary hydrogen atoms, with elementary fluorine and halogen fluorides

Elementary fluorine reacts vigorously with organic compounds under the usual conditions which frequently leads to destruction of the hydrocarbon skeleton.[39] During the last 10 years Rozen and co-workers have developed preparative methods of replacing tertiary hydrogen atoms by fluorine using low temperature fluorination with elementary fluorine.[40–48] Fluorination was effected by passing a gaseous mixture of F_2 and N_2 containing 1 to 10% fluorine through a strongly diluted (0.1–0.3%) solution of the substrate in a mixture of $CFCl_3$–$CHCl_3$ (1:1) at –75 to –78 °C. Chloroform was a necessary component of the solvent, in Freon alone fluorination did not take place.[46]

Exhaustive data on fluorination by this means including literature since 1985 have been presented in a review.[49] We will give only the most typical examples illustrating the possibilities of this method.

Best results (70–90% yield) were obtained for cyclic hydrocarbons (Table 2, compounds 2–6). Evidently these results are not explained by their hydrogen atoms reacting more readily with F_2 but by the greater stability of such alkyl fluorides compared with acyclic fluorides. A special feature characteristic of oxidative fluorination is the possibility of replacing the hydrogen atom at position 1 of the norbornane system (Table 2, compounds 7, 8) in which the formation of carbenium ions is extremely disfavoured. 1-Fluorocamphane and 2-(1-norbornyl)ethyl acetate were obtained in low yield (15–20%). Electron-accepting substituents hampered replacement, consequently tertiary hydrogen atoms furthest removed from such substituents were replaced more readily. Thus a better result was obtained with a steroid diol diacetate than with the ditrifluoroacetate (Table 2, compounds 9, 10), in both cases the hydrogen atom replaced was that located furthest from the acceptors. Similarly the tertiary hydrogen atom in the position γ to the ester group was replaced in better yield than that in the β position (Table 2, compounds 11, 12). The presence of two electron-accepting substituents in the position β to hydrogen hindered replacement so much that the yield of the corresponding fluoride was extremely low (Table 2, compound 13). The stereochemistry of replacement of tertiary hydrogen atoms by fluorine in cyclohexane derivatives has been investigated.[47] Replacement occurred with retention of configuration in all cases.



R = CH_3, $(CH_3)_3C$.

On fluorinating bicyclo[2.2.2]octane by this method a rearrangement

was observed typical of a reaction proceeding with the formation of carbenium ions.[48]

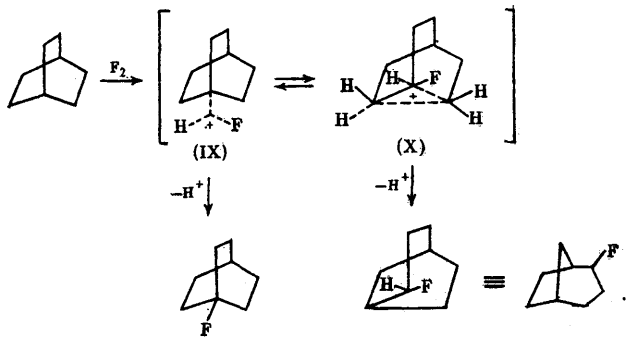
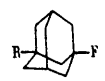
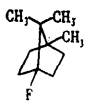
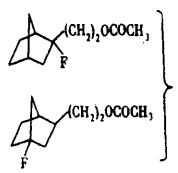
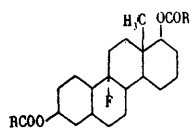
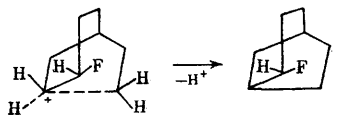


Table 2. Replacement of tertiary hydrogen atoms by fluorine using molecular fluorine in $CFCl_3-CHCl_3$ medium[a].

No.	Product[b]	Yield, %[c]	Refs.
1	$CH_3CH_2CH(CH_3)(CH_2)_6CH_3$	65	[47]
			
2	R=H	70	[40]
3	R=NHCOCF$_3$	83	[40]
4	R=OCOC$_6$H$_4$NO$_2$	90	[41]
5		90	[44]
6	*trans* *cis*	80	[44]
7		20	[48]
8		25	[48]
		15	[48]
9	R=CH$_3$	50	[45]
10	R=CF$_3$	34	[45]
11	$(CH_3)_2CF(CH_2)_3CO_2CH_2CCl_3$	55	[47]
12	$(CH_3)_2CFCH_2CO_2CH_2CCl_3$	30	[47]
13	$CH_3CFCH_2CO_2CH_3$ $CH_2CO_2CH_3$	2	[47]

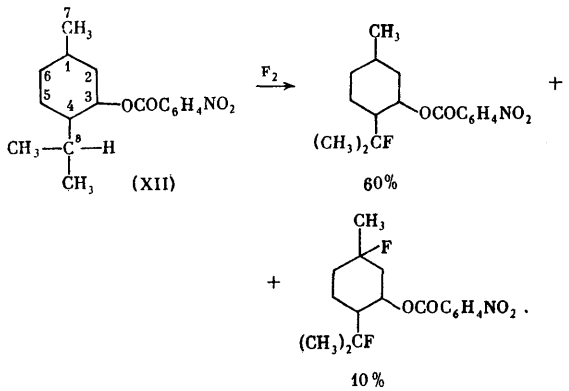
[a] Depending on the reactivity of starting material from 1 to 100 moles fluorine were passed in per mole substrate.
[b] Starting materials differed in that hydrogen replaces fluorine.
[c] Yield calculated on substrate.

1-Fluorobicyclo[2.2.2]octane and 2-fluorobicyclo[3.2.1]octane (rearrangement product) were obtained from the reaction. The authors proposed a scheme explaining the formation of these products. In the first stage a pentacoordinated carbonium ion (IX) is formed which is in equilibrium with the non-classical ion (X) having 8 electrons at each carbon atom. However such an explanation is hardly acceptable since conversion of ion (IX) to any other carbonium ion may only be effected by direct elimination of proton with subsequent protolysis of other σ bonds. Just such a scheme has been proposed for the isomerisation of saturated hydrocarbons in strongly acidic medium.[50] It is probable that the rearrangement product may be formed only from ion (XI) which has a strong electron-accepting substituent (fluorine atom) in the β-position and consequently must be less stable than ion (IX).



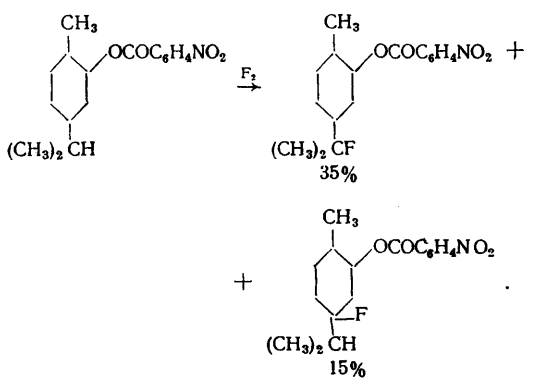
(XI)

A relationship was found between the contribution of the *p*-orbitals to the C−H bond and the ease of replacement of the hydrogen atom; the greater the contribution of *p*-orbitals then the easier substitution occurred.[46] According to semi-empirical calculations by the PRDDO method the contribution of *p*-orbitals to the C(1)−H bond is 2.7 and C(4)−H and C(8)−H about 2.9. The product with substitution at C(8) was obtained preferentially.

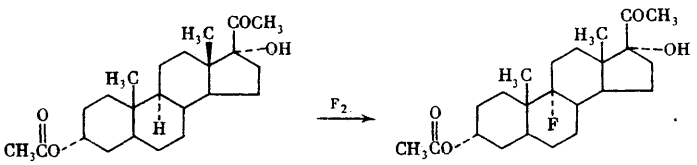


(XII)

The fact that substitution did not occur at C(4) was explained by the authors by the fact that fluorine approaches the reaction centre accompanied by at least one molecule of chloroform and the C(4) atom is the most sterically hindered. If the ester substituent is removed then the hydrogen atom at C(4) is also replaced.



However in our opinion it is more certain that this fact is explained by the deactivating influence of the electron-accepting ester group on the vicinal hydrogen atom of compound (XII). The synthesis of fluorosteroids is the most useful preparative application of the selective replacement of hydrogen atoms with elementary fluorine.[38] It was recorded that in all cases replacement occurred with retention of configuration. As a rule yields of products were not large (20–30%) but for 5α-pregnane-3α,17α-diol-20-one 3-acetate (XIII) the yield of 9α-fluorosteroid (XIV) reached 60%.



(XIII) (XIV)

The selectivity of the replacement attracts attention. Of the three tertiary hydrogen atoms in compound (XIII) only the 9α-hydrogen, which is furthest from the electron-accepting substituents, is replaced by fluorine.

The fact that fluorination takes place with complete retention of configuration and also the absence of typical carbocation rearrangements (excluding bicyclo[2.2.2]octane) and the absence of proton elimination reactions indicated, in the authors' opinion,[46] against a hydride transfer mechanism:

$$R_3CH + F_2 \rightarrow R_3C^+ + HF \xrightarrow{F^-} R_3CF.$$

They ascribed the selective fluorination to a type of electrophilic substitution at the saturated carbon atom proceeding through a pentacoordinated carbonium ion (XV) (Olah mechanism):

$$R_3CH + F_2 \rightarrow \left[R_3C\text{-}\overset{H}{\overset{|}{\underset{F}{\overset{\diagup}{\diagdown}}}}\ F^- \cdots HCCl_3\right] \xrightarrow{-HF} R_3CF.$$

In this reaction chloroform is a trapping agent for free radicals and a source of protons and serves as an acceptor of fluoride anion through a hydrogen bond which lowers the energy of the transition state.

It has recently been shown that not only elementary fluorine but also halogen fluorides may be used for the selective replacement of hydrogen atoms by fluorine.[51–53] Both tertiary and secondary hydrogen atoms are replaced by this method. Chlorine trifluoride in an inert solvent (Freon 114, 112, liquid CO_2) at −75 °C fluorinates hydrocarbons in good yield on observing experimental conditions such that ClF_3 itself and inorganic byproducts are in the reaction zone for no more than 2 min.[51] Reaction proceeds according to the scheme:

$$-\overset{|}{\underset{|}{C}}-H + ClF_3 \rightarrow -\overset{|}{\underset{|}{C}}-F + HF + ClF.$$

The formation of chlorine monofluoride as an inorganic byproduct was established by trapping it with cyclohexane or ethylene. Under these conditions first tertiary and then secondary hydrogen atoms are preferentially replaced. Methane and 2,2,3,3-tetramethylbutane, having only primary hydrogen atoms do not react. Since in the case of 2,2-dimethylbutane and 2-methylbutane products are obtained with 1,2-migration of methyl groups the authors preferred a heterolytic mechanism for the replacement of hydrogen by fluorine:

$$(CH_3)_3CCH_2CH_3 + ClF_3 \rightarrow ClF + HF + F^- + (CH_3)_3C^+CHCH_3 \rightarrow$$
$$\rightarrow (CH_3)_2C^+CH(CH_3)_2 \xrightarrow{F^-}$$
$$\rightarrow \underset{55\%}{(CH_3)_2CFCH(CH_3)_2} \xrightarrow{ClF_3} \underset{22\%}{(CH_3)_2CFCF(CH_3)_2},$$
$$(CH_3)_2CHCH_2CH_3 \xrightarrow{ClF_3} \underset{33\%}{(CH_3)_2CFCH_2CH_3} \xrightarrow{ClF_3}$$
$$\rightarrow \underset{5\%}{CH_3CF_2CH(CH_3)_2}.$$

Bromine trifluoride in a Freon medium at room temperature is also capable of replacing a hydrogen atom by fluorine. Reaction was carried out by direct addition of liquid BrF_3 to a 5–20% solution of substrate in Freon.[52,53] The process occurs according to the scheme:

$$R_3CH + {}^2/_3BrF_3 \rightarrow R_3CF + HF + {}^1/_3Br_2.$$

Selective fluorination of esters containing tertiary hydrogen atoms was effected by such a method.

$$(CH_3)_2CHCH_2OCOCF_3 + BrF_3 \rightarrow \underset{47\%}{(CH_3)_2CFCH_2OCOCF_3}.$$

Bromine trifluoride in the presence of anhydrous hydrogen fluoride (60 mol%) is capable of replacing tertiary hydrogen atoms in the position α to an ester group, which was unsuccessful with elementary fluorine.

$$(CH_3)_2CHCO_2R_F + BrF_3 \xrightarrow[\text{Freon 113}]{HF} \underset{50\%}{(CH_3)_2CFCO_2R_F} +$$
$$+ \underset{8\%}{CH_2BrCFCO_2R_F},$$
$$\quad\ |$$
$$\quad CH_3$$

$R_F = CH_2(CF_2)_2H.$

On replacing hydrogen atoms with bromine trifluoride the formation of cationoid moieties at the stage determining the reaction products was confirmed by the observation of a methyl group 1,2-migration in the reaction with 2-fluoro-2-methylbutane:[53]

$$(CH_3)_2CFCH_2CH_3 + BrF_3 \rightarrow$$
$$\rightarrow \underset{85\%}{CH_3CF_2CH(CH_3)_2} + \underset{15\%}{(CH_3)_2CFCHFCH_3}.$$

On extended reaction of bromine trifluoride with polyhaloalkanes in a Freon medium nonselective replacement of hydrogen atoms by fluorine was observed:[54]

$$CH_2FCHFCH_2Cl \xrightarrow[\text{Freon 112}]{BrF_3} \underset{29\%}{CH_2FCHFCH_2F} + \underset{35\%}{CHF_2CHFCH_2Cl} +$$
$$+ \underset{6\%}{CH_2FCF_2CH_2Cl} + \underset{29\%}{CHF_2CHFCH_2F}.$$

It should be mentioned that replacement of chlorine atoms in haloalkanes under the action of BrF_3 is catalysed by $SnCl_4$ and $SbCl_5$ (Lewis acids forming complex salts with BrF_3) while replacement of hydrogen atoms is catalysed by anhydrous HF.[55]

$$CH_2ClCHFCH_2Cl \xrightarrow[SnCl_4(1\%)]{BrF_3} \underset{28\%}{CH_2ClCF_2CH_3} + \underset{43\%}{CH_2ClCHFCH_2F},$$
$$CH_2ClCHFCH_2Cl \xrightarrow[HF]{BrF_3} \underset{30\%}{CH_2ClCF_2CH_3} + \underset{15\%}{CH_2ClCHFCH_2F} + \underset{25\%}{CHF_2CHFCH_2Cl}.$$

On fluorinating 1,3-dichloro-2-fluoropropane in Freon 113 in the presence of $SnCl_4$ only products of chlorine replacement were obtained while in HF 3-chloro-1,1,2-trifluoropropane, the product of replacing a hydrogen atom, was also obtained.

It has been shown[1] that in oxidative replacement of halogen atoms in organic halo-derivatives, halogen fluorosulphates are closest in reactivity to halogen fluorides. Consequently it might be expected that these reagents will also efficiently oxidise ether C–H bonds. However a single example of oxidative replacement of a hydrogen atom under the action of bromine trisfluorosulphate has been described in the literature.[56]

$$Cl(CF_2)_4H + Br(OSO_2F)_3 \rightarrow Cl(CF_2)_4OSO_2F + BrOSO_2F + HSO_3F.$$
65%

It is difficult to agree with a study[57] which considered that halogen fluorosulphates are inert towards C–H bonds at room temperature and only replace halogen atoms. In the case in question the matter consists not in the inertness of halogen fluorosulphate towards C–H bonds but in the fact that iodine and bromine atoms in alkyl halides are oxidised significantly more slowly than hydrogen atoms. The absence of data on reactions of halogen fluorosulphates with saturated hydrocarbons is also seemingly linked with the extremely low stability of alkyl fluorosulphates which complicates the isolation of the primary substitution products.

V. Reactions of saturated organic compounds with ozone

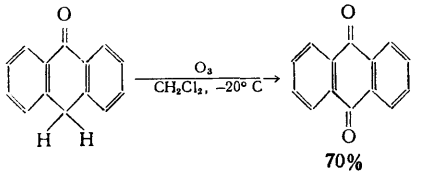
Linked with the current ecological concern about the opacity of the Earth's ozone layer, significant attention has been paid to the reaction of ozone with saturated hydrocarbons[58–70] and at the present time this is the most studied class of reactions for the oxidative replacement of hydrogen atoms. The reaction of ozone with σ C–H bonds leads to the formation of hydrotrioxides (XVI) as initial products which at temperatures greater than −40 °C readily decompose with the formation of alcohols and carbonyl compounds.

$$R_2CH_2 + O_3 \rightarrow \underset{(XVI)}{R_2CH_2OOOH} \rightarrow [R_2CHO^{\cdot} + {}^{\cdot}OOH]$$

$$\downarrow \qquad\qquad \downarrow \qquad\qquad \downarrow$$

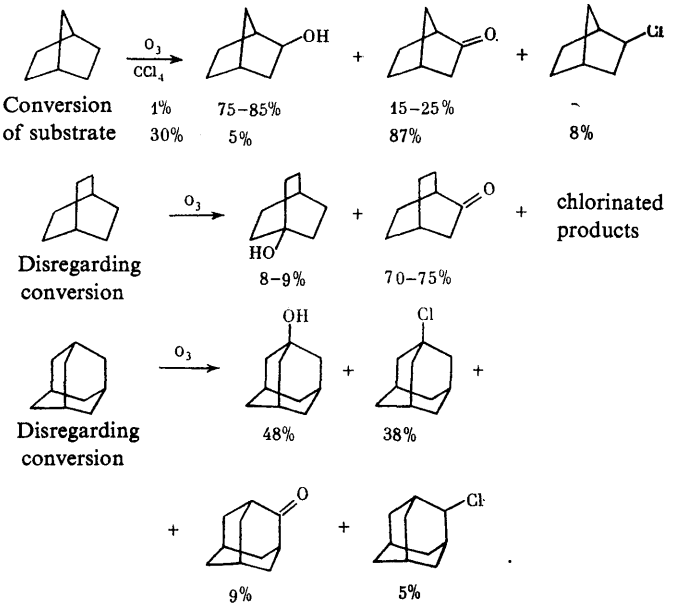
$$R_2CHOH + O_2 \qquad R_2C{=}O + H_2O_2 \qquad RCHO + R^{\cdot}.$$

$R_2CH\dot{O}$ and $\dot{O}_2H$ radicals escaping from the cage initiate radical processes. Usually ozonation of saturated hydrocarbons is effected by passing ozone diluted with nitrogen or oxygen into a solution of substrate in an inert solvent (CCl_4, CH_2Cl_2, Freons) at a temperature between −78 and +25 °C. Ozonation of anthrone carried out by this method leads to the formation of anthraquinone in 70% yield.[58]



70%

The authors showed that 2 moles O_3 were consumed and 2 moles O_2 were liberated on oxidising 1 mole anthrone confirming the sequential replacement of two atoms of hydrogen. An investigation of the oxidation products of norbornane, bicyclo[2.2.2]octane and adamantane has been described.[59] Both the tertiary hydrogen atoms at the bridge-head and the secondary hydrogen atoms were replaced in adamantane and bicyclo[2.2.2]octane but only secondary atoms in norbornane.



An interesting method of hydroxylation of tertiary C–H bonds has been developed.[60] Ozonation was carried out by absorbing substrate (1%) on silica gel and passing a stream of ozone (3% in O_2) at −45 °C. Rupture of C–C bonds was observed in addition to replacement of hydrogen atoms. Thus interaction of 2,3-dimethylbutane with O_3 led to the following set of products:

$$(CH_3)_2CHCH(CH_3)_2 \xrightarrow{O_3}$$

$$(CH_3)_2\underset{\displaystyle OH}{\underset{|}{C}}H(CH_3)_2 + (CH_3)_2CH\underset{\displaystyle O}{\underset{\|}{C}}CH_3 + (CH_3)_2CO.$$

35% 28% 37%

The total yield of ozonation products was 80–90%. The authors noted that on ozonation in Freon 112 solution at −45 °C the conversion of substrate was significantly less but the composition of products was the same as on silica gel. Thus on ozonation of 3-methylpentane the yield of products was only 6%.

Hydrotrioxides stable at low temperatures were obtained on ozonation of acetals with ozone and were characterised by their NMR spectra.[61] The hydrotrioxides decomposed by a radical mechanism to oxygen and the corresponding hydroxy derivatives, which gave esters and alcohols on acidic catalysis:

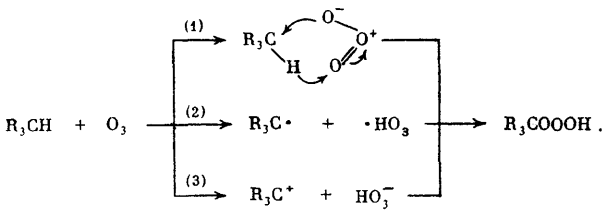
$$CH_3\underset{\displaystyle H}{\underset{|}{C}}(OR)_2 \xrightarrow{O_2} CH_3\underset{\displaystyle O_3H}{\underset{|}{C}}(OR)_2 \rightarrow$$

$$\rightarrow O_2 + CH_3\underset{\displaystyle OH}{\underset{|}{C}}(OR)_2 \xrightarrow{H^+} CH_3CO_2R + ROH.$$

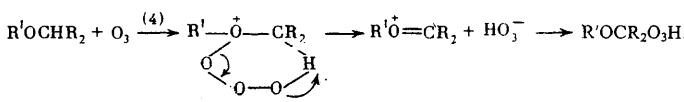
Replacement of hydrogen atoms at a saturated carbon atom by ozone occurs pre-eminently with retention of configuration. Thus on ozonation of *cis*- and *trans*-1,4-dimethylcyclohexanes 80–90% retention of configuration was observed,[62] oxidation of *cis*- and

trans-decalins to the corresponding 9-decalols occurred with complete retention of configuration.[63]

Many studies have been devoted to the kinetics and mechanism of ozonation of C–H bonds.[59,64–70] Three possible mechanisms have been proposed for the first stage of the oxidation of saturated hydrocarbons with ozone:



A mechanism with initial attack of ozone at the oxygen atom is possible for ethers and acetals in addition to those indicated above:



However it was shown that on oxidation of t-butylbenzyl ether[64] and also of a series of hydrocarbons[65,66] the kinetic isotope effect was approximately 4. These data make it possible to consider scheme (4) unlikely.

An assessment has been carried out of the possible routes of the ozonation reaction of saturated hydrocarbons by empirical calculation methods in the application of transition state theory based on recent thermochemical data.[62] It was shown that the most probable mechanism involved transfer of hydride ion and the formation of a tight ion pair:

$$R_3CH + O_3 \rightarrow R_3C^+,\ HO_3^- \rightarrow R_3CO_3H.$$

Table 3. Relative rates of ozonation,[67,68] bromination[71] and solvolysis.[72]

Type of C–H bond	O_3	Br·	Solvolysis[a]
Primary	0.003	0.005	—
Secondary	1	1	1
Tertiary	100	88	$10^{7.8}$

[a] Solvolysis rate in 80% alcohol of 2-bromoadamantane and 2-bromo-2-methyladamantane.

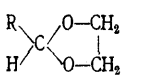
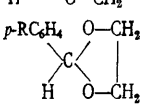
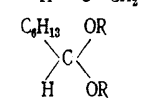
However study of the kinetics of oxidation of saturated hydrocarbons place the hydride ion transfer mechanism in doubt.

Relative rates of ozonation of primary, secondary and tertiary C–H bonds are shown in Table 3 as are relative rates of the free radical bromination and solvolysis.

The observed ratios of ozonation rates showed that a significant positive charge is not generated on the α-carbon atom in the transition state as in that case the difference in reactivity would be significantly greater. Since nucleophilic assistance by the solvent is absent from solvolysis of adamantane derivatives the ratio shown in Table 3 reflects the stability of transition states close in structure to a carbocation. It should be mentioned that ozonation is closer to free radical bromination in selectivity (a polar transition state is characteristic of the latter) than to a carbocationic reaction.

A kinetic study of oxidation processes with a change of substituent for various systems showed that the logarithm of the relative rate constants correlated well with the Hammett and Taft constants (Table 4).

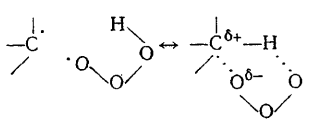
Table 4. Correlation of kinetic data and Hammett and Taft constants.[69,70]

No.	Substrate	ρ
1		−1.16
2		−1.10
3		−1.31
4	p-$RC_6H_4CH_3$	−2.07
5	p-$RC_6H_4CH_3$[a]	−1.42

[a] Reaction parameter for free radical bromination.[71]

The small values of ρ obtained for acetals were explained either by the fact that the positive charge in the transition state is stabilised by the acetal oxygens and to a significantly lesser degree by the substituents or by the fact that a small positive charge is generated in the transition state. For comparison values of ρ in acid hydrolysis reactions of acetals were from −3.6 to −4.2.[73] Comparison of ozonation and free radical bromination shows (Table 4, Nos. 4, 5) that oxidation with ozone proceeds through a more polar transition state than does bromination. The effect of solvent polarity on the ozonation rate of C–H bonds has been investigated.[68,69] It was shown that the oxidation rate of 2-hexyl-1,3-dioxan with ozone in acetic anhydride was two times greater than in n-hexane.[69] A similar increase in rate of 2–2.5 times on going from carbon tetrachloride (ε = 2.24) to acetonitrile (ε = 38) was observed on oxidation of a series of ethers. For comparison the solvolysis rate of t-butyl iodide was increased by more than one order of magnitude on going from benzene (ε = 2.28 to benzonitrile (ε = 25).[71] Thus the available data permit the view that the ozonation of C–H bonds proceeds through fairly polar transition states, however the charge separation in the transition state does not reach values characteristic of carbocationic reactions.

Activation parameters have been determined for the ozonation of a series of saturated hydrocarbons, ethers and acetals.[68,69] The energy of activation of these reactions is between the limits of 5 to 15 kcal/mol, the pre-exponential multiplier varies from 6 to 8. The values obtained for the pre-exponential factor are somewhat greater than would be expected for an insertion mechanism ($\log A < 7$) [74] and less than for the usual radical reactions ($\log A = 8-11$).[71] However the fact that ozonation proceeds through a more polar transition state than free radical substitution should be taken into consideration and this must lead, especially on carrying out the reactions in non-polar solvents, to an increase in the negative entropy of activation. Further the pre-eminent retention of configuration characteristic of ozonation may be explained not only by the insertion mechanism but also by the rapid collapse of the free radical pair in the solvent cage. Such an explanation of the pre-eminent retention of configuration was proposed[75] for the oxidation of saturated hydrocarbons by chromic acid to the corresponding alcohols. The mechanism of direct insertion of oxidising agent at a C–H bond is unlikely since it was shown that the sterically more hindered triethylmethane is oxidised 1.5 times more rapidly than isobutane. Thus the transition state in the ozonation reaction is most probably described by two resonance structures.

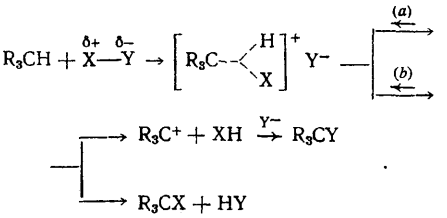


VI. General rules and mechanisms for oxidative replacement of hydrogen in saturated hydrocarbons

The experimental data considered in the previous sections show that in practice all strong oxidising agents, viz. elementary fluorine, ozone, nitronium salts or halogen fluorides are capable at low temperature in the liquid phase of selectively attacking a σ-C–H bond leading to the replacement of hydrogen by another element or functional group. The following factors are capable of increasing the selectivity of the oxidative replacement of hydrogen: 1) there must not be many C–H bonds in the substrate molecule of identical reactivity and 2) the more reactive the substrate the greater the dilution by inert solvent of substrate and reagent is required to bring about a selective reaction. An increase in electron density of the C–H bond favours attack by oxidising agent since the following series of C–H bond reactivities was observed for all the reactions considered in the previous sections: tertiary > secondary ⩾ primary. Correspondingly the introduction of electron-accepting substituents into the substrate molecule deactivates the neighbouring C–H bond and in this way the selectivity of replacing more distant hydrogen atoms is increased.

In the general case the non-radical reaction pathway of replacing hydrogen atoms under the action of oxidising reagents may be described by the scheme proposed by G Olah (Scheme 1).[50] Simple C–H bonds possess the ability to give a bonded electron pair to an electrophilic reagent with the formation of two-electron three-centre bonds. The electrophile attacks covalent bonds just from the front not the rear, and those portions of the covalent bond orbitals play a relatively small role. Subsequent breakdown of the three-centre bond in the pentacoordinate carbonium ion (XVII) may lead either to the formation of trivalent carbenium ions (route *a*) or directly to bonding carbon with the electrophile and ejection of a proton (route *b*).

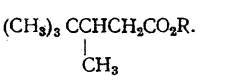
Scheme 1



Replacement of hydrogen atoms by scheme 1*a* should be referred to as a nucleophilic substitution reaction and by scheme 1*b* as a direct electrophilic replacement at a saturated carbon atom. At the present time it appears extremely difficult to choose between these directions for the majority of oxidative replacements of hydrogen. Thus in the case of homoatomic oxidising agents (F_2, O_2, Hal_2–Lewis acids) it is impossible to make this choice on the basis of the nature of the products since in both cases the same products will be formed. Consequently the scheme of direct electrophilic replacement quoted for these reactions in the fundamental publication[76] does not have adequate foundation.

The authors present a series of arguments in favour of electrophilic substitution as the course of the reaction of elementary fluorine with hydrocarbons, however in our view it is impossible to regard the mechanism of this reaction to be unequivocally established.

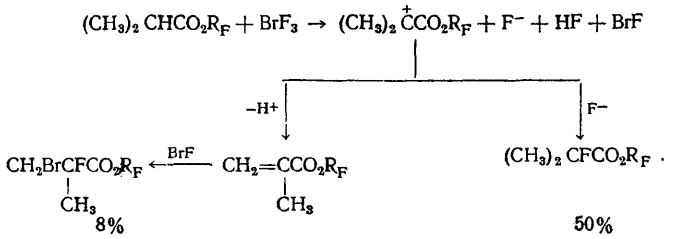
The first argument is the absence of rearrangements characteristic of carbenium ions. This principle, discovered by the authors, is not unexpected since only tertiary hydrogen atoms were subjected to substitution and rearrangements are not characteristic for tertiary carbocations. It would be extremely interesting to investigate fluorination of substrates for which rearrangements are possible, for example:



The second argument is the absence of elimination reactions. Proceeding from the general reaction rules of carbenium ions obtained from study of solvolysis reactions it would certainly be expected that unsaturated compounds would be formed on carrying out a fluorination reaction through a carbenium ion, especially in a non-polar solvent. However under these conditions the resulting olefins will be subjected to further fluorination and consequently small quantities of difluoro adducts will be difficult to detect among products of radical fluorination.

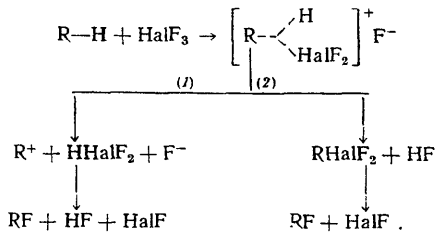
Further it should be mentioned that the formation of olefins is not a characteristic of hydrogen replacement reactions under the action of ClF_3 and BrF_3, although tertiary carbocations are formed in these reactions. Probably this is linked with the small steric volume of the nucleophile (fluorine anion) and also with conducting these reactions at low temperatures. Nonetheless in the reaction of fluoroalkyl isobutyrate with BrF_3 in addition to the main product, fluoroalkyl 2-fluoroisobutyrate, a small quantity of fluoroalkyl 2-fluoro-3-bromoisobutyrate was isolated[52] which was

probably formed as a result of bromofluorination of the unsaturated ester:



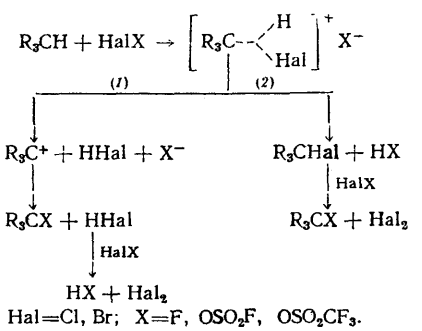
The main argument in favour of electrophilic substitution is the formation of products with complete retention of configuration from optically active substrates. However these results were obtained for conformationally stable cyclohexane derivatives, there are no data on the stereochemistry of oxidative substitution of hydrogen atoms in aliphatic compounds. It is known that the replacement reaction may proceed with the formation of carbenium ions and is accompanied by retention of configuration in the case when the reaction proceeds in a tight ion pair.[71]

In hydrogen replacement reactions with halogen fluorides (ClF_3, BrF_3) the formation of carbocationic intermediates at the stage determining the reaction products has been unambiguously confirmed by the observation of 1,2-migration of methyl groups. However two reaction routes may be proposed in this case:



Conversion of alkylhalogen(III) difluoride into final product may be accompanied by rearrangements. Thus dissociation of neopentyliodine(III) difluoride occurs with methyl group migration and the formation of t-amyl chloride and trimethylethylene derivatives.[1]

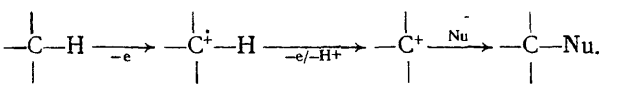
On the whole, for any oxidising agent containing an electropositive halogen atom, it is impossible to draw a conclusion as to the direction (route *1* or *2*) of the reaction based on the reaction products. At present it is well known that such oxidising agents preferentially attack the unshared electron pairs of halogen atoms covalently bonded to carbon rather than a C—H bond in identical surroundings.[1] Consequently if the reaction also proceeds according to route *2* then the product obtained R_3CHal will be slowly converted into product R_3CX undergoing in this route all the rearrangements and migrations typical of this reaction.



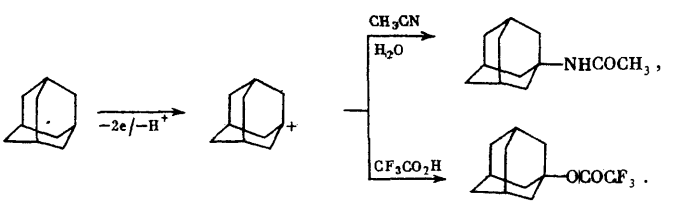
Therefore irrespective of the reaction route the final products of the interaction of hydrocarbons with halogen-containing oxidising agents will be the same.

It might have seemed that reasoned conclusions on the possible routes of hydrogen replacement by scheme 1 may be drawn on the basis of results of nitronium salt oxidation of hydrocarbons. In a non-nucleophilic medium (CH_2Cl_2, sulpholan) nitro derivatives are obtained in low yield the formation of which may be explained by electrophilic substitution (route *b*). The formation of 1-nitroadamantane shows that attack at a C—H bond is effected from the front since attack from the rear is impossible for adamantane. However on carrying out these reactions in nucleophilic solvents (CH_3CN, CF_3CO_2H) the corresponding acetamides and trifluoroacetates were formed in high yield which, together with the observed sextet rearrangements and elimination reactions, points in favour of splitting off a hydride ion with the formation of carbenium ion (route *a*).

The great similarity between the results of the hydrogen replacement reactions under the action of oxidising agents and the results of electrochemical oxidation of similar compounds has attracted attention.[34,77–79] In the light of modern ideas the formation of a carbenium ion in electrochemical oxidation of saturated hydrocarbons occurs as a result of two sequential one-electron oxidations, which is formally equivalent overall to hydride ion elimination by the reagent, i.e. the oxidising agent:[34]



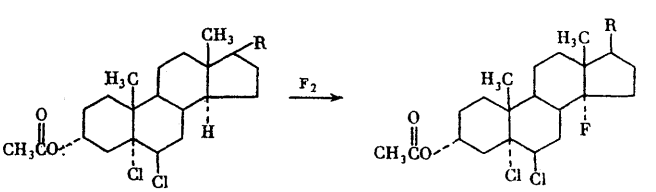
Depending on the solvent and electrolyte used, corresponding functional derivatives are formed, for example:



Yields of trifluoroacetates and acetamides were 50—90%.[69,77] As indicated previously similar results were obtained with nitronium salts.

It should be added that if terminology is applied strictly then the proposed elimination of hydrogen by an electron pair under the action of an oxidising agent cannot be called hydride ion elimination since the attacking electrophilic particle (E) possesses more strongly electron-accepting properties than hydrogen and a molecule with an electropositive hydrogen atom is the leaving group.

A particular special feature may be noted for certain oxidising agents containing electropositive oxygen or fluorine atoms, viz. their greater affinity towards hydrogen than towards chlorine (in the same environment). Such data are rare at present but they merit attention.



Oxidising agents with an electropositive halogen oxidise chlorine atoms under identical conditions.[1]

$$CH_3(CH_2)_5Cl + BrF_3 \rightarrow CH_3(CH_2)_3CHFCH_3.$$

The oxidising replacement reactions for hydrogen considered have one further special feature concerning their preparative use. Although tertiary and secondary C–H bonds are readily oxidised some final substitution products are unstable under the usual conditions in the case of simple hydrocarbon substrates. Thus secondary and tertiary fluorides, fluorosulphates and related compounds are readily decomposed especially in the presence of traces of strong acid. However introduction of electron-accepting substituents into a substrate increases the stability of such compounds and under these conditions interesting preparative applications may be considered for the oxidative hydrogen replacements.

Summarising the results considered the following conclusions may be drawn:

1. At the present time there are no conclusive data confirming the possibility of electrophilic substitution of hydrogen at an sp^3-hybrid carbon under the action of oxidising agents.

2. Carbenium ions are formed at the stage determining the products of oxidative replacement of hydrogen.

Further investigations are necessary for a deeper understanding of the mechanism of the above reactions. In particular it is necessary to expand ideas on the oxidation of C–H bonds at sp^3-hybrid carbon atoms by reagents such as halogen fluorides, hypohalites of strong acids and nitronium salts.

In conclusion it would be desirable to record that at present chemists have available a large selection of oxidising reagents for the selective functionalisation of saturated hydrocarbons and it may be expected that in the next few years the preparative potential of these reactions will be appreciably expanded.

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