The Functionalization of Saturated Hydrocarbons. Part 23.[+]
Gif-type Bromination and Chlorination of Saturated Hydrocarbons: A Non-radical Reaction

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Abstract: The bromination of saturated hydrocarbons was studied in the GoAgg[III] system using $CBrCl_3$ and other polyhaloalkanes. This bromination reaction was compared to free radical processes by (i) evaluating the rates of reactions for a series of polyhaloalkanes, by (ii) measuring the selectivity of the different systems towards various saturated hydrocarbons and by (iii) analyzing the product distribution arising from the bromination of cyclohexyl bromide under both the GoAgg[III] type conditions and from known processes for alkyl radical generation. Some chlorine containing reagents were also examined for C-Cl bond formation in the GoAgg[III] system. All the experimental findings support a mechanism for the reaction that is different from one involving free radicals. This non-radical pathway is common in all Gif-type systems, as seen in common patterns of selectivity.

INTRODUCTION

The substitution of the strong C-H bonds of saturated hydrocarbons is still a major challenge to chemists. The methods presently available include autooxidation processes currently used in industrial transformations[1] and the utilization of biological systems.[2] The former are unselective because of the vigorous conditions employed,[3] or selective only toward less strong (tertiary, benzylic or allylic) C-H bonds.[4] In enzymatic reactions the conformation of the enzyme interacting with that of the substrate imposes a high degree of selectivity in (say) a hydroxylation reaction.[5]

Although it is unlikely that equivalent selectivity can be secured in simple chemical models, we can at least make mimics of the active sites of the enzymes and study their capacity for selective reactions.

In the course of the past decade[6] we have reported the successful oxidation of saturated hydrocarbons by the Gif-family of chemical systems.[7] These are Fe- or Cu-containing oxidation systems which are capable of selective transformation of alkanes into oxidized products.[8] Peculiar selectivity is observed, since these

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systems show preference for secondary substitution versus tertiary or primary positions. Thus, adamantane (1) was found to give secondary/tertiary product ratios (C^2/C^3) of about 1.0.[7] The majority of other existing oxidation reactions give high selectivity for tertiary substitution of adamantane (C^2/C^3=0.01-0.16).[9] In Gif-type systems at secondary positions ketone formation is prevalent, with small amounts of accompanying alcohols.

Earlier reports found that the normal ketonization seen in the Gif[III] system could be intercepted by CCl_4, CH_2Br_2, $CHBr_3$ and CBr_4 to yield alkyl monobromides and monochlorides in addition to the usual oxidation products.[10] The halogenation of adamantane testified to the preservation of the usual Gif-selectivity: C^2/C^3 values of 1.16 and 1.06 were observed for bromination by $CHBr_3$ and chlorination by CCl_4, respectively.

Here we report the efficient and selective conversion of alkanes into alkyl bromides and chlorides in an Fe-catalyzed process by the GoAgg[III] system ($FeCl_3.6H_2O$/picolinic acid (2)/H_2O_2 in pyridine-acetic acid as solvent) in the presence of polyhaloalkanes.[11] During our investigations we observed that even though most of the reagents employed ($CBrCl_3$, CBr_4, etc.) are capable of producing alkyl bromides through chain radical reactions, the Gif-type bromination is different in its characteristics, and must take place *via* a different pathway, involving non-radical intermediates. We arrived at this conclusion after undertaking an extensive comparison of the various radical and Gif-type bromination reactions: considering the relative reactivities of various halogenating reagents; the selectivities toward different hydrocarbons; and the behaviour of a monohalogenated alkane (cyclohexyl bromide). Comparing the reactivity sequence of a series of cycloalkanes we can conclude that bromination in the presence of $CBrCl_3$ under GoAgg[III] conditions is a distinctly Gif-type reaction, representative of the general mechanism proposed for these systems in the oxygenation of saturated hydrocarbons.[12]

RESULTS AND DISCUSSION

Bromination of alkanes under Gif-type conditions: efficiency of different bromine-containing polyhaloalkanes

The GoAgg[III] system has been shown to share its chemical characteristics with other Gif-type systems such as Gif[III], Gif[IV], GoAgg[I] and GoAgg[II]. Since GoAgg[III] is a homogeneous system and is faster, and easier to handle than the others, it seemed to be advantageous to extend the preliminary observations on the effect of $CHBr_3$ and CBr_4 (giving alkyl monobromides when placed in the Gif[IV] mixture) to the GoAgg[III] system. These and other reagents shown in Table 1 were introduced in varying amounts. The oxidation of cyclododecane (3) was altered in the presence of these reagents, giving cyclododecyl bromide (4) in addition to the usual products: cyclododecanone (5) and cyclododecanol (6).
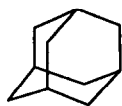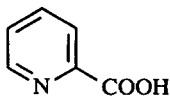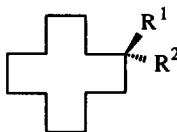
1   2   3: $R^1=R^2=H$
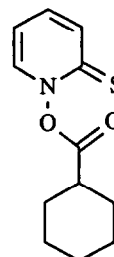   4: $R^1=H$; $R^2=Br$
                                          5: $R^1,R^2=O$
                                          6: $R^1=H$; $R^2=OH$

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Table 1. Bromination of cyclododecane under GoAgg^{III} conditions.[a]

Brominating Agent (mmol)	(%)	O (%)	Br (%)	Bromide/Ketone	Mass Balance (%)
CBr$_4$ (5.0)	80.5	3.1	11.1	3.6	94.7
CBr$_4$ (10.0)	83.0	1.0	16.6	16.6	100.6
CHBr$_3$ (5.0)	64.4	24.8	3.4	0.14	92.6
CHBr$_3$ (10.0)	70.1	20.1	4.2	0.21	94.4
CBrCl$_3$ (1.0)	65.4	21.5	7.0	0.33	93.9
CBrCl$_3$ (5.0)	59.8	10.0	21.9	2.2	91.7
CBrCl$_3$ (10.0)	69.8	< 0.2	28.6	>143	98.4
CBrCl$_3$ (25.0)	64.4	< 0.2	27.0	>135	91.4
CHBrCl$_2$ (10.0)	62.3	22.9	5.9	0.26	91.1
CBr$_2$Cl$_2$ (10.0)	74.9	17.4	2.0	0.11	94.3
CBr$_2$F$_2$ (10.0) [b]	70.3	8.6	16.9	2.0	95.8
(CBrCl$_2$)$_2$ (10.0)	66.4	4.3	18.1	4.2	88.8
LiBr (2.5)	76.8	20.5	---	---	97.3

a. For reaction conditions see Experimental.
b. Conducted at 0°C due to the volatility of CBr$_2$F$_2$

The extent of alkyl bromide formation was different for individual reagents. Bromoform, bromodichloromethane, dibromodifluoromethane and 1,2-dibromo-1,1,2,2-tetrachloroethane all gave total yields of products around 25-30%. Dibromodichloromethane decreased this overall yield to 19.4% and carbon tetrabromide gave a larger decrease, to 17.6-14.2%, depending on the amount of reagent used. The distribution of the products also showed some variation for individual cases: judging the effectiveness of the bromination reaction by looking at the alkyl bromide/ketone ratio, the most productive bromination reagent is clearly CBrCl$_3$, followed by (CBrCl$_2$)$_2$. The ratio of bromide to ketone was fairly high in the cases of CBr$_2$F$_2$ and CBr$_4$, but the volatility of the former and the overall yield reduction caused by the latter eliminated these reagents as practical alternatives for bromination by the GoAgg^{III} system. CBr$_2$Cl$_2$ and CHBrCl$_2$ did not reduce the total yield of functionalized compounds, but their presence still permitted a high proportion of ketone formation, with relatively little bromination. These qualitative differences in the behaviour of the above listed polyhaloalkanes called for a quantitative investigation of their reactivity in the Fe(III)-catalyzed GoAgg^{III} reaction.

Alkyl bromide formation does not arise from a reaction involving ionic bromide (formed *in situ* from the brominating reagent), since in the presence of LiBr no cyclododecyl bromide was detected. Instead, the normal ketonization yield was obtained. Also, since most of these brominating reagents are known to furnish alkyl bromides in radical chain reactions,[13] we needed to find out whether the GoAgg^{III} bromination reaction

proceeds through alkyl radicals possibly formed after H-abstraction from the alkane by an activated $Fe^n=O$ species (similarly to the Cytochrome P-450 oxygenations):

$$R\text{-}H + "Fe^n=O" \longrightarrow R^{\bullet} + "Fe^{n-1}\text{-}OH"$$

These radicals could then enter into radical chain reactions with the halogen-containing reagents:

$$R^{\bullet} + CBrCl_3 \longrightarrow RBr + [CCl_3]^{\bullet}$$
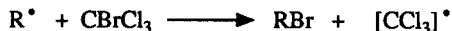
and this reaction would lead to the formation of alkyl bromides and chloroform from (say) $CBrCl_3$. In GoAgg^{III} reactions in the presence of $CBrCl_3$ neither chloroform, nor $(CCl_3)_2$ were detected among the products of the reaction even though blank experiments indicated that these compounds would be detectable even at low concentrations (> 5% conversion, while cyclododecane was converted to its bromide at 28% conversion). The only detectable product formed from the brominating reagent was CO_2, which was characterized both by ^{13}C-NMR spectroscopy (using $^{13}CBr_4$ as a substrate) and by precipitation as $BaCO_3$. Interestingly, $(CBrCl_2)_2$ only gave $Cl_2BrC\text{-}COOH$ (characterized as its trimethylsilyl derivative by GC/MS), without any tetrachloroethylene (elimination product) or oxalic acid (overoxidation product) visible by this analytical method.

Radical vs. *non-radical pathway: relative reactivities for the bromination of alkanes*

In order to confirm that the GoAgg^{III} reaction in the presence of the above described brominating reagents does not proceed through secondary free carbon radicals, a comparison was made of the relative reactivity of these reagents towards radicals generated by known methods, and their behavior under GoAgg^{III} conditions.

Some of these reagents have already been rated as far as their reactivity with methyl radicals is concerned, and in gas phase reactions the following sequence was found[14] (the numbers in parentheses represent relative reactivities compared to Cl-abstraction from CCl_4):

$$CBr_4 \ (4300) > CBr_2Cl_2 \ (2300) > CBrCl_3 \ (1000) > CBr_2F_2 \ (13).$$
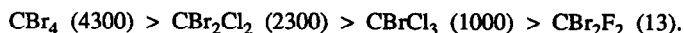
For our solution state radical experiments we chose the method of photolysis of the appropriate *N*-Hydroxy-2-thiopyridone derivatives of an alkanecarboxylic acid with visible light. This reaction represents a mild and effective way of generating carbon radicals:[15]
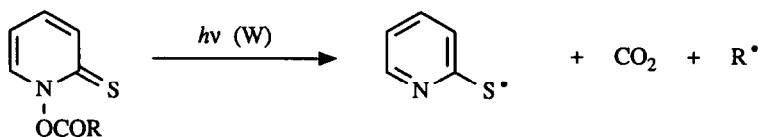
Cyclohexyl radicals were generated from the corresponding cyclohexane carboxylic acid derivative **7** (0.2 mmol) by this process, and were trapped by the haloalkanes shown in Table 2, in competition with a standard radical trap, thiophenol, giving alkanes in a H-abstraction step.[16] The relative reactivities of these polyhaloalkanes were then determined by taking the ratio of halogenated alkane versus the product of H-abstraction, cyclohexane. These product ratios are representative of the partition of cyclohexyl radicals between the two trapping reagents, since the mass balances for the total of the brominated and hydrogenated compounds were acceptable.

From Table 2 it is apparent that CBr_4 is the most active brominating reagent, followed by CBr_2Cl_2, then

Table 2. Relative rates of bromination under radical conditions for a series of polyhaloalkanes. For reaction conditions see experimental part.

Entry	Halogenating Reagent	⬡–H *mmol*	⬡–Br	$\dfrac{R\text{-}Br}{R\text{-}H}$	Total Products *mmol*
1	CBr_4	0.065	0.133	2.05	0.198
2	CBr_2Cl_2	0.108	0.093	0.86	0.201
3	$CBrCl_3$	0.099	0.072	0.73	0.171
4	$(CBrCl_2)_2$	0.124	0.072	0.58	0.196
5	CBr_2F_2	0.120	0.005	0.01	0.125

$CBrCl_3$ and $(CBrCl_2)_2$, the least reactive being CBr_2F_2. This order is in good accordance with the one found earlier for the relative reactivities of the same reagents in their gas phase reaction with methyl radicals, although we were initially apprehensive about the possible interfering cross reactions between CH_2Cl_2 and the reagents during the radical generation process. This similarity shows that, even though the conditions were somewhat different, the behaviour of secondary alkyl radicals towards the reagents mentioned in Table 2 is very similar to that of primary alkyl radicals.

The observed reactivity pattern also corresponds to general expectations about CBr_4 as the most reactive brominating agent of the group examined, in free radical reactions, and the trend is toward decreasing reactivity with increasing the electron-withdrawing properties of the substituents on the carbon of the C-Br bond being broken.

The GoAgg[III] system, however, displayed a completely different behavior. This could be anticipated already from the product distributions in Table 1, but quantitative measurements on cyclohexane as a substrate made it possible to compare GoAgg[III] reactivity with the above described radical behavior. Table 3 illustrates the results obtained when 2.5 mmol of the respective polyhaloalkanes were added to a GoAgg[III] reaction with 40.0 mmol of cyclohexane as the substrate, and 2.5 mmol H_2O_2 as the oxidant. The competition in this case was set up between the trapping of an intermediate on the usual oxidation pathway giving cyclohexanone, and the reaction with the bromine containing reagents. This competition was described also in terms of the product ratios: cyclohexyl bromide versus cyclohexanone.

In the GoAgg[III] system $CBrCl_3$ is clearly the most reactive reagent, with $(CBrCl_2)_2$ following, and CBr_4 is only third in line. Even CBr_2Cl_2, which ranked high in free radical reactions, showed poor reactivity under GoAgg[III] conditions. The relative reactivity sequence is thus quite different from the one found in free radical brominations of the same substrate.

From these results it can be concluded that the free radical and the GoAgg[III] processes differ from each other sufficiently to necessitate the suggested involvement of activated alkane intermediates other than free alkyl radicals. Free radicals are the proposed intermediates for cytochrome P-450 oxygenations, but their participation in other, non-heme enzymatic oxygenations of saturated hydrocarbons (e. g. by methane monooxygenase,[17] prolyl 4-hydroxylase[18] or γ-butyrobetaine hydroxylase[19]) is questionable, at best. If a non-radical type of intermediate was found in Fe-catalyzed oxygenation chemistry, it would certainly have further bearing on the mechanistic possibilities to be considered for these enzymatic transformations.

To further expose the contrast between free radical and GoAgg[III]-type brominations, the selectivity

Table 3. Relative rates of bromination under GoAgg[III] conditions for a series of polyhaloalkanes. For reaction conditions see experimental part.

Entry	Halogenating Reagent	(R=O) mmol	(R-Br) mmol	$\dfrac{R\text{-}Br}{R=O}$	Total Products mmol
1	$CBrCl_3$	0.024	0.686	28.6	0.710
2	$(CBrCl_2)_2$	0.031	0.529	17.1	0.560
3	CBr_4	0.070	0.396	5.6	0.466
4	CBr_2Cl_2	0.300	0.418	1.4	0.718
5	CBr_2F_2 [a]	0.352	0.079	0.2	0.431

a. Reaction carried out at $0^{\circ}C$ due to the volatility of CBr_2F_2. Reaction time:48 h.

towards different alkanes was examined. The brominating reagent of choice was $CBrCl_3$ for these measurements, since it was earlier shown that even a not very great excess of this compound eliminates ketonization completely under GoAgg[III] conditions. Since the only detectable reaction products are alkyl bromides, the amount of these is informative about the reactivity of the particular alkane. The mass balances (88-100%) generally were good enough to allow for this approximation.

Cyclopentane, cyclohexane, cyclooctane, cyclododecane and 2,3-dimethylbutane were competed in pairs of 5 mmol each. Table 4 shows the results from these experiments.

Table 4. Competitive experiments for the bromination reaction under GoAgg[III] conditions.

Substrates		Products (%)		Mass Balance (%)	
R^1H	R^2H	R^1Br	R^2Br	R^1H	R^2H
(hexagon)	(pentagon)	24.4	14.1	93.0	---[a]
(hexagon)	(cross)	19.5	24.7	88.0	100.0
(hexagon)	(octagon)	31.3	39.6	91.0	92.0
(cross)	(2,3-dimethylbutane)	23.3	0.57 (tert.) 1.15 (prim.)	99.0	---[a]

a. Not determined due to the volatility of the substrate.

From the data the relative reactivity of these alkanes (normalized by the number of the appropriate C-H bonds in the molecule and taking cyclohexane as the data base) is the following:

This reactivity sequence corresponds to the one found in both GoAgg[III] oxidations (with no polyhaloalkanes present) and the Cu-catalyzed GoChAgg oxygenations as well.[12] According to this, all these systems are likely to be operating via similar mechanisms.

1.00	0.76	0.69	0.63	0.18 *(prim.)*
				0.06 *(tert.)*
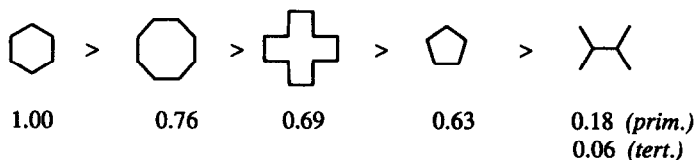
However, when for comparison the above listed hydrocarbons were exposed to radical bromination conditions, a different picture of relative reactivity emerged (Table 5).

Table 5. Competitive experiments for the bromination reaction under chain radical reaction conditions.[a]

| Substrates, mmol		CBrCl₃, mmol	Products Ratio	Normalized Relative Reactivity
R^1H	R^2H		R^1Br/R^2Br	
25.0	25.0	25.0	0.45 [b]	5.41
25.0	25.0	25.0	1.15	1.72
50.0	50.0	50.0	0.23	0.31
50.0	50.0	50.0	1.04	1.25

a. Reaction conditions: equimolar mixtures of R^1H and R^2H were heated at reflux with CBrCl₃ and *ca.* 50 mg of dibenzoyl peroxide. After 2 h about 30% of bromides were formed.
b. Only *tert.* bromide was detected from 2,3-dimethyl-butane (¹H-NMR analysis).

These numbers, after normalization, and taking cyclohexane as the data base, give the following reactivities:

10.2 *(tert.)*	3.3	1.9	1.3	1.0
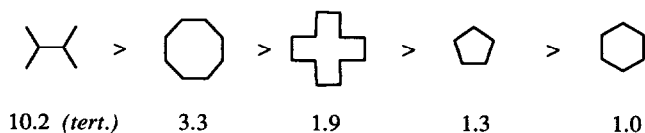
The sequence where tertiary C-H bonds are the most reactive, and cyclohexane the least, is in agreement with expectations of radical reactivity being correlated with the bond strength of the bonds to be homolytically cleaved. Also, the product of the bromination of the primary positions of 2,3-dimethylbutane was not observed at all. Blank experiments were carried out to ascertain the stability of both the primary and the tertiary bromides from this compound, and it was seen that they stand up to the normal GoAgg[III] conditions (95-98% recovery after 4 h).

From these two very different reactivity patterns it is clear that there is a need to invoke an intermediate unlike free alkyl radicals in order to explain the mechanism of the bromination and, consequently, the oxidation reactions taking place under Gif-type conditions (*e. g.* GoAgg[III]).

The "Skell-Walling effect" as a mechanistic diagnostic tool

Additional proof for this difference was obtained when cyclohexyl bromide was exposed to the conditions of the GoAgg^{III} system in the presence of CBrCl$_3$. The attack of radical initiators on alkyl bromides leads to the abstraction of a H-atom from the carbon β to the bromine substituent and, in correspondence with the "Skell-Walling effect",[20] this gives the *trans*-1,2-dibromides. This is what is observed, indeed, in radical chain brominations of cyclohexyl bromide.[21] Our experiments confirmed this effect, at least qualitatively, as shown in Table 6, entries 3 and 4.

In the GoAgg^{III} reaction, however, this was not the case. As entry 2 reflects, the two major products obtained from cyclohexyl bromide were the diequatorially substituted 1,4-*trans*-dibromocyclohexane, and the also diequatorial 1,3-*cis*-dibromocyclohexane. The "Skell-Walling product" 1,2-*trans*-dibromide was only present in minor quantities and the 1,1-dibromo compound could not be detected at all, even though both of these latter two dibromides were stable under the reaction conditions (blank experiments: 98% recovery). We can also observe, that instead of being more reactive and thus giving higher yields of brominated products than the corresponding alkane because of the weakened C-H bond beside the bromine substituent, cyclohexyl bromide is less reactive compared to the parent alkane. This is common Gif-type behaviour, attributed to the deactivating effect of electron-withdrawing substituents.[22]

Table 6. Comparison of the distribution of dibromocyclohexanes for a radical chain reaction and a GoAgg^{III} reaction.

Entry	⬡Br‴Br	⬡Br▸Br	⬡Br⁝Br	Br‴⬡Br	⬡Br⬍Br	Br‴⬡Br
1^a	94.0	3.5^b	0.9	0.5	0.5	0.5
2^c	7.7	---^{f}	1.9	45.2	27.9	17.3
3^d	41.0	14.0	0.8	21.0	16.0	7.2
4^e	33.0	25.0	7.0	15.0	13.0	7.0

a. Values for radical chain bromination (from reference 23). The conversion was 20%. *b.* 1,1-dibromocyclohexane and *cis*-1,2-dibromocyclohexane could not be distinguished. *c.* Values obtained in the GoAgg^{III} reaction on cyclohexyl bromide (for reaction conditions see experimental). *d.* Cyclohexyl bromide (1.0 mmol) and CBrCl$_3$ (4.0 mmol) irradiated in a Rayonet photoreactor with four 3000 Å light tubes under Ar at 35-38°C for 22 hs. *e.* Radical reaction initiated by (PhCOO)$_2$ in Py/AcOH. *f.* Not detected

Chlorination of alkanes

Parallel experiments were conducted with the GoAgg^{III} system in the presence of chlorinating reagents (Table 7). These reagents were generally less able to provide alkyl monochlorides as major products than the bromine-containing ones were to give bromides in their respective reactions, as we can see from the ratio of chlorinated and oxygenated products. The most reactive one was CCl$_4$, but even the less reactive CHCl$_3$ furnished valuable information: although the latter is known to serve as an H-source for free radicals to produce alkanes,[24] in its presence the combined yields of oxygenated and chlorinated products did not decrease. Thus CHCl$_3$ did not enter into H-transfer reactions (even though it was present in excess compared to the conversion of the hydrocarbon), but served as a chlorine source instead.

Table 7. Clorination of cyclododecane under GoAgg^{III} conditions.[a]

Chlorinating Agent (mmol)	(%)	O (%)	Cl (%)	Chloride/Ketone	Mass Balance (%)
CCl$_4$ (25.0)	70.3	21.6	6.4	0.30	98.3
CHCl$_3$ (25.0)	65.1	19.8	2.3	0.11	87.1
CHCl$_3$ (10.0)	65.0	22.6	1.5	0.07	89.1
CCl$_3$-CHCl$_2$ (10.0)	65.9	21.9	2.7	0.12	90.5
Ph-CHCl$_2$ (10.0)	67.0	21.5	0.7	0.03	89.2
(CCl$_3$)$_2$CHCl (10.0)	70.6	21.9	0.3	0.01	92.5
CCl$_3$-CCl$_2$-CHCl$_2$ (10.0)	74.1	20.4	4.0	0.20	98.5

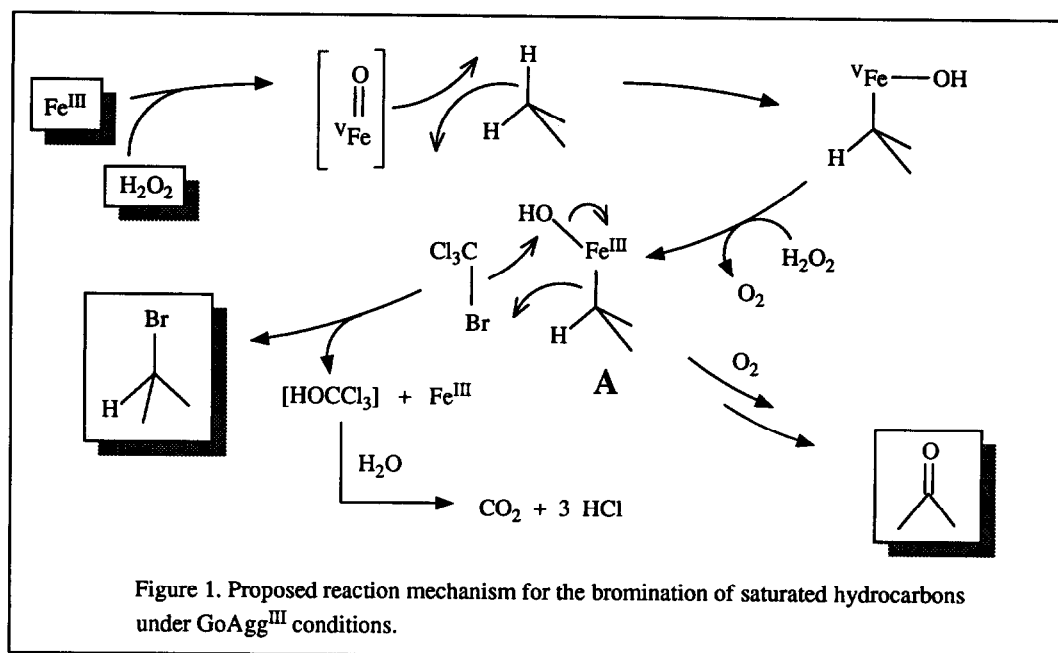a. For reaction conditions, see Experimental.

CONCLUSIONS

The studies herein reported expose the basically different nature of radical chain bromination and chlorination reactions and Gif-type halogenations. This difference is attributed to the non-radical nature of the hydrocarbon activation step under Gif conditions. We have rationalized our experimental observations by the postulated reaction mechanism shown in Figure 1. Thus, upon interaction between Fe(III) and hydrogen peroxide a high oxidation-state oxenoid species is produced. This is able to insert into the C-H bond, forming a high-valent organoiron derivative, which is responsible for the hydrocarbon activation under Gif-type conditions. Upon two electron reduction by hydrogen peroxide, a reduced organoiron (III) is produced. This has now two possible pathways: insertion of dioxygen (which affords the iron hydroperoxide precursor of the ketone or the alcohol), or reaction with CBrCl$_3$ (or other halogenating reagent) producing the alkyl halide and the unstable HOCCl$_3$, a precursor of CO$_2$. This mechanistic scheme explains every experimental fact known today on Gif chemistry. The formation of an Fe(V)=O species has considerable support[25]. Similarly, oxidative addition reactions are well known processes in metallo-organic chemistry[26].

EXPERIMENTAL PART

General. Unless otherwise stated, all the chemicals were the highest purity available from commercial sources and were used without further purification. Authentic samples of 2-bromo-2,3-dimethylbutane, 1-bromo - 2 , 3-dimethylbutane, 1 , 4 - *cis* - dibromocyclohexane, 1 , 4 - *trans* - dibromocyclohexane, 1,3-*cis*-dibromocyclohexane, and 1,3-*trans*-dibromocyclohexane were prepared by standard techniques,[27] and characterized by ^{1}H- and ^{13}C-NMR, IR, and MS.

The experimental methods (including work-up procedures and GC analyses) used throughout this work are as reported previously.[8] Mass spectrometric analyses were performed on a Hewlett-Packard 5790A Series gas chromatograph equipped with a mass-selective detector. ^{13}C-NMR experiments were carried out at room

Figure 1. Proposed reaction mechanism for the bromination of saturated hydrocarbons under GoAgg[III] conditions.

temperature on a Varian XL-200 or a Gemini-200 N.M.R. spectrometer operating at 50 MHz, using 5 mm tubes. Chemical shifts are reported relative to TMS (δ=0.00 ppm). Analyses involving silylation/GC-MS were done as reported elsewhere.[8]

Typical GoAgg[III] halogenation. Cyclododecane (420 mg, 2.5 mmol) and $FeCl_3.6H_2O$ (27 mg, 0.1 mmol) were dissolved in 14 mL pyridine in a 125 mL Erlenmeyer flask under air. Acetic acid (1.15 mL, 20 mmol) and picolinic acid (37 mg, 0.3 mmol) were added, followed by the appropriate amount of halogenating reagent. After 15 min incubation at room temperature 30% H_2O_2 was added in one portion, and the mixture was stirred at room temperature in the closed flask, for 4 hours. Following the usual work-up[8] samples were analyzed by gas chromatography using cycloheptane or naphthalene as internal standards.

Generation of cyclohexyl radicals from Barton-esters. Freshly distilled dichloromethane (10 mL) was purged by bubbling Ar through it at 0 °C for 10 min, after which thiophenol (1.03 mL, 10 mmol) and the appropriate polyhaloalkane (1 mmol) were added, still under Ar. Cyclohexanecarboxylic acid thiohydroxamic acid mixed anhydride (cyclohexyl Barton-ester) (47 mg, 0.2 mmol) was dissolved in this mixture in the dark, and the reaction was irradiated under Ar with a 150W tungsten lamp from a 15 cm distance for 10 min, while the solution was kept at 0 °C. Completion of the reaction was signalled by the disappearance of the bright yellow colour of the Barton-ester, after which an internal standard (naphthalene) was added and the reaction sample was analyzed by direct injection into the gas chromatograph. The R-Br/R-H ratios were obtained by simple comparison of the amount of products of Br- and H-abstraction, respectively.

Radical bromination of hydrocarbons with CBrCl₃. Equimolar mixtures of pairs of hydrocarbons were dissolved in $CBrCl_3$ in amounts as indicated in Table 5. Dibenzoyl peroxide (50 mg) was added as the radical initiator. Reaction mixtures were heated at reflux under Ar for 2 h. After cooling down to room temperature,

an aliquot of the reaction mixture was placed in an 5 mm NMR tube, and the relative amounts of alkyl bromides analyzed by ^{1}H-NMR spectroscopy.

UV-light-initiated bromination of cyclohexyl bromide. Cyclohexyl bromide (1.25 mL, 10.1 mmol) and bromotrichloromethane (0.40 mL, 4.06 mmol) were mixed in a 4 mL quartz cuvette. After purging with Ar for 10min, the cuvette was stoppered by a rubber septum. This reaction vessel was placed in the center of a Rayonet UV-reactor equipped with four 3000Å light tubes and was irradiated for 22 hours. The temperature of the solution remained 35-38 °C during the irradiation, due to the ventilation provided. Then an internal standard (naphthalene) was added and the mixture was analyzed by direct injection into a gas chromatograph.

Preparation of 1,1-dibromocyclohexane. Cyclohexanone-4-toluenesulfonhydrazone[28] (2.5 g, 9.4 mmol) and tetramethylguanidine (4.15 mL, 33 mmol) were dissolved in freshly distilled tetrahydrofuran (50 mL) under Ar. This mixture was added dropwise to a solution of Br_2 (1.53 mL, 30 mmol) in freshly distilled tetrahydrofuran (15 mL), while the reaction was vigorously stirred and maintained at -12°C to -14 °C. After completion of the addition, the solvent was removed in vacuum and the residue was dissolved in diethyl ether (200 mL), washed with 1:1 HCl-solution, sat. $NaHCO_3$-solution, and water, dried over $MgSO_4$ and evaporated to dryness in vacuum. The 6.8 mL pale oil obtained was subjected to vacuum distillation to give (in addition to some 1-bromocyclohexene at 34-36 °C) 1,1-dibromocyclohexane (0.90 g, 42%) at 58-62 °C/2 mmHg (lit.:[29] 84-89 °C/13 mmHg).

Determination of CO_2. The reaction mixture was purged with Ar (prepurified by bubbling through a 25% KOH solution) during the reaction, for 4 h. The gas leaving the mixture was bubbled through two consecutive traps containing saturated $Ba(OH)_2$ solution. After completion (no more precipitate was forming in the first trap), the precipitated $BaCO_3$ was filtered, washed with fresh distilled water, dried in a dessicator over KOH and weighed.

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