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The Functionalization of Saturated Hydrocarbons. Part 26.+ Ionic Substitution Reactions in GoAgg^{IV} Chemistry: The Construction of C-N, C-S and C-C Bonds

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Key Words: Gif systems, Selective functionalization, Iron catalysts, C-N bond formation, C-S bond formation, C-C bond formation.

Abstract: Utilization of the GoAgg^{IV} system in the presence of sodium azide, sodium nitrite, sodium thiocyanate, sodium disulfide and tetraethylamonium cyanide converts saturated hydrocarbons into the corresponding alkyl azides, nitroalkanes, alkyl thiocyanates, dialkyl disulfides and alkyl cyanides, respectively. Mechanistic studies suggest an Fe-centered ligand coupling reaction pathway.

INTRODUCTION

The selective transformation of saturated hydrocarbons into other classes of organic compounds has received much attention recently.[1] The systems catalyzed by metalloporphyrins providing oxygenated products under mild conditions are obvious examples.[2] Moreover, during the past few decades several non-heme containing chemical models which imitate the remarkable ability of biological systems have also been sucessfully developed.[3] Besides the ability to transform alkanes to oxygenated products, several systems have recently been shown to transform alkane C-H bonds into non-oxygenated functional groups.[4]

Gif-type reactions are another class of non-heme containing Fe- and Cu-based chemical models designed to mimic biological systems.[5] Since 1983, various Gif-type systems have been developed which use active oxygen sources such as superoxide ion ($O_2^{-}\cdot$) as in the Gif^{III} and Gif^{IV} systems; hydrogen peroxide (H_2O_2) as in GoAgg^{II}, GoAgg^{III} and GoChAgg systems.[6] All Gif-type reactions are performed in a solution of pyridine and

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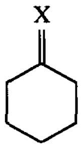
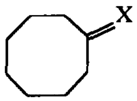
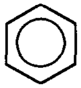


1 X = H_2
2 X = O
3 X = OH, H
4 X = N_3, H
31 X = NO_2, H
32 X = SCN, H
33 X = NCS, H
46 X = CN, H
47 X = Br, H



5 X = H_2
6 X = O
7 X = OH, H
8 X = N_3, H
34 X = SCN, H
35 X = NCS, H
48 X = *o*-pyridyl, H
49 X = *p*-pyridyl, H
50 X = Cl, H



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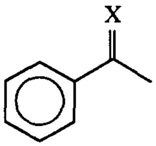

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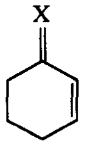
11 X = O
12 X = OH, H
13 X = N_3, H
42 X = SCN, H



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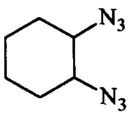
15 X = O
16 X = OH, H
17 X = N_3, H



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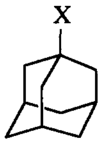
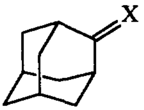
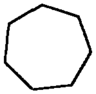


19 X = H
20 X = OH
23 X = *o*-pyridyl
24 X = *p*-pyridyl
25 X = N_3
40 X = SCN



21 X = OH, H
22 X = O
26 X = *o*-pyridyl, H
27 X = *p*-pyridyl, H
28 X = N_3, H
41 X = SCN, H



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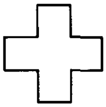

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36 X = H
37 X = SCN

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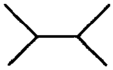

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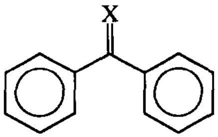
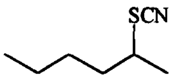


51 X = H_2
52 X = O
53 X = N_3, H
54 X = SCN, H



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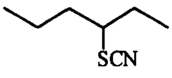

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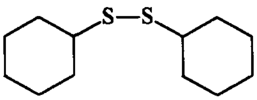

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acetic acid. These systems are capable of oxidizing saturated hydrocarbons under mild conditions to mainly ketones with unusual selectivity (secondary C-H bonds are preferentially oxidized over tertiary or primary C-H bonds).[5] Recent studies on the utilization of *tert*-butyl hydroperoxide (TBHP) as an oxidant (GoAgg^{IV} and GoAgg^{V}) have revealed several similarities and a common reaction pathway of these systems to those of the previous Gif-type reactions.[7] Mechanistic studies on the formation of the oxidized products have shown that there are at least two distinct intermediates along the reaction pathway. The second intermediate is fully characterized by both chemical and spectroscopic methods as an alkyl hydroperoxide.[8] The first intermediate is postulated to be a high-valent iron-carbon sigma bonded species. In the presence of appropriate trapping reagents, the production of oxidized products is diverted giving the corresponding monosubstituted alkyl derivatives. This process takes place *via* the interception of intermediate A.[5] For instance, in the presence of diphenyl diselenide (PhSeSePh) in the Gif$^{\underline{III}}$ or Gif^{IV} systems, the formation of alkyl phenylselenides is detected instead of ketone.[9] Alkyl bromides are found to be the sole products from the GoAgg$^{\underline{III}}$ reaction in the presence of bromotrichloromethane ($BrCCl_3$).[10] The production of alkyl chlorides and alkyl bromides is also attained employing the GoAgg^{IV} and GoAgg^{V} systems in the presence of halogenating agents. In addition, under the GoAgg^{IV} conditions in the presence of alkali metal salt such as LiCl, alkanes are efficiently converted into alkyl chlorides.[11] Continuing the exploration of the effects of the addition of other appropriate alkali metal salts to the GoAgg^{IV} oxidation systems, the formation of the corresponding monosubstituted alkyl derivatives was observed.

In this article, we wish to report the selective construction of C-N bonds (alkyl azides and nitroalkanes); C-S bonds (alkyl thiocyanates and dialkyl disulfides) and C-C bonds (alkyl cyanides) by utilizing the GoAgg^{IV} system in the presence of inexpensive alkali metal salts.

RESULTS AND DISCUSSION

The Formation of C-N Bonds

The direct conversion of unactivated C-H bonds into C-N bonds is important in synthesis. However, such a process is not generally facile. A limited number of successful studies concerned with the construction of C-N bonds have recently been reported. The introduction of an azido group into unactivated C-H bonds[4d,4j,12], the formation of *N*-alkylacetamide[13] and the formation of C-N bonds *via* nitrene (or its equivalents) insertion[14] are examples. However, under Gif-type conditions there has been no report on the construction of C-N bonds. Employing similar methodology to that applied in the formation of C-Cl bonds under GoAgg^{IV} conditions[11], the creation of C-N bonds such as alkyl azides and nitroalkanes by a simple system using $Fe(NO_3)_3 \cdot 9H_2O$ in the presence of sodium azide (NaN_3) or sodium nitrite ($NaNO_2$) could be accomplished.

Alkyl Azides

Replacing LiCl in the GoAgg^{IV} chlorination of cyclohexane (**1**) by NaN_3, gave cyclohexanone (**2**), cyclohexanol (**3**) and cyclohexyl azide (**4**). Appropriate blank experiments revealed that in the absence of either Fe$^{\underline{III}}$ or TBHP, there was no alkyl azide formation. Cyclohexyl azide (**4**) was also found to be stable (98% recovery) under the reaction conditions used.

A study of the effects of varying the Fe^{III} species on the formation of alkyl azide revealed that there was no significant influence by changing the Fe^{III} species used. However, the rate of the reaction was found to be dependent on the concentraton of Fe^{III}. The ratio of Fe^{III} and NaN_3 also highly affected the production of the desired product, alkyl azide. The optimal ratio of Fe^{III} to NaN_3 was found to be 1:15. Moreover, in contrast to the system developed by Que and coworkers[12a] where alkyl azide was reported to be directly proportional to the amount of Fe complex employed, the production of alkyl azide derived from the $GoAgg^{IV}$ system could be achieved by the use of catalytic amounts of Fe^{III} salts combined with excess NaN_3 present in the solution.

Various hydrocarbons, namely cyclohexane (**1**), cyclooctane (**5**), benzene (**9**), ethylbenzene (**10**) and cyclohexene (**14**) were selected to examine the regioselectivity of the reaction. The results are collected in Table 1.

Table 1. The $GoAgg^{IV}$ reaction of various hydrocarbons in the presence of NaN_3.[a]

Entry	Substrate (50 mmol)	Product (s) (mmol)
1	**1**	**2** (1.54), **3** (0.11), **4** (3.66)
2	**5**	**6** (1.52), **7** (0.10), **8** (5.17)
3	**9**	–
4	**10**	**11** (1.15), **12** (0.04), **13** (4.90)
5[b]	**14**	**15** (0.26), **16** (0.16), **17** (4.84)

a) employing $Fe(NO_3)_3 \cdot 9H_2O$ (1.0 mmol), NaN_3 (15 mmol) and TBHP (10 mmol) at 60°C. b) using TBHP (5 mmol).

The results from Table 1 show that saturated hydrocarbons such as cyclohexane (**1**) and cyclooctane (**5**) are converted into cyclohexyl azide (**4**) and cyclooctyl azide (**8**) under these conditions with efficiencies based on TBHP in the range of 53-68% (entries 1 and 2).[15] Under these conditions, benzene (**9**) did not give any functionalized products (entry 3), while the oxidation of alkyl benzenes such as ethyl benzene (**10**) yielded the corresponding azide (**13**) in high yield (entry 4). The activation process was observed to take place preferentially at the benzylic position of the molecule. The selective transformation of cyclohexene (**14**) to 1-azido-2-cyclohexene (**17**) was also accomplished in good yield by this methodology (entry 5). The formation of the latter provided informative results for the mechanistic pathway of the reaction. Schäfer[16] has reported that the products observed from the reaction of azide radicals ($N_3\cdot$) and cyclohexene (**14**) were 1,2-diazidocyclohexane (**18**, 54%), cyclohexyl azide (**8**, 30%) and 1-azido-2-cyclohexene (**17**, 15%). Therefore, the possibility that azide radical presumably generated from the oxidation of azide ion by TBHP was involved in the reaction pathway for the formation of alkyl azide under $GoAgg^{IV}$ conditions could be ruled out.

In order to avoid the formation of a mixture of oxidized products and alkyl azide, the reaction could be conducted under an argon atmosphere. Thus, the oxidation of cyclooctane (**5**) (50 mmol) employing 1 mmol of

$Fe(NO_3)_3 \cdot 9H_2O$ in the presence of 15 mmol of NaN_3 and 10 mmol of TBHP at 60°C under an atmosphere of oxygen-free argon resulted in the production of 7.79 mmol of cyclooctyl azide (**8**) (78% efficiency based on the oxidant). Under these conditions, the oxidation of ethyl benzene (**10**) yielded 6.60 mmol of 1-azido-1-phenyl ethane (**13**) (66% efficiency based on the oxidant) accompanied with a small amount of the oxidized products. The oxidation of cyclohexene (**14**) employing TBHP (2 mmol) gave 2.07 mmol of 1-azido-2-cyclohexene (**17**) (104% efficiency based on TBHP) as the only reaction product.

Regioselectivity studies using adamantane (**19**) as a substrate revealed an overall C^2/C^3 value for the azidification reaction of 0.53. This value is in the range typical of $GoAgg^{IV}$ systems (0.5-0.7).[7] The results are presented in Table 2.

Table 2. The oxidation of adamantane by the $GoAgg^{IV}$ system in the presence of NaN_3.[a]

Yield (%)[b]								Σ	C^2/C^3
19[c]	**20**	**21**	**22**	**23**	**24**	**25**	**28**		
68.8	4.9	tr.	4.1	3.2	1.4	8.4	4.1	94.9	0.53

a) employing $Fe(NO_3)_3 \cdot 9H_2O$ (1 mmol), NaN_3 (15 mmol) and TBHP (10 mmol) at 60 °C. b) based on substrate. c) recovered substrate. tr. = traces.

The results of a relative reactivity study in the azidification reaction between selected cycloalkanes are presented in Table 3. By normalization per C-H bond in the molecule, cyclooctane (**5**) was found to be more reactive than cycloheptane (**29**), cyclohexane (**1**) and cyclododecane (**30**) by the factors of 1.34, 2.17 and 2.65, respectively.

Nitroalkanes

The formation of nitroalkanes such as nitrocyclohexane (**31**) can be achieved by similar methodology to that applied for the production of alkyl chlorides and alkyl azides. Thus, the activation of cyclohexane (**1**) employing 1 mmol of $Fe(NO_3)_3 \cdot 9H_2O$, 15 mmol of sodium nitrite ($NaNO_2$) and 10 mmol of TBHP at 60°C resulted in the formation of 1.548 mmol of cyclohexanone (**2**), 0.124 mmol of cyclohexanol (**3**) and 0.504 mmol of nitrocyclohexane (**31**). The overall efficiency of the reaction based on TBHP was approximately 22%.

In an attempt to maximize the amount of the desired nitrocyclohexane (**31**), the reaction was performed under oxygen-free argon. However, the quantity of nitrocyclohexane formed under these conditions was found to be only slightly increased. The efficiency based on TBHP for the formation of nitrocylohexane was in the range of 7-10%.

Table 3. Competition studies between cycloalkanes towards the GoAgg^{IV} oxidation reaction in the presence of NaN_3.[a]

Cycloalkanes		Product (mmol)	
R^1	R^2	R^1-N_3	R^2-N_3
5	**29**	1.80	1.18
5	**1**	2.38	0.82
5[b]	**30**[b]	0.45	0.20

a) employing $Fe(NO_3)_3 \cdot 9H_2O$ (1 mmol), NaN_3 (15 mmol), TBHP (10 mmol) and a pair of subtrates (25 mmol each). b) using a pair of substrates (10 mmol each).

The Formation of C-S Bonds

Previous studies on the construction of C-S bonds under Gif-type conditions have shown that the formation of alkyl phenylsulfides; dialkyl disulfides, trisulfides and polysulfides can be accomplished using PhSSPh in the Gif^{III} or Gif^{IV} systems[9b] and Na_2S, H_2S, NaHS or S_8 in various Gif-type reactions.[17] Under GoAgg^{IV} conditions, upon the addition of sodium thiocyanate (NaSCN) and sodium sulfide ($Na_2S \cdot 9H_2O$), the formation of ketones was diverted giving alkyl thiocyanates and dialkyl disulfides, respectively.

Alkyl Thiocyanates

Preliminary experiments revealed that when the GoAgg^{IV} oxidation reaction of cyclohexane (**1**) was performed in the presence of 15 mmol of NaSCN at 60°C, cyclohexyl thiocyanate (**32**) was obtained as the main product accompanied with a very small amount of cyclohexyl isothiocyanate (**33**). Control experiments showed that in the absence of Fe^{III} or oxidant, no product was formed. Cyclohexyl thiocyanate (**32**) (95% recovery) and cyclohexyl isothiocyanate (**33**) (90% recovery) were found to be stable and not inter-converted under the conditions used.

The rate of the thiocyanation reaction was found to be surprisingly fast. At 60°C and at room temperature, the reaction was complete within 10 min. The half-life of the reaction at room temperature was approximately a few minutes, while at 0°C the half-life was around 20 min.

Variation of the Fe^{III} species and its concentration did not have any significant effect on the total activation achieved in this reaction. However, the ratio of Fe^{III} to NaSCN was found to have a major influence on the outcome of the reaction. The optimal ratio of Fe^{III} to NaSCN for the thiocyanation reaction at room temperature was found to be 1:5. When more NaSCN was added to the reaction, less products were obtained. The reason for this was possibly due to a competitive reaction between NaSCN and TBHP occurring parallel to the thiocyanation reaction of the saturated hydrocarbons.

Various hydrocarbons were selected to determine the regioselectivity of the system. The product distributions of these reactions are shown in Table 4.

Table 4. The GoAgg^{IV} oxidation of various hydrocarbons in the presence of NaSCN.

Entry	Substrate (mmol)	Product (mmol)
1	**1** (50)	**32** (2.80), **33** (0.02)
2	**5** (50)	**34** (2.91), **35** (0.05)
3	**36** (50)	**37** (0.17), **38** (1.40), **39** (0.99)
4	**19** (5)	**19** [a] (4.42), **40** (0.31), **41** (0.21)
5	**10** (25)	**42** (0.29)

The reaction was performed employing $Fe(NO_3)_3 \cdot 9H_2O$ (1.0 mmol), NaSCN (10 mmol) and TBHP (10 mmol) at room temperature. a) recovered substrate.

Utilizing this methodology, alkyl thiocyanates can be obtained directly from various hydrocarbons. For instance, cycloalkanes such as cyclohexane (**1**) and cyclooctane (**5**) were converted into the corresponding alkyl thiocyanates (**32**, **34**) accompanied with a trace amount of the corresponding alkyl isothiocyanates (**33**, **35**) with approximately 30% efficiency based on TBHP (entries 1 and 2). *n*-Hexane as an example of an open chain saturated hydrocarbon is also transformed into the corresponding alkyl thiocyanate (entry 3). The regioselectivity C^2/C^1 value was found to be 13.9. The oxidation of alkyl benzenes such as ethyl benzene (**10**) in the presence of NaSCN yielded the corresponding alkyl thiocyanate (**42**) preferentially at the benzylic position. Regiochemical evaluation of the system using adamantane (**19**) as a substrate resulted in the formation of 1-adamantyl thiocyanate (**40**) and 2-adamantyl thiocyanate (**41**) with trace amounts of pyridine-coupled products (**23**, **24**) detected only at the tertiary position. The overall C^2/C^3 value of the system was 0.69.

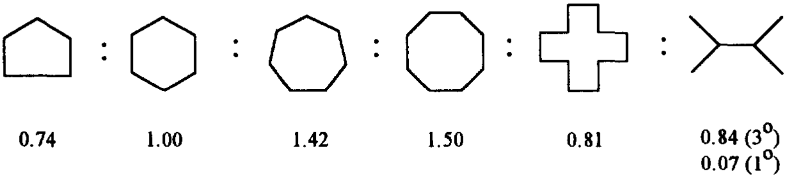
To avoid the undesired side reaction between NaSCN and TBHP, a modification of the reaction was performed. Thus, the dropwise addition of a solution of NaSCN (15 mmol) in pyridine to a mixture of $Fe(NO_3)_3 \cdot 9H_2O$ (1 mmol), TBHP (10 mmol) and cyclooctane (**5**) (50 mmol) at 0°C under an argon atmosphere, resulted in the formation of cyclooctyl thiocyanate (**34**) (4.26 mmol) and cyclooctyl isothiocyanate (**35**) (0.136 mmol). Thus, a 2-fold increase in the yield was observed and the efficiency based on TBHP was significantly improved from 29% to 44%.

The relative reactivity between cycloalkanes for the thiocyanation reaction employing 1 mmol of $Fe(NO_3)_3 \cdot 9H_2O$, 10 mmol of NaSCN, 10 mmol of TBHP and 25 mmol of each substrate at room temperature was conducted and the results are presented in Table 5.

By normalization per C-H bond in each molecule, cyclooctane (**5**) was found to be the most reactive substrate among the cycloalkanes selected. The relative reactivity ratio based on cyclohexane (1.00) is shown below. A competition reaction between cyclohexane (**1**) and 2,3-dimethylbutane (**44**) clearly showed that the activation process took place at the secondary position of the former preferentially over the tertiary or primary positions of the latter. Moreover, the relative reactivity between cyclohexane (**1**) and cyclopentane (**43**) was also indicative of the pathway of the reaction.

Table 5. Competition studies among cycloalkanes toward the GoAgg^{IV} thiocyanation.

Cycloalkanes		Product (mmol)	
R^1	R^2	R^1-SCN	R^2-SCN
43	**1**	0.74	0.99
1	**29**	0.90	1.50
1	**5**	0.89	1.77
5	**30**	1.65	1.34
1	**44**	0.46	0.13 (3°) 0.02 (1°)



Dialkyl Disulfides

The successful construction of C-S bonds giving dialkyl disulfides and polysulfides as reported for previous Gif-type reactions[17] could also be accomplished by the GoAgg^{IV} system. Thus, the oxidation of cyclohexane (**1**) (20 mmol) by a system comprising of 0.5 mmol of $FeCl_3 \cdot 6H_2O$, 1.5 mmol of picolinic acid, 4 mmol of $Na_2S \cdot 9H_2O$ and 10 mmol of TBHP at room temperature resulted in the formation of 0.163 mmol of cyclohexanone (**2**) and 0.426 mmol of dicyclohexyl disulfide (**45**).

Interestingly, unlike other Gif-type systems where the oxidation in the presence of $Na_2S \cdot 9H_2O$ produced a mixture of dialkyl disulfides, trisulfides and polysulfides[17], under GoAgg^{IV} conditions, the only product obtained from the reaction was the dialkyl disulfide.

The Formation of C-C Bonds

The formation of C-C bonds giving alkyl cyanides under GoAgg^{IV} conditions could be achieved by the addition of sodium cyanide (NaCN) to the oxidation system. The oxidation of cyclohexane (**1**) employing $Fe(NO_3)_3 \cdot 9H_2O$ (1 mmol) in the presence of NaCN (15 mmol) and TBHP (10 mmol) at 60°C resulted in the production of 1.24 mmol of cyclohexanone (**2**), 0.102 mmol of cyclohexanol (**3**) and 0.430 mmol of cyclohexyl cyanide (**46**). The overall efficiency of the reaction based on TBHP was found to be 18%.

Due to the low solubility of NaCN in pyridine-acetic acid, a more appropriate source of cyanide anion was found to be tetraethylammonium cyanide ($Et_4N^+CN^-$). Thus, by replacing NaCN with $Et_4N^+CN^-$ (10 mmol) in the oxidation of cyclohexane (**1**) by the GoAgg^{IV} system under an argon atmosphere, the resulting reaction mixture was found to be composed of cyclohexanone (**2**) (0.102 mmol) and cyclohexyl cyanide (**46**) (0.953 mmol). The efficiency for the formation of cyclohexyl cyanide based on TBHP was around 10%.

The addition of sodium cyanate (NaOCN), sodium or lithium acetate (NaOAc or LiOAc), sodium perchlorate ($NaClO_4$), sodium or lithium nitrate ($NaNO_3$ or $LiNO_3$) or nitromethane (CH_3NO_2) to the GoAgg^{IV} oxidation system did not produce any monosubstituted alkyl derivatives. The normal oxidation reaction was found to take place regardless of the presence or absence of these reagents.

Results showing the relative reactivity between ionic trapping reagents in the GoAgg^{IV} oxidation of cyclohexane (**1**) are presented in Table 6. The reactivity among ionic trapping agents was found to be in the following order: NaSCN > NaN_3 > LiBr > LiCl > $NaNO_2$.

Table 6. Competition study of the reactivity of ionic trapping reagents in the GoAgg^{IV} oxidation reaction of cyclohexane (**1**).[a]

Salts (mmol)		Product (mmol)					$\frac{R\text{-}X^1}{R\text{-}X^2}$
X^1	X^2	**2**	**3**	$R\text{-}X^1$	$R\text{-}X^2$	Σ	
LiCl (15)	NaN_3 (15)	1.10	0.14	0.34	1.64	3.22	0.21
LiCl (10)	NaSCN (10)	0.09	–	0.41	2.93	3.25	0.14
LiCl (10)	LiBr (10)	0.12	–	0.28	1.48	1.85	0.19
NaN_3 (10)	LiBr (10)	0.11	0.02	0.65	0.30	1.08	2.17
LiCl (10)	$NaNO_2$ (10)	1.44	0.03	3.24	0.12	4.82	27.00
NaN_3 (15)	NaSCN (15)	0.35	0.15	0.58	2.23	3.31	0.26

a) employing $Fe(NO_3)_3 \cdot 9H_2O$ (1 mmol), cyclohexane (**1**) (50 mmol) and TBHP (10 mmol) at 60°C.

Mechanistic Studies

The mechanism for the production of monosubstituted alkyl derivatives under GoAgg^{IV} conditions in the presence of alkali metal salts is believed to be the same as that proposed for the formation of alkyl chlorides in the presence of LiCl (Fig. 1).[11] The interception of a high valent carbon-iron bonded species (Intermediate A) was postulated to occur *via* Fe-centered ligand coupling.[11]

The results of competitive trapping in the GoAgg^{IV} system in the presence of ionic trapping (NaSCN) and covalent trapping ($BrCCl_3$) reagents are shown in Table 7. It was observed that the more $BrCCl_3$ was applied to the system, the more cyclohexyl bromide (**47**) was obtained, while less cyclohexyl thiocyanate (**32**) was observed. Nonetheless, the total activation of the process was found to remain constant. These results clearly illustrated that both trapping reagents were capturing the same intermediate along the reaction pathway.

Determination of the half-life of the GoAgg^{IV} reaction shows that in the absence of trapping reagents, the half-life for the formation of cyclooctyl pyridine-coupled products (**48**, **49**) is approximately 41 h at 60°C.

In contrast, in the presence of LiCl, NaN_3 and NaSCN the half-lives for the formation of cyclooctyl chloride (**50**), cyclooctyl azide (**8**) and cyclooctyl thiocyanate (**34**) were 110, 300 and less than 10 min. respectively.

Table 7. Competition study of the $GoAgg^{IV}$ oxidation of cyclohexane (**1**) in the presence of NaSCN and $BrCCl_3$.[a]

Trapping reagents (mmol)		Product (mmol)		
NaSCN	$BrCCl_3$	**32**	**47**	Σ
10	0	2.36	–	2.36
10	3	0.62	1.54	2.16
10	5	0.14	1.96	2.10
10	10	0.09	2.11	2.20

a) employing $Fe(NO_3)_3 \cdot 9H_2O$ (1 mmol), cyclohexane (50 mmol) and TBHP (10 mmol) at room temperature.

These values imply that the trapping process takes place at an early stage of the reaction and is much faster than the homolytic cleavage which occurs in the absence of O_2 and trapping reagents.[7]

For several non-heme chemical models it has been proposed that the first intermediate of the alkane activation process is a carbon-centered radical.[19] However, according to the accumulated results obtained from the study of Gif-type reactions, it has been clearly shown that the major pathway of the reaction, particularly at the secondary position of saturated hydrocarbons, does not involve free carbon-centered radicals.[5] Striking evidence against the participation of carbon-centered radicals as the first intermediate under $GoAgg^{IV}$ conditions is derived from a competition study between various hydrocarbons having different C-H bond energies. The compounds selected for this study were: cyclooctane (**5**), ethyl benzene (**10**) and diphenylmethane (**51**). The C-H bond strengths of the methylene groups in these compounds are 95.1, 85.4 and 81.4 kcal/mol, respectively.[20] The results of the competitive oxidation of these substrates in the presence of NaN_3 and NaSCN are shown in Table 8.

The corresponding alkyl azides (**8**, **13**, **53**) and alkyl thiocyanates (**34**, **42**, **54**) of these three compounds were synthesized and all of them were found to be stable (greater than 90% recovery) under the reaction conditions examined.

According to the C-H bond strengths, diphenylmethane (**51**) should be more reactive than the others if a radical process was operating in the reaction. Nevertheless, the experimental facts clearly show that by normalization per C-H bond in the molecule the relative reactivity of cyclooctane (**5**) was found to be comparable with ethyl benzene (**10**) in the azidification reaction with the ratio of 1:1.6 (entry 1). For the thiocyanation of these two compounds, cyclooctane was found to be more reactive than ethyl benzene by a factor of 2 (entry 2). Using cyclooctane (**5**) and diphenylmethane (**51**), the competitive azidification reaction provided a normalized C-H bond ratio of 0.78 (entry 3). Interestingly, performing this reaction under an argon atmosphere led to decreased amounts of oxidized products (**6**, **52**), whereas the amounts of the azides (**8**, **53**) were significantly increased. However, the ratio of the azides (**8**) and (**53**) was found to be constant (0.81).

Table 8. Competitive oxidation of cyclooctane (**5**), ethyl benzene (**10**) and diphenylmethane (**51**) in the presence of NaN_3 and NaSCN.[a]

Entry	Reagent	Hydrocarbons		Product (mmol)	
		R^1	R^2	R^1-X	R^2-X
1	NaN_3	**5**	**10**	**6** (0.601), **8** (5.116)	**11** (0.086), **13** (1.023)
2	NaSCN	**5**	**10**	**34** (1.861)	**42** (0.109)
3	NaN_3	**5**	**51**	**6** (0.606), **8** (2.803)	**52** (3.375), **53** (0.272)
4	NaSCN	**5**	**51**	**34** (1.683)	**54** (tr.)

a) employing $Fe(NO_3)_3\cdot9H_2O$ (1 mmol), a pair of substrate (25 mmol each), NaN_3 (15 mmol) or NaSCN (10 mmol) and TBHP (10 mmol) at 60°C for azidification and at RT for thiocyanation.

The most striking result, which is in complete contrast to the C-H bond strength value, was obtained from the competitive thiocyanation reaction between cyclooctane and diphenylmethane. The yield of cyclooctyl thiocyanate (**34**) was found to be the same in the presence or in the absence of diphenylmethane. In each case the thiocyanation product derived from diphenylmethane (**51**) was found only in trace amounts (entry 4).

In addition, recent studies comparing the behavior of Intermediate A in the $GoAgg^{IV}$ system with that of a carbon-centered radical towards various trapping reagents under conditions typically employed in the $GoAgg^{IV}$ system have shown that the relative reactivity of these two species towards trapping reagents is totally different. This informative finding has strengthened the postulation of a high valent iron-carbon sigma bonded species as the first intermediate of Gif-type systems.[21]

CONCLUSION

The direct transformation of C-H bonds of saturated hydrocarbons into C-N bonds (alkyl azides and nitroalkanes), C-S bonds (alkyl thiocyanates and dialkyl disulfides) and C-C bonds (alkyl cyanides) can be achieved by the use of the $GoAgg^{IV}$ system. A relatively long lived high valent Fe species is the first intermediate of the reaction and it can be captured by various anionic reagents giving monosubstituted alkyl derivatives. Competitive studies between various hydrocarbons have revealed the differences between the genuine carbon centered radicals and the first intermediate of this system.

EXPERIMENTAL

IR spectra were recorded on a Perkin Elmer 881 spectrophotometer. ^1H and ^{13}C NMR spectra were performed in deuterochloroform with tetramethylsilane (TMS) as an internal reference on a Varian Gemini 200 or Varian XL 200E. Gas chromatography was carried out on a Hewlett Packard 5890 series II instrument, on Chrompack Model 439 or 437S instruments equipped with a flame ionization detector with N_2 as a carrier gas. The columns used for chromatography were DB-WAX (30 m) or DB-5 (15 or 30 m) capillary columns from

J&W Scientific (0.32 mm i. d., 25 μm film thickness). Gas chromatography-mass spectrometry (GC-MS) was conducted on a Hewlett-Packard gas chromatograph Model 5790A coupled to a Hewlett-Packard 5970 mass selective detector (40 eV, electron impact). Thin layer chromatography (TLC) was performed on aluminium sheets precoated with silica gel (Merck, Kieselgel 60 F-254). Column chromatography was performed on silica gel (Merck, Kieselgel 60, 230-400 mesh). Solvents were used either as purchased or dried and purified by standard methods under pure, dry argon.

Unless otherwise stated, all chemicals were purchased as the highest purity commercially available and were used without further purification. Authentic samples of alkyl and cycloalkyl azides[22], 1-adamantyl azide[23], 1-azido-cyclohexene[24], alkyl and cycloalkyl thiocyanates[25], 1-adamantyl thiocyanate[26], dicyclohexyl disulfides[17], cyclohexyl cyanide[27] were prepared according to previously reported methods and their identities were confirmed by IR, ^{1}H- and ^{13}C-NMR spectroscopy. The *ortho-* and *para-* pyridine-coupled products: cyclooctyl-, 1-adamantyl- and 2-adamantyl-pyridine were obtained from the photolysis of the corresponding Barton ester in a pyridine-trifluoroacetic acid mixture as reported previously.[28]

General GoAgg^{IV} procedure for the construction of C-N bonds. A GoAgg^{IV} oxidation reaction of hydrocarbon (50 mmol) was carried out in the presence of $Fe(NO_3)_3 \cdot 9H_2O$ (404 mg, 1.0 mmol) or other iron complexes (1.0 mmol), NaN_3 (15 mmol) or $NaNO_2$ (15 mmol) in a solution of pyridine (30 ml), acetic acid (3 ml). The temperature of the reaction was raised up to 55-60°C and kept constant at that temperature prior to the addition of 90% TBHP (1.1 ml, 10 mmol). The reaction mixture was stirred for 10-12 h. The kinetic analysis or the quantification followed the same procedure reported elsewhere.[7] Samples were analyzed by gas chromatography using naphthalene or fluorene as internal standards.

The isolation of 1-azido-2-cyclohexene. The reaction mixture obtained from the GoAgg^{IV} oxidation of cyclohexene in the presence of NaN_3 was subjected to the normal work-up procedure. The combined ethereal extracts were concentrated to dryness. The crude mixture was purified by column chromatography (silica gel, 10% CH_2Cl_2 in hexanes) affording the title compound as a clear liquid (520 mg, 83.2% based on TBHP). IR (neat, cm^{-1}): 2095. ^{1}H NMR ($CDCl_3$): 5.95 (m, 1H), 5.68 (m, 1H), 3.85 (br, 1H) and 2.20-1.10 (m, 6H). ^{13}C NMR ($CDCl_3$): 132.69, 124.58, 55.89, 28.58, 24.67 and 19.10. All the spectroscopic data was identical with that reported in the literature for 1-azido-2-cyclohexene.[24]

The isolation of 1-azido-1-phenyl ethane. By the same prodecure described for the isolation of 1-azido-2-cyclohexene. 1-azido-1-phenyl ethane was obtained as a colorless liquid after purification by column chromatography (941 mg, 64.0% based on TBHP). IR (neat, cm^{-1}): 2095. ^{1}H-NMR ($CDCl_3$, ppm.): 7.25-7.55 (m, 5H), 4.64 (q, J = 6.74 Hz, 1H) and 1.56 (d, J = 6.86 Hz, 3H). ^{13}C-NMR ($CDCl_3$, ppm.): 140.85, 128.74, 128.10, 126.35, 61.07 and 31.60.

General GoAgg^{IV} and GoAgg^{V} procedures for the construction of C-S bonds.

For alkyl thiocyanates: Identical methodology described for the construction of C-N bonds was applied for the formation of C-S bonds (alkyl thiocyanates) except using NaSCN (10 mmol) instead of NaN_3 at room temperature.

For dialkyl disulfides: The reaction was carried out by the same procedure as that described for the GoAgg^{V} oxidation reaction[7] in the presence of sodium disulfides (4 mmol) at room temperature. Other procedures followed those described earlier for the typical GoAgg^{IV} or GoAgg^{V} reactions.[7]

General GoAgg^{IV} procedure for the construction of C-C bonds. The reaction was carried out in the same way as that described in the GoAgg^{IV} azidification reaction except employing NaCN *or* $Et_4N^+CN^-$ (15 mmol) instead of NaN_3.

General work-up procedure. An aliquot (1.0 ml) was taken from the reaction mixture, acidified with 25% H_2SO_4 to a pH of approximately 2-3 and extracted twice with diethyl ether (5 ml each). The combined organic extracts were washed with saturated solution of $NaHCO_3$ and water, dried ($MgSO_4$) and analyzed by gas chromatography after the addition of a known amount of an appropriate internal standard.

General procedure for the competition studies in the GoAgg^{IV} system. GoAgg^{IV} functionalization reactions were carried out employing a pair of hydrocarbons (25 mmol each or otherwise stated) in the presence of NaN_3 (15 mmol) at 60°C or NaSCN (10 mmol) at room temperature for the competition studies. Other procedures followed those described earlier for the typical GoAgg^{IV} reaction.

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