Synergistic oxidation of cyclohexane and hydrogen sulfide under Gif conditions

Derek H. R. Barton,* Tingsheng Li and John MacKinnon

Department of Chemistry, Texas A&M University, College Station, TX 77843-3255 USA

Saturated hydrocarbons and hydrogen sulfide can be synergistically oxidised by oxygen (or air) to give efficiently ketones (and the corresponding alcohols) and sulfur in the presence of a Gif catalyst based on Fe^{II}, picolinic acid and 4-*tert*-butylpyridine with acetonitrile as solvent at room temperature and nearly neutral pH.

We report an unusual reaction in which cyclohexane is oxidised to cyclohexanol and cyclohexanone whilst at the same time hydrogen sulfide is converted to sulfur. The only oxidant needed is oxygen or air.

In recent publications[1,2] we have presented a coherent theory of Gif ketonization chemistry. From the practical point of view the selective functionalization of hydrocarbons to furnish ketones, or other derivatives selectively substituted at secondary positions, requires the right kind of carboxylate ligands as, for example, in picolinic acid.[1] Exactly two picolinic acids are bonded to Fe^{III} as determined by quantitative ^{13}C NMR studies.[3] There is also an essential need for a certain kind of pyridine ligand as, for example, in 4-*tert*-butylpyridine or in pyridine itself. One of these ligands[2] is bonded to Fe^{III}. In practise, about 15 equiv. per Fe^{III} of the pyridine base give optimal results. As solvent the inert acetonitrile is satisfactory.

There are two ways in which the activated iron species can be formed.[1] The first is by addition of superoxide to Fe^{II}. This has been well established by electrochemical studies.[4] The second is by substitution chemistry on Fe^{III} by H_2O_2.

It occurred to one of us (D.H.R.B.) that if Fe^{II} and O_2 would furnish superoxide (and Fe^{III}) then the latter would react with more Fe^{II} to make the activated iron species and hence permit entry to Gif ketonization chemistry. If the Fe^{III} formed in the first step could be reduced by H_2S to give Fe^{II} and sulfur then it should be possible to concert the oxidation of saturated hydrocarbons to ketone (and alcohol) with the oxidation H_2S to sulfur. Indeed we have recently established that Fe^{III} is rapidly reduced to Fe^{II} by H_2S.[5]

In this way we would be able to coordinate the oxidation of (say) cyclohexane to cyclohexanone (and alcohol) with the removal of toxic hydrogen sulfide from (say) natural gas. The methane and ethane in the natural gas would not react under Gif conditions as evidenced by prior experiments.

For those not initiated into the unusual reactivity seen in Gif chemistry (the Gif paradox) the above sequence might seem improbable.[6] However, whatever oxidation species is present does have a special affinity for saturated hydrocarbons. The latter activates the iron reagent to attack the secondary position and make a species which is not a radical. We still formulate this as an iron–carbon bond.[7]

Be all this as it may, the experimental facts confirm the hypothesis. Using hydrogen sulfide and oxygen, cyclohexane is converted to cyclohexanone and cyclohexanol at the same time that hydrogen sulfide is oxidised to sulfur (see Table 1).

In contrast to our prior work[6] there is no limitation on the conversion. The formation of ketone and alcohol remains quantitative even up to a conversion of 36%. In blank experiments cyclohexanone is not transformed into any other derivatives as it is in prior Gif chemistry.[8] Thus the limit of 20–30% on the convertion previously observed[6] no longer pertains. Cyclohexanol is slowly converted into cyclohexanone. It did not seem likely that carbon radicals would be playing a role in the presence of excess H_2S and its derived radical $H{-}S^{\bullet}$. Indeed the addition of excess LiCl afforded no trace of cyclohexyl chloride. Of course, a blank experiment showed that cyclohexyl chloride did not react under the conditions of the oxidation. In agreement with Minisci[9] we accept that carbon radicals react rapidly with Fe^{III}–Cl species to make chloride.

As an industrial process, the selective oxidation of hydrocarbons is known to be very inefficient. The Dupont process converts cyclohexane to cyclohexanol and cyclohexanone in a 4% yield with 80% selectivity. The remaining 16% consists of various ring cleavage products and over oxidation products. The conversion is carried out at high temperatures (160 °C) and pressure (15 bar).[8] In this new system the reaction is carried out at room temperature and atmospheric conditions. Hydrogen sulfide (2–2.5 ml min^{-1}) and oxygen (25 ml min^{-1}) were simultaneously passed through a standard solution containing Fe^{III}Cl$_3$ (1 mmol), picolinic acid or its *N*-oxide (PA-N-oxide) (4 mmol), cyclohexane (20 mmol) and 4-*tert*-butylpyridine (15 mmol) in acetonitrile (33 ml). After a period of time the solution was filtered from the sulfur deposited and the mixture analysed. The efficiencies of the hydrocarbon oxidation are summarized in (Table 1).

Cyclohexane was oxidised to cyclohexanol and cyclohexanone with a 36% conversion after 9 h (Table 1, entry 3). When PA-N-oxide was used as a ligand, a conversion of 33% was achieved in 6 h (Table 1, entry 6). This oxidation procedure can be applied to different hydrocarbons (Table 1, entries 7 and 8).

Table 1 Efficiency of oxidation of hydrocarbons with hydrogen sulfide and oxygen

Entry	Hydrocarbon	mmol	Ligand	*t*/h	Ketone[a]/ mmol	Alcohol[a]/ mmol	Conversion (%)
1	Cyclohexane	20	Picolinic acid	3	2.10	1.87	19.9
2	Cyclohexane	20	Picolinic acid	6	2.76	2.57	26.7
3	Cyclohexane	20	Picolinic acid	9	3.00	4.13	35.7
4	Cyclohexane	30	PA-N-oxide	2	2.65	3.15	19.3
5	Cyclohexane	30	PA-N-oxide	4	4.18	4.52	29.0
6	Cyclohexane	30	PA-N-oxide	6	4.97	4.90	32.9
7	Cyclododecane	20	Picolinic acid	6	4.01	2.41	32.1
8	Cyclododecane	20	PA-N-oxide	4	2.47	1.97	22.2

[a] The products were analysed by GC, naphthalene was used as internal standard.

Cyclododecane was converted to cyclododecanone and cyclododecanol with a 32% conversion after 6 h. Elemental sulfur was also formed and filtered.

A major limitation with hydrocarbon oxidation was over oxidation of the oxygenated products.[6,10] Blank experiments were carried out to investigate the inherent stability of the products of oxidation. The results are summarized in Table 2.

Both cyclohexanone and cyclododecanone were stable under the oxidative conditions outlined above. It was also shown that the ketone produced as the major oxidation product (Table 1) was not the result of over oxidation of the alcohol. Since essentially no over oxidation occurs over 36 h the possibility of nearly 100% conversion of the hydrocarbon is now a realistic target.

Table 2 Stability of oxygenated products in hydrogen sulfide Gif oxidation[a]

Starting material	Recovered ketone (%)	Recovered alcohol (%)	Others (%)
Cyclohexanone	98.6	—	—[a]
Cyclohexanol	1.5	98.5	—[b]
Cyclododecanone	95.6	—	4.4[c]

[a] $Fe^{III}Cl_3 \cdot 6H_2O$ (1 mmol), ligand (4 mmol), ketone or alcohol (20 mmol), 4-*tert*-butylpyridine (15 mmol), MeCN (33 ml). Oxygen and hydrogen sulfide were passed through the homogeneous solution for 4 h. The products were analysed by GC, naphthalene was used as internal standard. [b] Not detected. [c] Four diketones in minor amounts.

Table 3 Conversion of cyclohexane to oxygenated products on a 784 mmol scale[a]

Entry	*t*/h	Cyclohexanone/ mmol	Cyclohexanol/ mmol	Total/ mmol	Conversion (%)
1	4	15.97	4.91	20.88	2.66
2	8	22.43	8.39	30.82	3.93
3	12	31.57	10.30	41.87	5.34
4	16	34.90	12.05	46.95	5.99
5	20	43.08	17.00	60.08	7.66
6	24	47.66	18.91	66.57	8.49
7	28	55.32	22.06	77.38	9.87
8	36	78.97	33.35	112.32	14.33

[a] $Fe^{III}Cl_3 \cdot 6H_2O$ (20 mmol), ligand (60 mmol), cyclohexane (784 mmol), 4-*tert*-butylpyridine (150 mmol), MeCN (80 ml). Oxygen and hydrogen sulfide were passed through the homogeneous solution. The solution was filtered to remove the sulfur deposited and the products were analysed by GC, naphthalene was used as internal standard.

Table 4 Effect of the amount of H_2S and O_2 on ketone/alcohol formation in presence of Fe^{II}[a]

Entry	H_2S/ mmol	O_2/ ml min^{-1}	*t*/h	Ketone/ mmol	Alcohol/ mmol	Sulfur/ mmol
1	35	25	8	1.23	0.79	17
2	35	50	8	1.55	1.27	30
3	35	100	4	2.16	1.45	28
4	35	120	4	2.17	1.98	30
5	25	100	4	1.24	0.55	21
6	25	50	8	1.07	0.97	20
7	25	25	8	0.75	0.61	19
8	15	100	4	0.56	0.38	11
9	15	50	4	0.87	0.78	11
10	15	25	4	0.71	0.65	10
11	15	15	4	0.60	0.36	11

[a] $Fe^{II}Cl_2 \cdot 4H_2O$ (1 mmol), ligand (3 mmol), hydrocarbon (20 mmol), 4-*tert*-butylpyridine (15 mmol), MeCN (33 ml). Oxygen and hydrogen sulfide were passed through the homogeneous solution for 4–8 h. The products were analysed by GC, naphthalene was used as internal standard. The H_2S is the total passed.

The oxidation of cyclohexane was not only limited to a 20 mmol scale. A large scale experiment was carried out (Table 3).

After 36 h the conversion of the hydrocarbon to ketone and alcohol was 14.33%. The lower conversion value was a result of a decrease in the rate of the reaction due to the increased hydrocarbon to solvent ratio. After filtration of the reaction mixture, 625 mmol of sulfur was obtained. In other experiments using variable H_2S and O_2 flow rates the sulfur formed was quantified (Table 4).

When the flow rates of one or both of H_2S and O_2 were varied from that of the standard flow rate (Table 4, entry 4), the total amount of ketone and alcohol decreased. A reasonable correlation between the amount of H_2S used and that of sulfur obtained was seen.

We have developed an efficient new procedure for the selective oxidation of hydrocarbons to the corresponding ketone and alcohol by simply passing through a stream of oxygen and hydrogen sulfide. At the same time we have provided an efficient route to dispose of hydrogen sulfide gas. This synergistic oxidation of hydrocarbons and removal of hydrogen sulfide provides a route for the nearly quantitative conversion of hydrocarbons to their oxygenated products. It is a significant improvement on our original work.[10]

Although there is considerable prior work on the oxidation of saturated hydrocarbons by non-haem systems[11] the normal substitution pattern according to the C–H bond strength is followed. Gif chemistry is a separate subject.[1,6,12] In the present work, as in general,[1] if the picolinic acid or the pyridine base are omitted from the system then very little oxidation takes place. A detailed mechanistic discussion has not been presented. The reactions differ from normal only in the enhancement of alcohol relative to ketone.

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