

Green Chemistry with Ozone

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Cyclic hydrocarbons are oxidized to ketones, alcohols, and carboxylic acids with no undesirable waste products.

The fundamental problem in the functionalization of saturated hydrocarbons is that their components, carbon and hydrogen, do not have electron pairs, and the molecules do not have orbitals of sufficient energy that they are easily accessible. Thus, very reactive reagents and/or extreme reaction conditions are typically required, for example, for the oxidation of alkanes. However, the initial products are almost always more reactive than the starting compounds, and undesired side reactions may occur (1).

This statement by Otto Reiser encapsulates the classical dilemma of derivatizing saturated hydrocarbons. The selective oxidation of alkanes at room temperature is one of the most important objectives of synthetic chemistry (2). Generally these reactions use metal-centered systems that mimic mono-oxygenases. Examples are cytochrome P-450 and methanemono-oxygenase mimics (3). This enzyme chemistry has been mimicked using the "Gif system", which consists essentially of air, catalytic amounts of iron or zinc, acetic acid, pyridine, and water (4).

The use of iron as the metal catalyst in these oxidations is recommended because of its low environmental impact. Iron oxide colloids generated by the hydrolysis of ferric nitrate nonahydrate catalyze the functionalization of the hydrocarbons that constitute the continuous phase of these micellar systems by reaction with *tert*-butyl hydroperoxide. The regioselectivity sequence tertiary > secondary >> primary was observed, in agreement with a homolytic cleavage of C–H bonds (5).

One review points to the mechanism of the oxidation of cycloalkanes by tertiary alkyl hydroperoxides catalyzed by iron(III) dichlorotris(2-pyridylmethyl)amine and by an acetate bridged (μ -oxo) di-iron complex (6). Product studies do not support oxidation via a high-valent iron intermediate, but they are consistent with a mechanism in which hydrogen atoms are abstracted from the alkane by alkoxy radicals derived from the hydroperoxide.

A manganese-centered version is also available: Alkanes are oxidized by hydrogen peroxide in air in acetonitrile in the presence of a manganese(IV) salt as the catalyst. The oxidation initially affords the corresponding alkyl hydroperoxides as the predominant products, but later these compounds decompose to produce the corresponding ketones and alcohols. The regioselectivity is high: The primary/secondary/tertiary ratio is in the range 1:15–40:180–300 (7).

Vanadium also has been used as the catalyst. The oxidation of decalin isomers with H_2O_2 catalyzed by a vanadium complex and pyrazine-2-carboxylic acid (PCA) in air is similar to that obtained from the photochemical oxidation with H_2O_2 in air and from air oxidation in the presence of anthraquinone. A proposed mechanism for the oxidation includes the initiation by hydroxyl radicals generated from H_2O_2 under the action of the vanadium–PCA system (8). The resulting alkyl radicals react rapidly with molecular oxygen to produce peroxy radicals that are transformed mainly into the hydroperoxides (9). Alternatively, in situ-generated RuO_4 has been used to oxidize alkanes (10).

The central problem of these procedures is the use of metals and organic solvents that generate waste. Some efforts at a metal-free technique use dioxiranes as oxidizing agents (11–15). Other procedures functionalize alkanes in superacidic media (16), insert oxygen with di(perfluoroalkyl)oxaziridines (17, 18), and oxidize with fluorine in aqueous acetonitrile (19).

Enter ozone

Ozonation is an alternative to these methods, for example, in the oxidation of cycloalkanes (20). The formation of the intermediate hydrotrioxides from alkanes has been reviewed in *Methoden der Organische Chemie* (21) and other sources. These studies suggest that conversion and selectivity in the use of ozone for alkane oxidation need to be improved.

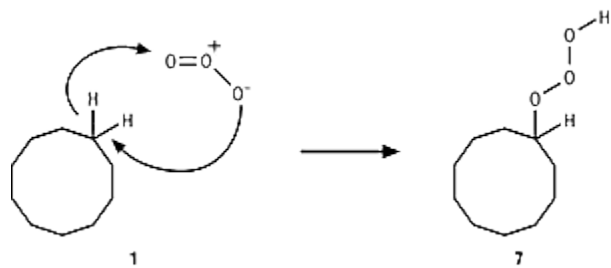
Some reports suggest that the use of ozone as a reactant in metal-catalyzed reactions, for example, the iron porphyrin-catalyzed oxygenation of alkanes (22, 23) or the oxidation of alkanes with manganese-substituted polyoxometalates (24). We have shown that the ozonation of ethers in acidic buffer forms esters (25) and that the ozonation of amines forms amides and N-dealkylation products (26–28).

We have reported the production of cyclodecanone (2) by ozonation of a suspension of cyclodecane (1) in water at pH 3 (Figure 1) (29). After 1 h at 25 °C, gas–liquid chromatography–mass spectroscopy (GLC–MS) analysis showed that the main product was cyclodecanone; cyclodecanol (3) was also observed. Because all of the mass was not accounted for, we repeated the analysis after derivatization with *N*-(*tert*-butyl dimethylsilyl)-*N*-methyltrifluoroacetamide. With this method, carboxylic acids can also be determined. This analysis showed that nearly equimolar amounts of cyclodecanone, 10-oxodecanoic acid (4), and decanedioic acid (5) were obtained (Table 1).

A trace of nonanedioic acid (6) was also observed. When the reaction was carried out at pH 7, the conversion was higher but selectivity for cyclodecanone was lower.

Ozonation of cyclodecane in organic solvents gave very similar results (Table 2). Higher selectivity for cyclodecanone was generally observed.

A possible reaction mechanism is shown in Figure 2.



Hydride transfer from the alkane forms a hydrotrioxide (7). In fact, hydrotrioxides from isopentane, 1,4-dimethylcyclohexane, 1,3-dimethylcyclohexane, decalin, and triphenylmethane have been synthesized by low-temperature ozonation of the corresponding hydrocarbons on a silica surface. Activation parameters of the thermal decomposition of

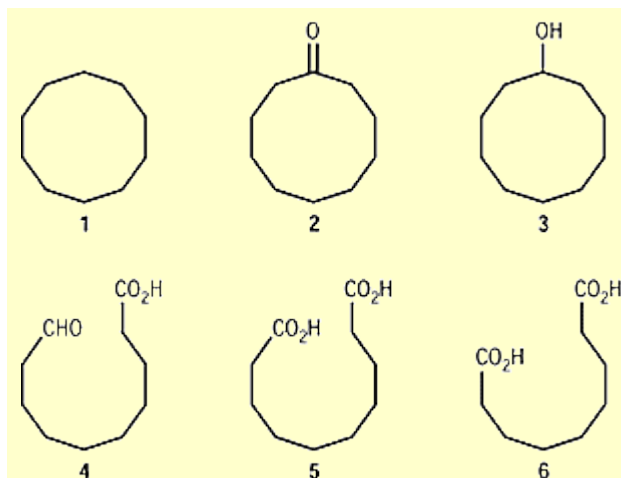


Figure 1. Cyclodecane (1) and its ozonation products: cyclodecanone (2), cyclodecanol (3), 10-oxodecanoic acid (4), decanedioic acid (5), and nonanedioic acid (6).

Table 1. Oxidation of cyclodecane with ozone in water

pH	Conversion, %	Reaction products, mol% ^a			
		2	3	4	5
3	61	29	2.4	24	29
7	75	20	1.4	–	8

^aAs a percentage of the converted material.

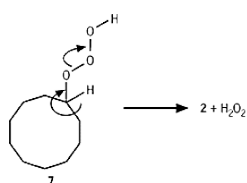
hydrotrioxides show a compensation effect ($\log A$ [the pre-exponential factor] vs E_a) that describes the available experimental and theoretical data for the homolysis of organic trioxides (30).

This mechanistic detail has been suggested to account for the oxygenation of some ethers (31) and agrees well with the fact that oxygen is inserted into the methylene group adjacent to the heteroatom in the oxygenation of ethers to esters (25) and in the oxygenation of amines to amides (26–28).

Table 2. Oxidation of cyclodecane with ozone in organic solvents

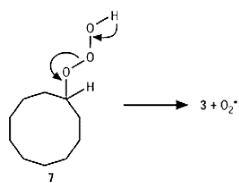
Solvent	Conversion, %	Reaction products, %	
		2	Others
MeCN	52.7	42.6	10.1
MeNO ₂	78.5	53.9	24.6
CH ₂ Cl ₂	52.3	39.4	12.9
CHCl ₃	64.4	39.1	25.3

Hydrotrioxide **7** is a key intermediate in the reaction. In fact, [Figure 3](#)

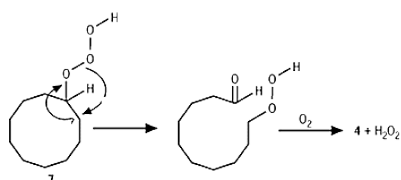


shows that it may

- dissociate to cyclodecanone and H₂O₂,
- dissociate to cyclodecanol and singlet oxygen, or
- rearrange to 10-oxodecanoic acid (**4**).



The alternative ozonation at pH 7 is probably less effective in converting cyclodecane into cyclodecanone because of the rapid further oxidation of the ketone. Organic solvents seem to direct the decomposition of hydrotrioxide **7** through the first pathway in Figure 3.



Ozonation of decalins

We have shown that ozone converts secondary carbons into carbonyl in aqueous solution. We had to use a different technique with decalins (**8** and **9**), because of their poor solubility in water. When the ozonation of *cis*-decalin (**8**) in nitromethane was performed at 5 °C over 30 min, we observed almost complete conversion. GLC–MS analysis of the reaction mixture showed that the major product was *cis*-9-hydroxydecalin (**10**) (see [Figure 4](#)), but a small amount of *trans*-9-hydroxydecalin (**11**) was also present. Calibration of the analytical response was performed by injecting known quantities of authentic specimens of starting material and reaction products and observing the signal,

and this allowed us to obtain the conversions and yields shown in [Table 3](#).

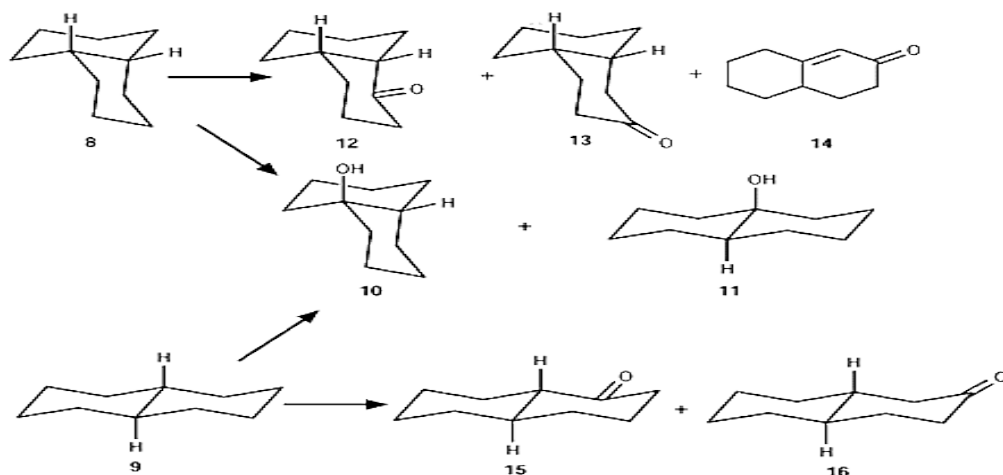


Table 3. Oxidation of *cis*- and *trans*-decalin with ozone in organic solvents

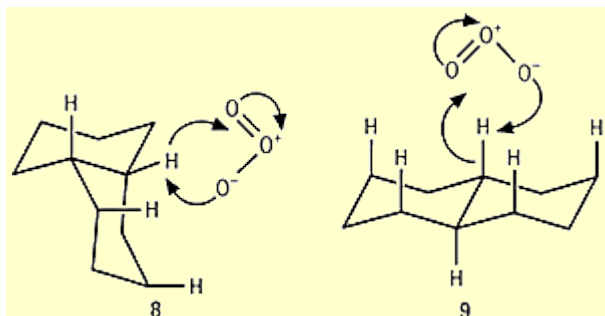
Starting material	<i>cis</i> -Decalin (8)		<i>trans</i> -Decalin (9)	
	MeNO ₂	CH ₂ Cl ₂	MeNO ₂	CH ₂ Cl ₂
Conversion, %	99	84	26	21
Reaction products, mol%				
<i>Functionalization at the tertiary carbon</i>				
<i>cis</i> -9-Hydroxydecalin (10)	57	71	0.4	0.3
<i>trans</i> -9-Hydroxydecalin (11)	4	2	12	10
<i>Functionalization at the secondary carbon</i>				
<i>cis</i> -Decalin-2-one (12)	6	3		
<i>cis</i> -Decalin-3-one (13)	6	3		
Unsaturated ketone (14)	22	4		
<i>trans</i> -Decalin-2-one (15)			5	4
<i>trans</i> -Decalin-3-one (16)			4	4

Small amounts of other reaction products were also observed. Some of them had the cyclic skeleton of the starting material: *cis*-decalin-2-one (**12**), *cis*-decalin-3-one (**13**), and the unsaturated ketone **14**. The ozonation of *cis*-decalin in methylene chloride produced similar results, but conversion was lower and selectivity for the *trans* tertiary alcohol **11** was higher than with nitromethane.

The ozonation of *trans*-decalin (**9**) in nitromethane and methylene chloride was run under the same conditions, but we observed much lower conversions. GLC–MS analysis of the reaction mixtures showed that the major product was *trans*-9-hydroxydecalin (**11**). Small amounts of *cis*-9-hydroxydecalin (**10**) and the decalones **15** and **16** were also present.

A first indication of the mechanism of the hydrogen transfer step comes from the observation that both *cis*- and *trans*-decalin undergo a highly stereospecific 9-hydroxylation reaction, as described for the 1,2-dimethylcyclohexanes (32). In fact, in the production of the 9-hydroxydecalins **11** and **12**, the stereochemistry of the starting material is highly retained. This suggests that formation of either a carbon radical or a carbocation in position 9 leading to inversion of this center is only a side pathway, and that the hydrogen atom transfer from carbon to oxygen in the ozonation is concerted.

Whether the transferred hydrogen species is a hydrogen atom or a hydride ion has been the subject of debate in earlier papers; however, the concerted nature of the reaction makes this discussion “more a difference in philosophy than reality” (20, p 268). Perhaps the relative reactivities of tertiary and secondary carbon–hydrogen bonds suggest that the transition state has some polar character. Moreover, the fact that *cis*-decalin **8** is 1 order of magnitude more reactive than *trans*-decalin **9** suggests that the concerted hydrogen atom transfer is rate-determining. In fact, fewer 1,3-diaxial interactions are found in the ozone attack on *cis*-decalin than in the attack on *trans*-decalin, as can be seen in Figure 5.

**Figure 5. Mechanism of ozone attack on *cis*- and *trans*-decalin.**

We have shown that ozone acts as a hydrocarbon oxidizing agent to produce carboxylic acids, ketones, and alcohols, generating only H₂O₂ as a byproduct—our contribution to green chemistry.

Acknowledgment

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