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Review

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Arkivoc **2023** (i) 202211942

Oxidative cleavage of alkynes: a review of the methods invented so far and their application possibilities in green organic synthesis

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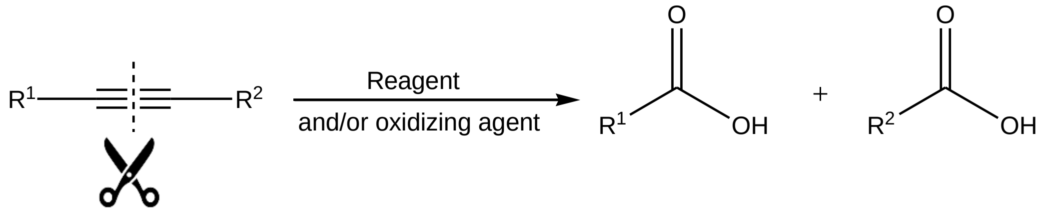
This work is dedicated to the people who died on February 6th, 2023 by earthquake in my homeland of Samandağ and Antakya

Received 12-06-2022 **Accepted** 03-09-2023 **Published on line** 04-08-2023

Abstract

Oxidative cleavage products of alkynes are used just as frequently in preparative organic synthesis as in industry. Compared to the number of methods for the oxidative cleavage of olefins, fewer methods for the oxidative cleavage of alkynes have been described, and most of these have only been tested on selected substrates. It is assumed that chemists avoid direct oxidative cleavage reactions of alkynes in their planning and instead prefer to use the corresponding oxidized olefin product for oxidative cleavage. In the review, the oxidative cleavage methods invented so far are presented in the literature. Among them are ozonolysis, transition metal-catalyzed oxidative cleavage methods, oxidative cleavages using main-group elements and lanthanide catalyzed oxidative cleavage methode.



Reagent: transition metal reagents, hypervalent main group compounds or lantanide reagents

Oxidizing agent: O_2, O_3, H_2O_2, TBHP, *m*-CPBA, $NaIO_4$...

Keywords: Oxidative cleavage, oxidative cleavage of alkynes, oxidative cleavage of olefins, transition metal-catalyzed cleavage

Cite as *Arkivoc* **2023** (i) 202211942
DOI: https://doi.org/10.24820/ark.5550190.p011.942

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1. Introduction

1. Introduction to Oxidative Cleavage of Alkenes and Alkynes

Oxidative cleavage of olefins is considered one of the most commonly used reactions both in preparative organic synthesis and in the industry.[1] The reaction consists of one or more C=C double bonds that normally are cleaved to aldehydes, ketones and/or carboylic acids. The reagents and/or catalysts are used here as strong oxidizing agents to react with olefins (Figure 1).

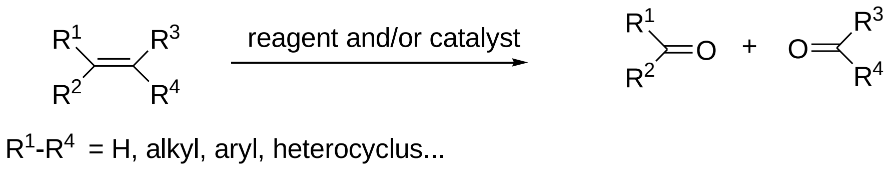


Figure 1. Oxidative cleavage of olefins to the corresponding aldehydes, ketones and/or carboxylic acids.

Oxidative cleavages of olefins were intensively studied. The reviews by Rajagopalan et al. and Bäckvall examine the methods often used in industry and in preparative synthesis.[1,2] Ozonolysis is one of the generally accepted standard methods and is used in both industrial and preparative chemistry for the oxidative cleavage of olefins.[3-7] This method has been used on a wide spectrum of substrates, as it usually brings good to very good yields, although there is a latent risk of explosion during use.[7,8]

No less common in preparative synthesis are the oxidative cleavage methods of olefins through the use of transition metals (Ti, V, Cr, Mn, Co, Cu, Ru, Rh, W, Re, Os, Ir, Au) at a higher oxidation state, which act as reagents in stochiometric amounts or as catalysts in amounts of 1-5 mol % relative to the substrate. Os[9,10] and Ru-based reagents[9,10] are the most commonly used transition metals.

Os-based catalysts: OsO_4 with $KHSO_5$; [11,12] OsO_4 with $NaIO_4$ and/or $NaClO_2$; [13-16] OsO_4 with Et_3N, KIO_4 and di-benzo-18-crown-6-ether.[17]

Ru-based catalysts: Ruthenium(II) $[RuCl(LL)_2]PF_6$ (LL = 1,3-bis(diphenylphosphino) propane, DPP; l-diphenylphosphino-2-(2'pyridyl)ethane with iodosylbenzene;[18] $RuCl_3$ with H_2O_2 [19]; *cis*-$[RuCl_2(bipy)_2]$ $2H_2O$ with $IO(OH)_5$;[20] $RuCl_3$ with $NaIO_4$ and/or pyridine,[21-23] $SiRu(H_2O)W_{11}O_3{}^{5-}$complex;[24] $[(Me_3tacn)(CF_3CO_2)_2Ru^{III}(OH_2)]CF_3CO_2$ (Me_3tacn=1,4,7-trimethyl-1,4,7-triazacyclononane);[25] Ru-(II)-perchlorate complexes;[26,27] RuO_4;[28] [*cis*-Ru(II)$(dmp)_2(H_2O)_2]^{2+}$ (dmp = 2,9-dimethylphenanthroline)[29]

Methods with the use of the remaining metals (Ti, V, Cr, Mn, Co, Cu, Rh, W, Re, Ir, Au)[9,10] for the oxidative cleavage of olefins were used and received good to very good yields.

Ti-based catalysts: Titanium- and cerium-containing mesoporous silicate with the use of H_2O_2,[30] titanium dioxide with the use of oxygen.[31]

V-based catalysts: Vanadyl acetylacetonate with H_2O_2 as an oxidizing agent.[32]

Cr-based catalysts/reagents: Pyridinium chlorochromate;[33] Chromium tristearate;[34] quinolinium dichromate.[35,36]

Mn-based catalysts/reagents: Permanganate[37] or Permanganate by adsorbed moist alumina;[38] Manganese porphyrin complex with the use of oxygen; [39,40] Mn-derived catalyst was prepared starting from the biomass of Mn-hyperaccumulating plants growing on metal-rich soils.[41]

Co-based catalysts: cobalt-salen complex with the use of oxygen;[42] $Co(acac)_2$ with the use of oxygen.[43]

Cu-based catalysts: copper chloride or copper chloride pyridine complex with the use of oxygen or TBHP; [44-49] Copper(II) complexes (CuL), wherein the ligand: 5,7,12,14-tetramethyl-1,4,8,11-tetraazacyclotetradeca-4,7,11,14-tetraene with the use of H_2O_2;[50] Binuclear copper complex where salicylate is used as ligand and oxygen as an oxidizing agent;[51] $Cu(ClO_4)_2$ with the use of oxygen.[52]

Rh-based catalysts: $(Ph_3P)_3RhCl$ with the use of oxygen.[53]

W-based catalysts: 12-tungstophosphate $[\pi\text{-}C_5H_5N^+\text{-}(CH_2)_{15}CH_3]_3(PW_{12}O_{40})^{3-}$ (CWP) with the use of H_2O_2; [54,55] $[Me(n\text{-}C_8H_{17})_3N]_3PO_4[WO(O_2)_2]_4$ with the use of H_2O_2;[56] H_2WO_4 with the use of H_2O_2;[57-60] $\{\alpha_2\text{-}Cu(L)P_2W_{17}O_{61}{}^{8-}$ or $[(Cu(L)]_2WZn(ZnW_9O_{34})_2{}^{12-}$, as catalysts, where L = NO_2.[61]

Re-based catalysts: in catalytic amount of Methyl trioxorhenium[62]

Ir-based catalysts: Iridium metal with oxygen[63]

Au-based catalysts: water soluble gold/silver nanoparticles with the use of *tert*-butyl hydroperoxides (TBHP);[64] Gold(I) neocuproine complex with the use of TBHP.[65]

In addition to these catalysts, a strong oxidizing agent is always used at least in stoichiometric amounts (such as O_2, TBHP, H_2O_2, $NaIO_4$, $NaIO_3$, etc.). The advantage of the transition metal catalyzed oxidative cleavage compared to ozonolysis is that no intermediate would be formed which poses a latent explosion risk. However, the disadvantage of the transition catalyzed methods is that these methods have not been tested for a comparably broad range of substrates as the ozonolysis method. The second disadvantage is that the used transition metals are either expensive and/or toxic, cause pollution and/or are not easily manageable in the lab. Because of latent risks of explosion using ozone, chemists apply the transition metal regents for preparative applications.

Last but not least, one of the methods developed so far can include oxidative cleavage with the use of enzymes[1,66-72] through the use of hypervalent iodine compounds[73-82] as reagents and/or oxidizing agents. In addition, reagents and/or oxidizing agents have been used for the oxidative cleavage of olefins, which do not fit into the above-mentioned categories. These include e.g. the radical oxidative cleavage of olefins using AIBN[83] or TEMPO;[84] electrochemical oxidative cleavage[85] or with the use of:

- $LiClO_4$[86]
- light and oxygen excited by porphyrin as a photosensitizer[87]
- $KHSO_5$ [88]
- triethylsilyl hydrotrioxide[89]
- disulfides[90]
- basic, neutral or acidic alumina and oxygen[91]
- $InCl_3$ and TBHP[92]
- Ceric ammonium nitrate[93]
- *N*-hydroxyphthalimide (NHPI) and oxygen[94,95]
- metal-organic framework (MOF): MIL-101 and H_2O_2 [96]
- Organoselenium compounds and H_2O_2 [97]
- Methane tetrabromide with the use of oxygen[98]
- KSF montmorillonite[99]
- CeO_2 using H_2O_2 [100,101]

Although the oxidative cleavage of olefins has been studied very well, so far, there is only one review about the oxidative cleavage of alkynes.[102] In this review, not all methods discovered so far were discussed. Therefore, we want to take a closer look at the oxidative cleavage of alkynes in some detail. In order to create a better overview, the methods have been grouped according to the type of oxidative cleavage.

2. Importance of the Oxidative Cleavage of Alkynes in Synthesis

Compared to the oxidative cleavage of alkynes, the methods of oxidative cleavage of olefins are mostly used in the preparative synthesis and total synthesis of natural products. Most chemists avoid the direct oxidative cleavage of the alkynes, instead reducing the alkynes to the corresponding olefins. After that they mostly use the ozonolysis method or the catalyst OsO4 with an oxidizing agent (e.g. *m*-CPBA or H_2O_2, etc.) (Figure 2).

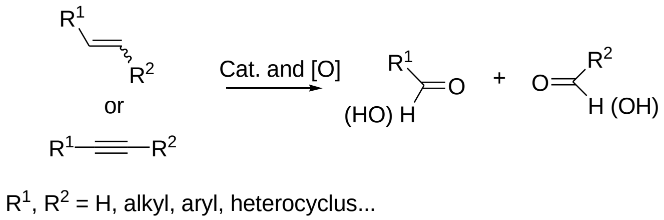


Figure 2. Oxidative cleavage of alkynes and its corresponding olefins.

In the third part, the oxidative cleavage of alkynes using ozone known as "*ozonolysis*" will be studied. In the fourth part, we want to study the oxidative cleavage of alkynes using transition metal and an oxidizing agent such as O_2, TBHP, *m*-CPBA, $NaIO_4$, $NaIO_3$, H_2O_2…etc. In the fifth part, the oxidative cleavage of alkynes using main group elements will be studied. Although the ozonolysis method can be subordinated to the part of the oxidative cleavage with the use of main group elements, we want to treat it in detail as a separate method.

3. Ozonolysis of Alkynes

Ozonolysis is a method that is used not only for the oxidative cleavage of alkenes but also for the oxidative cleavage of alkynes. The first known and widely accepted mechanism for the ozonolysis of alkynes was proposed by Criegee *et al.* and Bailey *et al.* Reaction intermediates **2**-**7** were detected and/or characterized based on the different acetylene derivatives that were produced in different reaction conditions.[103-105] When compound **1c** was used as a substrate in carbon tetrachloride, an amorphous, polymer product **12** was obtained. In contrast, in the ozonolysis of the same substrate in acetic acid, intermediate **4** was detected instead (G = $OCOCH_3$). The addition of pyridine to the reaction medium effected an oxidative cleavage of the C-C σ-bond to form the corresponding products **16a-b** over probable intermediates **4** and **5**. The investigation into the reaction mechanism of Bailey et al. confirmed the formation of these intermediates (Figure 3).

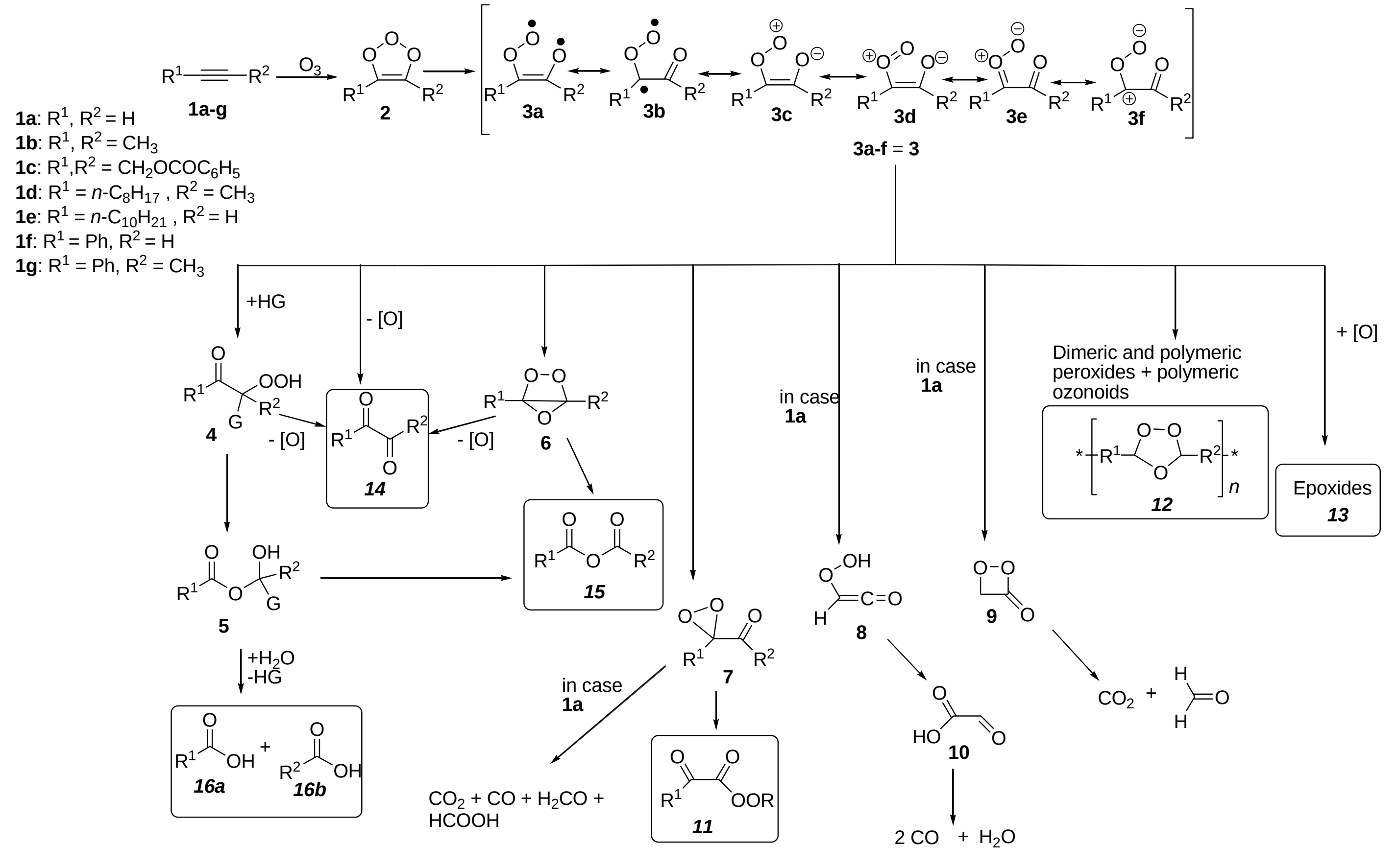


Figure 3. Criegee Mechanism of the ozonolysis of alkynes.

Silbert *et al.* have studied the ozonolysis of 2-undecyne (**1d**) and 1-dodecyne (**1e**)**.** They were able to show in both MS and GC analysis that intermediates **3a-f** are detected at -70 °C. However, with rising temperature, they have described that the intermediates **3a-f** convert to product **11.**[106]

Bailey *et al.* have further studied the mechanism of peroxide ozonolysis and non-peroxide ozonolysis with the use of the substrate **1f** and **1g** in methanol and ethanol. They have also confirmed that the first intermediate should be **3a-f**, resulting from a 1,3-dipolar cycloaddition. Intermediate **18** (**4**: G = OEt or OMe) was isolated with a 25% yield in the solvent. The decomposed main product was proven by the detailed studies as intermediate **19**, which could not be isolated. As a reason for the formation as the main product, they gave the resonance stabilization of the carbonyl oxide moiety in intermediate **17b** by the benzene ring. They suspect that the intermediate **17b** was formed in a ratio of 2.5:1 to the intermediate **17a** in the reaction environment. However, the intermediate **17b** is decomposed at room temperature[105,107] (Figure 4).

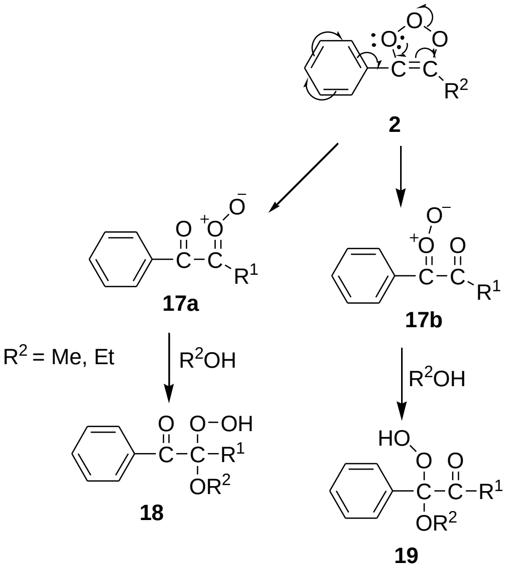


Figure 4. Study of Criegee mechanism by Bailey *et al.*

Miller et al. have conducted a number of kinetic studies on the ozonolysis of alkynes. They have tested a number of propargyl compounds [$HCCCH_2G$, where G = Cl, Br, $OCOCH_3$, OH, NMe_2, $(CH_2)_6CH_3$] in chlorinated solvents. Their results reinforce the assumption that ozone performs a 1,3-dipolar cycloaddition to the alkyne to form the first intermediate **2**.[108] DeMore et al. determined the rate constant, the Arrhenius parameters and the activation energy for the ozonolysis of acetylenes and simple alkynes.[109-111] Later in situ IR studies by DeMore et al.[111] and Dallwingk et al.[112] have shown that at -45 °C, the carbonyl oxide peak slowly disappears and an anhydride carbonyl peak is formed instead. Another study of the reaction mechanism was carried out by using 2-butyne as a substrate in methylene chloride at -70 °C. After completion of the ozonolysis of 2-butyne, the resulting intermediate was immediately epoxidized in order to capture the intermediate. The intermediates that they analyzed, which decomposed at -50°C, confirmed the formation of trioxolene (**2**, R^1, R^2 = CH_3).[113,114] Further investigations have shown that the intermediate **3** can immediately cleave using a reducing agent with dissociation of oxygen to form product **4** or rearrange to the product **6** (Figure 3 and Figure 5).[108,115]

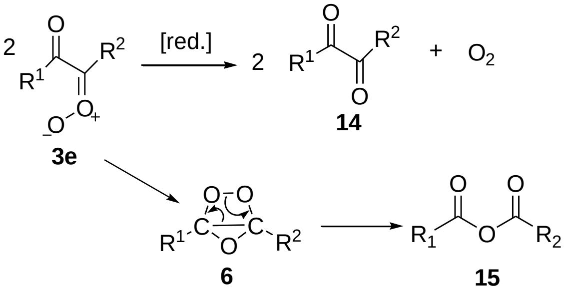
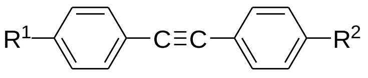


Figure 5. Mechanism in protic solvent suggested by Miller et al. and Jackson et al.

Later, Desvergne et al. studied the ozonolysis of crystals of diphenyl acetylene and methoxylated tolan and characterized adsorbed products on silica gel. The products resulting from crystalline diphenylacetylene and the products obtained from solutions were identical. For tolan, 80% benzoic anhydride and 15% benzil were obtained[116,117] (Figure 6).



20: $R^1 = R^2 = H$
21: $R^1 = OCH_3, R^2 = H$
22: $R^1 = R^2 = OCH_3$

Figure 6. Diphenylacetylene and methoxylated tolans.

Kinetic studies were conducted in the gas phase for the ozonolysis of acetylene and its derivatives. Studies have shown that ozonolysis in the gas phase differs from the liquid phase, which also have different intermediates and products compared to the gas phase reaction.[109,118-121]

The following reaction mechanism for the gas phase ozonolysis was proposed by DeMore (figure 7).[110]

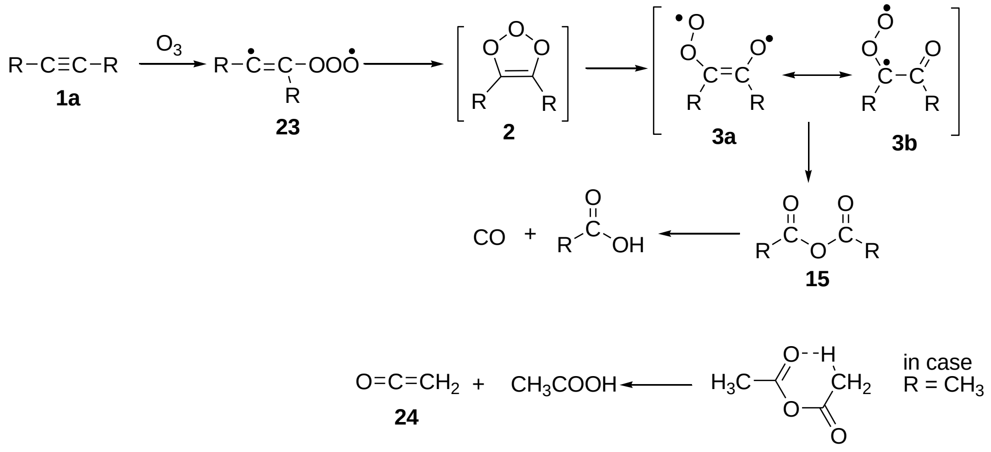


Figure 7. Mechanism of vapor-phase ozonation of alkynes.

According to DeMore et al., the trioxolene intermediate **2** is produced by two steps of radical reaction and has a very short lifetime. The main path of the reaction is via the transformation of intermediates **3a** and

3b to the anhydride **15**, which was obtained in the ozonolysis in the liquid phase in figure 4. Ketene **24**, which was observed in the ozonolysis of 2-butyne, was formed according to DeMore et al. by the decomposition of acetic acid anhydride (figure 3).

In 2001, the reaction mechanism of the ozonolysis of acetylene "**1a**" was theoretically calculated and described in detail by Cremer *et al.,* which is shown in figure 3 [122]. The ozonolysis of acetylene was investigated using CCSD(T), CASPT2, and B3LYP-DFT in connection with a 6-311+G (2d,2p) basis set. The reaction is initiated by the formation of a van der Waals complex followed by a [4+2] cycloaddition between ozone and acetylene (activation enthalpy ΔH_a = 298 kcal/mol; experiment, 10.2 kcal/mol), yielding 1,2,3-trioxolene **2**, which rapidly opens to α-ketocarbonyl oxide **3**. Alternatively, an oxygen atom can be transferred from ozone to acetylene, thus leading to formyl carbene, which can rearrange to oxirene or ketene. They found that the key compound is **3** in the ozonolysis of acetylene, because it is the starting point for the isomerization to the corresponding dioxirane **7**, for the cyclization to trioxabicyclo[2.1.0]pentane **6**, for the formation of hydroperoxy ketene **8**, and for the rearrangement to dioxetanone **9**. Intermediates **6**-**9** rearrange or decompose with barriers between 13 and 16 kcal/mol to yield as major products formanhydride, glyoxal, formaldehyde, formic acid, and (to a minor extent) glyoxylic acid.

Ozonolysis of alkynes has already been tested for a wide variety of substrates: an example of the oxidation of alkynes to 1,2-dicarbonyl compounds was investigated by Wisaksono et al. They have taken acetylenic ethers as the starting materials. They have obtained α-keto ester in moderate yields. In order to obtain α-keto ester, reducing agents were used in the reaction (Figure 8).[123,124]

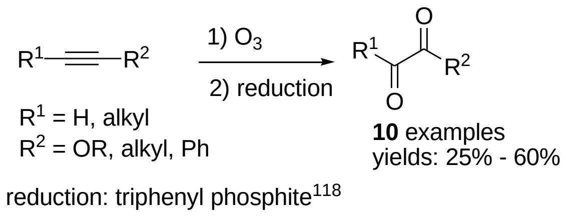


Figure 8. Ozonolysis of alkoxyacetlynes to α-ketoesters.

Cannon et al. have tested three different propargylic alcohols **24a**-**c** for ozonolysis. They obtained glycolic acid products **25a**-**c** in moderate to good yields as oxidative cleavage products, if ozone was not used in excess. When compounds **24b** was used as starting material by the application of ozone in excess, the product **26** was obtained quantitatively. Another experiment showed that when sodium hydrogen carbonate was added, product **27** was immediately formed in 15% yield upon ozonolysis of starting material **24b** (Figure 9).[125]

Another unusual reaction was performed by Lehmann et al.: the ozonolysis of 2,5-dimethyl-3-hexyne-2,5-diol (**28a)** in carbon tetrachloride, wherein only the oxidative aging product hydroxyisobutyric acid **36** was obtained. In aqueous solutions, **28a-b** react to form product **35** in ozonolysis. Lehmann et al. have also proven that the compound **32** reacts in hydrogen peroxide to compound **35**.[126] Bailey et al. suspected that the associated anhydride **31** should also be produced in aqueous hydrogen peroxide solution via Baeyer-Villiger rearrangement **30.** Their presumption was that compound **35** would arise in aqueous hydrogen peroxide solution via the cyclization of the intermediate **30** (Figure 10).[104]

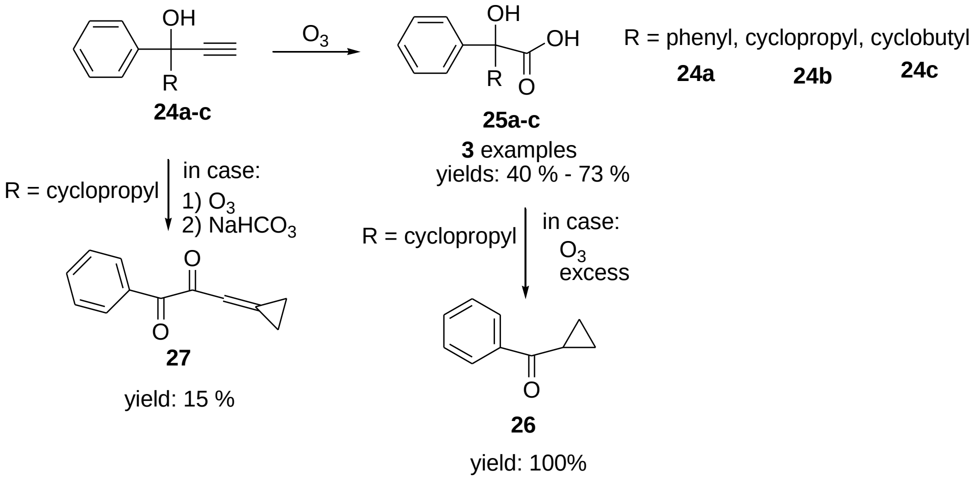


Figure 9. Ozonolysis of acetylenic alcohols

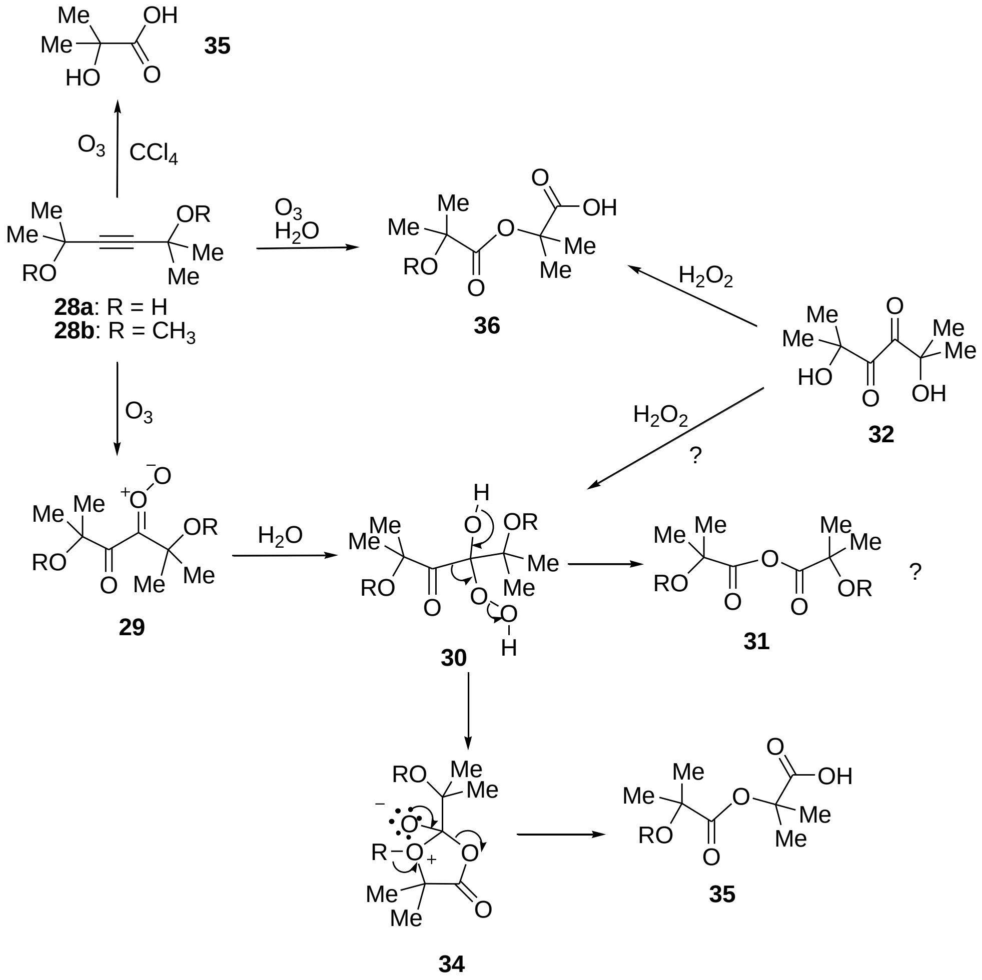


Figure 10. Ozonolysis of 2,5-dimethyl-3-hexyne-2,5-diol.

An interesting example in the literature is the ozonolysis of acetylene dicarboxylic acid **36** in concentrated formic acid. Bernatek et al. have received the compound **40** in good yield. The key step is the formation of ketene **38** by the decarboxylation of **37**. After that, the water adds to the ketene to form product **40.** The suspected mechanism is shown below (Figure 11).[127]

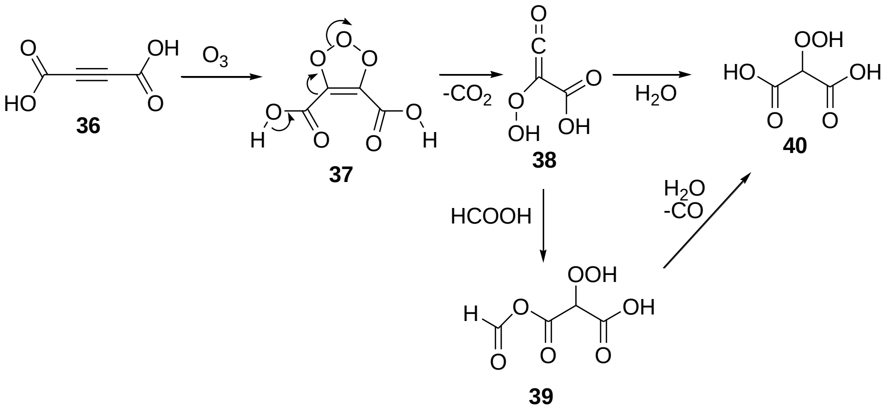


Figure 11. Ozonolysis of acetylenedicarboxylic acid **36**.

Eichelberger et al. developed a synthesis of phosphorus compounds which have an alkyne functional group in α-position. Ozonolysis of phenyl ethynyl diphenyl phosphine oxide (**41**) gave benzoic acid (**42**), formic acid (**45**), and diphenyl phosphinic acid (**44**), which was formed from diphenyl phosphinic carboxylic acid **43**. They obtained the products in very good yields (Figure 12).[128]

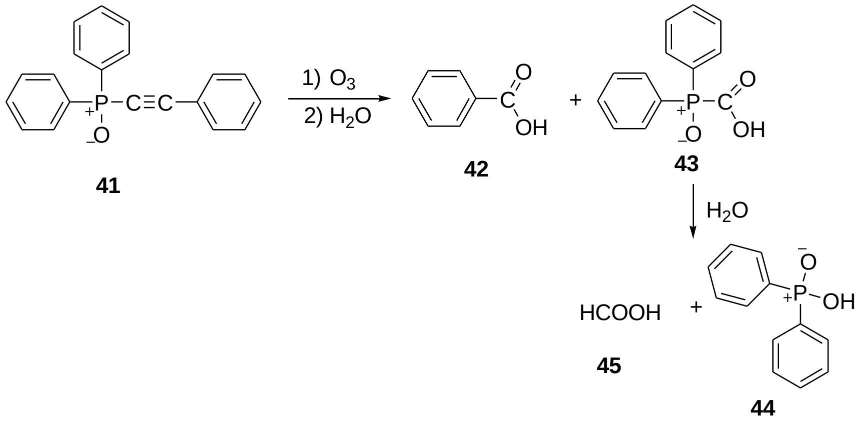


Figure 12. Ozonolysis of phenylethynylphosphine oxide (**41**).

As can be seen, it depends on the reaction condition whether 1,2-dicarbonyl compounds or a peroxo compound are obtained as the main product(s) in the ozonolysis of alkynes.

4. Transition Metal-catalyzed Oxidative Cleavage of Alkynes

4.1. Ru-catalyzed oxidative cleavage of alkynes

Ruthenium-catalyzed oxidative cleavage of the olefins was discussed above. It is mostly used for the oxidative cleavage of olefins; $RuCl_3$ is used as a catalyst with a strong oxidizing agent (see introduction).

Yang et al. described a method in 2003 using RuO_2 as a catalyst and $KHSO_5$ as an oxidizing agent in a mixture of acetonitrile, ethyl acetate and water, which covers a wide range of alkyl alkynes and aryl alkynes. They tested 12 substrates **46**, **48-59** and obtained yields ranging from good to very good. They found that when alkynes **55-57** are used as starting materials for the oxidative cleavage, the corresponding carboxylic acids are obtained. However, if they have β-halogenealkynes such as compound **59** used, then Yang et al. observed cyclization or lactone formation after the oxidative cleavage (Figure 13).[129]

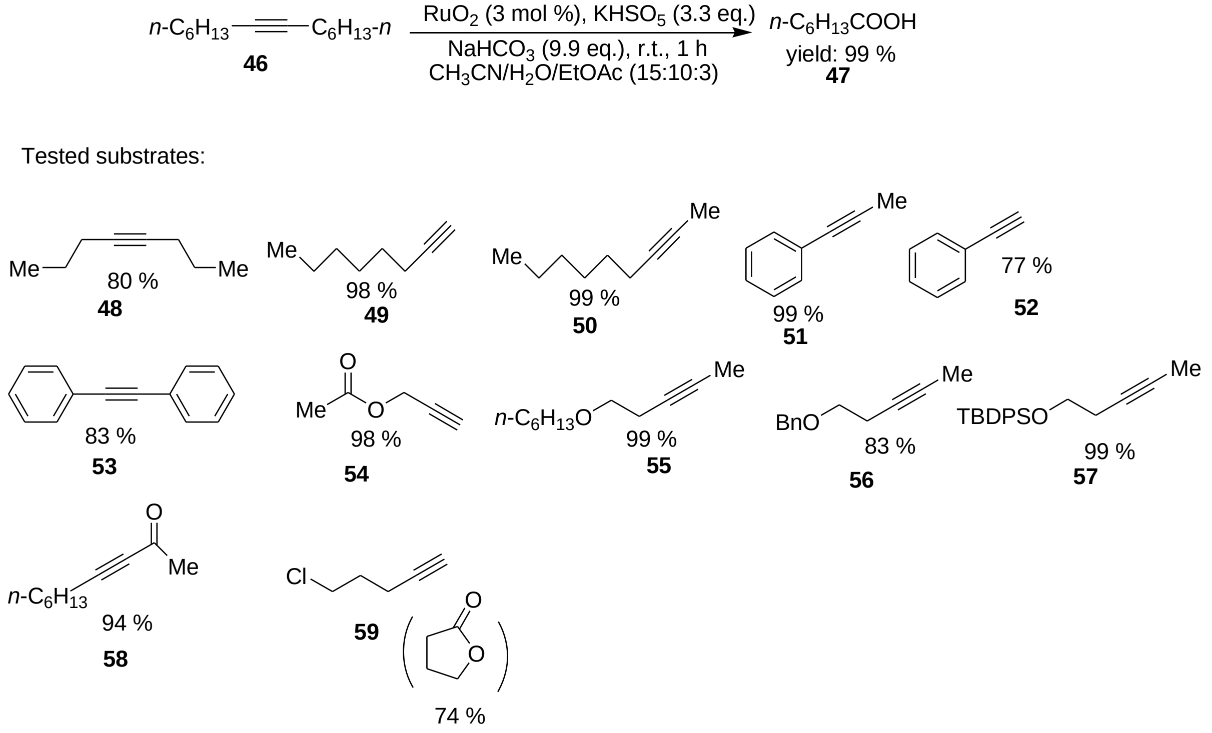


Figure 13. Ozonolysis of alkynes using RuO_2 as catalyst and $KHSO_5$ as oxidizing agent.

According to Yang et al., the reaction mechanism of oxidative cleavage consists mainly of two steps. The first step in the reaction mechanism is the formation of the active catalyst by peroxomonosulfate anion (HSO_5^-). This is responsible as an oxidizing agent to oxidize ruthenium dioxide in situ to produce the active catalyst ruthenium tetroxide “RuO_4”. The ruthenium tetroxide adds to alkyne to form intermediate **62**. This intermediate cleaves oxidatively to form 1,2-dicabornyl compound **63**. This creates the catalyst, which in turn is oxidized by an oxidizing agent (in this case HSO_5^-). This intermediate **63** can be isolated without problems if strong oxidants are not used. For example, Ren et al. tested as catalyst [Ru (cymene)Cl_2]$_2$ or $RuCl_3$, as oxidizing agent TBHP and obtained 1,2-diketones up to a very good yield. Miao et al. have tested “$RuCl_3$” as a catalyst and NaOCl as an oxidizing agent and obtained 1,2-diketones up to very good yields.[130-132]

In the second step, the peroxomonosulfate anion (SO_5^{2-}) **64** attacks the carbonyl carbon of intermediate **63** to form intermediate **65**. Intermediate **66** rearranges under thein a Baeyer-Villiger rearrangement. An anhydride **66** is thereby formed. In the presence of water and an acidic environment, the ester cleaves into carboxylic acids **67** and **68** (Figure 14).

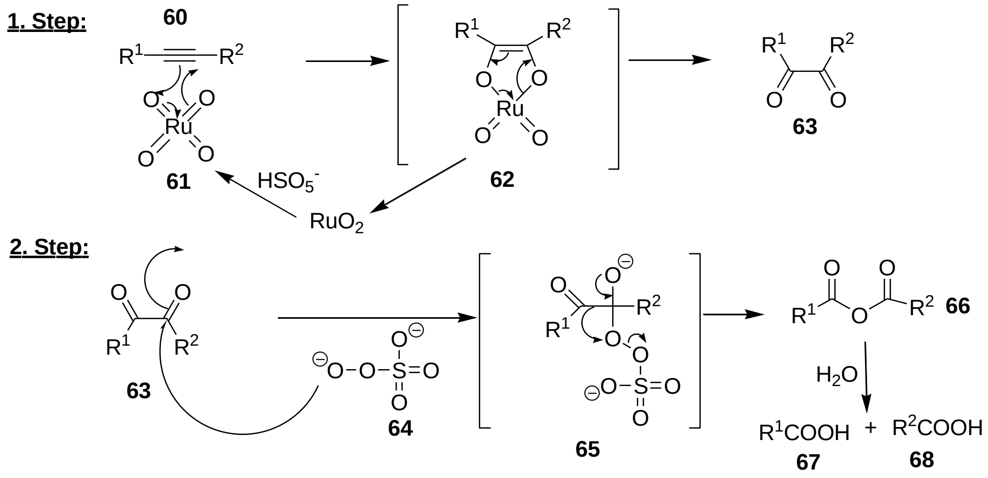


Figure 14. Proposed general mechanism of oxidative cleavage of alkynes using RuO_2 as catalyst and $KHSO_5/NaHCO_3$ as oxidazing agent.

Griffith et al. found out that the yields of the oxidative cleavage products using $RuCl_3$ as a catalyst and $IO(OH)_5$ as an oxidizing agent are strongly dependent on the used solvent(s). The best yields were obtained in carbon tetrachloride.[21] Griffith et al. have described the following in general terms in their detailed review of the ruthenium-based oxidation of organic substances: The reagent consists of a strong oxidizing agent (such as O_2, H_2O_2, TBHP, $NaIO_4$, $NaIO_3$,…etc.) and a catalyst, which is a salt of a transition metal (ruthenium dioxide) in oxidation state IV. Generally, the catalyst is first oxidized with a strong oxidizing agent to form the active catalyst in situ, which reacts with the starting material. In this case, ruthenium is oxidized by sodium periodate to achieve oxidation state VIII, whereby the oxidizing agent is reduced. In this case, sodium periodate is reduced to sodium iodate, which is used in stoichiometric amounts. In other words, Ru(VIII) oxidizes the substrate to the product, reducing itself to Ru(IV). During the oxidation, a total of two oxygen atoms is transferred to the substrate via the catalyst per using one molecule substrate. This, in turn, is oxidized by $NaIO_4$, whereby the catalytic cycle starts anew (Figure 15).[133]

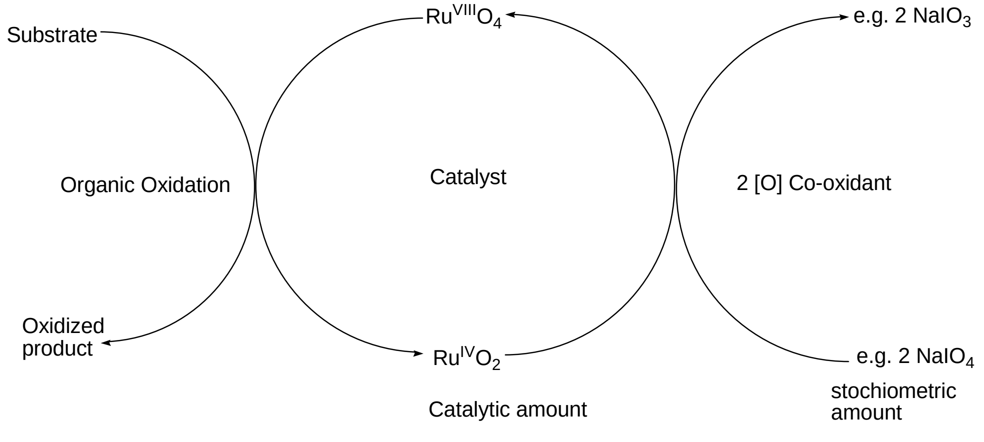


Figure 15. Catalysis cycle of ruthenium-catalyzed oxidative cleavage.[133]

Potential diagram of RuO_4 runs over $[RuO_4]^-$ to dianion $[RuO_4]^{2-}$, then to RuO_2 with +1.0 V, +0.59 V and +0.2 V respectively (Figure 16).[134,135]

$$RuO_4 \xrightarrow{1.0\ V} [RuO_4]^- \xrightarrow{0.59\ V} [RuO_4]^{2-} \xrightarrow{0.2\ V} RuO_2$$

Figure 16. Reaction of RuO_4 to RuO_2.

The infrared spectra of gaseous and pure liquid ruthenium tetroxide show that, on the assumption of T_d molecular symmetry, $v_3(F_2)$ is at 913 cm^{-l} and $v_4(F_2)$ at 330 cm^{-l}. The formation of RuO_4 was also confirmed by Raman spectroscopy (Figure 17).[136]

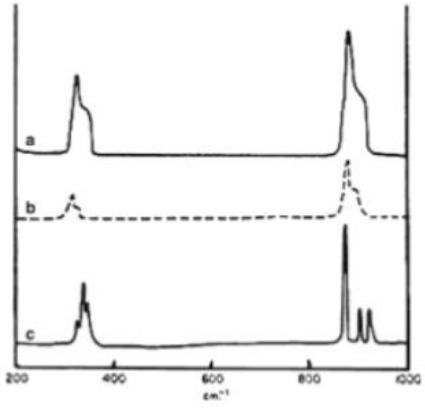


Figure 17. Raman spectra of RuO_4 (a) pure liq.; (b) 5% aqueous soln.; (c) solid (Reproduced from the Royal Society of Chemistry).

The first article about the oxidative cleavage using ruthenium was published in 1956 by Pappo et al. , who used RuO_4 as a catalyst. They generated the catalyst *in situ* for the oxidation of 1,2-bis (1-acetoxycyclohexyl) ethyne (**69**) by the unusual mixture $RuO_2/Pb(OAc)_4$/aq. AcOH to diketone **70** : minimal experimental details were given in the manuscript (Figure 18).[131]

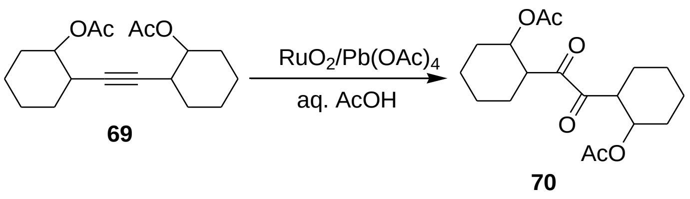


Figure 18. First tested oxidative cleavage reaction of alkynes using ruthenium metal.

Kumar et al. found a method using charcoal-supported and recyclable elemental ruthenium (Ru/C (5%)). The catalyst is prepared in benzene using charcoal (KB, 100 mesh, surface area 1500 m^2/g, 1.25 g) and $[RuCl_2(p\text{-cymene})]_2$ (250 mg) at room temperature, which is filtered off and washed with DMF.[137]

Herein, they report for the first time a recyclable catalytic system for performing the oxidative cleavage of alkynes to carboxylic acids and alkenes to aldehydes, respectively, by using Ru/C (5% grafted), which can be reused without loss of activity. In this methodology, Ru/C (5%) was used. Initially, oxidation of phenylacetylene (1 mmol, 120 mL) was checked using Ru/C (2.5 mol%, 50 mg) in a biphasic solvent of water–acetonitrile (1:1, 5 mL), $NaHCO_3$ (2.5 equiv.) at room temperature using oxone (614 mg, 1 mmol) as the stoichiometric oxidizing agent (Figure 19).[138]

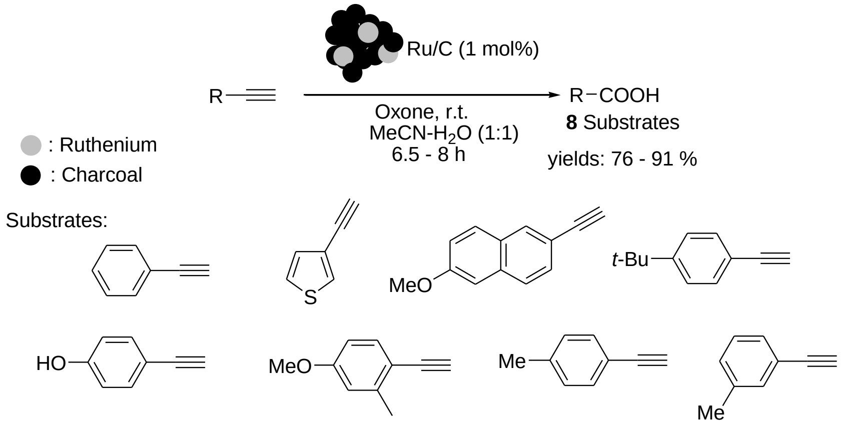


Figure 19. Oxidative cleavage using Ru/C (5 % grafted) as recyclable catalyst and oxone as oxidazing agent.

The advantage of this method is that the catalyst Ru/C is a heterogeneous catalyst and can be easily separated from the reaction environment by simple filtration and can be restored (Table 1). This catalyst also has the advantage that it can be used in environmental friendly solvents such as water.

Table 1. Recycling of the catalyst Ru/C in oxidative cleavage of 1-ethynyl benzene.

Ru/C	Yield (%)
Cycle 1	89
Cycle 2	89
Cycle 3	88
Cycle 4	88
Cycle 5	87

According to Kumar et al. the reaction mechanism proceeds as followed: first, the intercalated Ru/C **71** is oxidized to ruthenium dioxide intermediate **72** using oxone as an oxidizing agent. At this step, the active heterogeneous catalyst **72** attacks the substrate under formation of intermediate **73**. Electrocyclic reaction produces carboxylic acid as the end product, with catalyst **71** being regenerated (Figure 20).

Another catalyst ruthenium complex is $[(Me_3tacn(CF_3CO_2)_2Ru^{III}(OH_2)](CF_3CO_2)$ **76** which is used as a silica gel-immobilized or supported form "**76-SiO₂**" where Me_3tacn = 1,4,7-trimethyl-1,4,7 -triazacylcononane **74**, was prepared by Che et al. and used for the oxidative cleavage of alkynes (Figure 21). The catalyst is heterogeneous and recyclable that is easily separable from the reaction environment and for the oxidation of alcohols and also can be used for the oxidative cleavage of olefins.[25,139] Catalyst **76** was prepared from commercially available $[(Me_3tacn)Ru^{III}Cl_3]$ **75** in trifluoroacetic acid. For the synthesis of heterogeneous "**76-SiO₂**", immobilization of **76** was undertaken by stirring an ethanolic solution of **76** with chromatographic grade commercial silica gel at room temperature. Removal of the solvent by rotary evaporation at 40 °C afforded the heterogeneous Ru catalyst, designated as **76-SiO₂** (1% w/w), as a pale yellow solid (Figure 21).[139]

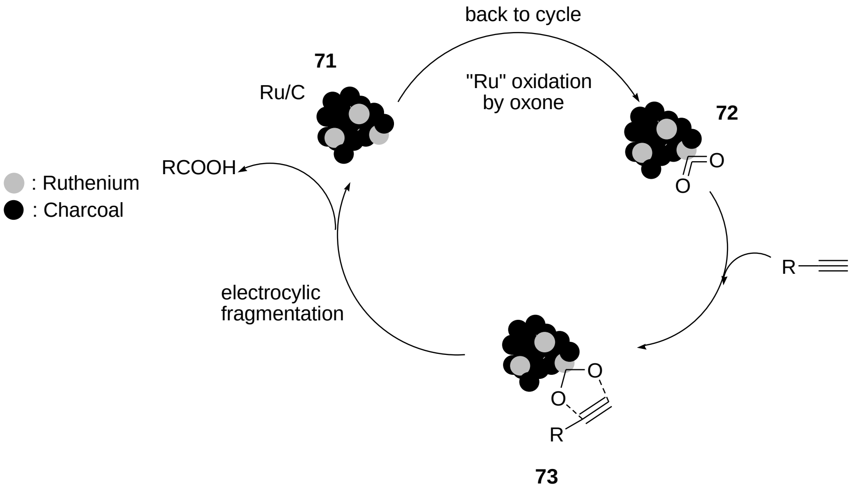


Figure 20. Reaction mechanism of oxidative cleavage of alkyne using Ru/C as catalyst and oxone as oxidizing agent.

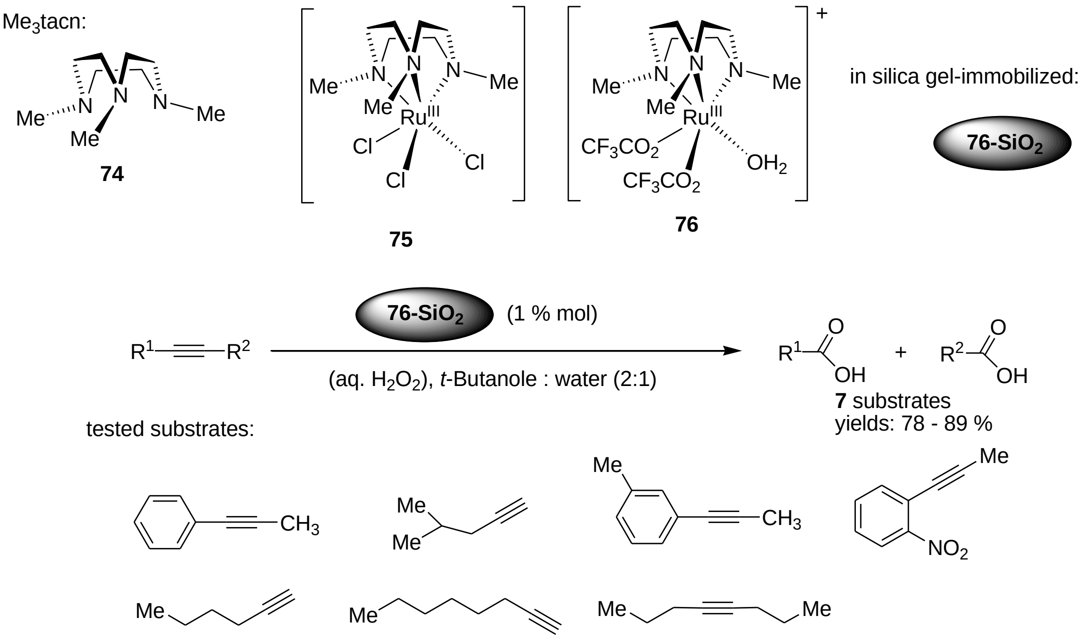


Figure 21. Oxidative cleavage of alkynes using [(Me$_3$tacn(CF$_3$CO$_2$)$_2$Ru^{III}(OH$_2$)](CF$_3$CO$_2$) 80 as catalyst and aqua H$_2$O$_2$ as oxidizing agent.

Che et. al. have tested not only alkyne substrates, but a range of olefin substrates and 1,2-diols. Unfortunately, they did not propose a mechanism for the oxidative cleavage of alkyne in their manuscript. Instead, they studied the reaction mechanism with a few substrates using ESI-MS.Based on their studies using the ESI-MS and starting materials, the reaction mechanism could proceed based on their studies as follow: [25,136] (Figure 22): first, the trifluoroacetate ligands and the water cleave from the catalyst **76**, which was fully characterized by X-Ray analysis[25], and at the same time the ruthenium is oxidized using the oxidizing agent (here is the oxidizing agent: hydrogen peroxide). The intermediate **77** is formed in situ, complexes the olefin under formation of **78**. The simultaneous addition of two oxygen atoms to olefin forms en-1,2-diol complex **79.** They believe that the rate-determining step is the [3+2] addition of the ruthenium dioxo compound to olefins, as shown in transition state **79**. This react further under the reorganisation of the σ-Bond of five ring intermediate **79** to the corresponding 1,2-dicarbonyl complex intermediate **81,** it is formed the oxidized products**.** The intermediates **77**, **80** and **81** were confirmed using ESI-MS. After oxidative cleavage of the intermediate **80** again, it is formed the corresponding carboxylic acids.

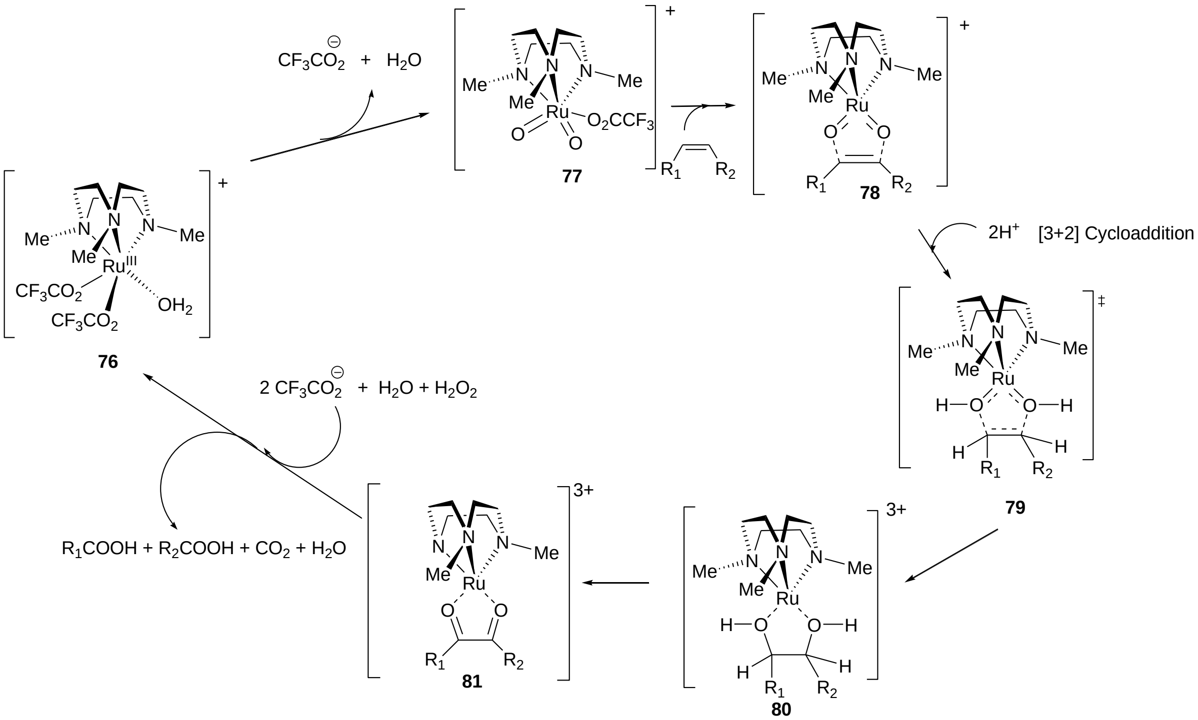


Figure 22. Proposed reaction mechanism for the oxidative cleavage of alkyne using catalyst 80 and aqua H_2O_2 as oxidizing agent.

Che et al. have tested the oxidative cleavage of alkynes and olefins with ruthenium nanoparticles immobilized on hydroxyapatite "*nano*-RuHAP", which is a heterogeneous catalyst and recyclable[140]. They mostly used this heterogeneous catalyst for the oxidative cleavage of olefins. In their manuscript, only one alkyne substrate is tested for the oxidative cleavage using "*nano*-RuHAP". The catalyst "*nano*-RuHAP" was prepared as followed: First, according to Fievet's protocol,[141] ruthenium colloids were synthesized by the reduction of $RuCl_3$•X H_2O (0.32 mmol) in 1,2-propanediol (100 mL) in the presence of sodium acetate (1 mmol) at 150 °C. The ruthenium reduction was scanned using UV/VIS spectroscopy. The disappearance of the peak in 400 nm indicated that the reaction has already ended. The ruthenium colloid (3.2 mm) that is produced in this way, showed excellent stability. Successful immobilization of the ruthenium nanoparticles was achieved by treating the colloidal solution with calcium hydroxyapatite (0.4 g) and H_2O (50 mL) for 24 h[140,142]. The following reaction was tested with the catalyst "*nano*-RuHAP". The nano-RuHAP with 1-(prop-1-ynyl)benzene (**82a**) as substrate and oxidant (oxone) in acetonitrile-water mixture was used. The oxidative cleavage took place in 82% yield for benzoic acid (**82b**) (Figure 23).

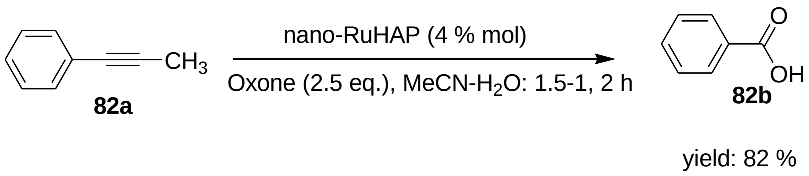


Figure 23. Oxidative cleavage of alkyne using ruthenium nanoparticles.

Che et al. have not suggested a mechanism in their manuscript. However, they propose that the oxidative cleavage of phenylacetylenes with *nano*-RuHAP would proceed in a similar way to the reaction mechanism described and discussed in figure 20. The only difference is that no charcoal is used here, instead the ruthenium nanoparticles are surrounded by calcium hydroxyapatite.

Another interesting example is presented by Datta et al. about the oxidative cleavage of 1,1-alkyl ethynyl alcohols.[143] This is the first example of a reaction, whereby no strong oxidizing agent is used. They synthesized first the catalyst **87** by using Chan et al.'s protocol (Figure 24).[144]

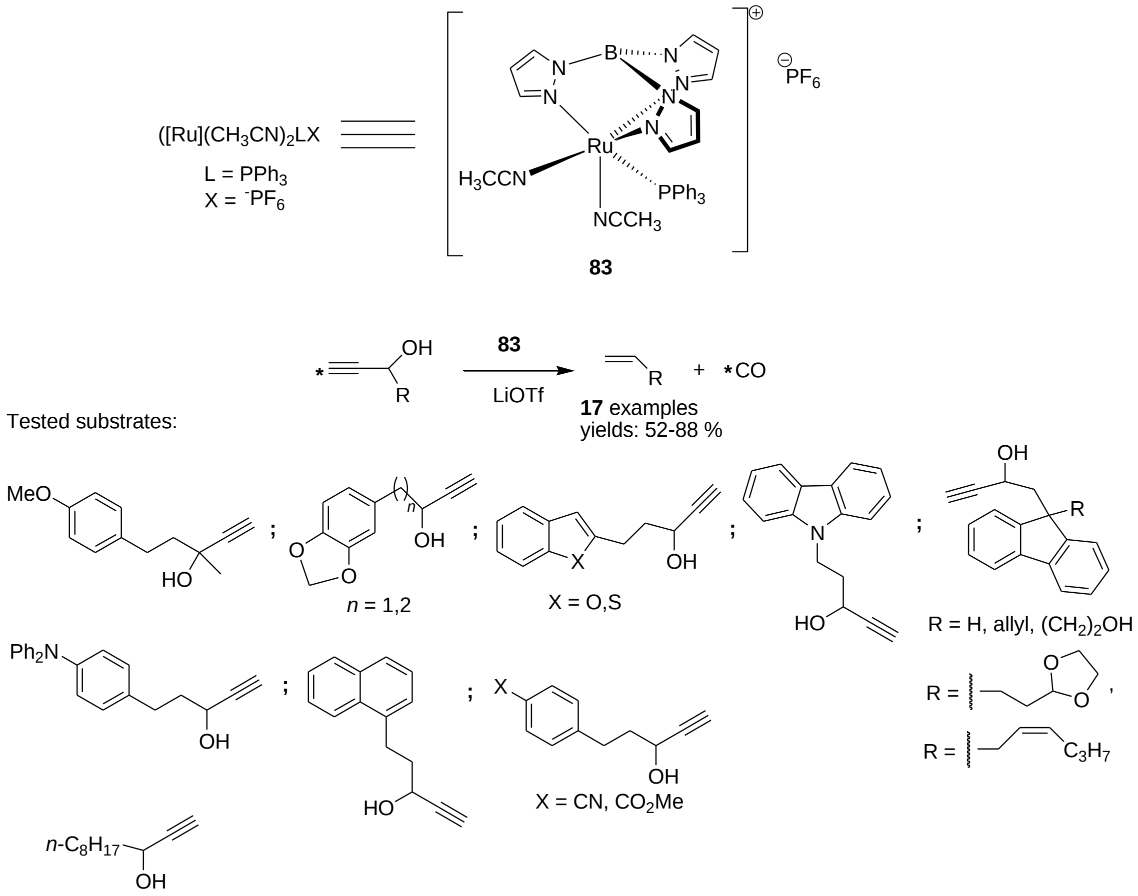


Figure 24. Oxidative cleavage of 1,1-alkyl ethynyl alcohols using **83**.

The following mechanism has been proposed for the oxidative cleavage of 1,1-dialkyl ethynyl alcohols: According to Datta et al. through the dissociation of the catalyst **83**, the active catalyst **84** is formed in situ. An acetonitrile ligand is removed and the triple bond coordinates to the Ru-metal forming a weak π-alkyne complex **85**.[145,146] The π-alkyne complex changes to a σ-complex through the rearrangement of the alkyne proton to ruthenium and the intermediate **86** is formed, whereby the triphenylphosphine ligand is cleaved. In the presence of lithium triflate, the hydroxide anion is cleaved by lithium, whereby ruthenium allenylidenium species **87** is formed.[147-151] The attack of the hydroxide anion produces ruthenium acyl species **88**, which is further formed into intermediate **89** through decarbonylation. The product is formed by the elimination of carbon monoxide, and the catalyst is regenerated in situ (Figure 25).[152-156]

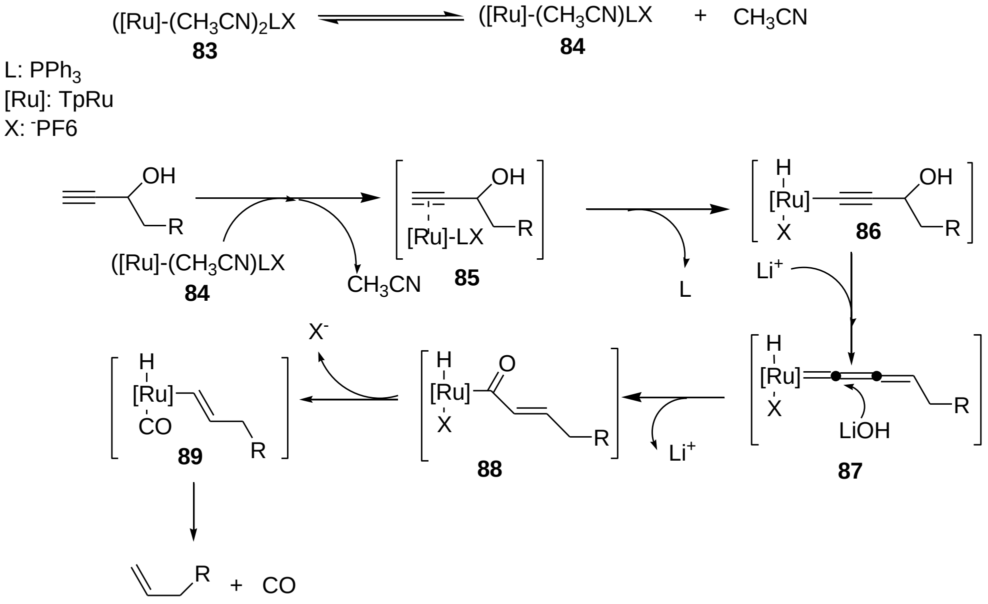


Figure 25. Proposed mechanism of the oxidative cleavage of 1,1-dialkyl ethynyl alcohols using **83** as catalyst.

The mechanism of this new process was elucidated on the basis of the results of an isotope-labeling experiment. The experiments using deuterated substrates confirmed the mechanism proposed by Datta et al. They first made substrate **90** and, as expected, the deuterium was found in the same place of compound **91**. A *cis* and *trans*-product mixture **93** was detected on the substrate **92**. Isotope labeling with O^{18} (56% enriched) of the hydroxy group of substrate **94** revealed 45% heavier carbon monoxide **95** (Figure 26).

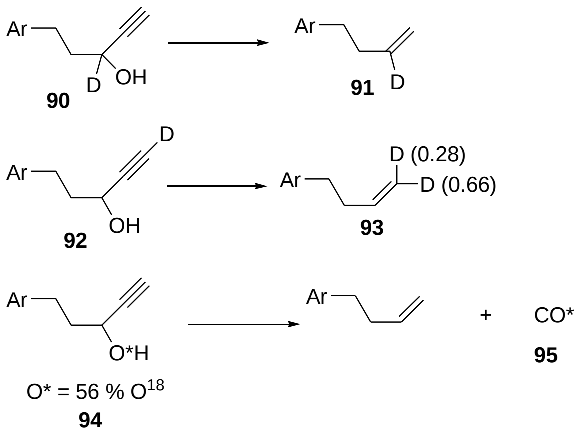


Figure 26. Isotope labeled substrates for the determination of the mechanism of oxidative cleavage of 1,1-dialkyl ethynyl alcohols.

Shen et al. have used aryl and alkynyl propargyl ethers as substrates for the oxidative cleavage using ruthenium metal. Aryl and alkynyl propargyl ethers react to aryl and alkynyl ketones by the use of $[TpRuPPh_3(CH_3CN)_2]PF_6$ **83** as a catalyst in a mixture from water and dichloroethane (Tp = tris (1-pyrazolyl) borate). Carbon dioxide and ethene were observed in the reaction. This reaction is another example of the indirect oxidative cleavage of the alkynes in the literature. Shen et al. tested the oxidative cleavage for 17 different alkynes and obtained good to very good yields (Figure 27).[157]

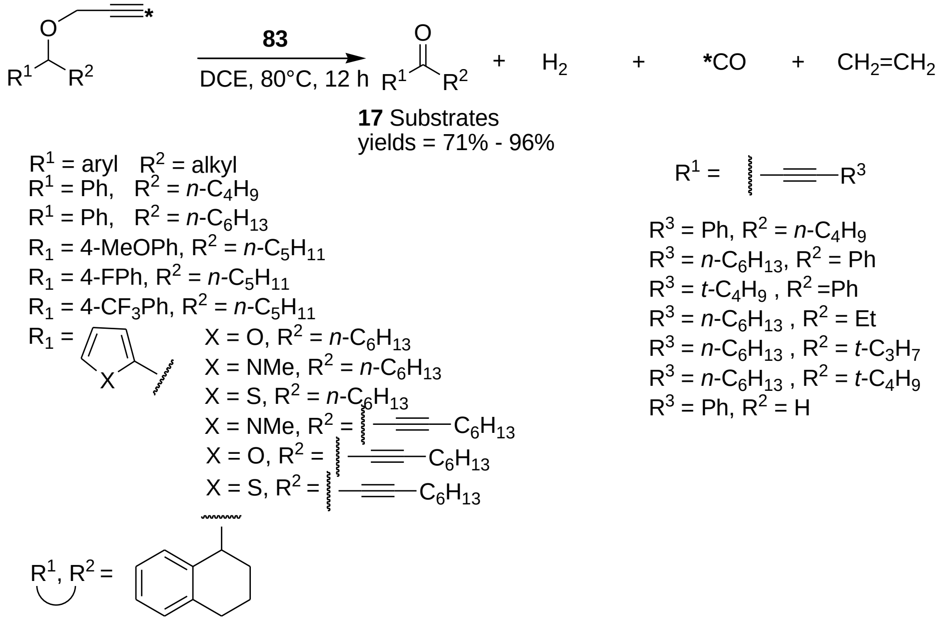


Figure 27. Oxidative cleavage of aryl and alkynyl propargyl ether using catalyst **83** and water.

Datta et al. published another article about the oxidative cleavage of other types of alkynes. The reaction mechanism is similar to the one in figure 24. With the addition of **96** to catalyst **83**, intermediate **97** is formed, whereby the proton of the alkynes rearranges to ruthenium metal. A proton of the ether is eliminated and ruthenium-allenylidenium intermediate **98** is formed, just like intermediate **87** in the reaction mechanism of 1,1-alkyl ethnyl alcohols, while the alcohol group cleaves from the ether. At this point, the reaction mechanism of 1,1-alkyl ethnyl alcohols (Figure 24) differs from that of aryl and alkynyl propargyl ether (Figure 28). In figure 24, the LiOH acts as an additive on the ruthenium-allenylidenium intermediate **91**, in contrast to the reaction mechanism in figure 28, the alcohol that is split off attacks on the ruthenium-allenylidenium intermediate **98**, thereby producing the intermediate **99**. This results from the cleavage and rearrangement of the proton intermediate **100**, which is attacked by water to the enol carbon. The product **101** and the intermediate **102** are formed. Hydrogen gas is split off by the addition of protons to ruthenium (**103**). Through the addition of two ligands (CH_3CN) to intermediate **104** and simultaneous elimination of the carbon monoxide and ethylene from intermediate **104**, catalyst **83** is regenerated (Figure 28).[157]

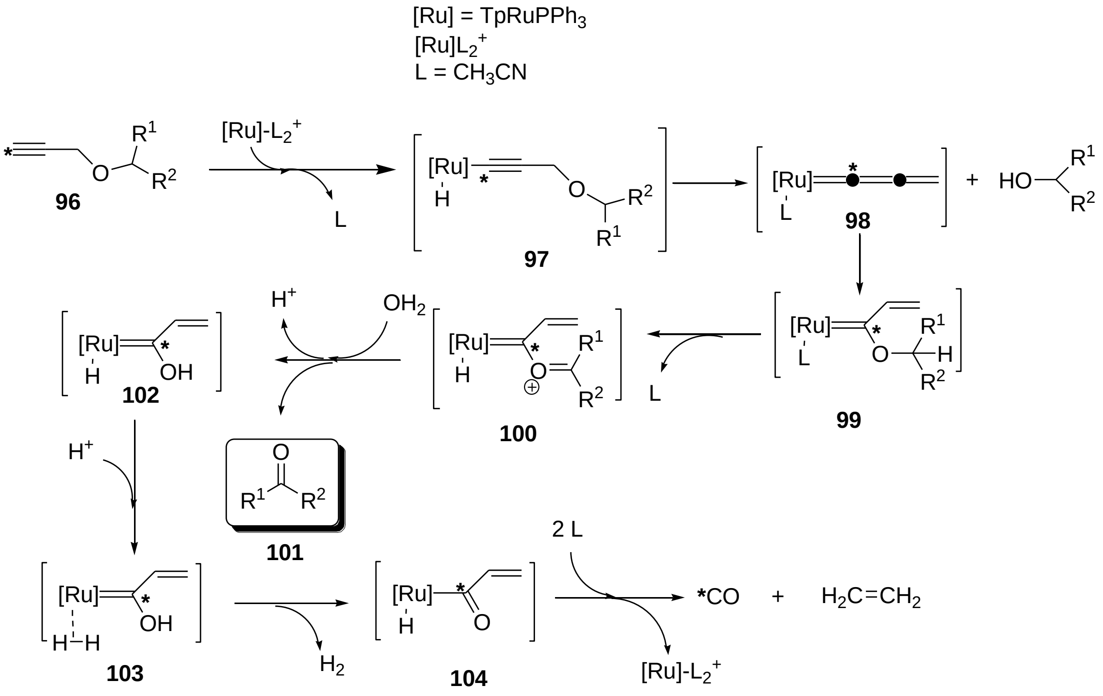


Figure 28. Oxidative cleavage of aryl and alkynyl propargyl ether using catalyst **87** and water.

Another interesting reaction was published by Shimada et al. in 2003. This type of reaction is the oxidative cleavage of alkyne followed by the addition of 2-aminophenol. They studied the oxidative cleavage of diynes. They found that the diynes react in the presence of $Ru_3(CO)_{12}$ as a catalyst and NH_4PF_6 as an additive to the corresponding ketones and benzoxazoles (Figure 29).[158] The reaction proceeds through oxidative cleavage of the C-C triple bond **(path a**) as well as of the C-C σ-bond (**path b**). They obtained a mixture of product(s) with relation 3:1 product mixtures (**path a** (benzoxazoles): **path b** (benzoxazoles)).

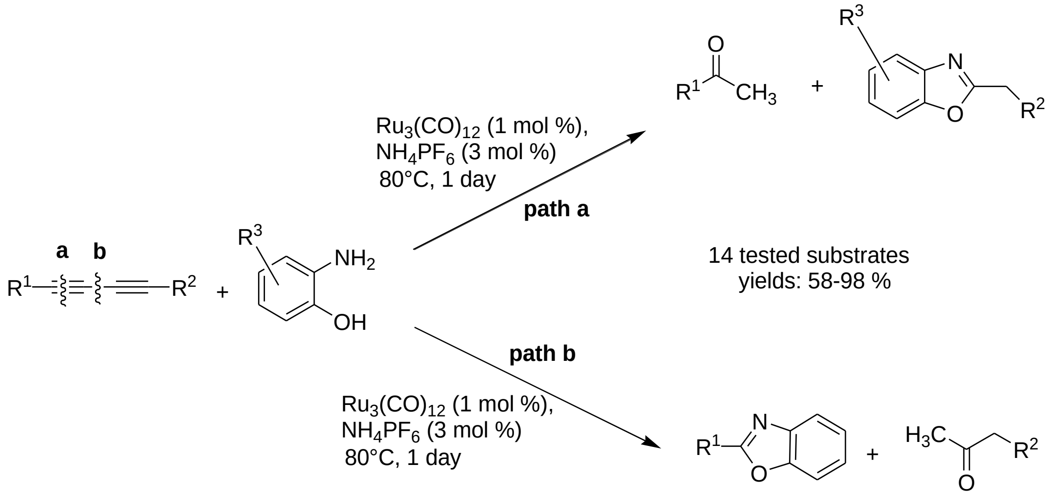
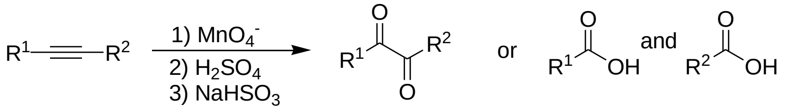


Figure 29. Oxidative cleavage of diynes using $Ru_3(CO)_{12}$ as catalyst.

4.2. Mn-catalyzed oxidative cleavage of alkynes

There are only a few references on the oxidative cleavage of alkynes with the use of potassium permanganate. Lee et al. have tested a series of alkyne using potassium permanganate. They have found that, depending on the alkyne used, either 1,2-dicarbonyl compounds or the corresponding acids were obtained. The Mn(VII) species is meanwhile reduced to Mn (IV) (Figure 30).



R^1 = n-C_4H_9 , R^2 = n-C_4H_9
R^1 = n-C_3H_5 , R^2 = n-C_2H_5
R^1 = Ph, R^2 = H
R^1 = n-C_4H_9 , R^2 = H
R^1 = Ph , R^2 = Ph
R^1 = Ph , R^2 = n-C_3H_5
R^1 = Ph , R^2 = n-C_4H_9
R^1 = n-C_6H_{13} , R^2 = n-C_6H_{13}
R^1 = n-C_7H_{15} , R^2 = n-C_7H_{15}
R^1 = n-C_8H_{17} , R^2 = -$(CH_2)_7COOH$

Figure 30. Oxidative cleavage of alkynes using potassium permanganate.

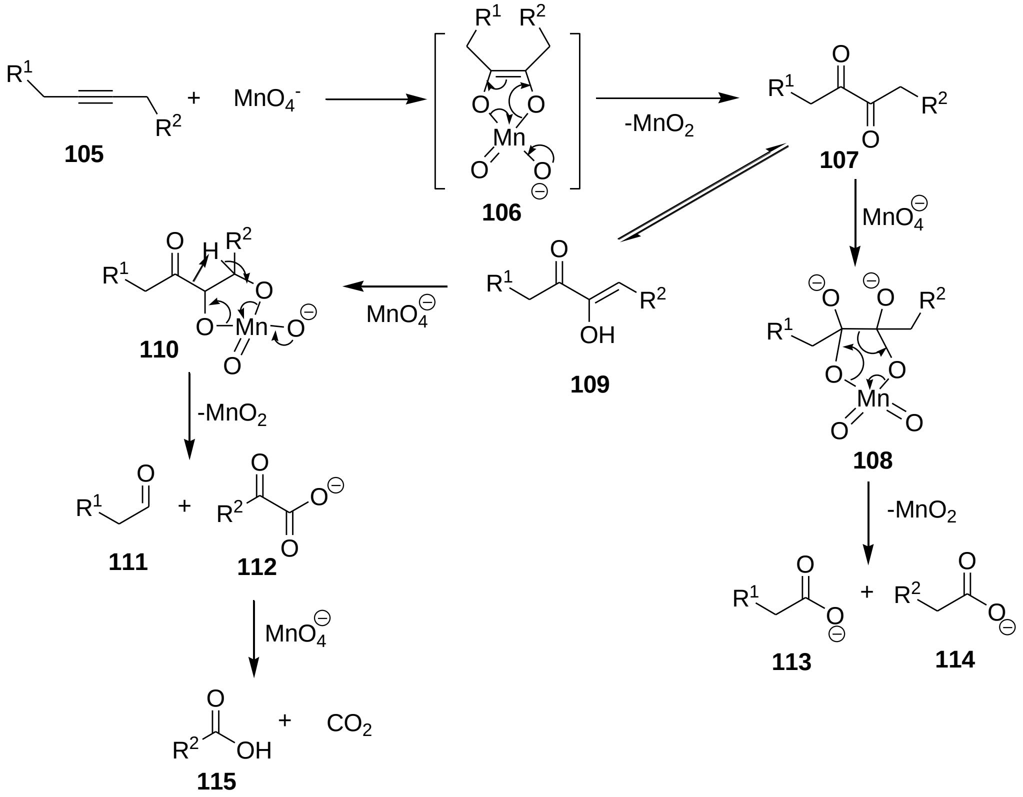


Figure 31. Reaction mechanism of oxidative cleavage of alkynes using permanganate.[159]

According to Lee et al., the reaction mechanism is similar to the mechanism of the oxidative cleavage of olefins using permanganate. With the use of permanganate, the oxidative cleavage of alkyne proceeds as followed: first, like all transition metal-catalyzed oxidative cleavages, the metal oxide, in this case, permanganate attacks the triple bond, producing the intermediate **106**. The oxidation in the step produces 1,2-dicarbonyl compound **107**, which can be isolated in the absence of water. However, this cleaves oxidatively in the presence of water and sulfuric acid to form the corresponding carboxylic acids **113** and **114**. Compound **107** can also react again with permanganate via keto-enol tautomerism (**107**), whereby intermediate **110** is formed. The oxidative rearrangement gives rise to products **111** and **112**. In this reaction condition, compound **112** cleaves oxidatively to carbon dioxide and **115**. Products **111** and **115** would form as by-products if **107** was bearing -CH_2- or -CHR group in the α-position (Figure 31).[159]

4.3. Fe-catalyzed oxidative cleavage of alkynes

Shaikh et al. published a method in 2011 that is cheap, environmentally friendly and non-toxic. They have used both olefins and alkynes as substrates. They used iron(III) chloride for the oxidative cleavage. *tert*-Butyl hydroperoxide (TBHP) was used as the oxidizing agent. They tested nine different substrates and obtained very good yields for 1-aryl alkynes (Figure 32).[160]

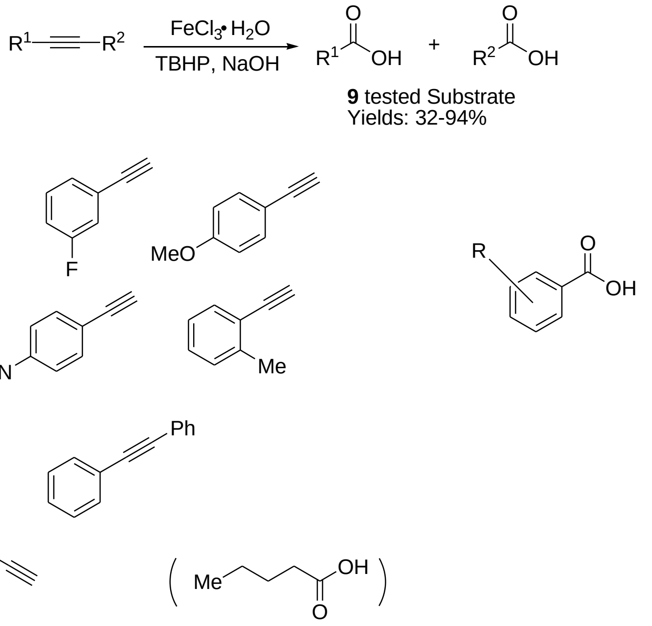


Figure 32. Oxidative cleavage of alkynes using $FeCl_3{\cdot}6\ H_2O$

Although Shaikh et al. investigated the reaction mechanism for the oxidative cleavage of olefins with GC-MS, however, there was no specific reaction-mechanistic investigation for the alkynes (see supporting information)[160]. The reaction mechanism of Fe-catalyzed oxidative cleavage of olefins has also been studied by Islam et al.[161]

Enthaler et al. have studied the Fe-catalyzed oxidative cleavage in more detail. They have tested a range of iron salts with different ligands and additives in hydrogen peroxide as an oxidant. They found out that ligands, additives and the different iron salts that they used in the reaction, have a very big effect on the yield of the products. Several salts such as $FePO_4$, $FeBr_3$ and $FeCl_3$ have been used. With the use of iron phosphate, they obtained less than 1% benzil as a product. With the use of iron bromide, they isolated 14% of benzil. The rest was unreacted tolane The best yield (99%) was isolated by the use of iron chloride. The reason for the difference in yields with the use of different iron salts was not explained in their paper. Without the use of ligands, they had a very good yield after a reaction time of 4 hours. Furthermore, the use of iron chloride leads to a reduction in the reaction time by one hour compared to the lack of use of a catalyst. For this purpose, they had carried out a GC-MS investigation for the formation of incorporated oxygen in diphenyl acetylene. The study of GC-MS confirmed their proposal and, (194 g*mol^{-1} (**116** + oxygen = **117**) was a peak detected. The best yield of benzil was achieved using *N,N,N',N'*-tretramethylethylenediamine (TMEDA). The unligated iron produced the intermediate **117** with 49% after one hour. Comparing the oxygen incorporation of the modified (49%) and unmodified (26%) iron-catalyzed oxidation reactions, significant advantages were observed with the addition of a ligand. A serious of aromatic amines were tested, the best performances were demonstrated by 4-dimethylamino pyridine (DMAP) with 55% incorporated oxygen. DMAP was tested as a ligand for 8 different alkynes as starting materials. In the case of R^1,R^2 = -COOEt or -COOMe, less than 1% cleavage product was obtained. The best yields (37-99%) were obtained using arylalkynes as substrates (Figure 33). They tested in total 9 different substrates. They obtained 82-99% of 1,2-carbonyl compounds as products.[162]

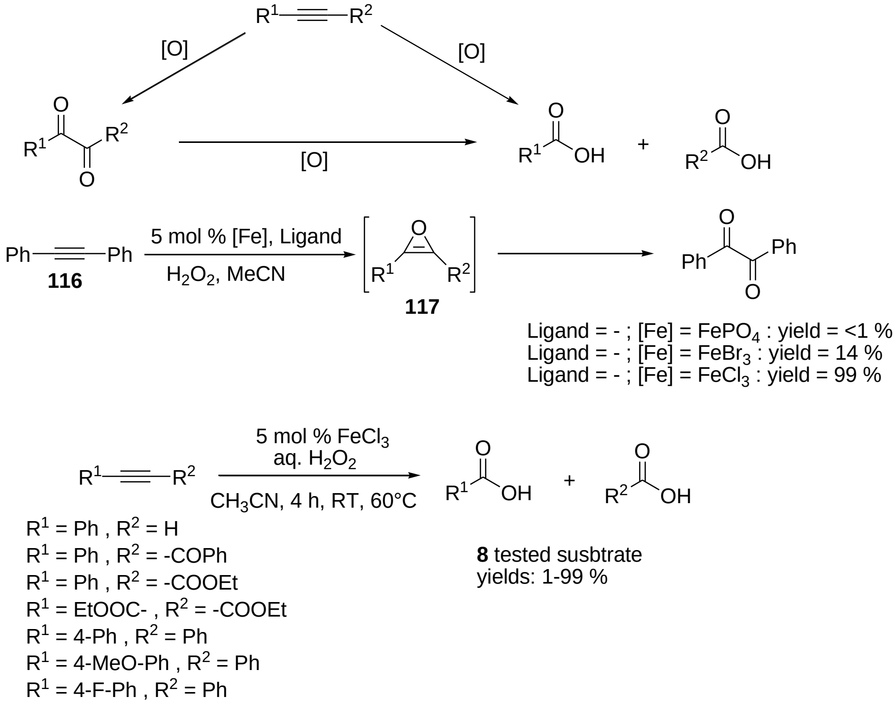


Figure 33. Oxidative cleavage of alkynes using FeCl$_3$ as catalyst, H$_2$O$_2$ as oxidizing agent and/or DMAP as ligand.[162]

Based on the reference, the reaction mechanism proceeds in the opinion of Enthaler et al. as follows.[163-170] As a key step, the oxidation reaction of the triple bond of starting material **116** proceeds to form an oxirene intermediate **117**, which was probably detected by using GC-MS.[162] The active catalyst is here iron(V)-oxo species.[160] Based on this, two follow-up reactions for the intermediate **117** are feasible. First, a rearrangement to a ketene **118** could occur, which would subsequently be either oxidized to a ketone **119** or hydrolyzed to a carboxylic acid **120**. Second, the oxirene could be oxidized to the corresponding 2,4-dioxa-bicyclo [1.1.0]-butane **121**, which could easily rearrange to the desired 1,2-dione **122** (Figure 34).

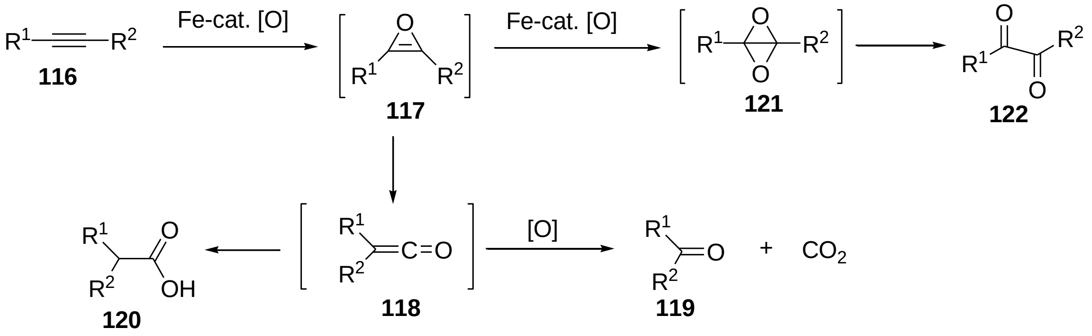


Figure 34. Reaction mechanism of iron(III) chloride catalyzed oxidative cleavage of alkyne.

In contrast to iron (III) compounds, the oxidation of alkynes proceeds radically using iron(II) compound: $[Fe(CH_3CN)_6][BF_4]_2$ as a catalyst and hydrogen peroxide as an oxidizing agent according to Yap et al. They have tested in total six alkynes. The aryl substituted alkynes cleave oxidatively to form the corresponding carboxylic acid or 1,2-dicarbonyl compound. However, alkyl substituted alkynes ($R^1 = C_3H_5$, C_2H_5, $R^2 = C_2H_5$, H) do not react under the same reaction conditions (Figure 35).

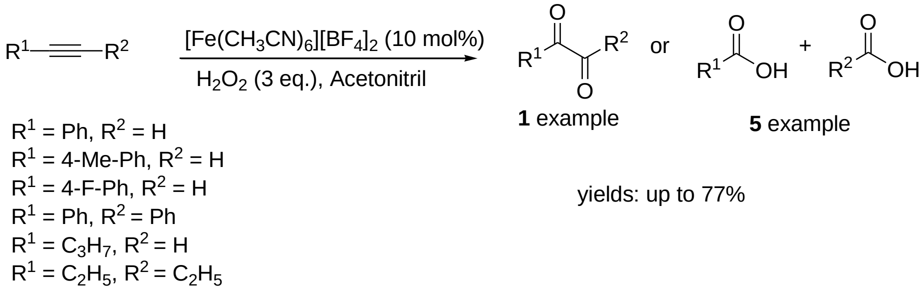


Figure 35. Oxidative cleavage of alkynes using Fe(II)-catalyst and H_2O_2 as oxidizing agent.

The method was not only tested for oxidative cleavage of alkynes but also for the oxidative cleavage of olefins. They tested in total ten olefins and obtained up to 84% yield. However, no oxidative cleavage was observed for the alkyl substituted olefins.[171] According to Yap et al. the reaction mechanism with 1-ethynylbenzene proceeds as followed: first the active catalyst **124** is formed in situ with hydrogen peroxide. According to Yap et al. the peroxo-iron (III) catalyst cleaves radically, the reactive hydrogen peroxo being formed radically. This radical attacks the triple bond of the alkyne, with the radical peroxo intermediate **125** being formed. The radical to intermediate **125** reacts with hydrogen peroxide molecule to form α-hydroxy peroxo-intermediate **126** with the formation of a hydroxide radical. The splitting of water gives the product 2-oxo-2-phenylacetaldehyde **127**. Yap et al. have commented that the terminal alkynes can react further to form the α-keto-carboxylic acid **128** through oxidation. As is well known, this intermediate product is not stable under heat and cleaves under decarboxylation to benzaldehyde and oxidizes with excess hydrogen peroxide to benzoic acid (Figure 36).[171]

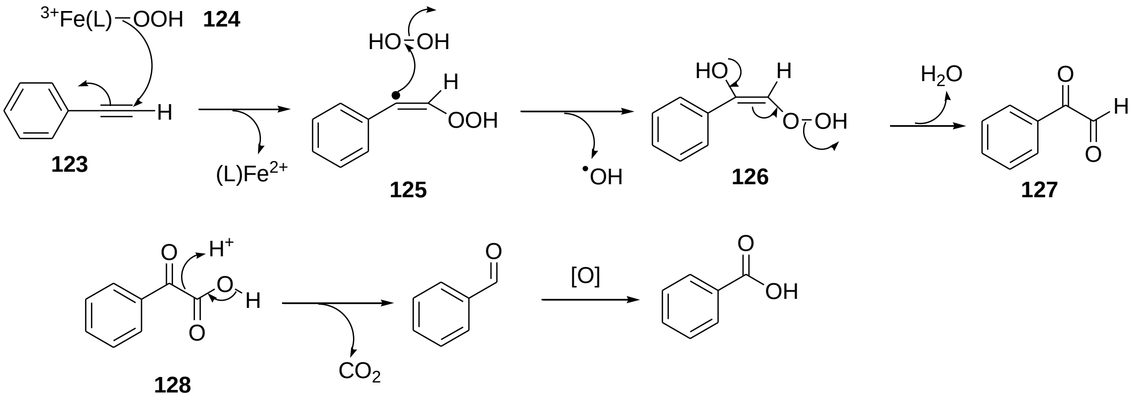
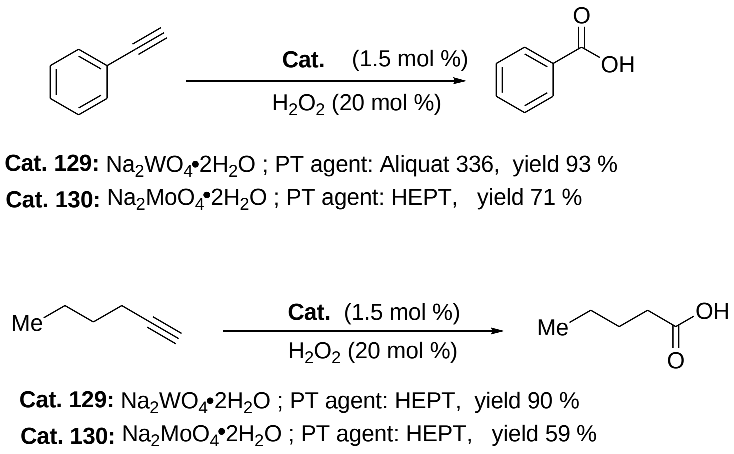


Figure 36. Reaction mechanism of oxidative cleavage of 1-ethynylbenzene to 2-oxo-2-phenylacetaldehyde or to benzoic acid using $[Fe(CH_3CN)_6][BF_4]_2$ as catalyst.[171]

4.4. Mo- and W-catalyzed oxidative cleavage of alkynes

Another method for oxidative cleavage of the alkynes was developed with the use of molybdenum or tungsten. However, there is a known method in the literature with the use of molybdenum, which was developed by Ballistreri et al. As additive a Na_2MO_4 (M = Mo (IV), W (VI)) and $Hg(OAc)_2$ salt were used and a dilute hydrogen peroxide solution as an oxidizing agent. This catalysis system is based on phase transfer catalysis. The catalysts were first tested in dioxane in homogeneous solution. However, low yields were obtained. A two-phase system brought much better results. The substrate, shown in figure 37, and $Hg(OAc)_2$ were placed in DCM and aqueous hydrogen peroxide and $Na_2MoO_4{\cdot}2H_2O$ or $Na_2WO_4{\cdot}2H_2O$ in a buffered solution. With these reaction conditions, the best yields for the oxidative cleavage of alkynes have been obtained. However, for two substrates the reaction conditions were optimized and applied. For the oxidative cleavage of 1-phenylacetylene with the catalyst $Na_2WO_4{\cdot}2H_2O$ **129** and **Aliquat 336** as phase transfer agent, they obtained 93% benzoic acid. In contrast, the yield decreased if they used $Na_2MoO_4{\cdot}2H_2O$ **130** as the catalyst instead and HEPT (hexaethylphosphoric triamide) as the phase transfer agent. In the oxidative cleavage of 1-hexyne, a better yield (90%) was also obtained when tungsten salt was used as the catalyst. With molybdenum as a catalyst, they were able to isolate a 59% yield of the cleavage product. In both cases, HEPT as the phase transfer agent was used. The tungsten (VI) apparently plays a crucial role in improving the yield regardless of which phase transfer agent is used [172]. In fact it is known that cationic PT agents such as Aliquat or Adogen extract anionic oxidant species such as $[MO_5(OH)(H_2O)]^-$ while neutral ligands such as HMPT or HEPT extract neutral species such as MO_5 (H_2O).[173,174] It has been reported that these two peroxo species display different reactivities toward substrates such as olefins or alcohols (Figure 37).



Cat. 129: $Na_2WO_4•2H_2O$; PT agent: Aliquat 336, yield 93 %
Cat. 130: $Na_2MoO_4•2H_2O$; PT agent: HEPT, yield 71 %

Cat. 129: $Na_2WO_4•2H_2O$; PT agent: HEPT, yield 90 %
Cat. 130: $Na_2MoO_4•2H_2O$; PT agent: HEPT, yield 59 %

Figure 37. Oxidative cleavage of alkynes using $Na_2MoO_4·2H_2O$ **130** or $Na_2WO_4·2H_2O$ **129** [172]

However, Ballistreri et al. did not suggest any reaction mechanism in their manuscript. It is assumed that the reaction mechanism proceeds with the use of W(IV) and Mo (IV) similarly to the standard Ru-catalyzed reaction mechanism (Figure 38).[172]

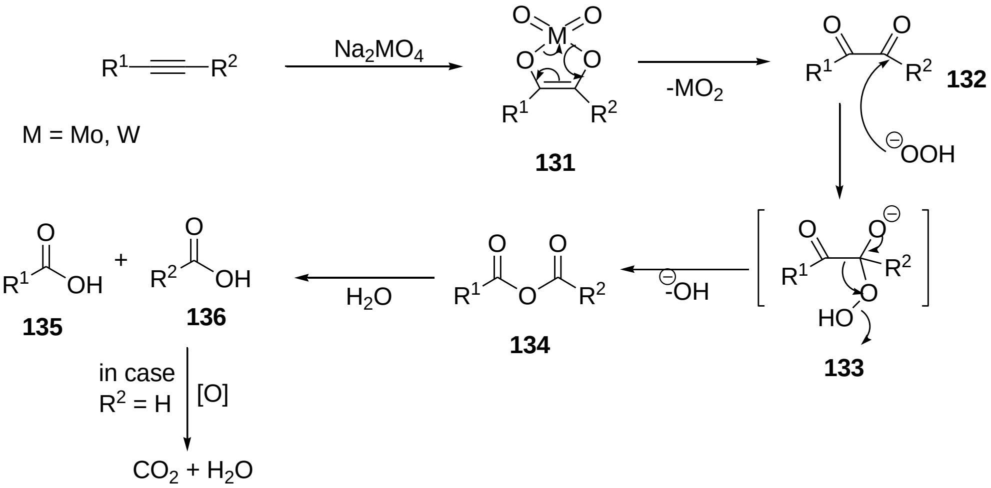


Figure 38. Suggested oxidative cleavage of alkynes using $Na_2Mo_4·2H_2O$ or $Na_2WO_4·2H_2O$ as catalysts.

That is, the attack of the tetraoxo metal anion occurs first to bind the alkyne triple, whereby the intermediate **131** is formed. The cleavage of metal dioxide forms the 1,2-dicarbonyl intermediate **132** which, among other things, can be isolated if the oxidizing agent is used in approximately equivalent amounts. If excess oxidizing agent (hydrogen peroxide) is used, the hydrogen peroxide anion attacks the carbonyl carbon to form intermediate **133**. At this stage, the intermediate **133** reacts through the Baeyer-Villiger rearrangement to form the corresponding anhydride **134**, which cleaves in the presence of water and heat to form the carboxylic acids **135** and **136**. In the case of terminal alkynes such as 1-hexyne or 1-phenylacetylene, formic acid is formed as the end product, which is further oxidized to carbon dioxide and water.

4.5. W-catalyzed oxidation and/or oxidative cleavage of alkynes

Ishii et al. have developed a method for the oxidation of alkynes. A catalyst has been synthesized that can be used to a large extent in the oxidation of various organic compounds.[54,175-183] The method was mainly tested on different substrates. For instance, it has been applied to 4-octyne and diphenylacetylenes. In the oxidation of diphenylacetylenes, benzil in a high yield of 93% was obtained. When 4-octyne was oxidized, three different products were isolated in 5%, 15% and 62%. These are as followed: butyric acid (5%), (*E,Z*)-oct-5-en-4-one (15%) and 1-(3-ethyloxiran-2-yl) butan-1-one (62%) (Figure 39).[184]

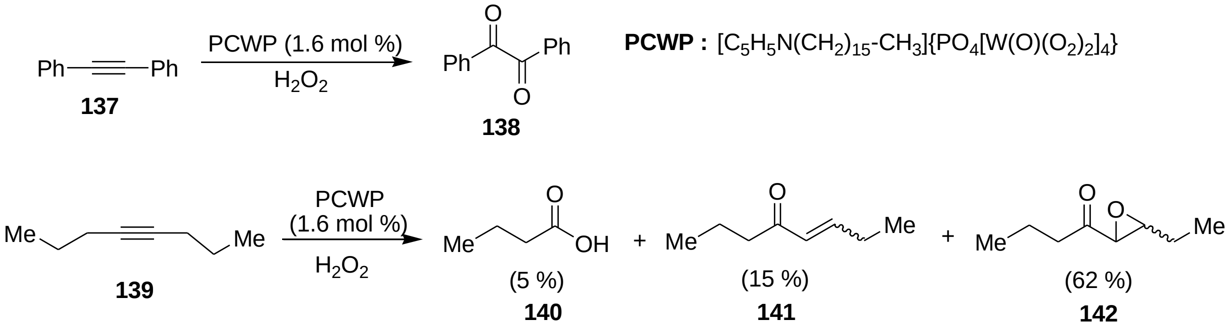


Figure 39. W-catalyzed oxidation and/or oxidative cleavage of alkynes

According to Ishii et al. the reaction mechanism proceeds exactly as described in Figure 74. The same intermediates result as in Figure 74. However, which active catalyst intermediates the reaction proceeds was not reported in the article.

4.6. Pd-catalyzed oxidative cleavage of alkynes

The oxidative cleavage of alkynes by $Pd(OAc)_2$, which was obtained commercially, to the ester was published in 2008 by Wang et al. (Figure 40).[185]

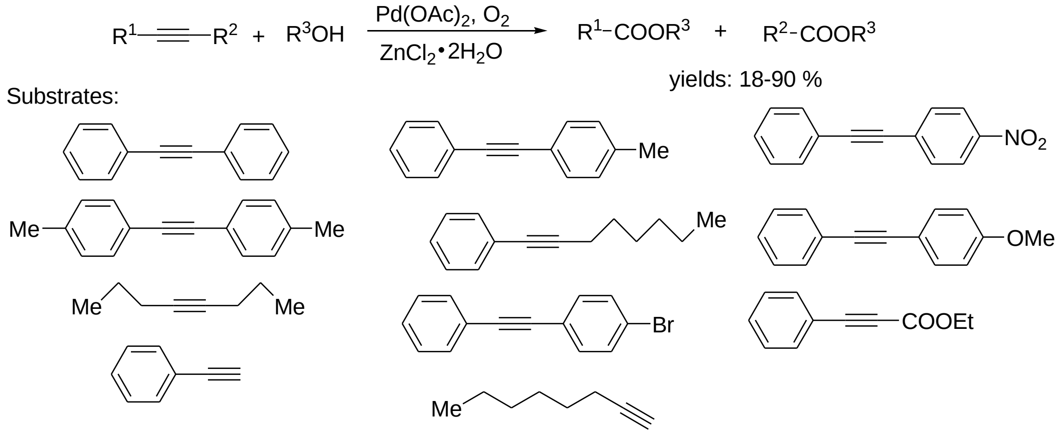


Figure 40. Oxidative cleavage of alkynes using $Pd(OAc)_2$ as catalyst

Totally 11 substrates were tested. During the oxidative cleavage of 4-octyne, they were able to isolate 18% butyric acid. With the remaining substrates, esters, as cleavage products between 73-89% yields were received. A number of additives were tested. It has been found out that the additives play a crucial role in improving the yields. For example, when they used $CuCl_2 \cdot 2H_2O$ as an additive, they isolated 43% yield of methyl benzoate for the oxidative cleavage of diphenylacetylene at 100 °C. When $ZnCl_2 \cdot 2H_2O$ was used as an additive at 100 °C, 90% yield Methyl benzoate was obtained. It has been also found that zinc chloride gives just a poor yield (43%) at 60 °C. Unfortunately, why the use of zinc chloride produces higher yields at high temperatures than the other additives in the same reaction conditions, this could not be explained. In addition to the normal alkynes, two 1,2-dialkyneses as substrates in the same reaction conditions were tested. In the oxidative cleavage of diphenyl-buta-1,3-diyne (**143a**) in methanol, 83% yield for methyl benzoate (**144a**) were able to be isolated. Use of hexadeca-7,9-diyne (**143b**), gave 77% yield on *n*-propyl heptanoate (**144b**) (Figure 41).[185]

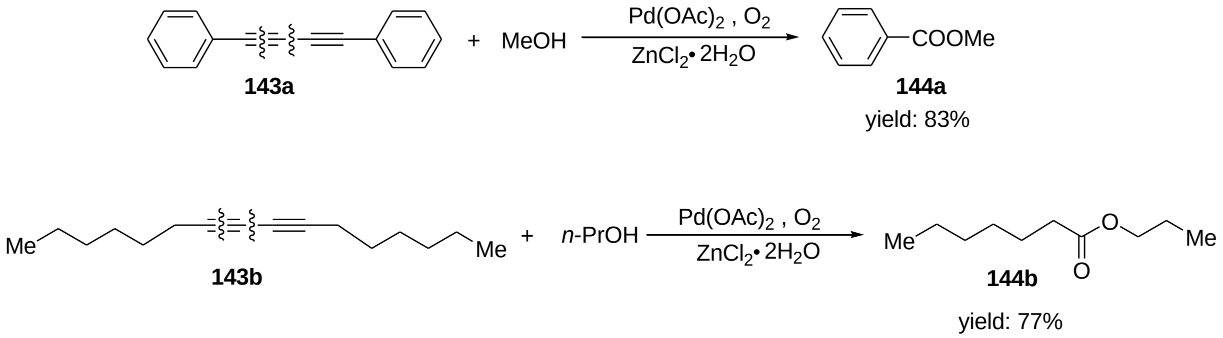


Figure 41. Oxidative cleavage of 1,2-dialkynes using $Pd(OAc)_2$

Here, according to the list of carbons for the substrates, formic acid, carbon monoxide and/or carbon dioxide should actually be produced as residual decomposition products. This is however not being mentioned in the article. The disadvantage of the method is that they did not test the reaction in solvents other than alcohols and used other alkyl substituted alcohols or aryl substituted alcohols which are solids as reactants. The reaction mechanism was investigated using the oxidative cleavage of diphenylacetylene. According to Wang et al. The reaction mechanism proceeds as follows (Figure 42): They propose that the alcohol used is first added to the triple bond of the alkyne, which is also used as a solvent, with the help of the catalyst, with methoxy-1,2-diphenyl ethene **145** as an intermediate, which further reacts with the active catalyst $Pd(OAc)_2$-$ZnCl_2 \cdot 2H_2O$-O_2 to form the intermediate **146**. The authors have proposed no structure at this point for the active catalyst using oxygen in their article. Intermediate **146**, which was detected using the GC-MS method, cleaves to methyl benzoate **147** oxidatively.[185]

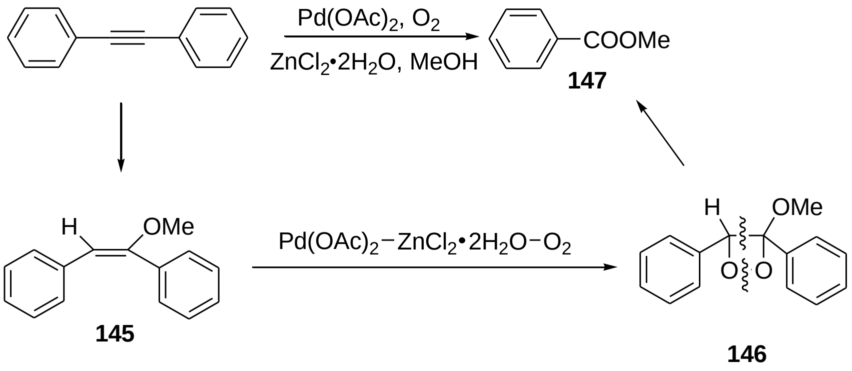


Figure 42. Proposed reaction mechanism of oxidative cleavage of $Pd(OAc)_2$ as catalyst.

However, following the suggestion of Wang et al. Benzaldehyde is also formed in the reaction through the oxidative cleavage of **146**. In the opinion of Wang et al., benzaldehyde oxidizes further to benzoic acid, which further reacts through esterification to form methyl benzoate **147**.[185]

A detailed review of the oxidation of alkynes to 1,2-dicarbonyl compounds using palladium salts such as $PdCl_2$, $PdBr_2$, $Pd(NO_3)_2$, $Pd(OAc)_2$ etc. was given by Muzart et al. (figure 41).[186] CuX_2, ZnX_2 salts in DMSO were mostly used as additives, where X is halogen. The general reaction mechanism with the use of DMSO has been described in the publication by Gao et al. based on diphenylacetylene assumed as followed (Figure 42).[187] According to Gao et al. Palladium salt first attacks the triple bond of the alkyne followed by addition, whereby the palladium-alkyne intermediate **149** is formed. This intermediate **149** then attacks a dimethyl sulfoxide molecule. This produces the palladium sulfoxoalkenes intermediate **150**. An aldol reaction then takes place. To this end, the intermediate **150** attacks the oxygen of another dimethyl sulfoxide molecule, whereby dimethyl sulfide is eliminated from the intermediate **150** and was 1,2-ketodione **153** formed. After the separation of second DMSO from intermediate **153**, the catalytic cycle is completed, with benzil **154** and active catalyst **148** is formed in situ (Figure 43).[187]

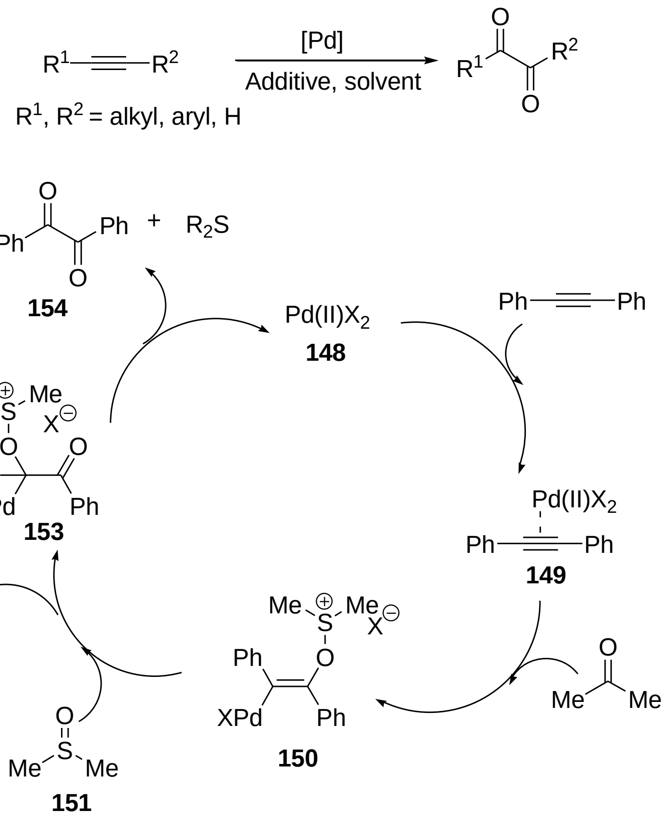


Figure 43. Oxidation of alkynes using Pd-metal to 1,2-dicarbonyl compounds.

Heterodimer nanocrystaline catalyst "Pd-Fe_3O_4" can also be used for the oxidation of alkynes to 1,2-diketones, which can be easily separated from the reaction environment by magnetic separation and can be reused. The Pd-Fe_3O_4 synthesis was performed by two-step thermal decomposition of a mixture solution composed of iron acetate, palladium acetate, oleic acid and oleylamine. In a general synthesis, $Pd(acac)_2$ and $Fe(acac)_3$ was added into a solution of containing oleic acid and oleylamine and the mixture was heated. Fifteen derivatives of diphenylacetylene were tested in the presence of Pd-Fe_3O_4 and $CuBr_2$ as additive in a solvent mixture of 1,4-dioxane-H_2O (5: 1). They obtained 1,2-diketones as products between 77 and 98% yields. However, the authors did not propose a reaction mechanism for the oxidation of alkynes in their manuscript (Figure 44).

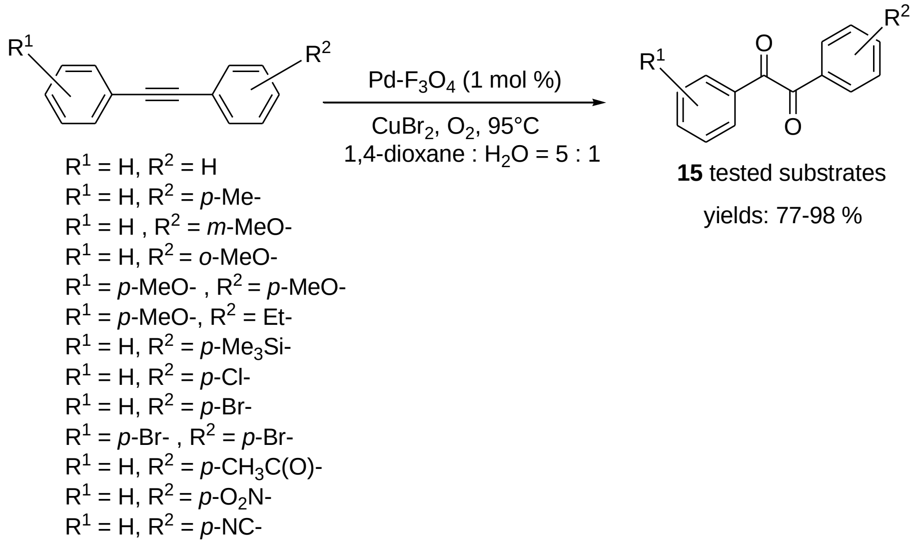


Figure 44. Oxidation of derivatives of diphenylacetylene using Pd-F_3O_4 as catalyst.

4.7. Rh-catalyzed oxidative cleavage of alkynes

Rhodium is a highly flammable, expensive and rare transition metal. In recent years, rhodium has been used frequently as a transition metal in catalysis. One would expect that it was also used in the oxidative cleavage of alkynes. However, few scientific articles on the Rh-catalyzed oxidative cleavage of alkynes have been published until now. For example; Park *et al.* have developed a method in which both an oxidative cleavage of the triple bond and an addition of the aryl groups were occurred. After phenylacetylene reacted with *N*-tosyl azide in the presence of copper (I) thiophene-2-carboxylate (CuTC, 10 mol%) in toluene, $Rh_2(Oct)_4$ (1 mol %) and azulene **156** were added to the reaction mixture, which was subsequently treated with Cs_2CO_3, resulting in the formation of 1-benzoyl azulene **157** in 66% yield in one pot (Figure 45). They tested the same reaction for the olefins and the reaction mechanism of the olefins was only studied. The reaction mechanism was proposed using the labeling method ($^{18}O_2$) in the manuscript. [188]

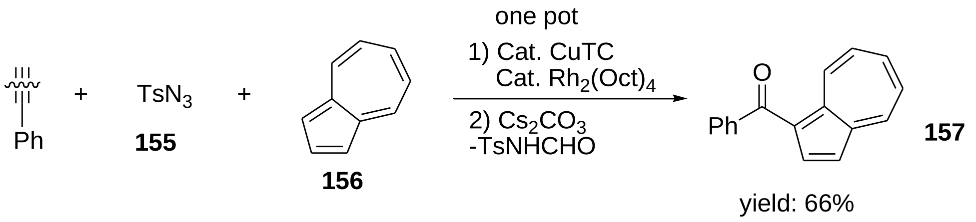


Figure 45. Oxidative cleavage of phenylacetylene using rhodium metal

The second interesting oxidative cleavage reaction is that alkyne reacts with 1-pyridinyl amine **158b**. A good to very good yield of amines were obtained (Figure 46). It is an oxidative cleavage combinated with a substitution reaction. Jun et. al. published this reaction, shown in figure 46, in 2001. They believe that the reaction occurs via imine. According to their opinion, the reaction goes as follows. First, the reaction starts through the addition of methylpyrdinylamine derivatives **158b** and the addition of alkyne **158a** to rhodium catalyst. The intermediate **159** is through this formed. With the internal attack of alkenyl on imine group of **159** and with the cleavage of the rhodium catalyst, α,β-unsaturated imine intermediate **160** is formed. This intermediate **160** in turn reacts internally via a six chair conformation with oxidative cleavage of a

Intermediate **162** and enamines intermediate **163**. The enamines, as is well known, also have corresponding imine tautomers. The imine is hydrolyzed to the corresponding ketone **168** at 130°C in toluene solution in the presence of water. Jun et. al. confirmed this reaction mechanism by preparing the intermediates **160**, **161**, **162** and **166** separately and testing them again separately under the same reaction conditions. They received the same results (Figure 46).[189]

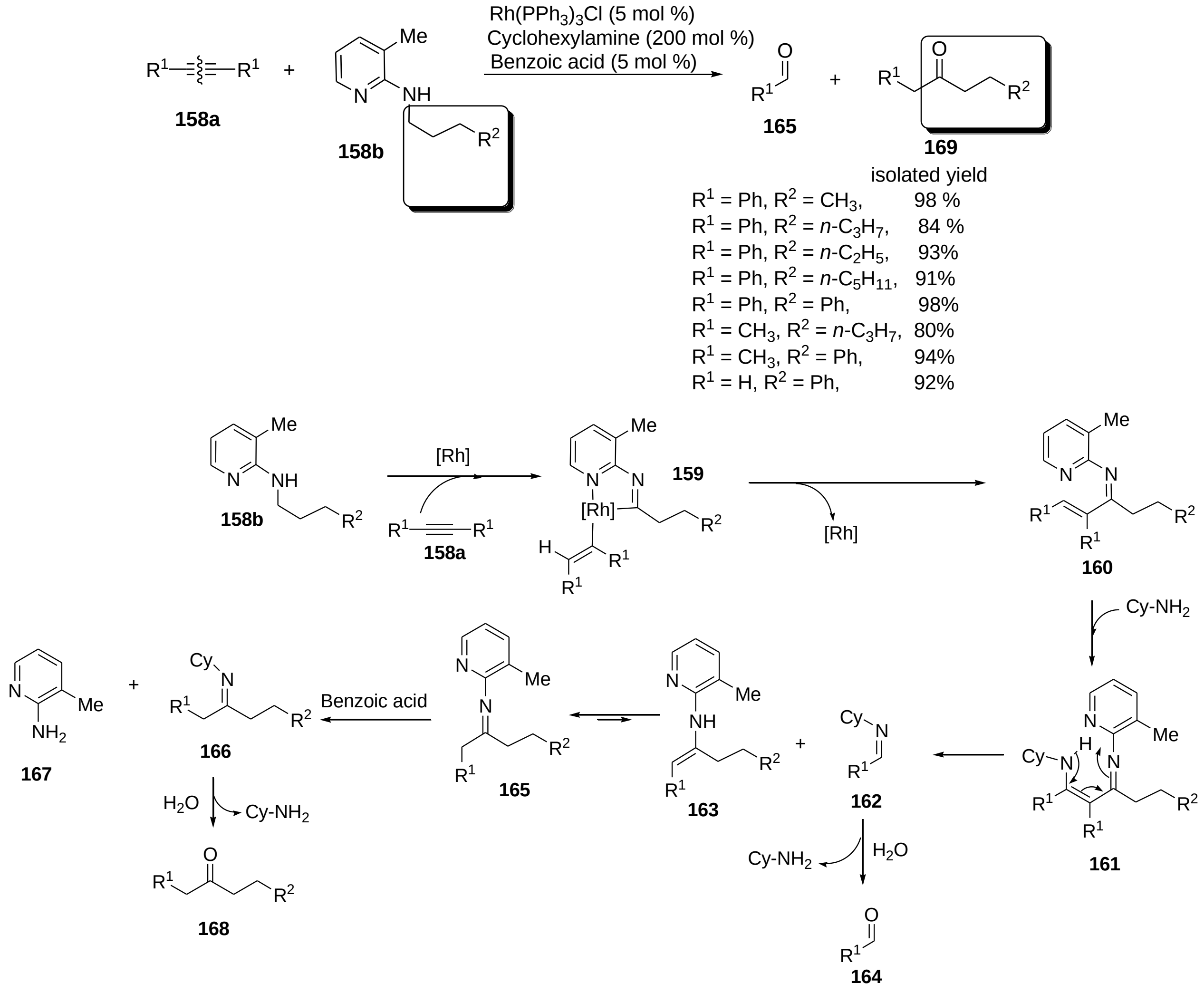


Figure 46. Cleavage of Carbon-Carbon Triple Bond of Alkyne via Hydroiminoacylation by Rh(I) Catalyst.

4.8. Ni-catalyzed oxidative cleavage of alkynes

Another oxidative cleavage method was presented by Urgoitia et al. in 2015. They found that mild oxidation conditions would be enough to split off the alkyne oxidative. In this method, atmospheric oxygen is used as the oxidizing agent under normal atmospheric pressure. They have tested a number of aryl substituted alkynes. The method is valuable because compared to other transition metals such as rhodium, ruthenium, osmium, palladium, tungsten and molybdenum, nickel is relatively cheap, nontoxic and often easy to handle. However, what may have been lacking for the industry to present a better method than ozonolysis is that the method has not been extended to include alkylalkynes (figure 47). They have dissolved fourteen substrates with the use of nickel bromide in 10^{-5} mol% as a catalyst in low-molecular-weight grade of polyethylene glycol (PEG-400) and **159** or **160** as ligands in 10-5 mol% in the presence of sodium acetate tested in acetonitrile. Except for (1-(4-(2-phenylethynyl)phenyl)ethanone), they got good to very good yields.[188] The ligands are either commercially available, such as Ligand **169**, or can simply be prepared in one step, such as ligand **170** (Figure 47).

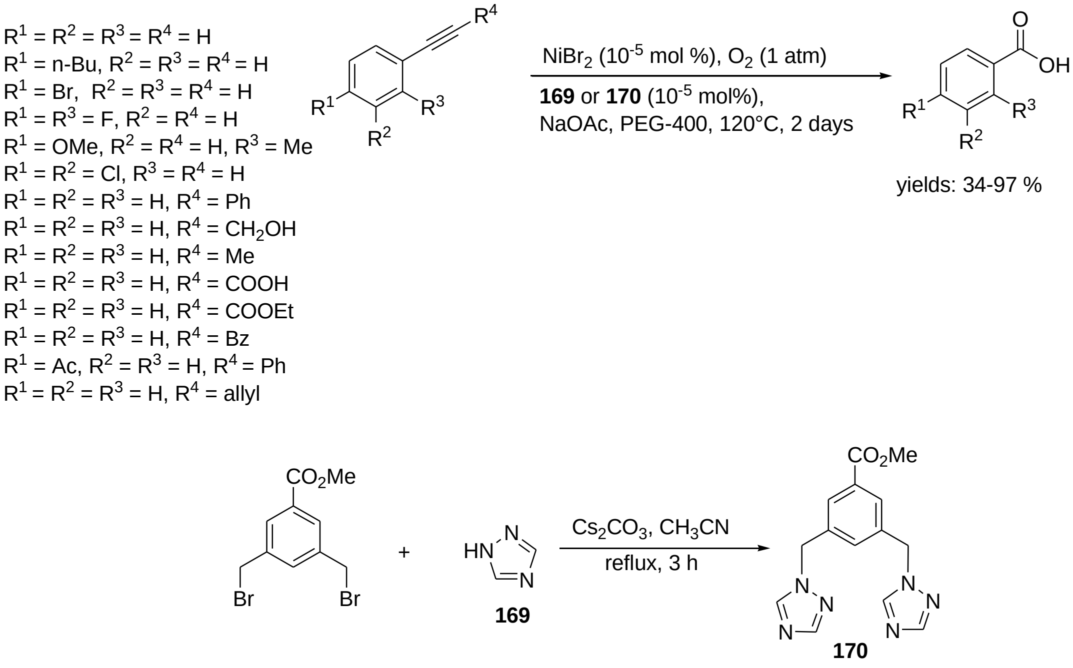
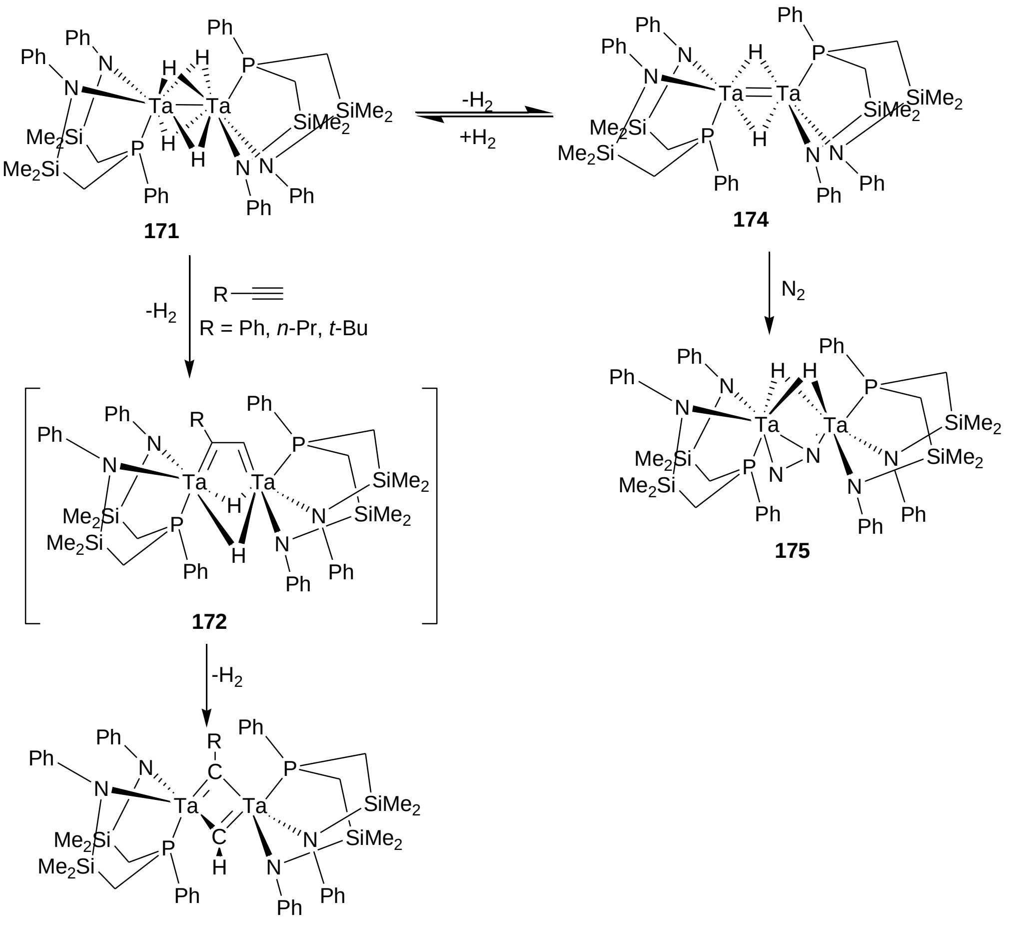


Figure 47. Oxidative cleavage of alkynes using nickel bromide in PEG-400 and **16** or **170** as ligands.

4.9. Ta-catalyzed oxidative cleavage of alkynes

Although there is no major application in industry and / or in preparative synthesis for the oxidative cleavage of alkynes with tantalum as a synthesis method, because tantalum is expensive and rare as a transition metal, we still want to take a brief look at what Shaver et al. have found out. This method has only been tested for phenylacetylene, 1-pentyne and tert-butylacetylene. Shaver et al. have succeeded in being able to isolate the important intermediate **172** (R = Ph) during the oxidative cleavage and to determine its structure by X-ray structure analysis. Reaction of terminal alkyne with the dinuclear tetrahydride complex $([NPN]Ta)_2(\mu\text{-}H)_4$ **171** gives the product $([NPN]Ta)_2(\mu\text{-}RCCH)(\mu\text{-}H)_2$ **172** (where NPN is $PhP(CH_2SiMe_2NPh)_2$). Storage of solutions of $([NPN]Ta)_2(\mu\text{-}RCCH)$ $(\mu\text{-}H)_2$ **172** under vacuum promotes the loss of H_2 and cleavage of the C≡C bond to give $([NPN]Ta)_2(\mu\text{-}CPh)(\mu\text{-}CH)$ **173**. It is also important at this point that this catalyst **171** has been used for the activation of nitrogen. This creates the intermediate **175**. Reaction of phenylacetylene with the dinitrogen complex $([NPN]Ta)_2(\mu\text{-}\eta^1\text{:}\eta^2\text{-}N_2)(\mu\text{-}H)_2$ **175** results in the dissociation of the bound dinitrogen and the formation of $([NPN]Ta)_2(\mu\text{-}PhCCH)(\mu\text{-}H)_2$ **172**, which is identical to that derived from the reaction with the dinuclear tetrahydride (Figure 48).[191]

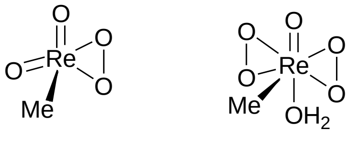


173

Figure 48. Oxidative cleavage of terminal alkynes (RCCH, R = Ph, *n*-Pr, *t*-Bu) using tantalum

4.10. Re-catalyzed oxidative cleavage of alkynes

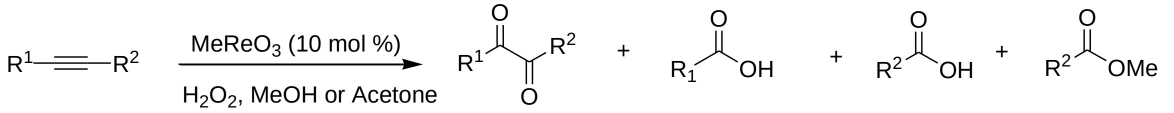
Rhenium is a transition metal which is not toxic but is very rare and expensive and some of its reagents flammable. Hence, using this metal in large quantities as a catalyst in industry would not be beneficial. Methylrhenium trioxide (CH_3ReO_3, MTO) is one of the catalysts, which is used for both the oxidative cleavage of olefins and alkynes.[168,192] The catalyst has two active forms **176** and **177**, which have been characterized crystallographically (Figure 49). Zhu et al. have found that the oxidation of both terminal and internal alkynes by hydrogen peroxide is also catalyzed by MTO.



176 **177**

Figure 49. Active catalyst of $MeReO_3$ *in situ.*

Zhu et al. have tested a number of alcohols as solvents for the oxidation of diphenylacetylene to benzil. They have achieved the best yield with the use of ethanol (Figure 50).



R^1 = Ph, R^2 = Ph	yield: 80 % (EtOH)	yield: 17 % (*t*-amyl)	yield: 9 % (MeOH)
R^1 = *n*-Pr, R^2 = *n*-Pr	yield: 43 % (Acetone)	yield: 24 % (Acetone)	yield: 15 %(MeOH)
R^1 = *t*-Bu, R^2 = Me		yield: 86 % (Acetone)	yield: 12% (MeOH)
R^1 = C_7H_{15}, R^2 = H		yield: 95 % (Acetone)	yield: 81% (MeOH)
R^1 = Ph, R^2 = H		yield: 65 % (Acetone)	yield: 95% (MeOH)

Figure 50. Oxidative cleavage of alkynes using $MeReO_3$ as catalyst and H_2O_2 as oxidizing agent in methanol or acetone.

Zhu et al. tested a total of 5 substrates in different solvents. They received either 1,2-diketones or carboxylic acids or esters, depending on the solvent and / or substrate. For example, when using acetone, the oxidative cleavage products were obtained to very good yields. When using methanol as a solvent, they have mainly obtained esters. Here, the solvent methanol not only acts as a solvent but reacts with one of the intermediates to form ester as the end product.

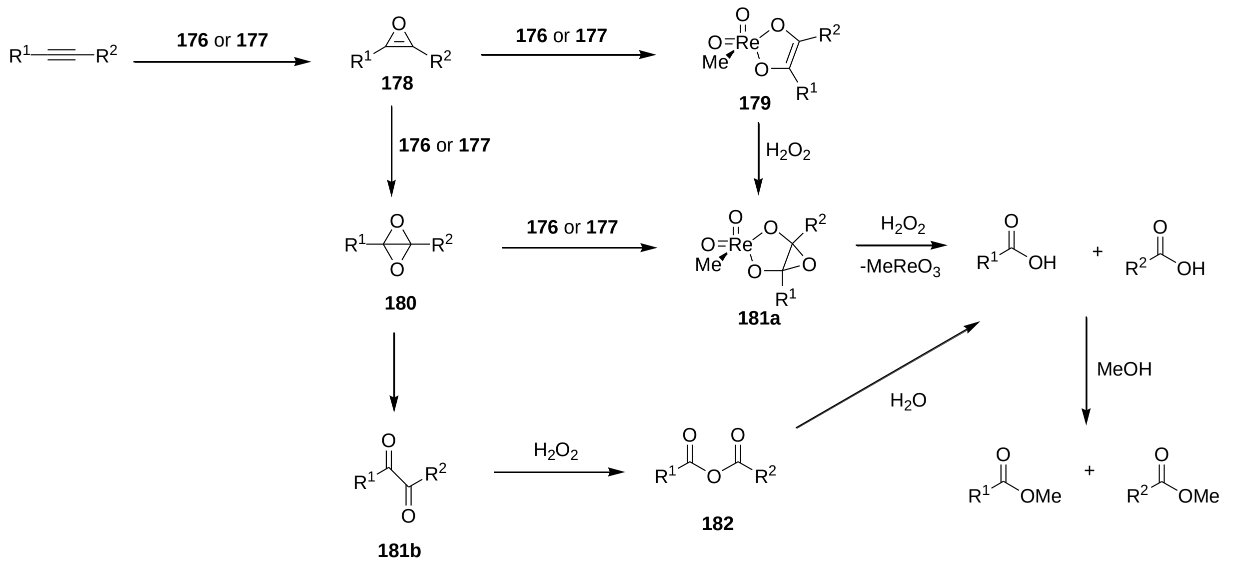


Figure 51. Mechanism of oxidative cleavage of alkynes using $MeReO_3$ as catalyst and H_2O_2 as oxidizing agent.

According to the suggestion by Zhu *et al.* the reaction mechanism proceeds as follows: first, the triple bond acts as a nucleophile on the active catalyst formed in situ (**176** or **177**), whereby the intermediate **178** is formed. This intermediate **178** responds to two pathways. The first reaction path is the reaction of methylrhenium oxide to form intermediate **179**. The second pathway is the attack of double bonds on the active catalyst (**176** or **177**) to form intermediate **180**. The double bond of intermediate **179** further reacts with hydrogen peroxide to form intermediate **181**. This intermediate is formed via intermediate **180**. Intermediate **171a** reacts with a hydrogen peroxide molecule and is cleaved to form the corresponding carboxylic acids. The catalyst ($MeReO_3$) is formed again in situ and the carboxylic acids are formed. The intermediate **180** can also be formed into 1,2-diketones **181b**, depending on the solvent. The attack of the hydrogen peroxide molecule on the carbonyl group of the 1,2-diketone **181b** and the Baeyer-Villiger rearrangement form the anhydride **182**. The anhydride **182** is unstable in an aqueous environment and when attacked by water cleaves into the corresponding carboxylic acids (Figure 51).[168]

4.11. Os-catalyzed oxidative cleavage of alkynes

Strangely enough, although osmium tetroxide is a toxic substance, it is often used in the oxidative cleavage of olefins. Because in many organic chemistry textbook is given as an example for the oxidative cleavage, the second famous method under the chemist after ozonolysis..The method leads to very good yields both in the oxidative cleavage of olefins and in the oxidative cleavage of alkynes. There are many examples of the oxidative cleavage of alkynes.[11-15,17] The first example is the selective oxidative cleavage of alkyne building blocks with the use of OsO_4 (5 mol%) as the catalyst and $NaIO_4$ (10 eq.) as the oxidizing agent. A general method for the solid-phase synthesis of carboxy-functionalized peptides by oxidative cleavage of the corresponding alkynes is presented. Clean and quantitative conversion is enabled by the addition of bases, such as DABCO (1,4-Diazabicyclo (2.2.2) octane) and hexamethylenetetramine (HMTA), to the classical $OsO_4/NaIO_4$ mixture. It is surprising with the method that the reaction proceeds quite selectively. This means that the strong oxidation reaction conditions ($OsO_4/NaIO_4$) do not decompose the starting material or a reaction only takes place between OsO_4 and alkyne. Nielsen et al. have shown that, regardless of the length of the peptides, the alkyne-functionalized peptide molecules bound to one side with a long amino acid polymer residue (eg Gly-HMBA-PEGA$_{800}$), which is also known as solid-phase synthesis, can be selectively oxidized be split off. Depending on the method, either DABCO (1,4-diazabicyclo (2.2.2)octane) or HMPA were used as additive bases in the method. A number of peptides were used in the method using the solid phase synthesis method. For example, peptide **184** with an alkyne group can be cleaved to the corresponding carboxylic acid peptide **185** in the presence of a strong base (hexamethylenetetramine = HMPA) and over 95% yield. It is important to note that the free amine groups were protected with a Boc group. This is done, for example, in the oxidative cleavage of **186** to **187**. Since OsO_4 reacts with $NaIO_4$ also with a double bond, the double bond and the triple bond of the compound **188** cleaves oxidatively to **189**. The resulting carbonyl group reacts with the nitrogen atom of the amide group and creates a cyclized peptide molecule **189**. Twenty amino acid residues were used in compound**190**. Besides tryptophan (yield: 32%), the oxidative cleavage product **191** was obtained in very good yields. Even simple α-alkynyl amino acids react like compound **190** under this reaction condition to give **191**, whereby the polymer residue (HMBA-PEGA800) is also split off (Figure 52).[193]

The development of the method with solid-phase oxidative cleavage with other substrates is Le Quement et al. succeeded. However, they used a different peptide-polymer residue (R = Ala-Phe-Gly-HMBA-PEGA$_{800}$). Just like the peptides, they had obtained good to very good yields. Three different reaction conditions were optimized and seven different substrates each based on (*ortho, meta* or *para*) trimethylsilylphenyl peptide polymer residue **194** were tested. In the first reaction condition, the corresponding carboxylic acids **195** were isolated in high yields by oxidative cleavage. Here, OsO_4 was used as the catalyst, $NaIO_4$ as the oxidizing agent, HMTA as the base and *tert*-butylammonium fluoride as the phase transfer catalyst in a THF and water mixture. The second reaction condition is optimized for the synthesis of α-ketocarboxylic acids **196**. A total of seven substrates were also tested here. The third optimization is the synthesis of (*ortho, meta or para*)-acylphenyl peptide polymer residue **197** only through the use of trifluoracetic acid (Figure 53).[194]

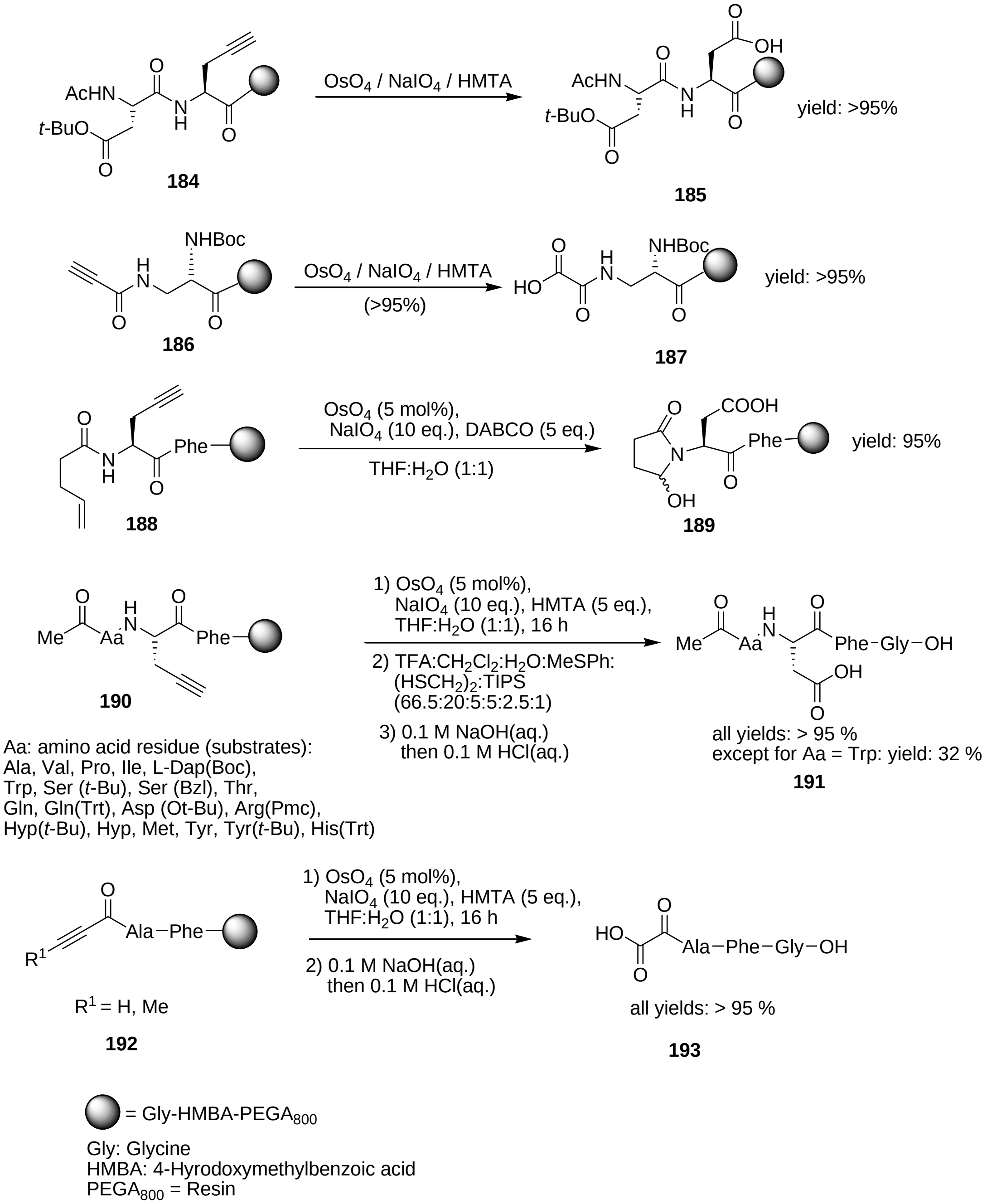
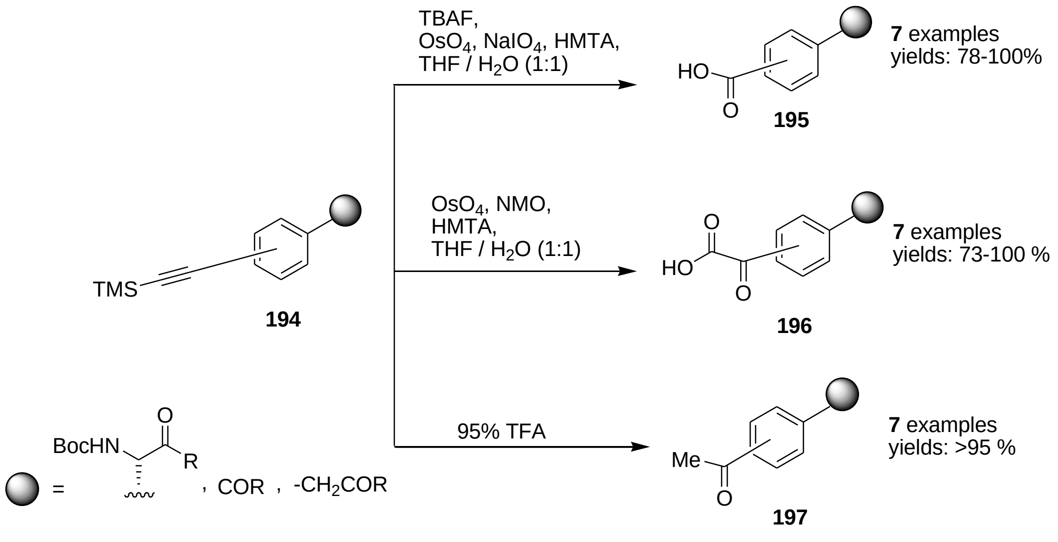


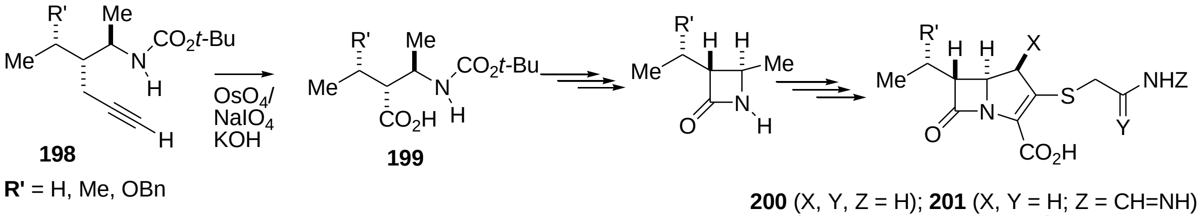
Figure 52. Oxidative cleavage of peptides using OsO_4 as catalyst and $NaIO_4$ as oxidizing agent.



R = Ala-Phe-Gly-HMBA-PEGA$_{800}$
HMBA: 4-Hydroxymethylbenzoic acid
PEGA$_{800}$ = Resin
TFA: Trifluoracetic acid
NMO: *N*-Methylmorpholin *N*-oxide
TBAF: *tert*-Butylammonium floride
HMTA: Hexamethylenetetramine
NaIO$_4$: Natriumperiodate

Figure 53. Solid-phase oxidative cleavage using OsO$_4$ and NaIO$_4$

Oxidative cleavage of alkynes with the use of OsO$_4$ and NaIO$_4$ are often used in the total synthesis of natural products. For example, one of the many examples is the synthesis of β-lactam antibiotics thienamycin and PS-5. Compound **188** was first treated with the KMnO$_4$/NaIO$_4$ oxidant. The compound decomposed and left many products that could not be characterized. However, with the use of OsO$_4$ and NaIO$_4$, the oxidative cleavage product **189** was obtained in high yield (Figure 54).[195,196]



R' = H, Me, OBn

200 (X, Y, Z = H); **201** (X, Y = H; Z = CH=NH)
202 (X = Me; Y = NMe$_2$; Z = H)

Figure 54. Total synthesis of Thienamycin and PS-5 antibiotics using OsO$_4$ and NaIO$_4$ for the oxidative cleavage of **188**.

Another example for the use of OsO$_4$ and NaIO$_4$ is the total synthesis of miharamycin A and B. During the synthesis of building blocks, compound **203** is oxidized to compound **204** by oxidative cleavage (Figure 55). [197]

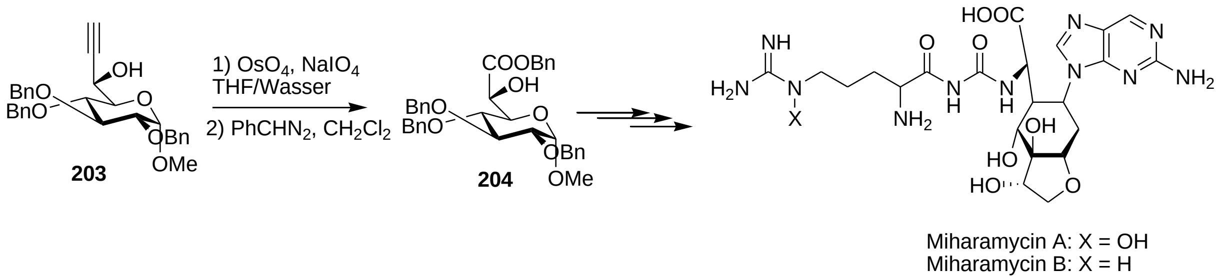


Figure 55. Total synthesis of Miharamycin A and B using OsO_4 as catalyst and $NaIO_4$ as oxidizing agent.

4.12.Au-catalyzed oxidative cleavage of alkynes

Gold is very expensive, but easy to handle a transition metal in the lab. A detailed review of the gold-catalyzed alkyne oxidation was given by Ye et al.[198] However, to date there has been no detailed review of oxidative cleavage with the use of gold via the alkynes. Here, we want to take a look at what has been researched so far on oxidative cleavage. Liu et al. have shown that starting from (*Z*)-enynols **205** butenolides can be formed as starting products **206** in the presence of $AuCl(PPh_3)$ as a catalyst and AgOTf as an additive. 13 substrates were tested using this method. The yields of the cyclized butenolides were obtained between 41-97% (Figure 56).[199]

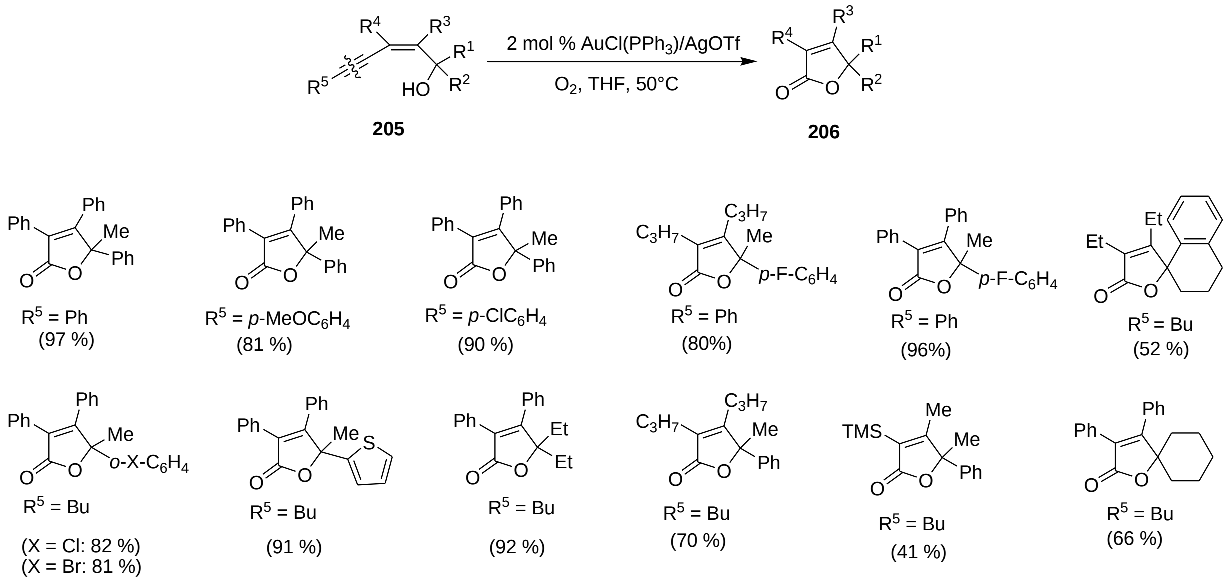
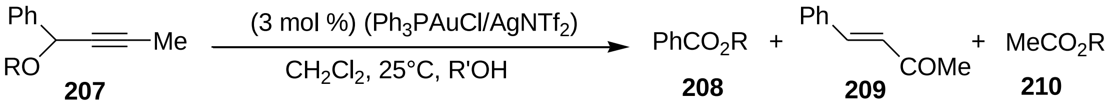


Figure 56. Oxidative cleavage of (*Z*)-enynols to cyclic butenolides using $AuCl(PPh_3)$ as catalyst and O_2 as oxidizing agent.

Although no precise reaction mechanism was described in their manuscript, according to Liu et al. in the reaction mechanism first Au(I) acts as a single-pot catalyst to catalyze cyclization to dihydrofurans followed by an efficient oxidative cleavage reaction, which resulted in the cleavage of C≡C triple bonds in (*Z*)-enynols **205** and converting it to butenolides **206** directly. It is also indicated that the cyclization was not hampered by the atmosphere of dioxygen.[199]

Another example of the oxidative cleavage of alkynes using gold as a catalyst was described by Das et al. They have found that the 1-(1-alkyloxybut-2-ynyl)benzenes are cleaved oxidatively to form the corresponding alkyl benzoate **208** and alkyl acetic acid **210**. Part of the starting material is oxidized to the olefins (E) -4-phenylbut-3-en-2-ones **209**.[200] The solvent plays a decisive role both for improving the yield and for the alkyl part of the ester formed, because the solvent attacks after the oxidative cleavage or after the formation of the carboxylic acid. When no solvent was used, poor yields were obtained. When methanol is used as the solvent, there is almost only an oxidative cleavage of the triple bond. In this reaction condition, the compounds **208** and **210** were isolated in very good yields. When the reaction was carried out in water, only the substrates were oxidized to (*E*)-4-phenylbut-3-en-2-one **210** in very good yield. Oxidative cleavage products **208** and **210** were mainly observed with the use of ethanol. With the use of long-chain alcohols such as *n*-propanol, the product contains more of compounds **208**, **209** and **210** (Figure 57).



R = Me; R'OH = -; **208** = 19 %; **209** = 43 %; **210** = nd
R = Me; R'OH = MeOH; **208** = 81 %; **209** = 4 %; **210** = 85 %
R = Me; R'OH = H_2O; **208** = 6 %; **209** = 83 %; **210** = nd
R = Et; R'OH = EtOH; **208** = 76 %; **209** = 12 %; **210** = 78 %
R = *n*-Pr; R'OH = *n*-PrOH; **208** = 56 %; 199 = 22 %; **210** = 57 %
R = H; R'OH = MeOH; **208** = nd; **209** = 72 %; **210** = nd

nd: not determined.

Figure 57. Oxidative cleavage of α-alkyloxy alkynes to ester and olefins using AuCl(PPh_3) as acatalyst.

Twelve further derivatives of the compound **207** were tested with the use of PPh_3AuCl as a catalyst and oxygen as the oxidizing agent in methanol and the oxidative cleavage products **212** were isolated in good yields. Surprisingly, the substrate **211** reacts by cleaving the C−C σ-bond to form the compound **213** if the *tert*-butyl group was used in the alkyl radical. They justified the formation of compound **213** through the mechanism of oxidative cleavage. Derivatives of thiophene (2-(1-methoxybut-2-ynyl)-3-methylthiophenes) and derivatives of naphthalene (2-(1-methoxybut-2-ynyl)naphthalenes) also cleave oxidatively to their corresponding esters in this reaction condition (Figure 58).[198]

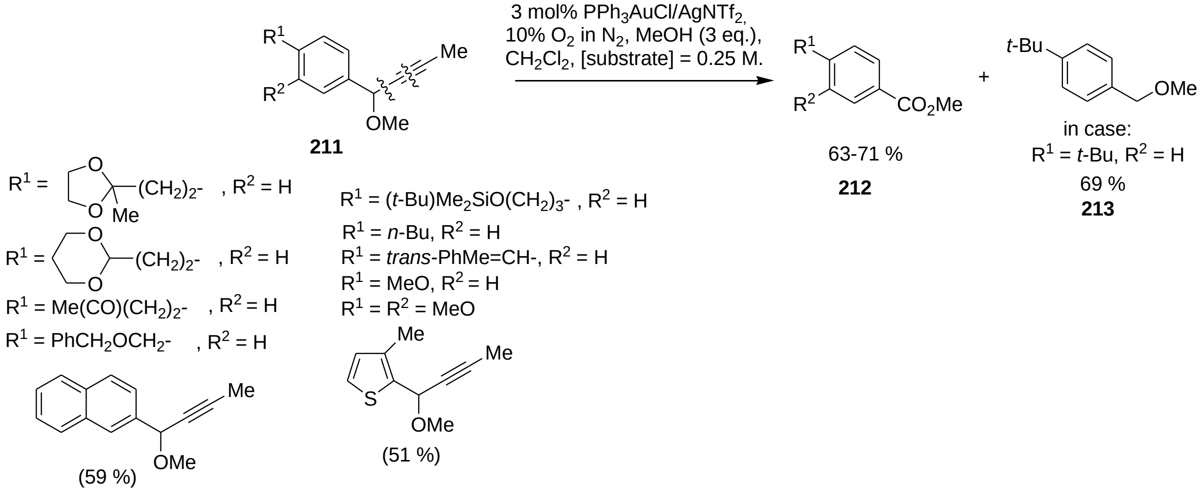


Figure 58. Oxidative cleavage of derivatives of compound **211** using (Ph_3P)AuCl and molecular oxygen as oxidizing agent.

With the use of substrates (-C≡C-(CH$_2$)$_3$-OBn and (-C≡C-(CH$_2$)$_3$-OH) **214**, the oxidative cleavage products **215** and **216** (Figure 59).

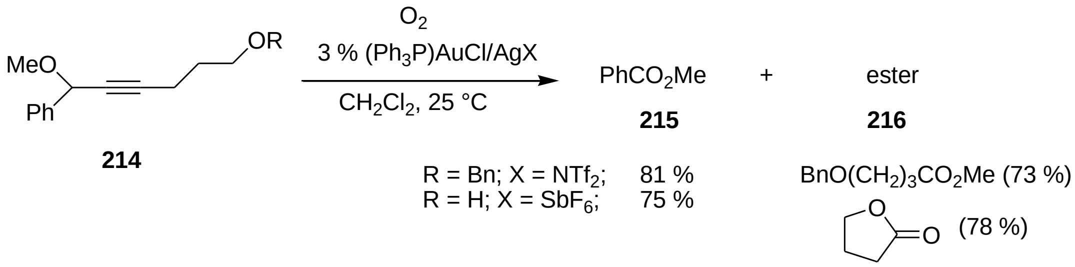


Figure 59. Oxidative cleavage of 1-(6-alkyoxy-1-methoxyhex-2-ynyl)benzene (**214**) using (Ph$_3$P)AuCl as catalyst and molecular oxygen as oxidizing agent to corresponding esters **215** and **216**.

According to Das et al. the reaction mechanism of the oxidative cleavage of figure 54-56 proceeds as followed: They have proposed the following reaction mechanism based on 1-(1-methoxybut-2-ynyl) benzene as starting materials **216**. First, the active catalyst (LAu$^+$) and methanol are added to the triple bond, whereby the intermediate **217** is formed. Intermediate **217** reacts with oxygen and active catalyst to form intermediate **218**. Oxidative cleavage of **218** produces formic acid and methyl benzoate **219**. Intermediate **217** can also only react with one oxygen molecule, with reactive dioxo-intermediate **220** being formed. This in turn reacts with elimination of methyl acetate to form intermediate **221a**. Instead of a phenyl group, *tert*-Bu group **221b**, the intermediate **221b** would further be formed with the elimination of carbon monoxide to the intermediate **222**, with this further elimination of the active catalyst, the cleavage products **226** and **227** are formed. The intermediate **221a** is in equilibrium with its enol **222**. This reacts further with molecular oxygen to form dioxo- intermediate **223**. With elimination of methyl benzoate (**219**), intermediate **224** is formed, which is further oxidized to carbon monoxide / water or carbon dioxide / water with elimination of the active catalyst (Figure 60).

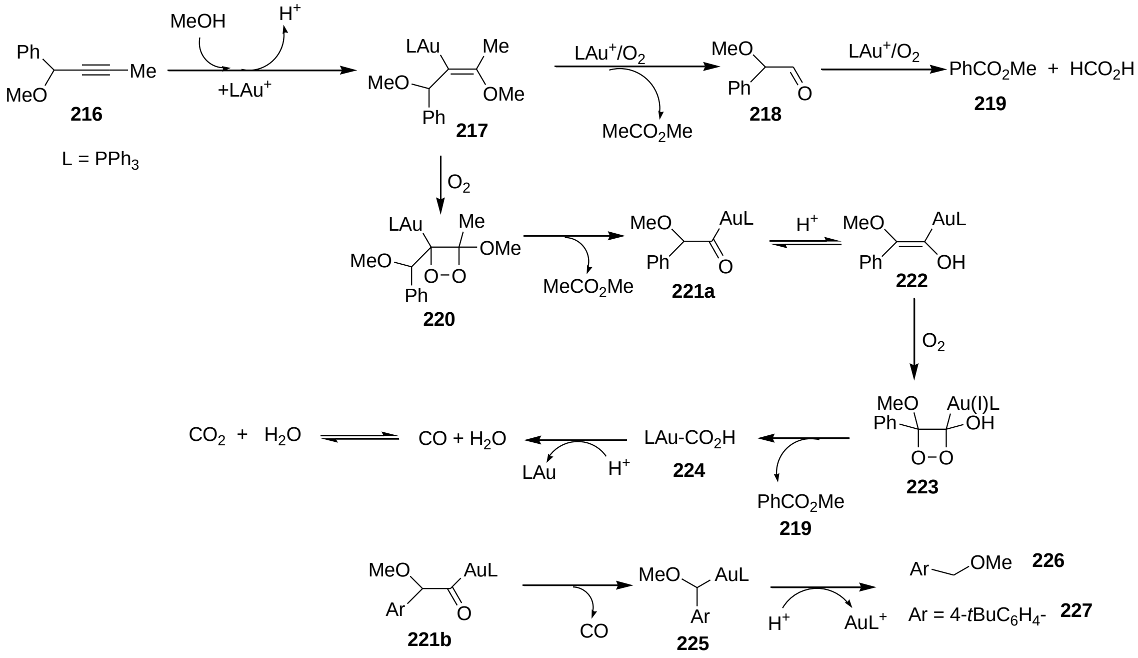


Figure 60. Reaction mechanism of oxidative cleavage of α-alkoxy alkynes using (PPh$_3$)AuCl as catalyst and molecular oxygen as oxidizing agent.

To confirm the proposed reaction mechanism, the starting material was labeled with heavy oxygen. They have carried out two experiments to clarify the mechanism. They first labeled the oxygen of the methoxy group and as a result, they discovered the labeled oxygen only formed on one of the esters. The second experiment was marking the water. They did not observe any labeled oxygen in the products (Figure 61).

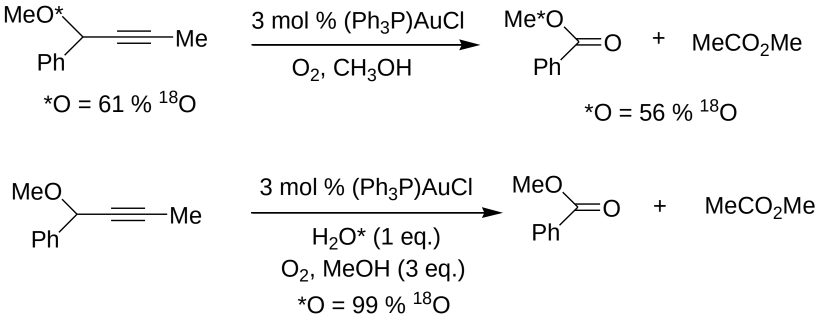


Figure 61. Two experiments for determination of mechanism of oxidative cleavage using ^{18}O labeling.

5. Oxidative Cleavage of Alkynes Using Main Groups Elements (C, Br, I, In)

Another method for the oxidative cleavage of alkynes is the use of the main group elements in high oxidation states. The hypervalent compounds with high oxidation levels are mostly used here. A great advantage of the method is that the reagents are relatively cheaper compared to transition metal reagents and that they have less environmental impact compared to transition metal reagents. However, they are mostly explosive reagents when exposed to heat.

5.1. Oxidative cleavage of alkynes using hypervalent λ^3-iodane reagents

Moriarty *et al.* developed a metal-free method in 1988 that can be used practically. This method is important because it is less polluting compared to using transition metals. They tested one of the many hypervalent iodine reagents in oxidative cleavage.[201-204] The hypervalent iodine reagents that are most commonly used in the oxidative cleavage of organic molecules are iodosylbenzene,[205] diacetoxyiodosylbenzene (PIA),[204] trifluorodiacetoxyiodosylbenzene (PIFA)[207] and [bis(trifluoroacetoxy)iodo]-pentodosylbenzene) **228**. Bis(trifluoroacetoxy)iodo]pentafluorobenzeneiodosylbenzene (FPIFA) **228**, which was used in oxidative cleavage by Moriarty et al. was simply prepared from pentafluoroiodobenzene in one step from pentafluoroiodobenzene and trifluoroacetic anhydride in the presence of nitric acid in 86% yield[208]. Moriarty et al. tested eight different substrates for oxidative cleavage and isolated the corresponding carboxylic acids in good yields (Figure 62).[209]

According to Moriarty et al., the reaction mechanism is as follows; first, the triple bond of the alkyne as a nucleophile attacks the positively charged iodine of FPIFA **228**, forming alkenyl iodine intermediate **229**. This intermediate precipitates with formation of salt **230** and reacts with water to form enol-iodine intermediate **232**. The water then attacks intermediate **231** again, forming α-hydroxyketone **232** and cleaves off pentafluorobenzene and trifluoroacetate. This intermediate **232** reacts according to Moriarty et al. again with **228** and oxidizes to the carboxylic acid end product. To prove that **232** should exist as an intermediate, another experiment was performed with 2-hydroxy-1-(4-nitrophenyl)ethanone **233**. They found that it oxidizes to the corresponding 4-nitrobenzoic acid **234** under the same reaction conditions (Figure 63).

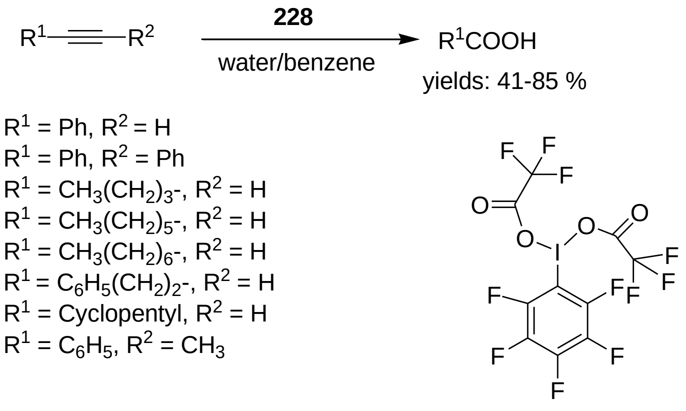


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Figure 62. Oxidative cleavage of alkyne using hypervalent iodine regant (FPIFA) in a mild reaction condition.

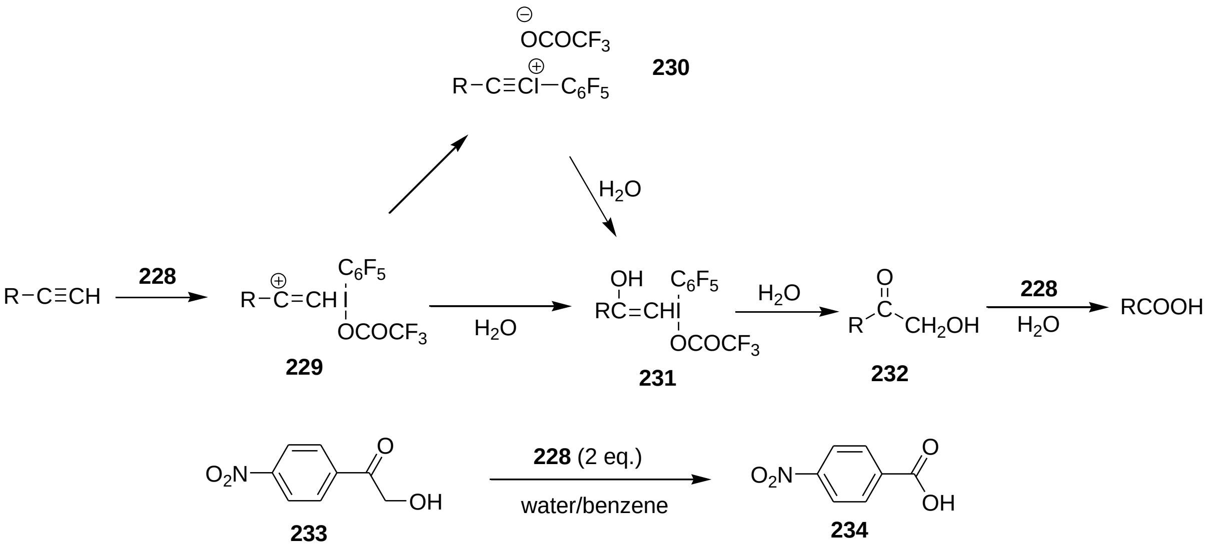


Figure 63. Mechanism of oxidative cleavage of alkynes using FPIFA.

A recently published work is on the use of phenyliodinebis(trifluoroacetate) **235** (PIFA) in the oxidative cleavage of alkynes in mild reaction conditions, which can be easily prepared in one step from iodobenzene in 87% yield.[207] Jiang et al. found out that the alkynes can be cleaved oxidatively directly to the ester. They tested a total of 28 substrates and isolated the esters in yields between 52 and 90%. No reaction took place with an 4-aminophenyl group (R = 4-H_2N-Ph-) and a 3-hydroxyphenyl group (R = 3-HO-Ph-). They suspect that the amine group and the hydroxyl group react with the iodine of the PIFA **235** and therefore there is no cleavage and therefore no esterification (Figure 64).[210]

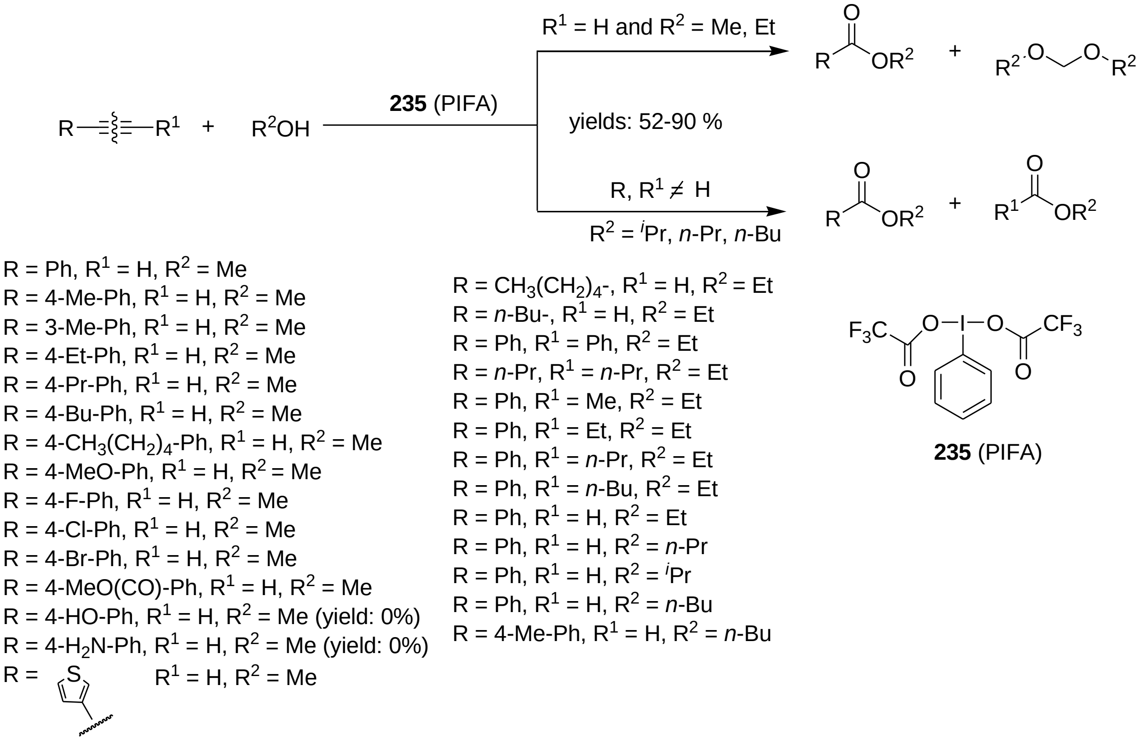


Figure 64. Oxidative cleavage of alkynes using PIFA.

According to Jiang et al. the mechanism proceeds as followed: the triple bond attacks the positively charged iodine of the PIFA, whereby the intermediate **236** is formed and trifluoroacetate is cleaved off . The intermediate **237** is formed by the attack of trifluoroacetate on carbon of the intermediate **236**. The intermediate **237** reacts further intermolecularly with elimination of iodobenzene and trifluoroacetate to form the intermediate **238**. Under attack by trifluoroacetate and twice the alcohol used, the intermediate **239** is formed, two molecules of trifluoroacetic acid alkyl ester being formed. According to Jiang et al., the intermediate **239** oxidizes again with PIFA to the corresponding 1,2-dicarbonyl intermediate **240**, which reacts one last time under Baeyer-Villiger rearrangement either to **241** and **242** or to **243** and **244**. The authors have not described a single step in the formation of intermediates **239** and **240**. They also carried out tests with phenylacetylene and 1-phenylpropyne to confirm intermediate products **239** and **240** GC-MS. To confirm this, they detected the masses of α-hydroxyacetophenone and 1-phenyl-1,2-propanedione. Separately, they conducted two experiments. α-hydroxyacetophenone and 1-phenyl-1,2-propanedione were tested again with PIFA in methanol and they have almost the same yields as the oxidative cleavage reaction starting from phenylacetylene and 1-phenylpropyne with PIFA to give the methyl benzoate (Figure 65).[210]

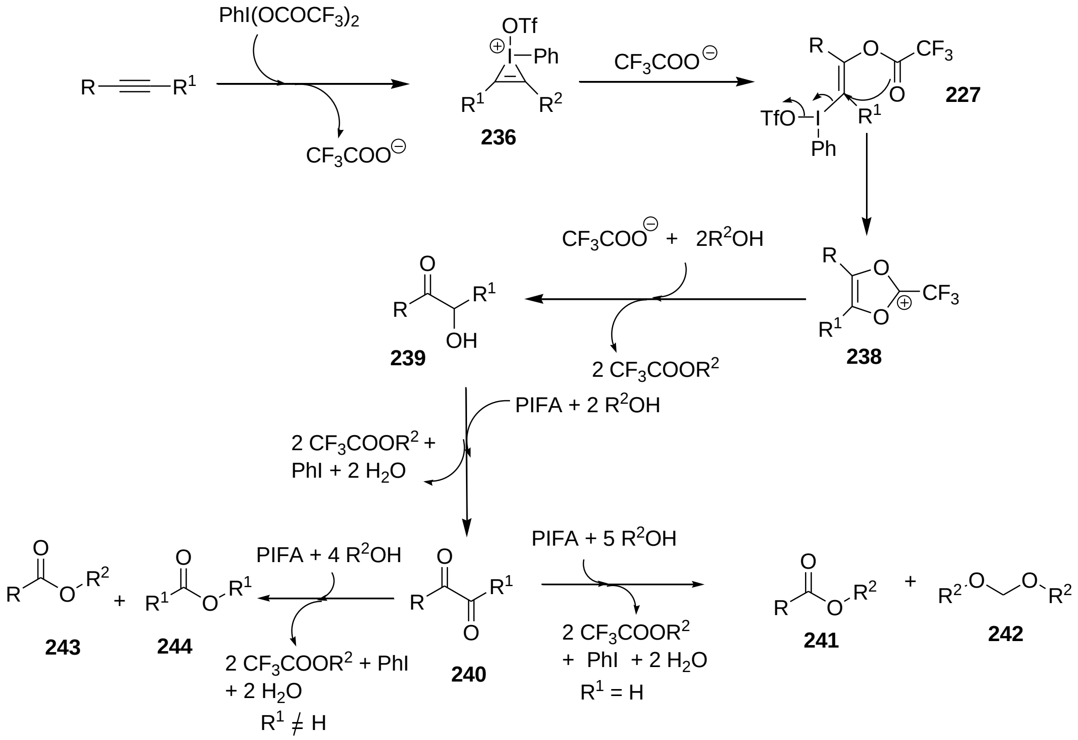


Figure 65. Mechanism of oxidative cleavage of alkynes using PIFA proposed by Jiang *et al.*

Sathyanarayana et al. discovered a method using molecular iodine (I_2), ammonium hydrochloride in dimethyl sulfoxide (DMSO). However, they only used this method for phenylacetylene and its derivatives. They did not comment on the mechanism in the article (Figure 66).[211]

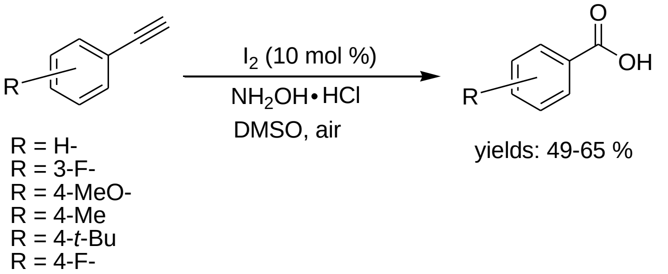


Figure 66. Oxidative cleavage of alkynes using iodine as oxidizing agent.

Miyamoto et al. have used iodomesitylene as a catalyst. They have tested this method not only for the alkynes but also for the oxidative cleavage of olefins. In this method the active reagent, which is the hypervalent iodine compound and is responsible for oxidative cleavage, was formed in situ. Compared to the above methods, the iodine compound is not used in the equivalent amount, but in the amount of catalyst (Figure 67).[77]

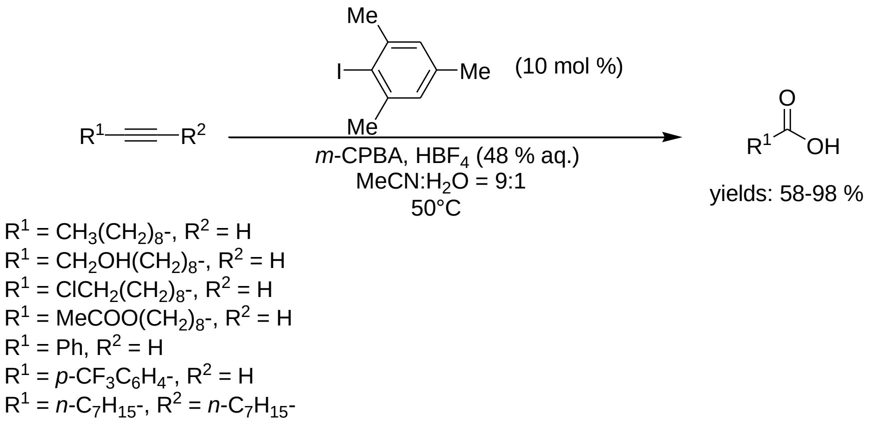


Figure 67. Oxidative cleavage of alkynes using iodomesitylene as catalyst and *m*-CPBA as oxidizing agent.

Miyamoto et al. have proposed a reaction mechanism for the oxidative cleavage of olefins. In the oxidative cleavage of olefins, the active catalyst hydroxy-λ^3-iodane **245** is first formed in situ with the oxidation of iodine using *m*-CPBA. This catalyst oxidizes the substrate (olefin) to 1,2-diol, which first oxidatively cleaves via **247** to give the corresponding aldehydes, which are further oxidized to the corresponding carboxylic acids. Cyclic dialkoxy-λ^3-iodane **247** is widely known in the literature.[79,201,205,212,213]

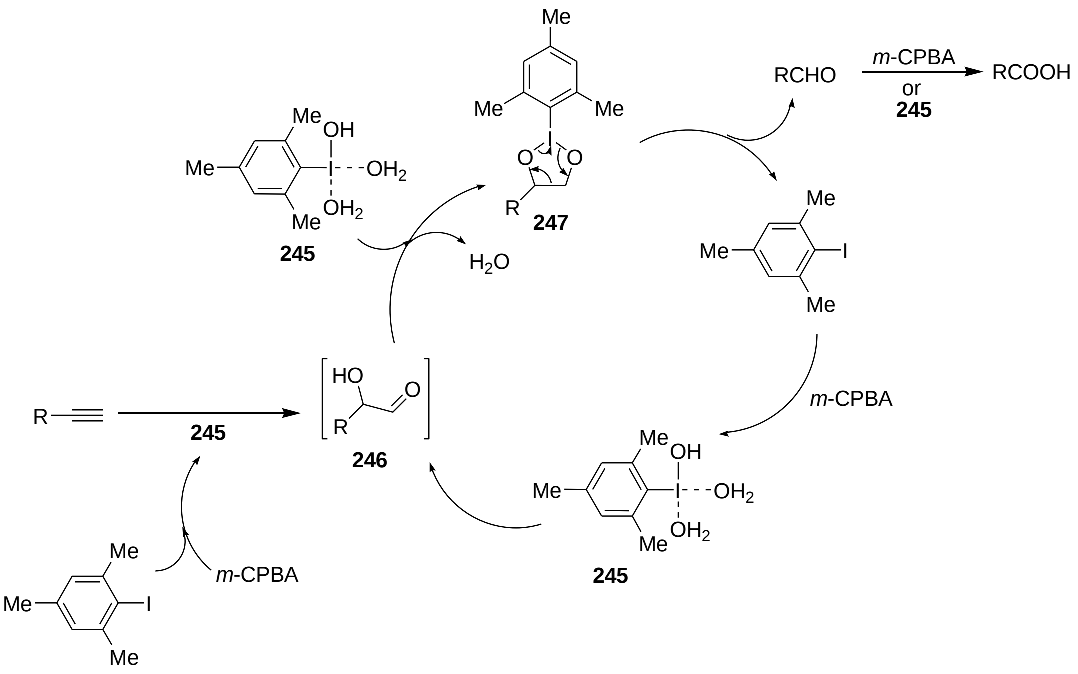


Figure 68. Proposed mechanism of oxidative cleavage of alkynes using iodomesitylene as catalyst and *m*-CPBA as oxidizing agent.

Miyamoto's CSI-MS studies have also confirmed the presence of **245** and **247**.[77] For the oxidative cleavage of alkynes, one can suggest the following reaction mechanism with the prior knowledge of the intermediates of the oxidative cleavage of olefins in situ [77,203] and the reaction mechanism of the other similar reagents (e.g. FPIFA) **218** for alkynes (Figure 68). First, just like in the oxidative cleavage of olefins,[77] the active catalyst hydroxy-λ^3-iodane **245** is formed in situ. This catalyst probably oxidizes the alkyne in several intermediate stages to *α*-hydroxy ketone **246**, while this intermediate product was previously detected with the use of FPIFA in GC-MS with different substrates (see figure 65) **218**. This intermediate product reacts with the active catalyst hydroxy-λ^3-iodane **235** to form the cyclic dialkoxy-λ^3-iodane **247**, which further cleaves oxidatively to the corresponding aldehydes. These aldehydes oxidize further under these strong oxidation conditions to the corresponding end products "carboxylic acids". Unfortunately, in the article no further studies were carried out on the reaction mechanism towards the formation of the aldehydes. This important intermediate for the explanation of the reaction mechanism could have been easily demonstrated with the variable temperature (VT)-NMR study. After the formation of the products, iodomesitylene is formed again in the reaction, which react again with *m*-CPBA to form the active catalyst hydroxy-λ^3-iodane **245** and the catalysis cycle starts again (Figure 68).

5.2. Oxidative cleavage of alkynes using carbon tetrabromide and molecular oxygen

Another environmentally friendly and metal-free method was developed by Yamaguchi et al. They used tetrabromomethane as the catalyst and molecular oxygen as the oxidant in a water/EtOAc mixture, where molecular oxygen was electronically excited with the use of a 400 W mercury lamp and water was used in catalytic amounts. A total of 12 substrates, including phenylacetylenes and its derivatives, 1-nonyne, 2-acetylenyl pyridine and 3-acetylenyl thiophene, were tested with this method. In the same reaction condition in the dark or with the use of a fluorescent lamp, no reaction took place. To optimize the reaction conditions, the oxidative cleavage of phenylacetylene was selected as the standard reaction and a number of catalysts such as CBr_4, NBS, Br_2, HBr (48% aq.), LiBr, NaBr, KBr, $AlBr_3$ and $SmBr_3$ were tested. The lowest yield (1%) was achieved with the use of sodium bromide and the highest yield (86%) was achieved with the use of tetrabromomethane. They also found that the addition of water in catalytic amounts plays a crucial role in improving the yield. Without ethyl acetate only in water as solvent, 8% benzoic acid was isolated (Figure 69).[214]

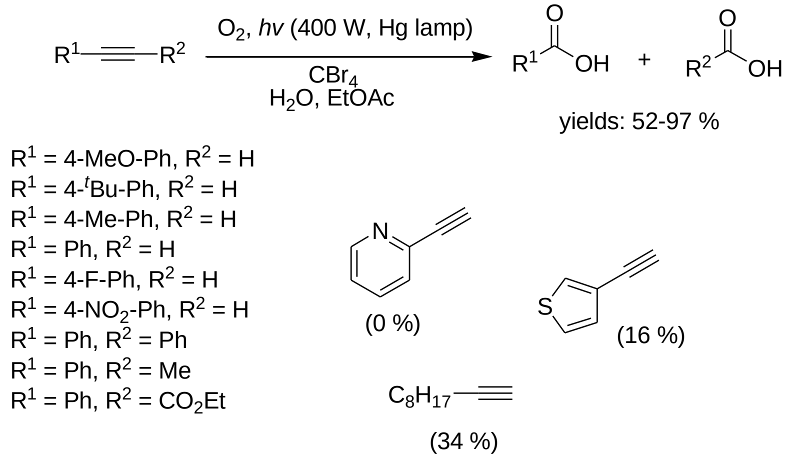


Figure 69. Oxidative cleavage of alkynes using CBr_4 as catalyst and molecular oxygen as oxidizing agent

According to Yamaguchi et al., the reaction proceeds radically first with the radical cleavage of tetrabromomethane to tribromocarbon radical and bromine radical with the help of light. With the help of light, bromine cleaves homolytically, which is then further oxidized in the presence of catalytic amounts of water to form hypobromous acid and hydrobromic acid. Br radicals also react with the alkyne to form a trans- β-bromoalkenyl radical **248**. This reactive radical intermediate reacts further with molecular oxygen and hydrogen radical in situ, which is formed by the radical cleavage of different intermediates in the catalysis cycle, whereby the (*Z*)-1-bromo-2-hydroperoxyalkenes intermediate **249** is formed. The reaction of HBr with the oxygen from peroxo intermediate **249** produces (*Z*)-2-bromoenol intermediate **250**, which further reacts with yet another bromine molecule on the basis of nucleophilic substitution to give α, α-dibromo acetylketone **251**. *α,α*-Dibrommethyl ketone **251** reacts according to Yamaguchi et al. in the three different reaction pathways A, B and C. In the first reaction path A, the intermediate product **251** reacts in the presence of light with elimination of a bromine radical to give α-bromomethyl ketone radical intermediate **252**. With molecular oxygen and hydrogen radical, this radical intermediate leads to the *α,α*-peroxo bromomethyl ketone **253**, which on treatment of HBr loses its peroxo group and reacts to *α,α*-hydroxy bromomethyl ketone **254**. With the elimination of hydrobromic acid, *α*-ketoaldehyde **245** is formed. According to Yamaguchi et al., *α*-ketoaldehyde **255** reacts further with elimination of a hydrogen atom to the α-keto acyl radical **256**, which forms its corresponding α-ketoperoxocarboxylic acid **257** with oxygen and hydrogen. *α*-Ketoperoxocarboxylic acid **257** in turn reacts with hydrobromic acid to form hydrobromic acid to give the corresponding α-ketocarboxylic acid **258**. This intermediate **258** cleaves with excitation of light to the acyl radical **259** (key intermediate), which is formed in reaction pathways **B** and **C**, upon excitation of light. In the proposal of reaction path B, the starting intermediate **251** reacts directly to the acyl radical **259** with the aid of light with radical elimination. In the reaction **path C**, the starting intermediate **251** reacts radically with the aid of light with the elimination of hydrogen to give the *α,α*-dibromomethyl ketone radical **262**, that then with oxygen molecule and hydrogen radical to form *α,α,α*-peroxo dibromomethyl ketone **263**, which in turn reacts with HBr to lose the peroxo group. This *α,α,α*-hydroxy dibromomethyl ketone **264** eliminates HBr, with the *α*-ketoalkonyl bromide 255 being formed. This reacts with water to form intermediate **268** with the formation of HBr. This means that the α-ketocarboxylic acid intermediate **268** is formed in reaction **path A** and **C**. This reacts radically with decarboxylation and with the formation of hydrogen to form the acyl radical **259**, which leads to the peroxocarboxylic acid intermediate **260** in the presence of oxygen and hydrogen. This peroxocarboxylic acid cleaves in the presence of hydrobromic acid to form the carboxylic acid product. According to Yamaguchi et al., the carboxylic acid product starting from alkyne requires two molecules of oxygen and two hydrogen radicals in reaction **path A**. The product requires one molecule of oxygen and one radical hydrogen in reaction **path B**. The product requires two molecules of oxygen and two hydrogen radicals in reaction **path C**. . ^{1}H-NMR measurements were carried out to confirm the entire reaction mechanism. They were able to detect intermediates **251** and **258**. However, the experiments are actually little in favor of proposing the three different reaction paths **A**, **B** and **C**. Many intermediates have been proposed without experimental evidence (Figure 70).

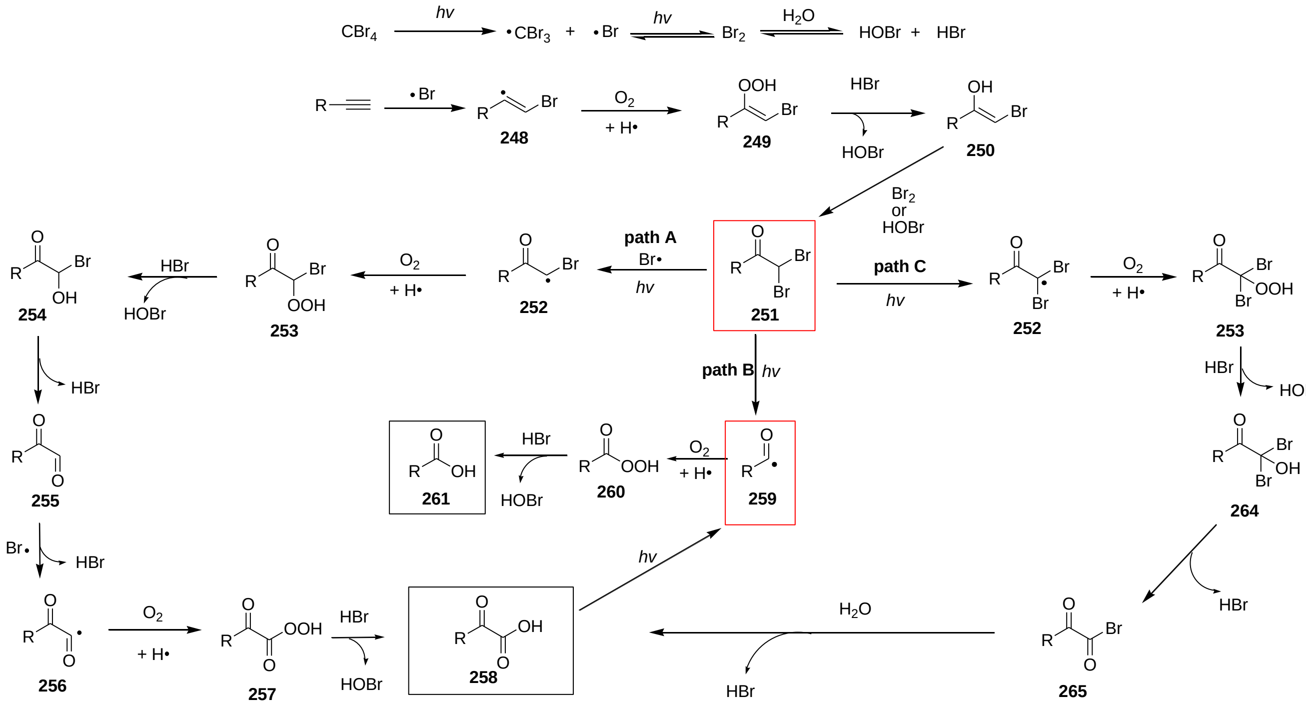


Figure 70. Proposed mechanism for the oxidative cleavage of alkynes using CBr_4 as catalyst and O_2 as oxidizing agent.

5.3. Oxidation of aryl substituted alkyne to 1,2-diketone using 9,10-dicyanoanthracene and biphenyl

A method for the synthesis of 1,2-diketones through the mild and metal-free catalytic photooxygenation of alkynes is described by Qin et al. This reaction, using 9,10-dicyanoanthracene (DCA) **266** as a catalytic sensitizer with / without biphenyl (BP) as a co-sensitizer, readily delivers a variety of desired products upon visible-light irradiation. They tested a total of 23 diaryl-substituted alkynes and arylalkyl-substituted alkynes (Figure 71). Without the use of biphenyl **271**, they received poorer yields for these substrates. The radical cation of biphenyl is more reactive and thus the radical cation can be more easily transferred to the substrate. The photocatalyst / redox mediator pair 9,10-dicyanoanthracene (DCA) and biphenyl (BP) has often been employed as a photooxidation system.[215-217] The singlet excited state of DCA (^{1}DCA*), which is traditionally generated in acetonitrile by irradiation with a Hg lamp, is an excellent one-electron oxidant [($E_{1/2}$) = 1.99 V vs. saturated calomel electrode (SCE)].[215,218] Moreover, BP might significantly increase the rate and chemical yield for DCA-catalyzed oxidations [oxidation potential (Eox) of BP = 1.85 V vs. SCE][215,219]. The oxidative potential of 1,2-diphenylethyne (1a) is 1.84 V (vs. SCE)[220]. According to Qin et al. the reaction mechanism proceeds as followed. First DCA is excited with visible light to DCA* **267** (Figure 72). Upon falling back to the ground state, BP **271** will be charged as radical cation **272** and DCA **266** as radical anion **268**. The charged radical anion DCA **268** transfers the radical cation to the air oxygen **269**. However, the radical cation of BP oxidizes the alkyne to the olefin radical cation **274**, which further reacts either with water and air oxygen or with the radical anion oxygen **270** to form 1,2 -dioxetane intermediate **275** or to form the radical *α*-peroxoketone intermediate **276**. These two intermediates **275** and **276** are then further oxidized to 1,2-diketone **277** (Figure 72).

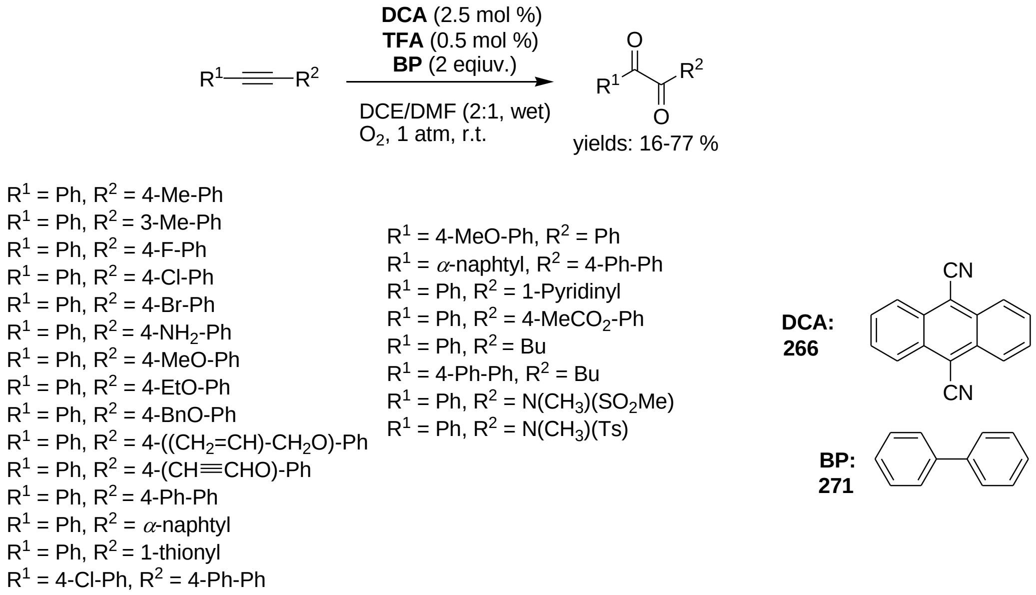


Figure 71. Oxidation of alkynes using DCA and BP as catalysts, O_2 as oxidizing agent.

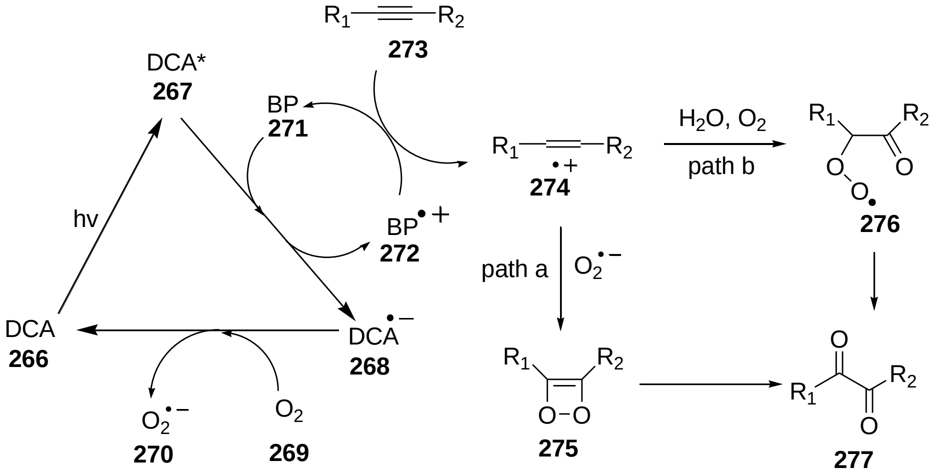


Figure 72. Oxidation of alkyne using DCA and BP as catalysts, O_2 as oxidizing agent

5.4. In-catalyzed oxidative cleavage of alkynes

An efficient and general method for the oxidative cleavage of alkenes and alkynes using tert-butyl hydroperoxide and indium (III) chloride as catalyst in water to give the corresponding carboxylic acids or ketones has been achieved by Ranu et al. They tested alkenes with peptide bonds, *tert*-butyl carboxylic esters and N-Boc-protected tryptophan and obtained very high chemoselectivity. The catalyst has been recycled successfully. They have tested transition metals such as $CuCl_2$, $CeCl_3$, $FeCl_3$, $ZnCl_2$ and $TiCl_4$ for oxidative cleavage. However, they were not as effective as $InCl_3$ and brought between 38 and 55% yield for the oxidative cleavage of α-phenylstyrene to benzophenones in the same reaction condition. Under the same reaction conditions, 84% benzophenone was isolated with the use of $InCl_3$ as a catalyst with no side product being obtained. Unfortunately, although they tested this method for 17 different olefins, they used this method only for a total of four alkynes. The corresponding carboxylic acids were obtained in good yields (Figure 73).[92]

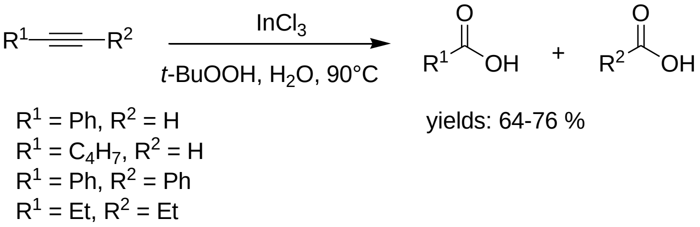


Figure 73. Oxidative cleavage of alkynes using $InCl_3$ as catalyst and *t*-BuOOH as oxidizing agent.

In their manuscript, a reaction mechanism was suggested only for the oxidative cleavage of olefins. According to Ranu et al., the oxidative cleavage of the olefins takes place via first the formation of epoxide, then the formation of 1,2-diol, which leads to the corresponding carboxylic acids. These intermediates were isolated from the reaction mixture. Unfortunately, no reaction mechanism for the oxidative cleavage of alkynes has been proposed.[92]

5.5. Oxidation of alkynes using dioxirane

Potassium peroxymonosulfate, well-known as oxone, can normally be synthesized from potassium carbonate and peroxomonosulfuric acid.[221] Potassium peroxomonosulfate is a crystalline white odorless solid that is readily soluble in water.[222] It decomposes when heated above 90 °C. Its aqueous solution is very acidic. This reagent is often used as a strong oxidant in chemical synthesis.[223] There is also a monohydrate with a monoclinic crystal structure. Curci et al. have the dioxiranes **278** and **279** from potassium peroxymonosulfate and acetone or trifluoroacetone in in aqueous buffer at pH 7.0-7.5. Curci et al. have developed a method for using these dioxiranes as oxidants for the oxidation of alkyne. They tested four alkynes in different reaction conditions. They have not isolated any oxidative cleavage products, instead a mixture of ketone, aldehyde, carboxylic acid and 1,2-dicarbonyl compounds. The yield of the products varies depending on the use of the dioxiranes (**278** or **279**). When phenylacetylene was reacted in the presence of dimethyldioxirane **278**, mainly 2-oxo-2-phenylacetic acid **279** was obtained in 20% yield and benzaldehyde in 64% yield. With the use of methyl (trifluoromethyl) dioxirane **279** as the oxidizing agent, mainly benzaldehyde was isolated in the oxidation of phenylacetylene. In the oxidation of diphenylacetylene, mainly benzilin 30% and benzophenone in approximately 60% yield were obtained using both dioxirane reagents (**278** and **279**). Using both oxidizing agents **278** and **279**, aliphatic alkynes such as hexadec-8-yne (e,f) oxidizes to form α,β-unsaturated ketone **288** in 77-78% and hexadecane-8,9-diones **289** in 18-19%. In the oxidation of cyclodecyne (a conformationally rigid cycloalkyne), *cis*-bicyclo (5.3.0] decan-2-one **290** was isolated in 86% yield and *cis*-bicyclo [4.4.0] decan-2-one **291** in 13% yield (Figure 74).[170]

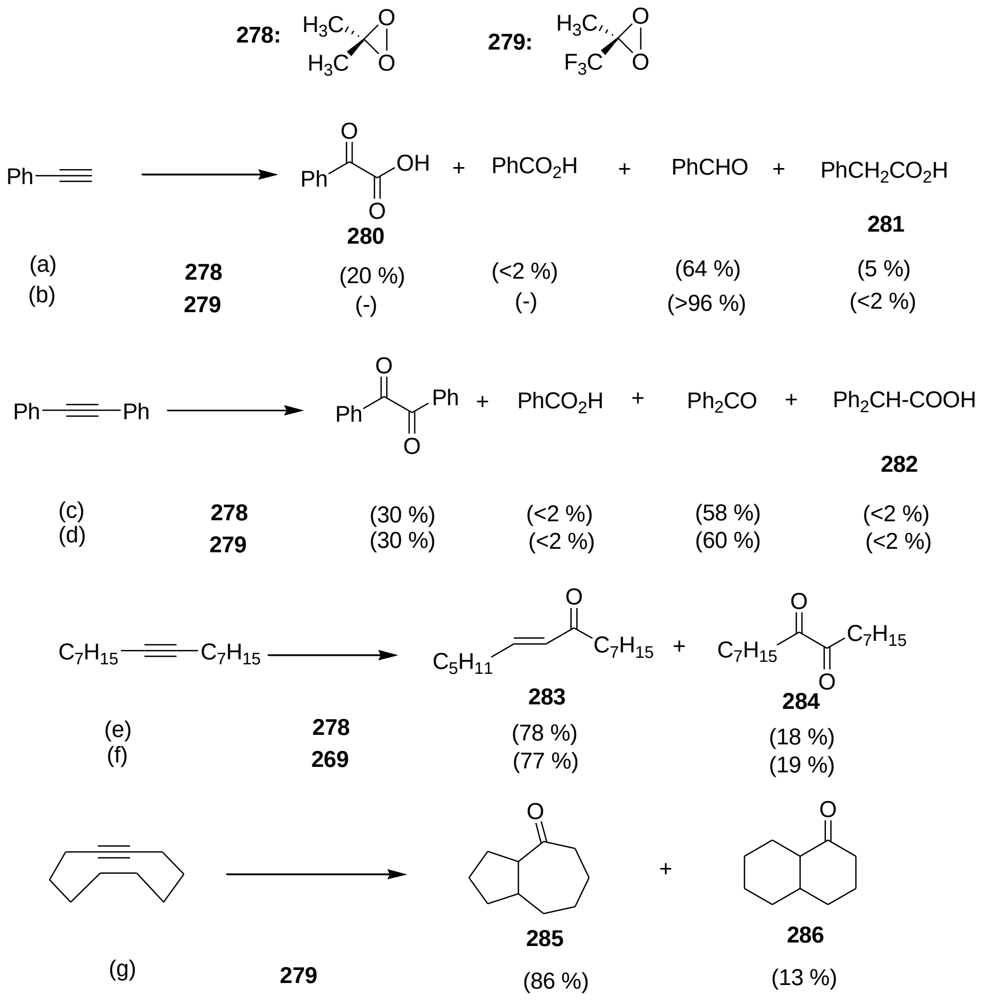


Figure 74. Oxidation of alkyne using dimethyl dioxirane **266** and methyl(trifluormethyl) dioxirane **267** to the corresponding ketone, aldehyde, carbonic acid and 1,2-dicarobonyl compounds.[170]

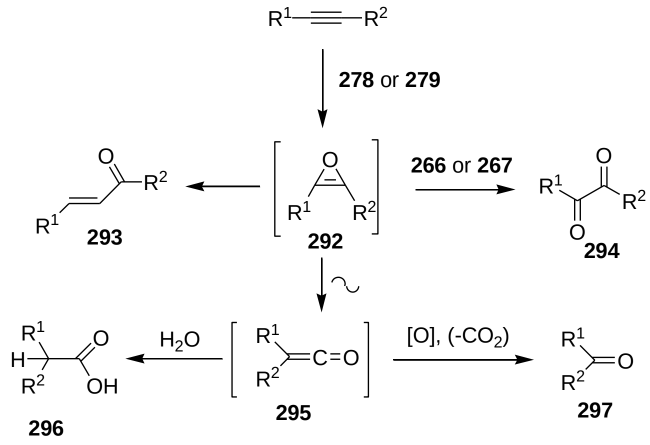


Figure 75. Oxidation of alkynes using dioxirane, which is synthesized by $KHSO_5$.

Dioxirane is prepared *in situ* or isolated as dimethyldioxirane (**278**) and methyl (trifluoromethyl) dioxirane (**279**) oxidize alkynes efficiently. The reaction occurs most likely via oxirene intermediates **280**, which convert to ketene **283**, to an α,β-unsaturated carbonyl **283** or rearrange to form 1,2-dicarbonyl compound **282**. Ketene intermediate **283** oxidizes again with **266** or **267** with decarboxylation to the corresponding ketone **285**, or intermediate **283** reacts in the presence of water to form dialkyl acetic acid (Figure 75).[170]

6. Lanthanide-catalyzed Oxidative Cleavage of Alkynes

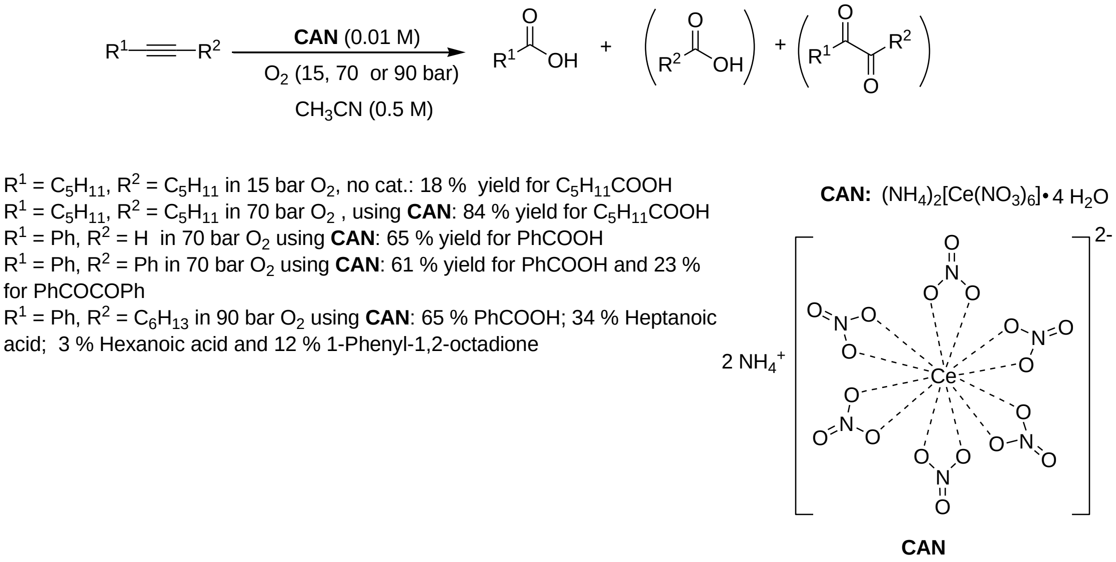
6.1. Ce-catalyzed oxidative cleavage of alkyne

Unlike transition metal-catalyzed oxidative cleavage of alkynes, there is only one example in the literature of oxidative cleavage of alkynes with the use of lanthanides such as cerium. Ceric ammonium nitrate tetrahydrate (also cerium (IV) ammonium nitrate, abbreviated CAN) is an inorganic compound with the formula $(NH_4)_2[Ce(NO_3)_6]\cdot 4H_2O$, which is commercially available. This chemical is also useful for the synthesis of quinoxaline derivatives which are useful as DNA cleaving agents, dyes, and organic semiconductors. When the metal is oxidized, carbon monoxide is produced, and the organic ligand is released.[224,225] The ammonium cation is not involved in the oxidation processes of ceric ammonium nitrate.[226] It is an orange-red crystalline solid and readily soluble in water. The rate enhancements observed with catalytic amounts of Ce are often dramatic relative to the background autoxidation of alkynes. Aryl substituted alkynes such as phenylacetylene, exhibit no autoxidation at 115 °C and 70 bar O_2 pressure in CH_3CN, but with a substrate/catalyst ratio of 20, CAN catalyzes the reaction under similar conditions such that complete substrate conversion is achieved in < 10 min. The Ce-catalyzed oxidation of alkynes gives with very high selectivity (> 90%) the cleavage products of the alkyne under mild conditions (70-100 °C and 100 psig O_2 pressure) with very high rates (TN> 100 min^{-l}) in many cases.

They have tested a total of four substrates in an oxygen pressure of 15, 70 and 90 bar with and without CAN. It is noteworthy that the oxygen has the ability to cleave the alkyl substituted alkyne “6-dodecyne” oxidatively at 15 bar. However, they isolated the hexanoic acid in 18% yield. With the use of CAN in 70 bar oxygen pressure, the yield of the acid was increased up to 84%. In the oxidative cleavage of the aryl substituted alkynes such as phenylacetylenes in 70 bar oxygen pressure 65% benzoic acid is isolated. In the oxidative cleavage of diphenylacetylene in addition to benzoic acid (61%), benzil (23%) was isolated as a by-product. In the oxidation of aryl and alkyl substituted alkyne, a complete homolytic oxidative cleavage was not observed, but a product mixture was obtained. The main products are the oxidative cleavage products: 65% benzoic acid and 34% heptanoic acid, and as byproduct was a 1,2-dicarbonyl compound 1-phenyl-1,2-octadione formed in 12 % yield (Figure 76).[227]

According to Riley et al. the oxidative cleavage proceeds radically in two stages, the first stage is the formation of 1,2-dicarbonyl compound. This intermediate product, which occurs as a by-product in the reaction when certain substrates are used, reacts further with oxidative cleavage to form the corresponding carboxylic acids. The reaction mechanism was studied on the basis of 3-hexyne and first proceeds either via the formation of radical 3-hexyne **305** or via the formation of radical olefin cation **307**. These two radical intermediates **305** and **307** are very reactive and react quickly with molecular oxygen to form the intermediates **306** and **309**. The 1,2-dioxetane intermediate **309** is a radical cation that accepts an additional electron. Then 1,2-dioxetane **310** either cleaves to the 1,2-dicarbonyl compound, which may be further oxidized to the carboxylic acids, or cleaves directly oxidatively to the corresponding carboxylic acids (Figure 78). 1,2-Dicarbonyl intermediate **311** was detected by GC/MS. According to Riley et al., the cerium(III) is oxidized to cerium(IV), the free electron is used in the reduction of the intermediate **309** to the intermediate

310. Which cerium-oxygen species plays a role and how this species reacts is not reported in the manuscript (Figure 77).



$R^1 = C_5H_{11}$, $R^2 = C_5H_{11}$ in 15 bar O_2, no cat.: 18 % yield for $C_5H_{11}COOH$
$R^1 = C_5H_{11}$, $R^2 = C_5H_{11}$ in 70 bar O_2 , using **CAN**: 84 % yield for $C_5H_{11}COOH$
R^1 = Ph, R^2 = H in 70 bar O_2 using **CAN**: 65 % yield for PhCOOH
R^1 = Ph, R^2 = Ph in 70 bar O_2 using **CAN**: 61 % yield for PhCOOH and 23 % for PhCOCOPh
R^1 = Ph, $R^2 = C_6H_{13}$ in 90 bar O_2 using **CAN**: 65 % PhCOOH; 34 % Heptanoic acid; 3 % Hexanoic acid and 12 % 1-Phenyl-1,2-octadione

Figure 76. Oxidative cleavage of alkynes using cerium(IV) ammonium nitrate (CAN) as catalyst and oxygen as oxidizing agent.

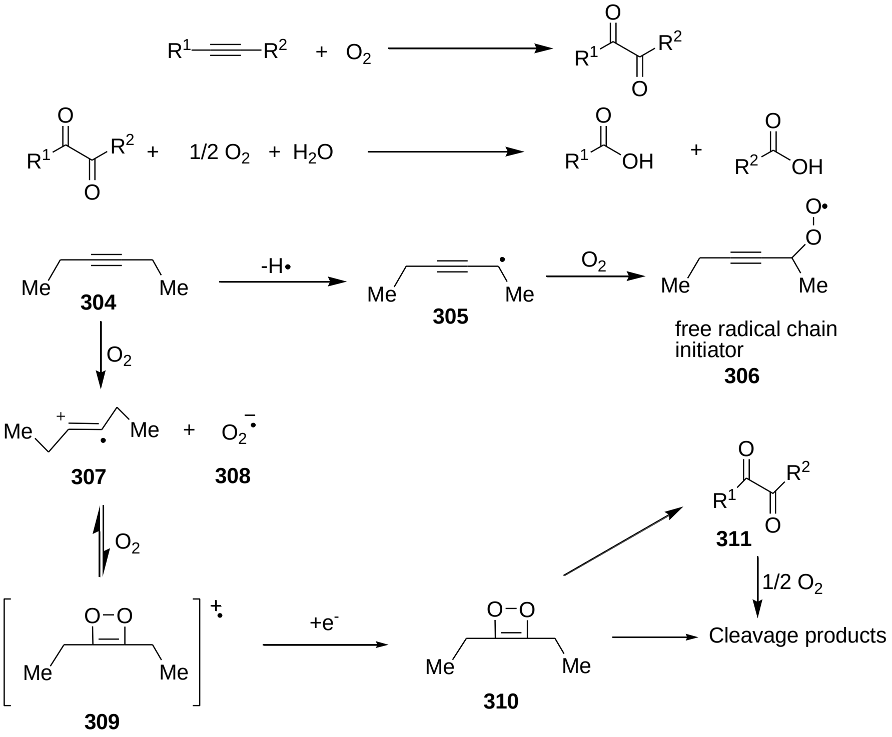


Figure 77. Oxidative cleavage of alkynes using CAN as catalyst and O_2 as oxidizing agent.

7. Summary and Outlook to Oxidative Cleavage of Alkynes in Green Synthesis

In general, the oxidative cleavage or oxidation of the alkynes mainly results in the following products, depending on the reaction conditions or on the substrates used: carboxylic acid anhydrides, 1,2-diketones, carboxylic acids, carboxylic acid esters, α,β-epoxy-ketones and α,β-unsaturated ketones (in case, bearing the substrate a CH_2 group in *α*-position) are mainly formed. Ketones, *α,α*-dialkyl-substituted carboxylic acid and *α*-hydroxyketones are mostly formed as by-products in the methods developed up to present. Unfortunately, no method has hitherto been developed that oxidatively cleaves the alkynes directly to the corresponding aldehydes (Figure 78).

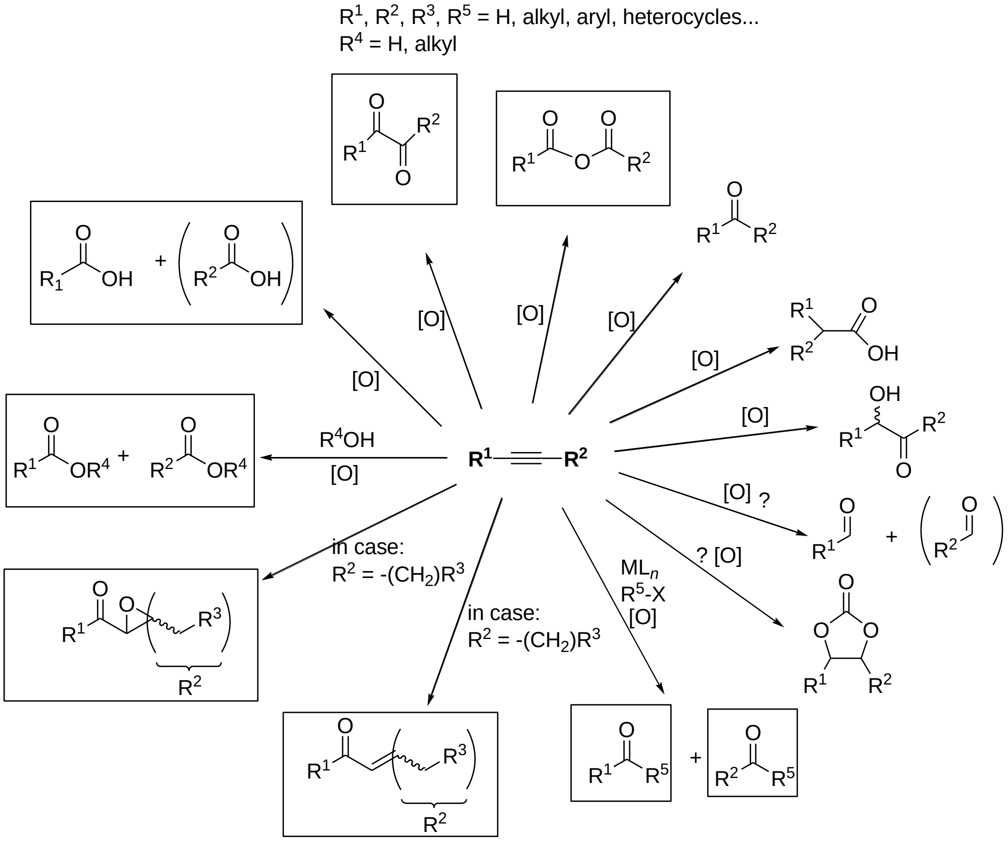


Figure 78. Oxidation and/or oxidative cleavage of alkynes to different products.

The principle of the ozonolysis of alkynes is the same as in the ozonolysis of olefins. The triple bond attacks react with ozone under [3+2] cycloadddition, with many more intermediates being formed compared to the oxidation of the olefins. These intermediates oxidize or cleave oxidatively to form 1,2-diketones, anhydrides or ultimately to carboxylic acids. When metals (Ru, Mn, Fe, Mo, W, Pd, Rh, Ni, Ta, Re, Os, Au and Ce) are used, the following principle was applied: the salts of the metals were used in combination with an oxidizing agent in a solvent. The salts are oxidized to a higher oxidation state under these conditions. The triple bond of the alkynes attacks the active catalyst formed in situ (mostly oxometallic complexes); after the bonds have been reformed, the intermediates are mostly cleaved to form the carboxylic acids or carboxylic acid esters. When using main group elements, the principle of oxidation or oxidative cleavage of the alkynes varies. For example, if hypervalent λ^3-iodanes are used, the hypervalent iodane is reduced to iodine, while alkynes are oxidized to the carboxylic acids or carboxylic acid esters. When using tetrabromomethane, the C-Br bond is first cleaved homolytically when the energy is transferred by light. Then a series of radical reactions begin that activate the oxygen in the air. The radically negatively charged oxygen in the air reacts with the substrate and causes this substrate to cleave oxidatively. When using the DCA-BP system (Figures 71-72). The reagent is activated with visible light, whereby a radical anion intermediate is formed. This intermediate activates the substrate used via BP. When using the dioxiranes, the reactive dioxiranes are in situ with the addition of oxones, which oxidizes the acetone or 1,1,1-trifluoropropane-2-oneto dioxiranes.

In the oxidation of olefins, no oxidative cleavage method for the alkyne that is enzyme-catalyzed has yet been published.

Unfortunately, apart from the oxidative cleavage method using the $OsO_4/NaIO_4$/HMPT system (Figure 50-52), only one method has been published that is chemoselective or that only reacts with alkyne triple bonds. For example, using gold as catalyst, triple bond of enyne as substrate is cleaved (Figure 56).

The best method in terms of environmental friendliness using metal-catalyzed oxidative cleavage seems to be the methods Fe-catalyzed oxidative cleavage with TBHP (chapter 4.3) and Ni-catalyzed oxidative cleavage with molecular oxygen (chapter 4.8). Because the catalyst is recyclable, the used reagent is not so expensive, it is not toxic and easy to handle in the laboratory. Ruthenium (chapter 4.1), rhenium (4.10) and osmium (chapter 4.11) are commonly used in the scientific world and are well-known transition metals for the oxidative cleavage of alkynes. However, these metals are under the category heavy metals and are more expensive and more toxic for human and environment compared to nickel and iron-catalyzed oxidative cleavage. The best methods without any use of transition metal in terms of efficiency, environmental friendliness, cost, easy handling in lab., non-toxicity and satisfying yield seem to be the methods: the ozonolysis (chapter 3), hypervalent λ^3-iodine catalyzed oxidative cleavage (chapter 5.1), DCA-catalyzed oxidative cleavage with molecular oxygen (chapter 5.1) and carbon tetrabromide catalyzed oxidative cleavage with molecular oxygen (chapter 5.2), because on one hand, it is a metal-free catalyzed oxidative cleavage, on the other hand a broad range of substrates were tested using these methods and the oxidizing agents are mostly molecular oxygen or the reagent itself. Using these methods, the oxidative cleavage products were isolated in up to very good yields. However, these methods are not chemoselective for the oxidative cleavage of triple bond of enyne substrate. Other methods have to be improved for a broad range of alkynes or be optimized with regard to stereo and/or chemoselectivity. With another words, the future of the oxidative cleavage of the alkyne should be more chemoselective, cheap, environmentally friendly and atom-efficient.

Conclusions

In conclusions, the best methods in relation to Green Synthesis to cleave the alkynes triple bonds to the corresponding carboxylic acids are the methods in chapters 3, 4.3, 4.8, 5.1, and 5.2.

References

1. Rajagopalan, A.; Lara, M.; Kroutil, W. *Adv. Synth. \& Catal.* **2013**, *355* (17), 3321. https://doi.org/10.1002/adsc.201300882
2. Bäckvall, J.-E. *Modern oxidation methods*; John Wiley \& Sons, 2011.

3. Hon, Y.-S.; Lin, S.-W.; Lu, L.; Chen, Y.-J. *Tetrahedron* **1995**, *51* (17), 5019.
   https://doi.org/10.1016/0040-4020(95)98699-I
4. Philip S Bailey. *Ozonation in Organic Chemistry*; Academic Press, 1978.
5. Criegee, R. *Angew. Chemie Int. Ed. English* **1975**, *14* (11), 745.
   https://doi.org/10.1002/anie.197507451
6. Fisher, T. J.; Dussault, P. H. *Tetrahedron* **2017**, *73*, 4233–4258.
   https://doi.org/10.1016/j.tet.2017.03.039
7. Ogle, R. A.; Schumacher, J. L. *Process Saf. Prog.* **1998**, *17* (2), 127.
   https://doi.org/10.1002/prs.680170209
8. Travaini, R.; Marangon-Jardim, C.; Colodette, J.; Morales Otero, M.; Bolado, S. **2015**;chapter 7, 105-135.
   https://doi.org/10.1016/B978-0-12-800080-9.00007-4
9. Spannring, P.; Bruijnincx, P. C. A.; Weckhuysen, B. M.; Gebbink, R. J. M. K. *Catal. Sci. \& Technol.* **2014**, *4* (8), 2182.
   https://doi.org/10.1039/C3CY01095C
10. Wójtowicz-Młochowska, H. *Arkivoc* **2017**, ii, 12-58.
    http://dx.doi.org/10.3998/ark.5550190.p009.578
11. Travis, B. R.; Narayan, R. S.; Borhan, B. *J. Am. Chem. Soc.* **2002**, *124* (15), 3824.
    https://doi.org/10.1021/ja017295g
12. Whitehead, D. C.; Travis, B. R.; Borhan, B. *Tetrahedron Lett.* **2006**, *47* (22), 3797.
    https://doi.org/10.1016/j.tetlet.2006.03.087
13. Kim, S.; Chung, J.; Kim, B. M. *Tetrahedron Lett.* **2011**, *52* (12), 1363.
    https://doi.org/10.1016/j.tetlet.2011.01.065
14. Nielsen, T. E.; Meldal, M. *Org. Lett.* **2005**, *7* (13), 2695.
    https://doi.org/10.1021/ol050870r
15. Saito, M.; Morita, T.; Takase, K. *Bull. Chem. Soc. Jpn.* **1980**, *53* (12), 3696.
    https://doi.org/10.1246/bcsj.53.3696
16. Pappo, R.; Allen Jr, D.; Lemieux, R.; Johnson, W. *J. Org. Chem.* **1956**, *21* (4), 478.
    https://doi.org/10.1021/jo01110a606
17. Marino, J. P.; Jaén, J. C. *Synth. Commun.* **1983**, *13* (13), 1057.
    https://doi.org/10.1080/00397918308080889
18. Morvillo, A.; Bressan, M. *J. Mol. Catal. A Chem.* **1997**, *125* (2–3), 119.
    https://doi.org/10.1016/S1381-1169(97)00086-1
19. Behr, A.; Tenhumberg, N.; Wintzer, A. *RSC Adv.* **2013**, *3* (1), 172.
    https://doi.org/10.1039/C2RA22370H
20. Shoair, A. G. F.; Mohamed, R. H. *Synth. Commun.* **2006**, *36* (1), 59.
    https://doi.org/10.1080/00397910500328944
21. Griffith, W. P.; Shoair, A. G.; Suriaatmaja, M. *Synth. Commun.* **2000**, *30* (17), 3091.
    https://doi.org/10.1080/00397910008086915
22. Zimmermann, F.; Meux, E.; Mieloszynski, J.-L.; Lecuire, J.-M.; Oget, N. *Tetrahedron Lett.* **2005**, *46* (18), 3201.
    https://doi.org/10.1016/j.tetlet.2005.03.052
23. Augier, C.; Malara, L.; Lazzeri, V.; Waegell, B. *Tetrahedron Lett.* **1995**, *36* (48), 8775.
    https://doi.org/10.1016/0040-4039(95)01873-G
24. Neumann, R.; Abu-Gnim, C. *J. Chem. Soc. Chem. Commun.* **1989**, No. 18, 1324.

https://doi.org/10.1039/C39890001324
25. Che, C.-M.; Yip, W.-P.; Yu, W.-Y. *Chem. Asian J.* **2006**, *1* (3), 453. https://doi.org/10.1002/asia.200600091
26. Bonaldo, M.; Borin, F.; Bressan, M.; Morvillo, A. *J. Organomet. Chem.* **1989**, *363* (1–2), 175. https://doi.org/10.1016/0022-328X(89)88051-9
27. Kanmani, A. S.; Vancheesan, S. *J. Mol. Catal. A Chem.* **1999**, *150* (1–2), 95. https://doi.org/10.1016/S1381-1169(99)00215-0
28. Berkowitz, L. M.; Rylander, P. N. *J. Am. Chem. Soc.* **1958**, *80* (24), 6682. https://doi.org/10.1021/ja01557a053
29. Kogan, V.; Quintal, M. M.; Neumann, R. *Org. Lett.* **2005**, *7* (22), 5039. https://doi.org/10.1021/ol052025e
30. Timofeeva, M. N.; Kholdeeva, O. A.; Jhung, S. H.; Chang, J.-S. *Appl. Catal. A Gen.* **2008**, *345* (2), 195. https://doi.org/10.1016/j.apcata.2008.04.039
31. Fox, M. A.; Chen, C.-C. *Tetrahedron Lett.* **1983**, *24* (6), 547. https://doi.org/10.1016/S0040-4039(00)81460-4
32. Anand, N.; Reddy, K. H. P.; Rao, K. S. R.; Burri, D. R. *Catal. Letters* **2011**, *141* (9), 1355. https://doi.org/10.1007/s10562-011-0668-1
33. Fetizon, M.; Goulaouic, P.; Hanna, I. *Tetrahedron Lett.* **1988**, *29* (48), 6261. https://doi.org/10.1016/S0040-4039(00)82320-5
34. Jarupinthusophon, S.; Thong-In, U.; Chavasiri, W. *J. Mol. Catal. A Chem.* **2007**, *270* (1–2), 289. https://doi.org/10.1016/j.molcata.2007.02.007
35. Nongkynrih, I.; Mahanti, M. K. *J. Org. Chem.* **1993**, *58* (18), 4925. https://doi.org/10.1021/jo00070a031
36. Nongkynrih, I.; Mahanti, M. K. *Bull. Chem. Soc. Jpn.* **1994**, *67* (8), 2320. https://doi.org/10.1246/bcsj.67.2320
37. Lee, D. G.; Brownridge, J. R. *J. Am. Chem. Soc.* **1974**, *96* (17), 5517. https://doi.org/10.1021/ja00824a031
38. Lee, D. G.; Chen, T.; Wang, Z. *J. Org. Chem.* **1993**, *58* (10), 2918. https://doi.org/10.1021/jo00062a046
39. Li, Y.-F.; Guo, C.-C.; Yan, X.-H.; Liu, Q. *J. Porphyr. Phthalocyanines* **2006**, *10* (07), 942. https://doi.org/10.1142/S1088424606000260
40. Liu, S.-T.; Reddy, K. V.; Lai, R.-Y. *Tetrahedron* **2007**, *63* (8), 1821. https://doi.org/10.1016/j.tet.2006.12.029
41. Escande, V.; Petit, E.; Garoux, L.; Boulanger, C.; Grison, C. *ACS Sustain. Chem. & Eng.* **2015**, *3* (11), 2704. https://doi.org/10.1021
42. Adilina, I. B.; Hara, T.; Ichikuni, N.; Shimazu, S. *J. Mol. Catal. A Chem.* **2012**, *361*, 72. https://doi.org/10.1016/j.molcata.2012.05.005
43. White, L. S.; Que Jr, L. *J. Mol. Catal.* **1985**, *33* (2), 139. https://doi.org/10.1016/0304-5102(85)85097-5
44. Hossain, M. M.; Shyu, S.-G. *Tetrahedron* **2014**, *70* (2), 251. https://doi.org/10.1016/j.tet.2013.11.075
45. Tsuji, J.; Kezuka, H.; Takayanagi, H.; Yamamoto, K. *Bull. Chem. Soc. Jpn.* **1981**, *54* (8), 2369. https://doi.org/10.1246/bcsj.54.2369
46. Tsuji, J.; Takayanagi, H. *Chem. Lett.* **1980**, *9* (1), 65.

https://doi.org/10.1246/cl.1980.65

47. Hossain, M. M.; Huang, W.-K.; Chen, H.-J.; Wang, P.-H.; Shyu, S.-G. *Green Chem.* **2014**, *16* (6), 3013. https://doi.org/10.1039/C3GC42624F
48. Tokunaga, M.; Shirogane, Y.; Aoyama, H.; Obora, Y.; Tsuji, Y. *J. Organomet. Chem.* **2005**, *690* (23), 5378. https://doi.org/10.1016/j.jorganchem.2005.05.018
49. Yukimasa, H. ; Sawai, H. ; Takizawa, T. *Chem. Pharm. Bull.* **1979**, *27* (2), 551. https://doi.org/10.1248/cpb.27.551
50. Mi, C.; Meng, X.-G.; Liao, X.-H.; Peng, X. *RSC Adv.* **2015**, *5* (85), 69487. https://doi.org/10.1039/C5RA14093E
51. Liu, Y.; Xue, D.; Li, C.; Xiao, J.; Wang, C. *Catal. Sci. \& Technol.* **2017**, *7* (23), 5510. https://doi.org/10.1039/C7CY01757J
52. Cossy, J.; Belotti, D.; Bellosta, V.; Brocca, D. *Tetrahedron Lett.* **1994**, *35* (33), 6089. https://doi.org/10.1016/0040-4039(94)88083-2
53. Bönnemann, H.; Nunez, W.; Rohe, D. M. M. *Helv. Chim. Acta* **1983**, *66* (1), 177. https://doi.org/10.1002/hlca.19830660119
54. Ishii, Y.; Yamawaki, K.; Ura, T.; Yamada, H.; Yoshida, T.; Ogawa, M. *J. Org. Chem.* **1988**, *53* (15), 3587. https://doi.org/10.1021/jo00250a032
55. Fujitani, K.; Mizutani, T.; Oida, T.; Kawase, T. *J. Oleo Sci.* **2009**, *58* (1), 37. https://doi.org/10.5650/jos.58.37
56. Khlebnikova, T. B.; Pai, Z. P.; Fedoseeva, L. A.; Mattsat, Y. V. *React. Kinet. Catal. Lett.* **2009**, *98* (1), 9. https://doi.org/10.1007/s11144-009-0054-9
57. Pyszny, D.; Piotrowski, T.; Orlińska, B. *Org. Process Res. \& Dev.* **2019**, *23* (3), 309. https://doi.org/10.1021/acs.oprd.8b00368
58. Santacesaria, E.; Ambrosio, M.; Sorrentino, A.; Tesser, R.; Di Serio, M. *Catal. today* **2003**, *79*, 59. https://doi.org/10.1016/S0920-5861(03)00045-2
59. Oguchi, T.; Ura, T.; Ishii, Y.; Ogawa, M. *Chem. Lett.* **1989**, *18* (5), 857. https://doi.org/10.1246/cl.1989.857
60. Santacesaria, E.; Sorrentino, A.; Rainone, F.; Di Serio, M.; Speranza, F. *Ind. \& Eng. Chem. Res.* **2000**, *39* (8), 2766. https://doi.org/10.1021/ie990920u
61. Rubinstein, A.; Jiménez-Lozanao, P.; Carbó, J. J.; Poblet, J. M.; Neumann, R. *J. Am. Chem. Soc.* **2014**, *136* (31), 10941. https://doi.org/10.1021/ja502846h
62. Herrmann, W. A.; Weskamp, T.; Zoller, J. P.; Fischer, R. W. *J. Mol. Catal. A Chem.* **2000**, *153* (1–2), 49. https://doi.org/10.1016/S1381-1169(99)00370-2
63. Karseboom, S. G.; Davis, J. E.; Mullins, C. B. *Surf. Sci.* **1997**, *383* (2–3), 173. https://doi.org/10.1016/S0039-6028(97)00160-X
64. Fisher, E.; Kenisgberg, L.; Carreira, M.; Fernández-Gallardo, J.; Baldwin, R.; Contel, M. *Polyhedron* **2016**, *120*, 82. https://doi.org/10.1016/j.poly.2016.06.012
65. Xing, D.; Guan, B.; Cai, G.; Fang, Z.; Yang, L.; Shi, Z. *Org. Lett.* **2006**, *8* (4), 693. https://doi.org/10.1021/ol052830t
66. Lara, M.; Mutti, F. G.; Glueck, S. M.; Kroutil, W. *J. Am. Chem. Soc.* **2009**, *131* (15), 5368. https://doi.org/10.1021/ja8097096

67. Auldridge, M. E.; McCarty, D. R.; Klee, H. J. *Curr. Opin. Plant Biol.* **2006**, *9* (3), 315. https://doi.org/10.1016/j.pbi.2006.03.005
68. Takemoto, M.; Iwakiri, Y.; Suzuki, Y.; Tanaka, K. *Tetrahedron Lett.* **2004**, *45* (43), 8061. https://doi.org/10.1016/j.tetlet.2004.08.175
69. Woggon, W.-D. *Pure Appl. Chem.* **2002**, *74* (8), 1397. https://doi.org/10.1351/pac200274081397
70. Mang, H.; Gross, J.; Lara, M.; Goessler, C.; Schoemaker, H. E.; Guebitz, G. M.; Kroutil, W. *Tetrahedron* **2007**, *63* (16), 3350. https://doi.org/10.1016/j.tet.2007.02.034
71. Schwartz, S. H.; Tan, B. C.; Gage, D. A.; Zeevaart, J. A. D.; McCarty, D. R. *Science (80-.).* **1997**, *276* (5320), 1872. https://doi.org/10.1126/science.276.5320.187
72. Kawata, S.; Minami, Y.; Tarui, S.; Marunaka, T.; Okamoto, m.; Yamano, T. *Jpn. J. Pharmacol.* **1984**, *36* (1), 43. https://doi.org/10.1254/jjp.36.43
73. Thottumkara, P. P.; Vinod, T. K. *Org. Lett.* **2010**, *12* (24), 5640. https://doi.org/10.1021/ol1023807
74. Nicolaou, K. C.; Adsool, V. A.; Hale, C. R. H. *Org. Lett.* **2010**, *12* (7), 1552. https://doi.org/10.1021/ol100290a
75. Atmaca, U.; Usanmaz, H. K.; Çelik, M. *Tetrahedron Lett.* **2014**, *55* (14), 2230. https://doi.org/10.1016/j.tetlet.2014.02.076
76. Henry, J. R.; Weinreb, S. M. *J. Org. Chem.* **1993**, *58* (17), 4745. https://doi.org/10.1021/jo00069a047
77. Miyamoto, K.; Sei, Y.; Yamaguchi, K.; Ochiai, M. *J. Am. Chem. Soc.* **2009**, *131* (4), 1382. https://doi.org/10.1021/ja808829t
78. Moorthy, J. N.; Parida, K. N. *J. Org. Chem.* **2014**, *79* (23), 11431. https://doi.org/10.1021/jo502002w
79. Havare, N. *Int. J. Chem. Stud.* **2018**, *2* (4), 10. http://www.chemistryjournal.in/archives/2018/vol2/issue4/2-5-12
80. Neumann, R.; Abu-Gnim, C. *J. Am. Chem. Soc.* **1990**, *112* (16), 6025. https://doi.org/10.1021/ja00172a018
81. Spannring, P.; Bruijnincx, P. C. A.; Weckhuysen, B. M.; Gebbink, R. J. M. K. *RSC Adv.* **2013**, *3* (18), 6606. https://doi.org/10.1039/C3RA40324F
82. Xu, J.-H.; Jiang, Q.; Guo, C.-C. *J. Org. Chem.* **2013**, *78* (23), 11881. https://doi.org/10.1021/jo401919h
83. Wang, G.-Z.; Li, X.-L.; Dai, J.-J.; Xu, H.-J. *J. Org. Chem.* **2014**, *79* (15), 7220. https://doi.org/10.1021/jo501203a
84. Wang, T.; Jiao, N. *J. Am. Chem. Soc.* **2013**, *135* (32), 11692. https://doi.org/10.1021/ja403824y
85. Bäumer, U.-S.; Schäfer, H. J. *J. Appl. Electrochem.* **2005**, *35* (12), 1283. https://doi.org/10.1007/s10800-005-9060-4
86. Wu, X.; Davis, A. P.; Fry, A. J. *Org. Lett.* **2007**, *9* (26), 5633. https://doi.org/10.1021/ol7026416
87. Murthy, R. S.; Bio, M.; You, Y. *Tetrahedron Lett.* **2009**, *50* (9), 1041.

https://doi.org/10.1016/j.tetlet.2008.12.069

88. Parida, K. N.; Moorthy, J. N. *J. Org. Chem.* **2015**, *80* (16), 8354. https://doi.org/10.1021/acs.joc.5b00292
89. Posner, G. H.; Oh, C. H.; Milhous, W. K. *Tetrahedron Lett.* **1991**, *32* (34), 4235. https://doi.org/10.1016/S0040-4039(00)92136-1
90. Deng, Y.; Wei, X.-J.; Wang, H.; Sun, Y.; Noël, T.; Wang, X. *Angew. Chemie Int. Ed.* **2017**, *56* (3), 850. https://doi.org/10.1002/ange.201607948
91. Aronovitch, C.; Mazur, Y. *J. Org. Chem.* **1985**, *50* (1), 149. https://doi.org/10.1021/jo00201a038
92. Ranu, B. C.; Bhadra, S.; Adak, L. *Tetrahedron Lett.* **2008**, *49* (16), 2588. https://doi.org/10.1016/j.tetlet.2008.02.089
93. Fisher, T. H.; Dershem, S. M.; Schultz, T. P. *J. Org. Chem.* **1988**, *53* (7), 1504. https://doi.org/10.1021/jo00242a030
94. Lin, R.; Chen, F.; Jiao, N. *Org. Lett.* **2012**, *14* (16), 4158. https://doi.org/10.1021/ol3018215
95. Pyszny, D.; Orlińska, B. *React. Kinet. Mech. Catal.* **2018**, *124* (1), 123. https://doi.org/10.1007/s11144-017-1307-7
96. Saedi, Z.; Tangestaninejad, S.; Moghadam, M.; Mirkhani, V.; Mohammadpoor-Baltork, I. *Catal. Commun.* **2012**, *17*, 18. https://doi.org/10.1016/j.catcom.2011.10.005
97. Wang, T.; Jing, X.; Chen, C.; Yu, L. *J. Org. Chem.* **2017**, *82* (18), 9342. https://doi.org/10.1021/acs.joc.7b01245
98. Hirashima, S.; Kudo, Y.; Nobuta, T.; Tada, N.; Itoh, A. *Tetrahedron Lett.* **2009**, *50* (30), 4328. https://doi.org/10.1016/j.tetlet.2009.05.012
99. Schäfer, C.; Ellstrom, C. J.; Török, B. *Top. Catal.* **2018**, *61* (7–8), 643. https://doi.org/10.1007/s11244-018-0961-y
100. Blair, R. G. US Patents: US8969603B2 2015. https://patentimages.storage.googleapis.com/6e/9f/9e/4a313cdd82638b/US8969603.pdf
101. Khan, M. L.; Tomkinson, J.; Fitchett, C. S.; Black, M. J. US Patents: US 6768029 B1 2004. https://patentimages.storage.googleapis.com/aa/f7/43/0ea5e13a81639c/US6768029.pdf
102. Urgoitia, G.; SanMartin, R.; Herrero, M. T.; Dominguez, E. *ACS Catalysis* **2017**, *7*, 3050-3060. https://doi.org/10.1021/acscatal.6b03654
103. Criegee, R. *Justus Liebigs Ann. Chem.* **1953**, *583* (1), 1. https://doi.org/10.1002/jlac.19535830102
104. Bailey, P. S. In *Ozonation in Chemistry: Volume 2 nonolefinic compounds*; Wasserman, H. H., Ed.; Academic Press: New York, 1982; pp 3–17.
105. Bailey, P. S.; Chang, Y.-G.; Kwie, W. W. L. *J. Org. Chem.* **1962**, *27* (4), 1198. https://doi.org/10.1021/jo01051a017
106. Silbert, L. S.; Foglia, T. A. *Anal. Chem.* **1985**, *57* (7), 1404. https://doi.org/10.1021/ac00284a050
107. Bailey, P. S.; Chang, Y.-G. *J. Org. Chem.* **1962**, *27* (4), 1192. https://doi.org/10.1021/jo01051a016
108. Miller, D. J.; Nemo, T. E.; Hull, L. A. *J. Org. Chem.* **1975**, *40* (18), 2675. https://doi.org/10.1021/jo00906a022

109. DeMore, W. B. *Int. J. Chem. Kinet.* **1969**, *1* (2), 209. https://doi.org/10.1002/kin.550010207
110. Demore, W. B. *Int. J. Chem. Kinet.* **1971**, *3* (2), 161. https://doi.org/10.1002/kin.550030208
111. DeMore, W. B.; Lin, C.-L. *J. Org. Chem.* **1973**, *38* (5), 985. https://doi.org/10.1021/jo00945a028
112. Dallwigk, E.; Paillard, H.; Briner, E. *Helv. Chim. Acta* **1953**, *36* (7), 1757. https://doi.org/10.1002/hlca.19530360710
113. Keay, R. E.; Hamilton, G. A. *J. Am. Chem. Soc.* **1975**, *97* (23), 6876. https://doi.org/10.1021/ja00856a054
114. Keay, R. E.; Hamilton, G. A. *J. Am. Chem. Soc.* **1976**, *98* (21), 6578. https://doi.org/10.1021/ja00437a028
115. Jackson, S.; Hull, L. A. *J. Org. Chem.* **1976**, *41* (20), 3340. https://doi.org/10.1021/jo00882a037
116. Bouas-Laurent, H.; Desvergne, J. P.; Lapouyade, R.; Thomas, J. M. *Molec. Cryst. Liq. Cryst.* **1976**, *32*, 143. https://doi.org/10.1080/15421407608083641
117. Desvergne, J.-P.; Bouas-Laurent, H. *J. Catal.* **1978**, *51* (1), 126. https://doi.org/10.1016/0021-9517(78)90246-4
118. Stedman, D. H.; Niki, H. *Environ. Lett.* **1973**, *4* (4), 303. https://doi.org/10.1080/00139307309435501
119. Pate, C. T.; Atkinson, R.; Pitts Jr, J. N. *J. Environ. Sci. \& Heal. Part A* **1976**, *11* (1), 19. https://doi.org/10.1080/10934527609385752
120. Dillemuth, F. J.; Schubert, C. C.; Skidmore, D. R. *Combust. Flame* **1962**, *6* (3), 211. https://doi.org/10.1016/0010-2180(62)90096-2
121. Cadle, R. D.; Schadt, C. *J. Chem. Phys.* **1953**, *21* (1), 163. https://doi.org/10.1063/1.1698576
122. Cremer, D.; Crehuet, R.; Anglada, J. *J. Am. Chem. Soc.* **2001**, *123* (25), 6127. https://doi.org/10.1021/ja010166f
123. Wisaksono, W. W.; Arens, J. F. *Recl. des Trav. Chim. des Pays-Bas* **1961**, *80* (8), 846. https://doi.org/10.1002/recl.19610800806
124. Knowles, W.; Thompson, Q. *J. Org. Chem.* **1960**, *25* (6), 1031. https://doi.org/10.1021/jo01076a044
125. Cannon, J. G.; Darko, L. L. *J. Org. Chem.* **1964**, *29* (11), 3419. https://doi.org/10.1021/jo01034a514
126. Lehmann, A.; Oertel, M. *Chem. Technol. Inst.* **1959**, *11*, 453.
127. Storesund, H. J.; Bernatek, E. *Acta Chemica Scandinavica* **1970**, *24*, 3237. https://doi.org/10.3891/acta.chem.scand.24-3237
128. Stille, J. K.; Eichelberger, J. L. *J. Org. Chem.* **1971**, *36* (13), 1840. https://doi.org/10.1021/jo00812a029
129. Yang, D.; Chen, F.; Dong, Z.-M.; Zhang, D.-W. *J. Org. Chem.* **2004**, *69* (6), 2221. https://doi.org/10.1021/jo0357925
130. Ren, W.; Liu, J.; Chen, L.; Wan, X. *Adv. Synth. \& Catal.* **2010**, *352* (9), 1424. https://doi.org/10.1002/adsc.201000250
131. Pappo, R. *Bull. Res. Counc. Isr. Sect. A* **1956**, *5*, 300.

132. Miao, Y.; Dupe, A.; Bruneau, C.; Fischmeister, C. *European J. Org. Chem.* **2014**, *2014* (23), 5071.
https://doi.org/10.1002/ejoc.201402447
133. Griffith, W. P. In *Ruthenium Oxidation Complexes*; Springer, 2009; pp 1–134.
https://doi.org/10.1007/978-1-4020-9378-4_1
134. Pagliaro, M.; Campestrini, S.; Ciriminna, R. *Chem. Soc. Rev.* **2005**, *34* (10), 837.
https://doi.org/10.1039/B507094P
135. Silverman, M. D.; Levy, H. A. *J. Am. Chem. Soc.* **1954**, *76* (12), 3319.
https://doi.org/10.1021/ja01641a073
136. Griffith, W. P. *J. Chem. Soc. A Inorganic, Phys. Theor.* **1968**, 1663.
https://doi.org/10.1039/J19680001663
137. Choi, E.; Lee, C.; Na, Y.; Chang, S. *Org. Lett.* **2002**, *4* (14), 2369.
https://doi.org/10.1021/ol0260977
138. Kumar, V.; Reddy, V. P.; Sridhar, R.; Srinivas, B.; Rao, K. R. *Synlett* **2009**, *2009* (05), 739.
https://doi.org/10.1055/s-0028-1087933
139. Cheung, W.-H.; Yu, W.-Y.; Yip, W.-P.; Zhu, N.-Y.; Che, C.-M. *J. Org. Chem.* **2002**, *67* (22), 7716.
https://doi.org/10.1021/jo0204404
140. Ho, C.-M.; Yu, W.-Y.; Che, C.-M. *Angew. Chemie Int. Ed.* **2004**, *43* (25), 3303.
https://doi.org/10.1002/anie.200453703
141. Viau, G.; Brayner, R.; Poul, L.; Chakroune, N.; Lacaze, E.; Fievet-Vincent, F.; Fievet, F. *Chem. Mater.* **2003**, *15* (2), 486.
https://doi.org/10.1021/cm0212109
142. Hayek, E.; Newesely, H.; Rumpel, M. L. *Inorg. Synth.* **1963**, *7*, 63.
https://doi.org/10.1002/9780470132388.ch17
143. Datta, S.; Chang, C.-L.; Yeh, K.-L.; Liu, R.-S. *J. Am. Chem. Soc.* **2003**, *125* (31), 9294.
https://doi.org/10.1021/ja036246w
144. Chan, W.-C.; Lau, C.-P.; Chen, Y.-Z.; Fang, Y.-Q.; Ng, S.-M.; Jia, G. *Organometallics* **1997**, *16* (1), 34.
https://doi.org/10.1021/om960627j
145. Bruneau, C.; Dixneuf, P. H. *Acc. Chem. Res.* **1999**, *32*, 311.
https://doi.org/10.1021/ar980016i
146. Bustelo, E.; Carbó, J. J.; Lledós, A.; Mereiter, K.; Puerta, M. C.; Valerga, P. *J. Am. Chem. Soc.* **2003**, *125* (11), 3311.
https://doi.org/10.1021/ja0291181
147. Trost, B. M.; Flygare, J. A. *J. Am. Chem. Soc.* **1992**, *114* (13), 5476.
https://doi.org/10.1021/ja00039a098
148. Trost, B. M.; Flygare, J. A. *Tetrahedron Lett.* **1994**, *35* (24), 4059.
https://doi.org/10.1016/S0040-4039(00)73111-X
149. Nishibayashi, Y.; Wakiji, I.; Hidai, M. *J. Am. Chem. Soc.* **2000**, *122* (44), 11019.
https://doi.org/10.1021/ja0021161
150. Yeh, K.-L.; Liu, B.; Lo, C.-Y.; Huang, H.-L.; Liu, R.-S. *J. Am. Chem. Soc.* **2002**, *124* (23), 6510.
https://doi.org/10.1021/ja012623y
151. Madhushaw, R. J.; Li, C.-L.; Shen, K.-H.; Hu, C.-C.; Liu, R.-S. *J. Am. Chem. Soc.* **2001**, *123* (30), 7427.
https://doi.org/10.1021/ja0106016
152. O'Connor, J. M.; Pu, L. *J. Am. Chem. Soc.* **1990**, *112* (24), 9013.
https://doi.org/10.1021/ja00180a075

153. Bianchini, C.; Casares, J. A.; Peruzzini, M.; Romerosa, A.; Zanobini, F. *J. Am. Chem. Soc.* **1996**, *118* (19), 4585.
https://doi.org/10.1021/ja9601393
154. Knaup, W.; Werner, H. *J. Organomet. Chem.* **1991**, *411* (3), 471.
https://doi.org/10.1016/0022-328X(91)83051-5
155. Chin, C. S.; Chong, D.; Maeng, B.; Ryu, J.; Kim, H.; Kim, M.; Lee, H. *Organometallics* **2002**, *21* (8), 1739.
https://doi.org/10.1021/om010953l
156. Davies, S. G.; McNally, J. P.; Smallridge, A. J. *Adv. Organomet. Chem* **1990**, *30*, 1.
https://doi.org/10.1016/S0065-3055(08)60498-0
157. Shen, H.-C.; Su, H.-L.; Hsueh, Y.-C.; Liu, R.-S. *Organometallics* **2004**, *23* (18), 4332.
https://doi.org/10.1021/om049711m
158. Shimada, T.; Yamamoto, Y. *J. Am. Chem. Soc.* **2003**, *125* (22), 6646.
https://doi.org/10.1021/ja034105o
159. Lee, D. G.; Chang, V. S. *J. Org. Chem.* **1979**, *44* (15), 2726.
https://doi.org/10.1021/jo01329a027
160. Shaikh, T. M.; Hong, F.-E. *Adv. Synth. \& Catal.* **2011**, *353* (9), 1491.
https://doi.org/10.1002/adsc.201000899
161. Islam, M.; Mondal, P.; Mukherjee, S.; Mobarak, M.; Roy, A. S.; Mondal, S.; Sarkar, S. *J. Chem. Technol. & Biotechnol.* **2010**, *85* (4), 460.
https://doi.org/10.1002/jctb.2311
162. Enthaler, S. *ChemCatChem* **2011**, *3* (12), 1929.
https://doi.org/10.1002/cctc.201100206
163. Rao, T. S. S.; Awasthi, S. *J. Mol. Struct. Theochem.* **2008**, *848* (1–3), 98.
https://doi.org/10.1016/j.theochem.2007.09.020
164. Meier, H.; Kolshorn, H. *Zeitschrift für Naturforsch. B* **1980**, *35* (8), 1040.
https://doi.org/10.1515/znb-1980-0822
165. Fowler, J. E.; Galbraith, J. M.; Vacek, G.; Schaefer III, H. F. *J. Am. Chem. Soc.* **1994**, *116* (20), 9311.
https://doi.org/10.1021/ja00099a057
166. Sawaki, Y.; Inoue, H.; Ogata, Y. *Bull. Chem. Soc. Jpn.* **1983**, *56* (4), 1133.
https://doi.org/10.1246/bcsj.56.1133
167. Dao, L. T. A.; Blau, K.; Pritzkow, W.; Schmidt-Renner, W.; Voerckel, V.; Willecke, L. *J. für Prakt. Chemie* **1984**, *326* (1), 73.
https://doi.org/10.1002/prac.19843260111
168. Zhu, Z.; Espenson, J. H. *J. Org. Chem.* **1995**, *60* (24), 7728.
https://doi.org/10.1021/jo00129a010
169. Sun, S.; Edwards, J. O.; Sweigart, D. A.; D'Accolti, L.; Curci, R. *Organometallics* **1995**, *14* (4), 1545.
https://doi.org/10.1021/om00004a001
170. Curci, R.; Fiorentino, M.; Fusco, C.; Mello, R.; Ballistreri, F. P.; Failla, S.; Tomaselli, G. A. *Tetrahedron Lett.* **1992**, *33* (51), 7929.
https://doi.org/10.1016/S0040-4039(00)74781-2
171. Yap, C. P.; Ng, J. K.; Madrahimov, S.; Bengali, A. A.; Chwee, T. S.; Fan, W. Y. *New J. Chem.* **2018**, *42* (13), 11131.
https://doi.org/10.1039/C8NJ02226G
172. Ballistreri, F. P.; Failla, S.; Tomaselli, G. A. *J. Org. Chem.* **1988**, *53* (4), 830.

https://doi.org/10.1021/jo00239a027
173. Bortolini, O.; Di Furia, F.; Modena, G.; Seraglia, R. *J. Org. Chem.* **1985**, *50* (15), 2688. https://doi.org/10.1021/jo00215a019
174. Bortolini, O.; Bragante, L.; Furia, F. Di; Modena, G. *Can. J. Chem.* **1986**, *64* (6), 1189. https://doi.org/10.1139/v86-197
175. Matoba, Y.; Inoue, H.; Akagi, J.; Okabayashi, T.; Ishii, Y.; Ogawa, M. *Synth. Commun.* **1984**, *14* (9), 865. https://doi.org/10.1080/00397918408075730
176. Oguchi, T.; Sakata, Y.; Takeuchi, N.; Kaneda, K.; Ishii, Y.; Ogawa, M. *Chem. Lett.* **1989**, *18* (11), 2053. https://doi.org/10.1246/cl.1989.2053
177. Sakata, Y.; Katayama, Y.; Ishii, Y. *Chem. Lett.* **1992**, *21* (4), 671. https://doi.org/10.1246/cl.1992.671
178. Yamawaki, K.; Nishihara, H.; Yoshida, T.; Ura, T.; Yamada, H.; Ishii, Y.; Ogawa, M. *Synth. Commun.* **1988**, *18* (8), 869. https://doi.org/10.1080/00397918808057856
179. Ishii, Y.; Yoshida, T.; Yamawaki, K.; Ogawa, M. *J. Org. Chem.* **1988**, *53* (23), 5549. https://doi.org/10.1021/jo00258a032
180. Ishii, Y.; Sakata, Y. *J. Org. Chem.* **1990**, *55* (21), 5545. https://doi.org/10.1021/jo00308a002
181. Sakaue, S.; Sakata, Y.; Nishiyama, Y.; Ishii, Y. *Chem. Lett.* **1992**, *21* (2), 289. https://doi.org/10.1246/cl.1992.289
182. Sakaue, S.; Tsubakino, T.; Nishiyama, Y.; Ishii, Y. *J. Org. Chem.* **1993**, *58* (14), 3633. https://doi.org/10.1021/jo00066a012
183. Ishii, Y.; Tanaka, H.; Nishiyama, Y. *Chem. Lett.* **1994**, *23* (1), 1. https://doi.org/10.1246/cl.1994.1
184. Sakaguchi, S.; Watase, S.; Katayama, Y.; Sakata, Y.; Nishiyama, Y.; Ishii, Y. *J. Org. Chem.* **1994**, *59* (19), 5681. https://doi.org/10.1021/jo00098a028
185. Wang, A.; Jiang, H. *J. Am. Chem. Soc.* **2008**, *130* (15), 5030. https://doi.org/10.1021/ja8002217
186. Muzart, J. *J. Mol. Catal. A Chem.* **2011**, *338* (1–2), 7. https://doi.org/10.1016/j.molcata.2011.01.030
187. Gao, A.; Yang, F.; Li, J.; Wu, Y. *Tetrahedron* **2012**, *68* (25), 4950. https://doi.org/10.1016/j.tet.2012.04.069
188. Park, S.; Jeon, H. W.; Yong, W.-S.; Lee, P.-H. *Org. Lett.* **2015**, *17(20)*, 5060. https://doi.org/10.1021/acs.orglett.5b02545
189. Jun, C.-H.; Lee, H.; Moon, W. C.; Hong, H.-S. *J. Am. Chem. Soc.* **2001**, *123*, 8600. https://doi.org/10.1021/ja011053z
190. Urgoitia, G.; SanMartin, R.; Herrero, M. T.; Domínguez, E. *Chem. Commun.* **2015**, *51* (23), 4799. https://doi.org/10.1039/C5CC00750J
191. Shaver, M. P.; Johnson, S. A.; Fryzuk, M. D. *Can. J. Chem.* **2005**, *83* (6–7), 652. https://doi.org/10.1139/v05-034
192. Johansson, M.; Lindén, A. A.; Bäckvall, J.-E. *J. Organomet. Chem.* **2005**, *690* (15), 3614. https://doi.org/10.1016/j.jorganchem.2005.04.033
193. Nielsen, T. E.; Le Quement, S. T.; Meldal, M. *Org. Lett.* **2007**, *9* (13), 2469.

https://doi.org/10.1021/ol070693p

194. Le Quement, S. T.; Nielsen, T. E.; Meldal, M. *J. Comb. Chem.* **2008**, *10* (4), 546.
https://doi.org/10.1021/cc8000037
195. Jacobi, P. A.; Murphree, S.; Rupprecht, F.; Zheng, W. *J. Org. Chem.* **1996**, *61* (7), 2413.
https://doi.org/10.1021/jo952092u
196. Jacobi, P. A.; Zheng, W. *Tetrahedron Lett.* **1993**, *34* (16), 2585.
https://doi.org/10.1016/S0040-4039(00)77631-3
197. Czernecki, S.; Horns, S.; Valery, J.-M. *J. Org. Chem.* **1995**, *60* (3), 650.
https://doi.org/10.1021/jo00108a030
198. Ye, L.; Zhang, L. In *Au-Catalyzed Synthesis and Functionalization of Heterocycles*; Springer, 2016; pp 87–115.
https://doi.org/10.1007/7081_2015_5002
199. Liu, Y.; Song, F.; Guo, S. *J. Am. Chem. Soc.* **2006**, *128* (35), 11332.
https://doi.org/10.1021/ja062610q
200. Das, A.; Chaudhuri, R.; Liu, R.-S. *Chem. Commun.* **2009**, No. 27, 4046.
https://doi.org/10.1039/B908338C
201. Wirth, T.; Kita, Y.; Wirth, T. *Hypervalent iodine chemistry*; Springer, 2016; Vol. 373.
202. Wirth, T. *Angew. Chemie Int. Ed.* **2005**, *44* (24), 3656.
https://doi.org/10.1002/anie.200500115
203. Varvoglis, A. *Synthesis (Stuttg).* **1984**, *1984* (09), 709.
https://doi.org/10.1055/s-1984-30945
204. Zhdankin, V. V; Stang, P. J. *Chem. Rev.* **2002**, *102* (7), 2523.
https://doi.org/10.1021/cr010003+
205. Havare, N. *Enantioselektive Epoxidierung mit Metall(salen)-Komplexen — Oxidative Spaltung und Umlagerung organischer Verbindungen*; University Freiburg: Freiburg, Germany, 2012.
https://freidok.uni-freiburg.de/fedora/objects/freidok:8526/datastreams/FILE1/content
206. Page, T. K.; Wirth, T. *Synthesis* **2006**, *2006* (18), 3153.
https://doi.org/10.1055/s-2006-942543
207. Kazmierczak, P.; Skulski, L. *Molecules* **2002**, *7* (11), 810.
https://doi.org/10.3390/71100810
208. Schmeisser, M.; Dahmen, K.; Sartori, P. *Chem. Ber.* **1967**, *100* (5), 1633.
https://doi.org/10.1002/cber.19671000531
209. Moriarty, R. M.; Penmasta, R.; Awasthi, A. K.; Prakash, I. *J. Org. Chem.* **1988**, *53* (26), 6124.
https://doi.org/10.1021/jo00261a031
210. Jiang, Q.; Zhao, A.; Xu, B.; Jia, J.; Liu, X.; Guo, C. *J. Org. Chem.* **2014**, *79* (6), 2709.
https://doi.org/10.1021/jo5003517
211. Sathyanarayana, P.; Upare, A.; Ravi, O.; Muktapuram, P. R.; Bathula, S. R. *RSC Adv.* **2016**, *6* (27), 22749.
https://doi.org/10.1039/C6RA02962K
212. Havare, N.; Plattner, D. A. *Org. Lett.* **2012**, *14* (19), 5078.
https://doi.org/10.1021/ol301675v
213. Havare, N.; Plattner, D. A. *Helv. Chim. Acta* **2012**, *95* (10), 2036.
https://doi.org/10.1002/hlca.201200444
214. Yamaguchi, T.; Nobuta, T.; Kudo, Y.; Hirashima, S.; Tada, N.; Miura, T.; Itoh, A. *Synlett* **2013**, *24* (05), 607.

https://doi.org/10.1055/s-0032-1318308

215. Yasui, S.; Tojo, S.; Majima, T. *J. Org. Chem.* **2005**, *70* (4), 1276.
https://doi.org/10.1021/jo049032l
216. Schaap, A. P.; Lopez, L.; Gagnon, S. D. *J. Am. Chem. Soc.* **1983**, *105* (3), 663.
https://doi.org/10.1021/ja00341a079
217. Pac, C.; Nakasone, A; Sakurai, H. *J. Am. Chem. Soc.* **1977**, *99*, 5806
https://doi.org/10.1021/ja00459a049
218. Hofstra, J. L.; Grassbaugh, B. R.; Tran, Q. M.; Armada, N. R.; de Lijser, H. J. P. *J. Org. Chem.* **2015**, *80* (1), 256.
https://doi.org/10.1021/jo502324z
219. Schaap, A. P.; Siddiqui, S.; Prasad, G.; Palomino, E.; Sandison, M. *Tetrahedron* **1985**, *41* (11), 2229.
https://doi.org/10.1016/S0040-4020(01)96597-4
220. Roth, H.; Romero, N.; Nicewicz, D. *Synlett* **2016**, *27* (05).
https://doi.org/10.1055/s-0035-1561297
221. Macintyre Jane E. *Dictionary of Inorganic Compounds*; CRC Press, 1992.
222. IFA. GESTIS-Stoffdatenbank: Pentakaliumbis(peroxymonosulfat)bis(sulfat)
http://gestis.itrust.de/nxt/gateway.dll/gestis_de/531291.xml?f=templates$fn=default.htm$3.0 .
223. Albert, M. *Introduction to Green Chemistry*, second edi.; CRC Press, 2010.
224. Itoh, K.; Horiuchi, C. A. *Tetrahedron* **2004**, *60* (7), 1671.
https://doi.org/10.1016/j.tet.2003.11.088
225. Horiuchi, C. A.; Fukunishi, H.; Kajita, M.; Yamaguchi, A.; Kiyomiya, H.; Kiji, S. *Chem. Lett.* **1991**, *20* (11), 1921.
https://doi.org/10.1246/cl.1991.1921
226. Brauer, G. *Handbook of Preparative Inorganic Chemistry*, Vol. 2.; Academic: New York, 1965.
227. Riley, D. P.; Correa, P. E. *J. Mol. Catal.* **1990**, *61* (2), 137.
https://doi.org/10.1016/0304-5102(90)85151-7

Authors' Biographies

Dr. Nizam Havare was born in Samandağ in Hatay province of Turkey. He studied Bachelor of Science from 1999 until 2003 in Department of Chemistry at University of Mersin and obtained his BS degree in July 2003 with very good (degree: 1.4) in Turkey. With DAAD (German Academic Exchange Service) fellowship he moved in 2002 to Germany, where he still lives. He performed his master studies and obtained his "*Dipl.-Chem.*" (equivalent to M.Sc.) degree from the University of Paderborn in 2006. He graduated his Ph.D. degree with very good at the University of Freiburg under the supervision of Prof. Dr. Dietmar A. Plattner in the field of asymmetric epoxidation using metal(salen) complexes/oxidative cleavage and rearrangement of different functional groups (olefins, epoxide, aldehydes and alcohols) using hypervalent iodine. He finished his first postdoc at the University of Tokyo under the supervision of Prof. Dr. Naokazu Kano in field hypervalent chemistry of main group elements from 2012 until 2013. He passed his second postdoc at Stanford University under the supervision of Prof. Barry M. Trost from 2016 until 2017. His research focus was on Pd-catalyzed asymmetric allylic alkylation (well-known as the *Tsuji-Trost* reaction) and Ru-catalyzed cycloisomarizations. Between 2014 and 2022, he also worked as a chemistry and physics teacher in various types of schools in Germany and still keeps oscillating between teaching in schools and research in universities.