[d002]

Selenium catalyzed oxidation of alkynes in aqueous media

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Abstract

3 equivalents of ammonium persulfate in a 3:1 mixture of MeCN and water slowly convert alkynes into the corresponding 1,2-dicarbonyl compounds.

The oxidation rate is enhanced by the presence of diphenyl diselenide that form in situ the electrophilic PhSeOSO₃H able to promote a "one pot" hydroxyselenenylation-deselenenylation reaction.

Introducrtion

The development of improved and eco-friendly oxidation reactions is an area of great current interest in both academic and industrial laboratories. Recently we reported the use of diphenyl diselenide as a pre-catalyst in the ammonium persulfate as well as in the hydrogen peroxide mediated dihydroxylation of olefins.[1]

In the first case[1a] the reactions were performed in a mixture of acetonitrile and water at 70° C proceeding through an hydroxyselenenylation followed by an oxidation of the corresponding selenide and a subsequent substitution by a molecule of water. This method resulted to be effective for the conversion of cyclic alkenes in 1,2-diols but it failed when applied to acyclic olefins. Using hydrogen peroxide as oxidant[1b] the method is of more general application and the mechanism has been demonstrated to involve an epoxidation by the "in situ" formed peracid, followed by the attack of a molecule of water that occurs as a S_N2 ring-opening reaction or through the formation of a carbocationic intermediate.

As an extension of our investigation concerning the use of organoselenium compounds as catalysts for greener synthetic procedures we take in consideration the oxidation of carbon carbon triple bond.

Tiecco *et al.*[2] previously demonstrated that diphenyl diselenide, in refluxing methanol in the presence of an excess of ammonium persulfate converts alkynes into the corresponding di- or monoprotected α-dicarbonylic compounds reporting also one example in which a stoichiometric amount of diphenyl diselenide produce the unprotected derivatives when the solvent is an MeCN/H₂O mixture.

1,2-Dicarbonyl derivatives are known to be useful and versatile synthones.[3] Recently they were successfully employed on the synthesis of the imidazole core[4] present in a series of well known drugs such as: hystidine, etomidate, cimetidine, omeprazole, ketoconazole and flumazenil.

Several methods are reported in literature for the preparation of these products starting from different compounds. Particular attention has been devoted to the oxidation of alkynes that, in most cases, are complicated by the overoxidation that afford the corresponding carboxylic acids.[5]

Results and Discussion

Here we report that ammonium persulfate in aqueous conditions can effect this oxidation and that the diphenyl diselenide can catalyze the process leading directly to the formation of unprotected 1,2-dicarbonyl derivatives.

Scheme 1. Oxidation of 1-phenyl-1-propyne

Preliminary experiments were carried out on 1-phenyl-1-propyne **1a** using as oxidant ammonium persulfate and hydrogen peroxide in the presence of a different concentration of catalyst (PhSe)₂ and different temperature (Scheme 1).

The results summarized on table 1 clearly demonstrated that the H₂O₂ is not a suitable oxidant for this reaction. On the contrary ammonium persulfate at 60°C slowly converts **1a** into the corresponding diketone **2a** and the reaction can be strongly accelerated by the presence of diphenyl diselenide.

Table 1. Preliminary investigation on reaction conditions.

Oxidant	% (PhSe)₂	Yield %[a]
(NH₄)₂S₂O₈	10	75
(NH₄)₂S₂O₈	100	80
(NH₄)₂S₂O₈	0	27
H₂O₂	10	--
H₂O₂	100	--
H₂O₂	0	--

[a] all the reactions were carried out at 60°C for 24h
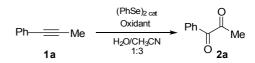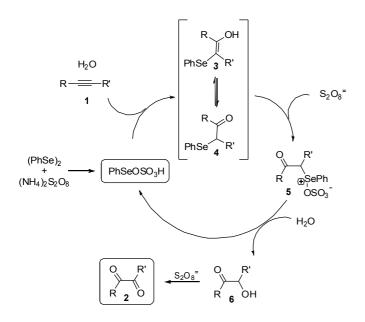
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Non appreciable differences have been observed between the reactions carried out with catalytic or stoichiometric amounts of diselenide. The role of the (PhSe)$_2$ is depicted in the mechanism proposed in scheme 2. The actual catalyst is the strong electophilic PhSe-sulfate produced by the reaction of diphenyl diselenide with ammonium persulfate.

Resonably the electrophile, in the presence of water, promote an hydroxyselenenylation on the triple bond leading to the enol **3** that exists in a tautomeric equilibrium with the ketone **4**. The excess of ammonium persulfate activate the phenyl selenium moiety to the nuclephilic substitution by a molecule of water as we reported for the dihydroxylation of olefins. The formation of the α-hydroxyketone **6** is demonstrated by the presence of a GC-MS peak [M+ m/z = 150] in the analysis effected during the ongoing reaction. In the used experimental conditions it is resonable to suppose a quick oxidation of **6** to afford the corresponding 1,2-dicarbonyl **2**.

Noteworthy these experimental evidences suggest that the reaction mechanism, in the presence of water, is different from those observed in 1991 by Tiecco *et al*[2] for similar reactions effected in methanol.
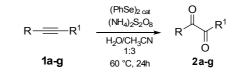

Scheme 2. Proposed mechanism

With the optimized conditions in hand we investigated the scope of this methodology starting from a series of substituted alkynes **1a-g**.
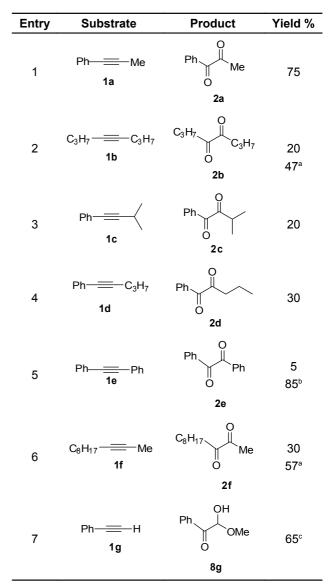
The results are collected in table 2. All the reaction were stopped after 24 hours and the corresponding 1,2-dicarbonyl derivatives **2a-g** were purified by flash chromatography and fully characterized on the basis of GC-MS analysis, ^{1}H and ^{13}C-NMR spectral data. The yields, referred to the amount of isolated compounds, are from moderate to good. Starting from the alkynes **1b** (entry 2), **1e** (entry 5) and **1f** (entry 6), we demonstrated that longer reaction time produce a positive effect on the yields even if for reaction time longer than 200 hours in some substrates the overoxidation seems to be the main process. The alkynes **1a**, **1d**, **1e**, and **1g** were quantitatively converted into benzoic acid in one week. In all the cases after purification on silica gel column

chromatography the pre-catalyst (PhSe)$_2$ can be completely recovered and then reused.

Starting from a terminal alkyne **1g**, in contrast with a previously reported result,[2] the α-ketoaldehyde **2g** cannot be isolated and its formation has been observed only from the ^{1}H-NMR of the crude in which it is in equilibrium with the hydrated form **7g**.
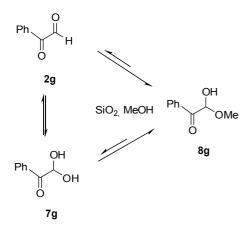
Table 2. Scope of the reaction

Entry	Substrate	Product	Yield %
1	Ph━━━Me **1a**	Ph—C(O)—C(O)—Me **2a**	75
2	C$_3$H$_7$━━━C$_3$H$_7$ **1b**	C$_3$H$_7$—C(O)—C(O)—C$_3$H$_7$ **2b**	20 / 47[a]
3	Ph━━━CH(CH$_3$)$_2$ **1c**	Ph—C(O)—C(O)—CH(CH$_3$)$_2$ **2c**	20
4	Ph━━━C$_3$H$_7$ **1d**	Ph—C(O)—C(O)—C$_2$H$_5$ **2d**	30
5	Ph━━━Ph **1e**	Ph—C(O)—C(O)—Ph **2e**	5 / 85[b]
6	C$_8$H$_{17}$━━━Me **1f**	C$_8$H$_{17}$—C(O)—C(O)—Me **2f**	30 / 57[a]
7	Ph━━━H **1g**	Ph—C(O)—CH(OH)(OMe) **8g**	65[c]

[a] reaction time 48h [b] reaction time 200h [c] after chromatography SiO$_2$-eluant CH$_2$Cl$_2$/MeOH

After silica gel chromatography, using a dichloromethane/methanol (99:1) mixture as eluant the methoxy hemiacetal **8g** is recovered in 65% of yield.

It is resonably to suppose that the equilibrium between **2g** and **7g** for the presence of methanol and the acidic catalysis of SiO$_2$ is shifted towards the more stable form **8g** (Scheme 3).

Scheme 3. Silica mediated formation of hemiacetal **8g**

Conclusion

In conclusion we present here a detailed study on the oxidation of internal alkynes using ammonium persulfate and diphenyl diselenide as catalyst in aqueous conditions.

These reactions lead directly to unprotected 1,2-dicarbonyl derivatives in moderate to good yields. Experimental evidences allow us to suppose a different reaction mechanism in respect to those previously observed for similar oxidations effected in methanol.

From terminal alkynes an interesting convertion of the resulting α-ketoaldehyde to the corresponding hemiacetal by treatment of the crude with silica gel and methanol has been observed and it will be the object of further investigation.

References

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