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Selective oxidation of acetylenic 1,4-diols with dioxiranes in comparison with the methyltrioxorhenium–hydrogen peroxide oxidant

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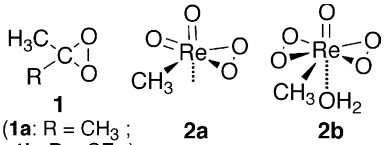
Dedicated to Professor Giorgio Modena (University of Padova, Italy) on the occasion of his 80th birthday

Abstract—Dimethyldioxirane (**1a**) and its trifluoro analog (**1b**) were employed to achieve selectively the direct transformation of hex-3-yne-2,5-diol **3a** and 1,4-diphenyl-but-2yne-1,4-diol **3b** (two representative acetylenic 1,4-diols) into the corresponding carbonyls, leaving the carbon–carbon triple bond moiety untouched. The results are compared with those recorded in the analogous oxidation using the methyltrioxorhenium (MTO)/85% H_2O_2 homogeneous system. The powerful methyl(trifluoromethyl)dioxirane (**1b**) is the reagent of choice to achieve optimum yields of the target alkyne-1,4-diones, which are extremely versatile synthons.

Simple acetylenic 1,4-diones are versatile building blocks in cycloaddition reactions,[1] for the synthesis of various heterocyclic compounds,[2] as well as for the preparation of other compounds of interest.[3] Thus, considerable effort has been devoted to the preparation of conjugated acetylenic diketones based on a wide variety of synthetic approaches[4] including multistep synthesis.[5] Besides these methods, particularly attractive is the one-step selective oxidation of acetylenic 1,4-diols since these substrates are readily available.[6] This transformation has been attempted previously with varying success. For instance, Li et al. have reported the direct radical α-oxidation of alkynes using Cu^{2+}/*t*-BuOOH under oxygen; they found that, in order to obtain acetylenic 1,4-diketones (e.g., hex-3-yne-2,5-dione) in fair yield (ca. 15%), the corresponding acetylenic diols have to be employed as the starting material.[7] As part of a continuing effort to devise selective oxidations of key organic compounds, we decided to apply two novel oxidants, namely dioxiranes **1**[8] and the methyltrioxorhenium–hydrogen peroxide reagent, CH_3ReO_3(MTO)/H_2O_2[9] to probe into the direct transformation of representative acetylenic diols into the corresponding carbonyls.

The catalytic cycle for oxidations with CH_3ReO_3[MTO]/H_2O_2 involves, besides the monoperoxo complex **2a**, the rhenium(VII) diperoxocomplex **2b** as the active species;[9,10] the latter became well characterized crystallographically.[10a]



Both dioxiranes and the MTO/H_2O_2 system have been the focus of much interest as oxidation catalyst in recent years. Numerous transformations have been reported for these versatile, highly reactive, and yet selective oxidants;[8–10] these include the recently reported oxidation of 1,2-diols to the corresponding 1,2-diketones by MTO/H_2O_2.[10e] The ever increasing number of their applications in synthesis has spurred intensive mechanistic studies of the related oxygen-transfer processes.[8–10] Akin to peracids[11] and metal peroxides,[12] both dioxiranes[13]

Keywords: Dioxiranes; Dimethyldioxirane; Methyl(trifluoromethyl)dioxirane; Methyltrioxorhenium; Hydrogen peroxide; Acetylenic 1,4-diols; Oxidation.
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and MTO/H_2O_2[14] have been found to allow the conversion of isolated alkynes into α-diketones and/or α,β-unsatured carbonyls, via intermediate α-ketocarbenes.[11–14]

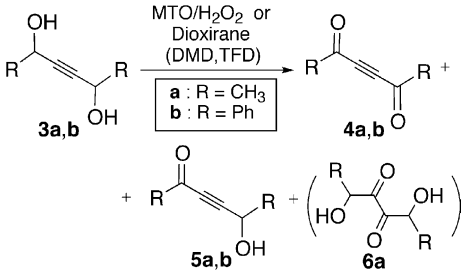
We have now applied both MTO/H_2O_2 and dioxiranes (either isolated or generated in situ)[8] to the direct oxidation of two representative acetylenic diols, namely the commercially available hex-3-yne-2,5-diol **3a** and 1,4-diphenyl-but-2yne-1,4-diol **3b**; an authentic sample of the latter could be synthesized by following literature procedures (Scheme 1).[15]

Dimethyldioxirane (DMD) (**1a**)[16] and methyl(trifluoromethyl)dioxirane (TFD)[17] (**1b**) solutions [0.08–0.1 M in acetone, and 0.7–0.8 M in 1,1,1-trifluoropropanone (TFP), respectively] were prepared as already reported in detail.

For the MTO catalyzed oxidation of the substrates at hand, we adopted the established homogeneous system using 85% H_2O_2 as bulk oxidant in methylene chloride.[18] It is well recognized that under the conditions adopted herein (i.e., with over a 50-fold excess of the oxygen donor H_2O_2 relative to the rhenium catalyst), the diperoxo complex **2b** is largely prevalent as the active oxygen-transfer agent, and practically no MTO is present in solution.[18] This was confirmed by our own ^1H and ^{13}C NMR control experiments in CD_2Cl_2.[19]

Data collected in Table 1 are representative of the oxidation of acetylenic diols **3a**,**b** using dioxiranes and MTO/H_2O_2.[20] Inspection of these reveals that either the MTO/H_2O_2 (entry 1–3) and the ketone/caroate system that is in situ dioxirane (entry 4 and 9) are capable to afford *catalytically* the acetylenic ketols in good to excellent yield with reasonable reaction times (12–30 h, in the majority of cases). While substrate conversion is only 35% during 12 h with in situ DMD (entry 4), this can be considerably improved using caroate/1,1,1-trifluoropropanone (in situ TFD), yielding acetylenic ketol **5a** in 90% isolated yield, with 75% substrate conversion occurring in just 1.2 h (entry 9).

High substrate conversions with short reaction times (0.3–6 h) are also generally accomplished using isolated dioxiranes as stoichiometric oxidants (entries 7, 8 and 10–12). Using DMD **1a**, both the acetylenic ketol **5** and the diketone **4** are produced (entries 6–8). While the ketol **5** is still the largely prevalent product using DMD in CH_2Cl_2 (entry 6), the balance can be changed to favor formation of the diketone (its sequential oxidation product) upon changing the solvent from CH_2Cl_2 to acetone (entries 7 and 8). The yield in the desired diketones **4a**,**b** climbs to a remarkable 90–96% using the highly reactive TFD in acetone/TFP (entries 11 and 12); substrate conversion is practically total in a matter of minutes, rather than hours. It is interesting to note that, when the oxidation of acetylenic diol **3a** is carried out with TFD in CH_2Cl_2, besides the diketone **4a** as the major product, a sizable amount (ca. 18%) of diketol **6a**



Scheme 1.

Table 1. Oxidation of two representative acetylenic 1,4-diols with methyltrioxo-rhenium(VII)/H_2O_2 and with in situ generated or isolated dioxiranes

No.	Oxidant	Method[a]	Substrate	*t*, °C	Ratio Ox/S[b]	Reaction time (h)	Convn %	Product (yield %)	
								Diketone	Ketol
1	MTO/H_2O_2	***A***	**3a**	20	6	20	90	—	**5a** (88)[c]
2		***A***	**3a**	20	20	30	95	—	**5a** (80)[c]
3		***A***	**3b**	20	20	30	60	—	**5b** (90)[c]
4	DMD (**1a**)	***A′***	**3a**	20	10	12	35	—	**5a** (90)[c]
5		***B***	**3a**	0	1	3	60	—	**5a** (98)[c]
6		***B***	**3a**	0	3	6	95	**4a** (3)[c]	**5a** (95)[d]
7		***B′***	**3a**	0	3	6	95	**4a** (65)[d]	**5a** (20)[d]
8		***B′***	**3b**	0	3	6	95	**4b** (70)[d]	**5b** (30)[d]
9	TFD (**1b**)	***A″***	**3a**	0	10	1.2	75	—	**5a** (90)[d]
10		***B″***	**3a**	0	3	0.5	95	**4a** (74)[d,e]	—
11		***B‴***	**3a**	0	3	0.3	95	**4a** (90)[d]	—
12		***B‴***	**3b**	0	3	0.3	95	**4b** (96)[d]	—

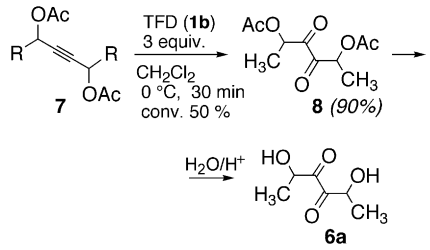
[a] ***A***: Methyldiperoxorhenium(VII) oxidant **2b** generated in situ from 85% H_2O_2/MTO (from 60:1 to 100:1), solvent CH_2Cl_2; ***A′***: DMD in situ from acetone/caroate 3:1; buffered aqueous solution, pH 7.5–8.0 [Ref. 16]. ***A″***: TFD in situ from 1,1,1-trifluoropropanone (TFP)/caroate 2:1; buffered aqueous solution, pH 7.5–8.0 [Ref. 17d]. ***B***: DMD in isolated form [Refs. 8 and 16] solvent CH_2Cl_2/acetone 50:50. ***B′***: DMD in isolated form [Refs. 8 and 16] solvent acetone. ***B″***: TFD in isolated form [Refs. 8 and 17] solvent CH_2Cl_2/TFP 1:1. ***B‴***: TFD in isolated form, solvent acetone/TFP 2:1.

[b] Ratio of bulk oxidant (H_2O_2, caroate, or isolated dioxirane) to substrate.

[c] As determined (±3%) by GC (ZB-1, 0.25 μm film thickness, 30 m × 0.25 mm ID, capillary column).

[d] Isolated yield (±5%).

[e] Byproduct 2,5-diidrossi-esan-3,4-dione (**6a**) was also isolated (yield 18%).



Scheme 2.

is also formed. The latter also represents a useful synthon.[21]

For the substrates examined, the feat of the selective conversion of the secondary alcohol moieties to carbonyls, leaving the carbon–carbon triple bond intact, should be credited to deactivation of the latter exercised by the flanking electron-withdrawing OH and/or C=O functionalities. This deactivating effect seems crucial since kinetic data point to a similar order of magnitude for the reactivity of isolated alkynes as compared to that of secondary alcohols R_2CH–OH toward DMD.[8a]

Likewise, the finding that the oxidation may proceed to the 2,5-diketone stage but no further, should be due to that acetylenic ketones, similar to acetylenic acids or esters, are strongly deactivated.[7] When the 'free' OH functionalities are masked by conversion into acetoxy, oxidation at the C≡C bond takes place instead. This is shown by the example reported in Scheme 2.

Certainly, deactivation of the carbon–carbon triple bond by the flanking oxygenated functionalities is diminished on going from OH to OAc. However, it is likely that transition state effects involving hydrogen bonding by free hydroxy groups to the incoming dioxirane or to the methyloxorhenium diperoxide also play a role[8a,22] in directing the oxidation toward the selective transformation of the secondary alcohol functionalities into carbonyls.

Be the mechanistic details as it may, data reported herein indicate that selective conversion of alkyne-1,4-diols into the corresponding carbonyls can be conveniently carried out using dioxiranes or MTO/H_2O_2 under mild conditions.

This new synthetic entry should prove useful since we verified that classical two-electrons electrophilic oxidants, such as *m*-CPBA or other peracids, are unreactive toward these substrates under standard conditions. Perhaps not surprising,[8,17] the powerful TFD oxidant is best suited if one wishes to obtain the target alkyne-1,4-diones in excellent yields.

Acknowledgements

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Supplementary data

Experimental details and supplemental characterization data for compounds **4a**, **5a**, **5b**, and **6a** (four pages). ^1H NMR and $\{^1H\}^{13}C$ NMR spectra recording the formation of peroxocomplexes **2b** from MTO and 85% H_2O_2 in CD_2Cl_2 (two pages). Supplementary data associated with this article can be found, in the online version, at doi:10.1016/j.tetlet.2004.09.110.

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18. For instance, see: (a) Adam, W.; Saha-Möller, C. H.; Weichold, O. *J. Org. Chem.* **2000**, *65*, 5001–5004; (b) It should be noted that, in carrying out oxidations of unsatured substrates by the MTO/H_2O_2 reagent, it is common practice to employ additives such as pyridine or urea; apparently, this serves to avoid undesirable side reactions (e.g., the hydrolytic opening of epoxides ring, ensuing pinacol-type rearrangements and C–C bond cleavage).[9,10] However, pyridine and other electron donors can bind to the metal center and might trigger MTO decomposition to HRO_4 and MeOH;[10d] also, the catalytically active rhenium species can no longer be defined with clarity.
19. We find that the $\{^1H\}^{13}C$ NMR (125.759 MHz) spectrum of CH_3ReO_3 (MTO) in CD_2Cl_2 presents a sharp C_3 resonance at 19.8 ppm; upon addition of 1 equiv of 85% H_2O_2, along with a residual MTO peak, two new resonances appear at 33.0 and 30.3 ppm (rel intensity ca. 6:1), pertaining to the diperoxo complex **2b** and to the monoperoxo complex **2a**, respectively. Then, after addition of excess 85% H_2O_2 (6 equiv), the mentioned ^{13}C NMR MTO and **2a** peaks disappear, and just the diperoxo complex **2b** resonance is present (cf., Supporting Info). This feature is confirmed by similar ^1H NMR experiments, in comparison with the CH_3 NMR shifts reported for MTO, **2b**, and **2a** in CD_3NO_2 [Ref. 10d]. Also, notably absent are ^{13}C or ^1H NMR resonances that could be attributed to 'free' or metal-bound CH_3OH in CD_2Cl_2.
20. General procedures for oxidations with MTO/H_2O_2, with dioxiranes in situ, and with isolated dioxiranes are reported in the Supplementary data.
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