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Oxidation of Alkynes by Dioxiranes

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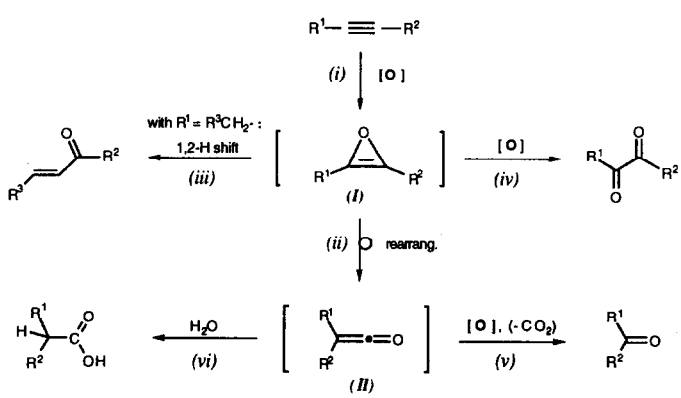
Abstract. *In situ* generated or isolated dimethyldioxirane (**1a**) and methyl(trifluoromethyl)dioxirane (**1b**) efficiently afford oxidation of alkynes, most likely via oxirene intermediates, which rearrange into ketene or α,β-unsaturated carbonyls, or else are further oxidized to α,β-dicarbonyls. Diphenylacetylene and phenylacetylene yield mostly ketene derived products, whereas 8-hexadecyne (an internal dialkyl alkyne) gives 9-hexadecen-8-one (both *trans* and *cis*) as the main product. Reaction of cyclodecyne (a conformationally rigid cycloalkyne) with isolated **1b** affords *cis*-bicyclo[*5.3.0*]decan-2-one (**15**) and *cis*-bicyclo[*4.4.0*]decan-2-one (**16**), which derive from the oxirene by stereoselective 1,5- and 1,6-transanular insertion, respectively.

It is known that alkynes can be converted into 1,2-dicarbonyl compounds or cleaved into carboxylic acids by metal oxidants such as permanganate salts,[1a,b] thallium nitrate,[1c] OsO_4,[1d,e] or RuO_4.[1f] Metal peroxides such as $(HMPA)MoO(O_2)_2$ or H_2O_2/Na_2MoO_4 (in the presence of Hg^{II} salts) allow the synthesis of α-oxoaldehydes in high yield,[1g,h] whereas peroxotungstophosphate (PCWP) or peroxomolybdophosphate (PCMP) convert internal dialkyl alkynes into α,β-unsaturated ketones and α,β-epoxyketones as principal products.[1i] By contrast, alkyne oxidations using organic peroxyacids[2] are rarely selective; in fact, they often yield complex mixtures whose composition of products depends markedly upon the nature of both the substrate and the peracid, as well as on reaction conditions.[2]

Scheme 1



The mechanism is envisaged as to involve alkyne π-bond oxidation to an oxirene ***(I)***, intrinsically unstable because of the strained antiaromatic moiety.[2a] Rapid subsequent oxidation of the oxirene (possibly via its isomeric α-oxo carbene R^1-CO-$\ddot{C}$-R^2) would led to an α-dicarbonyl (path *iv* , Scheme 1), and eventually to cleavage products.[2] With suitable substrates, *α,β*-unsaturated ketones can also be produced by 1,2-hydrogen shift (path *iii*).[2b] Besides these routes, the oxirene can rearrange by 1,2-alkyl or aryl migration into a ketene ***(II)*** (path *ii*), which is then rapidly cleaved to ketone (path *v*) or trapped by protic species, e.g. H_2O (path *vi*).[2]

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Table 1. Oxidation of Alkynes by Dimethyldioxirane (**1a**) and by Methyl(trifluoromethyl)dioxirane (**1b**)

Entry no.	Substrate	Dioxirane	T (°C)	Method [a]	Reactn time	Conversion (%) [b]	Products (% Yield) [c]			
	Ph-C≡C-Ph (2)						Ph-C(=O)-C(=O)-Ph (3)	$PhCO_2H$ (4)	$Ph_2C{=}O$ (5)	$Ph_2CH\text{-}CO_2H$ (6)
1		**1a**	5.	*in situ* [d]	60 h	88.	(17)	(8)	(53)	(16)
2		**1b**	5.	*in situ* [e]	12 h	75.	(16)	(6)	(59)	(8)
3		**1a**	0.	isol.	8 h	50.	(30)	(< 2)	(58)	(< 2)
4		**1b**	0.	isol.	6 min	82.	(30)	(< 2)	(60)	(< 2)
	Ph-C≡C-H (7)						Ph-C(=O)-C(=O)-OH (8)	$PhCO_2H$ (4)	PhCH=O (9)	$PhCH_2CO_2H$ (10)
5		**1a**	10.	*in situ* [f]	40 h	90.	(-)	(17)	(7)	(58)
6		**1b**	10.	*in situ* [g]	8 h	75.	(-)	(26)	(33)	(25)
7		**1a**	0.	isol.	6 h	60.	(20)	(< 2)	(64)	(5)
8		**1b**	0.	isol.	7 min	78.	(-)	(-)	(> 96)	(< 2)
	$CH_3(CH_2)_6C{\equiv}C(CH_2)_6CH_3$ (11)						$CH_3(CH_2)_5CH{=}CH\text{-}C(=O)(CH_2)_6CH_3$ (12)			$CH_3(CH_2)_6C(=O)\text{-}C(=O)(CH_2)_6CH_3$ (13)
9		**1a**	5.	*in situ* [h]	16 h	> 96	(58) [i]			(12)
10		**1a**	0.	isol.	8 h	> 96	(78) [i]			(18)
11		**1b**	0.	isol.	2 min	>96	(77) [i,k]			(19)
12	(14)	**1b**	0.	isol.	3 min	> 96.	(15) (86)			(16) (13)

[a] In the method using isolated dioxirane, the initial dioxirane to substrate molar ratio was ca. 2:1 in all experiments. [b] As determined (± 2%) by gc (OV 101, 30 m × 0.25 μm i.d. capillary column or DB5, 0.20 μm film thickness, 15 m × 0.32 mm i.d., wide-bore capillary column). [c] Unless noted otherwise, yields were determined by gc or gc/ms (Hewlett-Packard mod. 5970 mass selective detector and mod. 5890 gas chromatograph) and based on the amount of substrate consumed; products were identified upon comparison of their ^{1}H nmr spectra (Varian XL 200) and/or gc/ms, or gc/ftir (Perkin-Elmer FT-IR mod. 1710 and mod. 8700 gas chromatograph) with those of reported compounds or of commercially available materials. [d] Caroate to ketone to substrate molar ratio (hereafter C/K/S): 80:100:1. [e] C/K/S: 55:60:1. [f] C/K/S: 55:100:1. [g] C/K/S: 50:30:1. [h] C/K/S: 50:100:1. [i] Isolated yield of the *trans* stereomer. [j] Isolated as a ca. 60:40 mixture of the *trans* to *cis* stereomer (gc/ms and ^{1}H nmr analysis). [k] The corresponding epoxide, i.e. 9,10-epoxy-hexadecan- 8-one, was also detected by ^{1}H nmr.

With the introduction of the method using *in situ* generated dioxiranes R'R"CO_2 (**1**) as oxidants,[3] we tested its application to the oxidation of one water soluble alkyne, *viz.* phenylpropiolic acid Ph-C≡C-CO_2H employing excess aqueous potassium peroxomonosulfate $KHSO_5$ and acetone at pH 7.[3a] The combination of high reactivity and ease of product isolation now offered by the advent of isolated dioxiranes[4,5] on the chemical scene has encouraged us to carry out a more detailed screening of dioxirane oxidation of alkynes using isolated dimethyldioxirane (**1a**: R'=R"=CH_3)[4a-c] or the more reactive methyl(trifluoromethyl) dioxirane (**1b**: R'=CH_3, R"=CF_3).[4d,e] In Table 1 results obtained from oxidations of representative alkynes are summarized.

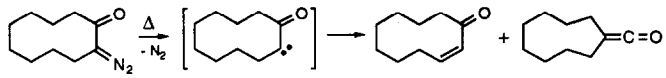
In the method using dioxiranes in the isolated form, the oxidations simply entailed addition of aliquots of standardized [4a-c] dioxirane solution to the alkyne substrates at the conditions given in Table 1; solutions of 0.06 - 0.09 M dimethyldioxirane (**1a**) in acetone or of 0.5 - 0.8 M methyl(trifluoromethyl)dioxirane (**1b**) in 1,1,1-trifluoropropanone (its ketone precursor, TFP[4d,e]) were obtained by following reported procedures.[4] According to the general protocol for *in situ* oxidations,[3] the dioxirane is generated from reaction of ketone with $KHSO_5$ in aqueous buffer at pH 7.0-7.5. In the oxidation of substrates of low nucleophilicity (such as alkynes), a large excess of $KHSO_5$ over substrate is necessary in order to achieve high conversions (Table 1), due to competing dioxirane-mediated decomposition of the economical

inorganic peroxide. A high ratio of ketone (the dioxirane precursor) to substrate (Table 1) is beneficial since reaction rates increase with ketone concentration.[5a,6]

The first four entries in Table 1 establish the dioxiranes as excellent agents for alkyne oxidation under mild conditions. In fact, diphenylacetylene (**2**) is reluctant to oxidation by common organic peracids[2d,e] (as well as by peroxomonosulfuric acid), affording complex product mixtures with poor yields and low conversion. However, the more reactive trifluoroperacetic acid CF_3CO_3H has been reported[2c] to react with **2** (according to a 2:1 stoicheiometry) to yield benzil (**3**) in 76% yield and benzoic acid (derived from oxidative cleavage of **2**) in 17% yield as the only identifiable products. Data in Table 1 indicate that oxidation of **2** with *in situ* dioxiranes can be carried to satisfactory substrate conversion (entry 1 and 2). However, using isolated dioxiranes (entry 3 and 4) has the advantage of much shorter reaction times (beside ease of product isolation); as expected,[4d,e] oxidation rates are much higher with dioxirane **1b**, which is several thousand-fold more reactive[5] than dimethyldioxirane (**1a**). Analogous considerations apply to the case of phenylacetylene (**7**) oxidation (entry 5 to 8, Table 1). Inspection of product distributions in Table 1 reveals that for diphenylacetylene (**2**), as well as for phenylacetylene (**7**), the ketene-derived (paths *ii* →*v* +*vi* , Scheme 1) products (i.e. benzophenone (**5**) plus diphenylacetic acid (**6**), and benzaldehyde (**9**) plus phenylacetic acid (**10**) respectively) largely dominate. In fact, in the oxidation of **7** with isolated methyl(trifluoromethyl) dioxirane (**1b**), benzaldehyde is practically the only product (entry 8). Product distributions also suggest that oxidation of the ketene by isolated dioxiranes (path *v*, Scheme 1) is faster than its trapping (path *vi*), at variance with what is normally observed using peracids.[2d,e]

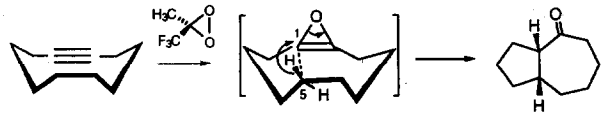
Entries 9-11 (Table 1) illustrate that the conversion of unbranched dialkyl alkynes such as 8-hexadecyne (**11**) into α,β-unsaturated carbonyls can be carried out successfully using dioxiranes either *in situ* or in the isolated form. This course (path *i* + *iii* , Scheme 1) is also prevalent when the oxidation of dialkyl alkynes is performed using peracids[2b] or H_2O_2 and PCWP (or PCMP);[2i] reportedly, the latter give exclusively the *trans*-α,β-unsaturated ketone. By way of contrast, oxidation of **11** by isolated dioxiranes yields both *trans*-9-hexadecen-8-one (**12a**)[6] and its *cis* stereomer (**12b**)[7] in a ca. 60:40 ratio. This suggests that, in the case at hand, the debated[2a] equilibration of the oxirene *(I)* to an α-oxo carbene $R^1\text{-}CO\text{-}\ddot{C}\text{-}R^2$ does not progress to any appreciable extent; in fact, should the α,β-unsaturated carbonyl have arisen from the α-oxo carbene, the thermodynamically more stable *trans* stereomer would have been formed in a much larger proportion.

As to the possible involvement of α-oxo carbenes, of interest is the case of cyclodecyne oxidation by isolated dioxirane **1b** (last entry, Table 1); in the reaction of this conformationally rigid alkyne, in fact, stereoselective 1,5- and 1,6-transanular insertion derivatives (i.e. **15**[8] and **16**,[9] respectively) account for over 95% of product, and no ring-contraction products are detected. By contrast, it is known[2f,10] that genuine medium-ring α-oxo carbenes generated from the corresponding α-diazoketones yield mainly enones and ring-contracted products (e.g., eq. 1).



(1)

This suggests that the first intermediate generated upon electrophilic *O*-transfer from the dioxirane to the alkyne may have *carbenoid* character only. Indeed, the products of cycloalkyne oxidation, at variance with those derived from α-diazoketones, may arise directly from intermolecular trapping of oxirenes as shown for the C_{10} system in eq 2.



(2)

(15)

With the completion of the present preliminary survey of dioxirane oxidation of alkynes, attempts to apply the potential of this new oxidant to more complex polyfunctional molecules encompassing the C≡C bond can begin. The mechanism of these reactions are also of interest; in fact, results reported herein indicate that their mechanism may differ in some respects from alkyne oxidations by peracids or peroxometals.

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6. According to a procedure which is representative of the *in situ* method, a concentrated aqueous solution (50 mL) of Curox® (triple salt $2KHSO_5 \cdot KHSO_4 \cdot K_2SO_4$, a gift from Peroxid-Chemie GmbH., Münich, FRG) containing 25 mmol of $KHSO_5$ (by iodometry) is added in portions during 2 h to a cooled (5-8 °C) and well stirred biphasic mixture of CH_2Cl_2 (20 mL) and buffered (pH 7.5, phosphate buffer) water (30 mL) containing acetone (7.5 mL, 100 mmol) , 8-hexadecyne (**11**) (2.5 g, 11 mmol), and $Bu_4N^+HSO_4^-$ (0.2 g, 0.6 mmol); the pH is kept constant at 7 - 7.5 by the addition of 5 M KOH. While substrate consumption is monitored by gc, further addition of solid Curox aliquots (up to 50 mmol of $KHSO_5$ total) during 16 h allows almost complete substrate conversion (Table 1). Then, the CH_2Cl_2 layer is separated, and the aqueous phase extracted with CH_2Cl_2 (10 mL); the combined methylene chloride extracts are dried ($MgSO_4$), the solvent removed in vacuo, and the residue purified by column flash-chromatography (silicagel, n-hexane/Et_2O), affording ***trans*-9-hexadecen-8-one (12a)** (1.52 g, 6.4 mmol, yield 58%): bp 117-118 °C (0.1 mmHg); ir (neat): 1676 (C=O str.), 1631 (C=C str.) cm^{-1}, etc.; ^1H nmr ($CDCl_3$, 200 MHz) δ 0.7-2.6 (m, 28 H), 6.05 (B part of ABX_2 system, apparent d of t , J_{AB}*(trans)* = 16 Hz, J_{BX} = 2 Hz, 1 H, =CH_B-CO-), 6.79 (A part of ABX_2 system, apparent d of t, J_{AB}*(trans)* = 16 Hz, J_{AX} = 6 Hz, 1 H, $C_5H_{11}CH_{2(X)}$-CH_A=); gc/ms (70 eV) *m/z* (r. i.) 238 (7, M^+), 181 (32), 139 (32), 127 (12), 96 (46), 69 (43), 67 (19), 55 (100), etc.

7. Column flash-chromatography (silicagel) afforded ***cis*-9-hexadecen-8-one (12b)** contaminated by its *trans* stereomer: ir (neat): 1695 (C=O str.), 1620 (C=C str.) cm^{-1}, etc.; ^1H nmr ($CDCl_3$, 200 MHz) δ 0.8-2.7 (m, 28 H), 6.08 (B part of ABX_2 system, apparent d of t, J_{AB}*(cis)* = 11.5 Hz, J_{BX} = 1.6 Hz, 1 H, =CH_B-CO-), 6.65-6.80 (A part of ABX_2 system, complex m, 1 H, $C_5H_{11}CH_{2(X)}$-CH_A=); gc/ms (70 eV) *m/z* (r. i.) 238 (5, M^+), etc.

8. ***Cis*-bicyclo[*5.3.0*]decan-2-one (15)**: bp 56-58 °C (0.02 mmHg);[2f,g] {^1H}^{13}C nmr ($CDCl_3$, 50 MHz) δ 24.47, 25.38, 26.19, 27.75, 32.50, 32.20, 40.39, 43.20, 54.60, 214.0 (C=O). Other spectral data in agreement with literature .

9. ***Cis*-bicyclo[4.4.0]decan-2-one** (*cis*-α-decalone) **(16)**: bp 65-67 °C (0.02 mmHg);[2f,g] {^1H}^{13}C nmr ($CDCl_3$, 50 MHz) δ 21.00, 21.73, 22.11, 23.10, 28.03, 29.69, 43.37, 58.31, 59.19, 206.5 (C=O). Other spectral data in agreement with literature .

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