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Oxidative Rearrangement of Internal Alkynes To Give One-Carbon-Shorter Ketones via Manganese Porphyrins Catalysis

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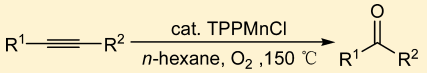
Supporting Information

ABSTRACT: Oxidative rearrangement of internal alkynes catalyzed by manganese(III) porphyrin is described, which opens a new access to one-carbon-shorter ketones using molecular oxygen. Under the standard conditions, a variety of alkynes including diarylalkynes and arylalkylalkynes rearranged smoothly to the corresponding ketones in high yields. Based upon experimental observations, a plausible reaction mechanism is proposed.

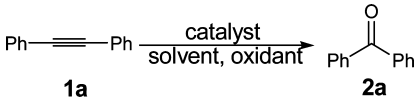


The oxidation of internal alkynes has received considerable attention for a long time because they can be converted to a wide variety of valuable compounds such as α,β-unsaturated ketones,[1] α-diketones,[2] 1,2-diols,[3] or cleavage products of the triple bond[4−6] that occur ubiquitously in natural and synthetic bioactive molecules. Over the past several decades, the stoichiometric oxidation of alkynes using organic peracids, thalium nitrate, ruthenium and osmium tetraoxides, permanganate, peroxomonophosphoric acid peroxomolybdenum complexes, and dioxiranes as oxidative reagents has been widely developed.[5,6] However, these are often stoichiometric, hazardous, expensive, and difficult to remove from the reaction solution. Recently, in the context of green and sustainable chemistry, transition-metal-catalyzed oxyfunctionalization of alkynes has emerged as an attractive alternative.[7] Despite considerable progress in the field, examples of catalytic methods are still limited: these established methods require the use of expensive transition-metal catalysts (often Pd and Ru). Consequently, it is still highly desirable to develop novel approaches for the oxyfunctionalization of alkynes.

Hydrocarbon functionalization mediated by transition-metal complexes based on porphyrins is of great interest in biomimetic investigation and is potentially useful in organic synthesis. The protocol of "metalloporphyrins/oxygen" used for mono-oxygenation of saturated C−H and epoxidation of olefin has been documented in many reports,[8] and mono-oxygenation of saturated C−H in alkane has been applied to large-scale industrial processes.[9] However, to the best of our knowledge, metalloporphyrins/oxygen used for the oxidation of internal alkynes has not been established. Herein, we report the first example of the oxidative rearrangement of alkynes using molecular oxygen as oxidant catalyzed by manganese(III) porphyrin.

Inspired by recent reports that metalloporphyrin can be used to catalyze epoxidation of alkenes with O_2,[8] we envision a metalloporphyrin-based strategy could be applied to alkynes. When the reaction of 1,2-diphenylacetylene **1a** was carried out in the presence of 10^{-6} mol *m*-tetraphenylporphyrin manganese(III) chloride (TPPMnCl) in *n*-hexane at 110 °C under 2 MPa of O_2 for 4 h, benzophenone **2a**, which was similar to the products of Wolff rearrangement,[2d,12b] was obtained in 54% yield based on **1a** (Table 1, entry 1). The

Table 1. Optimization of Reaction Conditions[a]



1a **2a**

entry	catalyst	solvent	T (°C)	oxidant	convn[b] (%)	yield[c] (%)
1	TPPMnCl	*n*-hexane	110	O_2	60	54
2	TPPMnCl	*n*-hexane	150	O_2	94	85
3	TPPMnCl	DMF	150	O_2	<1	trace
4	TPPMnCl	MeCN	150	O_2	<1	trace
5	TPPMnCl	benzene	150	O_2	<1	trace
6	TPPMnCl	*n*-hexane	150	H_2O_2	<1	trace
7	TPPMnCl	*n*-hexane	150	PhIO	<1	trace
8	TPPMnCl	*n*-hexane	150	$PhI(OAc)_2$	<1	trace
9	none	*n*-hexane	150	O_2	<1	trace
10	TPPMnCl	*n*-hexane	150	N_2	0	0

[a]Unless otherwise noted, the reaction conditions were as follows: **1a** (1 mmol), catalyst (10^{-6} mol), solvent (5.0 mL), pressure (2 MPa), reaction time (4 h). [b]Determined by GC. [c]Isolated yield based on **1a**.

desired product **2a** was obtained in 85% isolated yield when the reaction temperature was increased to 150 °C (Table 1, entry 2). Changing the solvent to DMF, CH_3CN, or benzene afforded a trace amount of product (Table 1, entries 3−5), which were consistent with the results that metalloporphyrins could not activate O_2 effectively in polar solvent.[10] In addition, some other oxidants, such as H_2O_2, PhIO, and $PhI(OAc)_2$, provided only a trace amount of the desired product (Table 1, entries 6−8). The controlled experiment also showed that no reaction occurred in the absence of either catalyst or O_2, thus suggesting that a metalloporphyrins/O_2 combination is

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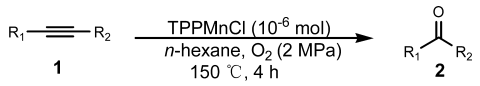
required for the success of the reaction (Table 1, entries 9 and 10). On the basis of these results, we decided to set heating the alkynes at 150 °C in the presence of 10^{-6} mol TPPMnCl in *n*-hexane under 2 MPa of O_2 as our standard conditions.

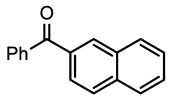
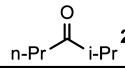
Under the optimized reaction conditions, we then examined the scope and limitations of the reaction, and the results are summarized in Table 2. We found that the reaction worked very well for a wide variety of internal alkynes including diarylalkynes and arylalkylalkynes, affording the desired ketones in yields ranging from 49% to 85% (Table 2, entries 1−10). Diarylalkynes bearing both electron-donating and electron-withdrawing groups on the phenyl group provided good results (Table 2, entries 6−8). The results indicated that the yield of the reaction was not very sensitive to the electron density of the phenyl group. The reaction of α- and β-naphthyl phenylacetylenes also worked well, furnishing the same ketone, β-naphthyl phenyl ketone **2i** in moderate yields (Table 2, entries 9 and 10). It was noteworthy that the reaction of α-naphthyl phenylacetylene gave β-naphthyl phenyl ketone, which was not consistent with the above results. In order to understand how the rearranged product obtained, we introduced α-naphthyl phenyl ketone, the proposed oxidative rearrangement intermediate of α-naphthyl phenylacetylenes, to the controlled experiment, and β-naphthyl phenyl ketone was obtained. This showed that the β-naphthyl phenyl ketone, the reaction product of α-naphthyl phenylacetylene, was probably generated via the rearrangement of α-naphthyl phenyl ketone formed in situ under the standard conditions. The results of aryl alkynes were all favorable; the reactions of aliphatic alkynes were messy. For example, the reaction of 4-octyne gave only a small amount of rearrangement product (Table 2, entry 13). It was interesting that one of the primary propyl groups that connected with the C−C triple bond was changed to isopropyl connected on the ketone, which was identified by GC−MS coinjection of commercially available authentic samples. Compared with the other ketones obtained, **2i** and **2m** were different from the others. Moreover, no reaction occurred when 1-trimethylsilyl-1-hexyne was subjected to the same reaction conditions (Table 2, entry 12). Unfortunately, phenylacetylene, which is a terminal alkyne, gave a complex mixture and only a trace amount of the desired product was detected by GC−MS (Table 2, entry 11).

Though the exact mechanism is still not clear at present, some information has been gathered: (1) When the reaction of **1a** was carried out in the presence of 1.5 equiv of radical inhibitor TEMPO (2,2,6,6-tetramethyl-1-piperidinyloxy), the desired product **2a** was not detected in an appreciable amount, thus suggesting that a radical mechanism could be involved. (2) When the competitive reaction of **1e** and **1n** was conducted under the same reaction conditions (Scheme 1, eq 1), only rearrangement products **2e** and **2n** were detected by GC−MS in addition to CO_2, and no cross-rearrangement products were detected. This result suggested that the rearrangement is strictly an intramolecular process and one carbon atom in the triple bond was oxidized to CO_2. (3) Benzil **3** and 2-diphenylacetic acid **4** seemed not to serve as intermediates in the reaction, as these species were introduced into the standard conditions and only a trace amount of **2a** could be detected (Scheme 1, eqs 2 and 3).

In a metalloporphyrin/O_2 system, the active species are recognized to be high-valent metal-oxo species ([TPPMn^{IV}=O]).[11] On the basis of these results and related reports,[2d,12] a plausible mechanism is proposed in Scheme 2. Under the reaction conditions, TPPMnCl reacted with O_2 to give intermediate [TPPMn^{IV}=O], which was then trapped by substrate **A** to produce oxirene **B**,[2d,12a,d] its subsequent rearrangement afforded **C**,[12b,d] and **C** was further oxidized to give the desired ketone and released carbon dioxide.

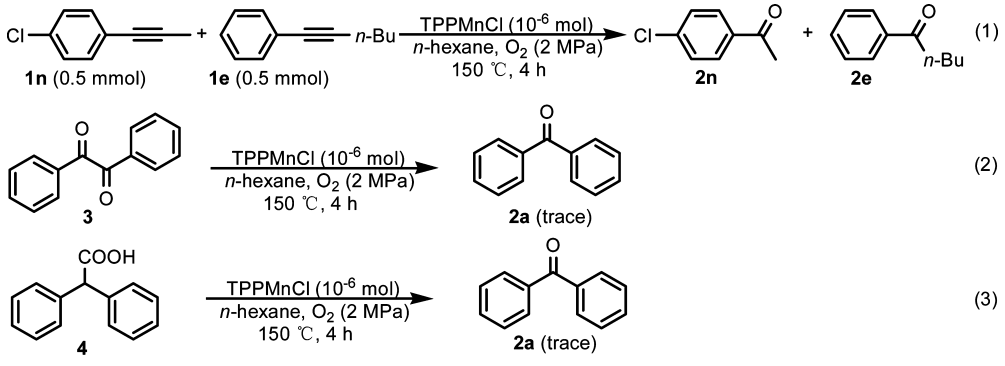
Table 2. TPPMnCl-Catalyzed Oxidative Rearrangement of Various Internal Alkynes[a]



Entry	R^1	R^2	Product	Conv.(%)[b]	Yield (%)[c]
1	Ph	Ph	**2a**	94	85
2	Ph	Me	**2b**	75	55
3	Ph	Et	**2c**	95	70
4	Ph	*n*-Pr	**2d**	94	74
5	Ph	*n*-Bu	**2e**	92	76
6	Ph	*p*-Cl-Ph	**2f**	95	82
7	Ph	*p*-NO_2-Ph	**2g**	95	82
8	Ph	*p*-MeO-Ph	**2h**	89	70
9	Ph	α-naphthyl	 **2i**	58	49
10	Ph	β-naphthyl	**2i**	62	54
11	Ph	H	**2k**	>99	trace
12	*n*-Bu	$SiMe_3$	--	0	0
13	*n*-Pr	*n*-Pr	 **2m**	>99	<5[d]

[a]Reaction conditions: **1** (1 mmol), TPPMnCl (10^{-6} mol) in 5 mL of *n*-hexane under 2 MPa of O_2 at 150 °C for 4 h. [b]Determined by GC. [c]Isolated yield based on **1**. [d]Detected by GC−MS.

Scheme 1. Investigation of Possible Reaction Intermediate



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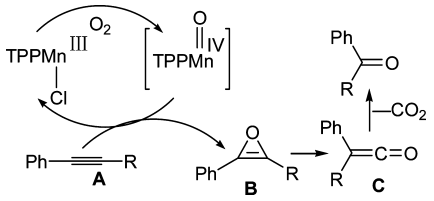
Scheme 2. Proposed Reaction Mechanism for the Oxidation of Internal Alkynes



In summary, we have developed a manganese(III) porphyrin catalyzed oxidative rearrangement of alkynes using molecular oxygen as oxidant. The reaction proceeded smoothly in *n*-hexane and a variety of ketones were obtained in yields of 49−85%, and substituents such as chloro, nitro, and alkoxy groups on the diarylacetylenes were well tolerated.

EXPERIMENTAL SECTION

General Comments. All reagents and solvent used were obtained commercially and used without further purification unless indicated otherwise. 1-chloro-4-(2-phenylethynyl)benzene (**1f**),[13a] 1-nitro-4-(2-phenylethynyl)benzene (**1g**),[13a] 1-(2-(4-methoxyphenyl)ethynyl)-benzene (**1h**),[13a] 1-(2-phenylethynyl)naphthalene (**1i**),[13b] and 2-(2-phenylethynyl)naphthalene (**1j**),[13b] and 1-chloro-4-(1-propynyl)-benzene (**1n**)[13b] were prepared according to literature procedures. All products were characterized by IR, MS, ^{1}H NMR, ^{13}C NMR, and elementary analysis. IR spectra were recorded on a FT-IR spectrometer. Mass spectra were measured on a mass instrument (EI). Analyses of the conversion of reagent were performed by gas phase chromatography, using a RX-5 capillary column and a frame ionization detector (FID). An elementary analyzer was used. ^{1}H NMR spectra were recorded on 400 MHz in $CDCl_3$, and ^{13}C NMR spectra were recorded on 100 MHz in $CDCl_3$ using TMS as internal standard. Copies of ^{1}H NMR and ^{13}C NMR spectra are provided as Supporting Information.

Typical Procedure for the Aerobic Oxidative Rearrangement of Internal Alkynes Catalyzed by TPPMnCl. A 10-mL homemade high-pressure kettle equipped with magnetic stirring bar was charged with 1 mmol alkynes, 10^{-6} mol TPPMnCl, and *n*-hexane (5 mL). The resulting mixture was stirring at 150 °C under 2 MPa of oxygen. After being stirred for the time indicated, the mixture was cooled to room temperature. Purification of the crude product by flash chromatography on silica gel using the indicated solvent system afforded the desired product.

ASSOCIATED CONTENT

Supporting Information

Copies of ^{1}H and ^{13}C NMR spectra. This material is available free of charge via the Internet at http://pubs.acs.org.

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Notes

The authors declare no competing financial interest.

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