Poly(ethylene glycol) dimethyl ether mediated oxidative scission of aromatic olefins to carbonyl compounds by molecular oxygen†

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A simple, and practical oxidative scission of aromatic olefins to carbonyl compounds using O2 as the sole oxidant with poly(ethylene glycol) dimethyl ether as a benign solvent has been developed. A wide range of monosubstituted, gem-disubstituted, 1,2-disubstituted, trisubstituted and tetrasubstituted aromatic olefins was successfully converted into the corresponding aldehydes and ketones in excellent yields even with gram-scale reaction. Some control experiments were also conducted to support a possible reaction pathway.

Introduction

The selective oxidative scission of olefins is a practiced transformation in organic synthesis. The produced carbonyl compounds are valuable intermediates in pharmaceuticals, fragrances, agrochemicals and bulk chemical industries.† The two-step ozonolysis is the conventional method to convert olefins into carbonyl compounds (Scheme 1a).‡ In recent years, the ozone was replaced by other oxidants, such as H2O2, oxone, TBHP, mCPBA, KMnO4, PhIO/HBF4 (Scheme 1b). However, the super stoichiometric use of expensive and toxic oxidants leads to a large amount of resource waste and environmental pollution.

Molecular oxygen is regarded as an ideal oxidant due to its easy availability, cheapness, environmental benignity and good functional-group tolerance. Recently, a series oxidative scission of olefins to carbonyl compounds with O2 as the sole oxidant, catalysed by organocatalysts NHPI, AIBN, Bz2PhI2, TEMPO, transitional-metal complexes Pd, Cu, Fe, Ni, CAN, as well as photocatalysts and electrocatalysts, have been reported (Scheme 1c). However, some shortcomings including non-commercial available catalysts, expensive additives, inevitable residual transitional-metals, and excess amount of volatile organic solvents limit their application in industry. Very recently, although a 1,2-diethoxyethane catalysed oxidative scission of olefins to ketones by air has been achieved, the olefins are limited to gem-disubstituted aromatic alkenes.‡ Therefore, developing a wide applicable strategy for the oxidative scission of olefins to aldehydes and ketones is highly desirable but still remains a challenge.

Poly(ethylene glycol) dimethyl ether (PEGDME) has been attracting increasing interest due to its benign characteristics involving lower cost, non-volatilization, and non-toxicity, etc.‡ To continue our interest in developing environmental benign synthetic reactions,‡ herein we report a simple and practical oxidative scission of a wide range of monosubstituted, gem- and 1,2-disubstituted, trisubstituted, and tetrasubstituted aromatic olefins to the corresponding aldehydes and ketones by O2 with PEGDME as a benign solvent.

Scheme 1 Oxidative scission of olefins to carbonyl compounds.
Results and discussion

Our studies were started with gem-diphenylethylene (1a) as a model substrate (Table 1). When the oxidation scission of 1a was performed in N,N-dimethylformamide (DMF), methyl tert-butyl ether (MTBE), tetrahydrofuran (THF), 2-methyltetrahydrofuran (2-MeTHF), ethylene glycol (EG), triethylene glycol (TEG), ethylene glycol dimethyl ether (EGDME), ethylene glycol diethyl ether (EGDEE), diethylene glycol monomethyl ether (DEGME), diethylene glycol dimethyl ether (DEGDME), dipropylene glycol monomethyl ether (DPGMME), and dipropylene glycol dimethyl ether (DPGDME) were screened as a solvent at 130 °C for 10 hours, providing 54–94% yields (entries 7–14). Moreover, it was found that the environmentally friendly poly(ethylene glycol) (PEG) and poly(ethylene glycol) dimethyl ether (PEGDME) gave 96% and 99% yield, respectively (entries 15–16). Therefore, PEGDME was demonstrated to be the best solvent. Next, the effect of the reaction temperature was examined. The yield of 2a remained at 99% when the reaction temperature dropped to 110 °C, but lower yield of 78% was observed at 100 °C (entries 17–18). Shorter reaction time was also attempted, the results revealed that the yield remained at 99% at 8 hours (entries 19–20). When the reaction was performed under air atmosphere, the yield decreased to 35% (entry 21). In addition, it was found that the higher concentration of 1a led to lower yield of 2a (entries 22–23). Finally, the entry 19 was regarded as the optimal reaction conditions: 1a (0.5 mmol), PEGDME (1 mL), under O2 atmosphere, 110 °C, and 8 hours.

With the optimized reaction conditions in hand, the scope of various olefins was investigated. As shown in Scheme 2, the oxidative scission of gem-diphenylethlenes bearing electron-donating group (Me, OMe) at the ortho-, meta- or para position of the phenyl proceeded successfully to give the corresponding 2b–2g with >98% yield. In addition, the halogen element (F, Cl, Br) substituted gem-diphenylethlenes were also gave corresponding ketones 2h–2i in 90–99% yields. The halogen substituents are useful entities amenable to further transformation in organic synthesis. The gem-diphenylethlenes with meta-substituted electron-withdrawing group CF3 gave higher yield than the ortho-substituted one (2m: 73%, 2n: 99%). The gem-diphenylethlenes with two or three substituents on the phenyls also gave the desired products 2o–2u in 86–99% yields. When phenyl of gem-diphenylethylene was replaced by naphthyl, thiethyl and pyridyl, the oxidative scission also proceeded smoothly, affording the corresponding products 2v–2x in 60–95% yields. To our delighted, the substrates containing fluorene or thioxanthene moiety also provided the desired ketones 2y and 2z in 87% and 85% yields. Furthermore, the aryl-alkyl disubstituted olefins like 2-aromatic olefins gave >95% yields. To our delighted, the substrates containing fluorene or thioxanthene moiety also provided the desired ketones 2y and 2z in 87% and 85% yields. Furthermore, the aryl-alkyl disubstituted olefins like 2-aromatic olefins gave >95% yields.

| Entry | Solvent | Temp. (°C) | t (h) | Yield (%) |
|-------|---------|------------|------|-----------|
| 1     | DMF     | 130        | 10   | <2%       |
| 2     | MTBE    | 55         | 10   | <2%       |
| 3     | THF     | 66         | 10   | <2%       |
| 4     | 2-MeTHF | 78         | 10   | <2%       |
| 5     | 1,4-Dioxane | 100 | 10 | 73        |
| 6     | Morpholine | 130 | 10 | 9        |
| 7     | EG      | 130        | 10   | 54        |
| 8     | TEG     | 130        | 10   | 85        |
| 9     | EGDME   | 86         | 10   | 61        |
| 10    | EGDEE   | 130        | 10   | 90        |
| 11    | DEGME   | 130        | 10   | 91        |
| 12    | DGDME   | 130        | 10   | 93        |
| 13    | DPGDME  | 130        | 10   | 94        |
| 14    | DPGMME  | 130        | 10   | 94        |
| 15    | PEG     | 130        | 10   | 96        |
| 16    | PEGDME  | 130        | 10   | 99        |
| 17    | PEGDME  | 110        | 10   | 99        |
| 18    | PEGDME  | 110        | 10   | 99        |
| 19    | PEGDME  | 110        | 10   | 78        |
| 20    | PEGDME  | 110        | 10   | 99        |
| 21*   | PEGDME  | 110        | 8    | 83        |
| 22*   | PEGDME  | 110        | 8    | 35        |
| 23*   | PEGDME  | 110        | 8    | 64        |
| 24*   | PEGDME  | 110        | 8    | 52        |

*Abbreviation: N,N-dimethylformamide (DMF), methyl tert-butyl ether (MTBE), tetrahydrofuran (THF), 2-methyltetrahydrofuran (2-MeTHF), ethylene glycol (EG), triethylene glycol (TEG), ethylene glycol dimethyl ether (EGDME), ethylene glycol diethyl ether (EGDEE), diethylene glycol monomethyl ether (DEGME), diethylene glycol dimethyl ether (DEGDME), dipropylene glycol monomethyl ether (DPGMME), dipropylene glycol dimethyl ether (DPGDME), poly(ethylene glycol) (average Mn, 400) (PEG400), poly(ethylene glycol) dimethyl ether (average Mn, 250) (PEGDME250). Reaction conditions: 1a (0.5 mmol), solvent (1 mL), O2 balloon. The yields were determined by HPLC.
bromobenzaldehyde (2ac), benzaldehyde (2ad) and diphenylmethanone (2a) were obtained in about 90% yields. Finally, the tetraphenylethylene (1ah) was also subjected to this oxidative scission, less than 5% yield was obtained even if elevating the temperature to 150 °C and extending the reaction time to 24 hours.

To understand the reaction pathway, control experiments were conducted. As shown in Scheme 4, when the oxidative scission of gem-diphenylethylene (1a) was carried out under N₂ atmosphere, no product 2a was observed. Only a trace amount of oxidation product 2a was detected in the presence of a radical scavenger 2,2,6,6-tetramethylpiperidine-N-oxyl (TEMPO) under optimal conditions. It means that a radical reaction pathway might be involved. When 2,2-diphenyloxirane (3a) was used as the starting material, the desired ketone 2a could be obtained in 99% yield, indicating that 3a might be a key intermediate of this oxidative scission reaction.

Based on the control experiments and reported work, a plausible reaction pathway was proposed as shown in Scheme 5. Firstly, PEGDME was oxidized by O₂ to produce a peroxyl radical 3a°. Secondly, 3,3-diphenyl-1,2-dioxetane (1a°) was formed by the oxidation of gem-diphenylethylene (1a) with 3a° as

Scheme 2 Scope of gem-disubstituted aromatic olefins. Reaction conditions: 1 (0.5 mmol), PEGDME (1 mL), O₂ balloon, 110 °C, 8 hours, isolated yield.

Scheme 3 Scope of mono, di-, tri-, and tetrasubstituted aromatic olefins.

Scheme 4 Control experiments.
an oxidant, regenerating PEGDME concurrently. And then, 1a’ is converted to the more stable key intermediate 2,2-diphenylethylene (3a) with one equivalent of 1a. Finally, 3a was converted to give the product 2a with 3a’ as an oxidant.

To further demonstrate the practicality of this oxidative scission reaction, as shown in Scheme 6, a gram-scale reaction of gem-diphenylethylene (1a; 1.80 g, 10 mmol) was conducted under O₂ atmosphere in PEGDME at 110 °C for 10 hours, the product diphenylmethanone (2a) was isolated in 96% yield (1.75 g).

Conclusions

In summary, we have developed an oxidative scission of aromatic olefins to carbonyl compounds using molecular oxygen as the sole oxidant with PEGDME as solvent. A wide range of monosubstituted, gem- and 1,2-disubstituted, trisubstituted, and tetrasubstituted aromatic olefins were oxidized to aldehydes and ketones in excellent yields. A reaction pathway was proposed based on some control experiments. A successful gram-scale reaction also demonstrated its practicability.

Experimental section

General information

Unless otherwise noted, all reagents, catalysts and solvents were purchased from commercial suppliers and used without further purification. Column chromatography was performed with silica gel (200–300 mesh). NMR spectra were recorded on Bruker AVANCE III (400 MHz) spectrometers. CDCl₃ was the solvent used for the NMR analysis, with tetramethyl silane as an internal standard. Chemical shifts were reported up field to TMS (0.00 ppm) for ¹H NMR and relative to CDCl₃ (77.0 ppm) for ¹³C NMR. HPLC analysis was conducted on an Agilent 1200 Series instrument with 5C18-MS-II Packed Column (4.6 mm I.D. × 250 mm).

General procedure for oxidation scission of aromatic olefin

The corresponding aromatic olefin 1 (0.5 mmol), PEGDME (1 mL) were added to a 10 mL Schlenk tube. The tube was evacuated and filled with oxygen three times. The mixture was stirred at 110 °C for 8 hours under O₂ atmosphere using a balloon. After cooling, the mixture was subjected to silica gel column chromatography (PE : EA = 15 : 1) to give the product 2.

Gram-scale oxidation scission of gem-diphenylethylene (1a)

The gem-diphenylethylene (1a, 1.80 g, 10 mmol), PEGDME (20 mL) were added to a 50 mL of round-bottomed flask equipped with a three-way jointer. The flask was then evacuated and filled with oxygen three times. The mixture was stirred at 110 °C for 10 hours under O₂ atmosphere using a balloon. After cooling, the mixture was subjected to silica gel column chromatography (PE : EA = 15 : 1) to give the product 2a (1.75 g, 96% yield).

Conflicts of interest

There are no conflicts to declare.

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