Household Ozone Disinfector as An Alternative Ozone Generator for Ozonolysis of Alkenes

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Abstract: Ozonolysis is an oxidative cleavage reaction of alkenes with ozone that is indispensable and has found many applications in organic synthesis. However, dedicated laboratory ozone generators are quite expensive equipment and may not be affordable by many laboratories. Recently, low-cost ozone disinfectors have become more common as a household appliance. Herein, we demonstrate the applicability of a household ozone disinfector, which can produce ozone in the order of 10 mmol/h, as alternative equipment for the laboratory scale ozonolysis of alkenes. The ozonolysis of 14 styrene derivatives bearing electron-donating and electron-withdrawing groups on aromatic rings including those with α- and β-substituents, as well as 8 natural products containing olefinic moieties were investigated. Ozonolysis of these alkenes at millimole scales proceeded to completion within 30–40 minutes and the carbonyl products were obtained in 68% to quantitative yields. Preparative-scale ozonolysis of 4-methoxystyrene (6.17 g, 46 mmol) was also demonstrated. The reaction proceeded smoothly to yield 4-anisaldehyde in 92% yield, which was subsequently converted to *p*-anisaldehyde dimethyl acetal in 66% yield. This work presents household ozone disinfector as an affordable, compact size, and practical synthetic equipment that does not require extra modification. Thus, the household ozone disinfector offers convenient access to ozonolysis or other reactions involving ozone for low-budget laboratories.

Introduction

Ozonolysis is one of the time-honored chemical reactions for oxidative cleavage of alkenes (C(sp²)-C(sp²) bond) or alkynes (C(sp)-C(sp) bond).[1] The 1,3-dipolar cycloaddition between ozone and alkene followed by reversion step produces secondary ozonide or hydroperoxy hemiacetal/ketal as an intermediate depending on the solvent.[1b] The intermediate is subsequently quenched by a reductive work-up to yield aldehyde, ketone, or alcohol. Alternatively, an oxidative work-up yields carboxylic acid or ester as final product. To reach the full potential of ozonolysis, several other variations have been developed such as the synthesis of 1,2,4-tetraoxolane *via* co-ozonolysis by Griesbaum's group,[2] the terminally differentiated ozonolysis by Schreiber's group,[3] and the end-group-differentiating ozonolysis by Carreira's group.[4] In 2019, Kwon's group reported a novel C(sp³)-C(sp²) bond cleavage utilizing ozonolysis. A hydrodealkenylative cleavage of C(sp³)-C(sp²) bond was exquisitely accomplished through tandem reactions of ozonolysis, reduction, and radical quenching.[5] This strategy was later applied to other functionalizations of olefins such as in the synthesis of aryl/alkyl sulfides by dealkenylative thiylation or the synthesis of carbonyls by oxodealkenylation.[6] Kwon's recent work on hydrodealkenylation represents the hidden potential of ozonolysis, despite its routine use in laboratories for several decades.[7]

Undoubtedly, ozonolysis has been one of the indispensable methods in synthetic toolbox due to its mild conditions, high atom economy, high efficiency, and compatibility with various functional groups.[8] Despite these obvious benefits, it is relatively underutilized due to the limited accessibility of laboratory ozone generators, which are generally far too expensive for underfunded laboratories, especially in developing countries.[9] Even when the budget is not a problem, investment in the acquisition of dedicated ozonolysis equipment may not be worthwhile if the reaction is to be performed only occasionally.[10] Renting of laboratory ozone generator is also a possible option but it is only available in some countries.[11] Alternatively, constructions of homemade ozone generators were reported in the past but have not been widely utilized due to several drawbacks such as low ozone production rate (15–30 mg/h),[12] the safety issues concerning high voltages (15–20 kVolts),[13] and elaborate equipment setup.[14] On the other hand, many research groups attempted to seek alternatives to ozonolysis for oxidative cleavages with oxidizing agents such as *meta*-chloroperoxybenzoic acid (*m*-CPBA),[15] Oxone®,[9a] PhIO/HBF₄,[16] Fe(OTf)₃/PyBisulidine/O₂,[9b] Pd(OAc)₂/O₂,[17] Cu₂(OH)₂CO₃/TBHP,[9c] H₂WO₄/H₂O₂,[18] and OsO₄/NaIO₄.[19] Some of these methods still suffered from harsh conditions, low yields, and production of toxic metal wastes.

The utilization of household appliances and products as alternatives for sophisticated scientific equipment has received

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considerable interest recently. For examples; kitchen pressure cookers were used as a substitute of an autoclave for sterilization in microbiology.[20] Espresso machines were used for the pressurized hot water extraction (PHWE) of natural products such as shikimic acid and eugenol,[21] Kitchen microwaves were used for chemical synthesis and modified into oven-vessel extraction.[22] Blood glucose meters were used as convenient and rapid equipment to measure glucose concentration during fermentation of cellulose, starch digestion, or biomass conversion.[23] A parallel spotting device for thin-layer chromatography (TLC) and a dark-box for fluorescence imaging had been constructed from LEGO bricks and used for a high-throughput monitoring the progress of chemical reactions (TLC).[24] Nowadays, household ozone disinfectors are readily available and inexpensive appliances for eliminating unpleasant odor in the kitchen, toilet, or pet caring area at home.[25] It was also used for the preparation of ozonated-water for the removal of residual pesticides and microorganisms in fruits and vegetables.[26] We became interested whether this readily accessible appliance, which costs less than 100 USD and can generate ozone up to 10 mmol ozone/hour according to the specification, could be used as a source of ozone for chemical synthesis. Herein, we examine the ozonolysis of alkenes by using a household ozone disinfector as an ozone supply. Styrene derivatives bearing electron-donating and electron-withdrawing groups on the aromatic rings as well as those with α- or β-substituents on the double bond, as well as several natural products containing olefinic group were selected as showcase substrates.

Results and discussion

The setup of the ozonolysis experiment using the household ozone disinfector is illustrated in Figure 1.

Gratifyingly, the household ozone disinfector can be used directly without the requirement of any extra modification. First, the inlet tube of the ozone disinfector was connected to an oxygen cylinder (99.995% purity) equipped with a pressure regulator, and the outlet tube was connected to a long-stem glass adaptor submerged in the solution of the ozonolysis substrate. The flow rate of the O_3/O_2 stream was controlled by the regulator at the oxygen cylinder. The excess ozone in the outlet gas stream was quenched by passing through a 1.0 M KI solution before being released to the atmosphere in the fume hood. The small footprint in the laboratory due to its compact size (Ø 22 cm×6.5 cm) was also another important advantage. Next, the ozonolysis of styrene and its derivatives **1–14** was investigated (Table 1). In general, the styrene derivatives (0.6–1.1 mmol) were totally consumed within 30–40 minutes after the ozone gas (as a mixture with oxygen as carrier gas) was passing through the solution.

The ozonolysis of styrene derivatives **1–5** bearing an electron-donating or an electron-withdrawing group on the aromatic ring afforded the corresponding aldehydes in a yield ranging from good to quantitative. The reaction of styrene (**1**) and electron-rich styrene derivatives (**2–3**) proceeded to completion within 30 minutes and yielded the aldehyde **1a**, **2a**, and **3a** in 91%, 80%, and 96% yield, respectively (Table 1, entries 1–3). Electron-poor styrene derivatives **4** and **5** resulted in the formation of aldehydes **4a** and **5a** in 89% and quantitative yield, respectively (entries 4–5). Next, less reactive
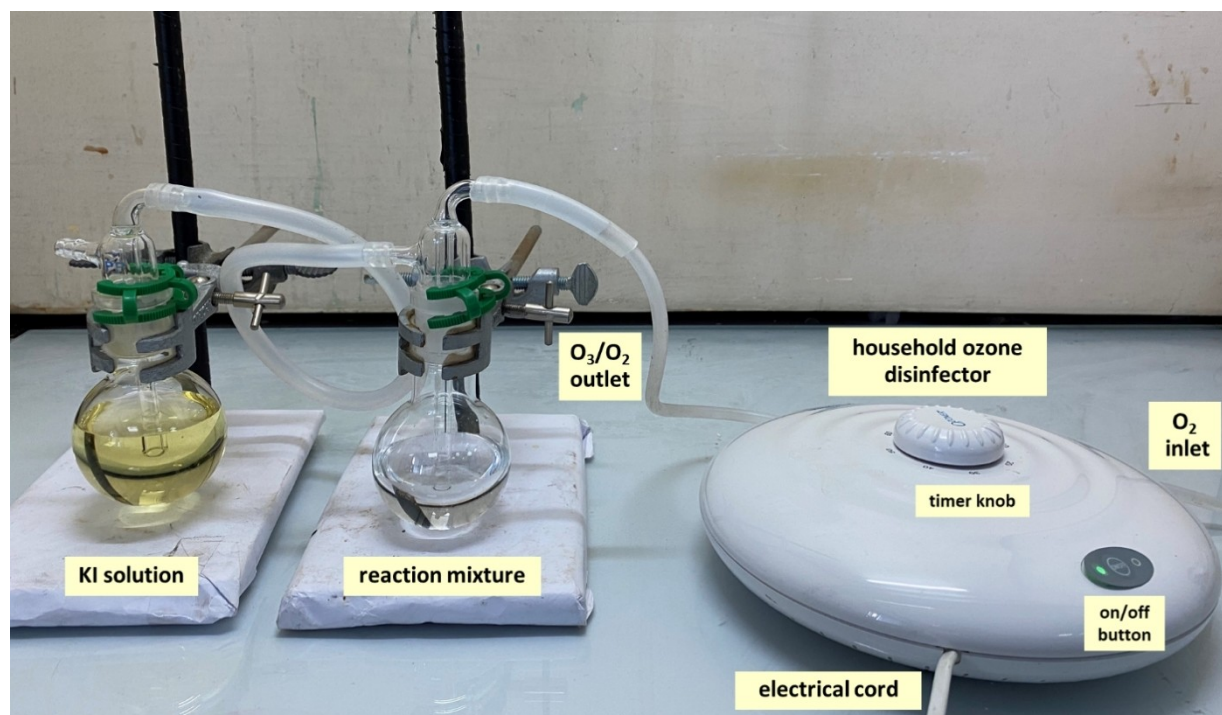

Figure 1. Experiment setup for ozonolysis using household ozone disinfector as an ozone supply.

Table 1. Ozonolysis of styrene derivatives with household ozone disinfector.

Entry	Olefin	Product	Yield[a] [O$_2$ as feed gas]	Yield[a,d] [air as feed gas]	Entry	Olefin	Product	Yield[a] [O$_2$ as feed gas]	Yield[a,d] [air as feed gas]
1	1	1a	91%[b]	67%	8	8	8a	quantitative (82%[f])	quantitative
2	2	2a	80%[b]	74%	9	9	1a	81%[b]	85%[b]
3	3	3a	96%	90%	10	10	1a	72%[b]	40%
4	4	4a	89% (85%[e])	89%	11	11	1a	92%[b]	65%
5	5	5a	quantitative	quantitative	12	12	1a	68%[b,c]	72%
6	6	6a	95%[c]	69%	13	13	1a	86%[b,c]	60%
7	7	7a	86%	86%	14	14	1a	75%[b]	64%

Standard conditions: 1. Styrene and derivatives (0.6–1.1 mmol), ozone generated by household ozone disinfector with oxygen as feed gas (flow rate = 250 mL/min), dichloromethane, room temperature (27–30 °C), 30–40 minutes; [styrene] = 0.03 M. 2. SMe$_2$ (5 equiv.) or PPh$_3$ (1.1 equiv.), room temperature (27–30 °C), 12 hours. [a] Yields were determined based on the isolated product after column chromatography. [b] Yields of volatile products were determined by ^{1}H NMR integration using 1,3,5-trimethoxybenzene as an internal standard. [c] Yields were based on recovered starting materials (brsm). [d] Ozonolysis under standard conditions with household ozone disinfector except using atmospheric air as feed gas (flow rate = 1.5 L/min), 80–240 minutes to completion. [e] Ozonolysis under standard conditions except using laboratory ozone generator and oxygen as feed gas (flow rate = 500 mL/min), 5 minutes to completion. [f] Ozonolysis using household ozone disinfector in larger scale by using 4-chloro-α-methylstyrene (8) for 1.00 g (6.58 mmol) and oxygen as feed gas, 2 hours to completion.

olefins such as α- and β-substituted styrene were examined. α-Substituted styrenes 6–8 provided the corresponding ketones 6a–8a in high yields, between 86% to quantitative yields, albeit requiring longer reaction time to complete (40 minutes) (entries 6–8). β-Substituted styrene 9–14 provided the unsubstituted benzaldehyde 1a in 68–92% yields after performing ozonolysis for 40 minutes (entries 9–14). It should be noted that when an electron-withdrawing group (formyl-, nitro-, nitrile- and amide group) was conjugated with the olefin substrate such as in trans-cinnamaldehyde (10), trans-β-nitrostyrene (12), trans-cinnamonitrile (13), and trans-cinnamamide (14), significant lower yields were obtained. This is in agreement with the previous reports whereby electron-deficient alkenes are much less reactive towards ozonolysis than electron-rich alkenes.[27] A comparison of the efficiencies of the household ozone disinfector and a laboratory ozone generator was carried out on 4-chlorostyrene (4) as the substrate (entry 4[e]). In both cases, the

same 4-chlorobenzaldehyde (4a) was obtained in comparable yields (85% yield for laboratory ozone generator versus 89% yield for household ozone disinfector). However, the ozonolysis with laboratory ozone generator went to completion within 5 minutes compared to 30 minutes when the household ozone disinfector was employed. This attributes to the higher ozone production rate by the laboratory ozone generator (4.00 g/h; model ED-OG-R6, EcoDesign Co. Ltd., Japan) compared with the household ozone disinfector (0.45 g/h; model OZONER-010, ProTechSci Co. Ltd., Thailand).[28] Moreover, larger scale ozonolysis of 4-chloro-α-methylstyrene (8) (1.00 g, 6.58 mmol) satisfyingly produced 4-chloroacetophenone (8a) in 82% yield within 2 hours of ozonolysis (entry 8[f]).

In regard to a source of oxygen gas for ozone production, atmospheric air could also be employed as feed gas for the household ozone disinfector instead of pure oxygen gas. The corresponding carbonyls 1a–8a were smoothly obtained from

alkene **1**–**14** in the range of 40% to quantitative yield (entries 1–14). However, the ozonolysis required a significantly longer time to reach completion (80–240 min.) due to the lower concentration of oxygen in the atmospheric air and thus resulting in lower ozone yields. Moreover, along with the O_3/O_2 stream, nitrogen oxides such as NO_2 and N_2O_5 were also generated from the reaction between nitrogen (N_2) and oxygen (O_2) in the atmospheric air supply due to the high voltage electrical discharge.[14,29] The NO_2 and N_2O_5 can further react with moisture to generate acidic species such as nitrous acid (HNO_2) and nitric acid (HNO_3). This was supported by the significant decrease of the pH in a control experiment when the ozone generated from atmospheric air was purged into pure water, the pH of solution decreased from 7.02 to 2.81 after 1 hour. Thus, although the use of atmospheric air as the feed gas is more convenient and more economical,[14] one must be aware of the longer reaction time and potential side reactions of acid-sensitive substrates.

Next, the ozonolysis of representative natural products containing an olefinic group (**15**–**22**) with the household ozone disinfector was investigated at 0.6–1.6 mmol scale (Table 2).

Natural products carrying both olefinic and phenolic groups such as caffeic acid (**15**), isoeugenol (**16**), and eugenol (**17**) were subjected to the standard ozonolysis protocol employing the household ozone disinfector. After the usual reductive work-up, the corresponding phenolic aldehydes including protocatechualdehyde (**15a**), vanillin (**16a**), and homovanillin (**17a**) were smoothly obtained in 87%, 89%, and 75% yield, respectively (Table 2, entries 1–3). Monoterpenes such as α-pinene (**18**), β-pinene (**19**), and acetyl-β-citronellol (**20**) were also successfully employed as additional test substrates. The ozonolysis products **18a**, **19a**, and **20a** were obtained as expected in 80%, 85%, and 80% yield, respectively (entries 4–6).[30] Next, limonene (**21**) was also tested as a representative monoterpene bearing two olefinic groups. The ozonolysis of limonene (**21**) in dichloromethane at room temperature gave a mixture of monocleavage **21a** (65% yield) and dicleavage **21b** (33% yield) (entry 7). The chemoselective ozonolysis of endocyclic alkene was achieved by using pyridine as additive at −60°C. Pyridine is known to form a complex with ozone and resulted in lower reactivity of ozone as an electrophile.[31] The formation of the double cleavage product **21b** was fully suppressed and only the

Table 2. Ozonolysis of natural products containing an olefinic group with the household ozone disinfector.

Entry	Olefin	Product/Yield[c]		Entry	Olefin	Product/Yield[c]
1	caffeic acid (**15**)	protocatechualdehyde (**15a**); 87%[b]		6	(±)-acetyl-β-citronellol (**20**)	**20a**; 80%[a]
2	isoeugenol (**16**)	vanillin (**16a**); 89%[a]		7	(+)-limonene (**21**)	**21a**; 65%[a] **21b**; 33%[a]
3	eugenol (**17**)	homovanillin (**17a**); 75%[a]		8	(+)-limonene (**21**)	**21a**; 83%[d]
4	(±)-α-pinene (**18**)	(±)-pinonaldehyde (**18a**); 80%[b]		9	methyl oleate (**22**)	**22a**; 85%[a] **22b**; 64%[a]
5	(−)-β-pinene (**19**)	(+)-nopinone (**19a**); 85%[b]				

Standard conditions: 1. Olefinic natural products (0.6–1.6 mmol), ozone generated by the household ozone disinfector with oxygen as feed gas (flow rate = 250 mL/min), room temperature (27–30 °C), 30–40 minutes; [olefin] = 0.03 M. 2. SMe$_2$ (5 equiv.) or PPh$_3$ (1.1 equiv.), room temperature (27–30 °C), 12 hours. [a] The ozonolysis was performed in dichloromethane. [b] The ozonolysis was performed in methanol. [c] Yields were determined from isolated product after column chromatography. [d] The ozonolysis was performed in dichloromethane and pyridine (5 equiv.) at −60 °C.

monoclevage product **21a** was obtained in 83% yield from the ozonolysis of the more reactive endocyclic alkene (entry 8).[1b] Finally, methyl oleate (**22**), when subjected to the ozonolysis, provided methyl 9-oxononanoate (**22a**) in 85% yield along with 1-nonanal (**22b**) in 64% yield (entry 8). The volatility of compound **22b** resulted in a moderate yield following the isolation by column chromatography.

p-Anisaldehyde dimethyl acetal (**23**) is a versatile reagent for protection of diols. It is widely used for the protection of hydroxyl groups at C-4 and C-6 positions of pyranosides in oligosaccharide synthesis.[32] The cyclic 1,3-dioxanes derived from *p*-anisaldehyde can be orthogonally cleaved in the presence of other protecting groups under mild conditions.[33] Direct preparations of *p*-anisaldehyde dimethyl acetal from 4-methoxystyrene were reported in moderate to good yields by using catalytic $FeSO_4$/pyridine-2-carboxylic acid with H_2O_2 as an oxidant in CH_3OH (method **A**: 45% yield)[34] or catalytic [(*p*-cymene)Ru(II)(imidazole-based ligand)MeOH]$^+$ with *tert*-butyl hydroperoxide (TBHP) as an oxidant in CH_3OH (method **B**: 79% yield).[35] An alternative metal-free preparative-scale synthesis of *p*-anisaldehyde dimethyl acetal (**23**) by using the household ozone disinfector was further demonstrated (Scheme 1).

The ozonolysis of 4-methoxystyrene (**3**) in preparative scales was carried out in two batches at 2.52 gram-scale (1st-run experiment) and 6.17 gram-scale (2nd-run experiment) (Scheme 1). The ozonolysis proceeded smoothly at 0 °C to completion within 5 and 8 hours, respectively. After a reductive work-up with Me_2S, catalytic *p*-TsOH and 3 Å molecular sieves were added to the reaction mixture (1st-run experiment) and was stirred at room temperature for 3 days. TLC analysis indicated incomplete conversion of the aldehyde **3a** to dimethyl acetal **23**. The isolation of the dimethyl acetal **23** and the aldehyde **3a** mixture proved challenging since the boiling points and polarities of both compounds are very close to each other. After vacuum distillation, a mixture of dimethyl acetal **23** and aldehyde **3a** was obtained as a colorless liquid. Thus, the product yields were determined by ^1H NMR analysis and *p*-anisaldehyde dimethyl acetal (**23**) was obtained in 42% yield (55% brsm yield), and 4-methoxybenzaldehyde (**3a**) was recovered in 22% yield. Alternatively, the 2nd-run experiment (6.17 gram-scale) was carried out in a 2-step synthesis approach. The crude mixture after the reductive work-up was first purified to yield 4-methoxybenzaldehyde (**3a**) in 92% yield. Then it was subjected to *p*-TsOH-catalyzed acetal formation using a continuous water extraction with molecular sieves technique recently reported by Stoltz's group.[36] The yield of *p*-anisaldehyde dimethyl acetal (**23**) was improved to 66% (74% brsm yield) and 4-methoxybenzaldehyde (**3a**) was recovered in 10% yield. It was thus demonstrated that the household ozone disinfector is capable of producing ozone in sufficient scale for performing ozonolysis in a synthetically useful scale. This is an indication of the practicality of the household ozone disinfector for general uses in the laboratories.

Despite the introduction of ozonolysis to organic synthesis by Harries since 1905,[7a] we believe there are hidden potentials for ozonolysis as a tool for organic synthesis that has not been discovered yet, partly due to the limited accessibility of ozone generator by many research groups. The reports of ozonolysis-initiated radical fragmentation between sp³-sp² carbon (instead of the traditional sp²-sp² carbon) from Kwon's group in 2019 was an example of such untapped potential.[5] We hope that our work would relieve this accessibility barrier and might help others to expand their research towards new applications of ozonolysis.

Conclusion

In summary, we have introduced a household ozone disinfector as an affordable, practical, compact size, and ready to use ozone generator for ozonolysis reactions without extra modification. The ozonolysis performance was demonstrated using a broad
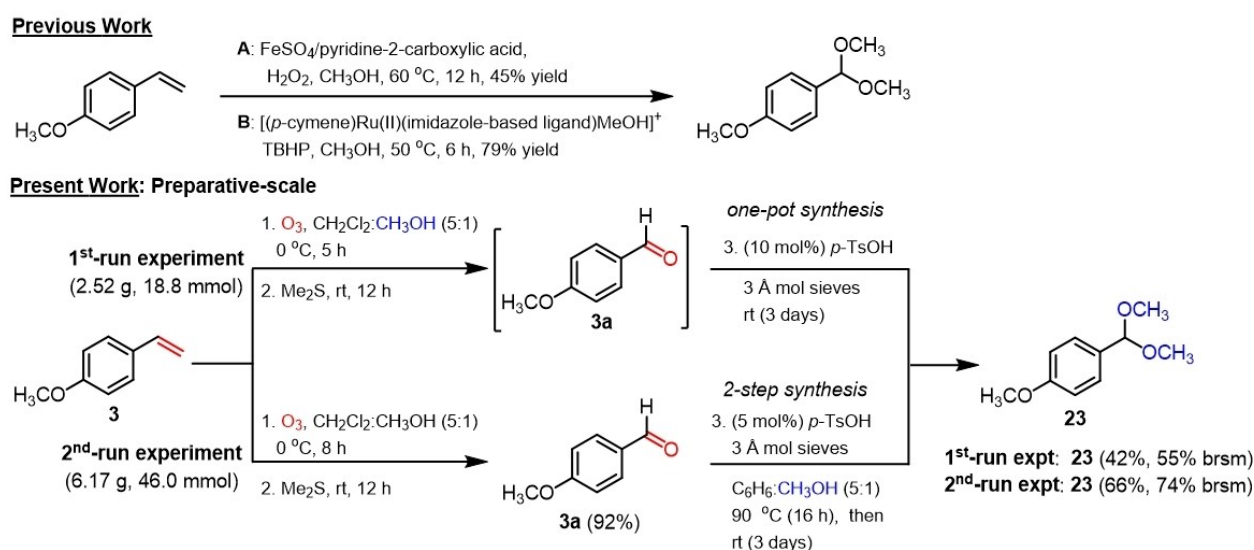
Scheme 1. Previous work and preparative-scale synthesis of *p*-anisaldehyde dimethyl acetal (**23**) using the household ozone disinfector.

range of olefinic substrates (**22** compounds) and high yields of the desired carbonyl products were obtained in all cases. Moreover, the household ozone disinfector was capable of generating ozone for the oxidative cleavage in preparative scales as demonstrated by the production of *p*-anisaldehyde dimethyl acetal (**23**). This process would enable underfunded laboratories to routinely perform the ozonolysis for oxidative cleavage of alkenes as well as discover its novel applications. It is noteworthy that reports of practical procedure/technique in organic synthesis have been valued and well-received within the community such as flash column chromatography technique,[37] drying organic solvents with desiccants,[38] and chemical shifts of impurities in NMR measurement.[39] We believe that the work presented here would be another addition to these useful techniques. Furthermore, this equipment should not only be beneficial for the organic synthesis community but also for other research areas. For example; the use of ozonolysis to determine the olefinic position on the synthetic polybutadiene rubber[40] and natural products such as fatty acid,[41] phospholipid,[42] alkaloids and coumarins[43] or the study on biomass conversion or degradation of renewable feedstock by ozonolysis.[44] Currently, demonstration of ozonolysis in an undergraduate laboratory class using household ozone disinfector is carrying out and will be reported in due course.

Experimental Section

All chemicals and solvents were purchased from Acros, Merck, Sigma-Aldrich, TCI, or RCI Lab Scan. Reaction monitoring by TLC was performed on silica gel 60 F254 0.2 mm pre-coated aluminium plates and purchased from Merck. Preparative thin layer chromatography was 0.5 mm thickness coated by silica gel 60 GF254 from Merck. Chemical spots on TLC were observed by visualization under 254 nm UV light or stained with 2,4-dinitrophenylhydrazine (2,4-DNP) staining solution or iodine (I_2). Silica gel 60 (70–230 mesh) from Merck was used in purification by column chromatography. Solvents for NMR experiments were purchased from Cambridge Isotope Laboratories or Euriso-top. Ozonolysis was carried out with a household ozone disinfector model OZONER-010 (from ProTechSci Co. Ltd., Thailand) with a maximum ozone output of 0.45 g/hour (components inside ozone disinfector model OZONER-010 was shown in Figure S2 and S3 of the supporting information material). Flowrate of atmospheric air supply can be adjusted between 50 mL–1.50 L/minute by installation of a valve at gas outlet tube. For comparison of the efficiency, laboratory ozone generator model ED-OG-R6 (from EcoDesign Co. Ltd., Japan) with a maximum ozone output of 4.00 g/hour was employed. Chemical structure characterization was conducted by nuclear magnetic resonance (NMR) spectrometer on Bruker Avance 400 NMR spectrometer operating at 400 MHz for ^{1}H NMR and 101 MHz for ^{13}C{^{1}H} NMR or JEOL JNM-ECZ500R/S1 spectrometer operating at 500 MHz for ^{1}H NMR and 126 MHz for ^{13}C{^{1}H} NMR. Exact masses of all products were determined by high resolution mass spectrometry (HRMS) on a Bruker Daltonics micrOTOF-QII-ESI-QqTOF Mass Spectrometer.

General procedure for ozonolysis with household ozone disinfector

In a typical procedure, the alkene (0.6–1.6 mmol) was dissolved in dichloromethane or methanol (*ca.* 0.03 M) in a round bottom flask. Ozone stream (O_3/O_2) from household ozone disinfector was bubbled through a long-stem glass adaptor submerged in the solution of the alkene for 30–40 minutes at room temperature (27–30 °C). The flow rate of the O_3/O_2 stream was set to 250 mL/min and controlled by a regulator at the oxygen cylinder. When atmospheric air was used as oxygen gas supply (flowrate = 1.5 L/min), the inlet tube was connected to air pump instead of the oxygen cylinder (see Figure S3 in the supporting information material). The excess ozone from the outlet gas stream was quenched by passing through a 1.0 M KI solution before releasing to the atmosphere in the fume hood. The reaction was monitored by thin-layer chromatography. Once the alkene was totally consumed, the ozone disinfector was switched off and oxygen gas (or atmospheric air) was passed through the solution for 10 minutes to remove the excess ozone. Then, triphenylphosphine (1.1 mmol per olefinic group) or dimethyl sulfide (5.0 mmol per olefinic group) was added into the reaction mixture and stirred at room temperature for 12 hours. It should be noted that triphenylphosphine exhibited greater reducing power towards the ozonide intermediate. However, the by-product, triphenylphosphine oxide, was occasionally difficult to separate from the desired carbonyl product, thus dimethyl sulfide was used instead.[45] Next, the solvent was removed by rotary evaporator to obtain the crude product. Purification by column chromatography on silica gel provided the carbonyl product. In case of volatile products, the yield was determined by ^{1}H NMR integration using 1,3,5-trimethoxybenzene as an internal standard.[24a]

Note on safety

The ozonolysis reactions with the household ozone disinfector have been carried out in our laboratory in both small (< 1 mmol) and large (up to 46 mmol) scales for more than 200 runs over several years without any incidents. However, there are some safety issues to be emphasized. Concentrating crude reaction mixture containing organic peroxides or ozonides could lead to spontaneous and exothermic decompositions.[46] It is mandatory to ascertain the absence of left-over organic peroxides or ozonides, especially when the ozonolysis was conducted in preparative-scale. It is recommended that the reaction mixture after the reductive work-up should be examined with a peroxide strip test to ensure the total consumption of the peroxides or ozonides. Alternatively, a small amount of reaction mixture (*ca.* 0.10–0.25 mL) may be sampled for a ^{1}H NMR analysis to confirm the absence of peroxides or ozonides.[47] Although the household ozone disinfector uses a high voltage to generate the ozone, there was no modification of the equipment in any way apart from connecting the oxygen gas inlet tube to the electrical discharge chamber within ozone disinfector, thus the risk of electrical shock is minimal. Nevertheless, the usual precaution should be taken when performing the experiments involving oxygen gas. All flammable organic solvents must be kept away from the fume hood and the tubing connections between the oxygen cylinder and the gas inlet of the household ozone disinfector must be tightly secured to avoid leakage of oxygen. Besides, ozone is a toxic and corrosive gas, thus the gas outlet must be quenched by passing through a KI solution before being released to the atmosphere only in the fume hood.

Benzaldehyde (1a) Table 1, entry 1

The ozonolysis was carried out as described in the general procedure by dissolving styrene (1) (107 mg, 1.02 mmol) in dichloromethane (30 mL). For ozonolysis using oxygen as the feed gas, the reaction completed within 30 minutes which was monitored by TLC (30% ethyl acetate in hexanes; 2,4-DNP, $R_f = 0.60$). The reductive work-up was carried out with triphenylphosphine (268 mg, 1.02 mmol) and the yield was determined by ^{1}H NMR integration using 1,3,5-trimethoxybenzene (70 mg, 0.42 mmol) as an internal standard. Benzaldehyde (1a)[9b] was obtained in 91% yield. For ozonolysis using atmospheric air as the feed gas, the reaction completed within 90 minutes and the product 1a was obtained in 67% yield after purified by column chromatography. ^{1}H NMR (400 MHz, CDCl$_3$) δ_H 10.03 (s, 1H), 7.87 (dd, $J = 7.9, 0.9$ Hz, 2H), 7.62 (t, $J = 7.7$ Hz, 1H), 7.51 (t, $J = 7.6$ Hz, 2H). ^{13}C{^{1}H} NMR (101 MHz, CDCl$_3$) δ_C 192.3, 136.4, 134.4, 129.7, 129.0.

4-Methylbenzaldehyde (2a) Table 1, entry 2

The ozonolysis was carried out as described in the general procedure by dissolving 4-methylstyrene (2) (110 mg, 0.93 mmol) in dichloromethane (27 mL). For ozonolysis using oxygen as the feed gas, the reaction completed within 30 minutes which was monitored by TLC (30% ethyl acetate in hexanes; 2,4-DNP, $R_f = 0.60$). The reductive work-up was carried out with triphenylphosphine (292 mg, 1.11 mmol) and the yield was determined by ^{1}H NMR integration using 1,3,5-trimethoxybenzene (49 mg, 0.29 mmol) as an internal standard. 4-Methylbenzaldehyde (2a)[9b] was obtained in 80% yield. For ozonolysis using atmospheric air as the feed gas, the reaction completed within 120 minutes and the product 2a was obtained in 74% yield after purified by column chromatography. ^{1}H NMR (500 MHz, CDCl$_3$) δ_H 9.96 (s, 1H), 7.77 (d, $J = 8.0$ Hz, 2H), 7.32 (d, $J = 8.0$ Hz, 2H), 2.43 (s, 3H). ^{13}C{^{1}H} NMR (126 MHz, CDCl$_3$) δ_C 192.1, 145.7, 134.3, 129.9, 129.8, 22.0.

4-Methoxybenzaldehyde (3a) Table 1, entry 3

The ozonolysis was carried out as described in the general procedure by dissolving 4-methoxystyrene (3) (101 mg, 0.79 mmol) in dichloromethane (24 mL). For ozonolysis using oxygen as the feed gas, the reaction completed within 30 minutes which was monitored by TLC (30% ethyl acetate in hexanes; 2,4-DNP, $R_f = 0.50$). The reductive work-up was carried out with triphenylphosphine (228 mg, 0.87 mmol) and the crude mixture was purified by column chromatography using 5% to 30% ethyl acetate in hexanes as gradient eluent. 4-Methoxybenzaldehyde (3a)[48] was obtained as yellow liquid (98 mg, 96%). For ozonolysis using atmospheric air as the feed gas, the reaction completed within 80 minutes and the product 3a was obtained in 90% yield after purified by column chromatography. ^{1}H NMR (400 MHz, CDCl$_3$) δ_H 9.89 (s, 1H), 7.84 (d, $J = 8.6$ Hz, 2H), 7.01 (d, $J = 8.5$ Hz, 2H), 3.89 (s, 3H). ^{13}C{^{1}H} NMR (101 MHz, CDCl$_3$) δ_C 190.9, 164.8, 132.1, 130.2, 114.5, 55.7.

4-Chlorobenzaldehyde (4a) Table 1, entry 4

The ozonolysis was carried out as described in the general procedure by dissolving 4-chlorostyrene (4) (95 mg, 0.69 mmol) in dichloromethane (21 mL). For ozonolysis using oxygen as the feed gas, the reaction completed within 30 minutes which was monitored by TLC (30% ethyl acetate in hexanes; 2,4-DNP, $R_f = 0.65$). The reductive work-up was carried out with triphenylphosphine (198 mg, 0.76 mmol) and the crude mixture was purified by column chromatography using 10% ethyl acetate in hexanes as eluent. 4-Chlorobenzaldehyde (4a)[9b] was obtained as white solid (86 mg,

89%). For ozonolysis using atmospheric air as the feed gas, the reaction completed within 120 minutes and the product 4a was obtained in 89% yield after purified by column chromatography. ^{1}H NMR (400 MHz, CDCl$_3$) δ_H 9.99 (s, 1H), 7.83 (d, $J = 8.4$ Hz, 2H), 7.52 (d, $J = 8.4$ Hz, 2H). ^{13}C{^{1}H} NMR (101 MHz, CDCl$_3$) δ_C 190.8, 141.0, 134.7, 130.9, 129.5.

4-Nitrobenzaldehyde (5a) Table 1, entry 5

The ozonolysis was carried out as described in the general procedure by dissolving 4-nitrostyrene (5) (131 mg, 0.88 mmol) in dichloromethane (27 mL). For ozonolysis using oxygen as the feed gas, the reaction completed within 40 minutes which was monitored by TLC (30% ethyl acetate in hexanes; 2,4-DNP, $R_f = 0.60$). The reductive work-up was carried out with triphenylphosphine (254 mg, 0.97 mmol) and the crude mixture was purified by column chromatography using 10 to 20% ethyl acetate in hexanes as gradient eluent. 4-Nitrobenzaldehyde (5a)[49] was obtained as pale yellow solid (114 mg, quantitative yield). For ozonolysis using atmospheric air as the feed gas, the reaction completed within 120 minutes and the product 5a was obtained in quantitative yield after purified by column chromatography. ^{1}H NMR (400 MHz, CDCl$_3$) δ_H 10.17 (s, 1H), 8.40 (d, $J = 8.4$ Hz, 2H), 8.09 (d, $J = 8.6$ Hz, 2H). ^{13}C{^{1}H} NMR (101 MHz, CDCl$_3$) δ_C 190.4, 151.3, 140.2, 130.6, 124.4.

Acetophenone (6a) Table 1, entry 6

The ozonolysis was carried out as described in the general procedure by dissolving α-methylstyrene (6) (100 mg, 0.86 mmol) in dichloromethane (27 mL). For ozonolysis using oxygen as the feed gas, the reaction completed within 30 minutes which was monitored by TLC (30% ethyl acetate in hexanes; 2,4-DNP, $R_f = 0.55$). The reductive work-up was carried out with dimethyl sulfide (314 μL, 4.28 mmol) and the crude mixture was purified by column chromatography using 10% ethyl acetate in hexanes as eluent. Acetophenone (6a)[9b] was obtained as colorless liquid (98 mg, 95%). For ozonolysis using atmospheric air as the feed gas, the reaction completed within 160 minutes and the product 6a was obtained in 69% yield after purified by column chromatography. ^{1}H NMR (400 MHz, CDCl$_3$) δ_H 7.96 (d, $J = 8.2$ Hz, 2H), 7.57 (t, $J = 7.4$ Hz, 1H), 7.47 (t, $J = 7.6$ Hz, 2H), 2.61 (s, 3H). ^{13}C{^{1}H} NMR (101 MHz, CDCl$_3$) δ_C 198.0, 137.2, 133.1, 128.6, 128.3, 26.5.

Benzophenone (7a) Table 1, entry 7

The ozonolysis was carried out as described in the general procedure by dissolving 1,1-diphenylethelene (7) (130 mg, 0.72 mmol) in dichloromethane (24 mL). For ozonolysis using oxygen as the feed gas, the reaction completed within 40 minutes which was monitored by TLC (30% ethyl acetate in hexanes; 2,4-DNP, $R_f = 0.65$). The reductive work-up was carried out with dimethyl sulfide (265 μL, 3.62 mmol) and the crude mixture was purified by column chromatography using 10% ethyl acetate in hexanes as eluent. Benzophenone (7a)[9b] was obtained as white solid (154 mg, 89%). For ozonolysis using atmospheric air as the feed gas, the reaction completed within 120 minutes and the product 7a was obtained in 86% yield after purified by column chromatography. ^{1}H NMR (500 MHz, CDCl$_3$) δ_H 7.80 (d, $J = 8.2$ Hz, 2H), 7.58 (t, $J = 6.9$ Hz, 1H), 7.47 (t, $J = 7.7$ Hz, 2H). ^{13}C{^{1}H} NMR (126 MHz, CDCl$_3$) δ_C 196.9, 137.7, 132.5, 130.2, 128.4.

4-Chloroacetophenone (8 a) Table 1, entry 8

The ozonolysis was carried out as described in the general procedure by dissolving 4-chloro-α-methylstyrene (**8**) (135 mg, 0.82 mmol) in dichloromethane (24 mL). For ozonolysis using oxygen as the feed gas, the reaction completed within 30 minutes which was monitored by TLC (30% ethyl acetate in hexanes; 2,4-DNP, $R_f = 0.50$). The reductive work-up was carried out with dimethyl sulfide (300 μL, 4.10 mmol) and the crude mixture was purified by column chromatography using 10% ethyl acetate in hexanes as eluent. 4-Chloroacetophenone (**8 a**)[9b] was obtained as pale yellow liquid (144 mg, quantitative yield). For ozonolysis using atmospheric air as the feed gas, the reaction completed within 120 minutes and the product **8 a** was obtained in quantitative yield after purified by column chromatography. **^{1}H NMR** (400 MHz, CDCl$_3$) δ_H 7.89 (d, $J = 8.6$ Hz, 2H), 7.44 (d, $J = 8.5$ Hz, 2H), 2.59 (s, 3H). **^{13}C{^{1}H} NMR** (101 MHz, CDCl$_3$) δ_C 196.8, 139.6, 135.6, 129.8, 129.0, 26.8.

Benzaldehyde (1 a) Table 1, entry 9

The ozonolysis was carried out as described in the general procedure by dissolving β-methylstyrene (**9**) (131 mg, 1.11 mmol) in dichloromethane (33 mL). For ozonolysis using oxygen as the feed gas, the reaction completed within 40 minutes which was monitored by TLC (30% ethyl acetate in hexanes; 2,4-DNP, $R_f = 0.60$). The reductive work-up was carried out with triphenylphosphine (320 mg, 1.22 mmol) and the yield was determined by ^{1}H NMR integration using 1,3,5-trimethoxybenzene (51 mg, 0.30 mmol) as an internal standard. Benzaldehyde (**1 a**) was obtained in 81% yield. For ozonolysis using atmospheric air as the feed gas, the reaction completed within 120 minutes and the product **1 a** was obtained in 85% yield based on ^{1}H NMR integration using 1,3,5-trimethoxybenzene as an internal standard.

Benzaldehyde (1 a) Table 1, entry 10

The ozonolysis was carried out as described in the general procedure by dissolving *trans*-cinnamaldehyde (**10**) (114 mg, 0.84 mmol) in dichloromethane (24 mL). For ozonolysis using oxygen as the feed gas, the reaction completed within 40 minutes which was monitored by TLC (30% ethyl acetate in hexanes; 2,4-DNP, $R_f = 0.60$). The reductive work-up was carried out with triphenylphosphine (242 mg, 0.92 mmol) and the yield was determined by ^{1}H NMR integration using 1,3,5-trimethoxybenzene (45 mg, 0.27 mmol) as an internal standard. Benzaldehyde (**1 a**) was obtained in 72% yield. For ozonolysis using atmospheric air as the feed gas, the reaction completed within 120 minutes and the product **1 a** was obtained in 40% yield after purified by column chromatography.

Benzaldehyde (1 a) Table 1, entry 11

The ozonolysis was carried out as described in the general procedure by dissolving *trans*-stilbene (**11**) (180 mg, 1.00 mmol) in dichloromethane (30 mL). For ozonolysis using oxygen as the feed gas, the reaction completed within 40 minutes which was monitored by TLC (30% ethyl acetate in hexanes; 2,4-DNP, $R_f = 0.60$). The reductive work-up was carried out with triphenylphosphine (262 mg, 1.00 mmol) and the yield was determined by ^{1}H NMR integration using 1,3,5-trimethoxybenzene (23 mg, 0.13 mmol) as an internal standard. Benzaldehyde (**1 a**) was obtained in 92% yield. For ozonolysis using atmospheric air as the feed gas, the reaction completed within 120 minutes and the product **1 a** was obtained in 65% yield after purified by column chromatography.

Benzaldehyde (1 a) Table 1, entry 12

The ozonolysis was carried out as described in the general procedure by dissolving *trans*-β-nitrostyrene (**12**) (109 mg, 0.73 mmol) in dichloromethane (21 mL). For ozonolysis using oxygen as the feed gas, the reaction completed within 40 minutes which was monitored by TLC (30% ethyl acetate in hexanes; 2,4-DNP, $R_f = 0.60$). The reductive work-up was carried out with triphenylphosphine (211 mg, 0.80 mmol) and the yield was determined by ^{1}H NMR integration using 1,3,5-trimethoxybenzene (32 mg, 0.19 mmol) as an internal standard. Benzaldehyde (**1 a**) was obtained in 68% yield. For ozonolysis using atmospheric air as the feed gas, the reaction completed within 240 minutes and the product **1 a** was obtained in 67% yield after purified by column chromatography.

Benzaldehyde (1 a) Table 1, entry 13

The ozonolysis was carried out as described in the general procedure by dissolving *trans*-cinnamonitrile (**13**) (123 mg, 0.95 mmol) in dichloromethane (30 mL). For ozonolysis using oxygen as the feed gas, the reaction completed within 40 minutes which was monitored by TLC (30% ethyl acetate in hexanes; 2,4-DNP, $R_f = 0.60$). The reductive work-up was carried out with triphenylphosphine (275 mg, 1.05 mmol) and the yield was determined by ^{1}H NMR integration using 1,3,5-trimethoxybenzene (49 mg, 0.29 mmol) as an internal standard. Benzaldehyde (**1 a**) was obtained in 86% yield based on recovery of starting material. For ozonolysis using atmospheric air as the feed gas, the reaction completed within 120 minutes and the product **1 a** was obtained in 60% yield after purified by column chromatography.

Benzaldehyde (1 a) Table 1, entry 14

The ozonolysis was carried out as described in the general procedure by dissolving *trans*-cinnamamide (**14**) (156 mg, 1.06 mmol) in dichloromethane (33 mL). For ozonolysis using oxygen as the feed gas, the reaction completed within 40 minutes which was monitored by TLC (30% ethyl acetate in hexanes; 2,4-DNP, $R_f = 0.60$). The reductive work-up was carried out with triphenylphosphine (279 mg, 1.06 mmol) and the yield was determined by ^{1}H NMR integration using 1,3,5-trimethoxybenzene (22 mg, 0.13 mmol) as an internal standard. Benzaldehyde (**1 a**) was obtained in 75% yield. For ozonolysis using atmospheric air as the feed gas, the reaction completed within 120 minutes and the product **1 a** was obtained in 64% yield after purified by column chromatography.

Protocatechualdehyde (15 a) Table 2, entry 1

The ozonolysis was carried out as described in the general procedure by dissolving caffeic acid (**15**) (112 mg, 0.62 mmol) in methanol (18 mL) and oxygen was used as the feed gas. The reaction completed within 40 minutes which was monitored by TLC (30% ethyl acetate in hexanes; 2,4-DNP, R_f 0.70). The reductive work-up was carried out with triphenylphosphine (326 mg, 1.24 mmol). The crude mixture was purified by column chromatography using 20 to 60% ethyl acetate in hexanes as gradient eluent. Protocatechualdehyde (**15 a**)[50] was obtained as white solid (75 mg, 87%). **^{1}H NMR** (400 MHz, DMSO-d_6) δ_H 10.11 (s, 1H), 9.70 (s, 1H), 9.55 (s, 1H), 7.40–7.14 (m, 2H), 6.90 (d, $J = 7.9$ Hz, 1H). **^{13}C{^{1}H} NMR** (101 MHz, DMSO-d_6) δ_C 191.0, 152.1, 145.9, 128.9, 124.4, 115.6, 114.4.

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Vanillin (16a) Table 2, entry 2

The ozonolysis was carried out as described in the general procedure by dissolving isoeugenol (16) (111 mg, 0.67 mmol) in dichloromethane (21 mL) and oxygen was used as the feed gas. The reaction completed within 40 minutes which was monitored by TLC (30% ethyl acetate in hexanes; 2,4-DNP, $R_f = 0.20$). The reductive work-up was carried out with dimethyl sulfide (250 μL, 3.37 mmol). The crude mixture was purified by column chromatography using 30 to 40% ethyl acetate in hexanes as gradient eluent. Vanillin (16a)[51] was obtained as pale yellow solid (91 mg, 89%).^{1}H NMR (400 MHz, CDCl$_3$) δ_H 9.83 (s, 1H), 7.42 (d, $J = 6.0$ Hz, 2H), 7.05 (d, $J = 8.5$ Hz, 1H), 6.22 (s, 1H), 3.97 (s, 3H). ^{13}C{^{1}H} NMR (101 MHz, CDCl$_3$) δ_C 191.0, 151.8, 147.3, 130.1, 127.6, 114.5, 109.0, 56.3.

Homovanillin (17a) Table 2, entry 3

The ozonolysis was carried out as described in the general procedure by dissolving eugenol (17) (136 mg, 0.83 mmol) in dichloromethane (25 mL) and oxygen was used as the feed gas. The reaction completed within 40 minutes which was monitored by TLC (20% ethyl acetate in hexanes; 2,4-DNP, $R_f = 0.20$). The reductive work-up was carried out with dimethyl sulfide (0.31 mL, 4.15 mmol). The crude mixture was purified by column chromatography using 5 to 20% ethyl acetate in hexanes as gradient eluent. Homovanillin (17a)[52] was as pale yellow liquid (103 mg, 75%). ^{1}H NMR (400 MHz, CDCl$_3$) δ_H 9.71 (t, $J = 2.4$ Hz, 1H), 6.91 (d, $J = 8.0$ Hz, 1H), 6.72 (dd, $J = 8.0$, 2.1 Hz, 1H), 6.68 (d, $J = 2.1$ Hz, 1H), 5.65 (s, 1H), 3.88 (s, 3H), 3.60 (d, $J = 2.5$ Hz, 2H). ^{13}C{^{1}H} NMR (101 MHz, CDCl$_3$) δ_C 199.7, 147.1, 145.2, 123.5, 122.7, 115.0, 112.1, 56.1, 50.3.

(+/−)-Pinonaldehyde (18a) Table 2, entry 4

The ozonolysis was carried out as described in the general procedure by dissolving (+/−)-α-pinene (18) (197 mg, 1.45 mmol) in methanol (45 mL) and oxygen was used as the feed gas. The reaction completed within 30 minutes which was monitored by TLC (30% ethyl acetate in hexanes; I$_2$, $R_f = 0.55$). The reductive work-up was carried out with dimethyl sulfide (0.53 mL, 7.25 mmol). The crude mixture was purified by column chromatography using 10% ethyl acetate in hexanes as eluent. (+/−)-Pinonaldehyde (18a)[53] was obtained as colorless liquid (194 mg, 80%). ^{1}H NMR (500 MHz, CDCl$_3$) δ_H 9.74 (s, 1H), 2.93 (dd, $J = 10.1$, 7.6 Hz, 1H), 2.53–2.40 (m, 3H), 2.05 (s, 3H), 2.03–1.91 (m, 2H), 1.34 (s, 3H), 0.85 (s, 3H). ^{13}C{^{1}H} NMR (126 MHz, CDCl$_3$) δ_C 207.5, 201.5, 54.4, 45.2, 43.4, 35.8, 30.4, 30.2, 22.9, 17.7.

(+)-Nopinone (19a) Table 2, entry 5

The ozonolysis was carried out as described in the general procedure by dissolving (−)-β-pinene (19) (223 mg, 1.64 mmol) in methanol (45 mL) and oxygen was used as the feed gas. The reaction completed within 30 minutes which was monitored by TLC (30% ethyl acetate in hexanes; I$_2$, $R_f = 0.65$). The reductive work-up was carried out with dimethyl sulfide (0.60 mL, 8.20 mmol). The crude mixture was purified by column chromatography using 10% ethyl acetate in hexanes as eluent. (+)-Nopinone (19a)[27b,54] was obtained as pale yellow liquid (192 mg, 85%). ^{1}H NMR (500 MHz, CDCl$_3$) δ_H 2.63–2.49 (m, 3H), 2.35 (ddd, $J = 19.1$, 9.2, 2.0 Hz, 1H), 2.24 (dq, $J = 4.5$, 2.2 Hz, 1H), 2.10–2.01 (m, 1H), 1.99–1.91 (m, 1H), 1.66–1.55 (m, 1H), 1.33 (s, 3H), 0.86 (s, 3H). ^{13}C{^{1}H} NMR (126 MHz, CDCl$_3$) δ_C 215.2, 58.1, 41.3, 40.5, 32.9, 26.0, 25.4, 22.2, 21.5.

3-Methyl-6-oxohexyl acetate (20a) Table 2, entry 6

The ozonolysis was carried out as described in the general procedure by dissolving acetyl-β-citronellol (20) (129 mg, 0.65 mmol) in dichloromethane (18 mL) and oxygen was used as the feed gas. The reaction completed within 30 minutes which was monitored by TLC (20% ethyl acetate in hexanes; I$_2$, $R_f = 0.30$). The reductive work-up was carried out with dimethyl sulfide (240 μL, 3.26 mmol). The crude mixture was purified by column chromatography using 5 to 15% ethyl acetate in hexanes as gradient eluent. 3-Methyl-6-oxohexyl acetate (20a)[55] was obtained as yellow liquid (92 mg, 80%). ^{1}H NMR (400 MHz, CDCl$_3$) δ_H 9.78 (s, 1H), 4.17–4.04 (m, 2H), 2.54–2.38 (m, 2H), 2.05 (s, 3H), 1.69 (qd, $J = 13.0$, 6.4 Hz, 2H), 1.62–1.52 (m, 1H), 1.47 (dt, $J = 19.6$, 6.4 Hz, 2H), 0.93 (d, $J = 6.3$ Hz, 3H). ^{13}C{^{1}H} NMR (101 MHz, CDCl$_3$) δ_C 202.3, 171.1, 62.5, 41.4, 35.2, 29.5, 28.7, 20.9, 19.1.

(3R)-3-(1-methylethenyl)-6-oxoheptanal (21a) and (3R)-3-acetyl-6-oxoheptanal (21b)

Table 2, entry 7

The ozonolysis was carried out as described in the general procedure by dissolving (+)-limonene (21) (126 mg, 0.93 mmol) in dichloromethane (28 mL) and oxygen was used as the feed gas. The reaction completed within 30 minutes which was monitored by TLC (30% ethyl acetate in hexanes; I$_2$, $R_f = 0.30$ and 0.10; 21a and 21b, respectively). The reductive work-up was carried out with dimethyl sulfide (0.34 mL, 4.65 mmol; two olefinic groups). The crude mixture was purified by column chromatography using 10 to 60% ethyl acetate in hexanes as gradient eluent. (3R)-3-(1-methylethenyl)-6-oxoheptanal (21a) was obtained as colorless liquid (105 mg, 65%) and (3R)-3-acetyl-6-oxoheptanal (21b) was obtained as pale yellow liquid (53 mg, 33%). (3R)-3-(1-Methylethenyl)-6-oxoheptanal (21a);[56] ^{1}H NMR (400 MHz, CDCl$_3$) δ_H 9.68 (s, 1H), 4.84 (s, 1H), 4.78 (s, 1H), 2.75–2.62 (m, 1H), 2.52–2.42 (m, 2H), 2.42–2.35 (m, 2H), 2.14 (s, 3H), 1.81–1.66 (m, 2H), 1.64 (s, 3H). ^{13}C{^{1}H} NMR (126 MHz, CDCl$_3$) δ_C 208.5, 202.0, 145.2, 113.4, 47.6, 41.0, 40.9, 30.2, 26.5, 18.5. (3R)-3-Acetyl-6-oxoheptanal (21b);[57] ^{1}H NMR (400 MHz, CDCl$_3$) δ_H 9.73 (s, 1H), 3.12–3.02 (m, 1H), 2.95 (dd, $J = 18.3$, 9.3 Hz, 1H), 2.43 (t, $J = 7.2$ Hz, 3H), 2.27 (s, 3H), 2.15 (s, 3H), 1.99–1.88 (m, 1H), 1.73 (t, $J = 7.3$ Hz, 1H). ^{13}C{^{1}H} NMR (126 MHz, CDCl$_3$) δ_C 210.2, 207.4, 200.2, 44.9, 44.8, 40.2, 30.1, 29.4, 24.5.

Table 2, entry 8

The ozonolysis was carried out as described in the general procedure by dissolving (+)-limonene (21) (150 mg, 1.10 mmol) in dichloromethane (35 mL), pyridine (0.44 mL, 5.50 mmol) was added as additive and oxygen was used as the feed gas. The reaction was carried out at −60°C and completed within 30 minutes which was monitored by TLC (30% ethyl acetate in hexanes; I$_2$, $R_f = 0.30$). The reductive work-up was carried out with dimethyl sulfide (0.44 mL, 5.50 mmol) for 2 hours. The reaction was quenched by addition of 5% HCl solution (10 mL), extracted with saturated aqueous NaHCO$_3$ solution (15 mL), diethyl ether (3 × 15 mL), and washed with brine (15 mL). The combined organic layer was dried over anhydrous Na$_2$SO$_4$. The solvent was removed by rotary evaporator and the crude mixture was purified by column chromatography using 10 to 20% ethyl acetate in hexanes as gradient eluent. (3R)-3-(1-Methylethenyl)-6-oxoheptanal (21a)[56] was obtained as colorless liquid (154 mg, 83%).

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Methyl 9-oxononanoate (22 a) and 1-nonanal (22 b) Table 2, entry 9

The ozonolysis was carried out as described in the general procedure by dissolving methyl oleate (**22**) (219 mg, 0.74 mmol) in dichloromethane (25 mL) and oxygen was used as the feed gas. The reaction completed within 30 minutes which was monitored by TLC (20% ethyl acetate in hexanes; I_2, $R_f = 0.25$ and 0.50 for **22 a** and **22 b**, respectively). The reductive work-up was carried out with triphenylphosphine (291 mg, 1.11 mmol). The crude mixture was purified by column chromatography using 5% to 10% ethyl acetate in hexanes as gradient eluent. Methyl 9-oxononanoate (**22 a**) was obtained as colorless liquid (117 mg, 85%) and 1-nonanal (**22 b**) was obtained as yellow liquid (54 mg, 64%). Methyl 9-oxononanoate (**22 a**)[58] ; **¹H NMR** (400 MHz, CDCl₃) δ_H 9.76 (t, $J = 1.5$ Hz, 1H), 3.67 (s, 3H), 2.42 (td, $J = 7.3$, 1.6 Hz, 1H), 2.30 (t, $J = 7.5$ Hz, 2H), 1.70–1.55 (m, 4H), 1.33 (s, 7H); **¹³C{¹H} NMR** (101 MHz, CDCl₃) δ_C 202.8, 174.3, 104.4, 51.2, 43.9, 34.1, 29.0, 29.0, 24.9, 22.1. 1-Nonanal (**22 b**)[58] ; **¹H NMR** (400 MHz, CDCl₃) δ_H 9.76 (s, 1H), 2.40 (dd, $J = 7.4$, 1.9 Hz, 2H), 1.63 (t, $J = 7.2$ Hz, 2H), 1.34–1.19 (m, 10H), 0.94–0.81 (m, 3H).

Preparative-scale synthesis of p–anisaldehyde dimethyl acetal (23) Scheme 1

Gram-scale synthesis from 4-methoxystyrene (3) 1st-run experiment; one-pot synthesis

4-Methoxystyrene (**3**) (2.52 g, 18.8 mmol) was dissolved in a mixture of dichloromethane: methanol (5 : 1, 60 mL, 0.30 M) in a 250 mL two-neck round bottom flask and oxygen was used as the feed gas. The solution was cooled down to 0 °C and the ozone stream (O₃/O₂) from household ozone disinfector was bubbled through a long-stem glass adaptor submerged in the solution. The flow rate of the O₃/O₂ stream was set to 250 mL/min by the regulator at the oxygen cylinder. The excess ozone in the outlet gas stream was quenched by passing through a 1.0 M KI solution before being released to the fume hood. The ozone stream (O₃/O₂) was stopped every hour to monitor the progress of ozonolysis by TLC. After 5 hours, the reaction reached to completion. The household ozone disinfector was switched off and oxygen was passed through the solution for 10 minutes. Dimethyl sulfide (4.10 mL, 56.3 mmol) was added dropwise into the reaction mixture at 0 °C and stirred from 0 °C to room temperature (27–30 °C) for 12 hours. The reaction mixture was then examined by a peroxide strip test to ensure a total consumption of ozonide or hydroperoxy hemiacetal intermediate. Moreover, a small amount of reaction mixture (*ca.* 0.25 mL) was sampled, concentrated to dryness, and subjected to ¹H NMR analysis which confirmed the disappearance of ozonide or hydroperoxy hemiacetal signals. Next, the reaction mixture was dried over anhydrous Na₂SO₄ (*ca.* 5 g) and was subjected to acetal formation without purification. To the crude solution of 4-methoxybenzaldehyde (**3a**), p-TsOH·H₂O (323 mg, 1.89 mmol) and flame-dried 3 Å molecular sieves (10 g) were added and stirred at room temperature. After 3 days, the TLC analysis of reaction mixture did not indicate further improvement in the formation of the dimethyl acetal **23**. The reaction was quenched by adding saturated aqueous NaHCO₃ solution (50 mL), extracted with ethyl acetate (3 × 30 mL), and washed with brine (50 mL). The combined organic layer was dried over anhydrous Na₂SO₄. Solvents were removed by rotary evaporator and the crude mixture was purified by vacuum distillation (152 °C, 50 torr) to yield a mixture of p-anisaldehyde dimethyl acetal (**23**) and 4-methoxybenzaldehyde (**3a**) as a colorless liquid in 2.01 g. The isolation of dimethyl acetal **23** and aldehyde **3a** mixture was troublesome since boiling points and polarities of both compounds are very close to each other. Thus,

the product yields were determined by ¹H NMR integration using 1,3,5-trimethoxybenzene (641 mg, 3.82 mmol) as an internal standard. p-Anisaldehyde dimethyl acetal (**23**) was obtained in 7.87 mmol (42% yield, 55% brsm yield, over 2 steps) and 4-methoxybenzaldehyde (**3a**) was recovered in 4.56 mmol (22% yield) based on ¹H NMR analysis of a mixture. A small amount of the mixture was purified by column chromatography over ammonium hydroxide-neutralized silica gel using 5% ethyl acetate in hexanes as eluent to provide both compound **23** and **3a** for the purpose of NMR characterization. It is worth noting that dimethyl acetal **23** rapidly decomposed to aldehyde **3a** during silica gel column chromatography. Performing the column chromatography with ammonium hydroxide-neutralized silica gel was necessary to avoid such decomposition. p-Anisaldehyde dimethyl acetal (**23**);[34] **¹H NMR** (500 MHz, C₆D₆) δ_H 7.50 (d, $J = 8.8$ Hz, 2H), 6.81 (d, $J = 8.7$ Hz, 2H), 5.38 (s, 1H), 3.28 (s, 3H), 3.16 (s, 6H). **¹³C{¹H} NMR** (126 MHz, C₆D₆) δ_C 160.5, 131.4, 114.2, 103.2, 55.1, 52.2.

Gram-scale synthesis from 4-methoxystyrene (3) 2nd-run experiment; 2-step synthesis

The ozonolysis was carried out as described earlier in the 2.52-gram-scale synthesis (1st-run experiment) by dissolving 4-methoxystyrene (**3**) (6.17 g, 46.0 mmol) in a mixture of dichloromethane: methanol (5 : 1, 180 mL, 0.25 M) in a 500 mL three-neck round bottom flask and oxygen was used as the feed gas. The flow rate of the O₃/O₂ stream was set to 1 L/min. After 8 hours, the reaction reached to completion and the reductive work-up was carried out with dimethyl sulfide (8.42 mL, 115 mmol). The solvent was removed by rotary evaporator to obtain a crude product and purified by column chromatography using 10% ethyl acetate in hexanes as eluent. 4-Methoxybenzaldehyde (**3a**) was obtained as colorless liquid (5.74 g, 92%).

To a solution of 4-methoxybenzaldehyde (**3a**) (5.74 g, 42.1 mmol) in a mixture of benzene: methanol (5 : 1, 105 mL, 0.40 M) in a 250 mL two-neck round bottom flask was added p-TsOH·H₂O (363 mg, 2.11 mmol). An addition funnel was plugged with cotton at the stopcock valve and flame-dried 3 Å molecular sieves (30 g) were added to the funnel according to a continuous water extraction technique reported by Stoltz's group.[36] The addition funnel was attached to the round bottom flask, and a reflux condenser was connected to the top of addition funnel. The system was purged with Ar and heated to 90 °C in an oil bath. The progress of acetal formation was monitored in every 4 hours by TLC. After 16 hours, the TLC analysis of reaction mixture did not indicate further improvement in the formation of the dimethyl acetal **23**. Next, flame-dried 3 Å molecular sieves (20 g) was added into the reaction mixture and stirred at room temperature for additional 3 days to ensure the maximum conversion. The reaction was quenched by adding saturated aqueous NaHCO₃ solution (100 mL), extracted with ethyl acetate (3 × 50 mL), and washed with brine (100 mL). The combined organic layer was dried over anhydrous Na₂SO₄. Solvents were removed by rotary evaporator and the crude mixture was purified by distillation (146 °C, 50 torr) to yield a mixture of p-anisaldehyde dimethyl acetal (**23**) and 4-methoxybenzaldehyde (**3a**) as a colorless liquid in 5.39 g. The product yields were determined by ¹H NMR integration using 1,3,5-trimethoxybenzene (1.32 g, 7.89 mmol) as an internal standard. p-Anisaldehyde dimethyl acetal (**23**) was obtained in 27.7 mmol (66% yield, 74% brsm yield) and 4-methoxybenzaldehyde (**3a**) was recovered in 4.44 mmol (10% yield) based on ¹H NMR analysis of a mixture. Small amount of the mixture was purified by ammonium hydroxide-neutralized silica gel column chromatography using 5% ethyl acetate in hexanes as eluent to provide both of compound **23**

and **3a** for the purpose of NMR characterization, which gave consistent results with the previous report.[34]

Conflict of Interest

The authors declare no conflict of interest.

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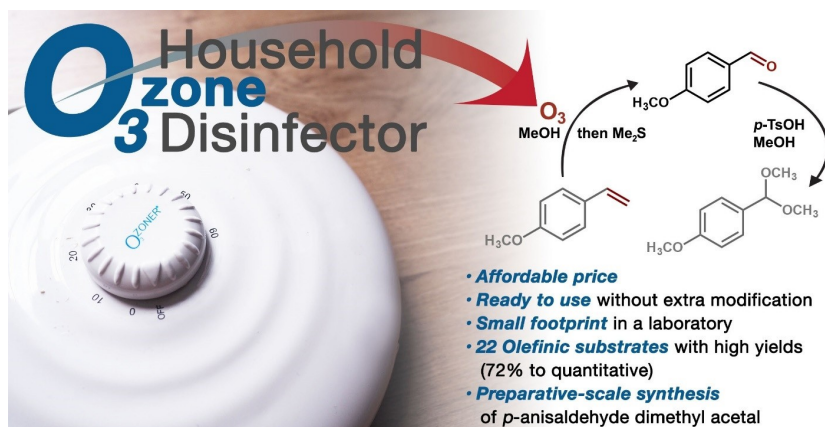
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Household Ozone Disinfector as An Alternative Ozone Generator for Ozonolysis of Alkenes

A low-cost household ozone disinfector can produce ozone for ozonolysis of alkenes without extra modification. The ozonolysis of 14 styrene derivatives bearing electron-donating and electron-withdrawing groups on aromatic rings including those with α- and β-substituents, as well as 8 natural products containing olefinic moieties were performed in good yields. Moreover, the household ozone disinfector was capable of generating ozone for the oxidative cleavage in preparative scales (46 mmol) as demonstrated by the production of *p*-anisaldehyde dimethyl acetal.