

FACILE ONE-POT SYNTHESIS OF ANISALDEHYDE

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At room temperature, anisaldehyde (4-methoxybenzaldehyde) is synthesized based on the ozonolysis of anethole (1-methoxy-4-(1-propenyl)-benzene) in a novel and environmentally friendly system composed of water and ethyl acetate. In the presence of water, ozonolysis of anethole results in the direct formation of anisaldehyde, avoiding the isolation or decomposition of ozonide.

Keywords: anethole, anisaldehyde, ozone, ozonide, ozonolysis.

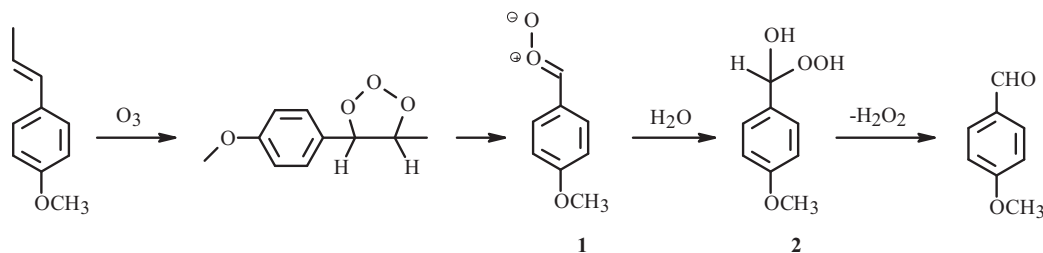
Anisaldehyde is commonly encountered in the fragrances, both synthetic and natural. It is widely used in the flavor, food, and cosmetic industry [1–3]. Also, anisaldehyde is used as an intermediate in the synthesis of other compounds in pharmaceuticals, pesticides, and perfumery [4].

In traditional methods [5–7], inorganic salts [8–10] are usually used as oxidants. Unfortunately, anisic acid, which is the oxidation product of anisaldehyde, is the main product. Furthermore, these protocols generally involve long processes [11–13] and produce significant quantities of chemical wastes.

Ozonolysis reaction [14–20], which has attracted many chemists' attention in recent years, can solve the problems mentioned above. However, recent research shows that the reaction usually requires low temperatures and rigorous conditions. Moreover, the reaction requires two steps to complete [21]. Little attention is focused on the one-pot synthesis of anisaldehyde from ozonolysis of anethole. We report here a facile and convenient synthesis of anisaldehyde based on ozonolysis of anethole in a novel and environmentally friendly system composed of water and ethyl acetate.

Our research grew from the traditional ozonolysis reaction of anethole. It was found that in the presence of water, anisaldehyde could be obtained directly, avoiding a separate ozonide reductive step and very low temperatures. The addition of water to the reaction was believed to generate a gem-hydroperoxy alcohol **2**, which in the substrate decomposed with liberation of anisaldehyde and H₂O₂.

To testify the above mechanism, ozonolysis was performed until the anethole was consumed. The product was isolated after extraction, with no separate reduction. FT-IR of the product showed no strong absorption at ca. 1080–1110 cm⁻¹, which was the characteristic peak of the ozonides. On the contrary, there was an obvious carbonyl peak of aromatic aldehyde at 1685 cm⁻¹. This showed that no ozonide existed in the product, and anisaldehyde was produced directly. A more quantitative postreaction assay, performed on the UV spectrum, tested the H₂O₂ produced in the ozonolysis of water–ethyl acetate solvent and a mixture of anethole in water–ethyl acetate solvent.



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The absorption value of the reference solution is zero. The water–ethyl acetate solvent oxidized by ozone for 60 min has a low absorption value. However, the mixture of anethole and water–ethyl acetate solution oxidized by ozone for 60 min has a high absorption value. It can be surmised that, in water–ethyl acetate solvent, ozone reacts with water to produce a small quantity of H₂O₂. In contrast, in anethole and water–ethyl acetate solution, ozone firstly reacts with anethole to generate carbonyl oxide **1**, and then carbonyl oxide **1** reacts with water to produce gem-hydroperoxy alcohol **2**, which decomposes with liberation of the anisaldehyde and a larger quantity of H₂O₂.

The optimal conditions for synthesis of anisaldehyde were as follows: water–ethyl acetate solvent with water content 10%; ratio m(anethole)–m(solvent) = 1:3; O₃/O₂ flow 0.06 m³·h⁻¹; reaction time 100 min; and reaction taken at room temperature. The yield reaches about 81.7%. Gas chromatography detected a decrease in anethole and an increase in anisaldehyde.

In conclusion, in a mixture of anethole and water–ethyl acetate solvent, anisaldehyde is directly synthesized by ozonolysis in a one-pot reaction at a relatively high yield. The process reported here is convenient and economical.

EXPERIMENTAL

GC spectrum was recorded on a Shimadzu 2010 gas chromatograph with FID (flame ionization detector). The injection temperature was 250°C and the column temperature increased gradually from 50°C to 260°C at a growth rate of 10°C per minute. The air, hydrogen, and nitrogen flow was 400 mL, 47 mL, and 30 mL per minute, respectively. ¹H NMR spectra were recorded on a Bruker DRX-400 NMR spectrometer in CDCl₃ with TMS as internal standard, and chemical shifts are recorded as δ values in parts per million (ppm). IR spectrum was measured with an Analect RFX-65 spectrometer, and wave numbers are given in cm⁻¹. MS was carried out on a Shimadzu QP-2010 mass spectrometer at an ion source temperature of 200°C. UV spectrum was recorded on a Shimadzu UV-2550 ultraviolet spectrophotometer. The wavelength was between 350 and 600 nm. All solvents and reagents were purchased from commercial sources and used as received without further purification.

General Experimental Procedure. Anethole substrate 20 g (0.135 mol) was placed in a bubble column with a water-jacketed condenser and dissolved in water–ethyl acetate (10% in mass fraction) solvent. The solution was maintained at room temperature, and a stream of O₃/O₂ (0.06 m³·h⁻¹, approximately 6% in mass fraction) was bubbled into the reaction solution through a bubbling pipe. A sample was taken out every scheduled time by an injector from the reactor and recorded on a gas chromatograph. When the sampling was completed, the ozonizer voltage was set to zero. Nitrogen was passed through the solution until the blue color disappeared. The crude reaction mixture was diluted with 50 mL ethyl acetate and 10 mL distilled water. The separated aqueous layer was extracted twice with 10 mL of ethyl acetate. The organic layers were combined and dried with anhydrous sodium sulfate. The solvent was removed under reduced pressure to give a colorless liquid. The desired product, anisaldehyde, was obtained in a yield of 81.7% (16.4 g) with 99.5% purity. ¹H NMR (400 MHz, CDCl₃, δ): 3.87 (3H, s, OCH₃), 6.98 (2H, s, Ar-H), 7.82 (2H, s, Ar-H), 9.87 (1H, s, CHO). IR (neat, ν_{max}, cm⁻¹): 3076 (Ar-H), 2968 (CH₃), 2842 and 2742 (O=C-H), 1685 (C=O), 1600 and 1512 (Ph), 1462 (CH₃), 1261 (Ar-O), 1028 (CH₃-O), 835 (Ph). MS (EI, 70 eV, *m/z*, *I*_{rel.} %): 136 (M⁺, 75), 135 (100), 119 (2), 107 (19), 92 (21), 77 (38), 65 (12), 64 (11), 63 (11), 51 (11), 50 (9), 39 (13), 27 (2).

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