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Letter

Highly Selective Isobutane Hydroxylation by Ozone in a Pressure-Tuned Biphasic Gas−Liquid Process

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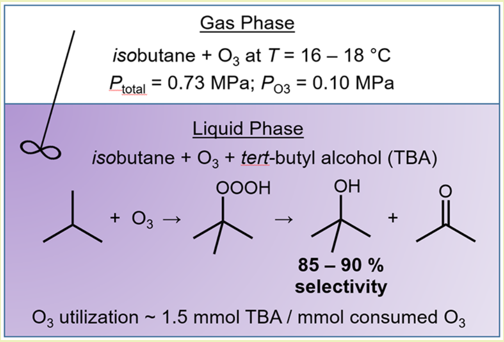
ABSTRACT: We have demonstrated a simple process for isobutane ozonation to *tert*-butyl alcohol (TBA) with 85%−90% selectivity in a biphasic gas−liquid process at ambient temperatures (16−18.5 °C) and mild pressures (∼0.6 MPa). The observed TBA selectivity is much higher than the value reported for either gas-phase ozonation or conventional noncatalytic air oxidation in liquid isobutane. The O_3 utilization to form TBA is maximized (∼1.5 mol TBA/mol O_3 consumed) by (a) adding optimum amounts of protic compounds (water and alcohols) in the reaction mixture, and (b) maintaining an optimum O_3 partial pressure in the gas phase that limits the liquid-phase O_3 concentration and minimizes O_3 decomposition. The relatively low CO_2 formation (<6% selectivity at optimal conditions) suggests that TBA formation occurs with high economy, predominantly via hydrotrioxide formation.



KEYWORDS: *tert-Butyl alcohol, Noncatalytic, Ozone utilization efficiency, Protic additive, Hydrogen bonding*

■ INTRODUCTION

Oxyfunctionalization of alkanes by partial oxidation is an important process since it produces a variety of building-block precursors for the chemical industry. Conventional oxidation with O_2 entails the selective activation of C−H bonds with relatively high dissociation energies of 330−460 kJ/mol, which generally requires catalytic processes at high temperatures.[1−3]

Isobutane is frequently chosen as a simple model substrate for evaluating the oxidation of C−H bonds on tertiary carbon atoms. Further, isobutane is abundantly available from refineries and as a component of natural gas liquids.[4] Isobutylene, produced via either isobutane dehydrogenation or *tert*-butyl alcohol (TBA) dehydration, is an important alkylating reagent for the production of fine-chemical and pharmaceutical precursors.[5] The dehydrogenation of lower alkanes for producing alkenes is highly endothermic and equilibrium limited. Hence, oxygen is used to selectively titrate away the hydrogen thereby overcoming equilibrium limitations. The exothermic oxidation also provides energy for the endothermic dehydrogenation reaction. However, even in the presence of oxygen, temperatures around 400 °C are required to achieve single-pass isobutane conversions around 10% on various catalysts.[6−8] In sharp contrast, the low temperatures required to dehydrate TBA (<90 °C)[9−12] provide an alternative route that also avoids the energy-intensive separation of isobutane + isobutylene mixtures. The separations of TBA from isobutane and water from isobutylene (resulting from TBA dehydration) are less energy intensive.

Industrial isobutane oxidation uses O_2 as oxidant and is performed at 120−140 °C and 2.5−3.5 MPa, with ∼3%−10% O_2 in the gas phase.[13,14] At these conditions, isobutane exists as a liquid, and O_2 is bubbled through the liquid phase. The vapor phase is typically maintained above the upper flammability limit for isobutane. Free radical initiators such as *tert*-butyl hydroperoxide (TBHP) and di-*tert*-butyl peroxide (DTBP) are usually co-fed to reduce the induction period. Also, transition metal (such as cobalt) salts may be used as homogeneous catalysts. At these conditions, the isobutane conversion is ∼4%−8% per hour, producing nearly equimolar amounts of TBA and TBHP, at up to 96% combined selectivity. The TBHP is used as an oxidant for propylene oxidation to propylene oxide, producing TBA as a coproduct.

For isobutane oxidation with O_2, the initiation mechanisms in the liquid phase and gas phase are similar. However, the product selectivities strongly depend on the relative concentrations of the substrate and oxidant.[13] Compared to liquid-phase oxidation, isobutane oxidation in a gas phase requires longer induction periods even at 260−360 °C and produces a wider spectrum of products. This is caused by side reactions,[15,16] including overoxidation of terminal carbons and C−C bond cleavage. Therefore, liquid-phase isobutane oxidation is preferred to achieve better product selectivity and atom economy toward desired products.

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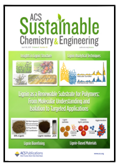

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Ozone has been reported as a potent oxidant for gas-phase activation of alkanes at temperatures as low as 50 °C.[17−22] In gas-phase reactions, ozone produces significant quantities of CO_2.[17] Ozonation of alkanes including *n*-heptane, 2,2,4-trimethylpentane, and cyclohexane in liquid CO_2 at sub-ambient temperatures has been reported to produce ketones and alcohols with undetectable combustion products.[23,24] Despite faster rates[25] and better selectivities, liquid-phase ozonation faces challenges related to effective O_3 utilization. For example, ozone is known to decompose faster in the liquid phase compared to the gas phase.[26] Further, ozone can undergo decomposition on the metal surface of pressurized liquid-phase reactors.[21,26,27] Indeed, in our previous work,[23] only 12%−21% of the ozone was utilized to produce oxygenates. Thus, a key challenge in liquid-phase ozonation of alkanes is to maximize ozone utilization toward the desired reaction, minimizing substrate overoxidation and ozone decomposition.

In this work, we investigated isobutane ozonation in a liquid phase using a Teflon-lined Parr reactor to avoid metal surface-induced O_3 decomposition. Because liquid isobutane possesses some compressibility at near-ambient temperatures, it should be able to accommodate O_3 at higher concentrations compared to a traditional organic solvent. In liquid CO_2, our group reported unusually high O_3 concentrations that were also pressure tunable.[28] We expect similar pressure tunability of the O_3 concentration in liquid isobutane. Another advantage of liquid-phase operation is the ability to easily maintain the isobutane-rich vapor phase above the upper flammability envelope. We demonstrate herein that isobutane undergoes facile ozonation in its liquid phase at near ambient temperature, directly producing TBA at ~90% selectivity. Further, we demonstrate in this noncatalytic system that ozone utilization can be improved by using protic additives in the feed. Our experimental results strongly suggest that isobutane hydroxylation to TBA proceeds via the formation of the isobutyl hydrotrioxide intermediate that, unlike ozonides that form during alkene ozonolysis, decomposes easily to form TBA without major release of energy.

■ RESULTS AND DISCUSSION

Table 1. Comparison of Product Yields with and without Initial Water Addition[a]

No.	Water, mmol	O_3, mmol	TBHP, mmol	TBA, mmol	Acetone, mmol
1	0	0.57	0.084	0.089	0.008
2	5.53	0.57	–	0.426	0.034

[a] Conditions: T = 17 °C, 40 mL iC_4 (~0.39 mol, as liquid at 17 °C and 0.86 MPa in Teledyne ISCO pump), O_3 mole fraction = 4% in O_3 + O_2, iC_4 saturation $P \sim 0.25$ MPa, total $P \sim 0.42$ MPa (~0.08 mmol O_3 each cycle), gas-phase iC_4 concentration ≥ 65% (UFL = 48%[29]), reaction time = 30 min each cycle, stirring rate 1000 rpm.

Batch Runs. Preliminary experiments of isobutane ozonation at −30 °C in an open vessel suggested beneficial effects of condensed ambient moisture on the reaction. A setup described in the Supporting Information (SI) (Figure S1) was used to systematically evaluate the effects of controlled addition of water in a closed Parr reactor. Procedural details for the batch runs are provided in the SI (Sections 2.3 and 2.4). Briefly, approximately 40 mL of isobutane (iC_4) at 17 °C (saturation vapor pressure = 0.86 MPa) was added to the batch reactor. A known amount of water was also added initially to study its effect. The products were analyzed by GC/FID and ^{1}H NMR methods. Please refer to Figures S2−S7 and related discussion in Section 2 of the SI for details on the analysis protocol. Table 1 compares the liquid-phase products after seven sequential cycles of pressurization with the O_3/O_2 mixture and depressurization to the isobutane vapor pressure at 17 °C. In each cycle, the O_3 depleted in the previous cycle was replenished to generate additional TBA from the excess isobutane. When water was added, ozone utilization was enhanced, and the product distribution was shifted toward predominantly TBA, with the formation of only a small amount of acetone (entry #2, Table 1). In the absence of added water, we observed nearly equimolar TBA and TBHP formation at significantly lower yields of these products (entry #1, Table 1). Therefore, the remaining experiments were carried out with added water. Designed experiments confirmed that the role of water was not to aid TBHP decomposition as initially suspected. Rather, water appears to favor the hydrotrioxide pathway for TBA formation, which is different from the free radical pathway for TBHP formation via conventional O_2 oxidation of isobutane. The reaction mechanism is discussed in more detail later.

To gain insights into the kinetics of TBA formation, the effect of batch time on product yield in Figure 1 was studied via multiple batch runs of various durations under otherwise similar operating conditions as listed in Table 1. The molar product quantities were normalized to the moles of ozone fed in each batch. The end-of-run TBA profile was regressed with a kinetic model assuming a first-order dependence on O_3 concentration with isobutane in a large excess. It is implicitly assumed that the O_3 concentration in the liquid phase is linearly proportional to the O_3 partial pressure in the gas phase. This assumption is justified based on a similar trend observed in liquid CO_2.[28] Such an analysis yielded a pseudo-first-order rate constant of ~0.56 min^{-1} for O_3 consumption. The minor coproducts acetone and CO_2 show overlapping profiles, suggesting that they result from the same pathway. We propose that these products occur via the *β*-scission of the *tert*-butoxy radical, which would form a methyl radical and acetone. The methyl radical is most likely converted to CO_2. Clearly,

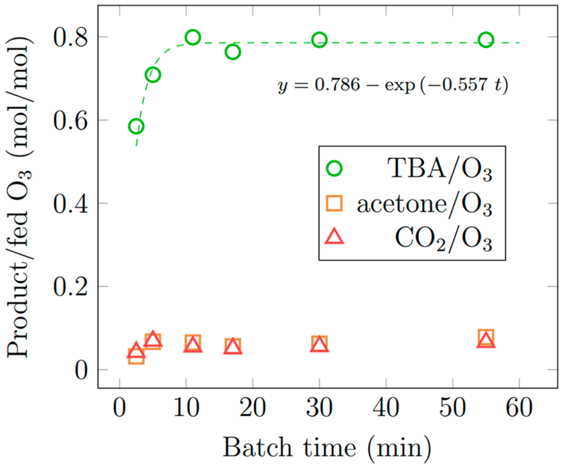


Figure 1. Temporal product profiles from batch reactor experiments of isobutane ozonation (reaction conditions other than batch time are identical to those provided in Table 1).

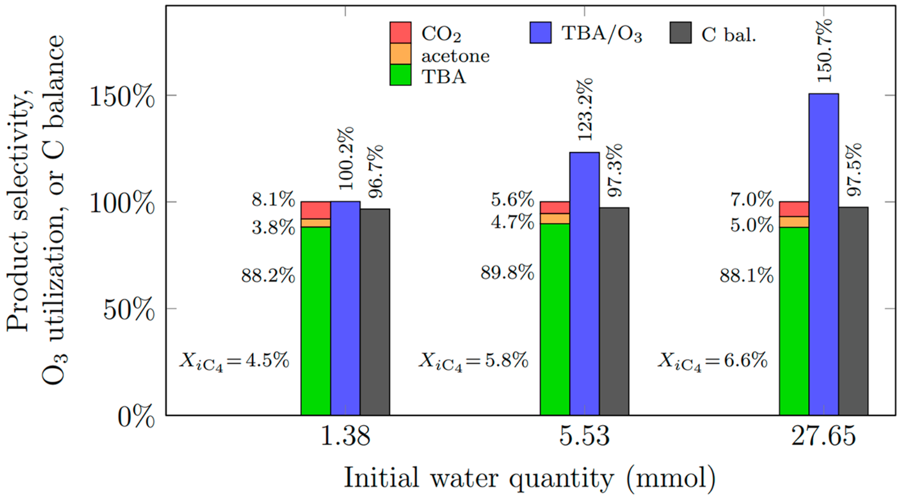


Figure 2. Effect of initial water quantity on product distribution and O_3 utilization. Conditions: T = 18.5 °C, 5% $O_3/(O_3 + O_2 + N_2)$, $P_{O3+O2+N2}$ = 0.34 MPa.

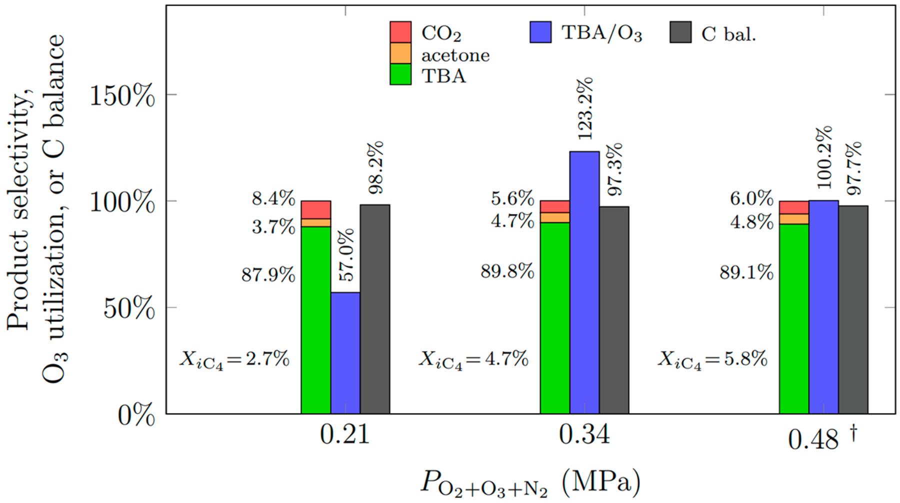


Figure 3. Effect of noncondensable gas partial pressure on product distribution and ozone utilization. Conditions: T = 18.5 °C, 5% $O_3/(O_3 + O_2 + N_2)$, initial H_2O quantity = 5.53 mmol. †Other byproducts in small quantities: TBHP selectivity ~0.01%, hydroxyacetone, and one unidentified.

the rate of the β-scission pathway is much lower than the parallel pathway to produce TBA.

Semibatch Ozonation and Parametric Studies. The remarkable TBA selectivity observed in the batch runs motivated us to investigate semicontinuous ozonation in which ozone was continuously fed into the reactor containing an initial charge of isobutane (~220 mmol). The experimental procedures are discussed in SI Section 2.5. Specifically, the effects of water, O_3 partial pressure, and TBA were evaluated during semibatch runs at 18.5 °C. The total gas-phase pressure was maintained at 0.75 MPa, consisting of 0.27 MPa isobutane and up to 0.48 MPa of other gases (O_3, O_2, and N_2). N_2 was added as an inert component to maintain the gas phase outside the flammability envelope. The molar $(O_3 + O_2)$:N_2 ratio was 1, and the O_3 mole fraction in the $(O_3 + O_2 + N_2)$ mixture was 5%. The partial pressure of the noncondensable gases $(O_3 + O_2 + N_2)$ was chosen as 0.34 MPa for the base case. The liquid products were analyzed by both GC/FID (Figure S3b) and ^{1}H NMR (Figure S5) methods. The carbon balances were closed within experimental error (a sample calculation is provided in Table S1).

Effect of Water. As shown in Figure 2, varying water quantities caused only slight variations in the product distributions, with the TBA selectivity being 88%−90%. However, O_3 utilization (defined as moles of TBA formed/mol of O_3 fed) toward TBA formation increased by 1.5 fold as the initial water charge was increased from 1.38 to 27.65 mmol (~20 fold). In other words, while an increase in the initial water concentration has only a marginal effect on TBA selectivity, it greatly increases the O_3 utilization toward TBA formation.

Effect of O_3 Partial Pressure. Due to the higher O_3 decomposition rates in the liquid phase, O_3 partitioning between the gas and liquid phases dictates ozone utilization toward TBA formation. Liquid-phase O_3 solubility depends on gas-phase O_3 partial pressure as well as the properties (e.g., density, polarity) of the liquid phase. The O_3 partial pressure may be varied by changing either the total pressure of the gas phase of a fixed composition or the O_3 fraction in the gas phase at a fixed total pressure. During these investigations, the initial water added was constant at 5.53 mol.

As shown in Figure 3, varying the partial pressure of the noncondensable gas mixture at a fixed O_3 mole fraction caused

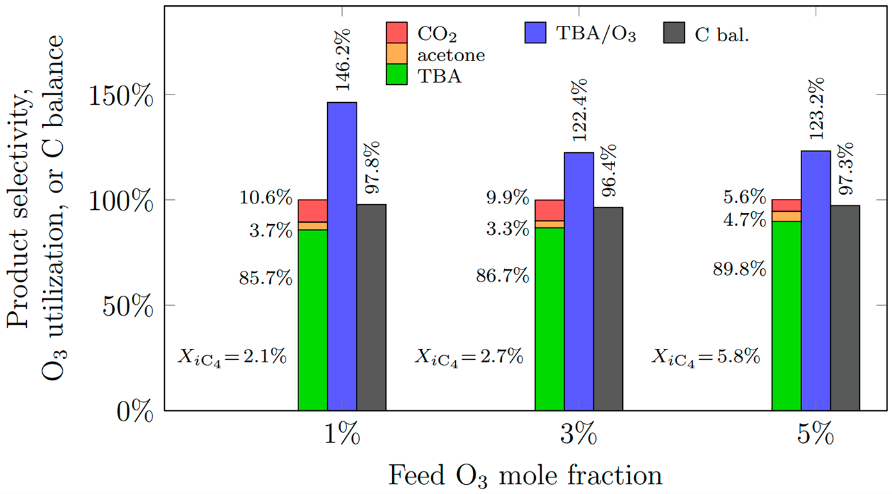


Figure 4. Effect of $O_3/(O_3 + O_2 + N_2)$ mole fraction on product distribution and O_3 utilization. Conditions: T = 18.5 °C, $P_{O3+O2+N2}$ = 0.34 MPa, initial H_2O quantity = 5.53 mmol.

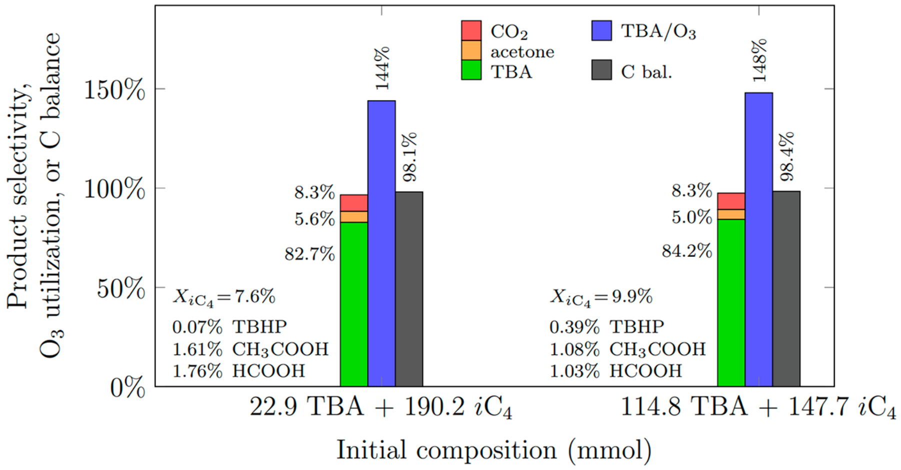


Figure 5. Effect of initial TBA addition on product distribution and O_3 utilization. Conditions: T = 18.0 °C, 5% $O_3/(O_3 + O_2 + N_2)$, $P_{O3+O2+N2}$ = 0.34 MPa, no initial H_2O addition.

only marginal changes in product distribution. The ozone utilization, however, varied quite significantly, displaying a maximum at an intermediate pressure (0.34 MPa). At lower partial pressures, the ozone partitioned more into the gas phase, oxidizing some of the gas-phase isobutane to CO_2, as evidenced by the highest CO_2 selectivity at 0.21 MPa. In contrast, at the highest partial pressure investigated (0.48 MPa), the O_3 concentration in the liquid phase increases, resulting in increased O_3 decomposition rates and overoxidation of liquid-phase products. Hence, O_3 utilization decreases significantly at higher partial pressures.

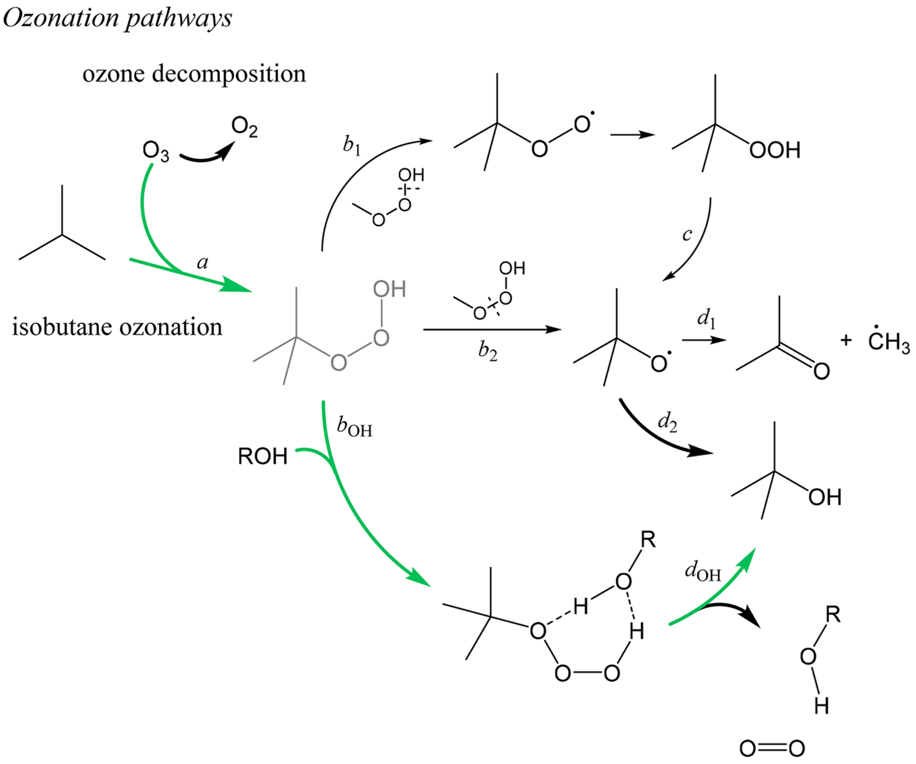
When the partial pressure of the noncondensable gases is held at 0.34 MPa and the O_3 concentration varied, a substantial increase in O_3 utilization was observed even at 1% O_3 (Figure 4). The CO_2 selectivity increased slightly at the lower ozone partial pressure. While the increased gas-phase O_3 partitioning increases overoxidation of gas-phase isobutane, the slower O_3 decomposition in the gas phase also enhances overall O_3 utilization toward TBA formation. Collectively, these data demonstrate that there is a pressure-tunable optimum at which O_3 utilization is maximized.

In summary, even though gas-phase ozonation is less selective,[25] the gas phase may serve as a desirable reservoir at low temperatures, where O_3-based combustion and decomposition are quite slow. On the other hand, increased O_3 concentrations in the liquid may promote facile decomposition in the liquid phase, which would compete with the activation of substrate C−H bonds with high bond dissociation energies (320−450 kJ/mol).[3] With the appropriate choice of temperature and gas-phase partial pressure, the vapor−liquid equilibrium of O_3 may be harnessed to optimize its liquid-phase concentration and thereby to minimize both O_3 decomposition and substrate overoxidation in the liquid phase.

Effect of TBA in the Initial Mixture. The highest quantity of TBA produced in previous runs was approximately 6% of the isobutane fed to the system. In order to assess the effect of TBA accumulation on the product distribution, ozonation of mixtures of TBA + isobutane was evaluated. The net product formation (with initially added TBA subtracted) is shown in Figure 5, with quantified minor products listed on the left side of each group. Also, traces of hydroxyacetone were detected in the GC/FID chromatogram, suggesting oxidation of the methyl group in the acetone coproduct.

In general, the presence of TBA in the initial mixture promoted O_3 utilization, which is similar to the effect of added

Scheme 1. Reaction Pathways of Isobutane Ozonation[a]



[a]Green pathway is dominant.

water. However, the net TBA formation in such reactions decreased. Most likely, TBA underwent oxidation to form acetic acid and formic acid with a combined selectivity of greater than 2% (Table S2, Section 3 in the SI). For comparison, the combined selectivity of acetic acid and formic acid was less than 0.02% in the isobutane ozonation runs without added TBA. Peroxyacetic acid is a possible intermediate that decomposes to acetic acid. The TBHP detected during the runs with initial TBA added was at least 10^2 times greater compared to previous runs with initially added water. Two factors could contribute to the observed results: (a) The solvent polarity (and hence the O_3 solubility) is significantly affected as TBA is more soluble in isobutane than water. (b) Compared to water, the bulkier *tert*-butyl group could pose a hindrance to the formation of hydrogen-bonded cyclic structures[30−32] from TBA and other molecules containing hydroxyl, hydroperoxyl, or hydrotrioxyl groups.

Ozonation Pathways. Scheme 1 summarizes plausible reaction pathways based on the observed major product spectrum. Possible alternate pathways are reviewed elsewhere.[30,31,33] For the ozonation of alkanes, the formation of an alkyl hydrotrioxide adduct (step *a*) is generally accepted as the first initiation step.[23] One of the O−O bonds in the *tert*-butyl hydrotrioxide intermediate can cleave to give either TBHP (via b_1) or TBA (via b_2) via free radical formation. On the basis of O_3 utilization and the observed selectivity without water addition in Table 1, pathways b_1 and b_2 likely occurred slower in the liquid phase relative to O_3 decomposition. The observed high ozone utilization and low yields of di-*tert*-butyl peroxide (formed by the coupling of the *tert*-butyl peroxyl radicals)[34] suggest that the concentrations of the peroxyl radicals are low. If one assumes that the *tert*-butyl peroxyl radicals are consumed exclusively by hydrogen abstraction to form TBHP, the rate ratio is estimated to be $r_{b_1}/r_{b_2} \approx 0.94$ based on the product yields at 17 °C in the absence of water. Although Lee and Coote estimated computationally that pathway b_2 was preferred over b_1 by ∼3 kcal/mol,[33] such a preference was not evident from our data (Table 1), possibly due to solvent effects not considered in the computations.

When isobutane ozonation was performed in the presence of water or TBA, the TBA formation was substantially more selective than TBHP formation. These observations suggest a role for these protic components in aiding the decomposition of the alkyl hydrotrioxide intermediate (Scheme 1, pathway b_{OH}) to give TBA. This pathway avoids the formation of TBHP, consistent with the low formation of this product in the presence of either water or TBA. While the low TBHP yields could alternatively be explained by TBHP decomposition during the course of the reaction (Scheme 1, pathway *c*), the slow TBHP decomposition rates (Figures S6 and S8, Section 4 in the SI) are inconsistent with the observed low peroxide selectivities. In the absence of O_3, TBHP decomposes extremely slowly following long induction periods (∼9−44 h), even in the presence of water, TBA, or acetic acid (Figures S6, S8, and S9). In the presence of O_3 and water (or TBA), the TBHP decomposed more rapidly[35] (Figure S10 and Table S3, Section 5 in the SI) without the long induction period. However, in the presence of water, the peroxide likely also formed free radicals that promote O_3 decomposition in the liquid phase, resulting in lower ozone utilization (Table S3).

Due to the competing O_3 decomposition, the TBA formation per mole of consumed O_3 cannot surpass unity based on considering only the two pathways for unimolecular hydrotrioxide decomposition (b_1 and b_2). The observed TBA/O_3 ratios of up to 1.5 suggest alternative pathways including hydrotrioxide decomposition[32] (via d_{OH}) and ROOOH formation[30,31] via solvated hydrotrioxide intermediates. Also, water may promote several intermolecular reactions among ROOOH, HOOOH, HOOH, and HOH,[30,31] producing caged radical pairs to aid alkane activation. While such complexes were observed at lower temperatures,[32] the absence of similar signals in ^{1}H NMR spectra (e.g., Figure S5) in this work suggests that they are potential active species that are involved in promoting O_3 utilization. Thus, the progressive accumulation of TBA and water (as products) during the semicontinuous runs will promote alternative pathways and eventually completely inhibit TBA formation.

Byproducts including acetone, acetic acid, formic acid, and CO_2 formed during all runs, while hydroxyacetone and methanol were detected only under certain reaction conditions. At low ozone exposure (i.e., at short contact time and low O_3 partial pressures), nearly equimolar amounts of acetone and CO_2 (Figure 1) are formed, suggesting that even in the presence of water, β-scission of a *tert*-butoxyl radical (d_1) can still occur. However, the low yields of these products suggest that this pathway is a minor contributor. As revealed by studies on the cumyloxyl and the *tert*-butoxyl radicals,[36,37] while the rate of hydrogen abstraction (d_2) was nearly independent of the reaction media, a strong solvent effect was observed on the rate of β-scission (d_1). At higher ozone exposure (i.e., longer contact time and higher O_3 partial pressures), overoxidation in the liquid phase (suggested by Figure 4 and Table S2) along with ozonation of gas-phase isobutane to CO_2 diminish the carbon economy. A number of oxygenate oxidation pathways,[38] shown in Scheme S1 of Section 6 in the SI, are likely the major contributors under these conditions, forming acetic acid, formic acid, and CO_2.

The foregoing results suggest that in order to maximize TBA yield and O_3 utilization, reactor operation in which the gas and liquid phases are continuously admitted and withdrawn is needed to control the O_3 partial pressure in the gas phase as well as the TBA/water accumulation in the liquid phase. Also, less polar protic additives to the mixture may also benefit TBA selectivity and O_3 utilization by minimizing β-scission rate and O_3 decomposition, respectively.

SUMMARY

We have demonstrated facile isobutane ozonation with 85%−90% TBA selectivity in a biphasic gas−liquid process at room temperature (16−18.5 °C) and mild pressures (~0.6 MPa). The process can be operated safely with a nonflammable vapor phase that is well above the upper flammability limit. In contrast to oxidation with O_2 (the conventional industrial process), hydroperoxide formation was drastically reduced. We suggest the reduced formation of such products results from an alternate reaction mechanism when protic compounds and O_3 coexist. With O_3, conventional free radical initiators like TBHP and DTBP are not required to initiate the reaction. In fact, such free radical initiators promote O_3 decomposition. Isobutane most likely undergoes hydroxylation via an alkyl hydrotrioxide intermediate that decomposes releasing much less energy compared to ozonides formed during alkene ozonolysis.[39]

The O_3 utilization to form TBA is maximized by (a) an optimum concentration of protic compounds, such as water and alcohols in the liquid phase, and (b) an optimum O_3 partial pressure in the gas phase. Beyond the optimum concentration of TBA and water, undesired free radical pathways adversely affect product selectivity. Similarly, beyond the optimum gas-phase O_3 partial pressure, the increased liquid-phase O_3 concentrations promote O_3 decomposition as well as overoxidation of TBA. Even though TBA selectivity is 85%−90% during the first 2−3 h, TBA is susceptible to further oxidation upon prolonged contact with ozone. Hence, to enhance overall atom economy, continuous reactor operation is essential to operate the gas phase at the optimum O_3 partial pressure and to optimize the O_3 contact time with the liquid phase in order to simultaneously maximize O_3 utilization and TBA (desired product) yield, avoiding overoxidation involving C−C bond cleavage. The proposed method could potentially be extended to activating higher alkanes with tertiary carbons where the C−H bonds are more susceptible to ozonation than those on the primary carbons.

ASSOCIATED CONTENT

Supporting Information

The Supporting Information is available free of charge at https://pubs.acs.org/doi/10.1021/acssuschemeng.1c01004.

> Safety considerations, experimental details for batch and semibatch runs, analysis details, and figures and tables for supplementary experimental results (product overoxidation and *tert*-butyl hydroperoxide decomposition) (PDF)

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Notes

The authors declare no competing financial interest.

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