Synthesis and Low Temperature Spectroscopic Observation of 1,3,5-Trioxane-2,4,6-Trione: The Cyclic Trimer of Carbon Dioxide

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Supporting Information

ABSTRACT: 1,3,5-Trioxane-2,4,6-trione (cyclic trimer of CO2) is the product of a four-step synthesis: chlorination of isobutyraldehyde; cyclotrimeration of 2-chloro-2-methylpropanal; dehydrochlorination of 2,4,6-tris(2-chloropropan)-2-yl-1,3,5-trioxane; ozonolysis at –80 °C of 2,4,6-tri(propan-2-ylidene)-1,3,5-trioxane. This trioxane-trione is detected in solution at temperatures between –80 to –40 °C, and its conversion to CO2 is monitored by 13C NMR and FTIR. The CO2 trimer has a half-life of approximately 40 min at –40 °C.

INTRODUCTION

As a product of combustion and respiration whose accumulation in the atmosphere has become a cause for significant concern, carbon dioxide has been the subject of much research directed at its reutilization. Various approaches toward this CO2 reutilization goal have been described in excellent reviews over the past two decades. Important processes involve reduction with hydrogen, coupling with other small molecules, incorporation into polymers, and artificial photosynthesis. The main products include fuels, solvents, chemical intermediates and polymers. The efficiency of these commercial processes in terms of reagent usage is relatively low with respect to the fraction of CO2 incorporated into the product; the highest being for urea (57%), and decreasing for salicylic acid (36%) and methanol (10%). This could be raised to 100% if a CO2 self-fixation chemistry could be developed. Ideally with a sufficient input of energy, CO2 would react with itself to yield a liquid or solid product from which this energy could be extracted when needed for useful work. Such chemistry has been the subject of theoretical calculation for structures representing the linear polymer and cyclic oligomers of CO2. With respect to thermodynamic stability, the cyclic trimer has been described as "feasible" although energetically less stable than three CO2 molecules by 27 kJ/mol per CO2 unit. Regarding kinetic stability of the cyclic trimer toward fragmentation to CO2, calculated barriers for this decomposition have ranged from activation energies of 61 to 172 kJ/mol depending on the computational method with calculated half-lives ranging from days to milliseconds at ambient conditions and substantially longer at lower temperatures.

The cyclic trimer of CO2 has also been proposed as a low-energy intermediate in the transformation of CO2 to an extended solid. The formation of an orthocarbonate extended covalent structure of interconnected six-membered rings was predicted by model calculation with the finding of a stabilization energy that increased with molecular size. Later experimental work found under extreme pressure/temperature (40 GPa/1800 K), CO2 will transform to a metastable extended solid which has been characterized as a Phase V form of CO2 with a sigma bonded quartz-like structure. It has also been proposed that sorption of CO2 into the isolated nanoscale confined spaces of sulfur- or nitrogen-treated porous carbon at 30 bar pressure can produce a polymeric structure of carbon dioxide as has been reported for other molecules in nanoconfined spaces.

The 1,3,5-trioxane-2,4,6-trione structure of the CO2 cyclic trimer, I, may represent an important intermediate or product in the self-fixation of gaseous CO2. Theoretical studies on this molecule have indicated a possibility of kinetic stability at room temperature and as well as a possibility for it to be thermodynamically feasible. To date, no experimental evidence has been reported for its existence. The objective of this work is to synthesize compound I and to make an assessment of its stability. The approach is that of a model compound synthesis where the trioxane ring is first generated from substituted aldehydes and then the peripheral carbonyl structures are incorporated at low temperature in the final step. As will be shown, compound I does not possess the stability for facile isolation and storage.

RESULTS

A retrosynthetic route for the synthesis of compound 1 is illustrated in Scheme 1. The three steps are an oxidative cleavage of a triolefin-trioxane, 2, a dehydrochlorination of α-chloroaldehyde trimer, 3, and a trimerization of two candidate
\( \alpha \)-chloroaldehydes, 4 and 5. The chemical properties of triolefin-trioxane compounds are not well-known, nor has the susceptibility of this type of olefin toward oxidative cleavage been reported. This synthesis requires that all three olefin bonds of 2 be cleaved thereby adding great importance to the yield of this reaction. Thus, both the unsubstituted 2,4,6-tris-methylene-1,3,5-trioxane, 2b, and the hexamethyl-substituted analog 2,4,6-tris-isopropylidene-1,3,5-trioxane, 2a, were both targeted for comparative purposes as well as a strategy of having an alternative if difficulties are encountered en route to 1. In Scheme 1 the absence or presence of methyl substituents on the oxycyclic olefin structure 2 may affect the oxidative cleavage to compound 1 and will determine detectable byproducts, both of which are issues of interest. The synthesis of the hexamethyl triolefin-trioxane 2a is depicted in Scheme 2. Isobutyr aldehyde, 6, was chlorinated by a procedure using sulfuryl chloride\(^1\) to afford the corresponding \( \alpha \)-chloroaldehyde, 4. This aldehyde was then trimerized to 2,4,6-tris(1-chloro-1-methylethyl)-1,3,5-trioxane, 3a, in good yield by a procedure using concentrated H\(_2\)SO\(_4\)\(^2\) and isolated as a crystalline solid (see Supporting Information for crystal structure). The third step of dehydrohalogenating 3a to the hexamethyl triolefin-trioxane 2a was problematic. In our hands a patented procedure\(^2\) for preparation of compound 2a (Route A, reaction of 3a with sodium hydroxide dispersed in dimethylheptanol at 185 °C) produced no yield of product. An alternate approach of using potassium tert-butoxide in THF (Route B) afforded 2a in good yield. Compound 2a prepared via Route B is a liquid while that reported from Route A was a solid with a very broad melting point (54–62 °C).\(^3\) A thorough analysis of this product was conducted (\(^1\)H NMR, \(^13\)C NMR, IR, UV–vis, HR-MS, elemental analysis and differential scanning calorimetry; see Experimental Section and Supporting Information for data and discussion), and these results are in good agreement with the structure assigned to compound 2a.

Attempts to synthesize the unsubstituted triolefin-trioxane 2b met with considerable challenges (Scheme 3). Trimerization of the commercially available aqueous solution of 5 with concentrated H\(_2\)SO\(_4\) produced low yields (26%) of 3b and often inconsistent results. Multiple attempts to dehydrohalogenate trioxane 3b, using either the previously reported conditions\(^2\) (Route A) or our modified procedure (Route B) failed to yield the desired unsubstituted triolefin-trioxane 2b. Confident in the structure of the methyl substituted triolefin-trioxane and the reproducibility of our procedure; our focus was placed on the oxidation chemistry of 2a. The initial approach to oxidative transformation of the 2a olefin bonds to carbonyl bonds involved preliminary experiments to determine if the three C–C double bonds could be oxidatively cleaved in a stepwise manner. Cleavage using oxo metals such as OsO\(_4\),\(^22\)–\(^23\) or combinations of RuCl\(_3\),\(^24\)–\(^25\) and co-oxidants was unsuccessful as was using singlet oxygen generated from ozone and phosphine.\(^26\) Byproducts interfered with analyses and obscured isolation of anticipated products of unknown stability.

A complete oxidation approach using ozonolysis was then explored.\(^27\)–\(^29\) The Criegee mechanism\(^30\) for this chemistry as applied to compound 2a is depicted in Scheme 4. Ozone and

\[ \text{Scheme 4. Criegee Ozonolysis Mechanism Applied to Compound 2a}^{34} \]

the olefin bonds of 2a initially at low temperature may or may not form a \( \pi \) or charge-transfer complex,\(^7\)\(^31\)–\(^33\) followed by formation of the primary ozonide, 8, which breaks down to the carbonyl oxide “Criegee intermediate”, 9, and the complementary carbonyl compound. In an inert solvent these moieties recombine to form the secondary ozonide, 10, which is sometimes sufficiently stable for isolation but which is usually reacted with a reductant to yield the desired pair of carbonyl compounds as indicated by the left route in Scheme 4. Initially, our selected reaction conditions (–78 °C, saturated solution of 2a in CH\(_2\)Cl\(_2\) with a flowing 5% O\(_2\)/O\(_3\) mixture until the blue coloration of excess ozone persists followed by purging the O\(_3\) then by the addition of (CH\(_3\))\(_2\)S to quench the reaction and warming to ambient temperature) did not result in the detection of the desired trione-trioxane product 1. However,
the resultant oxidation byproduct, (CH₃)₂SO, was observed consistent with the action of some ozonide intermediate on Me₂S. As some secondary ozonides are known to be sufficiently stable for ambient isolation, limited attempts were made to isolate an ozonide intermediate by withholding the addition of the reducing agent, but a stable and structurally characterized product was not obtained. The intramolecular constraint of three olefin bonds initially held in close proximity when the primary ozonide and the reactive carbonyl oxide are generated from one of them is conjectured to be a route to a complex product mixture.

The reaction path on the right side of Scheme 4 was then pursued. Methanol is employed as a well-known and quantitative trapping agent for the carbonyl oxide intermediate and converts it into the relatively stable 2-methoxyprop-2-yl hydroperoxide, 11. The hypothesis for using methanol in this manner is that, when the primary ozonide 8 fragments, the carbonyl oxide intermediate will incorporate the exocyclic methyl groups of 2a (structure 9) and not incorporate the trioxane ring structure of 2a. In favor of this hypothesis is the reported ozonolysis of 1,1-dimethoxyethylene preferentially yielding dimethyl carbonate and the carbonate functional group’s resistance to further reaction with carbonyloxides. The presence of methanol is also useful in preventing the self-coupling of the acetone carbonyl oxide 9 to form dimeric and oligoperoxidic compounds. As a proof of concept, the ozonolysis reaction of 2a was carried out in a similar manner as before in a chilled (1:1) mixture of CH₂Cl₂ and CH₃OH in the absence of any reducing agent. After the reaction warmed to ambient temperature, NMR analysis of the evaporated mixture revealed hydroperoxide 11 (average of 62% over two reactions) as the dominant product. This observation indicates that the oxidative cleavage is, in fact, occurring as planned since the trapped carbonyl oxide is concomitant with the generation of the new carbonate functionality. Due to the lack of any other observable product, it seems possible that the trione-trioxane 1 is formed but subsequently degrades. If this is the case, further support for its existence was needed.

To obtain evidence for the existence of the trione-trioxane 1, a variable temperature ¹³C NMR experiment was conducted. A solution of 2a dissolved in a 1:1 CD₂Cl₂:CD₃OD mixture was prepared in an NMR cell, and an initial spectrum is obtained. This solution is then cooled to −78 °C, and a 5% O₂/O₃ stream was passed into this solution until the blue coloration of excess ozone was observed. The cell was then purged with oxygen and quickly transferred into a precooled NMR probe at −80 °C. Spectra were acquired at progressive temperatures of −80, −60, −40, −20, and 0 °C. These spectra are presented in Figure 1 with expansions of important resonances depicted in inserts. The initial 20 °C spectrum displayed the three resonances of triolefin-trione 2a at chemical shifts of 15.0 (−CH₃), 87.5 (==C(CH₃)₂) and 145.2 (==C(O)₂) ppm. After cooling and completion of the ozone treatment, these resonances disappeared, and the three resonances attributable to the hydroperoxide compound 11 appeared at 22.0 (−CH₃), 49.1 (−OCH₃ obscured by the CD₃OD) and 104.1 (C-OOH) ppm in excellent agreement with those previously reported for this compound. At this −80 °C temperature an additional new resonance appeared at 156 ppm which we assign to the new carbonate functionality. Due to the lack of any other observable product, it seems possible that the trione-trioxane 1 is formed but subsequently degrades. If this is the case, further support for its existence was needed.

Figure 1. ¹³C NMR spectra from the triolefin-trione–ozone reaction. The lowest spectrum is the substrate 2a CD₂Cl₂/CD₃OD solution prior to ozone treatment. The series spectra above were recorded after the −78 °C ozone saturation and purging from this solution at successive 20 °C temperature increments from −80 to 0 °C. The compound structures for which resonances are assigned are depicted at the left of each spectra and the chemical shifts discussed in the text are indicated by the dashed lines and values at the top of this figure. Those resonances of particular importance have a magnified insert.
was present at low temperatures then decomposes to its monomeric form as CO$_2$ gas.$^{41,42}$ As further support for assignment of the 156 ppm resonance to the carbon nucleus in compound 1, SCF GIAO magnetic shielding tensor calculations were carried out on this compound, CO$_2$ and TMS. The calculated chemical shifts relative to TMS are 150.2 and 123.9 ppm respectively which are in reasonably good agreement with the 156 and 125 experimental values.

To complement this NMR evidence for the existence and stability of this trione-trioxane, compound 1, an in situ FTIR experiment was conducted under essentially the same conditions. Instead of an NMR cell, the reaction was conducted in a 25 mL flask which was fitted with an ozone inlet and the ATR probe of a ReactIR reaction monitoring system. With the capability of generating several spectra per minute, this method is better suited for quantitative kinetic analysis, but it does require sophisticated software for spectral deconvolution and tracking of the time dependent profiles of species in the reaction medium. Control spectra of the CH$_2$Cl$_2$ and CH$_3$OH solvents, the triolefin-trioxane 2a and O$_3$ reagents and the hydroperoxide 11 and CO$_2$ byproducts were input to the software, and the reaction is monitored by repetitive recording of FTIR spectra in real time. The composite spectra are deconvoluted for individual species, and the corresponding trend lines depict the quantities of reactants, intermediates and products as a function of time. The upper half of Figure 2 presents trend lines for the in situ −80 °C ozonolysis of 2a, depicting this reagent, intermediates and the trione-trioxane product 1. Three distinct intermediates appear to form and are consumed during the course of this reaction. The product once
formed has an indefinite stability at −80 °C. In the lower half of Figure 2, this product is monitored as a function of time for 1.5 h intervals at −80, −60, and −40 °C. Once the temperature and baseline have stabilized, the decomposition of I in the −40 °C interval is readily apparent and is accompanied by the generation of CO₂. This is in good agreement with the NMR experiment of Figure 1. From the slope of the trend line in this region (indicated by the dashed window in Figure 2), a half-life of 40 min is estimated at this temperature which is in reasonable agreement with a range of half-lives calculated by various theoretical methods.⁹

The infrared spectrum of the trione-trioxane 1 was deconvoluted from the accumulated spectra during the ozonolysis reaction and from the postreaction spectra as the temperature was increased to assess the thermal stability of this compound. As presented in Figure 3, these spectra duplicate each other closely. Assignment of the major bands may be correlated with the anhydride and carbonate functional groups experimentally observed for molecules of closely related structure and with calculated from the MP2 and DFT(B3LYP) levels of theory.

Experimentally, infrared bands characteristic of the cyclic anhydride functional group as part of a six-membered ring (a doublet of comparable intensity derived from the symmetric and asymmetric C=O stretching modes in the 1750 to 1850 cm⁻¹ range and a single C=O band in the 1160–1260 cm⁻¹ range)⁴³ are consistent with those observed. As a closely related structure, pyran-2,4,6-trione (acetonedicarboxylic anhydride, 3-oxoglututaric anhydride) displays such bands at 1810, 1740, and 1245 cm⁻¹, which are in relatively close conformity with the 1821, 1733, and 1272 cm⁻¹ bands in Figure 3. The carbonate group displays C=O and C–O bands in a similar range although less sensitive to ring strain and with a different intensity ratio between the symmetric and antisymmetric C=O bands.⁴⁴ The broad bands in the 1380–450 cm⁻¹ range are difficult to assign as most model compounds have C–H bands in that range. However, in ring systems containing carboxyl groups and an absence of C–H bonds, such bands are observed and correlated with out-of-plane deformations.⁴⁵ While the functional group character of compound 1 combines structural elements of both anhydride and carbonate, its infrared spectrum more resembles the anhydride. Vibrational calculations for compound 1 have been reported at the MP2(FC)/6-31G* level with a scaling factor of 0.94.⁹ Infrared frequencies calculated for the C=O symmetric and asymmetric stretching modes are 1991 cm⁻¹ (corrected to 1987 cm⁻¹; relative intensity 0) and 1918 cm⁻¹ (corrected to 1803 cm⁻¹; relative intensity 89) respectively, and those for the C–O asymmetric and symmetric ring stretching modes are 1302 cm⁻¹ (corrected to 1224 cm⁻¹; relative intensity 100) and 1043 cm⁻¹ (corrected to 980 cm⁻¹; relative intensity 3) respectively. Comparable infrared frequency calculation at the BL3YP/6-31G* level without a scaling factor have been reported as 2015 cm⁻¹ (relative intensity 26), 1931 cm⁻¹ (relative intensity 764) and 1286 cm⁻¹ (relative intensity 742) for the respective C=O symmetric and C=O asymmetric and C–O ring stretching modes.⁴⁴ These calculated band frequencies, when corrected by a scaling factor, correlate with those of the experimentally observed bands centered at 1821, 1733, and 1272 cm⁻¹ in Figure 3. The 1821 and 1733 cm⁻¹ bands display weak unresolved satellite bands. This feature has been observed in a study of 5- and 6-membered lactone compounds comparing experimental and MP2 and DFT calculated spectra and was attributed to a Fermi-resonance interaction between the C=O vibration and overtone or combination bands.⁴⁵

As final evidence in this study for the formation of 1 from 2a and its subsequent decomposition into CO₂, quantitative yield measurements of the hydroperoxide byproduct 11 from the ozonolysis and of the CO₂ evolved during the postreaction warming were conducted. The yield measurement for compound 11 was conducted on a 200 mg scale following the ozonolysis procedure of the NMR and IR experiments and produced a 67% yield. A small quantity of residual impurities was also observed which may be due to incomplete trapping of the carbonyl oxide 9 in Scheme 4 or to some decomposition or side reaction of this hydroperoxide byproduct 11. Measurement of the yield of CO₂ evolved from 1 after warming to room temperature was conducted by two procedures utilizing infrared spectroscopy and the reaction conditions employed above in the measurement of compound 11. The first procedure utilized an infrared solution cell with CaF₂ windows to quantify the CO₂ band intensity at 2339 cm⁻¹. Immediately after the ozonolysis of 1 was completed and warmed to near room temperature, a measured aliquot of the reaction mixture was transferred to fill the IR solution cell and the spectrum recorded. An analytical solution of CO₂ in the 1:1 CH₃Cl₂:CH₃OH solvent was then prepared with a CO₂ concentration having a comparable 2339 cm⁻¹ band intensity in its IR spectrum. The CO₂ yield derived from 1 was then determined from a proportionality between the integrated intensities of this band in the ozonolysis reaction and analytical spectra. This method resulted in a 37% yield based on quantity of 2a and on assumptions of quantitative conversions of the ozonolysis and of the CO₂ evolution reactions. There was also the possibility of CO₂ escape from the solution IR cell during transfer and measurement of the condensed phase reaction mixture. A second procedure was conducted using a gas IR cell with an attached cylindrical well in which the ozonolysis reaction and subsequent warming of the product were conducted. After completion of the ozonolysis, the reaction solution was cooled from −78 °C to −195 °C, the cell was evacuated to remove the O₂/O₃ from the headspace and then slowly warmed to 20 °C while monitoring gas phase species in the isolated cell. This procedure was repeated with a quantitatively prepared CO₂/CH₃Cl₂:CH₃OH solution (volume and CO₂ concentration calculated for a 100% yield from 2a) placed in the cylindrical well. The yield of CO₂ measured in the gas phase for the ozonolysis reaction was 61% relative to that measured from the CO₂/CH₃Cl₂:CH₃OH analytical solution. This 61% yield of CO₂ appears to complement the above 67% yield of the hydroperoxide byproduct 11. On the basis of these measurements, a 64% yield is supported for the formation of the trione-trioxane 1 in Scheme 4.

### DISCUSSION

While the self-condensation of CO₂ into larger molecules is attractive for the perspective of a high efficiency in CO₂ utilization and perhaps energy storage, the kinetic stability of such compounds is a key issue. For the case of the 2,4,6-trione-1,3,6-trioxane 1, the result of this work indicates that its preparation from CO₂ would be very tedious and would require maintenance of low temperatures, high pressures and a yet to be defined catalyst. This molecule has received significant theoretical analyses, and estimates of its kinetic stability or half-life are useful information even if variable. Older calculation methods appear to significantly overestimate these parameters.⁹
while those based on density functional theory are low (41 ms/298 °K) and to be regarded as lower limits. Half-life calculation based on CCSD coupled cluster theory (~100 s/298 °K) is in reasonable good agreement with the 40 min/233 °K experimental value.

A comparison of this kinetic stability of 1 with known compounds of related structure is worthy of comment. Molecules composed of multiple CO₂ units are known for the oligo-carbonate series (CH₃)ₙCO–[O(O)O]ₙ–C(CH₃)ₙ, n = 1, 2, 3. All are stable at ambient conditions and have progressively decreasing decomposition temperatures: n = 1 (>200 °C), 46 n = 2 (100 °C); 47 n = 3 (65 °C). 48 For polymer analogs of undefined end groups claims are made of subambient stability both theoretically 49,50 and experimentally. 16 While a kinetic instability increases with an increasing –[O(O)O]ₙ– chain length, a chain length of three units can be considered stable at ambient conditions. However, at such a short chain length end group effects play a role, and it has been reported that changing the tert-butyl to the isopropyl end group diminished stability and precluded purification. 45 Ring strain may also play a role in the stability of 1. Calculation has optimized the conformation of 1 as planar with small nonpolar coreactant would be advantageous.

The work reported here provides substantial evidence for the existence and kinetic stability of 2,4,6-trione-1,3,5-trioxane 1 prepared in a model compound synthesis for the cyclic trimer of carbon dioxide. This compound is synthesized in four steps: chlorination of isobutylaldehyde 6; trimerization of chloroisobutyraldehyde 4; dehydrochlorination of chloro-isobutyraldehyde 3a; and ozonolysis of the hexamethyl triolefin-trioxane 2a to the trione-trioxane 1. During the ozonolysis reaction, it is critical that methanol be present to trap the carbonyl oxide intermediate 9 and to prevent side reactions. Analysis of 1 during its formation and decomposition to CO₂ by both ¹³C NMR and in situ mid-FTIR spectroscopy is consistent with assigned spectral features. The FTIR spectral features are interpreted to indicate that 1 is more related to a cyclic anhydride than to a cyclic carbonate. Its yield from the ozonolysis of 2a is 64% as derived from yield measurements of the hydroperoxide byproduct 11 and of the CO₂ decomposition product. Compound 1 has a half-life of 40 min at −40 °C in 1:1 CH₂OH.CH₂Cl₂ solution, is stable at ambient pressures and decomposes quantitatively to carbon dioxide above −40 °C.

## EXPERIMENTAL SECTION

### General Information

All reactions were conducted in oven-dried glassware under an inert atmosphere of dry argon unless otherwise specified. Solvents were refluxed and distilled over Na/benzophenone ketyl or CaH₂ prior to use. All commercial reagents were used as received without further purification. Ozonolysis was performed using an LG-7 CD Laboratory Ozone Generator by Ozone Engineering. Analytical TLC was done using precoated silica gel 60 F254 plates and visualized with either UV light (254 nm), KMnO₄ or Cerium Molybdate staining solution. NMR spectra were recorded at 300 MHz for ¹H NMR and at 75.4 MHz for ¹³C NMR. All chemical shifts for ¹H and ¹³C NMR spectroscopy were referenced to residual signals from CDCl₃ (¹H) 7.26 ppm and (¹³C) 77.2 ppm or from CDCl₃ (¹³C) 53.8 ppm. FTIR spectra were obtained in transmission with sample supported on a NaCl plate under a nitrogen purge of 40 cm³/min and in ATR reflection with sample supported on a diamond window. The ozonolysis reaction was monitored by real time in situ FTIR spectra and in obtained with a Mettler-Toledo ReactIR 15 using a silver halide fiber optic probe assembly containing a silicon or diamond ATR sensor at the tip of the probe. Mass spectral analyses of parent ion were conducted with an ESI-TOF instrument. Elemental analysis was performed by a commercial contractor. Compounds 3a, 3b, 4 and 11 were prepared using known procedures. Compound 2a was prepared using a modified procedure.

### Synthetic Procedures

#### 2,4,6-Tris(chloromethyl)-1,3,5-trioxane (3b)

In an atmosphere of air, chloroacetaldehyde (245% in H₂O, 1.95g, 25.0 mmol) was added to a round-bottom flask equipped with a stir bar and cooled to 0 °C via ice bath. Conc. H₂SO₄ was added dropwise with vigorous stirring until precipitation occurs. The suspension was then poured over ice (ca. 50 mL). The suspension was then vacuum filtered and washed liberally with water. The material was then resuspended in a 2:1 mixture of ethanol and ice cold water followed by vacuum filtration to remove any colored material. The material was then dried on high vacuum to give a white powder (0.23 g, 26%). mp 85–86 °C (Lit. 86 °C); ¹H NMR (CDCl₃, 300 MHz) δ = 3.61 (d, 3J = 4.71 Hz, 6 H), 5.16 (t, 3J = 4.71 Hz, 3 H) ppm; ¹³C NMR (CDCl₃, 75 MHz) δ = 43.2, 99.8 ppm; IR (cm⁻¹) 3127, 1024, 760 cm⁻¹. X-ray crystal structure (Tables S1–S6, Supporting Information).

#### 2-Chloro-2-methylpropanal (4)

Isobutyaldehyde (23.2 g, 0.32 mmol) was added to a two-neck round-bottom flask equipped with a magnetic stir bar, pressure equalizing funnel and reflux condenser. Sulfuryl chloride (33.8 g, 0.32 mmol) was then transferred to the addition funnel and added dropwise at a rate to maintain an external oil bath temperature below 40 °C. The evolved gases were vented through a trap containing water (ca. 50 mL). Once the sulfuryl chloride was added, the reaction was heated to 45 °C with stirring for 1.5 h then stirred at RT for an additional 2.5 h. The addition funnel and reflux condenser were replaced with a stopper and a distillation head fitted with a receiving flask. The crude material was distilled under a vacuum (95 °C, 115 mmHg). A second distillation was necessary to achieve the pure material as a colorless liquid (12.48 g, 72%). mp 156–157 °C (Lit. 156–157 °C); ¹H NMR (CDCl₃, 300 MHz) δ = 1.56–1.87 (m, 6 H), 9.42 (s, 1 H) ppm; ¹³C NMR (CDCl₃, 75 MHz) δ = 25.8, 69.3, 194.9 ppm.

#### 2,4,6-Tris(2-chloropropan-2-yl)-1,3,5-trioxane (3a)

In an atmosphere of air, aldehyde 4 (20.0 g, 0.18 mmol) was added to a round-bottom flask equipped with a stir bar. Conc. H₂SO₄ was added

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dropwise with vigorous stirring until precipitation occurs. The suspension was then poured into ice cold water (ca. 50 mL). Large chunks of material were finely pulverized with a large glass stir rod. The suspension was then vacuum filtered and washed liberally with water. The material was then resuspended in a 2:1 mixture of ethanol and ice cold water followed by vacuum filtration to remove any colored material. The material was then dried on high vacuum to give a white powder (12.2 g, 61%). mp 106–108 °C (Lit.,10 106–107 °C).

H NMR (CDCl3, 300 MHz) δ = 1.54–1.63 (m, 18 H), 4.86–4.90 (m, 3 H) ppm; 13C NMR (CDCl3, 75 MHz) δ = 26.7, 67.2, 103.0 ppm; IR νmax (solid) 1154, 1122, 1107 cm−1. X-ray crystal structures (Tables S7–S12, Supporting Information).

2,4,6-Tri(propan-2-ylidene)-1,3,5-trioxane (2a). A 100 mL Schlenk flask equipped with a magnetic stir bar was charged with KOr-Bu (10.48 g, 93.8 mmol) in a glovebox under an atmosphere of dry argon. The flask was then removed from the glovebox and connected to a Schlenk line under argon. Dry THF (35 mL) was then added via syringe, this mixture was then cooled to 0 °C via ice bath and a solution of trioxane 3a (4.97 g, 15.6 mmol) dissolved in dry THF (10 mL) was added slowly to the cooled reaction mixture. After stirring 15 min at 0 °C, the ice bath was removed and the mixture warmed to room temperature. The flask was then fitted with a reflux condenser and heated to 75 °C for 18 h. The mixture was then cooled to room temperature, and the THF removed under a vacuum. Et2O (20 mL) was then added, and the resultant suspension was vacuum filtered over a bed of Celite, washing with Et2O (20 mL). The solvent was then removed under a vacuum, and the crude product was purified by vacuum distillation (10 mmHg at 185 °C) to yield the title compound as a colorless liquid (2.32 g, 71%). 1H NMR (CDCl3, 300 MHz) δ = 1.63 (s, 18 H) ppm; 13C NMR (CDCl3, 75 MHz) δ = 15.0, 86.9, 144.7 ppm; IR νmax (liquid) 2991, 2919, 2863, 1726, 1284, 1212 cm−1; UV (CH2Cl2) λmax = 210 nm (ε = 1.57 × 104 L/mol·cm); HRMS (ESI) m/z calculated for C12H18O3: 178.1134 found 178.1132. Anal. Calcd for C12H18O3: C, 68.48; H, 8.76. Note: in an earlier published procedure21 for the literature procedure39 1H NMR (CDCl3, 300 MHz) δ = 26.7, 67.2, 103.0 ppm.

Variable Temperature 13C NMR of 2a-Ozonolysis Reaction. A solution of trioxane 3a (30.0 mg, 0.143 mmol) in 0.5 mL 1:1 CD2Cl2:CH3OH solvent mixture was prepared in a 5 mm NMR tube until a persistent blue coloration was observed (15 min). After warming to 20 °C, solvents were removed by rotary evaporation to yield 11 (215 mg, 2.03 mmol, 67%).

Byproduct CO2 Yield from 2a-Ozonolysis Reaction. Two IR transmission spectroscopy based techniques were used: a solution measurement and a gas phase measurement. The first procedure utilized an infrared solution cell with CaF2 windows to quantify the CO2 band intensity at 2339 cm−1. Immediately after the ozonolysis of 2a as described above was completed and warmed to near room temperature, a measured aliquot of the reaction mixture was transferred by syringe to fill the IR solution cell, and the spectrum was recorded. An analytical solution of CO2 in the 1:1 CH2Cl2:CH3OH solvent was then prepared via transfer of CO2 from a calibrated bulb to provide a solution spectrum with a comparable 2339 cm−1 band intensity. This method resulted in a 37% CO2 yield on quantity of 2a and on assumptions of quantitative conversions of the ozonolysis and of the CO2 evolution reactions. There was also the possibility of CO2 escape from the solution IR cell during transfer and measurement of the condensed phase reaction mixture. A second procedure was conducted using a gas IR cell with an attached cylindrical well in which the ozonolysis reaction and subsequent warming of the product were conducted. After completion of the ozonolysis, the reaction solution was cooled from −78 °C to −195 °C, the cell was evacuated to remove the O3/O2 from the headspace and slowly warmed to 20 °C while monitoring gas phase species. This procedure was repeated with an analytically prepared CO2/1:1 CH2Cl2:CH3OH solution (volume and CO2 concentration calculated for a 100% yield from 2a) placed in the cylindrical well, frozen, evacuated and subsequently warmed to 20 °C in the isolated cell. The yield of CO2 measured in the gas phase for the ozonolysis reaction was 61% relative to that measured from the CO2/CH2Cl2:CH3OH analytical solution.

ASSOCIATED CONTENT

Supporting Information

The Supporting Information is available free of charge on the ACS Publications website at DOI: 10.1021/acs.joc.6b00647.

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