

# A Titration Method for Standardization of Aqueous Sodium Chlorite Solutions Using Thiourea Dioxide<sup>†</sup>

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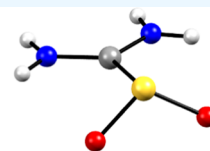
Supporting Information

**ABSTRACT:** Accurate and cost-effective methods for the analysis of oxychlorine compounds in water are critical to modern chlorine-based water treatment. With alternatives to elemental chlorine and hypochlorite bleaches growing in popularity, simple quantification methods for the disinfectant chlorine dioxide ( $\text{ClO}_2$ ) in water, as well as chlorite ( $\text{ClO}_2^-$ ) and chlorate ( $\text{ClO}_3^-$ ), which are commonly used precursors in  $\text{ClO}_2$  generation, are required. However, currently, regulated standard methods require specialized equipment and do not effectively discriminate between molecular and ionic species. In this contribution, we present a simple titration-based method for chlorite determination in water using commercially available and easy-to-handle reagents. Specifically, chlorite is reduced with a slight excess of thioureadioxide (TUD). The remaining reductant is then back-titrated against a known amount of potassium permanganate, affording calculatable chlorite concentrations through measured consumption of a reductant and a clear visual endpoint upon accumulation of excess  $\text{KMnO}_4$ . Straightforward methods for chlorite standardization with reasonable error and accuracy for field and/or lab application have the potential to greatly enhance quality assurance and therefore assist in resource deployment in water treatment.

✓ Simple

✓ Cost-effective

✓ Trackable by eye



*$\text{ClO}_2^-$  quantification using thiourea dioxide!*

## INTRODUCTION

Water-borne disease and contamination are serious global problems, with both urban<sup>1</sup> and remote communities at risk.<sup>2</sup> While elemental chlorine ( $\text{Cl}_2$ ) and hypochlorite ( $\text{ClO}^-$ ) bleaches are routinely employed in large-scale sanitation systems due to their bactericidal efficacy and simplicity of use, the use of alternative chlorine-based disinfectants is growing in popularity in a number of sectors, including food, water treatment, and air quality.<sup>3–9</sup> Chlorine dioxide ( $\text{ClO}_2$ ), for example, has been used to control off-tastes, odors, and colors in drinking water.<sup>10</sup>  $\text{ClO}_2$  is a particularly attractive disinfectant compared with  $\text{Cl}_2$ , as  $\text{ClO}_2$  produces minimal carcinogenic halogenated organic byproducts,<sup>11,12</sup> and functions as a stronger bactericide over a wide pH range (due to higher oxidation capacity) with high water solubility.<sup>13</sup> In drinking water,  $\text{ClO}_2$  presents operational advantages with cost levels comparable to ultraviolet (UV) disinfection and standard chlorination.

As the storage of  $\text{ClO}_2$  is impractical and hazardous, production is typically carried out on-site through the oxidation of sodium chlorite ( $\text{NaClO}_2$ ).  $\text{ClO}_2$  generators often rely on specific feed ratios of hydrochloric acid (HCl) and  $\text{NaClO}_2$  solutions. US Environmental Protection Agency (EPA) approved chlorite standardization methods include iodometric titrations, ion chromatography, and commercial analyzers.<sup>14</sup> Spectrophotometric methods have also been reported,<sup>15</sup> based on the absorbance of chlorite in the ultraviolet region of the electromagnetic spectrum.<sup>16</sup> In resource-limited settings, accurate, quick, and cost-effective

methods for verifying solution concentrations of  $\text{ClO}_2^-$  can enable simple pump adjustments to maintain effective water decontamination<sup>17</sup> without costly additional equipment.<sup>15</sup> Here, a robust titration method capable of quickly and accurately determining the concentration of  $\text{ClO}_2^-$  in aqueous solution is presented, accompanied by an investigation into the relevant redox reactions involved.

## MATERIALS AND METHODS

Potassium permanganate ( $\geq 99\%$ , Fisher Scientific), thiourea dioxide, also known as formamidinium sulfonic acid (TUD, 99% Aldrich), oxalic acid (Univar, 99.6%), and sodium chlorite ( $\text{NaClO}_2$ , 80% w/w, Oxychem) were used as-received unless otherwise noted. Sodium oxalate ( $\geq 99\%$ , J.T. Baker) was dried at 120 °C for a minimum of 5 h prior to use. Unless otherwise noted, all aqueous solutions were prepared using distilled water supplied by Osorno Enterprises Inc. Unless otherwise noted, Class A volumetric glassware (Fisher Scientific) was used for titrations and solution preparation. One-dimensional (1D) NMR spectra were recorded on a Bruker Avance 400 MHz or a Bruker Avance – III 500 MHz spectrometer. Ultraviolet–visible (UV–vis) spectroscopy was performed on a Thermo

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Scientific Genesys 10S UV–Vis spectrophotometer. Chronoamperometric analysis was carried out using a Palintest ChlordioX Plus using chlorine dioxide and chlorite sensors. Ion chromatography was performed by Element (7217 Roper Road NW, Edmonton, Alberta, T6B 3J4, Canada). Iodometric titrations were performed as described in the Oxychem Sodium Chlorite Handbook.<sup>18</sup> The theoretical limit of detection (LOD) for the colorimetric titration method described herein is approximately 7.5 ppm. The actual value is dependent on the concentration of the prepared titrant as well as the quality of the glassware used. A low-concentration titrant will result in a lower LOD. When titrated spectrophotometrically, the LOD will be determined by the instrument used.

#### Preparation of $\text{KMnO}_4$ Stock Solutions for Titration.

To prepare  $\sim 0.020$  M solutions,  $\text{KMnO}_4$  (6.953 g, 44.00 mmol) was dissolved in  $\sim 2$  L of distilled water. The solution was heated to  $80^\circ\text{C}$  and stirred for 1 h. The solution was removed from the heat source and left to stand for 3 days and then filtered through an 'F' porosity filter, leaving the last 50 mL of solution (containing most of the precipitated  $\text{MnO}_2$ ) behind. Standardization via repeated titrations ( $4\times$ ) with sodium oxalate in 5% (v/v)  $\text{H}_2\text{SO}_4$  or oxalic acid was performed to determine the final concentration.

#### Preparation of TUD Stock Solutions for Titration.

Targeting 0.055 M solutions, a 1 L solution of 2.5 M  $\text{H}_2\text{SO}_4$  in distilled water was prepared in a light-filtering glass container. The solution was cooled in an ice bath. Solid TUD (5.9466 g, 55.000 mmol) was then slowly added and swirled to dissolve. The solution was then standardized via repeated titrations ( $4\times$ ) against  $\text{KMnO}_4$  in an oil bath held at  $60^\circ\text{C}$ .

#### Method of $\text{NaClO}_2$ Solution Preparation for Titration.

At higher concentrations of  $\text{NaClO}_2$ , the assumption of  $\rho_{\text{H}_2\text{O}} = 1$  g/mL does not hold due to the addition of salt mass and is also affected by the concentration-dependent ionic strength of the solution. Solutions were prepared on a weight-percent (wt %, or w/w) basis. A mass of  $\text{NaClO}_2$  was weighed into a 20 mL vial. Water was then added to the vial until the desired total mass was reached. The vial was swirled vigorously until the solution appeared homogeneous. Calculations to determine  $\text{NaClO}_2$  concentration in solutions prepared through this method are described in Supporting Information: [Sample Calculation 1](#). Conversion between per-weight and per-volume concentrations was done using an experimentally determined calibration curve (Supporting Information: [Figure S1](#)), generated by determining the density of several solutions prepared on a per-weight basis as described above.

**General Titration Procedure.** A known volume of a standardized solution of TUD was added to a 250 mL Erlenmeyer flask containing a stir bar and kept in a bath held at  $60^\circ\text{C}$  for the duration of the titration. 25.0 mL of 2.5 M  $\text{H}_2\text{SO}_4$  was added to the flask. The volumetric flask used to measure the TUD solution was rinsed multiple times into the Erlenmeyer to ensure that the entirety of the TUD solution was transferred. The flask was left to stir for 1 min to allow the temperature of the solution to equilibrate. A known volume of a  $\text{NaClO}_2$  solution was then added to the warm TUD solution. The resulting mixture was left to stir for 2 min to ensure all of the  $\text{NaClO}_2$  was consumed by the TUD present. The remaining TUD was then titrated against standardized  $\text{KMnO}_4$ . The endpoint of the titration was identifiable by the persistence of a pink color associated with excess

permanganate. The rate of addition was controlled to ensure that the solution remained at  $60^\circ\text{C}$ .

**Example Titration of 25 wt %  $\text{NaClO}_2$  (Table 2).** The procedure for preparing a titration-ready  $\text{NaClO}_2$  solution was as noted above, using  $\text{NaClO}_2$  (3.18370 g, 28.161 mmol); the final mass of water and  $\text{NaClO}_2 = 10.09341$  g; the solution was diluted by transferring 1.000(6) mL into a 10.00(2) mL volumetric flask via a volumetric pipet to make a titration-ready solution. 1.000(6) mL of this titration-ready solution was used for titration. The procedure for quenching and back-titration was as noted above, using 25.00(4) mL of a standardized 0.0554(2) M TUD solution and a standardized solution of 0.0201(5) M  $\text{KMnO}_4$ . Titration results (repeated twice): titration 1:  $\Delta V = 24.69$  mL ( $2.32 \times 10^5$  mg/L); titration 2:  $\Delta V = 24.40$  mL ( $2.43 \times 10^5$  mg/L). Chronoamperometric analysis (repeated twice): using appropriate analytical techniques and glassware, the 25 wt %  $\text{NaClO}_2$  solution was diluted by a factor of 10,000.  $\text{ClO}_2^-$  was then measured using the instrumental protocol.<sup>19</sup> Chronoamperometric analysis 1:  $\text{ClO}_2^- = 15.8$  mg/L ( $\text{NaClO}_2 = 2.113 \times 10^5$  mg/L); chronoamperometric analysis 2: 16.6 mg/L ( $\text{NaClO}_2 = 2.220 \times 10^5$  mg/L).

**Example Titration of 7.5 wt %  $\text{NaClO}_2$  (Table 2).** The procedure for preparing a titration-ready  $\text{NaClO}_2$  solution was as noted above, using  $\text{NaClO}_2$  (0.93870 g, 8.3034 mmol); the final mass of water and  $\text{NaClO}_2 = 10.02903$  g; the solution was diluted by transferring 5.00(1) mL into a 10.00(2) mL volumetric flask via a volumetric pipet to make a titration-ready solution. 1.000(6) mL of the titration-ready solution was used for titration. The procedure for quenching and back-titration was as noted above, using 25.00(4) mL of a standardized 0.0554(2) M TUD solution and a standardized solution of 0.01960(8) M  $\text{KMnO}_4$ . Titration results (repeated twice): titration 1:  $\Delta V = 23.08$  mL ( $5.94 \times 10^4$  mg/L); titration 2:  $\Delta V = 22.45$  mL ( $6.42 \times 10^4$  mg/L). Chronoamperometric analysis (repeated twice): using appropriate analytical techniques and glassware, the 7.5 wt %  $\text{NaClO}_2$  solution was diluted by a factor of 2000.  $\text{ClO}_2^-$  was then measured using the instrumental protocol.<sup>19</sup> Chronoamperometric analysis 1:  $\text{ClO}_2^- = 15.8$  mg/L ( $\text{NaClO}_2 = 2.113 \times 10^5$  mg/L); chronoamperometric analysis 2: 16.6 mg/L ( $\text{NaClO}_2 = 2.220 \times 10^5$  mg/L).

**Example Titration of 0.70 wt %  $\text{NaClO}_2$  (Table 2).** The procedure for preparing titration-ready  $\text{NaClO}_2$  solution was as noted above, using  $\text{NaClO}_2$  (0.2220 g, 1.964 mmol); the final mass of water and  $\text{NaClO}_2 = 22.716$  g; 5.000(1) mL of this solution was then used directly for titration. The procedure for quenching and back-titration was as noted above, using 25.00(4) mL of a standardized 0.0554(2) M TUD solution and a standardized solution of 0.0201(5) M  $\text{KMnO}_4$ . Titration results (repeated twice): titration 1:  $\Delta V = 20.85$  mL ( $7.67 \times 10^3$  mg/L); titration 2:  $\Delta V = 20.45$  mL ( $7.99 \times 10^3$  mg/L). Chronoamperometric analysis (repeated twice): using appropriate analytical techniques and glassware, the 0.70 wt %  $\text{NaClO}_2$  solution was diluted by a factor of 200.  $\text{ClO}_2^-$  was then measured using the instrumental protocol.<sup>19</sup> Chronoamperometric analysis 1:  $\text{ClO}_2^- = 22$  mg/L ( $\text{NaClO}_2 = 5.900 \times 10^3$  mg/L); chronoamperometric analysis 2: 19.9 mg/L ( $\text{NaClO}_2 = 5.336 \times 10^3$  mg/L).

**Example Titration of 0.14 wt %  $\text{NaClO}_2$  (Table 2).** The procedure for preparing a titration-ready  $\text{NaClO}_2$  solution was as noted above, using  $\text{NaClO}_2$  (0.1883 g, 1.666 mmol); the final mass of water and  $\text{NaClO}_2 = 90.016$  g; 10.00(2) mL of this solution was then used directly for titration. The

procedure for quenching and back-titration was as noted above, using 25.00(4) mL of a standardized 0.0554(2) M TUD solution and a standardized solution of 0.0201(5) M  $\text{KMnO}_4$ . Titration results (repeated twice): titration 1:  $\Delta V = 26.42$  mL ( $1.64 \times 10^3$  mg/L); titration 2:  $\Delta V = 26.40$  mL ( $1.64 \times 10^3$  mg/L). Chronoamperometric analysis (repeated twice): using appropriate analytical techniques and glassware, the 0.14 wt %  $\text{NaClO}_2$  solution was diluted by a factor of 250.  $\text{ClO}_2^-$  was then measured using the instrumental protocol.<sup>19</sup> Chronoamperometric analysis 1:  $\text{ClO}_2^- = 2.8$  mg/L ( $\text{NaClO}_2 = 9.38 \times 10^2$  mg/L); chronoamperometric analysis 2: 3.7 mg/L ( $\text{NaClO}_2 = 1.240 \times 10^3$  mg/L).

**Preparation and Standardization of the  $\text{KMnO}_4$  Solution for Electronic Absorption Spectroscopy Reactivity Experiments.** Targeting an  $\sim 0.25$  M solution,  $\text{KMnO}_4$  (3.650 g, 23.10 mmol) was dissolved in  $\sim 0.110$  L of distilled water. The solution was heated to 80 °C and stirred for 1 h. The solution was cooled to ambient temperature and left to stand for 3 days and then filtered through an 'F' porosity filter, leaving the last 10 mL of solution (containing most of the precipitated  $\text{MnO}_2$ ) behind. The filtered solution was diluted by transferring 25.00(3) mL via a volumetric pipet to a 100.00 mL volumetric flask and filling with water to the calibration line. The flask was repeatedly inverted until the solution was homogeneous (minimum 30 $\times$ ). Standardization via titration (4 $\times$ ) with sodium oxalate in 5% (v/v)  $\text{H}_2\text{SO}_4$  was used to determine the final concentration. The solution was stored in a light-filtering container at room temperature. All experiments using this solution were carried out within 3 days of standardization.

**Preparation of the TUD Solution for Electronic Absorption Spectroscopy Reactivity Experiments.** A 1000.00(15) mL volumetric flask was charged with  $\sim 800$  mL of water and cooled to 0 °C in an ice bath. Next, 140 mL of concentrated  $\text{H}_2\text{SO}_4$  was slowly added to target a final concentration of 2.5 M  $\text{H}_2\text{SO}_4$ . Solid TUD (0.0530 g, 0.490 mmol) was then slowly added while the temperature was cold. The solution was allowed to reach room temperature, which was followed by the addition of water until the solution reached the fill line. The flask was repeatedly inverted until the solution was homogeneous (minimum 30 $\times$ ). The resulting solution was kept in a light-filtering container and stored in a refrigerator. All experiments using this solution were completed within 3 days of preparation.

**Preparation of the  $\text{NaClO}_2$  Solution for Electronic Absorption Spectroscopy Reactivity Experiments.**  $\text{NaClO}_2$  (3.7592 g, 33.253 mmol) was placed in a 500.0(2) mL volumetric flask. Water was added until the calibration line was reached. The flask was repeatedly inverted until the solution was homogeneous (minimum 30 $\times$ ). The resulting solution was kept in a light-filtering container and stored in a refrigerator. All experiments using this solution were completed on the day of preparation.

**Determination of TUD: $\text{NaClO}_2$ /TUD: $\text{KMnO}_4$  Reaction Stoichiometry Using Electronic Absorption Spectroscopy.** A portion of the TUD solution prepared as above (3.000(18) mL) was added to a cuvette and fitted loosely with a screw-top cap. The cuvette was then inserted into a UV-vis spectrometer sample holder preheated to 60 °C. Electronic absorption spectra (4–6) were collected spanning 600–250 nm with the scan range repeated every  $\sim 30$  s. Over that time, the internal temperature of the sample is assumed to have equilibrated. An aliquot of the  $\text{NaClO}_2$  or  $\text{KMnO}_4$  solution

prepared as noted above was then added via a microsyringe. The cuvette was then recapped loosely, and electronic absorption spectra were collected spanning 600–250 nm, with the scan range repeated every  $\sim 30$  s until no further changes in peak intensities were observed. Fresh solutions were used for each stoichiometry investigated, and the data points used in our analysis were derived from spectra collected after equilibrium had been reached (Figure S8).

**Chemical Stability Tests Using Electronic Absorption Spectroscopy.** Solutions were prepared using the above solutions and were diluted to concentrations appropriate for electronic absorption spectroscopy measurements ( $\sim 10^{-4}$  M) while maintaining a 2.5 M  $\text{H}_2\text{SO}_4$  concentration for the solutions of TUD. The resulting mixtures were then added to a cuvette and inserted into a preheated UV-vis spectrometer sample holder held at a specified temperature. Each sample was then repeatedly scanned at a specified rate, and the changes in spectra were tracked.

**NMR Spectroscopic Investigation of TUD and  $\text{NaClO}_2$  Reaction Products.** TUD (16.0 mg, 0.148 mmol) and  $\text{NaClO}_2$  (16.3 mg, 0.145 mmol) were added to an NMR tube.  $\text{D}_2\text{O}$  (400  $\mu\text{L}$ ) was added to the tube, forming a yellow solution and the vigorous production of a gas. The solution quickly turned colorless. Water (200  $\mu\text{L}$ ) was added to the NMR tube which was then placed in a sonicated bath to help dissolve the remaining solids.  $^{13}\text{C}\{^1\text{H}\}$  NMR spectroscopic analysis (Figure S13) indicated the presence of urea<sup>20</sup> (162.16 ppm), cyanamide<sup>21</sup> (117.85 ppm), and unreacted TUD (177.38 ppm) (Figure S3).

**NMR Spectroscopic Investigation of TUD and  $\text{NaClO}_2$  Reaction Products in the Presence of  $\text{H}_2\text{SO}_4$ .** In a 10 mL vial, TUD (17.2 mg, 0.159 mmol),  $\text{NaClO}_2$  (18.20 mg, 0.162 mmol),  $\text{D}_2\text{O}$  (300  $\mu\text{L}$ ), water (300  $\mu\text{L}$ ), and  $\text{H}_2\text{SO}_4$  (80  $\mu\text{L}$ , 1.482 mmol) were mixed. The solution visibly released a gas, turned yellow, and then turned colorless.  $^{13}\text{C}\{^1\text{H}\}$  NMR was taken of the resulting solution (Figure S14), indicating the production of urea<sup>20</sup> (160.97 ppm) (Figure S4).

**NMR Spectroscopic Investigation of TUD and  $\text{KMnO}_4$  Reaction Products in  $\text{H}_2\text{SO}_4$ (aq).**  $\text{D}_2\text{O}$  (800  $\mu\text{L}$ ) was added to a 20 mL vial, followed by the addition of 100  $\mu\text{L}$  of concentrated  $\text{H}_2\text{SO}_4$ . After the solution was left to cool in a refrigerator for 10 min, TUD (0.0405 g, 0.375 mmol) was slowly added, and the resulting mixture was sonicated until it appeared all added material had dissolved. The solution was again left to cool in a refrigerator for 10 min, after which potassium permanganate (0.0272 g, 0.172 mmol) was added, and the resulting solution was sonicated until it appeared all added solids were dissolved. The solution was then analyzed by  $^{13}\text{C}\{^1\text{H}\}$  NMR. The resulting NMR spectrum indicates the presence of urea (163.3 ppm) (Figure S5) with no other signals observed. Note: the chemical shift and signal intensity of the analyte were observed to be sensitive to factors including temperature, pH, and the ionic strength of the solution.

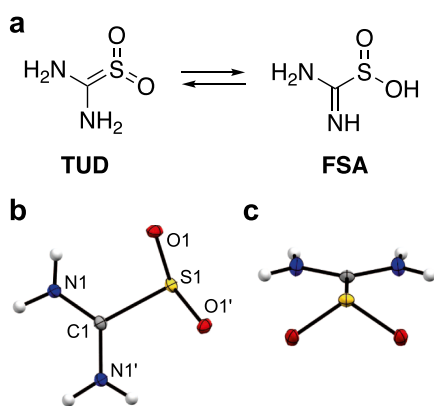
**NMR Spectroscopic Investigation of TUD Stability in 2.5 M  $\text{H}_2\text{SO}_4$ .**  $\text{D}_2\text{O}$  (800  $\mu\text{L}$ ) was placed in a vial containing TUD (0.020 g, 0.18 mmol). The vial was placed in an ice bath, and concentrated  $\text{H}_2\text{SO}_4$  (200  $\mu\text{L}$ ) was slowly added. A sample of the resulting solution was then analyzed via  $^1\text{H}$  and  $^{13}\text{C}$  NMR spectroscopy at ambient temperature. In the NMR spectrometer cavity, the temperature was raised to 60 °C, and the spectra were recollected. A  $^1\text{H}$  spectrum was collected upon reaching 60 °C and again after 10 min at this temperature, revealing no obvious change. A  $^{13}\text{C}\{^1\text{H}\}$  NMR

spectrum was then collected over a period of ~1 h. Two additional  $^{13}\text{C}\{^1\text{H}\}$  spectra were collected over 3 h per spectrum, with a final spectrum collected over a period of 7 h (Figure 2d). At this time, a final  $^1\text{H}$  NMR spectrum was also obtained (Figure S6)

**X-ray Crystallography Experiment.** X-ray crystal structure data was collected from a multifaceted crystal of suitable size and quality selected from a representative sample of crystals of the same habit using an optical microscope. The crystal was mounted on a MiTiGen loop, and data collection was carried out in a cold stream of nitrogen (150 K; Bruker D8 QUEST ECO). All diffractometer manipulations were carried out using Bruker APEX3 software.<sup>22</sup> The structure solution and refinement were carried out using XS, XT, and XL software embedded within the Bruker SHELXTL suite.<sup>23</sup> The absence of additional symmetry was confirmed using ADDSYM incorporated in the PLATON program.<sup>24</sup> CCDC No. 2267651 contains the supplementary crystallographic data for this paper. The data can be obtained free of charge from The Cambridge Crystallographic Data Centre via [www.ccdc.cam.ac.uk/structures](http://www.ccdc.cam.ac.uk/structures).

## RESULTS AND DISCUSSION

The titration functions as follows.  $\text{NaClO}_{2(\text{aq})}$  is first reduced with a slight excess of a standardized reductant. The remaining reductant is then back-titrated against a known amount of oxidant, affording calculatable chlorite concentrations through measured consumption of the reductant. The selected reductant, TUD (Figure 1a), is a commercially available,



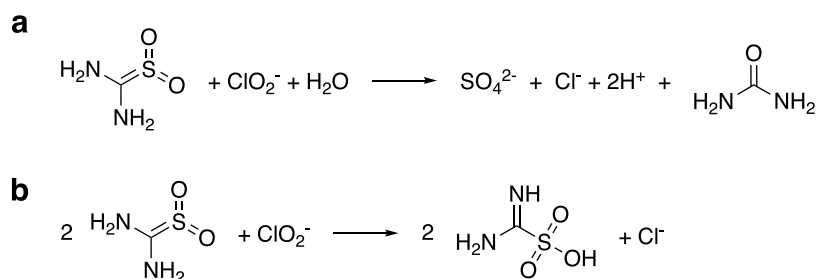
**Figure 1.** (a) Chemical structure of thiourea dioxide (TUD) and its tautomer, formamidine sulfinic acid (FSA) and (b, c) two orientations of the solid-state structure of TUD shown with thermal ellipsoids set at 50% probability levels.

water-soluble reducing agent,<sup>25</sup> first prepared by Barnett over 100 years ago via the oxidation of thiourea with hydrogen peroxide.<sup>26</sup> TUD has experienced a relatively recent resurgence of interest,<sup>27–29</sup> with applications in the reduction of graphene oxide to graphene<sup>30,31</sup> and porous graphene hydrogels,<sup>32</sup> the production of nanoscale metal sulfides,<sup>33</sup> and bitumen modification.<sup>34</sup> Reactions involving decomposition and consumption of TUD typically generate only common commercial wastes such as sodium sulfite and urea.<sup>35</sup> TUD exhibits one of the longest (and weakest) known C–S bonds [ $1.8592(6)$  Å]<sup>36</sup> confirmed here by an updated crystal structure (Figure 1b,c); as such, its reactivity is typically confined to the sulfinic moiety.<sup>37</sup>

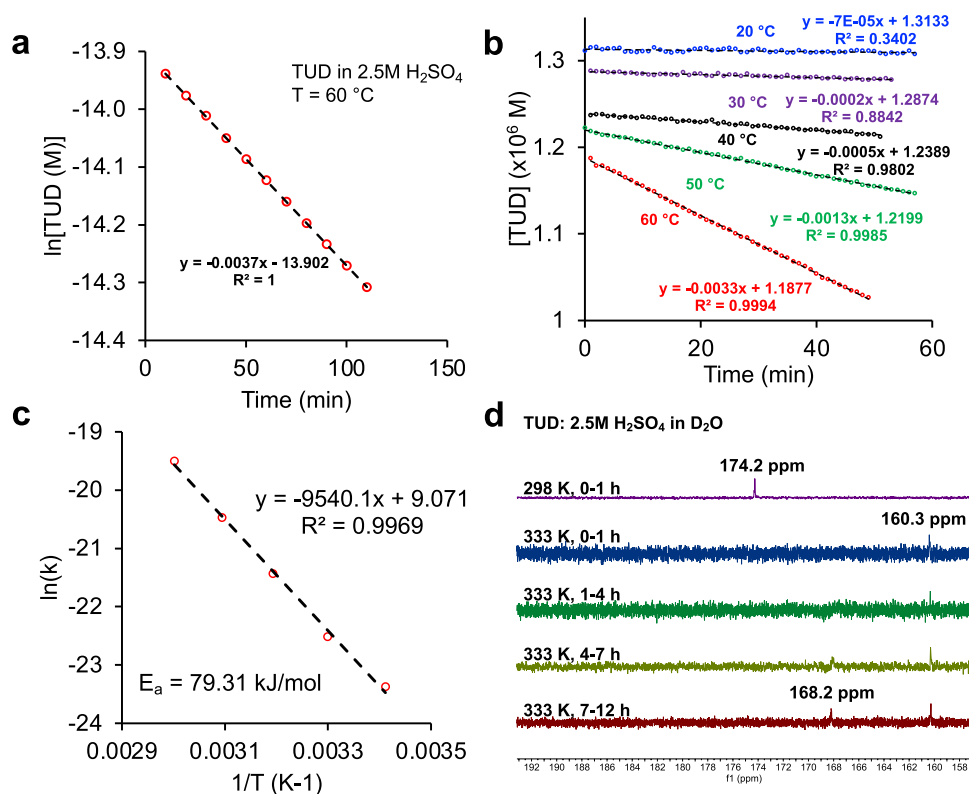
The ground-state structure<sup>36,38</sup> and tautomerization of TUD to formamidine sulfinic acid (FSA) under acidic conditions<sup>39</sup> has been discussed extensively in the literature. The FSA tautomer is considered to be more acidic and reactive than TUD, which is the more stable form in aqueous solution.<sup>28,39</sup> While stable under anaerobic conditions, TUD is known to decompose in alkaline solution in air to produce dithionite ( $[(\text{SO}_2)_2]^{2-}$ ) via generation and subsequent oxidation of  $[\text{SO}_2]^{2-}$ .<sup>35</sup> However, in acidic solution, TUD is stable on the order of weeks,<sup>40</sup> though solutions have been reported to establish a tautomeric equilibrium upon aging that can exhibit differences in reaction rates with oxidants.<sup>39</sup> Importantly, TUD reacts rapidly with chlorite ( $\text{ClO}_2^-$ ), only slowly with chlorine dioxide ( $\text{ClO}_2$ ), and not at all with chlorate ( $\text{ClO}_3^-$ ). We envisaged that this selective reactivity under acidic conditions would make TUD advantageous for use in a simple and selective method for  $\text{NaClO}_2$  concentration determination in water. The use of thiourea dioxide<sup>41</sup> and thiourea itself<sup>42,43</sup> in colorimetric probes does have some precedence.

Reactions of TUD and chlorite have been investigated in the literature in the context of oscillating chemical reactions. Since appearing in the first systematically designed chemical oscillator,<sup>44</sup> the chlorite ion has been a popular choice for investigating nonlinear reaction dynamics in both oxidations and reductions.<sup>45</sup> The reaction of TUD with  $\text{ClO}_2^-$  has been noted to proceed with a 1:1 stoichiometry when the pH of the solution is between 1 and 3, and if the reaction takes place in the presence of excess  $\text{ClO}_2^-$  (Scheme 1a). Reports have discussed that increasing concentrations of TUD can introduce a competitive reaction pathway bearing a 2:1 TUD/ $\text{ClO}_2^-$  stoichiometric relationship (Scheme 1b).<sup>46</sup> At low pH, concentrations of  $\text{ClO}_2$  transiently found in solution as a result of oligooscillatory behavior are low and the reaction of  $\text{ClO}_2^-$  with TUD is fast compared to the reaction of TUD with  $\text{ClO}_2$ , which is around 1000 times slower.<sup>46</sup>

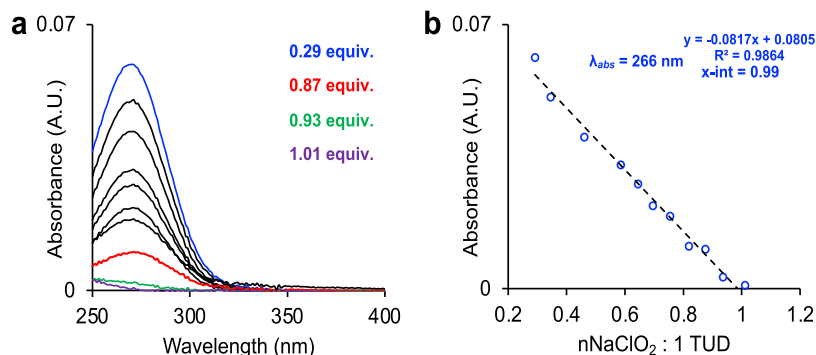
### Scheme 1. Relevant Reactions of TUD and $\text{ClO}_2^-$ in Acidic Aqueous Media<sup>a</sup>



<sup>a</sup>(a) Targeted reaction with 1:1 stoichiometry and (b) the potential competitive reaction bearing a 2:1 TUD/ $\text{ClO}_2$  stoichiometry.



**Figure 2.** (a) Natural log of TUD concentration in 2.5 M H<sub>2</sub>SO<sub>4(aq)</sub> ( $\lambda_{\max} = 266$  nm) as a function of time, fitted to be 1st order in TUD at 333 K; (b) initial rates of TUD decomposition in 2.5 M H<sub>2</sub>SO<sub>4(aq)</sub>; (c) Eyring plot of TUD decomposition in 2.5 M H<sub>2</sub>SO<sub>4(aq)</sub>; and (d) <sup>13</sup>C{<sup>1</sup>H} NMR spectra in D<sub>2</sub>O of TUD in 2.5 M H<sub>2</sub>SO<sub>4(aq)</sub>.

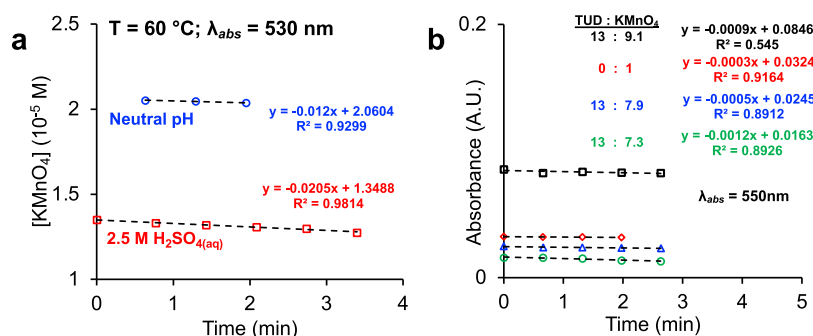


**Figure 3.** (a) UV–vis traces of solutions containing  $n$  equivalents of NaClO<sub>2</sub> and TUD in 2.5 M H<sub>2</sub>SO<sub>4(aq)</sub> at 60 °C and (b) TUD absorbance ( $\lambda_{\text{abs}} = 266$  nm) as a function of added NaClO<sub>2</sub>.

When acidic solutions of TUD were held at elevated temperatures, a slight decrease in the intensity of the main absorption band ( $\lambda_{\text{abs}} = 266$  nm) could be observed by electronic absorption spectroscopy. When held at 60 °C, the degradation of TUD over time was shown to be first-order in TUD (Figure 2a). To examine whether this decay was promoted by light, the same experiment was conducted with the absorbance scan collected at different time intervals; no effect on the rate was noted. The initial rates of decay were measured at various temperatures (Figure 2b), showing that TUD in 2.5 M H<sub>2</sub>SO<sub>4(aq)</sub> shows almost no degradation at room temperature, with a slight decay starting to become evident at 30 °C. Using the initial rate data, the activation energy of this decay was determined to be 79.31 kJ/mol (Figure 2c). TUD in 2.5 M H<sub>2</sub>SO<sub>4(aq)</sub> is therefore stable for longer periods of time when stored in a cool environment and a drop of ~1% in TUD

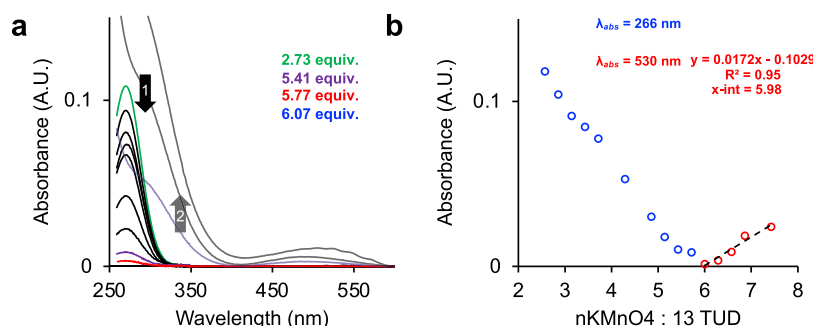
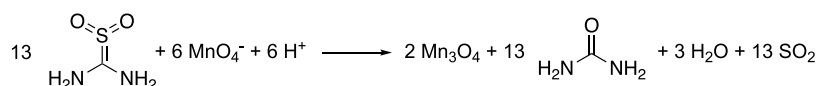
concentration over the course of the titration experiment (3 min) may thus be expected at 60 °C. Following this process by <sup>13</sup>C{<sup>1</sup>H} NMR spectroscopy, the <sup>13</sup>C resonance attributed to the TUD peak (174.2 ppm) shifts significantly to 160.3 ppm upon heating an acidified solution to 60 °C with a new peak (168.2 ppm) emerging after 4 h of heating (Figure 2d).

Satisfied with the relative stability of TUD in titration-relevant conditions, electronic absorption spectroscopy was then used to determine the stoichiometry of the reaction between TUD and chlorite. In 2.5 M H<sub>2</sub>SO<sub>4</sub>, the addition of one full equivalent of NaClO<sub>2</sub> was required to quench peaks attributed to TUD (Figure 3). Sodium chlorite in 2.5 M H<sub>2</sub>SO<sub>4</sub> rapidly produces ClO<sub>2</sub>, which appears as a broad feature centered at 354 nm (Figure S7). No appreciable amount of ClO<sub>2</sub> was detected in the reaction of NaClO<sub>2</sub> with TUD in 2.5 M H<sub>2</sub>SO<sub>4</sub>, indicating that the reaction rate of



**Figure 4.** (a) Monitoring the stability of  $\text{KMnO}_4$  in water as a function of time and (b) monitoring the stability of  $\text{MnO}_4^-$  ( $\lambda_{\text{abs}} = 530 \text{ nm}$ ) in the presence of TUD and 2.5 M  $\text{H}_2\text{SO}_4$  as a function of time.

### Scheme 2. Balanced Reaction of TUD and $\text{KMnO}_4$ in Acidic Aqueous Media at a 13:6 TUD:[ $\text{MnO}_4^-$ ] Stoichiometry



**Figure 5.** (a) Monitoring changes in UV–vis absorbance of 2.5 M  $\text{H}_2\text{SO}_4(\text{aq})$  solutions of  $n$  equivalents of  $\text{KMnO}_4$  and TUD. The numbered arrows signify the addition of (1) 0–5.77 equiv and (2) 6.07–6.98 equiv of  $\text{KMnO}_4$  relative to 13 equiv of TUD. (b) Plot of the peak height of the TUD absorbance (blue;  $\lambda_{\text{abs}} = 266 \text{ nm}$ ) and  $\text{MnO}_4^-$  absorbance (red;  $\lambda_{\text{abs}} = 530 \text{ nm}$ ) as a function of added  $\text{KMnO}_4$  equivalents.

$\text{NaClO}_2$  with TUD is sufficiently high so as not to be affected by any competitive reaction between  $\text{NaClO}_2$  and  $\text{H}_2\text{SO}_4$ . Mixing equimolar amounts of TUD and  $\text{NaClO}_2$  in acidified  $\text{D}_2\text{O}$  yielded only a single resonance at 161.0 ppm in the  $^{13}\text{C}\{^1\text{H}\}$  NMR spectrum consistent with urea production at low pH (Figure S4). When the same experiment was repeated with no added acid, urea (162.2 ppm), cyanamide (117.9 ppm), and unreacted TUD (177.4 ppm) were all evident in the solution, confirming the necessity of a low pH for selective reactivity.

Focusing on widely available reagents that are operationally simple to deploy using standard laboratory techniques, potassium permanganate ( $\text{KMnO}_4$ ) was selected as the titratable oxidant.  $\text{KMnO}_4$  offers suitable chemical reactivity and acts as its own indicator, with complete consumption easily monitored by the naked eye. The stability of  $\text{KMnO}_4$  in titration-relevant conditions was investigated through UV–vis spectroscopic analysis. A solution of  $\text{KMnO}_4$  was prepared in neutral aqueous conditions as well as in 2.5 M  $\text{H}_2\text{SO}_4(\text{aq})$ , and the absorbance intensity ( $\lambda_{\text{abs}} = 530 \text{ nm}$ ) at 60 °C was monitored for both solutions over time (Figure 4a). A slight but constant reduction in peak intensity was observed in both samples over time. The presence of acid seems to increase the rate of decomposition, with the decomposition of the neutral solution occurring at a rate of  $0.012 \times 10^{-5} \text{ M/min}$ , which increases to  $0.0205 \times 10^{-5} \text{ M/min}$  at low pH. The rate of degradation is minimal, however, and is not expected to affect

the results of the titration as the reaction of  $\text{KMnO}_4$  with TUD proceeds much more rapidly. Several solutions containing TUD and an excess of  $\text{KMnO}_4$  were prepared. The permanganate quickly consumed all of the TUD, and the decay of the remaining characteristic permanganate peak was investigated (Figure 4b). The change in decay rate compared to the solution of only  $\text{KMnO}_4$  was negligible and within experimental error, indicating that  $\text{KMnO}_4$  is sufficiently stable in the presence of the products of its reaction with TUD for the purposes of this titration.

To examine the stoichiometry of the reaction between TUD and  $\text{KMnO}_4$  under conditions relevant to our titration protocol, solutions of a known concentration and volume of TUD were prepared at 60 °C and then subjected to various amounts of standardized  $\text{KMnO}_4$  (Figure S8a). The change in absorbance was expressed as the change in moles of TUD and fitted as a function of moles of added  $\text{KMnO}_4$  (Figure S8b). The resulting slope of  $-2.16$  implies a stoichiometry of 13:6 TUD/ $\text{KMnO}_4$  (Scheme 2; see Scheme S1 for a list of other potentially contributing reactions). Indeed, the broad absorption peak associated with TUD ( $\lambda_{\text{abs}} = 266 \text{ nm}$ ) completely disappeared upon reaching this stoichiometry (Figure 5a), followed by the appearance of a characteristic absorption feature ( $\lambda_{\text{abs}} = 530 \text{ nm}$ ), indicating the persistence of excess permanganate. The growth of the main absorbance of  $[\text{MnO}_4^-]$  was plotted as a function of the amount of  $\text{KMnO}_4$  added (Figure 5b), giving an intercept of 5.98 equiv of  $\text{KMnO}_4$

**Table 1. Comparison of NaClO<sub>2</sub> Concentrations Determined for Solutions of Recrystallized NaClO<sub>2</sub> by Using Different Analytical Techniques**

target solution wt % <sup>a</sup>	calculated concentration of NaClO <sub>2</sub> (mg/L) <sup>b</sup>	TUD titration NaClO <sub>2</sub> (mg/L) <sup>c</sup>	iodometric titration (mg/L) <sup>d</sup>	chronoamperometric NaClO <sub>2</sub> (mg/L) <sup>e</sup>	ion chromatography (mg/L) <sup>f</sup>
25%	3.002 × 10 <sup>5</sup>	2.597 × 10 <sup>5</sup>	3.016 × 10 <sup>5</sup>	2.55(37) × 10 <sup>5</sup>	3.426(9) × 10 <sup>5</sup>
7.50%	7.899 × 10 <sup>4</sup>	6.785 × 10 <sup>4</sup>	7.650 × 10 <sup>4</sup>	6.70(76) × 10 <sup>4</sup>	1.019 × 10 <sup>4</sup>
0.70%	7.045 × 10 <sup>3</sup>	7.118 × 10 <sup>3</sup>	6.801 × 10 <sup>3</sup>	6.972 × 10 <sup>3</sup>	9.3(5) × 10 <sup>3</sup>
0.14%	1.469 × 10 <sup>3</sup>	1.435 × 10 <sup>3</sup>	1.341 × 10 <sup>3</sup>	1.341 × 10 <sup>3</sup>	1.66(5) × 10 <sup>3</sup>

<sup>a</sup>wt % of NaClO<sub>2</sub> in the solution based on the mass of 100% (w/w) NaClO<sub>2</sub> (SI: [Sample Calculation 1](#)) <sup>b</sup>Calculated through the use of a calibration curve relating the mg/L to the fractional wt % of the solution. (SI: [Sample Calculation 4](#)) <sup>c</sup>NaClO<sub>2</sub> wt % determined by TUD back-titration ([Materials and Methods](#) section: General Titration Procedure, and SI: [Sample Calculation 2](#)). <sup>d</sup>NaClO<sub>2</sub> wt % determined by iodometric titration. <sup>e</sup>NaClO<sub>2</sub> wt % determined using the Palintest ChlordioX Plus chronoamperometric method (see SI [Sample Calculation 3](#)). Numbers in brackets are the standard deviation from two runs. <sup>f</sup>NaClO<sub>2</sub> wt % determined using ion chromatography. Numbers in parentheses represent the standard deviation from two runs.

added (relative to 13 equiv TUD) consistent with a 13:6 TUD: [MnO<sub>4</sub><sup>-</sup>] stoichiometry.

To identify the reaction products, a solution of KMnO<sub>4</sub> and TUD was prepared in acidified D<sub>2</sub>O. The resulting solution mixture was probed via <sup>13</sup>C{<sup>1</sup>H} NMR, which revealed a single peak (163.3 ppm), indicating the presence of urea. It is worth noting that the strength of the signal is likely dampened due to the low pH of the solution, as well as the presence of potassium, manganese, and oxygen-containing salts, as the ability of the probe to precisely tune to NMR active nuclei is adversely affected by the increased ionic strength of a solution. The exact mechanism of the reaction between TUD and KMnO<sub>4</sub> is not known, and the observed stoichiometry could be complicated by the potential reactivities, rates, and degradative properties of the initial products of TUD and KMnO<sub>4</sub>.

Back-titration using KMnO<sub>4</sub> to oxidize the excess TUD remaining following the quenching of a sample of chlorite gave reproducible results. An important observation was that the solution pH and the addition rate of KMnO<sub>4</sub> must both be kept low enough to prevent brown discoloration indicative of MnO<sub>2</sub> formation, which can hamper the visualization of a sharp endpoint otherwise observed in the form of the onset of a pink color. Solutions of a series of initial concentrations of NaClO<sub>2</sub> were prepared, targeting 25, 7.5, 0.70, and 0.14 wt %. The titration procedure was performed using solutions of recrystallized solid NaClO<sub>2</sub> ([Table 1](#)) and as-received 80% (w/w) NaClO<sub>2</sub> ([Table 2](#)), which revealed a determination dependence on the initial solution concentration. When using more concentrated solutions, the titration-derived concentration was below the expected value calculated from the initial mass of the analyte and water of the solution using either recrystallized or as-received NaClO<sub>2</sub>. For example, solutions of 25 and 7.5 wt % yielded experimentally determined concentrations ~14–21% lower than the calculated value for solutions of recrystallized/as-received NaClO<sub>2</sub> ([Tables 1–2](#) and [S2–S3](#)). The relative difference between the calculated and experimental values is smaller for more dilute solutions ( $\Delta_{\text{mg/L}} \text{ experimental/calculated} \times 100\% = +1.0\%$  (0.70 wt %),  $-2.3\%$  (0.14 wt %) using recrystallized NaClO<sub>2</sub>;  $-0.4\%$  (0.70 wt %),  $+2.6\%$  (0.14 wt %) using as-received NaClO<sub>2</sub>). We note that higher concentration 25 and 7.5 wt % solutions require a dilution step to be titratable, whereas lower concentration solutions do not. Thus, restricting the concentration range of test solutions sufficiently so as not to require a pre-dilution step could obviate a potential source of experimental error. A graphical description of the results in [Tables 1–2](#) (and [Tables S2–S3](#)) is shown in [Figure 6](#).

**Table 2. Comparison of NaClO<sub>2</sub> Concentrations Determined for Solutions of As-Received 80% w/w NaClO<sub>2</sub> Using Different Analytical Techniques**

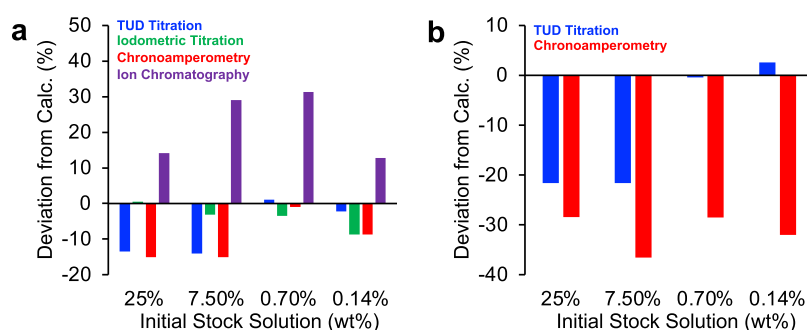
target wt % <sup>a</sup>	calc. concentration NaClO <sub>2</sub> (mg/L) <sup>b</sup>	TUD titration NaClO <sub>2</sub> (mg/L) <sup>c</sup>	chronoamperometric NaClO <sub>2</sub> (mg/L) <sup>d</sup>
25%	3.03 × 10 <sup>5</sup>	2.38(5) × 10 <sup>5</sup>	2.17(8) × 10 <sup>5</sup>
7.50%	7.9 × 10 <sup>4</sup>	6.2(2) × 10 <sup>4</sup>	5.0(5) × 10 <sup>4</sup>
0.70%	7.9 × 10 <sup>3</sup>	7.83(15) × 10 <sup>3</sup>	5.6(4) × 10 <sup>3</sup>
0.14%	1.603 × 10 <sup>3</sup>	1.645(3) × 10 <sup>3</sup>	1.1(2) × 10 <sup>3</sup>

<sup>a</sup>wt % of NaClO<sub>2</sub> in the solution based on the mass of 80% (w/w) NaClO<sub>2</sub> (SI: [Sample Calculation 1](#)) <sup>b</sup>Calculated through the use of a calibration curve relating the mg/L to the fractional wt % of the solution. (SI: [Sample Calculation 4](#)) <sup>c</sup>NaClO<sub>2</sub> wt % determined by TUD back-titration ([Materials and Methods](#) section: General Titration Procedure, and SI: [Sample Calculation 2](#)). Numbers in brackets are the standard deviation from two runs. <sup>d</sup>NaClO<sub>2</sub> wt % determined using the Palintest ChlordioX Plus chronoamperometric method (see SI [Sample Calculation 3](#)). Numbers in brackets are the standard deviation from two runs.

We next compared our titration-based methodology to results from other commonly employed analytical techniques. Using the same solutions analyzed above, the concentration of chlorite was also determined using iodometric titration, commercially available chronoamperometry, and ion chromatography. Comparing experimentally determined NaClO<sub>2</sub> concentration using iodometric titration to the calculated values, the deviation is minimal ( $-0.5\%$ ) for ~25 wt % solutions but gradually increases to  $-8.7\%$  for ~0.14 wt % solutions. Chronoamperometric analysis using commercially available analytical equipment consistently under-reported the concentration compared to the calculated value ( $-15.1$  to  $-1.0\%$ , recrystallized NaClO<sub>2</sub>;  $-28.6$  to  $-36.6\%$ , as-received NaClO<sub>2</sub>). Ion chromatography consistently over-reported the concentration when compared to the calculated values ( $+12.7$  to  $+31.3\%$ ) at all solution concentrations. Ion chromatography was performed off-site, and while solutions were shipped in sealed vials, the possibility of solvent evaporation (leading to increased sample concentration) cannot be excluded.

## CONCLUSIONS

In pursuit of a simple, titration-based method for the standardization of aqueous sodium chlorite solutions, a series of experiments were carried out to verify the utility of thiourea dioxide (TUD) as a titrant and to probe elements of the mechanism of the process. TUD undergoes first-order decomposition in acidified aqueous solutions; however, this process is slow enough to allow relatively long term storage in



**Figure 6.** Comparison of % deviation against the calculated  $\text{NaClO}_2$  concentration based on the measured mass of (a) recrystallized  $\text{NaClO}_2$  and (b) as-received 80% (w/w)  $\text{NaClO}_2$  using different analytical techniques.

cool, dark settings. From the initial rates of TUD degradation at different temperatures, the activation energy of TUD decomposition was determined to be 79.31 kJ/mol.

UV-vis spectrophotometric analysis of the reaction between TUD and  $\text{NaClO}_2$  is consistent with a 1:1 stoichiometry, and the analysis of the  $^{13}\text{C}\{^1\text{H}\}$  NMR spectrum containing a representative solution of TUD and  $\text{NaClO}_2$  showed a single peak associated with the production of urea. Similar analysis of mixtures of TUD and  $\text{KMnO}_4$  indicate a 13:6 stoichiometry operates in the back-titration, with  $^{13}\text{C}\{^1\text{H}\}$  NMR spectroscopic analysis again showing the production of urea. Overall, the TUD- $\text{KMnO}_4$  back-titration method for the analytical determination of chlorite concentration in aqueous media provides reproducible results with deviations comparable to those of industrially standard methods (iodometric titration) while outperforming others. The method performs best when using lower concentrations of initial solutions and provides determined concentration values considerably lower than expected when using high-concentration initial solutions. This method uses inexpensive, commercially available reagents and provides a cost-effective alternative to methods that may require expensive instrumentation such as electrochemical sensing or ion chromatography.

## ■ ASSOCIATED CONTENT

### SI Supporting Information

The Supporting Information is available free of charge at <https://pubs.acs.org/doi/10.1021/acsomega.3c05490>.

Calculation section; plot relating the fractional wt% to the concentration in terms of mg/L in solutions of  $\text{NaClO}_2$ ; (a) crystal structure of thiourea dioxide (110 K), crystallized from water at room temperature; (b) alternate view; (c) hydrogen bonding network in the solid state;  $^1\text{H}$  NMR (500 MHz,  $\text{D}_2\text{O}$ ) of TUD in 2.5 M  $\text{H}_2\text{SO}_4$  (aq) with varying temperature and times of acquisition; UV-vis trace of a solution prepared by slowly adding  $\text{NaClO}_2$  to a 2.5 M solution of  $\text{H}_2\text{SO}_4$  (aq) kept around 5 °C; solid-state structural characterization results; deviation from expected concentration of thrice recrystallized  $\text{NaClO}_2$  by the analysis technique; and deviation from expected concentration of [80% (w/w)]  $\text{NaClO}_2$  by the analysis technique (PDF)

TUD (CIF)

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### Notes

The authors declare no competing financial interest.

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## ■ DEDICATION

†Dedicated to the memory of Dr. H. Peter Hombach.

## ■ REFERENCES

- Baum, R.; Bartram, J.; Hruday, S. The Flint Water Crisis Confirms That U.S. Drinking Water Needs Improved Risk Management. *Environ. Sci. Technol.* **2016**, *50*, 5436–5437.
- Schaidler, L. A.; Rodgers, K. M.; Rudel, R. A. Review of Organic Wastewater Compound Concentrations and Removal in Onsite Wastewater Treatment Systems. *Environ. Sci. Technol.* **2017**, *51*, 7304–7317.
- Han, Y.; Selby, T. L.; Schultze, K. K.; Nelson, P. E.; Linton, R. H. Decontamination of Strawberries Using Batch and Continuous Chlorine Dioxide Gas Treatments. *J. Food Prot.* **2004**, *67*, 2450–2455.



- (4) Popa, I.; Hanson, E. J.; Todd, E. C. D.; Schilder, A. C.; Ryser, E. T. Efficacy of Chlorine Dioxide Gas Sachets for Enhancing the Microbiological Quality and Safety of Blueberries. *J. Food Prot.* **2007**, *70*, 2084–2088.
- (5) Wu, V. C. H.; Rioux, A. A Simple Instrument-Free Gaseous Chlorine Dioxide Method for Microbial Decontamination of Potatoes during Storage. *Food Microbiol.* **2010**, *27*, 179–184.
- (6) Ogata, N.; Sakasegawa, M.; Miura, T.; Shibata, T.; Takigawa, Y.; Taura, K.; Taguchi, K.; Matsubara, K.; Nakahara, K.; Kato, D.; Sogawa, K.; Oka, H. Inactivation of Airborne Bacteria and Viruses Using Extremely Low Concentrations of Chlorine Dioxide Gas. *Pharmacology* **2016**, *97*, 301–306.
- (7) Hsu, M. S.; Huang, Y. T.; Wu, M. Y.; Liao, C. H. Efficacy of Chlorine Dioxide Disinfection to Non-Fermentative Gram-Negative Bacilli and Non-Tuberculous Mycobacteria in a Hospital Water System. *J. Hosp. Infect.* **2016**, *93*, 22–28.
- (8) Hsu, C.-S.; Lu, M.-C.; Huang, D.-J. Disinfection of Indoor Air Microorganisms in Stack Room of University Library Using Gaseous Chlorine Dioxide. *Environ. Monit. Assess.* **2015**, *187*, No. 17.
- (9) Zhou, S.; Hu, C.; Zhao, G.; Jin, T.; Sheen, S.; Han, L.; Liu, L.; Yam, K. L. Novel Generation Systems of Gaseous Chlorine Dioxide for Salmonella Inactivation on Fresh Tomato. *Food Control* **2018**, *92*, 479–487.
- (10) Hoehn, R. C.; Rosenblatt, A. A.; Gates, D. J. In *Considerations for Chlorine Dioxide Treatment of Drinking Water*, AWWA Water Quality Technology Conference; Boston, MA, 1997; pp 63/B–74/B.
- (11) Sharma, V. K.; Sohn, M. Reactivity of Chlorine Dioxide with Amino Acids, Peptides, and Proteins. *Environ. Chem. Lett.* **2012**, *10*, 255–264.
- (12) Yang, X.; Guo, W.; Zhang, X.; Chen, F.; Ye, T.; Liu, W. Formation of Disinfection By-Products after Pre-Oxidation with Chlorine Dioxide or Ferrate. *Water Res.* **2013**, *47*, 5856–5864.
- (13) Al-Otoum, F.; Al-Ghouti, M. A.; Ahmed, T. A.; Abu-Dieyeh, M.; Ali, M. Disinfection By-Products of Chlorine Dioxide (Chlorite, Chlorate, and Trihalomethanes): Occurrence in Drinking Water in Qatar. *Chemosphere* **2016**, *164*, 649–656.
- (14) Appendix A to Subpart C of Part 141; US Environmental Protection Agency (EPA), Office of Water, 40 CFR 141131, 2016.
- (15) Philippi, M.; dos, S. H. S.; Martins, A. O.; Azevedo, C. M. N.; Pires, M. Alternative Spectrophotometric Method for Standardization of Chlorite Aqueous Solutions. *Anal. Chim. Acta* **2007**, *585*, 361–365.
- (16) Hong, C. C.; Rapson, W. H. Analyses of Chlorine Dioxide, Chlorous Acid, Chlorite, Chlorate, and Chloride in Composite Mixtures. *Can. J. Chem.* **1968**, *46*, 2061–2064.
- (17) Long, B. W.; Miller, R. F.; Rosenblatt, A. A. Pilot Study: The Use of High-Purity, Chlorine-Free Chlorine Dioxide to Minimize Trihalomethane Formation. *Chem. Oxid.* **1997**, *6*, 126–133.
- (18) Oxychem Sodium Chlorite Handbook 2015 <https://www.oxy.com/siteassets/documents/chemicals/products/other-essentials/Sodium-Chlorite-Handbook.pdf>. (accessed May 29, 2023).
- (19) Palintest ChlordioX Plus: User Manual 2023 [https://www.palintest.com/wp-content/uploads/2019/04/ChlordioX\\_Plus\\_User-Manual\\_Web.pdf](https://www.palintest.com/wp-content/uploads/2019/04/ChlordioX_Plus_User-Manual_Web.pdf). (accessed May 29, 2023).
- (20) Coxon, B.; Fatiadi, A. J.; Sniegowski, L. T.; Hertz, H. S.; Schaffer, R. A Novel Acylative Degradation of Uric Acid. Carbon-13 Nuclear Magnetic Resonance Studies of Uric Acid and Its Degradation Products. *J. Org. Chem.* **1977**, *42*, 3132–3140.
- (21) Kamo, T.; Hiradate, S.; Fujii, Y. First Isolation of Natural Cyanamide as a Possible Allelochemical from Hairy Vetch *Vicia villosa*. *J. Chem. Ecol.* **2003**, *29*, 275–283.
- (22) Bruker-AXS. APEX3 V2016.1–0. 2016.
- (23) Sheldrick, G. M. A Short History of SHELX. *Acta Crystallogr., Sect. A: Found. Crystallogr.* **2008**, *64*, 112–122.
- (24) Spek, A. L. Structure Validation in Chemical Crystallography. *Acta Crystallogr., Sect. D: Biol. Crystallogr.* **2009**, *65*, 148–155.
- (25) Makarov, S. V.; Horvath, A. K.; Silaghi-Dumitrescu, R.; Gao, Q. Recent Developments in the Chemistry of Thiourea Oxides. *Chem. - Eur. J.* **2014**, *20*, 14164–14176.
- (26) Barnett, E. D. Action of Hydrogen Dioxide on Thiocarbamides. *J. Chem. Soc., Trans.* **1910**, *97*, 63–65.
- (27) Makarov, S. V.; Kudrik, E. V.; van Eldik, R.; Naidenko, E. V. Reactions of Methyl Viologen and Nitrite with Thiourea Dioxide. New Opportunities for an Old Reductant. *J. Chem. Soc., Dalton Trans.* **2002**, 4074–4076.
- (28) Lewis, D.; Mama, J.; Hawkes, J. An Investigation into the Structure and Chemical Properties of Formamidinium Sulfonic Acid. *Appl. Spectrosc.* **2014**, *68*, 1327–1332.
- (29) Ayazi-Nasrabadi, R. Thiourea Dioxide: A Multi-Purpose Reagent. *Synlett* **2015**, *26*, 1281–1282.
- (30) Wang, Y.; Sun, L.; Fugetsu, B. Thiourea Dioxide as a Green Reductant for the Mass Production of Solution-Based Graphene. *Bull. Chem. Soc. Jpn.* **2012**, *85*, 1339–1344.
- (31) Chua, C. K.; Ambrosi, A.; Pumera, M. Graphene Oxide Reduction by Standard Industrial Reducing Agent: Thiourea Dioxide. *J. Mater. Chem.* **2012**, *22*, 11054–11061.
- (32) Xing, L.-B.; Zhang, J.-L.; Zhang, J.; Hou, S.-F.; Zhou, J.; Si, W.; Cui, H.; Zhuo, S. Three Dimensional Reduced Graphene Hydrogels with Tunable Pore Sizes Using Thiourea Dioxide for Electrode Materials in Supercapacitors. *Electrochim. Acta* **2015**, *176*, 1288–1295.
- (33) Wang, H.; Li, Q.; Gao, C. Preparation of Nanometer Nickel Powder from Spent Electroless Nickel Plating Baths by Using Thiourea Dioxide as a Green Reductant. *J. Cleaner Prod.* **2014**, *84*, 701–706.
- (34) Cuadri, A. A.; Partal, P.; Navarro, F. J.; Garcia-Morales, M.; Gallegos, C. Bitumen Chemical Modification by Thiourea Dioxide. *Fuel* **2011**, *90*, 2294–2300.
- (35) Svarovsky, S. A.; Simoyi, R. H.; Makarov, S. V. Reactive Oxygen Species in Aerobic Decomposition of Thiourea Dioxides. *J. Chem. Sci., Dalton Trans.* **2000**, 511–514.
- (36) Lee, C.-R.; Tang, T.-H.; Chen, L.; Wang, Y. A Combined Experimental and Theoretical Electron Density Study of Intra- and Intermolecular Interactions in Thiourea S,S-Dioxide. *Chem. - Eur. J.* **2003**, *9*, 3112–3121.
- (37) Xu, L.; Valkai, L.; Kuznetsova, A. A.; Makarov, S. V.; Horvath, A. K. Kinetics and Mechanism of the Oxidation of Thiourea Dioxide by Iodine in a Slightly Acidic Medium. *Inorg. Chem.* **2017**, *56*, 4680–4688.
- (38) Wang, Y.; Chang, N. L.; Pai, C. T. Charge Density Study of Thiourea S,S-Dioxide. *Inorg. Chem.* **1990**, *29*, 3256–3259.
- (39) Xu, L.; Cseko, G.; Petz, A.; Horvath, A. K. Kinetics and Mechanism of the Oxidation of Pentathionate Ion by Chlorine Dioxide in a Slightly Acidic Medium. *J. Phys. Chem. A* **2014**, *118*, 1293–1299.
- (40) Svarovsky, S. A.; Simoyi, R. H.; Makarov, S. V. A Possible Mechanism for Thiourea-Based Toxicities: Kinetics and Mechanism of Decomposition of Thiourea Dioxides in Alkaline Solutions. *J. Phys. Chem. B* **2001**, *105*, 12634–12643.
- (41) Gao, W.; Qi, W.; Lai, J.; Qi, L.; Majeed, S.; Xu, G. Thiourea Dioxide as a Unique Eco-Friendly Coreactant for Luminol Thiourea Chemiluminescence in the Sensitive Detection of Luminol, Thiourea Dioxide and Cobalt Ions. *Chem. Commun.* **2015**, *51*, 1620–1623.
- (42) Bakir, E. M.; Sayed, A. R.; El-Lateef, H. M. A. Colorimetric Detection of Hg<sup>2+</sup> Ion Using Fluorescein/Thiourea Sensor as a Receptor in Aqueous Medium. *J. Photochem. Photobiol., A* **2022**, *422*, No. 113569.
- (43) Jose, D. A.; Kumar, D. K.; Ganguly, B.; Das, A. Efficient and Simple Colorimetric Fluoride Ion Sensor Based on Receptors Having Urea and Thiourea Binding Sites. *Org. Lett.* **2004**, *6*, 3445–3448.
- (44) De Kepper, P.; Epstein, I. R.; Kustin, K. A Systematically Designed Homogeneous Oscillating Reaction: The Arsenite-Iodate-Chlorite System. *J. Am. Chem. Soc.* **1981**, *103*, 2133–2134.
- (45) Sagués, F.; Epstein, I. R. Nonlinear Chemical Dynamics. *Dalton Trans.* **2003**, 1201–1217.
- (46) Jones, J. B.; Chinake, C. R.; Simoyi, R. H. Oxyhalogen-Sulfur Chemistry: Oligooscillations in the Formamidinesulfonic Acid-Chlorite Reaction. *J. Phys. Chem. A* **1995**, *99*, 1523–1529.