Supporting information

Reaction pathway and selectivity control of tetraethyl thiuram disulfide synthesis with NaHCO₃ as pH regulator

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1. Experimental materials

Hydrogen peroxide (30 wt%) was purchased from Sinopharm Chemical Reagent Co., Ltd. (Shanghai, China). Carbon dioxide (99.99 vol%) was supplied by Beijing Hua Yuan Gas Chemical Industry (Beijing, China). Sodium diethyldithiocarbamate (99 wt%) was purchased from Aladdin Industrial Corporation (Shanghai, China). Sodium bicarbonate (AR) was purchased from Beijing Chemical Works (Beijing, China). TEMPO was purchased from Nanjing Likson biological Technology Co., Ltd. All chemicals were used without any further purification.

2. The solubility of NaHCO₃ in different concentration of sodium diethyldithiocarbamate solution

| Concentration of NaEt₂DTC solution (mol/L) | Molar ratio of NaHCO₃ to NaEt₂DTC | phenomena |
|------------------------------------------|----------------------------------|-----------|
| 0.92                                     | 1:1                              | insoluble |
| 0.60                                     | 1:1                              | soluble   |
| 0.60                                     | 1.5:1                            | insoluble |
| 0.30                                     | 1:1                              | soluble   |
| 0.30                                     | 1.5:1                            | soluble   |
| 0.30                                     | 2:1                              | soluble   |

3. Analytical method

The concentration of the NaEt2DTC solution was measured using a variable wavelength UV-VIS detector (UV 2450, Shimadzu). The relative maximum ultraviolet absorption wavelengths of NaEt2DTC in water of 257 nm and 280.5 nm (at 23 °C) were used to set up two standard curves of concentration - UV absorption values separately and determine the concentration of the test solution.

An additional HPLC (Agilent 1260 Series, USA, Waters Xbridge-C18, 5 μm, 4.6mm×250 mm column, equipped with a programmable variable wavelength UV-VIS...
detector and an autosampler injector) method was also built to determine the concentration and the purity of NaEt2DTC. Chromatographic separations were performed at 25 °C, and the UV detection wavelength was 254 nm. The mobile phase consisting of methanol-water (containing ammonium acetate-ammonium hydroxide buffer salt) was delivered at a 5:95 volume ratio in gradient mode at a flow rate of 1 mL/min.

The HPLC-MS method was used to analyze the composition of the mother liquor after the reaction. The instrument consisted of an Ultra Performance Liquid Chromatography (Waters ACQUITY UPLC) and a quadrupole time-of-flight mass spectrometer interfaced to an electrospray ionization (ESI) source (Waters Xevo G2 QTof), and mass spectrometry software (Waters MassLynx v4.1 software). The ionization of analytes was carried out using the following setting of ESI: source temperature 100 °C, desolvation temperature 450 °C, cone gas flow 50 L/h, desolvation gas flow 800 L/h, capillary voltage 2000 V and both positive and negative polarity modes. The HPLC separation was achieved on an Xbridge-C18 HPLC column (4.6 mm i.d×250 cm, 5μm) from Waters.

4. Selectivity calculation

As the purity of produced TETD after three times washing with 50 mL ultrapure water could reach at least 99%, the reaction selectivity could be calculated from the amount of TETD solid \( m_{\text{TETD}} \), g and NaEt\(_2\)DTC as follow. \( V_{\text{NaEt}_2\text{DTC}} \) is the volume of NaEt\(_2\)DTC solution and \( c_{\text{NaEt}_2\text{DTC}} \) is the molar concentration of NaEt\(_2\)DTC solution. The subscripts “0” represents initial NaEt\(_2\)DTC solution and “1” represents final reaction solution.
\[
S = 1.15 \times \left( \frac{m_{TETD}}{V_0(\text{NaEt}_2\text{DTC}) \times c_0(\text{NaEt}_2\text{DTC}) - V_{p}(\text{NaEt}_2\text{DTC}) \times c_p(\text{NaEt}_2\text{DTC})} \right)
\]

(1)

5. One typical HPLC-MS detection result of NaHCO\textsubscript{3} method

![HPLC graph of mother liquor in experiment entry 4 in Table 1](image)

**Figure S1** The HPLC graph of mother liquor in experiment entry 4 in Table 1

| Residence time (min) | Substance       |
|----------------------|-----------------|
| 6.52                 | RC(O)SNa        |
| 7.177                | NaEt\textsubscript{2}DTC |

6. Pre-experiments of preparing NaEt\textsubscript{2}DTCS

To obtain the maximum amount and highest purity of NaEt\textsubscript{2}DTCS, the amount of hydrogen peroxide and aging time were optimized based on the pH value and UV absorbance value change at 326nm. H\textsubscript{2}O\textsubscript{2} (0.58mol/L, 1mL/min, molar ratio of H\textsubscript{2}O\textsubscript{2} to NaEt\textsubscript{2}DTC = 1:1) was titrated into the NaEt\textsubscript{2}DTC aqueous solution (0.3 mol/L, 30 g) and started to age with introduction of nitrogen. When the pH value of solution stopped increasing at eight-minute aging time, 1% moore dosage of H\textsubscript{2}O\textsubscript{2} was added. After five-minute aging, same amount of H\textsubscript{2}O\textsubscript{2} was added again. After repeating four times, pH value of solution started to decrease. The data of process were recorded as
shown in the following figures.

![Figure S2 The pH value change during experiments](image)

**Figure S2** The pH value change during experiments

![Figure S3 The UV absorbance value change during experiments](image)

**Figure S3** The UV absorbance value change during experiments

(Ratio means the ratio of absorbance value at 256nm to 326nm, absorbance value is the product of absorbance value at 326nm and dilution factor of detected solution, Number means the $n^{th}$ $\text{H}_2\text{O}_2$ titrated up and aging 5-minute)

As 326nm is characteristic absorption wavelength of NaEt$_2$DTCS, its absorbance value was major consideration. As shown in Figure S3, with first addition of 1% moore dosage of $\text{H}_2\text{O}_2$ and subsequent five-minute aging, the absorbance value at 326 nm reached the maximum. So the preparation procedure was determined as follow: $\text{H}_2\text{O}_2$ (0.58mol/L, 1mL/min, molar ratio of $\text{H}_2\text{O}_2$ to NaEt$_2$DTC = 1:1) was titrated into
the NaEt₂DTC aqueous solution (0.3 mol/L, 30 g) and aging 8 minutes with
introduction of nitrogen. Then 1% moore dosage of H₂O₂ was continued to titrate and
aging 5 minutes. The obtained solution was diluted and detected by UV-Vis
absorption spectrometry.

7. The standard concentration curve of NaEt₂DTCS

![Figure S4 The standard concentration curve of NaEt₂DTCS](image)

257nm:

\[ Y = 55207.03X, \quad R^2 = 1 \quad (2) \]

326nm:

\[ Y = 24140.02X, \quad R^2 = 1 \quad (3) \]

(X: Mass fraction of NaEt₂DTCS, Y: Absorption value)

8. UV-Vis calculation

The structure of these two substances were fully optimized by employing the
B3LYP \(^1\)\(^, \)\(^2\) density functionals and the 6-311+G(d,p) basis sets\(^3\). And PCM solvent
model\(^4\) was used to stimulate an aqueous environment. The optimized structures were
all converged with the default self-consistent-field (SCF) convergence cutoffs without
any restrictions. The TD-DFT \(^5\) calculations are conducted considering 30 states to
realize valence excitation to predict the UV-Vis absorption of the substances. And the
output files were analyzed by Multiwfn\textsuperscript{6}, which can output corresponding calculated UV-Vis absorption curve based on the transition energy from the ground state to each electron excited state and the oscillator intensity. And the hole-electron analysis\textsuperscript{7} was also carried out to investigate type of excitation.

Optimized structure of NaEt\textsubscript{2}DTC (Figure S5) and NaEt\textsubscript{2}DTCS (Figure S6) are shown below.

![Figure S5 Optimized structure of NaEt\textsubscript{2}DTC](image1)

![Figure S6 Optimized structure of NaEt\textsubscript{2}DTCS](image2)

The UV-Vis absorption of NaEt\textsubscript{2}DTC was calculated at first to verify the reliability of the calculation method. The results are shown below, two maximum UV absorption
wavelengths are 247 and 287.5nm, which are consistent with the experimental results. So this calculation method is suitable for UV-Vis spectrum calculation of these materials.

![Graph showing UV-Vis absorption](image)

**Figure S7 The calculated UV-Vis absorption graph of NaEt₂DTC**

The electron-hole analysis on this substance is also carried out by Multiwfn (Figure S8, Figure S10). And in order to judge types of transition, the molecular orbitals involved in the transition of NaEt₂DTC molecule are also shown below (Figure S9). From the output file, the transition from S0 to S7 comes from the electron being excited from molecular orbital 44 to 46 and from 45 to 47. The transition from S0 to S18 comes from the electron being excited from molecular orbital 43 to 46. These two transitions are typical transitions of this molecule which are main contributions of the two UV absorption peaks. The absorption of short wavelength ~247nm mainly comes from \( n \rightarrow \pi^* \) transition, the long wavelength ~287.5nm comes from \( \pi \rightarrow \pi^* \) transition. And because of the highly electronegative oxygen atom, the longer wavelength absorption redshift to 324nm which can be concluded by comparing electron-hole graphs S7, S18 of NaEt₂DTC and S4, S5 of NaEt₂DTCS. This could be one of the explanations for the
different nucleophilicity between NaEt$_2$DTC and NaEt$_2$DTCS.

Figure S8 The electron-hole graph of excited states of NaEt$_2$DTC

(isosurface value of S7, S18 and S20 : 0.01, isosurface value of S22 : 0.005)

Num.43 (isosurface value: 0.07) Num.44 (isosurface value: 0.03)
Figure S9 Some molecular orbital graphs of NaEt$_2$DTC

Figure S10 The electron-hole graph of excited states of NaEt$_2$DTCS

(isosurface value of S4, S5, S19 and S20 : 0.01)

9. TETD hydrolysis experiments

Sample 1: TETD (0.14 g) was added into water (4.96 g), which was equivalent to 3.17 wt% NaEt2DTC converting to TETD. This suspension was stirred at room
Sample 2: TETD (0.14 g) and Na₂CO₃ (0.1 g) was added into water (6.66 g), which was equivalent to 2.34 wt% NaEt₂DTC converting to TETD. This suspension was stirred at room temperature (~30 °C) for 1 hour.

These samples were detected by HPLC. The chromatographic peak position of sodium diethylcarbamothionic S-acid and NaEt₂DTC can be determined by the existing mother liquor detection results of HPLC-MS, retention time at ~7.2 min and ~7.8 min.

The results are shown in Table S3.

**Table S3 HPLC detection results of TETD hydrolysis**

| Sample | Mass fraction of NaEt₂DTC (ppm) | Estimated mass fraction of sodium diethylcarbamothionic S-acid (ppm) |
|--------|-------------------------------|---------------------------------------------------------------|
| 1      | 7                             | -                                                             |
| 2      | 105                           | 31.7                                                          |

As the Introduction part mentioned, the TETD hydrolyze into NaEt₂DTC and NaEt₂DTCS under alkaline environment and NaEt₂DTCS decompose to generate sodium diethylcarbamothionic S-acid has been reported long time ago. Based on these evidences, it is easy to explain how NaEt₂DTC and sodium diethylcarbamothionic S-acid come from. TETD hydrolyze into NaEt₂DTC and NaEt₂DTCS under alkaline environment, and NaEt₂DTCS decompose into sodium diethylcarbamothionic S-acid further because of its instability.

The hydrolysis rate of TETD became faster under alkaline environment while only 0.02 % of TETD hydrolyzed within 1 hour in sample 2. And it did hydrolyze to sodium diethylcarbamothionic S-acid and NaEt2DTCS. The hydrolysis of TETD produced NaEt2DTCS, which decomposed into sodium diethylcarbamothionic S-acid further. And the estimated mass fraction of sodium diethylcarbamothionic S-acid was only 31.7 ppm according to stoichiometric ratio. Thus, the hydrolysis of TETD has little effect on
the loss of raw materials.

References

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