Formation of Ozonic Compound and Used as Therapeutic Agent in Medicine

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Abstract. It has some encouraging results to use ozone in medicine. However, as ozone is usually in gas state, unstable and strong oxidability, it is difficult to be stored and used commonly. Ozone, ethylene, acrylic acid and the ozonic compounds were calculated to study the interaction between ozone and carrier material to form ozonide. The stability of the ozonide, or the bond strength between ozone and ions of carrier are controlled felicitously to release ozone from the ozonide with proper velocity. Ozone antimicrobial has been composed on the above principle. It can be used conveniently, especially for common families. There are some characteristics of ozone antimicrobial or ozone, such as universal applicability, efficiency and rapidity, security, strong penetrability, no drug resistance and sterilization and treatment simultaneity.

1. Introduction

Ozone was discovered and used for a long time. The strong oxidability of ozone (only lower than fluorine and S₂O₈²⁻) has been used in wide field. When oxidation takes places, the products of ozone are oxygen and water generally, which has the good ecological environment effect. Recently, ozone has been researched in some new important aspects, such as the therapeutic agent in medicine. In despite of some debates, it has some encouraging results [1-7] in faith to use ozone in treatments. Now when a man falls ill, such as inflammation, he may eat or be injected antibiotics or bacteriophages. There is latent danger for him. If he does in this way from time to time, some serious consequences may be resulted in, such as antibiotic may have no effect to him when he falls serious illness again. Namely, he has the drug resistance in his body. When ozone is used to treat, there is different mechanism of the ozone from the bacteriophage, as ozone is the strong oxidant. As the special merits of ozone, some beneficial effects of ozone have been observed in treating some diseases, such as chronic ulcers [8], vaginitis [9], atherosclerosis [10], lumbar disk herniation [11], HIV [12], and so on [1-7].

Ozone has some advantages over common medicament. As it is in gas state, low stability and strong oxidation, ozone is difficult to be stored. It should be produced when it is needed. The ozone generator is equipped where
ozone is used. If ozone is used as common medicament in hospitals, families, open fields, journey or other places, it lets to difficulty as the problems of production and storage. Therefore, the “fixation” of ozone is the key matter in use of ozone commonly or conveniently. There the study is to solve this problem of fixation of ozone. In the recent ten years, we have being searched the materials that can fix ozone for us to use ozone conveniently. Firstly, the carrier material needs to bond with ozone to form “ozonic compound”. The stability of the ozonic compound, or the bond strength between ozone and carrier, must be felicitous. If the bond strength is too small, the ozonic compound is less stable and ozone is difficult to store. On the other hand, if the bond strength is too large, the ozonic compound is too stable and ozone is difficult to release when we need to use ozone. In other words, the reaction “Ozone + Carrier = Ozonic compound” should react in both of positive and negative reactions, and there is no large difference of the rate constants of two directions. Secondly, the solvent needs to dissolve the ozonic compound, and the concentration of ozone in solution is large enough to be use (the ozone solubility is only 3-7mg/L in water at 25°C and hardly has treating effect). At the same time, the production is required to be kept, transited and used conveniently. In other words, we need felicitous carrier and solvent. In this paper, ozonic compound and related single molecules were calculated to study the interaction between ozone and carrier to form ozonic compound with density function theory and discrete variational method (DFT-DVM) [13]. The carrier and ozonic compound are designed from the calculations. The stabilities of the ozonic compound or the bond strength between ozone and carrier are controlled felicitously to release ozone from the ozonic compound with proper velocity.

2. Calculated method

DFT-DVM method [13] is to resolve the Kohn-Sham equation firstly:

\[ h_\nu \varphi_i (\mathbf{r}) = \left[ -\frac{\nabla^2}{2} + \sum_j Z_j \left( \frac{1}{|\mathbf{r} - \mathbf{R}_j|} \right) + \int \frac{\rho(r')}{|\mathbf{r} - \mathbf{r}'|} \, dr' + V_\text{xc} \right] \varphi_i (\mathbf{r}) = \varepsilon_i \varphi_i (\mathbf{r}) \]

(1)

Here there is

\[ \rho(r) = \sum_i n_i \left| \varphi_i (\mathbf{r}) \right|^2 \]

(2)

\[ h_\nu \] is Hamilton function of single electron. \( \varepsilon_i \) is energy value of single electron to be resolved. \( \rho(r) \) is density function. \( \varphi(r) \) is single electron wave function of molecule or cluster. \( n \) is the number of occupied electrons. The first term in the middle of equation (1) is kinetic energy operator. The second term is Coulomb potential due to that the electrons are absorbed by nuclei. The third is Coulomb potential due to that the electrons repel each other. \( V_\text{xc} \) is exchange potential. \( \varphi(r) \) is expanded to functions of atomic orbitals:

\[ \varphi_i (\mathbf{r}) = \sum_j \varphi_j (\mathbf{r}) \chi_{ij} \]

(3)

The error function is found as:

\[ \Delta_v = \langle \varphi_v, \left[ h_\nu, \varepsilon_v \right] \varphi_v \rangle \]

(4)

A number of discrete sampling points in a three-dimensional grid are chosen. Variation is made to the parameter of \( C_\mu \) in the error function to obtain all the minima for the points and the Secular equation. Using the multi-dimensional numeral integer method, self-consistent process is carried out to obtain \( \varepsilon_v, \varphi(r) \) and others.

3. Results and discussions

Criegee [14] had put forward and proved the mechanism as below 3 steps. The last productions can be aldehyde, ketone or carboxylic acid commonly.
Ozone, ethylene (C$_2$H$_4$), acrylic acid (C$_2$H$_3$COOH), ozonic compounds of [C$_2$H$_4$]O$_3$ and [C$_2$H$_3$COOH]O$_3$ were calculated. Ozone is with symmetry of C$_{2v}$, ethylene with D$_{2h}$, acrylic acid with C$_s$ and [C$_2$H$_4$]O$_3$ or [C$_2$H$_3$COOH]O$_3$ with C$_1$ point groups. The electronic population, energy level and so on of the highest occupied molecule orbital (HOMO) and lowest unoccupied molecule orbital (LUMO) of them are shown in table 1. The LUMO of ozone is 2b$_2$ and the skeleton map of which is shown in Figure 1. The p orbital with dumbbell shape is perpendicular to the plane of oxygen atoms. The HOMO of ethylene is 1b$_{1u}$ and is shown in Figure 2. The electronic population of 1b$_{1u}$ is from carbon atoms (table I). There is less difference of energy level between HOMO of ethylene and LUMO of ozone. The bonding overlapping can form if the underside of 2b$_2$ contact the upside of 1b$_{1u}$ (as shown in Figure 1 and 2), and the symmetries of 2b$_2$ of two side oxygen atoms and 1b$_{1u}$ orbitals are matched each other. In other wards, the ozonic compound forms. As the electronegativity of carbon is less than that of oxygen, some electrons of ethylene transfer to ozone, and the compound can be shown as [ethylene]$^+$[ozone]$^-$. The electron transfer can be seen in table 2 of some ionic changes of the models. On the other hand, if this bonding overlapping strength increase, the antibonding overlapping in ozone increases too, as the orbital phase of middle oxygen is different from that of bonding carbons or other oxygen in ozone. Afterward, the system becomes unstable and steps 2 and 3 may occur, such as for common fat alkenes.

If the actions can stop at step 1, the ozonic compound that accord with our request may be prepared. The skeleton map of main atoms of [C$_2$H$_3$COOH]O$_3$ ozonic compound and the number of atoms are shown as in Figure 3. The skeleton map of atom 4 and 5 of HOMO of acrylic acid is same as those of Figure 2. The difference of energy level between HOMO of acrylic acid and LUMO of ozone is less than that between HOMO of ethylene and LUMO of ozone (Table 1). The bonding overlapping also can form if the underside of ozone 2b$_2$ contact atom 4 and 5 of HOMO of acrylic acid. Some electrons of acrylic acid transfer to ozone, and the compound can be shown as [acrylic acid]$^+$[ozone]$^-$. Actually, the electronic populations of HOMO of [C$_2$H$_4$]O$_3$ or [C$_2$H$_3$COOH]O$_3$
are mainly from oxygen and carbon atoms (Table 1), and there are interaction among orbitals of oxygen and carbon atoms in these HOMO’s.

**Figure 1.** HOMO of ozone  
**Figure 2.** LUMO of ethylene  
**Figure 3.** Skeletom map of [C₂H₃COOH]O₃

| Model             | O1  | O2  | O3  | C4  | C5  |
|-------------------|-----|-----|-----|-----|-----|
| O₃               | 0.172 | -0.086 | -0.086 | -0.457 | -0.457 |
| C₂H₄             |       |       |     |     |     |
| [C₂H₃]O₃        | -0.018 | -0.128 | -0.128 | -0.397 | -0.397 |
| C₂H₃COOH        |       |       |     |     |     |
| [C₂H₃COOH]O₃   | 0.013 | -0.121 | -0.081 | -0.435 | -0.099 |

Table 2. Some ionic changes of the models

If this bonding overlapping strength increase, the antibonding overlapping also increases in ozone, as the phase of middle oxygen is different from that of other oxygen. However, it is different from [ethylene]⁺[ozone]⁻ that the electrons transferred from acrylic acid is not absolute bonding, because carbon atoms 5 and 6 are anti-phase and the electrons transferred is antibonding between carbon atoms 5 and 6, though carbon atoms 4 and 5 are with the same phase and the electrons transferred is bonding between these two carbons. Therefore, compare with single molecules, the energy change of [acrylic acid]⁺[ozone]⁻ is less than that of [ethylene]⁺[ozone]⁻. The energy change is defined as

\[
\Delta E_1 = E_{\text{total}}(\text{ethylene})^\gamma - E_{\text{total}}(\text{ozone})^\gamma - E_{\text{total}}(\text{ethylene})
\]

\[
\Delta E_2 = E_{\text{total}}(\text{acrylic acid})^\gamma - E_{\text{total}}(\text{ozone})^\gamma - E_{\text{total}}(\text{acrylic acid})
\]

The calculated results shown that \(\Delta E_1\) and \(\Delta E_2\) are both negative values and the absolute value of \(\Delta E_1\) is larger than that of \(\Delta E_2\). Comparing [acrylic acid]⁺[ozone]⁻ with [ethylene]⁺[ozone]⁻, \(\zeta\) is less than \(\delta\), so the antibonding overlapping of ozone in [acrylic acid]⁺[ozone]⁻ is weaker than that in [ethylene]⁺[ozone]⁻. Therefore, the possibility of step 2 of Criegee reaction of [acrylic acid]⁺[ozone]⁻ is less than that of [ethylene]⁺[ozone]⁻. Moreover, the electrons distribute in the limited field for non-conjugated alkene, but the electrons distribute over the larger field for conjugated system of acrylic acid. The C-C bond in [ethylene]⁺[ozone]⁻ is more easily broken and steps 2 and 3 easier to happen than that in [acrylic acid]⁺[ozone]⁻. Meanwhile, there is delocalized large π bond in acrylic acid, and the π electrons move in larger range and in a more stable state than those in ethylene. The stability of acrylic acid is significantly stronger than that of fat alkenes. Therefore, the stability of [acrylic acid]⁺[ozone]⁻ is larger than that of [ethylene]⁺[ozone]⁻. The reaction steps 2 and 3 isn’t easy to happen in [acrylic acid]⁺[ozone]⁻.

Table 3 is overlapping population between some ions of the models. Comparing with single molecules of ethylene and ozone, the strengths of covalent bond O-O and C-C of [ethylene]⁺[ozone]⁻ become weaker, and the
O-C bonds form, which is the precursor step 2 of Criegee reaction. The strength of C-C bond of acrylic acid is weaker than that of ethylene too, because there is delocalized large π bond in acrylic acid. Comparing [acrylic acid][conjugate-base][ozone][conjugate-base] with acrylic acid and ozone, the change trend of covalent bond strength is similar to that of comparing [ethylene][conjugate-base][ozone][conjugate-base] with ethylene and ozone. The strengths of covalent bond O-O and C-C of [acrylic acid][conjugate-base][ozone][conjugate-base] are stronger than those of [ethylene][conjugate-base][ozone][conjugate-base], and O(ethylene)-C of [acrylic acid][conjugate-base][ozone][conjugate-base] is weaker than that of [ethylene][conjugate-base][ozone][conjugate-base], so the possibility of step 2 of Criegee reaction of [acrylic acid][conjugate-base][ozone][conjugate-base] is less than that of [ethylene][conjugate-base][ozone][conjugate-base].

Several types of conjugated system are used as carriers. The effects of position-arrestment or electrical-repulsion of the groups in carrier, as well as the effect of the solvent, may prevent strong overlapping between ozone and –C=O and let steps 2 and 3 not to occur. For example, the solvent can be a type of modified soya oil. The production in liquid state, called ozone antimicrobial, can be in small bottle (such as about 10 mL) to be used conveniently, especially for common families. The high effective concentration of ozone (40g/L) and the long conserved period, about two years, are the advantages of the ozone antimicrobial. The ozonic compound decomposes and releases ozone with proper velocity when it is used, and let to good effect of treatment. The sterilizing capability is observed from the experiment of bacteriostasis with nature keeps. The ozone antimicrobial still has the bacteriostasis effect to aruginosa pseudomonas and golden staphylococcus after it preserves at the room temperature for two years. There are some characteristics of ozone antimicrobial or ozone, such as universal applicability, efficiency and rapidity, security, strong penetrability, no drug resistance and sterilization and treatment simultaneity.

Table 3. Overlapping population of some ions of the models

| Model          | O1-O2 | O1-O3 | O2-C4 | O3-C5 | C4-C5 |
|----------------|-------|-------|-------|-------|-------|
| O3             | 0.443 | 0.443 |       |       |       |
| C2H4           |       |       | 1.335 |       |       |
| [C2H4]O3      | 0.276 | 0.276 | 0.311 | 0.311 | 0.915 |
| C2H3COOH      |       |       |       | 1.268 |       |
| [C2H3COOH]O3 | 0.295 | 0.282 | 0.233 | 0.335 | 0.925 |

4. Conclusion

The bonding overlapping can form if ozone contact ethylene, and the compound of [ethylene][conjugate-base][ozone][conjugate-base] forms. Some electrons of ethylene transfer to ozone. On the other hand, if this bonding overlapping strength in ozone increase, the antibonding overlapping increases too, as the phase of middle oxygen is different from that of bonding carbons or other oxygen in ozone. Afterward, the system becomes unstable and steps 2 and 3 occur, such as for common fat alkenes.

The bonding overlapping also can form if ozone contact the carbon atoms in double bond of acrylic acid. Some electrons of acrylic acid transfer to ozone, and the ozonic compound of [acrylic acid][conjugate-base][ozone][conjugate-base] also forms. However, it is different from [ethylene][conjugate-base][ozone][conjugate-base] that the electrons transferred from acrylic acid is not absolute bonding, because carbon atoms in double bond and in carboxyl are anti-phase and the electrons transferred is antibonding between these carbon atoms, though carbon atoms in double bond are with the same phase and the electrons transferred is bonding between these two carbons. Therefore, compare with single molecules, the energy change of [acrylic acid][conjugate-base][ozone][conjugate-base] is less than that of [ethylene][conjugate-base][ozone][conjugate-base]. The effect on the bond strength of [ethylene][conjugate-base][ozone][conjugate-base] form decrease of bonding electrons is more obviously than that on [acrylic acid][conjugate-base][ozone][conjugate-base] from decrease of bonding or antibonding electrons. Moreover, the electrons distribute in the limited field for non-conjugated alkene, but the electrons distribute over the larger field for conjugated system of acrylic acid. Therefore, the stability of [acrylic acid][conjugate-base][ozone][conjugate-base] is larger than that of [ethylene][conjugate-base][ozone][conjugate-base]. The reaction steps 2 and 3 isn’t easy to happen in [acrylic acid][conjugate-base][ozone][conjugate-base]. The stabilities of the ozonic compound, or the bond strength between ozone and carrier are controlled felicitously to release ozone from the ozonic compound with proper velocity.
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