

Control of Biohazards: A High Performance Energetic Polycyclized Iodine-Containing Biocide

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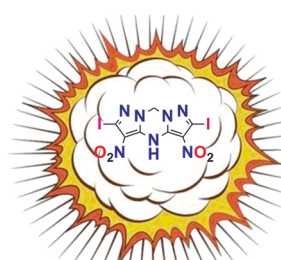
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Supporting Information

ABSTRACT: Biohazards and chemical hazards as well as radioactive hazards have always been a threat to human health. The search for solutions to these problems is an ongoing worldwide effort. In order to control biohazards by chemical methods, a synthetically useful fused tricyclic iodine-rich compound, 2,6-diiodo-3,5-dinitro-4,9-dihydrodipyrzolo [1,5-*a*:5',1'-*d*][1,3,5]triazine (**5**), with good detonation performance was synthesized, characterized, and its properties determined. This compound which acts as an agent defeat weapon has been shown to destroy certain microorganisms effectively by releasing iodine after undergoing decomposition or combustion. The small iodine residues remaining will not be deleterious to human life after 1 month.

Deal With Biological Threats Effectively

$D_v = 5834$ m/s
 $P = 21.48$ GPa
 $T_d = 323$ °C
 $d = 2.56$ g/cm³



I₂ Gas
49.67 wt% kg⁻¹

1. INTRODUCTION

Biohazards are biological substances such as microorganisms, viruses, or toxins that threaten living organisms,¹ including humans as exemplified by smallpox,² plague,³ cholera,⁴ and more recently, SARS,⁵ bird flu,⁶ and Ebola viruses.⁷ Although the use of biological weapons is prohibited under international humanitarian law⁸ as well as by a variety of international treaties and their use in armed conflict is deemed a war crime, some countries and organizations continue to synthesize and utilize biological agents. Because of the attractive properties of *Bacillus anthracis*,⁹ including physical shape, thermal stability, and resistance to many disinfectants (including 95% ethanol),¹⁰ its endospores are extraordinarily well-suited for use (in powdered and aerosol form) as a biological weapon as demonstrated by some countries in the past.¹¹ Large quantities of chemical and biological weapons are stored by various countries and illegitimate groups around the world.¹¹

Since a biological weapon may be a bacterium, virus, protozoan, parasite, or fungus that can be used as a weapon in bioterrorism or biological warfare,¹² it is necessary to develop agent defeat weapons (ADWs) in order to destroy or neutralize the active agents by releasing large amounts of strong biocides after detonation.^{13–17} Based on molecular biology, the mechanism of iodine as a bactericide may arise from oxidation and iodination reactions of cellular proteins and nucleic acids.¹⁵ Iodine damages the walls of the cells that make up the micro-organisms and causes the contents to leak out.¹⁵

This prevents the micro-organisms from being able to make important proteins that are necessary for survival, so they die. The destruction of certain bacteria, amoebic cysts, and viruses (a 99.999% kill in 10 min at 25 °C) may require I₂ residuals of 0.2, 3.5, and 14.6 ppm, respectively.¹⁵ However, due to the ready sublimation of iodine, it is not practical to use the element itself as an ingredient in an ADW. Iodine-rich compounds in which the iodine exists as C–I, iodide or iodate exhibit relatively better thermal stability and therefore, can be used as potential ingredients for ADWs.¹⁶

Many polyiodide compounds have been synthesized and developed over two generations of ADWs. Among these compounds, 3,4,5-triiodo-1*H*-pyrazole (TIPy) (**a**),^{16,18} tetraiodofuran (TIF) (**b**),¹⁶ and 4,5-diiodo-[1*H*]-1,2,3-triazole (**c**)¹⁹ are typical compounds of first-generation ADWs (Figure 1). They exhibit good thermal stability but low detonation performance.

However, one of the problems with application of first-generation ADWs is the difficulty in obtaining complete combustion because of their low detonation performance ((**a**) $P = 5.32$ GPa; $D_v = 2859$ m/s; (**b**) $P = 4.29$ GPa; $D_v = 2417$ m/s), thus reducing the bactericidal effect.²⁰ Residual compounds may also pollute the environment, so an oxidizer

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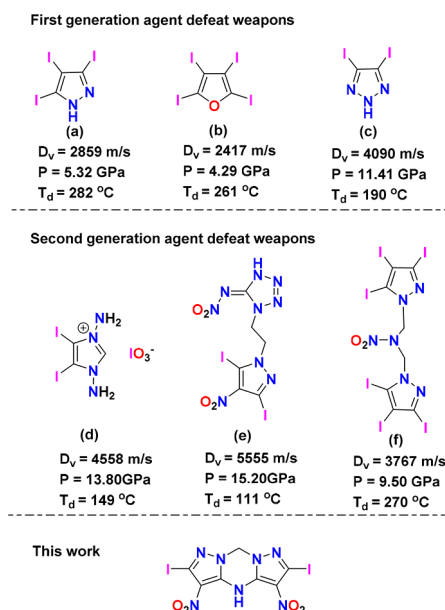


Figure 1. (a–c) First-generation ADWs. (d–f) Second-generation ADWs. Bottom panel: target molecule.

or combustion adjuvant must be used with these polyiodide compounds in order for complete combustion to occur.

Further work was focused on improving the detonation performance of iodine-rich compounds by introducing energetic groups which resulted in the second-generation of agent defeat weapons. The introduction of nitro, nitramine, or tetrazole groups was a successful strategy such as seen in (e) and (f) [(e) $P = 15.20$ GPa; $D_v = 5555$ m/s; (f) $P = 9.50$ GPa; $D_v = 3767$ m/s].^{20,21} Additionally, the combination of an iodine-rich cation with IO_3^- , IO_4^- , or I_3O_8^- as anion in a prospective biocide to ensure a high iodine content and improve the oxygen balance as well was attempted. For example, (d) has a good detonation performance ($P = 13.80$ GPa; $D_v = 4558$ m/s) and oxygen balance.¹⁷ However, the introduction of energetic groups reduces thermodynamic stability. The decomposition temperatures of (d) and (e) are 149 and 111 °C, respectively. Compound (f) has a high decomposition temperature (270 °C) but low detonation performance.

2. RESULTS AND DISCUSSION

In an attempt to realize an ideal balance between high performance and molecular stability, 2,6-diiodo-3,5-dinitro-4,9-dihydro-1H-pyrazolo [1,5-*a*:5',1'-*d*][1,3,5]triazine (5) was synthesized and characterized. Incorporating the nonaromatic 1,3,5-triazinane with pyrazoles results in the fused tricyclic (5) which has a nearly planar structure with enhanced thermal behavior as well as better detonation performance.

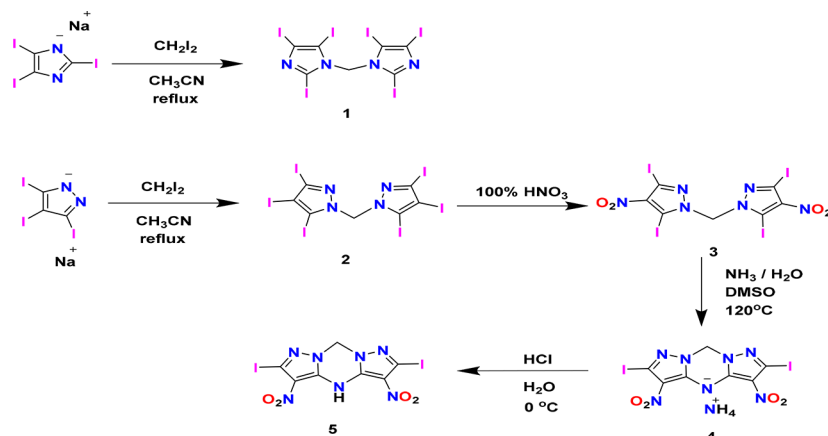
The synthesis of fused tricyclic compound 5 takes advantage of bis(3,4,5-triiodo-1H-pyrazol-1-yl)methane (2) as the starting material, which was obtained readily from 3,4,5-triiodopyrazolium with diiodomethane (Scheme 1). Compound 1 was synthesized analogously. Nitration of 2 gave bis(3,5-diiodo-4-nitro-1H-pyrazol-1-yl)methane (3) which was treated with ammonia–DMSO solution to form pure ammonium salt 4 with a tricyclic framework. Neutralization of 4 using 10% aqueous hydrochloric acid gives 5. All compounds were confirmed by NMR, IR, DSC and elemental analysis. The carbon–nitrogen ratio is a very important indicator of detonation performance for ADWs. The smaller the carbon–nitrogen ratio (mass), the more energetic and effective the materials are.²⁰ Compounds 1 and 2 have the same carbon–nitrogen ratio of $C/N = 1.5$, while 3 is lower at $C/N = 1.0$. Compounds 4 and 5 have carbon–nitrogen ratios of $C/N = 0.75$ and 0.85 , respectively. Therefore, they are expected to be the most energetic. In the ^1H NMR spectrum, the methylene bridge resonates between 6.06 and 6.65 (s) ppm. In the ^{13}C NMR spectra, the peak assigned to the methylene bridge carbon is at 62–67 ppm and the chemical shift for C–I is at 86–110 ppm.

Crystallographic data and data collection parameters, bond lengths, and bond angles are given in the Supporting Information. Compounds 3 and 4 crystallize in the triclinic space group $P\bar{1}$, while 5 crystallizes in the tetragonal space group $P4_32_12$ (Figures 2–4).

Compound 3 is in a gauche conformation with the angles between the pyrazole rings along the C–C axis at $81.5(6)^\circ$. The dihedral angle between the mean planes through the tetrazole rings is $100.7(2)^\circ$. The nitro groups in 3 bonded to the pyrazole ring are not coplanar with an angle $(26.6(3)^\circ)$ due to steric hindrance. For 4 and 5, all the atoms of the fused tricyclic framework are nearly coplanar.

Impact sensitivity (IS) measurements were made by using standard BAM techniques.²² All the iodine-rich compounds

Scheme 1. Preparation of Compounds 1–5



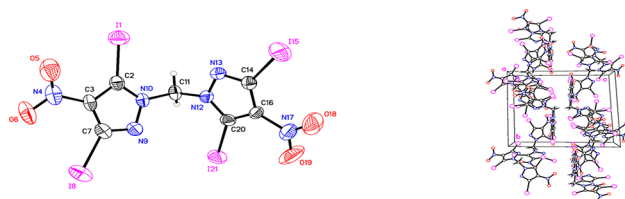


Figure 2. (a) Thermal ellipsoid plot (50%) and labeling scheme for **3**. (b) Ball-and-stick packing diagram of **3** viewed down the *b* axis. Dashed lines indicate strong hydrogen bonds.

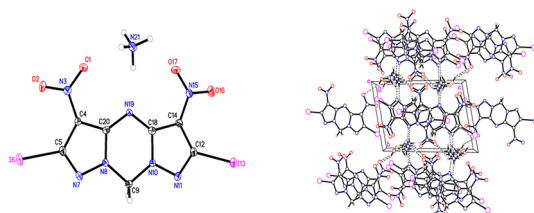


Figure 3. (a) Thermal ellipsoid plot (50%) and labeling scheme for **4**. (b) Ball-and-stick packing diagram of **4** viewed down the *b* axis. Dashed lines indicate strong hydrogen bonds.

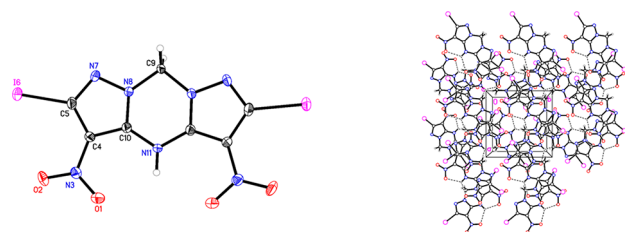


Figure 4. (a) Thermal ellipsoid plot (50%) and labeling scheme for **5**. (b) Ball-and-stick packing diagram of **5** viewed down the *b* axis. Dashed lines indicate strong hydrogen bonding.

have IS values ranging between 9 and 40 J. Compounds **1** and **2** are insensitive at 40 J. After introducing nitro groups, the impact sensitivity of **3** is found to be 11 J. Although **5** has a more stable fused tricyclic frame structure and a higher nitrogen content, it has an impact sensitivity (8 J) greater than **3**. This probably arises because of the higher nitrogen content and additional molecular strain and crystal packing of **5** (Table 1).

Heats of formation were calculated using the Gaussian 03 (Revision D.01) suite of programs.²³ For iodine-rich cations, the (15s, 11p, 6d) basis of Stromberg et al.²⁴ was augmented with another p shell and the five valence sp exponents optimized, resulting in a [5211111111, 411111111, 3111] contraction scheme in conjunction with 6-31+G** for first- and second-row elements. The heats of formation were

obtained by combining the MP2/6-311++G** energy difference for the reactions, the scaled zero-point energies (ZPE), values of thermal correction (HT), and other thermal factors. Compound **5** has the highest heat of formation (1192.69 kJ mol⁻¹). The heat of formation of **3** is larger than those of **1** and **2** due to introduction of nitro groups (976.87 kJ mol⁻¹). On the basis of the calculated values for heats of formation and experimental densities, the detonation velocities (*D_v*) and pressures (*P*) were obtained using Cheetah 7.0. Compared with 3,4,5-triiodopyrazole (TIPy) (Table 1), **3** and **5** have higher detonation pressures ranging from 17.31 to 21.48 GPa and higher detonation velocities from 4627 to 5834 m/s. With a detonation performance of 21.48 GPa: 5834 m/s, **5** approaches TNT (19.50 GPa: 6881 m/s). The decomposition products of the iodine-rich compounds are important in evaluating the ability to destroy or neutralize an active agent (Table 2). Given are the major detonation products of **1**–**3**

Table 2. Detonation Products: Cheetah 7.0 [wt% kg⁻¹]

comp	I ₂ (g)	N ₂ (g)	HI (g)	CH ₄ (g)	C (s)	CO ₂ (g)
1	84.21	6.20	0.06	0.88	8.64	
2	84.21	6.20	0.06	0.88	8.64	
3	67.74	11.33	0.92	1.05	7.31	11.86
5	49.67	19.49	0.80	2.36	10.18	17.48
TIPy	52.10	6.22	22.87			8.00

and **5** at STP (*T* = 298 K, *P* = 1 atm). On the basis of the detonation products, they are potential candidates to be effective bio agent-defeat materials because of the high percentage of I₂: **1** and **2** have markedly higher iodine concentrations at 84.21%, while **3** and **5** have iodine concentrations at 67.74 and 49.67%, respectively.

Thermal stability is a very important property for any energetic molecule. The thermal behavior of compounds **1**–**3** was determined with a differential scanning calorimeter (DSC) scans at a heating rate of 5 °C/min. Compounds **1** and **2** decompose at 264 and 351 °C (onset temperatures), respectively. After introducing the nitro groups, **3** has a good thermal stability, decomposing at 320 °C (onset temperature). Because of the fused tricyclic framework, **5** has an excellent thermal stability decomposing at 323 °C (Figure 5). Densities were measured using a gas pycnometer at 25 °C and found between 2.56–3.66 g cm⁻³. The replacement of an iodine atom with a nitro group leads to a decrease in density (Table 1). Compound **5** has a density of 2.56 g cm⁻³. If an ADW does not decompose completely upon heating or combustion, then there will be a reduced bactericidal effect. The DSC curve of **5** shows a sharp peak at 323 °C suggesting that **5** decomposed or

Table 1. Physicochemical Properties of Compounds 1–5

comp	<i>T_d</i> (°C) ^a	<i>d</i> (g/cm ³) ^b	Δ <i>H_f</i> ^o (kJ/mol) ^c	<i>D</i> (m/s) ^d	<i>P</i> (GPa) ^e	iodine (%)	OB (%) ^f	IS (J) ^g
1	264	3.60	536.59	2670	4.34	84.27	−14	>40
2	351	3.66	520.71	2766	4.76	84.27	−14	>40
3	320	2.94	976.87	4625	17.31	68.44	−8	11
5	323	2.56	1192.69	5834	21.48	50.46	−14	9
TIPy ¹⁶	272	3.38	461.1	2859	5.32	85.4	−12	>40
TNT ¹⁷	295	1.65	−31.7	6881	19.5	0	−25	15

^aDecomposition temperature (onset). ^bMeasured density at 25 °C. ^cCalculated heat of formation. ^dDetonation velocity, CHEETAH 7. ^eDetonation pressure, CHEETAH 7. ^fOxygen balance C_aH_bO_cN_dI_e: OB = 1600(*c* − *b*/2 − *a*)/MW. ^gImpact sensitivity measured via BAM method.

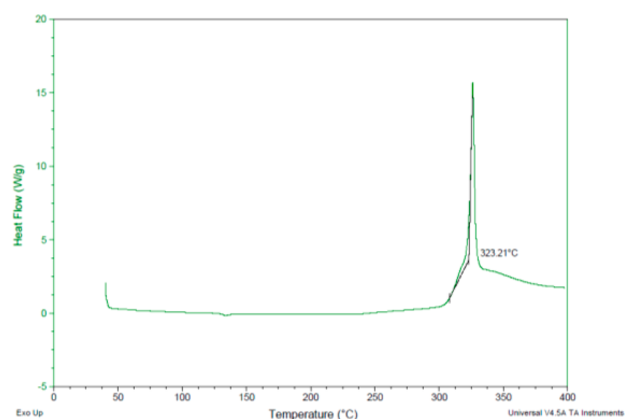


Figure 5. DSC curve of **5**.

combusted completely. Therefore, **5** may have the potential to be an excellent ADW.

In order to determine the qualitative biocidal capability of **5**, a modified method to test this property of these materials based on a reported procedure was used.²⁰ We chose skin surface and airborne bacteria (may contain *B. subtilis* and *Staphylococcus aureus*, *Salmonella*, etc.) to simulate a real environment since there are many different kinds of bacteria in the actual environment and since iodine is a broad-spectrum bactericide. In order to better understand the bactericidal effect of iodine, *Escherichia coli* representing Gram-negative bacteria and *S. aureus* representing Gram-positive bacteria were chosen since these bacteria are widely distributed on the earth and they are readily available. Methicillin-resistant *S. aureus* is often referred to as a “superbug”,²⁵ and *B. anthracis* also belongs to the Gram-positive bacteria group.

In a 25 mL round-bottomed flask, **5**, 10, 25, or 50 mg of iodine-rich **5** was decomposed by heating at about 400 °C for ~3 min. The flask was cooled to room temperature in a water

bath, and 5 mL of deionized water was added. This mixture was poured onto a culture medium (lysogeny broth (LB), a nutritionally rich medium, primarily used for the growth of bacteria, and agar) that was coated with bacteria (mixed bacteria, *E. coli* or *S. aureus*, labeled as a–d, separately). The blank test (BL) was run by pouring 5 mL of deionized water onto the culture medium that was coated with bacteria. Because ADWs deal with microorganisms in air, water, and topsoil in the infected zone, carrying out the biotest at 25 °C is reasonable. The antibacterial activity experiment was incubated at 25 °C for 13 days and then evaluated. In Figures 6–8, BL and a–d correspond to the blank test and the decomposition products of **5**, 10, 25, and 50 mg of **5**, respectively. Carbon produced during decomposition (black spot) is seen in a–d.

In Figure 6, BL1 shows the growth of *S. aureus* from 24 h. From a1–a5, b1–b5, c1–c5, d1–d5 in Figure 6, even treated with decomposition products of 5 mg of (a1–a5), no colony of *S. aureus* can be seen for more than 13 days. Therefore, it can be seen that the decomposition products of **5** have very good antibacterial activity against Gram-positive bacteria.

In Figure 7, from BL2, *E. coli* covers the entire medium, and the medium becomes cloudy because of its growth after 96 h. As in Figure 6, treating *E. coli* with decomposition products of different amounts of **5**, a1–a5, b1–b5, c1–c5, and d1–d5 in Figure 7 show a very good bactericidal effect, and no colony of *E. coli* can be seen for more than 13 days. This indicates the decomposition products of **5** have very good antibacterial activity against Gram-negative bacteria.

In Figure 8, coating mixed bacteria after 72 h, BL3 shows that the growth of mixed bacteria starts after 96 h. For a–d, after 312 h (13 days), a1–a5, b1–b5, c1–c5, and d1–d5 show that the exposed bacteria do not survive in the culture medium. It can be seen that the decomposition products of **5** kill almost all microorganisms in air and surface soil in the infected zone. From the biotest, after decomposition of **5**, all microorganisms appear to have been killed effectively and the environment was

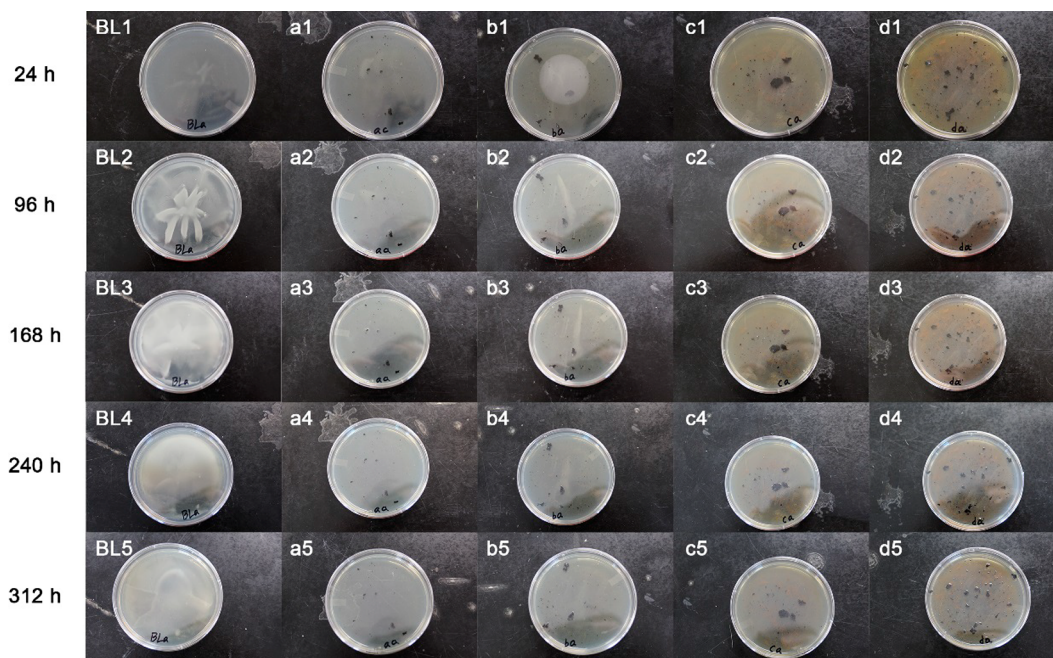


Figure 6. Comparison [312 h (13 days) after treatment] of the treatment of *S. aureus* with decomposition products of different amounts of **5** (BL: blank test, a: 5 mg, b: 10 mg, c: 25 mg, d: 50 mg).

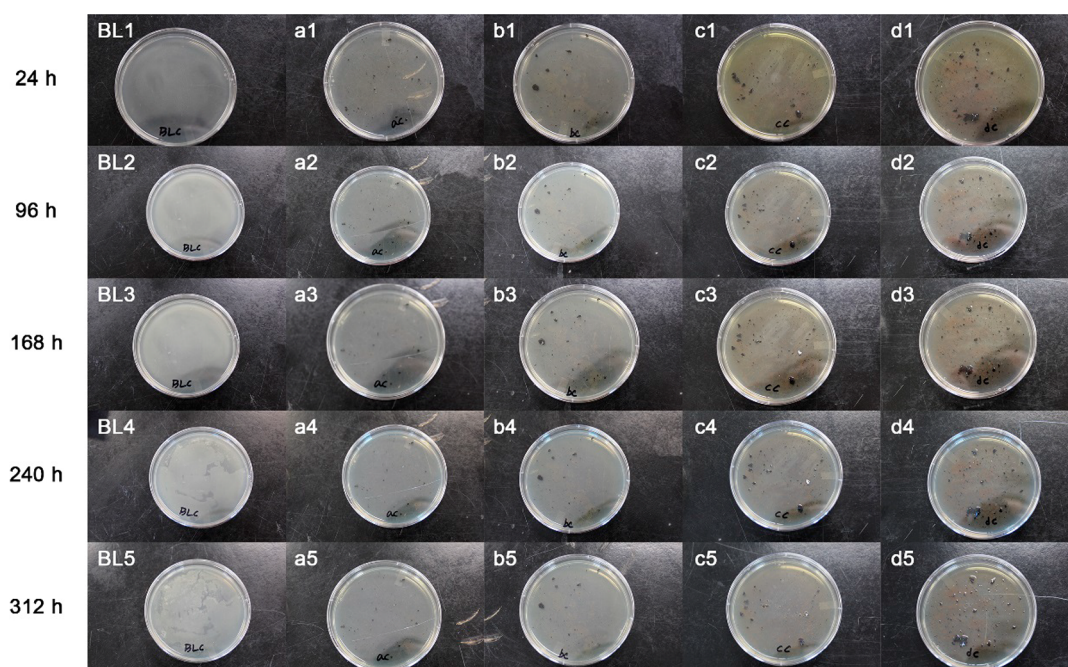


Figure 7. Comparison [312 h (13 days) after treatment] of the treatment of *E. coli* with decomposition products of different amounts of **5** (BL: blank test, a: 5 mg, b: 10 mg, c: 25 mg, d: 50 mg).

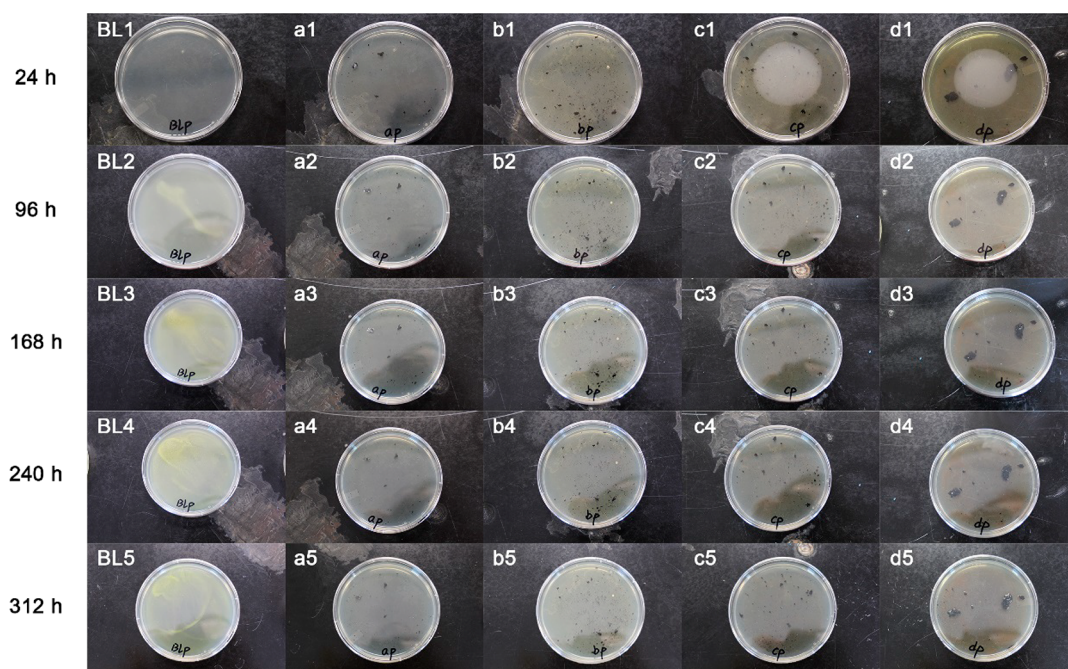


Figure 8. Comparison [312 h (13 days) after treatment] of the treatment of skin surface bacteria and airborne bacteria (may contain *B. subtilis*, *S. aureus*, *Salmonella*, etc.) with decomposition products of different amounts of **5** (BL: blank test, a: 5 mg, b: 10 mg, c: 25 mg, d: 50 mg).

kept clean for more than 13 days. As an ADW, **5** may control areas of outbreak of any epidemic and effectively reduce the risk of cross infection for affected areas of people and animals as well as medical staff. From the biotest, it is seen that the decomposition products of 5 mg of **5** might control an area of one plate (about 63 cm²). Assuming an outbreak or attack by biological weapons in a big city (100 km²), about 79.4 tons of **5** would be required as an ADW to annihilate most of the microorganisms in air, water and topsoil in the infected zone.

In an infected zone treated with ADWs, the residual amount of biocide would be a very important index for determining whether compounds as ADWs are good or bad. If the compounds are to be useful as Agent Defeat Weapons, the quantity of released biocide after decomposition must be a small amount with low toxicity, decomposition or biological metabolism last for a short time, and not cause long-term environmental pollution. Studies concerning residual biocides released after decomposition or combustion of ADWs have rarely been reported. Iodine-rich compounds are excellent

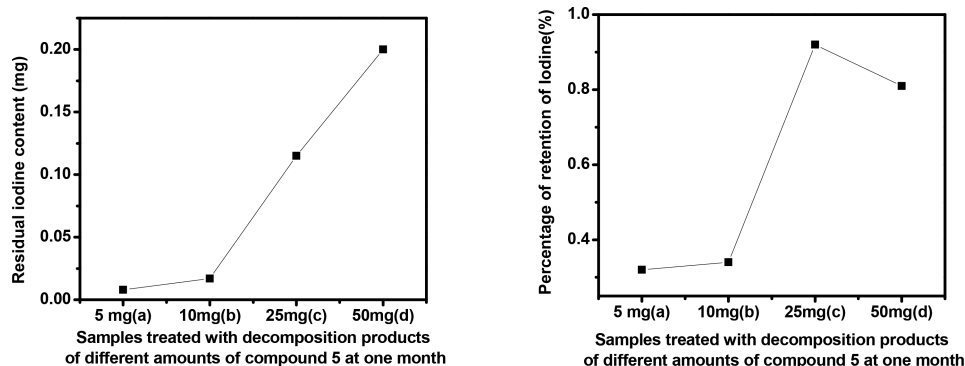


Figure 9. Residual iodine content of culture-media treated with decomposition products of different amounts of **5** (left) and percentage of retention of I₂ in the media after one month (right).

ADWs due to the iodine released upon decomposition or combustion. Iodine is volatile and undergoes redox reactions but does not cause substantial environmental pollution. In our work, the amount of residual iodine was characterized by using a reported UV spectrophotometric method (Supporting Information).²⁶ The iodine remaining on the media treated with decomposition products of **5** after one month had decreased to 0.008 mg (a: 5 mg), 0.017 mg (a: 10 mg), 0.115 mg (a: 25 mg), and 0.200 mg (a: 50 mg) (Figure 9). From Table 2, the amount of I₂ released after decomposition or combustion of **5** is 49.67% which says 2.5 mg of I₂ is obtained when 5 mg of **5** is decomposed and so on. Therefore, the percentages of retention of I₂ on the media after one month are 0.32% (a), 0.34% (b), 0.92% (c), and 0.81% (d), respectively which indicates that the quantity of residual iodine is so low after one month in the affected areas that there will be no deleterious effects on humans.

3. CONCLUSION

Compound **5** (2,6-diiodo-3,5-dinitro-4,9-dihydrodipyrzolo-[1,5-*a*:5',1'-*d*][1,3,5]triazine) was synthesized and characterized. The structures of three iodo compounds, **3–5**, were determined by single crystal X-ray diffraction. Compound **5** has a high density and iodine content and good detonation properties ($P = 21.48$ GPa; $D_v = 5834$ m/s) approaching TNT ($P = 19.50$ GPa; $D_v = 6881$ m/s), all of which suggest it as a candidate as an ADW. With a sharp peak at 323 °C in the DSC scan, **5** is likely combusted or decomposed at that temperature. Because of the polycyclic dipyrzolo-1,3,5-triazine backbone, there are several advantages in density, planarity, molecular stability, and energetic performance. From the biotest, after decomposition of **5**, all microorganisms in air, water, and topsoil would have apparently been killed effectively, and the environment remained uncontaminated for more than 13 days. After 1 month, the residual iodine on the medium treated with decomposition products of **5** has decreased to very low levels indicating that there would likely be no deleterious effects on living things from the iodine and pathogenic microorganisms.

4. EXPERIMENTAL SECTION

4.1. General Methods. Reagents were purchased from Aldrich and Acros Organics and were used as received. ¹H₂ and ¹³C spectra were recorded on a 300 MHz (Bruker AVANCE 300) nuclear magnetic resonance spectrometer operating at 300.13 and 75.48 MHz, respectively. DMSO-*d*₆ was used as solvent and locking solvent. Chemical shifts in the ¹³C spectra are reported relative to Me₄Si. The melting and decomposition points were obtained with a differential

scanning calorimeter (TA Instruments Co., model Q2000) at a heating rate of 5 °C/min. IR spectra were recorded using KBr pellets for solids on a BIORAD model 3000 FTS spectrometer. Densities were determined at 25 °C by employing a Micromeritics AccuPyc 1340 gas pycnometer. Elemental analyses were carried out using an Exeter CE-440 elemental analyzer. Impact sensitivity measurements were made using a standard BAM Fallhammer. The residual iodine amount was characterized by a reported UV spectrophotometric method²⁶ for content determination of iodine using a VWR spectrophotometer UV-3100PC UV-vis. Potassium iodate (5.0×10^{-5} mol/L), potassium iodide (2.5×10^{-3} mol/L), starch (0.5%), sulfuric acid (1.0 mol/L), and distilled water were used. A wavelength of 575 nm was chosen as the maximum absorption. The cell length was 1 cm.

Caution! Although no explosions or hazards were observed during the preparation and handling of these compounds, all the compounds investigated are potentially explosive materials. Mechanical actions involving scratching or scraping must be avoided. In addition, all of the compounds must be synthesized only on a small scale. Manipulations must be carried out in a hood behind a safety shield. Eye protection and leather gloves must be worn at all times.

4.2. Bis(2,4,5-triiodo-1H-imidazol-1-yl)methane (1). To a solution of the sodium salt of 3,4,5-triiodopyrazole (936 mg, 2 mmol) in acetonitrile (20 mL) was added diiodomethane (268 mg, 1 mmol), and the reaction was maintained at 80 °C for 4 h. After cooling, the mixture was poured into cold water (40 mL), the off-white precipitate obtained was filtered, washed with water (3 mL), and dried in the air to give 812 mg of an off-white solid. Yield: 90%; $T_{d(onset)}$ = 264 °C; ¹H NMR (300 MHz, DMSO-*d*₆, δ): 6.16 (s, 2H); ¹³C NMR (75 MHz, DMSO-*d*₆, δ): 100.97, 97.87, 99.68, 86.79, 65.30 ppm; IR (KBr): $\nu = 1452$ (m), 1380 (s), 1360 (m), 1320 (s), 1273 (m), 1208 (s), 1175 (m), 1085 (m), 996 (m), 938 (m), 789 (m), 761 (m), 651 (m), 615 (w), 481 (w), 425 cm⁻¹ (m); Anal. Calcd for C₇H₂I₆N₄ (903.45): C 9.31, H 0.22, N 6.20. Found: C 9.40, H 0.27, N 6.21.

4.3. Bis(3,4,5-triiodo-1H-pyrazol-1-yl)methane (2). To a solution of the sodium salt of 3,4,5-triiodopyrazole (936 mg, 2 mmol) in acetonitrile (20 mL) was added diiodomethane (268 mg, 1 mmol), and the reaction was maintained at 80 °C for 4 h. After cooling, the mixture was poured into cold water (40 mL), and the white precipitate was filtered, washed with water (3 mL), and dried in the air to give 857 mg white solid. Yield: 95%; $T_{d(onset)}$ = 351 °C; ¹H NMR (300 MHz, DMSO-*d*₆, δ): 6.49 (s, 2H); ¹³C NMR (75 MHz, DMSO-*d*₆, δ): 110.89, 100.14, 89.20, 67.65 ppm; IR (KBr): $\nu = 1534$ (w), 1435 (s), 1408 (m), 1380 (m), 1366 (m), 1297 (s), 1230 (m), 1147 (w), 1039 (w), 1011 (s), 978 (m), 946 (w), 765 (m), 647 (w), 506 (w), 477 (w), 416 cm⁻¹ (w); Anal. Calcd for C₇H₂I₆N₄ (903.45): C 9.31, H 0.22, N 6.20. Found: C 9.39, H 0.26, N 6.24.

4.4. Bis(3,5-diiodo-4-nitro-1H-pyrazol-1-yl)methane (3). Compound **2** (903 mg, 2 mmol) was added to 100% nitric acid (4 mL), and the reaction mixture was stirred at room temperature for 12 h and then poured into cold water (60 mL). The yellowish brown

precipitate was filtered, washed with water (30 mL), and dried in air to obtain 518 mg. Yield: 70%; $T_{d(onset)} = 320\text{ }^{\circ}\text{C}$; ^1H NMR (300 MHz, $\text{DMSO}-d_6$, δ): 6.65 (s, 2H); ^{13}C NMR (75 MHz, $\text{DMSO}-d_6$, δ): 140.28, 99.32, 95.93, 67.28 ppm; IR (KBr): $\nu = 3433$ (w), 3035 (w), 2814 (w), 1757 (w), 1600 (w), 1517 (s), 1441 (m), 1391 (m), 1376 (s), 1348 (s), 1315 (m), 1129 (w), 1070 (m), 1040 (w), 999 (w), 954 (w), 834 (w), 773 (w), 756 (w), 586 cm^{-1} (w); Anal. Calcd for $\text{C}_7\text{H}_2\text{I}_4\text{N}_6\text{O}_4$ (741.63): C 11.33, H 0.27, N 11.33. Found: C 11.45, H 0.341, N 11.45.

4.5. Ammonium 2,6-Diiodo-3,5-dinitro-9H-dipyrzolo[1,5- α :5',1'- d][1,3,5]triazin-4-ide (4). Compound 3 (741 mg, 1 mmol) was dissolved in 10 mL of DMSO and aqueous ammonia (10 mL) was added slowly at room temperature. Then the mixture was heated at $120\text{ }^{\circ}\text{C}$ in a sealed tube. After 8 h, the mixture was cooled to room temperature and was blown dry by air. Water (30 mL) was added to the system giving rise to an orange-red precipitate. It was filtered, washed with cold water, and dried in vacuo to obtain 370 mg of orange-red solid. Yield: 70%; $T_{d(onset)} = 325\text{ }^{\circ}\text{C}$; ^1H NMR (300 MHz, $\text{DMSO}-d_6$, δ): 7.08 (s, 4H), 6.06 (s, 2H); ^{13}C NMR (75 MHz, $\text{DMSO}-d_6$, δ): 145.56, 120.83, 98.04, 62.14 ppm; IR (KBr): $\nu = 3420$ (w), 3216 (w), 3114 (w), 1525 (s), 1505 (s), 1451 (s), 1436 (s), 1368 (s), 1315 (m), 1216 (m), 1130 (m), 1085 (m), 1024 (m), 996 (m), 946 (m), 891 (w), 811 (w), 770 (m), 761 (w), 715 (w), 630 (w), 414 (w), 403 cm^{-1} (w); Anal. Calcd for $\text{C}_7\text{H}_6\text{I}_2\text{N}_8\text{O}_4\cdot\text{DMSO}$ (569.84): C 18.07, H 2.02, N 18.73. Found: C 18.24, H 1.926, N 18.88.

4.6. 2,6-Diiodo-3,5-dinitro-4,9-dihydrodipyrzolo[1,5- α :5',1'- d][1,3,5]triazine (5). To an ice-cold aqueous solution of hydrochloric acid (1 M, 5 mL), compound 4 (300 mg 0.57 mmol) was added slowly, while the reaction temperature was maintained at $0\text{--}5\text{ }^{\circ}\text{C}$. The final suspension was stirred at $0\text{--}5\text{ }^{\circ}\text{C}$ for 30 min and was filtered. The pale yellow solid was washed with water and dried in vacuum to yield 240 mg of compound 5. Yield: >95%; $T_{d(onset)} = 323\text{ }^{\circ}\text{C}$; ^1H NMR (300 MHz, $\text{DMSO}-d_6$, δ): 6.38 (s, 2H); ^{13}C NMR (75 MHz, $\text{DMSO}-d_6$, δ): 135.39, 121.10, 97.83, 62.47 ppm; IR (KBr): $\nu = 3374$ (w), 1613 (m), 1585 (s), 1496 (s), 1480 (m), 1321 (m), 1286 (s), 1239 (m), 1112 (m), 1099 (m), 1035 (w), 892 (m), 817 (w), 775 (w), 760 (w), 716 (w), 627 (w), 617 (w), 524 cm^{-1} (w); Anal. Calcd for $\text{C}_7\text{H}_3\text{I}_2\text{N}_7\text{O}_4$ (502.83): C 16.72, H 0.60, N 19.49. Found: C 16.42, H 0.69, N 19.12.

■ ASSOCIATED CONTENT

● Supporting Information

The Supporting Information is available free of charge on the ACS Publications website at DOI: 10.1021/acs.inorgchem.8b01600.

X-ray crystal diffraction data and crystal structures for compounds 3, 4- CH_3OH , and 5; isodesmic reactions; titration curve (PDF)

Accession Codes

CCDC 1834212 and 1834214–1834215 contain the supplementary crystallographic data for this paper. These data can be obtained free of charge via www.ccdc.cam.ac.uk/data_request/cif, or by emailing data_request@ccdc.cam.ac.uk, or by contacting The Cambridge Crystallographic Data Centre, 12 Union Road, Cambridge CB2 1EZ, UK; fax: +44 1223 336033.

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Notes

The authors declare no competing financial interest.

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