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New Promises from an Old Friend: Iodine-Rich Compounds as Prospective Energetic Biocidal Agents

Jinjie Chang,[‖] Gang Zhao,[‖] Xinyuan Zhao, Chunlin He,* Siping Pang,* and Jean'ne M. Shreeve*

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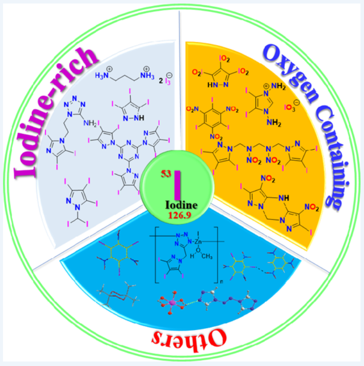

CONSPECTUS: For a very long time, frequent occurrences of biocrises have wreaked havoc on human beings, animals, and the environment. As a result, it is necessary to develop biocidal agents to destroy or neutralize active agents by releasing large amounts of strong biocides which are obtained upon detonation. Iodine is an efficient biocidal agent for bacteria, fungi, yeasts, viruses, spores, and protozoan parasites, and it is the sole element in the periodic table that can destroy microbes without contaminating the environment. Based on chemical biology, the mechanism of iodine as a bactericide may arise from oxidation and iodination reactions of cellular proteins and nucleic acids. However, because of the high vapor pressure causing elemental iodine to sublime readily at room temperature, it is inconvenient to use this material in its normal solid state directly as a biocidal agent under ambient conditions. Iodine-rich compounds where iodine is firmly bonded in molecules as a C—I or I—O moiety have been observed to be among the most promising energetic biocidal compounds. Gaseous products comprised of large amounts of iodine or iodine-containing components as strong biocides are released in the decomposition or explosion of iodine-rich compounds. Because of the detonation pressure, the iodine species are distributed over a large area greatly improving the efficacy of the system and requiring considerably less effort compared to traditional biocidal methods. The commercially available tetraiodomethane and tetraiodoethene, which possess superb iodine content also have the disadvantages of volatility, light sensitivity, and chemically reactivity, and therefore, are not suitable for use directly as biocidal agents. It is absolutely critical to synthesize new iodine-rich compounds with good thermal and chemical stabilities.

In this Account, we describe our strategies for the syntheses of energetic iodine-rich compounds while maintaining the maximum iodine content with concomitant stability and routes for the synthesis of oxygen-containing iodine-rich compounds to improve the oxygen balance and achieve both high-energy and high-iodine content. In the other work, which involves cocrystals, iodine-containing polymers were also summarized. It is hoped that this Account will provide guidelines for the design and syntheses of new iodine-rich compounds and a route for the development of inexpensive, more efficient, and safer iodine-rich antibiological warfare agents of the future.

KEY REFERENCES

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- Zhao, G.; He, C.; Kumar, D.; Hooper, J. P.; Imler, G. H.; Parrish, D. A.; Shreeve, J. M. 1,3,5-Triiodo-2,4,6-trinitrobenzene (TITNB) from benzene: Balancing performance and high thermal stability of functional energetic materials. *Chem. Eng. J.* **2019**, *378*, 122119.[2] TITNB, which was synthesized in a two-step reaction from benzene, exhibiting a high density (3.057 g cm^{-3}), high decomposition temperature of 367 °C, an iodine content of 64.44%, and calculated detonation properties approaching that of trinitrotoluene (TNT).
- Zhang, J.; Hooper, J. P.; Zhang, J.; Shreeve, J. M. Well-balanced energetic cocrystals of H_5IO_6/HIO_3 achieved by a small acid−base gap. *Chem. Eng. J.* **2021**, *405*, 126623.[3] The formation of cocrystals using commercially available iodine-containing acids (H_5IO_6/HIO_3) and weakly basic energetics gives a simple and efficient route to achieve energetic biocidal agents.

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- Zhang, J.; Zhu, Z.; Zhou, M.; Zhang, J.; Hooper, J. P.; Shreeve, J. M. Superior High-Energy-Density Biocidal Agent Achieved with a 3D Metal−Organic Framework. *ACS Appl. Mater. Interfaces* **2020**, *12*, 40541−40547.[4] The utilization of an easily coordinated IO_3 anion with metal forming 3D MOFs to exchange with $[Cu(atrz)_3(NO_3)_2]_n$ (atrz = 4,4′-azo-1,2,4-triazole) gives novel 3D MOFs with superior detonation performance combined with excellent biocidal effects.

1. INTRODUCTION

During winter 2019, the entire world suffered from a new corona virus disease (COVID-19) with millions of people being infected. Even more painful was that hundreds of thousands of people have died in this COVID-19 pandemic. The history of human society tells that hundreds of millions of people have died in epidemics. Over these many years, human health has been threatened by bacteria, viruses, and toxins, such as plague, smallpox, cholera, and more recently, SARS, bird flu, and Ebola viruses. Therefore, the development of effective biocidal agents has become an urgent problem crying out for solutions. Some representative virus structures are shown in Figure 1.

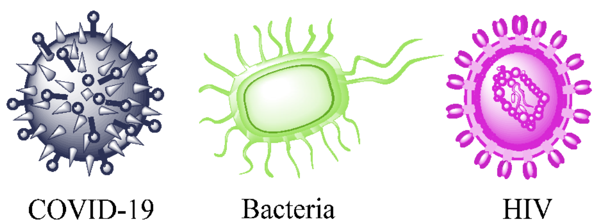

Figure 1. Some representative structures of bacterium and viruses.

Humankind has a long history of using disinfectants as an important way to prevent the invasion of bacteria and viruses and to protect health of living things. Because of their high-efficiency and broad-spectrum characteristics, halogen-containing fungicides have attracted extensive attention from researchers everywhere. Chlorine-containing disinfectants have the advantages of simple synthetic processes, low prices and strong killing ability. HF performs a better biocidal activity, 200 ppm of HF can destroy most bacteria, including Anthrax spores in 5 min. However, their potential toxicity, instability and causticity limit their applications. Iodine is the only element in the periodic table that will kill microbes without contaminating the environment. Iodine can penetrate the cell wall of microorganisms rapidly and react with cellular nucleic acids and S−H groups of the amino acids, which play important factors in the synthesis of proteins. Eventually, the structure of bacteria and viruses is disordered, leading to their inactivation and death. The use of iodine as a disinfectant to the destruction of certain bacteria, amoebic cysts, and viruses (a 99.999% kill in 10 min at 25 °C) only require I_2 concentrations of 0.2, 3.5, and 14.6 ppm, respectively.[5] However, because of its high vapor pressure, solid iodine sublimes easily at room temperature, and therefore, it is not convenient to be used neat directly as a biocidal agent. When the threat of highly pathogenic and highly infectious bacteria and viruses, such as the coronavirus disease 2019 (COVID-19), SARS, H7N9, etc., are being fought, it is often inefficient, limited, and not convenient to use traditional disinfectants to destroy them. Since these methods are difficult to implement for large-scale killing over a short time, it is necessary to find new ways to solve the threat of harmful microorganisms to humans.

To solve this problem, the development of agent defeat weapons (ADWs), which can be used to destroy or neutralize active agents by releasing large amounts of strong biocides after detonation of an explosive device, has been proposed.[5−8] Iodine-rich compounds are a class of compounds with an iodine content higher than 50%, where the iodine is stabilized in molecules by the formation of C−I or I−O bonds or as iodide. Through the combustion or explosion of an iodine-rich compound itself or the composite of iodine-rich compounds with energetic content, the biocide (mainly iodine) is released to achieve the destruction of bacteria and viruses in the environment. This kind of material can not only address the elimination of a wide range of viruses and improve the efficiency of killing organisms, but it also solves the problems of sublimation and instability inherent in elemental iodine. It is an effective weapon for inhibiting rapidly spreading bacterial viruses.

This Account summarizes the recent strategies from our group to tune the energetic and biocidal properties of iodine-rich compounds and directions to synthesize novel iodine-rich compounds. Development of more efficient and safer iodine-rich anti-biological warfare agent formulations is proposed.

2. SYNTHESES OF IODINE-RICH COMPOUNDS

For a very long time, frequent occurrences of biocrises have wreaked havoc on human beings, animals, and the environment. As a result, it is necessary to develop biocidal agents to destroy or neutralize active agents by releasing large amounts of strong biocides, which are obtained upon detonation. On the basis of the chemical biology, the mechanism of iodine as a bactericide may arise from oxidation and iodination reactions of cellular proteins and nucleic acids.[9] Because of 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. As shown in Figure 2, introduction of the C−I bond into a variety of moieties or salts, which contain the triiodide ion, leads to an iodine content in iodine-rich compounds as high as 97.69%. The commercially available tetraiodomethane and tetraiodoethene possess superb iodine content, but they are volatile, light sensitive, and chemically reactive, and therefore, not suitable to be used in formulations.[10] It is critical to synthesize new iodine-rich compounds with good thermal and chemical stabilities. Much research effort has been devoted to the syntheses of energetic iodine-rich compounds while maintaining the maximum iodine content with concomitant stability.

Iodine content and energy level are two key factors in evaluating biocidal agents. Increasing the iodine content can markedly improve the proportion of effective bactericidal components in the explosion or decomposition products, while concomitantly reducing their energy. An increase in the number of nitrogen atoms enhances the heat of formation, and therefore, the energy level of the biocidal agent. More nitrogen atoms in the molecule gives rise to fewer positions for substitution for iodination which results in the decrease of the iodine content. Among the iodine-rich compounds that have been studied, mostly use pyrazole, imidazole, triazole, and other energetic skeletons, which are also often utilized as skeletons in energetic materials.

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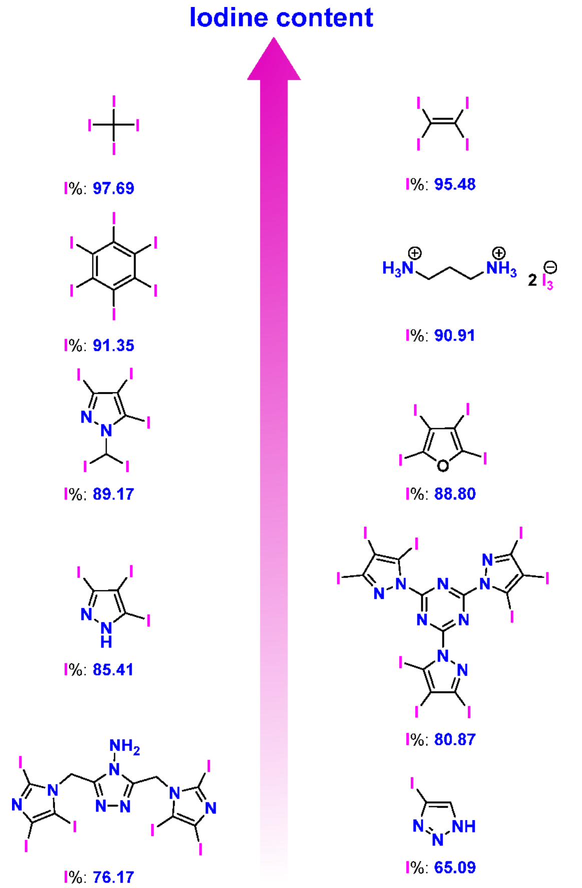


Figure 2. Selected iodine-rich compounds.

2.1. Neutral Iodine-Rich Compounds

In 2013, iodine-rich azole compounds were suggested as biocidal agents for the first time by our group.[11] Compounds with various iodine content, for instance, 4-iodo-1*H*-pyrazole (**1**) (I = 65.42%), 3,4-diiodo-1*H*-pyrazole (**2**) (I = 79.35%), 3,4,5-triiodo-1*H*-pyrazole (**3**) (I = 85.41%),[11] tris(4,5-diiodoimidazolyl)-2,4,6-triazine (**6**) (I = 73.59%), tris(3,4,5-triiodopyraolyl)-2,4,6-triazine (**7**) (I = 80.87%),[12] 2,3,4,5-tetraiodofuran (**8**) (I = 88.80%), and 2,3,4,5- tetraiodo-1H-pyrrole (**9**) (I = 89.00%), were synthesized using different iodination reactions (Figure 3). Although tetraiodofuran and tetraiodopyrrole possess high iodine content, their preparation procedures involve the use of large amounts of toxic and expensive mercuric acetate which is not environmentally friendly and not economical for industrial scale syntheses (Scheme 1).

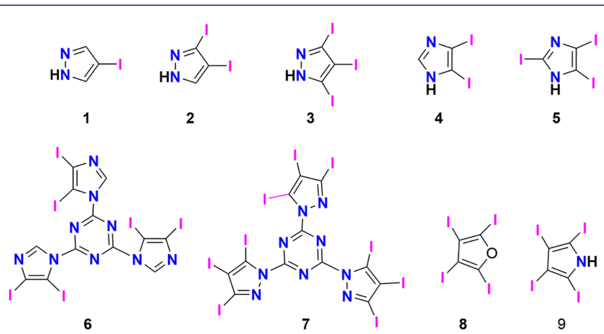
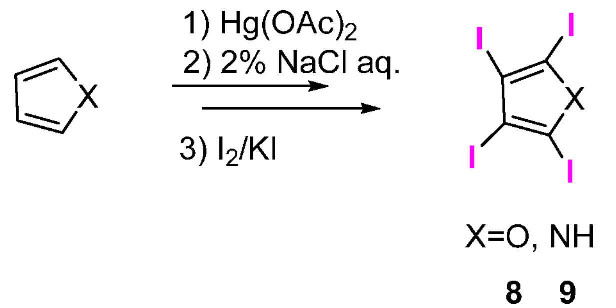


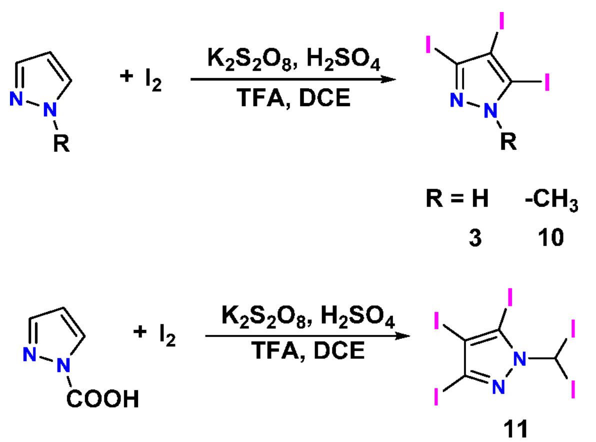
Figure 3. Structures of iodine-rich compounds **1**−**9**.

Scheme 1. Syntheses of Tetraiodofuran (8) and Tetraiodopyrrole (9)



In 2015, we optimized the iodination method by adding potassium persulfate, sulfuric acid and trifluoroacetic acid to a mixture of iodine and substrate in dichloroethane via a one-pot method.[13] By employing this method, some iodine-rich compounds were synthesized, such as compounds **3** and **10**, which were prepared in one step with good yields (Scheme 2). 1-

Scheme 2. Preparing Iodine-Rich Compounds Using a One Pot Method



Diiodomethyl-3,4,5-triiodopyrazole (**11**) with an iodine content of 89.17% was synthesized by using pyrazole-1-acetic acid as the starting material and reacted with a mixture of iodine, potassium persulfate, sulfuric acid and trifluoroacetic acid in dichloroethane in one-pot (Scheme 2).[13] In addition, compounds with more iodine atoms in one molecule, such as 4,5,6,7-tetraiodo-1*H*-benzimidazole (**16**) and tris(3,4,5-triiodopyrazolyl)-1,3,5-benzene (**18**), which has nine iodine atoms in a single molecule were synthesized in one step (Figure 4). In follow-up studies, compounds **12**−**17** using different precursors were synthesized via a one-pot method, which verified the universality of this method.[14]

For designing iodine-containing compounds with high iodine content and good thermal stability, we proposed the syntheses of materials with bridges.[15−18] This method not only maintains the iodine content but also improves the thermal stability. In 2016, a series of methylene- and ethylene-bridged 4,5-diiodoimidazoles (**19** and **20**) through the reaction of 4,5-diiodoimidazoles with dihaloalkanes was prepared successfully (Scheme 3).[19] The introduction of methylene and ethylene bridges not only provides a new method for the syntheses of iodine-rich energetic compounds, but also maintains a high iodine content (about 80%), and improves their thermal stability. The same method was employed to synthesize iodine-rich energetic compounds

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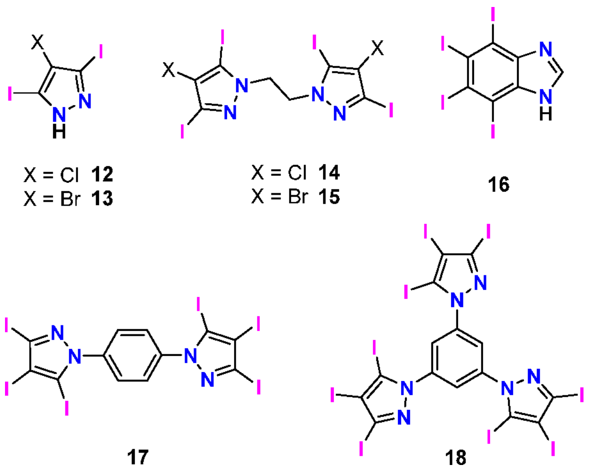
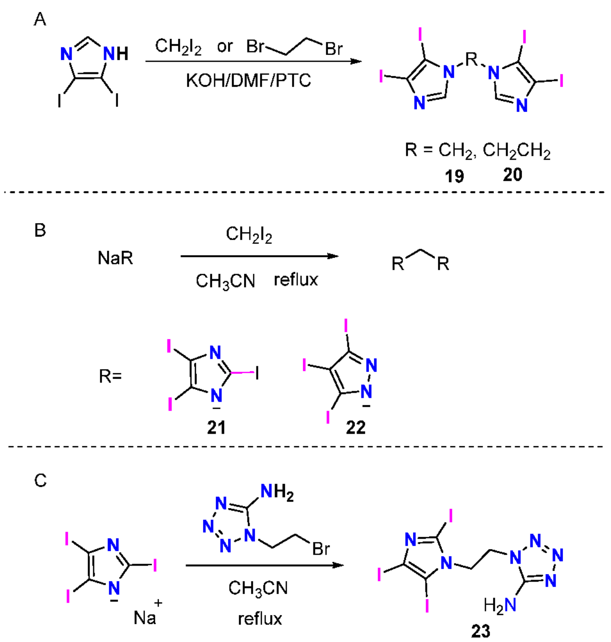


Figure 4. Iodine-rich compounds prepared by "one pot" method.

Scheme 3. *N,N′*-Bridged Iodine Compounds



that are methylene-bridged 2,4,5-triiodoimidazoles (**21**) and methylene-bridged 3,4,5-triiodopyrazoles (**22**).[19]

In the syntheses of iodine-rich compounds with high bactericidal efficiency, iodine content has always been an important factor. We developed a new strategy to synthesize compounds with high iodine content and high enthalpy of formation.[20] The *N,N′*-ethylene-bridged polyiodoazole compounds were synthesized by connecting polyiodopyrazole or imidazole and aminotetrazole rings (**23**).

The triazole ring with the same number of iodine atoms has a higher enthalpy of formation and better detonation performance than that of imidazole or pyrazole. Therefore, an improved iodination method that used the triazole ring as the precursor and iodine chloride as the iodine reagent to synthesize the triazole iodine-rich compounds **24** and **25** was developed (Scheme 4).[12]

These iodination methods have been improved continuously providing simpler ways for the introduction of iodine atoms into energetic molecules. Similarly, in 2019, we linked 4*H*-1,2,4-triazol-4-amine with a triiodopyrazole or triiodimidazole ring using a bridging reaction (Scheme 4),[21] and obtained compounds **26** and **27** with higher iodine content (76.32%). These compounds have high iodine content and good detonation properties, which are more suitable for iodine-rich biocidal agents.

2.2. Iodine-Rich Salts

Salts have the characteristics of low vapor pressure, good thermal stability, and adjustable anion and cation types. Therefore, it is possible to meet the requirements of different energy and sterilization efficiency by adjusting the type of iodine-containing anions and cations.

In 2014, a variety of aliphatic iodide-containing salts **28−50** (Scheme 5) were synthesized by our group,[22] which were characterized by using quaternary ammonium salt as cations and using I^-, I_3^-, I_5^-, etc., as anions. In addition, I_3^-, I_5^-, and I_8^{2-} are generated by adding elemental iodine to an aqueous I^- solution. Salts **28−50** have high iodine content, with salt **30** having an iodine content of 90.91%. However, the cations of such compounds lack energetic groups or positions available for substitution by such groups, resulting in an imbalance of energy and iodine content for the entire compound. For example, the theoretical detonation velocity of salt **30** with the highest iodine content is only 1800 m s^{-1}, and the detonation pressure is 2.28 GPa. The theoretical detonation velocity of salt **40** is 4610 m s^{-1}, and the denotation pressure is 10.05 GPa, but the iodine content is only 62%.

As shown in Table 1, the iodine content of CHNI compounds easily reaches above 70%, but the energy level is low. Although their density increases with the increase of iodine content, the energy level decreases as the iodine content improves. The theoretical detonation velocity of most of the current known compounds is 1800−3500 m·s^{-1}, and the theoretical detonation pressure usually falls between 2−8 GPa. Such materials require adding additional oxidizers and energetic components to further increase their oxygen balance and energy level for practical applications.

3. SYNTHESIS OF OXYGEN-CONTAINING IODINE-RICH COMPOUNDS

The introduction of an oxygen-containing group into an iodine-rich compound can improve the oxygen balance of the compound effectively. When the oxygen balance of the oxygen-containing iodine-rich compound approaches zero, it has the potential to be used directly as an agent defeat weapon (ADWs) charge as a single component. When the oxygen balance is positive, the compound has the potential to be used as an oxidant for ADWs charge by combining with other negative oxygen balanced iodine-rich compounds.

3.1. Synthesis of Iodyl Compounds

The iodyl group ($-IO_2$) is an attractive functional group, which possesses a structure similar to that of the nitro moiety and which can be readily prepared by oxidizing the corresponding iodo compound. The conversion of an iodo group into an iodyl substituent is an efficient way to improve the oxygen balance for iodine-rich compounds. In 2013, six iodyl compounds (**51−56**) were synthesized by oxidizing polyiodo compounds using oxone (potassium peroxymonosulfate, $2KHSO_5 \cdot KHSO_4 \cdot K_2SO_4$) (Scheme 6).[11] The iodyl compounds show an obvious improvement in oxygen balance (between −24.8% and −1.5%) and detonation performance (D_v = 4125−6166 m s^{-1}, P = 9.89−23.11 GPa) when compared with their parent iodo compounds. However, the presence of the iodyl group also

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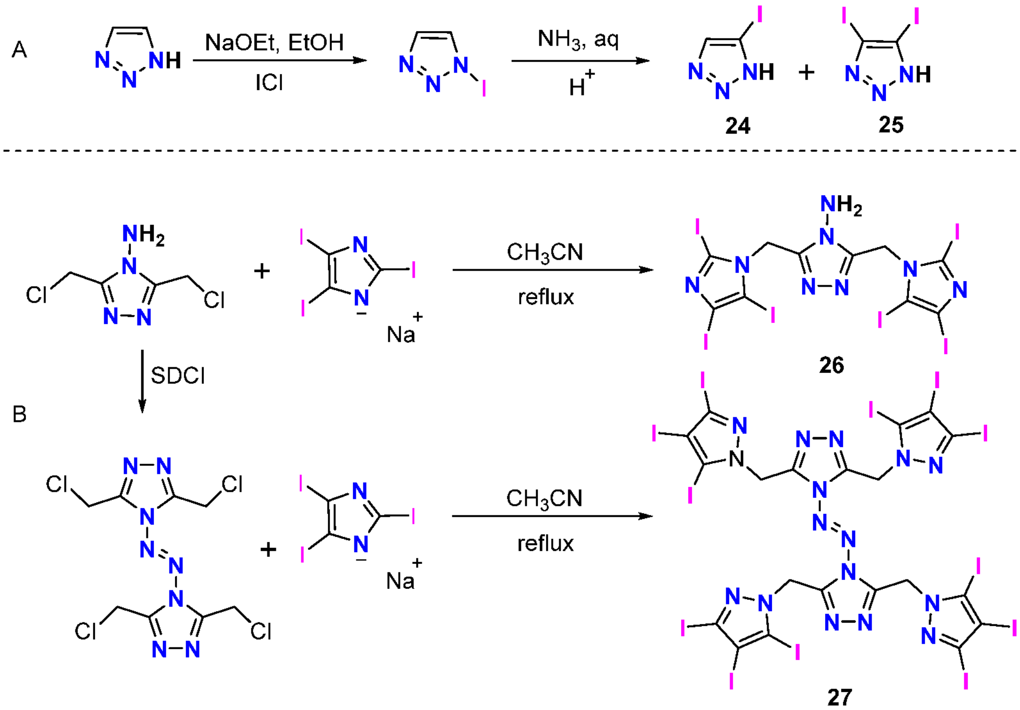
Scheme 4. Iodination and Coupling of Triazole



results in high sensitivities and gives rise to safety concerns when used as biocidal agents.

3.2. Iodine-Rich Imidazolium Iodate and Periodate Salts

Another efficacious route to improve the oxygen balance of iodine-containing compounds in lieu of forming the iodyl group, is the incorporation of an iodine-containing anion, namely, IO_3^- or IO_4^- into an iodine-rich cation. In 2011, iodide-containing salts were used as biocidal agents for the first time by Fischer et al.,[23] and decomposition of the new compounds $[NH_4]^+[IF_2O_2]^-$ and $[C(NH_2)_3]^+[IF_2O_2]^-$ generated HF and I_2, both of which are highly effective fungicides. In 2016, aromatic iodine-rich salts **57−67** were prepared by our group[15] through the metathesis reactions of $AgIO_3$ or $AgIO_4$ with aromatic salts (Scheme 7). All of the compounds have high densities (2.86−3.20 g cm^{-3}), high iodine content (70.3−78.1%), desirable detonation properties (D_v = 2958−4558 m s^{-1}, P = 4.1−13.8 GPa), and acceptable oxygen balances that make these compounds potential candidates as single-based biocidal agents. However, because of their high impact sensitivity, which ranges from 3−6 J, the treatment with coating agents of those compounds to achieve desirable impact sensitivities will be needed to make them useful in future applications.

3.3. Nitro Group-Containing Iodine-Rich Compounds

To circumvent the high sensitivity of iodyl compounds and iodate or periodate salts, taking advantage of the introduction of the nitro group to improve the energy level and oxygen balance is a well-established method in the area of energetic compounds.[24−30] Although the nitro group increases the energy while replacing an iodine atom, which results in a decrease in biocidal activity, this method provides an excellent route for the synthesis of high-energy and high-iodine biocidal agents.

Compounds **68−69**,[20] **70−73**,[19] **74−76**,[14] **77−78**,[9] and **79**[2] were obtained successively by our group through nitrification reactions (Scheme 8). In 2016, Chand et al. synthesized the tricyclic iodine-containing compound **76** by a ring closing reaction.[14] In another study, compound 77 was formed by Zhao et al. through a nitration reaction, in which a ring-closing reaction occurred when reacting with aqueous ammonia to form fused ring compound **78**. Specifically, the thermal decomposition temperature of compound **78** is 323 °C; the theoretical detonation velocity is 5834 m s^{-1}; and the detonation pressure is 21.48 GPa with an iodine content of 50.46%. Most importantly, the impact sensitivities of 77 and **78** are 11 and 9 J, respectively.[9] They incorporate the nonaromatic 1,3,5-triazane with pyrazole through a ring-closing reaction to produce a fused tricyclic ring. The compound has a nearly planar structure, so its thermal stability and detonation performance are enhanced. The 1,3,5-triiodo-2,4,6-trinitrobenzene (**79**) with a higher density of 3.05 g cm^{-3} and decomposition temperature of 367 °C was synthesized by our group using a two-step reaction from benzene.[2] The replacement of selected iodo groups by nitro groups in iodine-rich compounds by nitration increases the oxygen balance and enhances the detonation performance.

To solve the problem of the decrease in iodine content by a direct nitration method, we used *N*,*N*-bis(2-chloroalkyl)-nitramide as a bridging group. A series of triiodopyrazoles or triiodoimidazoles were linked by 2-nitrazapropane, 2,4-nitrazapentane, 2,4,6-trinitro-2,4,6-triazaheptane, or 2,2-dinitropropane moieties to give hexaiodo-containing compounds **80−87** (Scheme 9).[1] The energy of the new compound was higher than that of the triiodoazole before bridging. For example, the detonation velocity of compound **81** is 4321 m·s^{-1}; the detonation pressure is 12.4 GPa, and the iodine content is maintained at 72.4% while its impact sensitivity is 10 J. The introduction of energetic groups, such as nitro or nitramino groups, into iodine-rich compounds is an effective method to improve their detonation performance with acceptable sensitivity, while maintaining the iodine content at a high level.

As seen in Table 2, the existence of oxygen in iodine-rich compounds not only improves the oxygen balance but also

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Scheme 5. Preparation of Alkyl Ammonium Iodide, Triiodide, or Pentaiodide

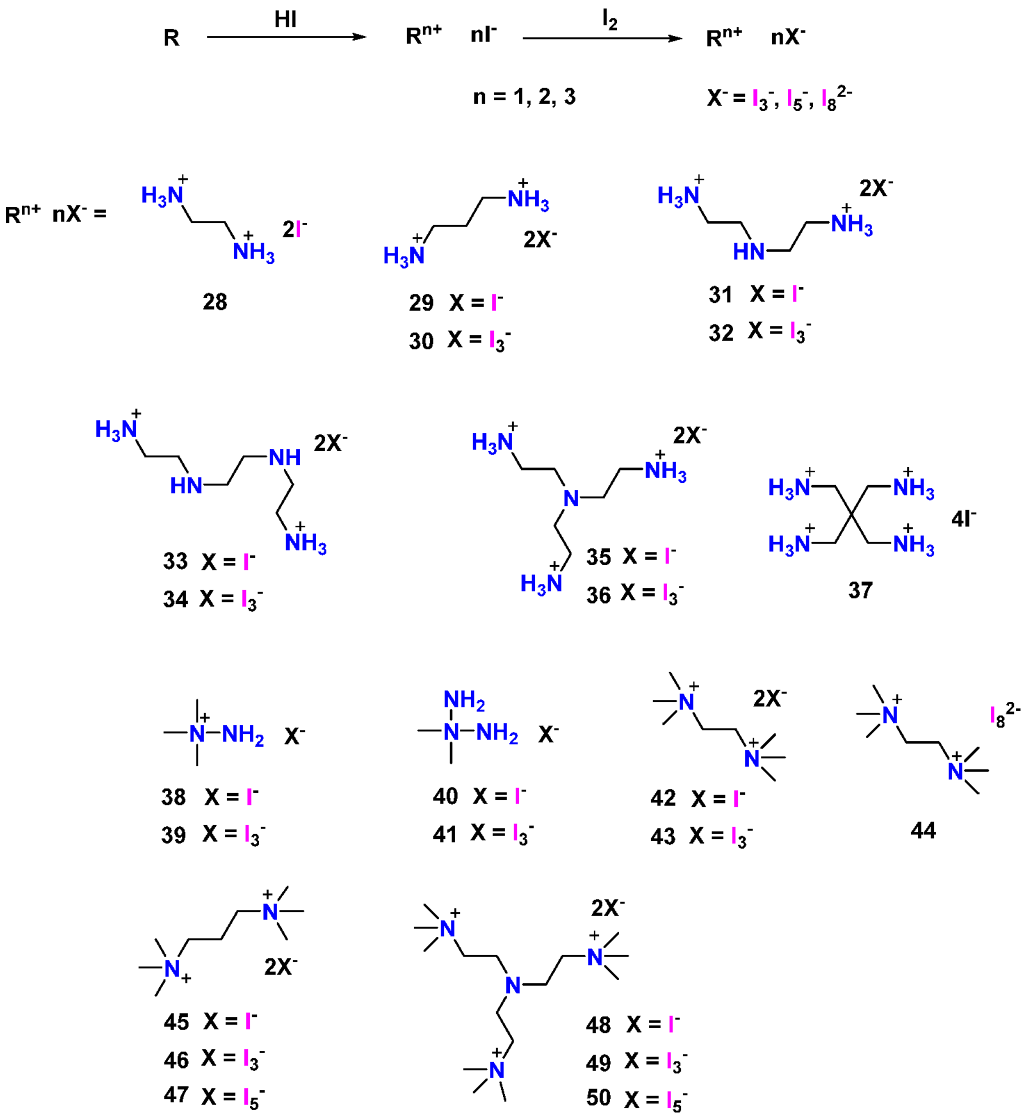
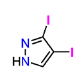
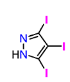
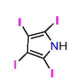
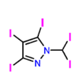
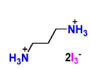


Table 1. Physicochemical Properties of Selected Iodine-Rich Compounds[a]

Compound	Structure	T_d[(a)] °C	d[(b)] $g \cdot cm^{-3}$	D[(c)] $m \cdot s^{-1}$	P[(d)] GPa	I[(e)] %	IS[(f)] J
2[11]		290	3.14	3475	7.63	79.4	>40
3[11]		282	3.38	2859	5.32	85.4	>40
9[11]		168	3.62	2253	3.27	89.0	28
11[13]		371	3.94	2605	4.59	89.2	>40
30[22]		233	3.33	1800	2.28	90.9	>40

[a]Note: (a) T_d, decomposition temperature; (b) d, density; (c) D, calculated detonation velocity; (d) P, calculated detonation pressure; (e) I, iodine content; (f) IS, impact sensitivity.

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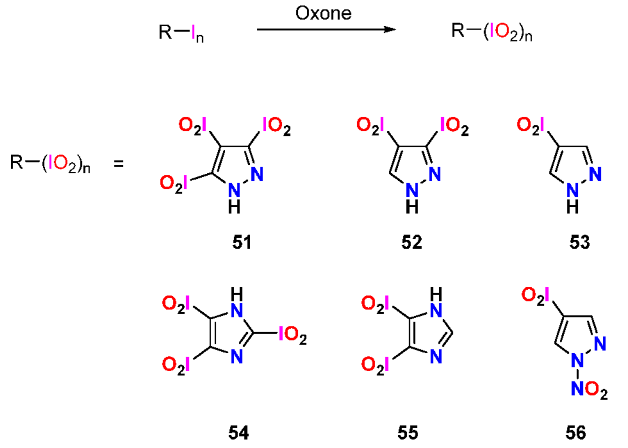
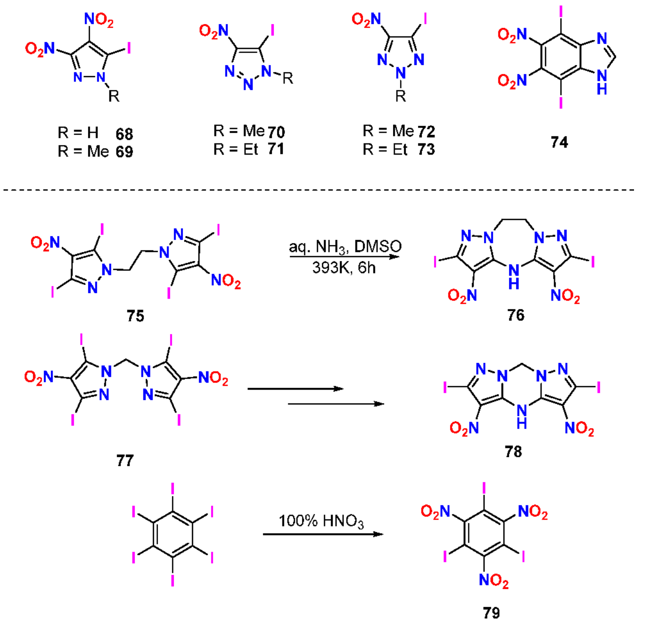
Scheme 6. Synthesis of Iodyl Compounds



Scheme 8. Oxidation and Nitration of Iodine-Rich Compounds

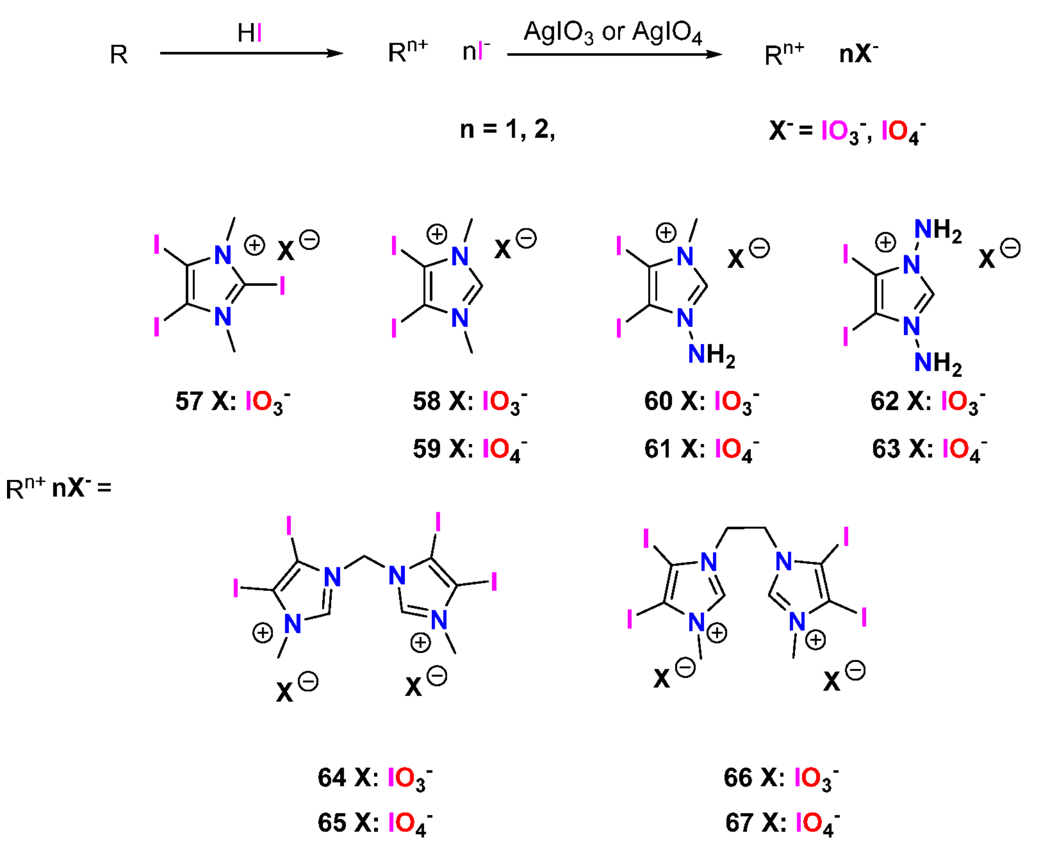


increases their detonation velocity and pressure. Among the strategies reported in the literature, the formation of the iodyl group or the introduction of iodate or periodate anion are effective ways to improve the oxygen balances of iodine-rich compounds without reducing the number of iodine atoms in the compound; however, this method always increases their impact sensitivity which lowers the safety. The substitution of the iodo group by nitro or the link of iodine-rich compounds via energetic groups have the advantages of improving oxygen balance and the energy level, as well as maintaining their sensitivity in an acceptable range.

4. OTHER IODINE-RICH COMPOUNDS

Energetic cocrystals[31−33] are a new type of energetic material, which generally refers to two or more compound molecules that form a regular arrangement of crystals through intermolecular interaction forces such as hydrogen bonding or $\pi-\pi$ interactions between donor−acceptor. The iodine atom in an iodine-

Scheme 7. Preparation of Aryl Ammonium Iodates and Periodates



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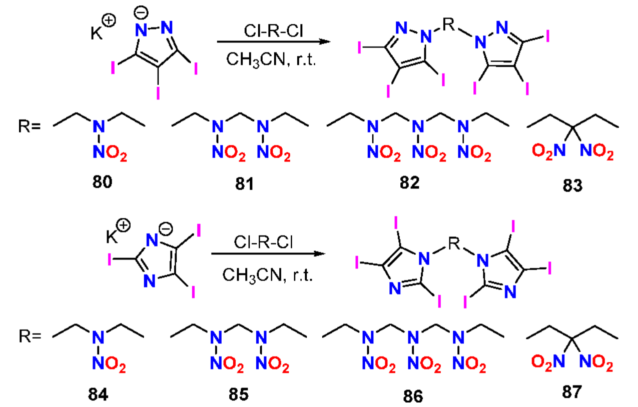
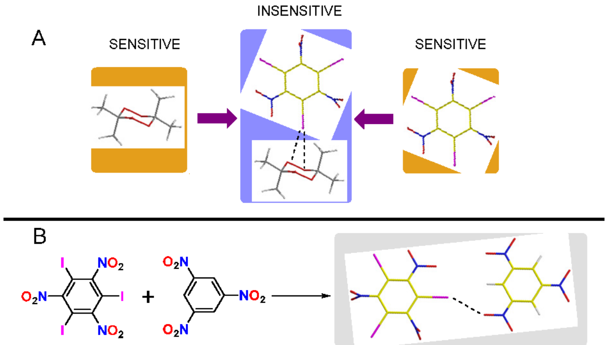
Scheme 9. Synthesis of N−NO_2-Bridged Iodine-Rich Compounds



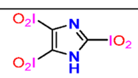
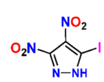
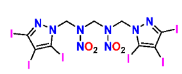
containing compound and the strong electronegative element on the other ligand compound form a halogen bond, and the two compounds are alternately arranged to form a cocrystal. In 2015, Matzger' group obtained a series of 1:1 diacetone diperoxide (DADP)/1,3,5-triiodo-2,4,6-trinitrobenzene (TITNB) cocrystals (Scheme 10).[34] Then, another cocrystal based on TITNB was developed by the same group. These energetic cocrystals containing 1,3,5-trinitrobenzene (TNB) were obtained with the energetic materials 1,3,5-triiodo-2,4,6-trinitrobenzene (TITNB) and 1,3,5-tribromo-2,4,6-trinitrobenzene (TBTNB) in a ratio of 2:1 TNB/TITNB or TBTNB. These iodine-containing cocrystals not only have an increased density and a reduced sensitivity but also exhibit a strong detonation performance and iodine content. They may have future potential as insensitive biocidal materials.[35] Recently, our group obtained four energetic cocrystals through a close acid−base gap.[3] Oxygen-rich iodine-containing acids, H_5IO_6/HIO_3 were used to combine with three weakly basic energetics (btrz, 4,4′-bis-1,2,4-triazole; atrz, 4,4′-azo-1,2,4-triazole; ICM-102, 2,4,6-triamino-5-nitropyrimidine-1,3-dioxide) to form four cocrystals (**C1**, H_5IO_6/ btrz; **C2**, H_5IO_6/atrz; **C3**, 2HIO_3/atrz; and **C4**, HIO_3/ICM-102) (Scheme 11). When H_5IO_6/HIO_3 were introduced into energetic materials, the iodine content and oxygen balance of the four cocrystals increased significantly. With high iodine content and detonation performance, cocrystals **C3** and **C4** shows potential as biocidal agents.

Scheme 10. (A) Cocrystals of 1:1 DADP/TITNB and (B) Isostructural Cocrystals of 1,3,5-Trinitrobenzene



To efficiently improve the energy characteristics of energetic materials, in addition to the method of introducing nitrogen-containing components into the compound, another important method is to form a 2D (two-dimensional) or 3D (three-dimensional) metal−organic framework (MOF).[27−38] These materials not only have high energy density, but also have good

Table 2. Physical Properties of Selected Oxygen-Containing Iodine-Rich Compounds[a]

Compound	Structure	$T_d$$^{(a)}$ °C	d$^{(b)}$ g·cm^{-3}	$D^{(c)}$ m·s^{-1}	$P^{(d)}$ GPa	I$^{(e)}$ %	$IS^{(f)}$ J
54[11]		183	3.68	4891	16.98	70.27	5
62[19]		149	3.20	4558	13.8	72.4	4
68[20]		292	2.46	5922	20.63	44.70	>40
78[9]		323	2.56	5834	21.48	50.46	9
79[2]		367	3.05	5632	24.51	64.44	8
81[1]		243.9	2.94	4321	12.4	72.40	10
TNT		295	1.65	6881	19.53	0	15

[a]Note: (a) T_d, decomposition temperature; (b) *d*, density; (c) *D*, calculated detonation velocity; (d) *P*, calculated detonation pressure; (e) I, content of iodine; (f) IS, impact sensitivity.

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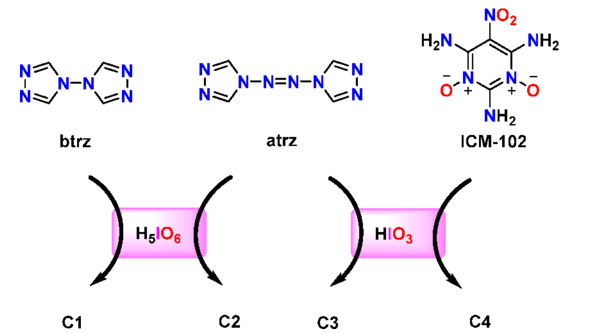
Scheme 11. Four Energetic Cocrystals



thermal stability. Since the first 3D energetic MOF, $[Cu(atrz)_3(NO_3)_2]_n$ (atrz = 4,4′-azo-1,2,4-triazole) was synthesized by Pang's group,[39] energetic 3D MOF materials have attracted great interest.[40] On the basis of this, the energetic 3D MOF is also suitable for iodine-containing biocidal agents. We reported a 3D MOF biocidal agent with high throwing capacity for biosafety application.[4] An iodine-containing 3D MOF, $\{[Cu(atrz)(IO_3)_2]_n$ (atrz = 4,4′-azo-1,2,4-triazole)$\}$, which was prepared using a post synthetic method from $\{[Cu(atrz)_3(NO_3)_2]_n\}$, and IO_3^- has strong coordination ability and can be used as both the ligand and a counterion. This 3D MOF has high density, good thermal stability and excellent biocidal effects, which can play the role of a potentially valuable biocidal agent in infection control (Figure 5).

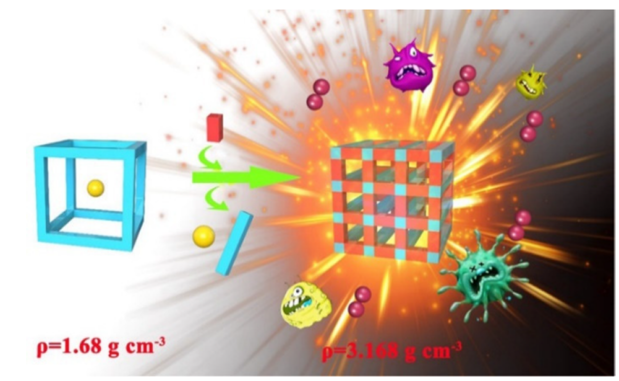
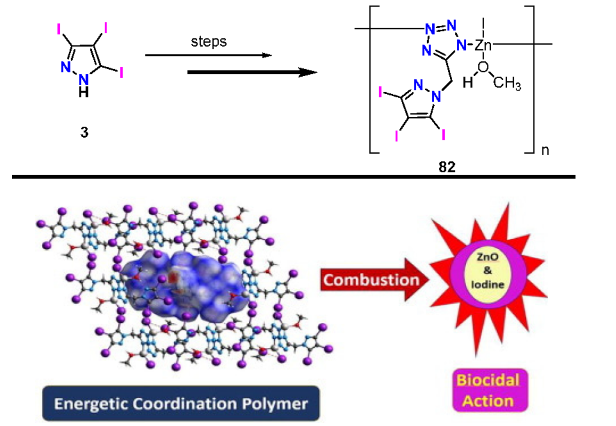


Figure 5. Iodine-containing 3D Metal–Organic Framework. Reproduced with permission from ref 4. Copyright 2020 American Chemical Society.

In addition to energetic cocrystals and 3D MOFs, organic polymers are also used in the field of biocidal agents. Chinnam et al.[41] reported the synthesis of iodine-containing biocidal agent polymers for the first time by starting from **3** (Scheme 12). Compared with small molecules, the polymers have good thermal stability, iodine content and sensitivity. The compound produces iodine and ZnO during decomposition, which have good bactericidal effects, and the decomposition products of the polymer can be combined to form iodine-coated zinc oxide nanoparticles, which have a certain synergistic sterilizing effect.

When considering practical applications of agent defeat weapons, formulations which normally consist of fuels, oxidizers, and binders are always used to achieve a balance between the energy level and sterilization efficiency. The diversity of iodine-containing fuels or oxidizers, which are the main components in a formula makes them favorable to adjust the output of the energy and biocidal, giving the study and development of the biocidal agent formula a perspective strategy (Figure 6). Therefore, the formulation study of iodine-containing biocidal agents has gained increasing interest from researchers.[42−47]

Scheme 12. Energetic Iodine-Rich Coordination Polymer



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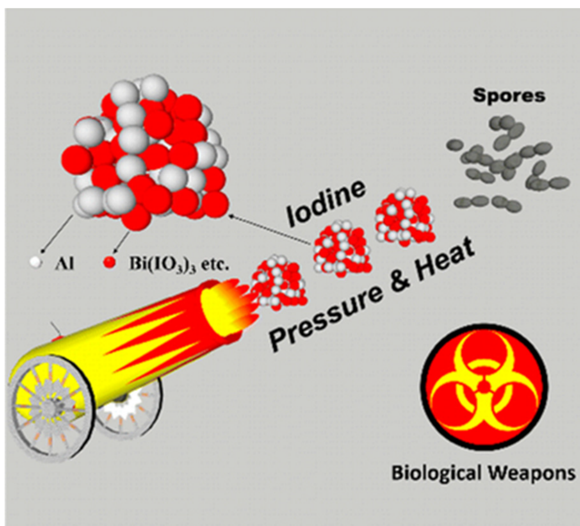

Figure 6. Iodine-containing formulation materials for biological warfare agents. Reproduced with permission from ref 42. Copyright 2015 American Chemical Society.

5. CONCLUSIONS

Iodine-rich compounds, which have good thermal and chemical stabilities, moderate energy, and high iodine content, have gained extensive attention from scholars all over the world. In the past 100 years, the frequent occurrence of biological crises, which result from the outbreak of pestilences and the use of bioweapons by extremists, have brought great harm to human beings. The research and development of iodine-rich biocidal agents may make it possible for humans to overcome harmful microorganisms in both civilian and military applications.

This Account mainly summarizes the design strategies and synthetic methods for iodine-rich organic compounds. One of the main purposes for synthesizing iodine-rich compounds is to push the limit of the stable storage of iodine in a molecule. Much effort has been expended to increase the number of iodine atoms, as well as iodine content of a molecule. On the other

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hand, the introduction of oxygen atoms into iodine-rich compounds effectively improves their energy and oxygen balance. However, the design and synthesis of oxygen balanced iodine-rich compounds suitable for single component materials as ADWs remains a challenge. With the development of the field of materials chemistry, advanced functional materials have also been introduced into iodine-containing energetic materials. The advanced functional materials studies of iodine-rich compounds are currently mainly focused on cocrystals, 3D metal−organic frameworks, and iodine-containing polymers, etc. These materials with simple preparation, relatively better thermal stability, and higher detonation performance, have more potential as biocidal agents.

By summarizing the recent research methodology, synthetic strategy and new biocidal agents of iodine-rich compounds, the authors believe that, in the future, the research on iodine-rich compounds will focus mainly on the following aspects: (1) improve the atomic economy of iodination, which is able to introduce multiple iodo groups to the backbone in one step with high yield; (2) design iodine-containing functional materials with cage frameworks by using advanced functional materials (energetic cocrystals, supramolecular self-assembly materials, covalent organic frameworks, and metal organic framework); and (3) improve the preparative methods of iodine-rich energetic materials by using new technologies (such as 3D printing). These iodine-rich energetic materials are expected to become new biocidal agents with low sensitivity, good thermal stability, high energy, and high sterilization efficiency.

■ AUTHOR INFORMATION

Corresponding Authors

Chunlin He − *School of Materials Science & Engineering and State Key Laboratory of Explosion Science and Technology, Beijing Institute of Technology, Beijing 100081, China; Department of Chemistry, University of Idaho, Moscow, Idaho 83844-2343, United States;* orcid.org/0000-0002-4099-6477; Email: chunlinhe@bit.edu.cn

Siping Pang − *School of Materials Science & Engineering and State Key Laboratory of Explosion Science and Technology, Beijing Institute of Technology, Beijing 100081, China;* Email: pangsp@bit.edu.cn

Jean'ne M. Shreeve − *Department of Chemistry, University of Idaho, Moscow, Idaho 83844-2343, United States;* orcid.org/0000-0001-8622-4897; Email: jshreeve@uidaho.edu

Authors

Jinjie Chang − *School of Materials Science & Engineering, Beijing Institute of Technology, Beijing 100081, China*

Gang Zhao − *Department of Chemistry, University of Idaho, Moscow, Idaho 83844-2343, United States;* orcid.org/0000-0002-3061-8341

Xinyuan Zhao − *State Key Laboratory of Explosion Science and Technology, Beijing Institute of Technology, Beijing 100081, China*

Complete contact information is available at: https://pubs.acs.org/10.1021/acs.accounts.0c00623

Author Contributions

‖J.C. and G.Z. contributed equally. The manuscript was written through contributions of all authors. All authors have given approval to the final version of the manuscript.

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Notes

The authors declare no competing financial interest.

Biographies

Jinjie Chang completed his master's degree in analytical chemistry at Shandong Normal University in 2019. After that, he joined the Beijing Institute of Technology to study for a PhD degree under the supervision of Prof. Siping Pang and Prof. Chunlin He. His research interests are focused on the design and synthesis iodine-rich compounds.

Gang Zhao received his PhD degree in organic chemistry in 2013 in Prof. Qing-Yun Chen's group from Shanghai institute of Organic Chemistry, CAS. He has been a postdoctoral fellow in Professor Jean'ne Shreeve's team at the University of Idaho since 2016. His research interest includes design, synthesis, and characterization of high density energetic materials and high-density green oxidizers for rocket propellants and developing new polyiodo compounds.

Xinyuan Zhao completed her bachelor's degree at China University of Labor Relations in 2019. Since 2019, she has pursued her master's degree at Beijing Institute of Technology under the supervision of Prof. Siping Pang and Prof. Chunlin He. Her research interests are the design and preparation iodine-rich biocidal formulations.

Chunlin He received his PhD in 2010 from Beijing Institute of Technology. From 2011 to 2018, he worked in Prof. Jean'ne M. Shreeve's group as a postdoctoral fellow at the University of Idaho. Since 2018, he has served as a professor at Beijing Institute of Technology. His research interests include the design, synthesis and characterization of nitrogen-rich and iodine-rich compounds.

Siping Pang is a full professor at the Beijing Institute of Technology (BIT, China). He is working on the syntheses and characterization of highly energetic materials, guided by theoretical calculations. He obtained his PhD from the BIT, where his research was focused on the synthesis of HNIW. Since 2016, he has been the Dean of the School of Material Sciences and Engineering at BIT and he also serves as a member of the Editorial Boards of the Chinese Journal of Energetic Materials and Acta Armamentarii.

Jean'ne M. Shreeve is a Montana native. She received a B.A. in chemistry at the University of Montana, an M.S. in analytical chemistry at the University of Minnesota, and a Ph.D. in inorganic chemistry at the University of Washington, Seattle. She has been at the University of Idaho since 1961, where she has served as chemistry department head and vice president for research and graduate studies. In 2011, Shreeve was named a University Distinguished Professor. Her research interests include the design, syntheses, characterization, and reactions of energetic materials, fluorine-containing compounds, and energetic ionic liquids.

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