Benzylamine-Free, Heavy-Metal-Free Synthesis of CL-20

SERDP SEED Project WP-1518

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The main objective of this SERDP SEED project was to demonstrate the feasibility of preparing the hexaazaisowurtzitane cage in a form that is efficiently directly nitrolyzable to CL-20 without a requirement for expensive benzylamine starting material or heavy metals, including palladium, involved in its production. We applied a known chemical transformation, base-catalyzed isomerization of allylamines into 1-propenylamines, to the recently reported hexaallylhexaazaisowurtzitane to prepare hexa(1-propenyl)-hexaazaisowurtzitane (HPIW). We next performed photooxygenation of this intermediate, using singlet oxygen gas, in order to oxidize the 1-propenyl substituents to formyl substituents. Although the oxidation reaction did not go to completion to produce hexaformylhexaazaisowurtzitane, the partially oxidized product formed did undergo nitrolysis to form CL-20 in a clean reaction. Furthermore, we demonstrated that the new intermediate, HPIW, underwent direct nitrolysis to form CL-20, though initial conditions did not do so as cleanly as with its oxidation product as a precursor for nitrolysis.

15. SUBJECT TERMS
CL-20; hexaallylhexaazaisowurtzitane; hexa(1-propenyl)hexaazaisowurtzitane; singlet-oxygen; nitrolysis

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List of Acronyms

BINAP	2,2′-Bis(diphenylphosphino)-1,1′-binaphthalene
CL-20	Hexanitrohexaazaisowurtzitane
COD	Cyclooctadiene
DMAC	Dimethylacetamide
DMSO	Dimethyl sulfoxide
HAIW	Hexaacetylhexaazaisowurtzitane
HAllylIW	Hexaallylhexaazaisowurtzitane
HBIW	Hexabenzylhexaazaisowurtzitane
HHTDD	2,4,6,8,10,12-Hexanitro-2,4,6,8,10,12-hexaazatricyclododecane-5,11-dione
HMX	Octahydro-1,3,5,7-tetranitro-1,3,5,7-tetrazocine
HNW	Hexanitrohexaazawurtzitane
HPIW	Hexa(1-propenyl)hexaazaisowurtzitane
MsOH	Methanesulfonic acid
NMR	Nuclear magnetic resonance
RDX	Hexahydro-1,3,5-trinitro-1,3,5-triazine
TADA	Tetraacetylhexaazaisowurtzitane
TADF	Tetraacetyldiformylhexaazaisowurtzitane
TADH	Tetraacetylhexaazaisowurtzitane
TAIW	Tetraacetylhexaazaisowurtzitane
TEX	4,10-Dinitro-2,6,8,12-tetraoxa-4,10-diaza-tetracyclododecane
THF	Tetrahydrofuran
TsOH	*p*-Toluenesulfonic acid

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Executive Summary

SERDP Statement of Need PPSON-06-03 called for new "green chemistry" approaches to the preparation of precursors to important energetic ingredients, such as nitrogenous polycycles. One of the most important new ingredients for DoD applications is CL-20, but its production process suffers from several economic and environmental disadvantages, mostly related to requirements for benzylamine starting material and for heavy metal (typically, palladium) catalysts used in debenzylation steps. Besides its high material cost, benzylamine is an environmentally undesirable starting material. The main objective of this SEED project was to demonstrate the feasibility of preparing the hexaazaisowurtzitane cage in a form that is directly nitrolyzable to CL-20 without a requirement for expensive benzylamine starting material or heavy metal catalysts, thereby introducing a new, preferably lower-cost, less wasteful, and environmentally cleaner process to produce CL-20.

Ultimately, this project was fully successful in demonstrating a new route to CL-20 that met these requirements, but many unsuccessful reaction runs were carried out along the way.

Many attempts were made to achieve the transformation originally proposed for this project: the condensation of 1,4-diformyl-2,3,5,6-tetrahydroxypiperazine (**1**) with any 1,1,2,2-tetraamidoethane (**2**) to form a hexaacylhexaazaisowurtzitane suitable as a precursor to CL-20. All of our attempts at this condensation, under many different conditions, were unsuccessful. We next performed degradation chemistry on a known nitramine, HHTDD, in attempts to reorganize its degradation intermediates into a hexaazaisowurtzitane cage, but initial attempts were unsuccessful.

The recent publication by French researchers of a new hexaazaisowurtzitane derivative, hexaallylhexaazaisowurtzitane (HAllylIW), presented a new opportunity to prepare a superior precursor to CL-20 without a requirement for benzylamine or heavy metal catalysts. We applied a known transformation—base-catalyzed isomerization of allylamines into 1-propenylamines—to HAllylIW to prepare a new derivative, hexa(1-propenyl)hexaazaisowurtzitane (HPIW). We next performed photooxygenation of this intermediate by singlet oxygen—using oxygen gas photolyzed by a quartz halogen headlamp in the presence of a tetraphenylporphine sensitizer—in order to oxidize the 1-propenyl substituents to formyl substituents. The resulting hexa- or polyformylhexaazaisowurtzitane was expected to be a new suitable precursor to CL-20. Although the oxidation reaction did not go to completion to produce hexaformylhexaazaisowurtzitane, the partially oxidized product formed did indeed undergo nitrolysis to form CL-20 in a clean reaction. Furthermore, we demonstrated that the new intermediate, HPIW, underwent direct nitrolysis to form CL-20, though initial conditions did not do so as cleanly as with its oxidation product as a precursor for nitrolysis. This reactivity of the enamine HPIW is explained to be a mechanistically reasonable transformation.

This SEED project constituted only a feasibility demonstration that new synthetic routes to CL-20 are available. Significant process development would be needed in order to demonstrate their overall superiority to the current production process.

Objective

SERDP Statement of Need PPSON-06-03 called for new "green chemistry" approaches to the preparation of precursors to important energetic ingredients, such as nitrogenous polycycles. The main objective of this SEED project was to demonstrate the feasibility of preparing the hexaazaisowurtzitane cage in a form that is directly nitrolyzable to CL-20 without a requirement for expensive benzylamine starting material or heavy metal catalysts, thereby introducing a new, preferably lower-cost, less wasteful, and environmentally cleaner process to produce CL-20.

Background

One of the most important new ingredients for DoD applications is CL-20,[1] but its production process (Figure 1) suffers from several economic and environmental disadvantages, mostly related to requirements for benzylamine starting material and for heavy metal (typically, palladium) catalysts used in debenzylation steps. Besides its high material cost, benzylamine is an environmentally undesirable starting material because it is produced from benzyl chloride (plus ammonia[2]), which in turn is produced by α-chlorination of toluene.[3] CL-20 production therefore entails all of the problems inherent in the chlorine manufacturing industry,[4] such as the long-term toxicity of environmental organochlorine by-products[5] and mercury involved in the industrial chlor-alkali process to produce chlorine.[6] The alternative chemistry proposed for this project would avoid halogenated materials as reagents and as solvents. The proposed process would also eliminate hydrogenolysis reactions used in the current process, thereby eliminating heavy metals required for those steps.

---

[1] (a) Nair, U.R.; Sivabalan, R.; Gore, G.M.; Geetha, M.; Asthana, S.N.; Singh, H. *Combust. Explos. Shock Waves* **2005**, *41*, 121; (b) Sysolyatin, S.V.; Lobanova, A.A.; Chernikova, Yu.T.; Sakovich, G.V. *Russ. Chem. Rev.* **2005**, *74*, 757; and references therein.

[2] "Benzylamine", *Hawley's Condensed Chemical Dictionary*, 14th Edition; John Wiley & Sons, 2002.

[3] "Benzyl chloride", in: Lowenheim, F.A.; Moran, M.K. *Faith, Keyes, and Clark's Industrial Chemicals*, 4th Edition; John Wiley & Sons, 1975; p. 145.

[4] "The Many Faces of Chlorine"; http://pubs.acs.org/cen/ncw2004/8242chlorine.html

[5] "The Global Chlorine Crisis"; http://archive.greenpeace.org/toxics/reports/cfap/cfapm2.html

[6] "Mercury Process for Making Chlorine"; http://www.eurochlor.org/upload/documents/document109.pdf

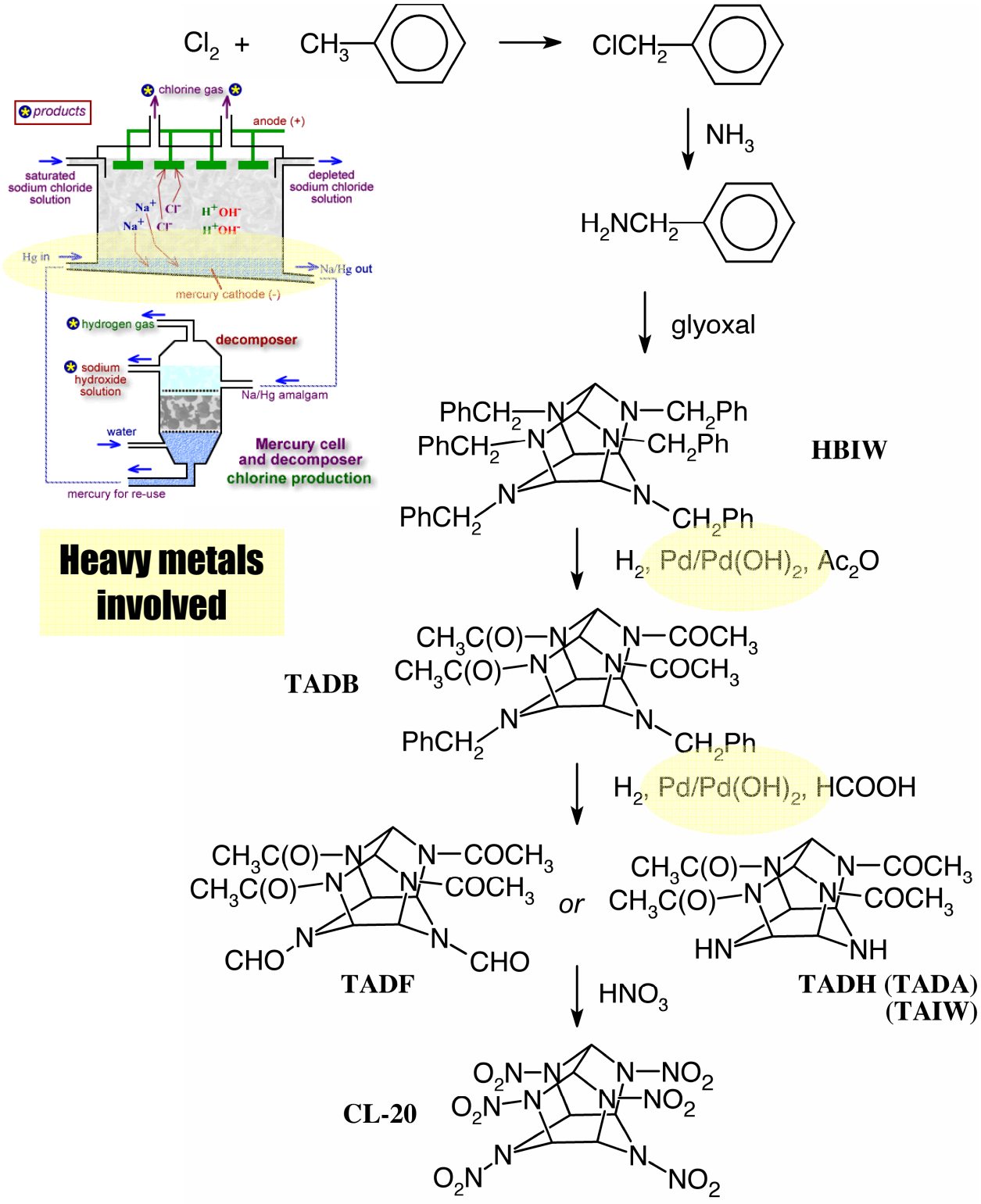

Figure 1. Current production process for CL-20 (mercury cell schematic[7] used with permission)

[7] "Chlorine"; http://www.greener-industry.org/pages/chlorine/6chlorine_PM1.htm

All synthetic routes used to prepare the hexaazaisowurtzitane cage for production of CL-20 depend on the condensation of benzylamine with glyoxal, originally developed by Nielsen.[8] CL-20 has remained nearly prohibitively expensive, however (as a potential large-scale replacement for HMX), mainly due to the high cost of benzylamine starting material and of hydrogenolysis steps involving palladium catalyst used in the debenzylation of hexabenzylhexaazaisowurtzitane (HBIW) intermediate in the course of preparing acylhexaazaisowurtzitane intermediates, such as tetraacetyldiformylhexaazaisowurtzitane (TADF), tetraacetylhexaazaisowurtzitane (TADA or TADH or TAIW), or hexaacetylhexaazaisowurtzitane (HAIW). The byproduct of hydrogenolytic debenzylation of HBIW, toluene, is not economically or cleanly reconverted to benzylamine (only via chlorination followed by amination), so benzyl is not a clean, recoverable protecting group in that system. Various R&D projects, including Navy ManTech programs,[9] have addressed process development for reducing the cost of CL-20 production, but most have not approached potential cost reduction by developing a fundamentally different synthetic approach to the hexaazaisowurtzitane cage.

Thiokol researchers have expended the most effort on developing process improvements in CL-20 production.[10] Most of these improvements have involved variations in conditions and parameterizations of hydrogenolytic debenzylation of HBIW followed by nitrolysis. Recently, Thiokol adopted process variations[11] devised by Japanese researchers in which tetraacetylhexaazaisowurtzitane (TADA)—a preferable intermediate for the nitrolysis conditions used in Thiokol's CL-20 process—is made from HBIW.[12]

Materials and Methods

While many attempts at amide–glyoxal condensations have failed to produce the hexaazaisowurtzitane cage in one step, there are two compounds reported in the literature, each formed in one step from inexpensive reagents, that appear to be ideal precursors to the formation of a hexaacylhexaazaisowurtzitane which would be a suitable immediate precursor to CL-20. 1,4-Diformyl-2,3,5,6-tetrahydroxypiperazine (**1** in Figure 2 below) is made efficiently from formamide plus glyoxal.[13] (Other amides, including simple ones such as acetamide, do not form the piperazine structure.[14]) Various 1,1,2,2-tetraamidoethane derivatives (**2**), including tetraacetamidoethane (**2a**), have been prepared by amide–glyoxal reactions under appropriate conditions.[15] It may be apparent that a single bimolecular condensation of these two reactants under appropriate conditions would produce the hexaazaisowurtzitane cage.

---

[8] Nielsen, A.T.; Nissan, R.A.; Vanderah, D.J.; Coon, C.L.; Gilardi, R.D.; George, C.F.; Flippen-Anderson, J. *J. Org. Chem.* **1990**, *55*, 1459.

[9] "Lower Cost, Improved Quality CL-20 Energetic Material"; https://www.dodmantech.com/successes/Navy/weapons/weapons_LowerCostCL20_120805.pdf

[10] (a) Wardle, R.B.; Hinshaw, J.C. *U.S. Patent* 6,147,209 (2000); (b) Wardle, R.B.; Hinshaw, J.C. *U.S. Patent* 7,129,348 (2006); and references therein.

[11] Sanderson, A.J.; Warner, K.; Wardle, R.B. *U.S. Patent* 6,391,130 (2002).

[12] Kodama, T.; Tojo, M.; Ikeda, M. *U.S. Patent* 6,472,525 (2002).

[13] Vail, S.L.; Moran, C.M.; Barker, R.H. *J. Org. Chem.* **1965**, *30*, 1195.

[14] Currie, A.C.; Dinwoodie, A.H.; Fort, G.; Thompson, J.M.C. *J. Chem. Soc. (C)* **1967**, 491.

[15] Gilbert, E.E. *J. Chem. Eng. Data* **1974**, *19*, 182.

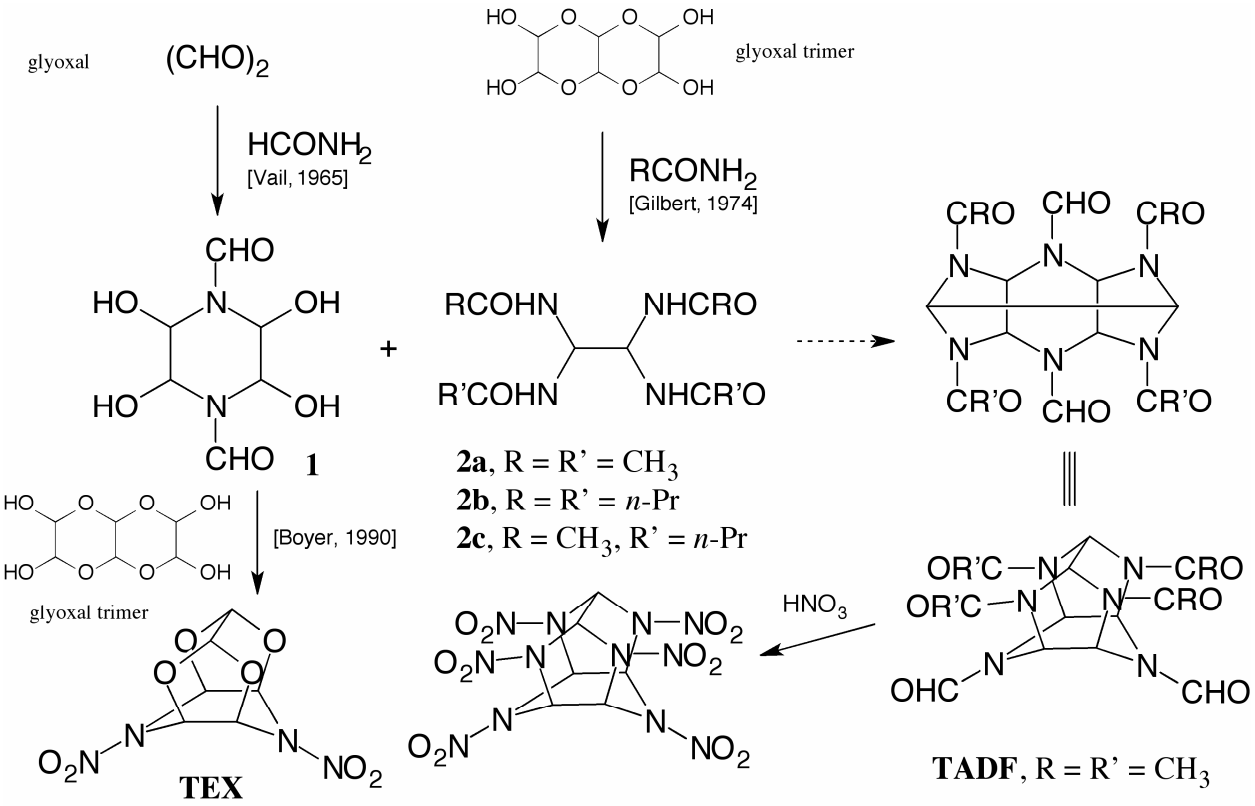

Figure 2. Proposed benzylamine-free preparation of CL-20 precursor

(Conceivably, an alternative structure that could form from these two reactants would be the *wurtzitane* structure, with all carbon–carbon linkages parallel; but a hexanitrohexaazawurtzitane product made from such an intermediate would have even higher density than CL-20 and would be an even more desirable new product.)

The feasibility of reactivity of the tetrahydroxypiperazine intermediate (**1**) in the desired mode is suggested by its similar reaction with glyoxal (trimer) to make the diazatetraoxaisowurtzitane cage system,[16] whose *N,N'*-dinitro derivative was named "TEX" by Thiokol researchers.[17] Thus, the reaction of the tetrahydroxypiperazine **1** with a tetraamidoethane **2** under appropriate conditions should produce the hexaazaisowurtzitane cage system. Tetraacetamidoethane (**2a**) is the most attractive candidate because of the lowest cost of acetamide starting material. The expected hexaazaisowurtzitane product, TADF, is known to be a feasible immediate precursor to CL-20 by nitrolysis,[18] and a recent Russian patent improves that nitrolysis by showing a 98% yield of CL-20 using ammonium nitrate–nitric acid mixture as the nitrolysis reagent.[19] Finally, the proposed process would offer the advantage that the acetyl protecting

[16] Ramakrishnan, V.T.; Vedachalam, M.; Boyer, J.T. *Heterocycles* **1990**, *31*, 479.
[17] Highsmith, T.K.; Edwards, W.W.; Wardle, R.B. *U.S. Patent* 5,498,711 (1996).
[18] Wardle, R.B.; Edwards, W.W. *U.S. Patent* 5,739,325 (1998).
[19] Sysolyatin, S.V.; Lobanova, A.A.; Chernikova, Yu.T. *Russ. Patent* RU 2,199,540 (2003); *Chem. Abstr.* **2004**, *140*, 146176.

group introduced at the beginning is easily regenerated after nitrolysis: acetamide is made by thermolysis of ammonium acetate, formed by neutralization of acetic acid by-product made upon deprotection.

Nurgatin et al. reported in 1985 that compound **1**—as well as its tetraacetate ester—was completely destroyed by concentrated hydrochloric acid.[20] Even earlier, Reynolds et al. reported the general sensitivity of *N*-acyl-α,α′-dihydroxyazaheterocycles to acid degradation with examples of *N*-acylisoindolines (benzopyrrolidines), which undergo complex decomposition and recombination reactions in strong acids.[21] We therefore proposed that condensations of **1** with **2** should be conducted avoiding acidic conditions—at least Brønsted acidic conditions. It has been reported that condensations between amides and acid-sensitive carbonyl equivalents, acetals, can be driven by catalysis with *Lewis acids*, such as boron trifluoride etherate, instead of Brønsted acids.[22] Also, condensations between carbonyl equivalents and carboxamides to make acid-sensitive hemiaminal products (such as *N*-acyl-1,3-dihydroxyisoindolines) can be driven by increasing the nucleophilicity of the amide under *basic* conditions, to generate the amide anion as a reactive species.[21] Condensations involving **2** should therefore be conducted using their anionic form, generated by a non-hydrolytic base such as sodium hydride.[23] The solubilization of sodium salts of organics in aprotic solvents may be improved by the use of crown ether catalysts,[24] and this condition may be beneficial in this system as well.

In parallel with the new approach described above to prepare hexaacylhexaazaisowurtzitanes, another potential alternative route to CL-20 that avoids hydrogenolysis with heavy metal catalysts—though not a requirement for benzylamine—is the possible debenzylation of HBIW by *nitrosolysis* instead of hydrogenolysis. The feasibility of debenzylating benzylhexaazaisowurtzitane derivatives by nitrosolysis with N_2O_4 has been demonstrated using tetraacetyldibenzylhexaazaisowurtzitane (TADB).[25] Thus, it was proposed to attempt similar debenzylation with the initial hexaazaisowurtzitane intermediate, HBIW. The resulting hexanitrosohexaazaisowurtzitane would be directly nitrolyzable to CL-20, thereby avoiding catalytic hydrogenolysis and acylation steps and also generating a benzyl by-product (presumably the nitrate ester) that is directly convertible to benzylamine starting material, unlike the by-product of hydrogenolytic debenzylation, toluene.

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[20] Nurgatin, V.V.; Ginzburg, B.M.; Kovalenko, V.I.; Marchenko, G.A. *Chem. Heterocycl. Comp. (USSR)* **1985**, 1057.

[21] (a) Reynolds, R.D.; Conboy, R.J. *J. Org. Chem.* **1965**, *30*, 2251; (b) Reynolds, R.D.; Arendsen, D.L.; Guanci, D.F.; Wickman, R.F. *J. Org. Chem.* **1970**, *35*, 3940.

[22] Murfin, D.L. *U.S. Patent* 3,803,091 (1974).

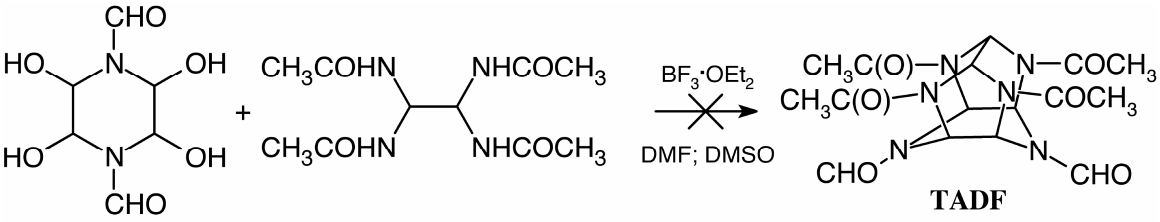
[23] Fones, W.S. *J. Org. Chem.* **1949**, *14*, 1099.

[24] Aspinall, H.C.; Greeves, N.; Lee, W.-M.; McIver, E.G.; Smith, P.M. *Tetrahedron Lett.* **1997**, *38*, 4679.

[25] (a) Latypov, N.V.; Wellmar, U.; Goede, P.; Bellamy, A.J. *Org. Proc. Res. Dev.* **2000**, *4*, 156; (b) Lü, L.-Y.; Ou, Y.-X.; Wang, J.-L. *Chinese J. Expl. Prop.* **2003**, *26*, 41.

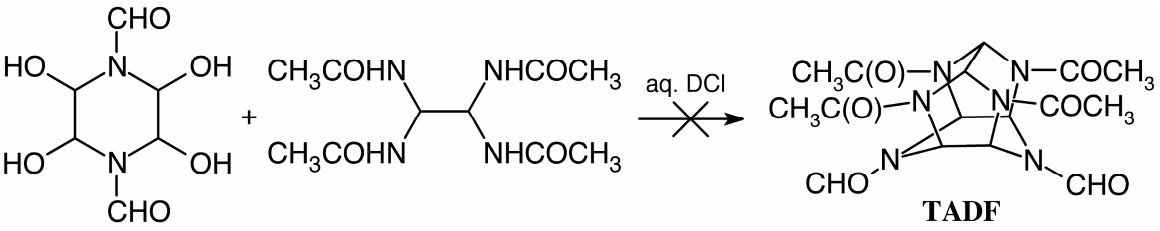
Results and Accomplishments

Initial reactions between 1,4-diformyl-2,3,5,6-tetrahydroxypiperazine (**1**) and tetraacetamidoethane (**2a**) using a Lewis acid, boron trifluoride etherate (Eq. 1),



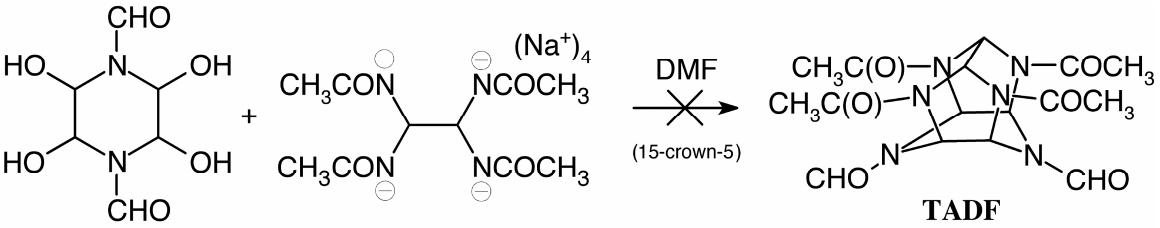
(1)

and a Brønsted acid, deuterium chloride (Eq. 2), as catalysts failed to produce evidence of the desired reactivity, i.e., formation of the hexaazaisowurtzitane cage. Instead, degradation of reactant **1** occurred before the desired bimolecular reaction.



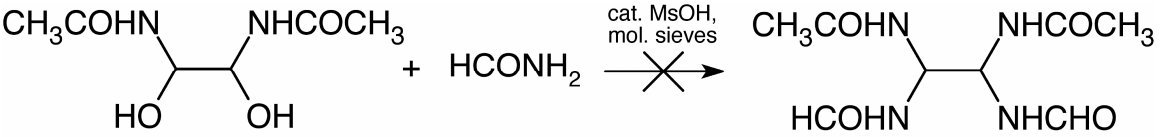
(2)

Under basic conditions in order to improve the nucleophilicity of **2a** as its sodium salt using sodium hydride, that tetraamide appeared to be too insoluble, even in the presence of 15-crown-5 phase transfer catalyst, to allow the desired reaction (Eq. 3).



(3)

Several reactions were conducted in order to prepare asymmetric tetraamidoethanes (similar to **2c**) in hopes of improving the solubility of **2**. Reaction of 1,2-bisacetamido-1,2-ethanediol with formamide in the presence of catalytic methanesulfonic acid and molecular sieves (Eq. 4) produced only a sludge rather than the desired 1,2-bisacetamido-1,2-bisformamidoethane.



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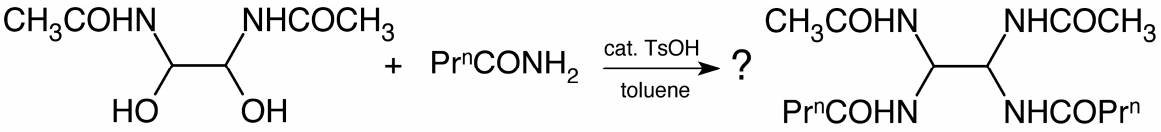
A similar reaction of 1,2-bisacetamido-1,2-ethanediol and butyramide in toluene solvent (Eq. 5), for azeotropic drying instead of molecular sieves,



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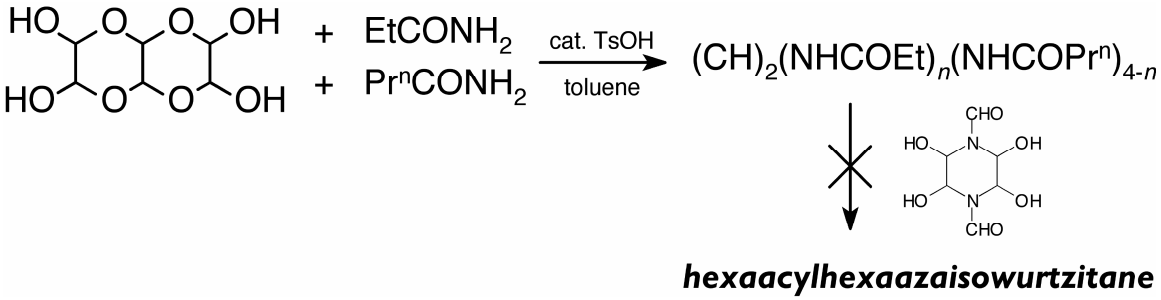
and a reaction of glyoxal (trimer) with a mixture of propionamide and butyramide under similar conditions (Eq. 6) both gave *possible* desired asymmetric tetraamidoethanes, but the products still had quite poor solubility in common solvents and were thus difficult to characterize (and not superior for the intended application). Neither intermediate led to formation of a hexaacyl-hexaazaisowurtzitane upon reaction with **1**.



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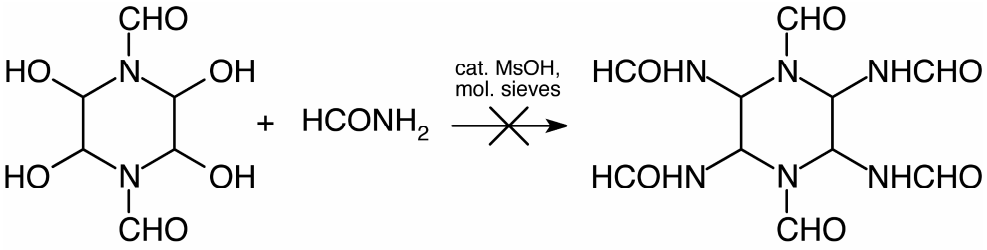
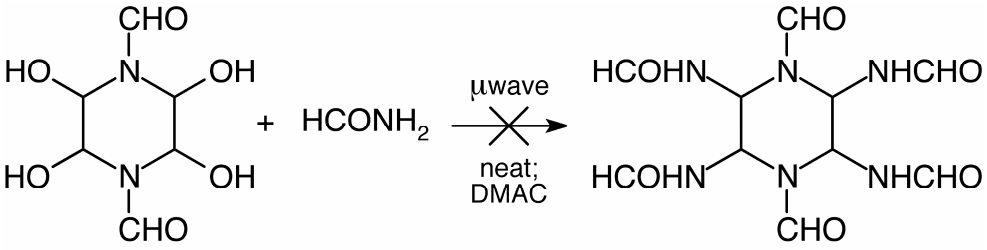
An alternative class of potentially attractive intermediate, a 2,3,5,6-tetraamido-1,4-diformylpiperazine, was attempted to be prepared from 1,4-diformyl-2,3,5,6-tetrahydroxy-piperazine (**1**) and simple amides: with formamide in the presence of catalytic methanesulfonic acid and molecular sieves (Eq. 7), only a sludge was produced;



(7)

similar results were obtained with these reactants under conditions of microwave assistance, both as neat reactants and in dimethylacetamide (Eq. 8);



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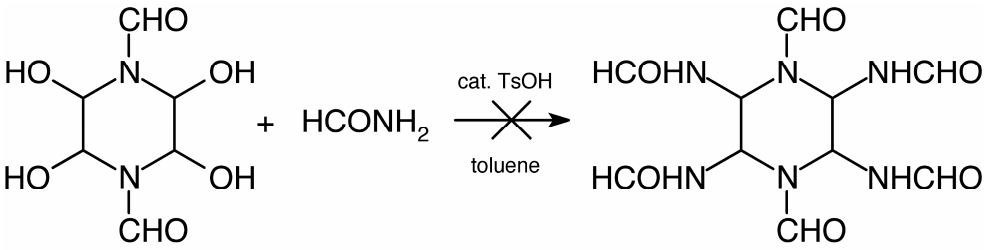
similar results were obtained with formamide in toluene solvent, for azeotropic drying instead of molecular sieves (Eq. 9);



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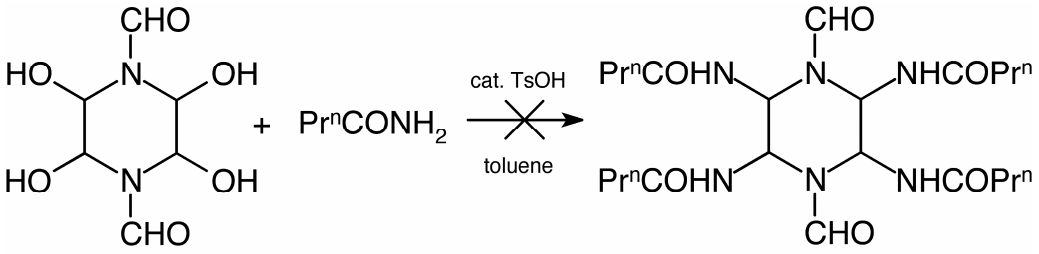
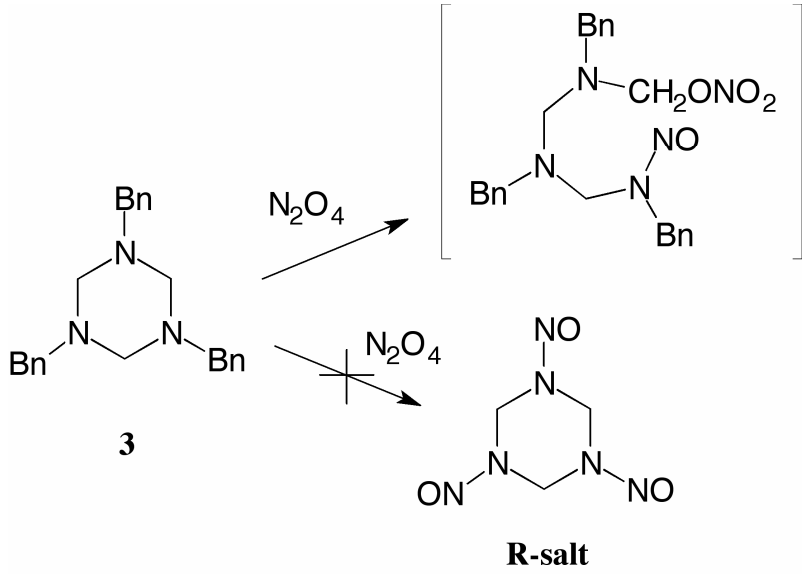
with butyramide in toluene solvent (for azeotropic drying instead of molecular sieves), only starting materials were recovered (Eq. 10).



(10)

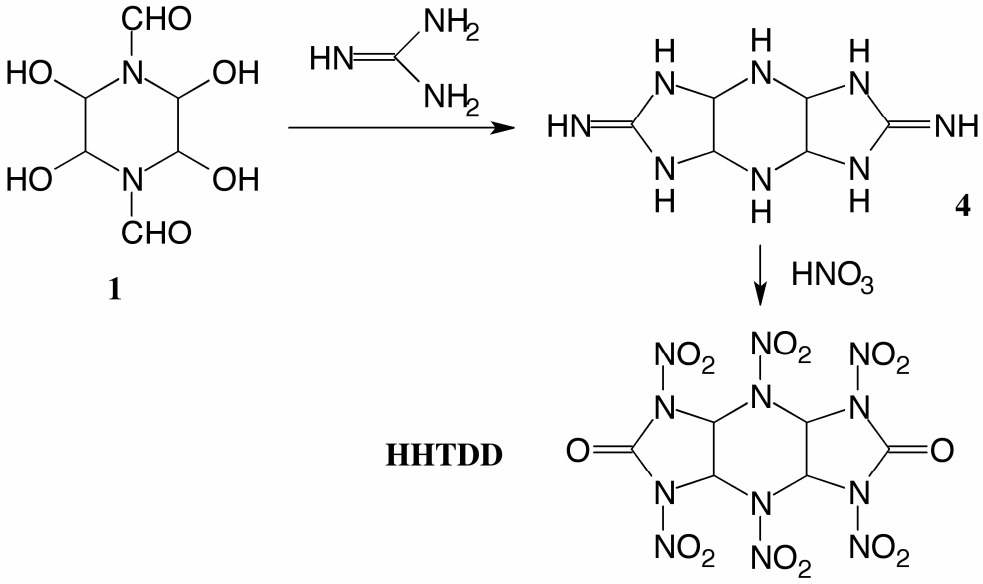
A test of the technical feasibility of nitrosolytic debenzylation of HBIW used 1,3,5-tribenzylhexahydro-1,3,5-triazine (**3**) as a model *N*-benzylaminal, analogous in reactivity to HBIW, in reactions with nitrogen tetroxide (N_2O_4) both neat and in carbon tetrachloride solvent. The choice of this model compound was based on the better available characterization of the desired nitrosolysis product, hexahydro-1,3,5-trinitroso-1,3,5-triazine ("R-salt"), than of the unknown and spectroscopically very complex HBIW product, hexanitrosohexaazaisowurtzitane. Analysis of the reaction product(s) indicated that nitrosolysis occurred via cleavage of the methylene bridges instead of at the *N*-benzyl substituents (Eq. 11).



(11)

This result suggests a fundamental flaw in attempts to electrophilicly displace *N*-benzyl in HBIW: the alkylene bridges in *N,N′*-dibenzylaminals are more susceptible to cleavage than are the *N*-benzyl "protecting groups," which would rupture the heterocyclic ring or cage. This approach was therefore abandoned within the scope of a SEED project.

Another known polycyclic nitramine was recognized as a potentially attractive intermediate that might lead to CL-20 or its structural isomer, hexanitrohexaazawurtzitane (HNW): 2,4,6,8,10,12-hexanitro-2,4,6,8,10,12-hexaazatricyclododecane-5,11-dione (HHTDD). Two known precursors to HHTDD were prepared: 2,4,6,8,10,12-hexaazatricyclododecane-5,11-dione from the reaction of **1** with urea in aqueous HCl;[26] and dodecahydro-2,6-diimino-1*H*,5*H*-diimidazo[4,5-*b*:4′,5′-*e*]pyrazine (**4**) from the reaction of **1** with guanidine.[27] The latter intermediate was used to prepare HHTDD (Eq. 12).[28]



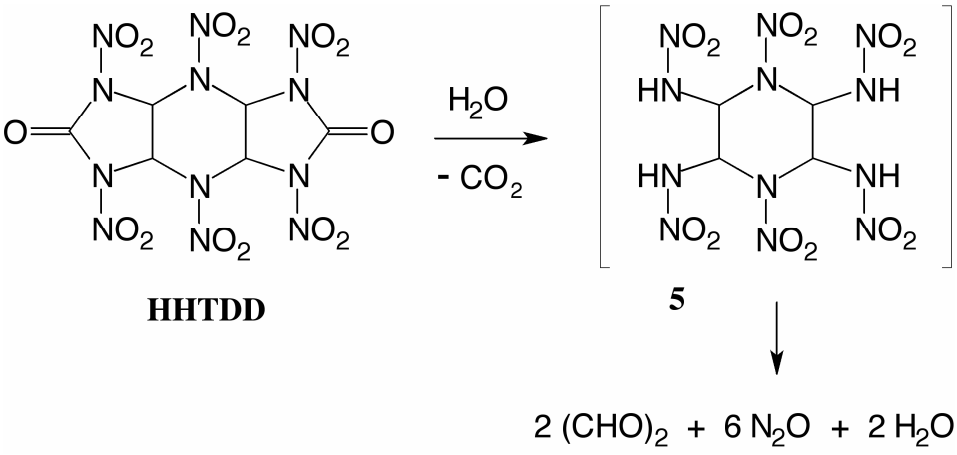
(12)

[26] Vedachalam, M.; Ramakrishnan, V.T.; Boyer, J.H.; Dagley, I.J.; Nelson, K.A.; Adolph, H.G.; Gilardi, R.; George, C.; Flippen-Anderson, J.L. *J. Org. Chem.* **1991**, *56*, 3413.

[27] Dagley, I.J.; Flippen-Anderson, J.L. *Aust. J. Chem.* **1994**, *47*, 2033.

[28] Vedachalam, M.; Ramakrishnan, V.T.; Boyer, J.H. *Heteroatom Chem.* **1991**, *2*, 313.

HHTDD is attractive as a potential precursor to a hexanitrohexaaza cage compound because Chinese research on the compound suggests that 2,3,5,6-tetrakisnitramino-1,4-dinitropiperazine (**5**) may be an intermediate in the hydrolysis of HHTDD (Eq. 13).[29]



(13)

It may be visualized that the four primary nitramine substituents of this intermediate may be linked with glyoxal (via known methodology for nitramine–aldehyde condensations) to produce the desired cage compound (such as CL-20). Although attempted hydrolyses of HHTDD in acetonitrile with added water, in concentrated sulfuric acid, and in concentrated sulfuric acid with added glyoxal trimer showed no evidence of the desired intermediate or a cage compound product, hydrolysis of HHTDD in the system nitromethane–concentrated sulfuric acid (1:1) with excess glyoxal trimer behaved differently, producing predominantly one compound that was consistent (by ^{1}H NMR) with the desired intermediate. However, an opportunity that was assessed to be a superior route to CL-20 presented itself at this time, and this approach was abandoned within the context of the SEED project.

An alternative benzylamine-free route to a hexaacylhexaazaisowurtzitane precursor to CL-20 was envisioned following the recent report by Hervé et al. (SNPE France) of a preparation of hexaallylhexaazaisowurtzitane (HAllylIW) from allylamine and glyoxal.[30] The new route we envisioned was to utilize HAllylIW in a well-known isomerization reaction of allylamines into 1-propenylamines catalyzed by rhodium(I) catalysts.[31] Although this would not be strictly a heavy-metal-free route, the amount of catalyst required (≤1 mol%) is much less than the amount of palladium required (5~10%) in the catalytic hydrogenolysis of hexabenzylhexaazaisowurtzitane (HBIW), and the turnover number (typically, many thousands) is higher for the Rh(I)-catalyzed isomerization of allylamines than for Pd-catalyzed debenzylation. The resulting hexa(1-propenyl)hexaazaisowurtzitane could then be oxidized by singlet oxygen (generated by dye-sensitized photolysis of oxygen gas) via another well-known transformation: cleavage of the C=C bond of propenylamines to produce formamides.[32] The resulting hexaformylhexaaza-

[29] Hu, R.; Lu, X.; Fang, Y. *J. Energ. Mater.* **1993**, *11*, 219.

[30] (a) Cagnon, G.; Eck, G.; Hervé, G.; Jacob, G. *U.S. Patent Appl.* 2004/0260086 (2004); (b) Hervé, G.; Jacob, G.; Gallo, R. *Chem. Eur. J.* **2006**, *12*, 3339.

[31] Inoue, S.; Takaya, H.; Tani, K.; Otsuka, S.; Sato, T.; Noyori, R. *J. Am. Chem. Soc.* **1990**, *112*, 4897.

[32] Foote, C.S.; Lin, J.W.-P. *Tetrahedron Lett.* **1968**, 3267.

isowurtzitane would be another example of the class of hexaacylhexaazaisowurtzitanes that should be susceptible to direct nitrolysis to CL-20.

Following several failed attempts to reproduce the allylamine–glyoxal reaction according to conditions reported in the French publications, some process development successfully prepared the desired intermediate by modifying the isolation conditions (cf. Appendix Experimental Section). Thus, hexaallylhexaazaisowurtzitane (HAllylIW) was prepared by us in 33% yield, better than the 20-25% reported by Hervé et al.[30]

We made several attempts to isomerize this allyl derivative into the corresponding 1-propenyl derivative via rhodium(I) catalysis, a well known transformation for other allylamines. Rhodium(cyclooctadiene)BINAP perchlorate was prepared for this purpose.[33] However, no reaction occurred with HAllylIW treated with this catalyst in tetrahydrofuran at 60 °C, even on prolonged reaction. The quality of the prepared catalyst was proven by successful isomerizations of allyl-*N*,*N*-dimethylamine and *N*-allyl-*N*-methylaniline as model amines; nevertheless, HAllylIW proved recalcitrant toward isomerization. Another rhodium–BINAP catalyst was prepared *in situ* from rhodiumbis(acetonitrile)(cyclooctadiene) tetrafluoroborate plus BINAP in THF.[34] With or without hydrogen gas bubbled through the reaction solution (to reduce and eliminate the COD ligand in order to generate a coordinatively unsaturated cationic rhodium species), HAllylIW proved resistant to isomerization. Yet another rhodium(I) catalyst, hydridocarbonyltris(triphenylphosphine)rhodium(I), was employed in benzene solvent (another catalytic system previously used for allylamine-to-propenylamine rearrangements[35]), but HAllylIW still proved resistant to the required isomerization.

The required rearrangement of HAllylIW was finally successfully achieved (Eq. 14) by a different mechanism, base-catalyzed isomerization:[36] clean, efficient isomerization of HAllylIW to hexa(1-propenyl)hexaazaisowurtzitane (HPIW) was effected—essentially quantitatively—by potassium *t*-butoxide base in dimethyl sulfoxide at room temperature in ~6 hours (also at 80 °C in ~¼ hour). We also demonstrated that the isomerization was efficiently achieved by introducing potassium *t*-butoxide as its conveniently available tetrahydrofuran solution into a solution of HAllylIW in DMSO or in dimethylformamide. Reactions in such ~1:1 solvent mixtures typically proceeded to completion in an overnight run. (However, THF as the sole solvent did not allow isomerization at room temperature, even on prolonged reaction.) As in previous similar transformations of this type,[37] the allylamine-to-propenylamine isomerizations require only catalytic *t*-butoxide; some of our successful runs employed ⅓ equivalent of potassium *t*-butoxide per allyl substituent.

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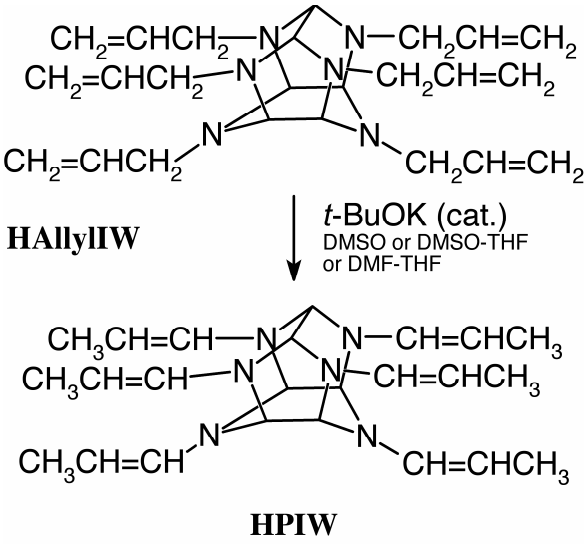
[33] Tani, K.; Yamagata, T.; Akutagawa, S.; Kumobayashi, H.; Taketomi, T.; Takaya, H.; Miyashita, A.; Noyori, R.; Otsuka, S. *J. Am. Chem. Soc.* **1984**, *106*, 5208.

[34] Oi, S.; Sato, T.; Inoue, Y. *Tetrahedron Lett.* **2004**, *45*, 5051.

[35] Krompiec, ,S.; Pigulla, M.; Krompiec, M.; Baj, S.; Mrowiec-Białoń, J.; Kasperczyk, J. *Tetrahedron Lett.* **2004**, *45*, 5257.

[36] Price, C.C.; Snyder, W.H. *Tetrahedron Lett.* **1962**, 69.

[37] (a) Sauer, J.; Prahl, H. *Tetrahedron Lett.* **1966**, 2863; (b) Carlsen, P.H.J.; Jørgensen, K.B. *J. Heterocycl. Chem.* **1997**, *34*, 797.



(14)

HPIW was most easily purified (sufficiently for subsequent reactions) by removing solvent(s) under high vacuum and redissolving the HPIW in a suitable solvent in which residual potassium *t*-butoxide is insoluble. We initially chose benzene-d_6 for the sake of characterizing the dissolved HPIW and subsequent reaction products by NMR. Potassium *t*-butoxide has sufficiently low solubility in benzene that this is an effective purification method; however, other hydrocarbon solvents in which potassium *t*-butoxide has low solubility, such as toluene or xylene or even some aliphatics, should be suitable for this process.

We tested other methods of "neutralizing" potassium *t*-butoxide *in situ* so that the processed solution might be used directly without workup of the HPIW. In one case, methylation of contained potassium *t*-butoxide was attempted by reaction with stoichiometric dimethyl sulfate injected into the crude HPIW product solution, with the intention of producing *t*-butyl methyl ether and potassium sulfate by-product. This approach was partially successful in a single attempt, but it was fraught with complications. Actual *t*-butoxide content must be determined in order to distinguish it from *t*-butanol formed from adventitious hydrolysis of *t*-butoxide during handling of the hygroscopic solutions. Otherwise, excess toxic dimethyl sulfate—beyond that required to methylate *t*-butoxide—might alkylate HPIW intermediate or interfere in other ways. In the course of this approach, we developed a potentially useful diagnostic measure of potassium *t*-butoxide–*t*-butanol mixture compositions in DMSO-d_6 solvent using ^{13}C NMR spectrometry. In ^{13}C NMR spectra of mixtures of *t*-butanol and potassium *t*-butoxide, the quaternary carbon resonance occurs at an average chemical shift (δ) of the two species, weighted by the mole fraction (X) of each:

$$\delta_{\text{obsd}} = X_{t\text{-BuOK}}\delta_{t\text{-BuOK}} + X_{t\text{-BuOH}}\delta_{t\text{-BuOH}} \tag{15}$$

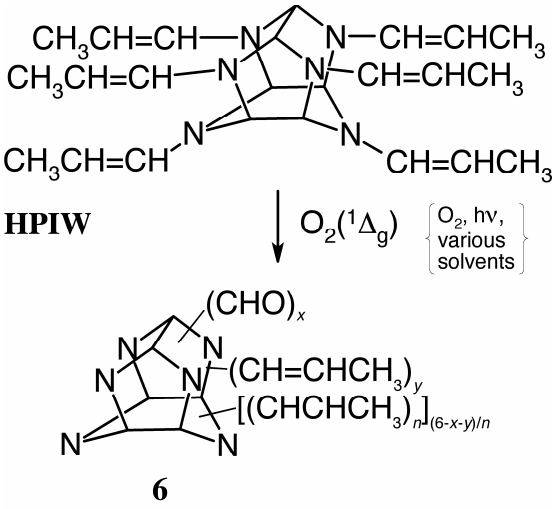
From analyses of four solutions of *t*-butanol–potassium *t*-butoxide mixtures in DMSO-d_6—quantified by integration of the quaternary carbon absorptions vs. those of DMSO-d_6 (i.e., all non-protiated carbons)—linear regression of a plot of mole fraction of *t*-butoxide vs. quaternary carbon chemical shift produced the following relationship, useful for determining potassium *t*-butoxide content in DMSO-d_6 solutions by ^{13}C NMR:

$$X_{t\text{-BuO}^-} = 49.17 - \delta^{\text{quat}}_{^{13}\text{C}}/1.36 \tag{16}$$

This regression estimates a chemical shift of δ 66.87 for pure *t*-butanol in DMSO-d_6, comparing very favorably with a literature value of δ 66.88.[38]

The ^{1}H and ^{13}C NMR spectra of HPIW in various solvents indicate that it exists in a few (two to four) rotational isomers (rotamers) due to cis-trans isomerism of the propenyl substituents and restricted rotation about the *N*–propenyl bonds. Other examples of exo-heterocyclic enamines, *N,N*-dimethylaminomethylene-substituted pyrazoles, exhibit complex NMR spectra due to rotamers, as well.[39]

HPIW was next subjected to oxidation by singlet oxygen, generated by halogen-lamp photolysis of oxygen gas, sensitized by catalytic amounts of zinc tetraphenylporphine (Eq. 17). The transformation of enamines to formamides via photooxygenation has been reported to occur in a variety of different solvents.[40] We conducted this reaction several times in a variety of solvents under various conditions because all runs produced tentative evidence that polymerization of one or more enamine intermediate(s) was occurring: precipitation of an organic solid that was soluble in DMSO-d_6 but otherwise poorly soluble in most other solvents, including acetone.



(17)

Also, the ^{1}H NMR spectra of the reaction products showed quite broad absorptions of all signals attributable to hexaazaisowurtzitane species (Figure 3). However, a mixture of several different compounds containing various numbers of 1-propenyl and formyl substituents might be expected to exhibit unusually complex ^{1}H NMR spectra due to potentially even more rotamers than in HPIW. (TADF[10a] and triacetyltribenzylhexaazaisowurtzitane[41] exhibit complex ^{1}H NMR spectra due to rotamers of these polyacylhexaazaisowurtzitanes.) Other tentative evidence that initially suggested that the product(s) formed in these reactions included polymeric species rather than "simple" polyformylpoly(1-propenyl)hexaazaisowurtzitane intermediates (i.e., a mixture of cages with various multiple numbers of both substituents, rather than polymeric species) included the chemical shift of the methyl protons in the ^{1}H NMR spectra in DMSO-d_6: δ ~1.14 (rather than δ ~1.60 seen in the HPIW reactant), which is tentatively more consistent with methyl

[38] Gottlieb, H.E.; Kotlyar, V.; Nudelman, A. *J. Org. Chem.* **1997**, *62*, 7512.
[39] Kölle, U.; Kolb, B.; Mannschreck, A. *Chem. Ber.* **1980**, *113*, 2545.
[40] Foote, C.S.; Dzakpasu, A.A. *Tetrahedron Lett.* **1975**, 1247.
[41] Han, W.-R.; Ou, Y.-X.; Liu, J.-Q.; Chen, B.-R. *Youji Huaxue* **2005**, *25*, 1259.

groups on a saturated chain rather than on a 1-propenyl substituent. The crude oxidation product (**6**) is therefore shown (Eq. 17) as a hexaazaisowurtzitane cage with indeterminate numbers of formyl, 1-propenyl, and saturated polymer chain substituents.

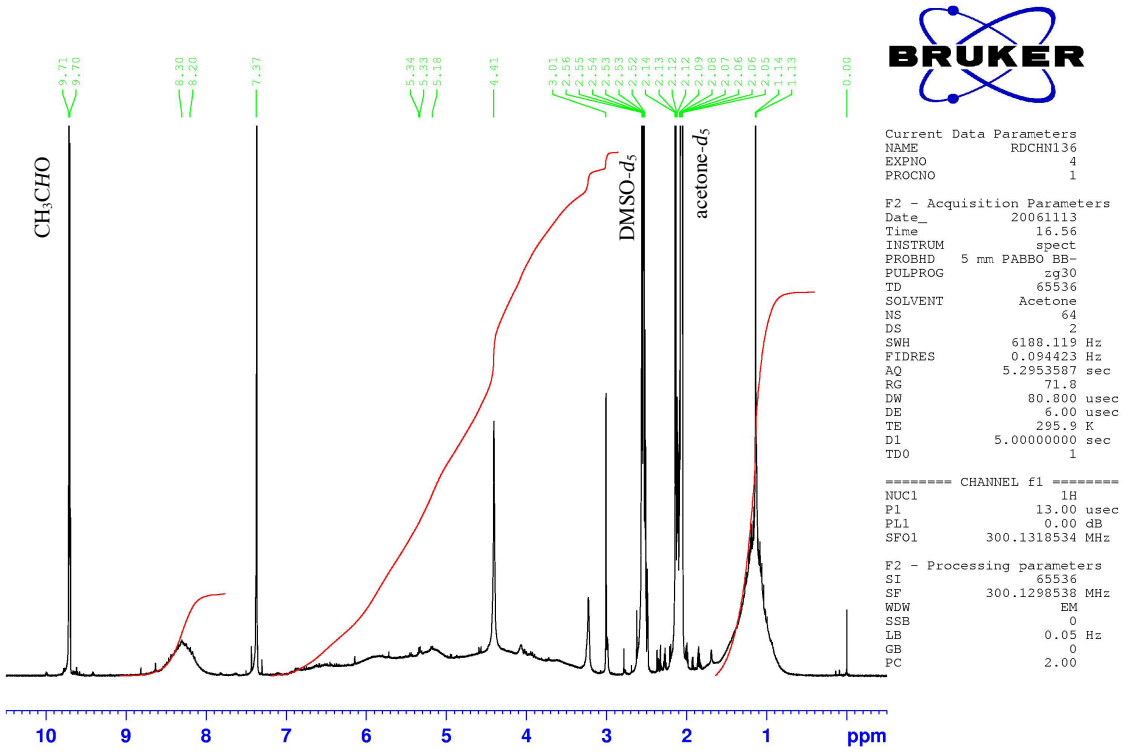
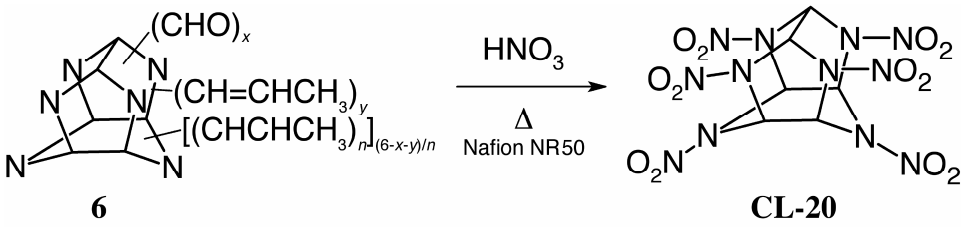


Figure 3. ^{1}H NMR spectrum of crude reaction sample: photooxygenation of HPIW

Integration of the various broad absorptions of the ^{1}H NMR spectra suggested that the average extent of oxidation of 1-propenyl substituents to formyl was typically between three and four substituents per hexaazaisowurtzitane cage (i.e., x = 3~4) before significant precipitation may have prevented further oxidation (which would require heterogeneous gas–solid reactions for further progress). In order to minimize the polymerization that tentatively appeared to be occurring, one run was conducted at a much lower concentration than others (1–10% of the HPIW concentration of any other run) *and* at low temperature (cooled in a dry ice–ethanol bath). Even at 0.8 h reaction time, a sample withdrawn for analysis yielded a ^{1}H NMR spectrum that exhibited (in addition to expected acetaldehyde, which was always apparent in spectra of the crude reaction mixtures) *broad* resonances at chemical shifts consistent with polyformylpoly(1-propenyl)hexaazaisowurtzitane intermediates (but with a formyl content of significantly less than three substituents per cage); broad methyl absorptions were apparent over a range of δ 0.9–1.6. Table 1 lists the variety of conditions that were attempted to effect photooxygenation of HPIW to polyformylhexaazaisowurtzitane derivatives.

Table 1. Conditions of photooxygenation of HPIW		
Solvent system	Temperature	Reaction time
C_6D_6	R.T.	3 h
2:1 C_6D_6–acetone-d_6	0 °C	8 h
3:5 $CDCl_3$–CD_2Cl_2	0 °C	3 h
1:1 C_6H_6–DMSO-d_6	0 °C	3 h
acetone-d_6	dry ice–EtOH bath	6 h
1:5 CD_2Cl_2–$CDCl_3$	dry ice–EtOH bath	0.8 h

The products of some photooxygenation reactions were subjected to nitrolysis after isolation from reaction suspensions by removal of all volatiles (solvent and acetaldehyde by-product). An initial run utilizing a mixture of 98~100% nitric acid and acetonitrile-d_3 produced a minor amount of CL-20 (<10%)—confirmed by HPLC analysis as well as ^{1}H and ^{13}C NMR spectrometry—in a complex mixture after 6 days of reaction at ambient temperature. (Such prolonged reaction conditions significantly hydrolyzed acetonitrile ultimately to acetic acid.) In another run, the very viscous oily residue from a photooxygenation reaction was subjected to nitrolysis conditions using 98~100% nitric acid in the presence of Nafion NR50 beads as a strong Brønsted acid catalyst (Eq. 18).



6 **CL-20** (18)

Reflux of the reaction solution for a total of 30½ hours resulted in a surprisingly clean conversion of the crude polyformyl intermediate to CL-20, which is the predominant constituent in the spectral region attributable to hexaazaisowurtzitane species. Figure 4 is the ^{1}H NMR spectrum of a sample of crude reaction solution (in HNO_3) dissolved into acetonitrile-d_3. Sharp peaks in other regions of the spectrum are certainly attributable to the by-products of nitrolysis of N-substituents from the cage intermediate. These include a clean doublet at δ 1.52, likely attributable to C$\underline{H}_3$CH in a functionalized propenyl substituent removed during nitrolysis. Other sharp peaks from such a by-product are not assigned.

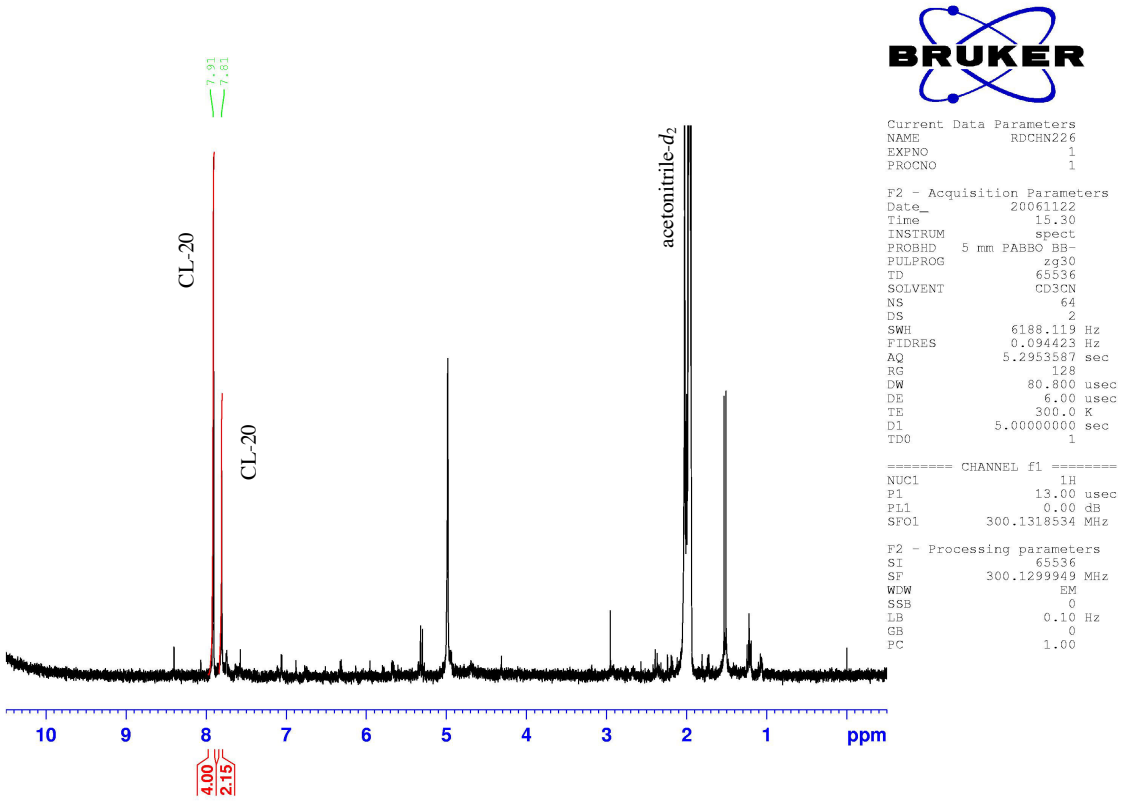


Figure 4. [1]H NMR spectrum of crude reaction sample: nitrolysis of oxidation product **6** to CL-20

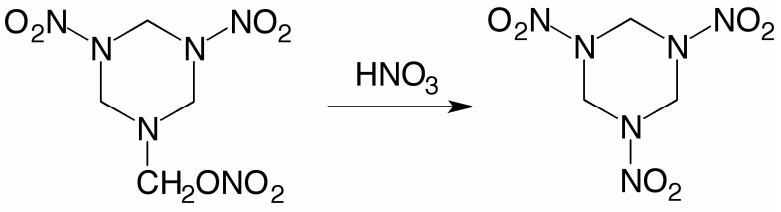
One attempt to isolate CL-20 from the reaction solution involved distillation of the nitric acid at reduced pressure, but concentration resulted in degradation of the quality of the product. Alternative isolation conditions should be developed, but better options are apparent for larger-scale experiments: solutions may be quenched onto ice, precipitating contained CL-20.

The cleanliness of the nitrolysis of the oxidation product (**6**) calls into question the assignment of the broad NMR absorptions as being due to polymeric species containing saturated alkyl substituents on hexaazaisowurtzitane cages. Such saturated substituents would not be expected to be as easily nitrolyzed as formyl or 1-propenyl (*vide infra*), so the different *chemical shift range* of the methyl resonances (vs. those in HPIW) might be attributable to the influence of partial oxidation of other substituents on the cage systems in the mixture of polyformylpoly(1-propenyl)hexaazaisowurtzitanes. That the photooxygenation reactions yielded products with NMR characteristics reminiscent of polymers regardless of the temperature (dry ice–ethanol, 0 °C, or room temperature) or reaction time (0.8–8 h) also leaves in question the actual presence of significant polymeric substitution in the reaction product.

In parallel with the success of the nitrolysis of a crude product (**6**) of photooxygenation of HPIW, an experiment to directly nitrolyze HPIW itself was carried out. Out of concern for possible hydrolysis of enamine HPIW—which could lead to disruption of the cage and degradation of intermediates—from the minor water content of 98~100% nitric acid, fuming sulfuric acid

was added to nitric acid to ensure anhydrous conditions for nitrolysis. An aliquot of the reaction mixture after 4 hours' reflux, added to dichloromethane-d_2 for NMR analysis, showed significant CL-20 content. (The mixture was not quite as clean as the nitrolysis of the photooxygenation product of HPIW, but neither had the nitrolysis reaction proceeded as long.)

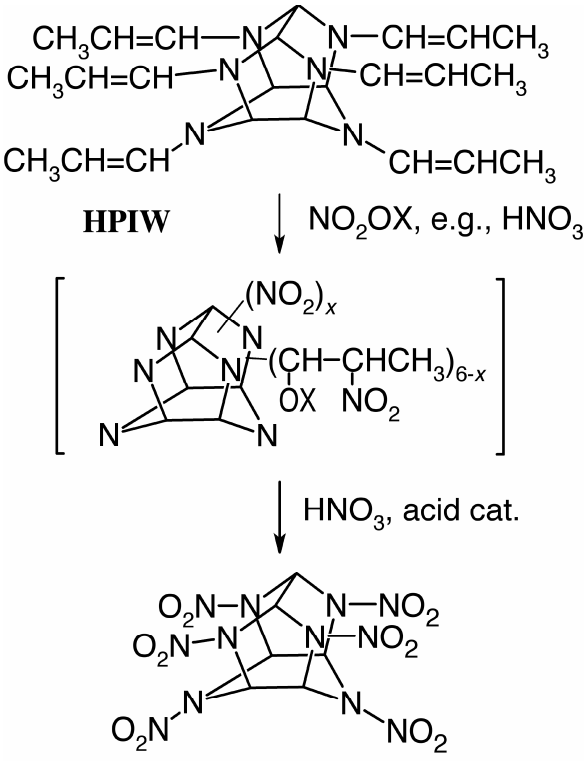
It may be expected that HPIW could be a feasible intermediate for nitrolysis. Enamines are known to undergo electrophilic attack at the β carbon, such as by acylating reagents and halogens, preferentially over the complete displacement of an *N*-alkenyl substituent.[42] A similar initial nitration of the 1-propenyl substituent(s) by a nitrating reagent such as nitric acid would produce an α-(nitratoalkyl)amine, a class of tertiary amine—along with various other electronegatively α-substituted alkylamines—that is known to be nitrolyzable to the corresponding nitramine, such as the case of hexahydro-5-nitratomethyl-1,3-dinitro-1,3,5-triazine nitrolyzed to RDX (Eq. 19):[43]



(19)

This mechanistic route to displacement of substituents on the hexaazaisowurtzitane cage makes it superior to nitrolysis of α-unsubstituted alkyl derivatives, such as would be formed by initial nitration of allyl substituents in hexaallylhexaazaisowurtzitane (HAllylIW). Thus, in the French report of new hexaazaisowurtzitanes,[30a] treatment of 1 g of HAllylIW with mixed acid produced a yellow solid (CL-20 is white) that had a detectable content of CL-20, but no yield was specified. In contrast, the isomerization performed here on HAllylIW produces more easily removed substituents—tentatively following their initial nitration in HPIW—and the content of CL-20 in the nitrolysis mixture is high. It is speculated that transient intermediates of β-nitration of HPIW could be mixed polynitropoly(α-substituted β-nitropropyl)hexaazaisowurtzitanes (Eq 20, wherein X = NO_2, Ac, etc.). (X = H, such as with simple nitric acid, would leave α-hydroxy sites susceptible to further nitration by the nitrating reagent, still forming nitrolyzable intermediates with X = NO_2.)

[42] Hickmott, P.W. in Rappaport, Z. (Ed.), *The Chemistry of Enamines*; John Wiley, 1994; Chapter 14.
[43] Bonner, T.G.; Hancock, R.A.; Roberts, J.C. *J. Chem. Soc. Perkin Trans. 1* **1972**, 1902.


CH3CH=CH
CH=CHCH3
HPIW
NO2OX, e.g., HNO3
(NO2)x
(CH–CHCH3)6-x
OX
NO2
HNO3, acid cat.
O2N
NO2

(20)

Conclusions

By improving the efficiency of converting HAllylIW to CL-20 with one or two additional steps, a potentially practical benzylamine-free, heavy-metal-free synthesis of CL-20 has been successfully achieved. The overall process now avoids the preparation of benzyl chloride, which uses elemental chlorine, and catalytic hydrogenolysis steps—requiring palladium metal/compounds—are avoided. A heavy-metal-free sequence leading to CL-20 is shown in Figure 5: glycerol (available from biodiesel) is dehydrated in formic acid to make allyl alcohol;[44] the alcohol is efficiently converted to allyl bromide[45] or chloride[46] by treatment with the corresponding hydrohalic acid; and the allyl halide is aminated to make allylamine.[47] This commercially available reagent condenses with glyoxal, as recently reported, to make HAllylIW;[30] and the subsequent steps have been developed in the current SEED project, leading to CL-20 with apparently high efficiency.

[44] Kamm, O.; Marvel, C.S. *Org. Synth.* **1941**, *Coll. Vol. I*, 42.
[45] Norris, J.F.; Watt, M.; Thomas, R. *J. Am. Chem. Soc.* **1916**, *38*, 1071.
[46] McCullough, R.; Cortese, F. *J. Am. Chem. Soc.* **1929**, *51*, 225.
[47] Peters, L.M.; Marple, K.E.; Evans, T.W.; McAllister, S.H.; Castner, R.C. *Ind. Eng. Chem.* **1948**, *40*, 2046.

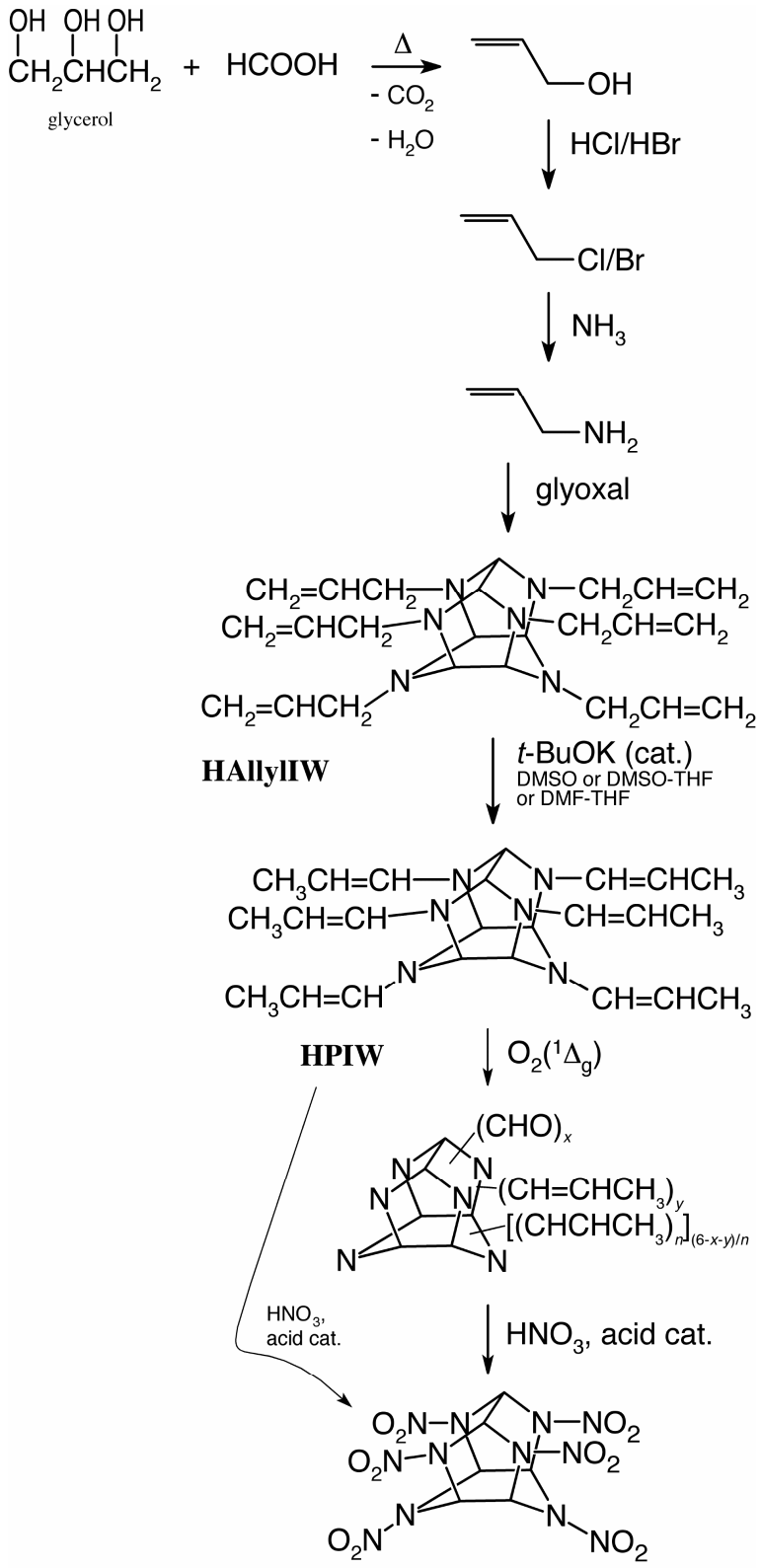


Figure 5. Benzylamine-free, heavy-metal-free route to CL-20

The following recommendations derive from the results of this SEED project, which was only a small-scale feasibility demonstration:

- Process development is needed to improve efficiency of certain steps. Hervé et al. reported 20–25% yields of HAllylIW,[30] and our slight modification of their published procedures yielded 33% HAllylIW. It is clear that further process development should make the allylamine–glyoxal condensation similar in efficiency to that which has been achieved with benzylamine–glyoxal, since the chemistry and conditions are fundamentally similar. In fact, the development of HAllylIW is approximately paralleling that of HBIW: the first yield of HBIW was 12.7%, reported in March 1986;[48] by October 1986, it had improved to 30–40%;[49] and upon an August 1989 manuscript submission, process development had brought it to ~80%.[8]
- The HAllylIW-to-HPIW isomerization has proven to be very efficient, but more-economical alternative solvents might be found for this transformation.
- The limits of catalysis by *t*-butoxide in effecting this isomerization have not been determined. Still-lower quantities of potassium *t*-butoxide could improve the economics of the process.
- The possibly viable "direct" nitrolysis of HPIW—technically, via likely poly(α-nitratoalkyl)-hexaazaisowurtzitane transient intermediates—should be investigated considerably more, as it offers the prospect of avoiding an additional step of oxidizing HPIW by singlet oxygen.
- Nitrolysis of the crude product (**6**) of photooxygenation proceeded very cleanly and efficiently in one example we demonstrated, but overall yield and efficiency should take into account the extra oxidation step in a comparison to the "direct" nitrolysis of HPIW.
- If the photooxygenation product remains desirable, its composition should be better characterized, especially with respect to polymeric vs. propenyl components, and process development in conducting the photooxygenation most efficiently should be carried out. Known alternative methods of generation of singlet oxygen—e.g., solid metal peroxide–gaseous hydrogen halide reactions[50]—should also be considered.
- Further process development of this nature could reasonably be conducted in a follow-on SERDP project.
- Eventually, success in improving the overall sequence should transition a new CL-20 manufacturing process to an industrial partner, such as ATK. However, non-energetic intermediates, such as HAllylIW or HPIW, could be produced by Eurenco[51] or any number of specialty chemical houses, such as Parish Chemical,[52] to whom ATK currently subcontracts the preparation of HBIW and TADB used for CL-20 production.

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[48] Nielsen, A.T.; Nissan, R.A. "Polynitropolyaza Caged Explosives Part 5", Naval Weapons Center (China Lake, CA) *TP 6692*, March 1986.

[49] Nielsen, A.T. *American Defense Preparedness Association Compatibility of Plastics and Other Materials with Explosives, Propellants, Pyrotechnics & Processing of Explosives, Propellants and Ingredients [Proceedings]*, Long Beach CA, October 1986; p. 118.

[50] Christe, K.O; Alfano, A.J. *U.S. Patent* 6,623,718 (2003).

[51] "Eurenco – about – profile"; http://www.eurenco.com/en/about/index.html

[52] "Parish Chemical: Product Details: Product #5200"; http://www.parishchemical.com/product_details.pl?id=2177

Appendices

Experimental Section (Supporting Data)

Hexa(1-propenyl)hexaazaisowurtzitane (HPIW) (Procedure A). Hexaallylhexaazaisowurtzitane (HAllylIW) was prepared as reported by Hervé et al.,[30] except that the product solution was basified with saturated aqueous $NaHCO_3$ and then stored at –16 °C for two days, precipitating HAllylIW, which was filtered off and dried further by dissolving it in CH_2Cl_2, drying over $MgSO_4$, filtering, and removing solvent. To 5 mL of a solution of 204 mg HAllylIW (0.50 mmol) in DMSO-d_6 was added 224 mg (2.00 mmol) of solid potassium *t*-butoxide, and the mixture was magnetically stirred in a capped vial at ambient temperature. Progress of the isomerization was monitored occasionally by ^{1}H NMR analysis of small aliquots and was seen to be complete with essentially quantitative conversion after 6 h. ^{1}H NMR (DMSO-d_6) of HPIW in the crude reaction mixture (Figure A-1): δ 1.52–1.63 (m, CH_3), 4.24–4.33 (m, C*H*CH_3), 4.84 (s, 4 H, cage CH), 4.89 (s, 2 H, cage CH), 5.88–5.96 (NCH).

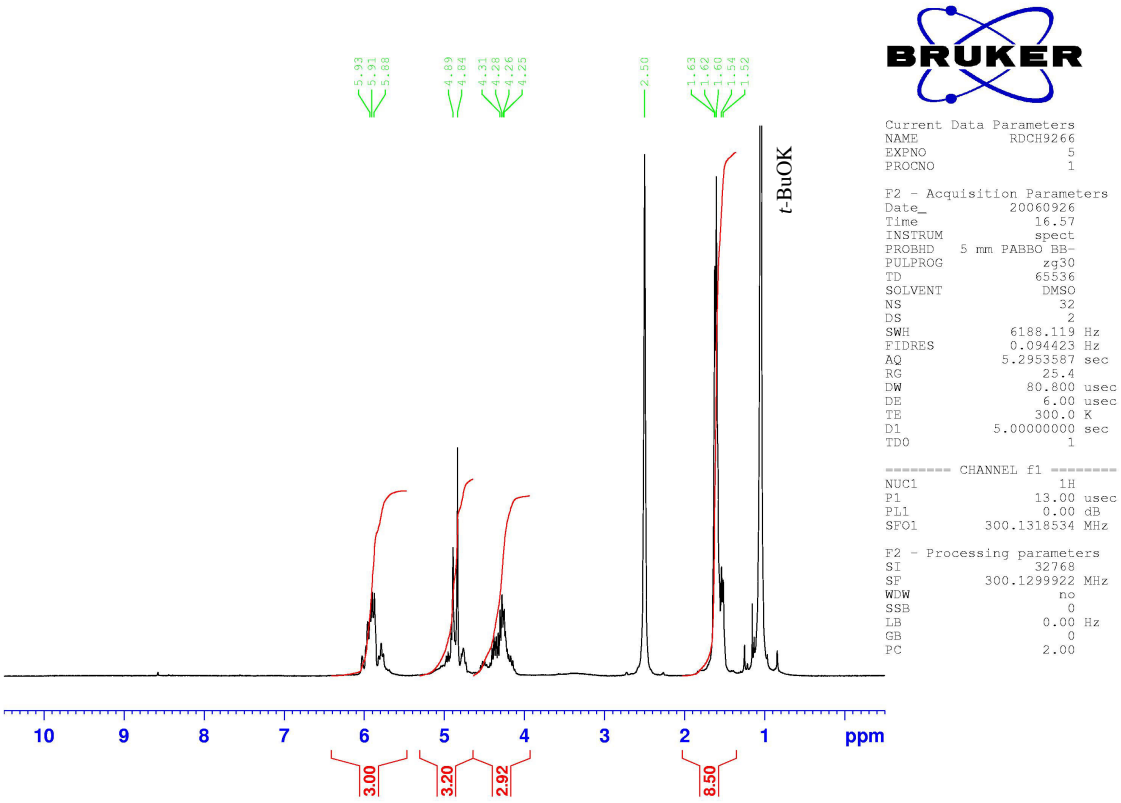

Figure A-1. ^{1}H NMR spectrum of crude reaction sample: preparation of HPIW

^{13}C NMR (DMSO-d_6) of the crude reaction mixture (Figure A-2): δ 11.78, 11.89, 12.20, 15.08, 74.07, 76.61, 77.14, 81.02, 82.11, 82.60, 92.75, 100.24, 100.96, 101.62, 101.77, 102.51, 134.84, 135.30, 135.46, 135.58.

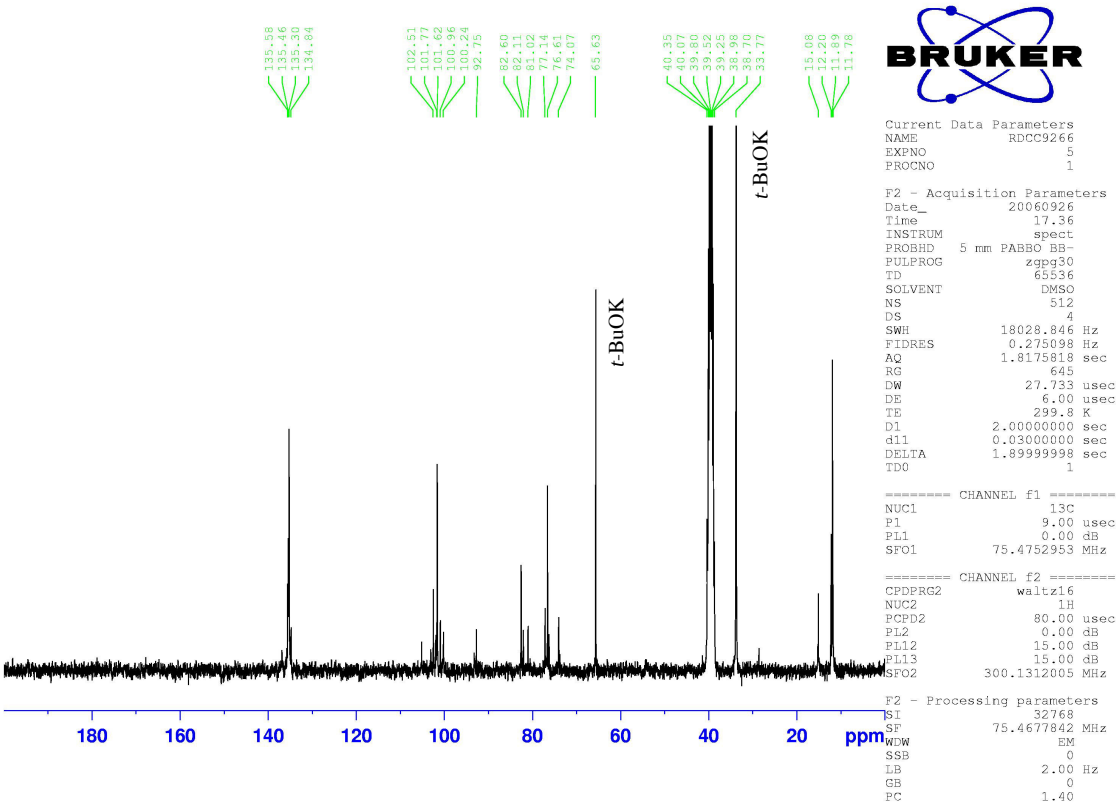

Figure A-2. ^{13}C NMR spectrum of crude reaction sample: preparation of HPIW

HPIW was separated from residual potassium *t*-butoxide by pumping off DMSO-d_6 under high vacuum at room temperature, redissolving HPIW in ~25 mL benzene, filtering off insoluble salt (and minor possible polymeric by-products), removing benzene under vacuum at room temperature, and redissolving in CD_2Cl_2. ^{1}H NMR (CD_2Cl_2): δ 1.59–1.70 (m, CH_3), 4.42–4.76 (m, C*H*CH_3), 4.75 (s, 4 H, cage CH), 4.84 (s, 2 H, cage CH), 5.93–6.02 (NCH). ^{13}C NMR (CD_2Cl_2): δ 12.46, 12.57, 12.82, 15.49, 75.67, 75.81, 77.95, 78.30, 78.71, 78.85, 78.94, 81.92, 82.48, 83.35, 83.89, 95.45, 102.85, 103.78, 104.38, 104.87, 105.90, 135.47, 135.59, 135.76, 135.88, 136.09.

Hexa(1-propenyl)hexaazaisowurtzitane (HPIW) (Procedure B). To 1 mL of a solution of 204 mg HAllylIW (0.50 mmol) in DMSO-d_6 was added 1.0 mL of 1 *M* solution of potassium *t*-butoxide in tetrahydrofuran, and the mixture was magnetically stirred in a capped vial at ambient temperature. After 18 h, isomerization of HAllylIW to HPIW was complete; the product was worked up as in Procedure A, and the isolated product was identical by NMR.

Photooxygenation of HPIW (Example). The HPIW product from an isomerization by Procedure B, following extraction into benzene and concentration, was redissolved in 6 mL of acetone-d_6 in a 10-mL graduated cylinder (with a standard-taper joint) fitted with a Claisen

adapter to allow inlet as well as egress of an oxygen purge via a glass capillary; a few mg of zinc(II) tetraphenylporphine sensitizer was added to the solution, and the base of the cylinder was submerged in a dry ice–ethanol bath. With a purge of oxygen passing through, the solution was irradiated with a quartz halogen headlamp. After 6 h of treatment, a pale pink flocculent solid was suspended in the solution. A representative sample of the suspension was withdrawn for NMR analysis after adding DMSO-d_6 to dissolve it (Figure 3). (Acetaldehyde by-product was clearly apparent in the ^{1}H NMR spectrum of the crude reaction mixtures.) ^{1}H NMR (~1:1 acetone-d_6–DMSO-d_6) of the hexaazaisowurtzitane product (**6**): δ 1.0–1.4 (bm, CH_3), 3.3–6.9 (bm, all CH), 8.1–8.5 (CHO). After filtration of the precipitate from acetone-d_6 and drying under vacuum over P_4O_{10}, the product was a pale peach solid.

Nitrolysis of oxidation product 6 to CL-20. The product suspension of a photooxygenation reaction was concentrated to dryness under vacuum and pumped under high vacuum at room temperature overnight. The very viscous oily residue in a round-bottom flask—fitted with an addition funnel containing 15 mL of cold 98~100% nitric acid (Fluka "100%" nitric acid) and a nitrogen bubbler—was cooled in a dry ice–ethanol bath. The nitric acid was added quickly via the addition funnel. When the nitric acid started freezing, the cooling bath was removed, and the organic reactant dissolved in the acid upon warming adventitiously. After reaching room temperature, the solution was heated to reflux—with a nitrogen bubbler atop the reflux condenser—in an oil bath maintained at 85–95 °C. After 8½ h reflux, NMR analysis of an aliquot showed little conversion to CL-20, so several beads of Nafion NR50 were added. Reflux was resumed and continued for a total of 30½ h. An aliquot of the crude reaction solution withdrawn into acetonitrile-d_3 showed, by ^{1}H NMR (Figure 4), very clean conversion of all hexaazaisowurtzitane species to CL-20. By-products of nitrolysis of the substituents from **6** are also fairly simple in the spectrum. ^{1}H NMR (CD_3CN with HNO_3) of crude CL-20: δ 7.81 (s, 2 H), 7.91 (s, 4 H).

Nitrolysis of HPIW to CL-20. Half of the purified product solution (in benzene) from a preparation of HPIW by Procedure B was evaporated to dryness under vacuum; 10 mL CCl_4 was added, and the solution was again evaporated to dryness under vacuum. The residue in a round-bottom flask—fitted with an addition funnel containing 11 mL of cold 98~100% nitric acid (Fluka "100%" nitric acid) and a nitrogen bubbler—was cooled in a dry ice–ethanol bath. The nitric acid was added quickly via the addition funnel. When the nitric acid started freezing, the cooling bath was removed, and the organic reactant dissolved in the acid upon warming adventitiously. After stirring while warming for 1 h, ~1 mL of 30% fuming sulfuric acid was added, and the solution was heated to reflux—with a nitrogen bubbler atop the reflux condenser—for 4 h. A sample withdrawn into dichloromethane-d_2 showed, by ^{1}H NMR (Figure A-3), significant simplification of the hexaazaisowurtzitane region and formation of CL-20, confirmed by addition of a small amount of authentic CL-20 to the NMR sample and observation of the increase of specific peaks. ^{1}H NMR (CD_2Cl_2 with HNO_3, vs. trimethylsilylpropionic-d_4 acid as δ 0.00) of contained CL-20: δ 7.11 (2 H), 7.45 (s, 4 H).

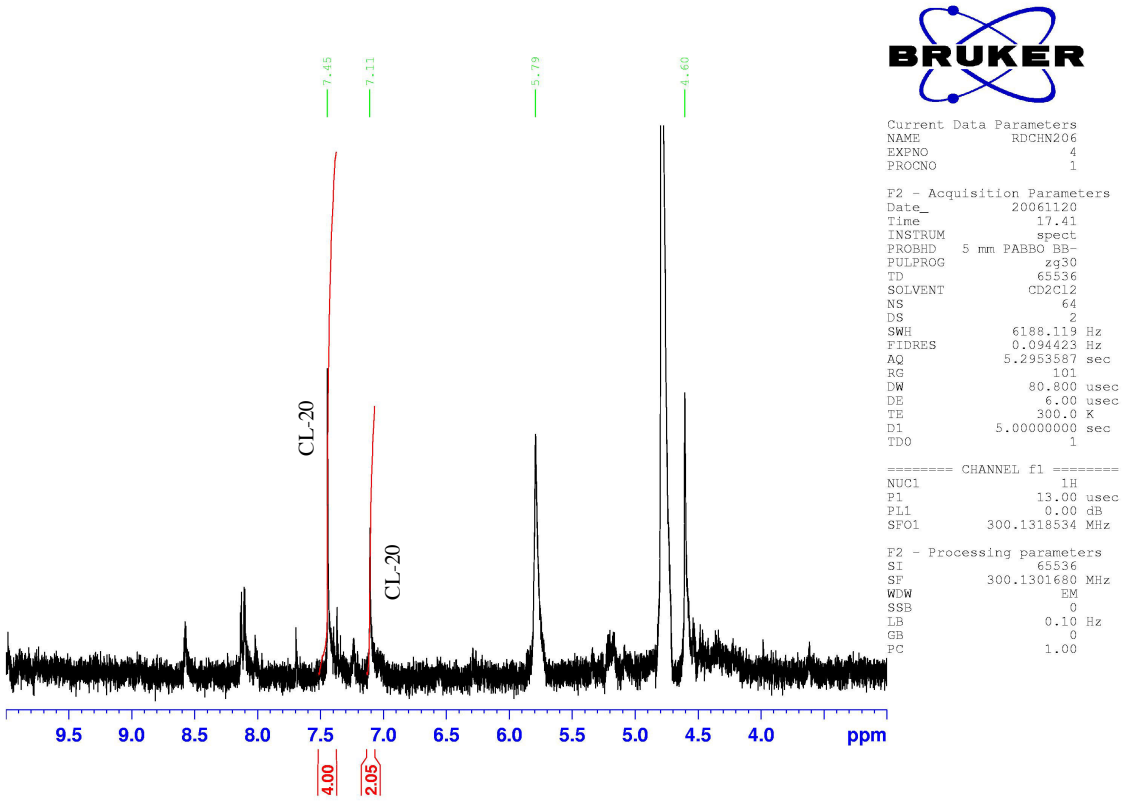

Figure A-3. ^{1}H NMR spectrum of crude reaction sample: nitrolysis of HPIW

List of Technical Publications

"Benzylamine-Free, Heavy-Metal-Free Synthesis of CL-20" Robert D. Chapman, Richard A. Hollins, Thomas J. Groshens, David A. Nissan, *2006 Partners in Environmental Technology Technical Symposium & Workshop [Abstracts]*; Poster Number 94 (http://www.serdp.org/Symposium/upload/Wednesday%20Poster%20Abstracts-after%20Symposium.pdf).