EurJOC
European Journal of Organic Chemistry

A Journal of
ChemPubSoc Europe

Accepted Article

Title: Energetic Functionalization of the Pyridazine Scaffold: Synthesis and Characterization of 3,5-Diamino-4,6-dinitropyridazine-1-oxide

Authors: Thomas M. Klapötke, Joerg Stierstorfer, and Ivan Gospodinov

To be cited as: *Eur. J. Org. Chem.* 10.1002/ejoc.201800068

Link to VoR: http://dx.doi.org/10.1002/ejoc.201800068

Supported by
ACES Asian Chemical Editorial Society

WILEY-VCH

10.1002/ejoc.201800068

WILEY-VCH

Energetic Functionalization of the Pyridazine Scaffold: Synthesis and Characterization of 3,5-Diamino-4,6-dinitropyridazine-1-oxide

Ivan Gospodinov,[a] Thomas M. Klapötke*[a] and Jörg Stierstorfer[a]

Abstract: The synthesis of 3,5-diamino-4,6-dinitropyridazine-1-oxide (**8**) is reported. It is prepared in a six step synthetic procedure starting from the acyclic compounds and shows good properties (detonation velocity $D_{C\text{-}J}$ = 8486 m·s^{-1}, detonation pressure $p_{C\text{-}J}$ = 302 kbar and sensitivity toward mechanical stimuli). Compound **8** and its precursor (**7**, 3,5-dimethoxy-4,6-dinitropyridazine-1-oxide) were characterized by means of multinuclear (^{1}H, ^{13}C, ^{14}N, ^{15}N) NMR spectroscopy, mass spectrometry, vibrational spectroscopy (IR and Raman), elemental analysis and DTA measurements. Compounds **4**, **5**, **6**, **7**, **8** and **9** were also characterized by low-temperature single-crystal X-ray diffraction. The heats of formation for **7** and **8** were calculated using the atomization method based on CBS-4M enthalpies. With the experimentally determined (X-ray) densities and the calculated standard molar enthalpies of formation, several detonation parameters such as the detonation pressure, energy and velocity were predicted by using the EXPLO5 code (V6.03). The sensitivities of 3,5-dimethoxy-4,6-dinitropyridazine-1-oxide (**7**) and 3,5-diamino-4,6-dinitropyridazine-1-oxide (**8**) toward impact, friction and electrical discharge were tested according to BAM standards. In addition, the shock reactivity of **8** was measured by applying the small-scale shock reactivity test, showing similar values to HNS, PYX and TKX-55.

Introduction

Due to increasing safety regulations the research on new energetic materials based on nitrogen-rich heterocycles has attracted considerable interest in the past decades, not only for military application but also for industrial.[1] The arising challenge on combining good detonation performance and sensitivity for the synthesis of new high-energy density materials has come into focus.[2] There are different strategies reported in the literature for achieving this goal; introduction of conjugation into the system, formation of nitrogen-rich salts or introduction of an alternating C−NH_2/C−NO_2 into the system, which leads to the formation of intra- and intermolecular hydrogen bonds.[3] A well-known example for a heat resisting and insensitive explosive is 2,4,6-triamino-1,3,5-trinitrobenzene (TATB) consisting of alternating amino and nitro groups on the benzene scaffold.[4] In recent years, the synthesis of new energetic materials based on nitrogen-rich heterocycles has received great interest.[5] Some synthesized and well known heterocyclic, energetic materials based on pyridines (TANPyO)[6] and 1,4-diazines (ANPZ and LLM-105)[7,8] are shown in Figure 1. LLM-105 and TANPyO exhibit good thermal stability and sensitivity combined with good detonation performance. The introduction of the N-oxide moiety to the energetic backbone has been proven to increase not only the performance of the energetic material, but also its oxygen balance and improves the crystal packing, leading to higher density of the material.[9] For example, 2,6-diamino-3,5-dinitropyrazine-1-oxide (LLM-105, ρ = 1.92 g·cm^{-3} and D = 8516 m·s^{-1}) shows higher energetic performance compared to its precursor 2,6-diamino-3,5-dinitropyrazine (ANPZ, ρ = 1.84 g·cm^{-3} and D = 7892 m·s^{-1}).[5,10]

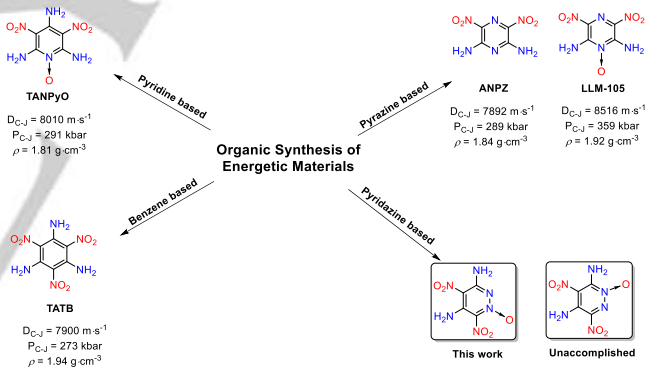


Figure 1. Energetic compounds TATB, TANPyO, ANPZ, LLM-105 and the investigated pyridazine derivatives.

Although 1,4-diazines have been well investigated in the literature as energetic materials, 1,3- and 1,2-diazines are relatively unexploited systems. This can be explained by the fact that electrophiles directly attack the ring N-atoms in the pyridazine/pyrimidine system resulting for instance in protonation, alkylation or N-oxidation, thus hindering nitration attempts.[11] In addition, the nitro group is an excellent leaving group and can be easily substituted even by weak nucleophiles.[12] However, recently reported literature shows that 1,2-diazine (pyridazine) derivatives and their N-oxides can be synthesized and may be interesting new building blocks for the synthesis of new energetic materials.[13] The idea of this work was to synthesize 3,5-diamino-4,6-dinitropyridazine-1-oxide and 4,6-diamino-3,5-dinitropyridazine-1-oxide (Figure 1); two structural isomers to LLM-105 which are based on the pyridazine scaffold. Due to the additional N–N bond both

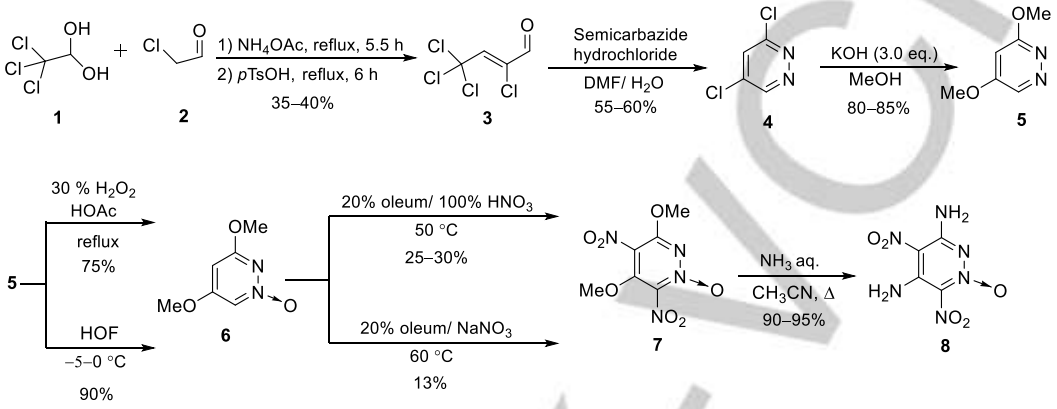
[a] *Prof. Dr. Thomas M. Klapötke, Ivan Gospodinov, Dr. Jörg Stierstorfer.*
Ludwig-Maximilian University Munich, Department of Chemistry
Butenandtstr. 5-13 (D), 81377 München, Germany
Fax: (+) 49 (0) 89 - 2180 77492
E-mail: tmk@cup.uni-muenchen.de
Homepage: http://www.hedm.cup.uni-muenchen.de

Supporting information for this article is given via a link at the end of the document.((Please delete this text if not appropriate))

pyridazine derivatives should exhibit even higher heat of formation compared to LLM-105.

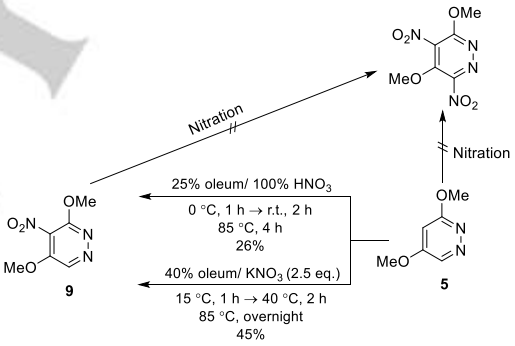
Results and Discussion

Herein, we report the selective functionalization of the pyridazine scaffold (Scheme 1).



Scheme 1. Synthesis of 3,5-dimethoxy-4,6-dinitropyridazine-1-oxide (**7**) and 3,5-diamino-4,6-dinitropyridazine-1-oxid (**8**).

The target molecules 3,5-dimethoxy-4,6-dinitropyridazine-1-oxide (**7**) and 3,5-diamino-4,6-dinitropyridazine-1-oxide (**8**) were synthesized by using 3,5-dichloropyridazine (**4**) as the starting material. Initially, compound **4** was synthesized according to the literature.[14] Treatment of chloral hydrate (**1**) with chloroacetaldehyde (**2**) in the presence of ammonium acetate and *p*-toluenesulfonic acid monohydrate on the DEAN-STARK apparatus gave (*Z*)-2,4,4,4-tetrachlorobut-2-enal (**3**). The cyclization of compound **3** with semicarbazide hydrochloride yielded 3,5-dichloropyridazine (**4**). Subsequently, compound **4** was converted into 3,5-dimethoxypyridazine-1-oxide (**6**)[15] by first reacting it with potassium hydroxide in methanol, which gave 3,5-dimethoxypridazine (**5**),[16] followed by oxidation of the pyridazine nitrogen with 30% hydrogen peroxide in glacial acetic acid. The introduction of the N-oxide was also accomplished by using HOF increasing the yield of the reaction up to 90%.[17] The insertion of the N-oxide and the introduction of electron-donating functional groups (−OMe) into the pyridazine scaffold allowed the nitration with 20% oleum and 100% nitric acid of compound **6** to the desired product 3,5-dimethoxy-4,6-dinitropyridazine-1-oxide (**7**). Nitration of **6** was also possible with a mixture of 20% oleum and sodium nitrate at elevated temperature. The second nitro group in compound **7** was able to be introduced only when the N-oxide was present in the parent molecule. Finally, 3,6-diamino-4,6-dinitropyridazine-1-oxide (**8**) was synthesized by reacting compound **7** with concentrated ammonia solution in acetonitrile.



Scheme 2. Nitration reactions with 3,5-dimethoxypyridazine (**5**).

The first step in the synthesis of 4,6-diamino-3,5-dinitropyridazine-1-oxide was the nitration of 3,5-dimethoxypridazine (**5**). As shown in Scheme 2 the nitration of compound **5** gave only 3,5-dimethoxy-4-nitropyridazine (**9**) and not the desired product 3,5-dimethoxy-4,6-dinitropyridazine. Further nitration of compound **9** was not successful and yielded either the starting material or decomposition products. The crystal structure of compound **9** is reported in the Supporting Information. As it seems without the N→O moiety the introduction of the second nitro group into the pyridazine system cannot be achieved. Different strategies toward the synthesis of 4,6-diamino-3,5-dinitropyridazine-1-oxide are currently under investigation.

Suitable crystals of **7** and **8** for X-ray diffraction analysis were obtained by slow evaporation from a solution of **7** in dichloromethane and a solution of **8** in water, respectively. In addition the crystal structures of compounds **4**–**6** are shown in the Supporting Information. CCDC-1590457 (**4**), CCDC-1590458 (**5**), CCDC-1590459 (**6** • 3 H_2O), CCDC-1590461 (**7**), CCDC-1590460 (**8**) and CCDC-1816507 (**9**) contain the supplementary

crystallographic data for this paper. These data can be obtained free of charge from The Cambridge Crystallographic Data Centre via www.ccdc.cam.ac.uk/data_request/cif. Compound **7** crystallizes in the orthorhombic space group *Pbcn* and has a calculated density of 1.637 g·cm^{-3} at 123 K (Figure 2). The bond angles and bond lengths in the pyridazine ring are between typical C−N/N−N single and C=N/N=N double bonds due to the aromaticity. Among them, the bond lengths of N2−C1 and N1−N2 are 1.329(3) and 1.347(3) Å, respectively. The N−O bond length in the N→O moiety is 1.268(2) Å.

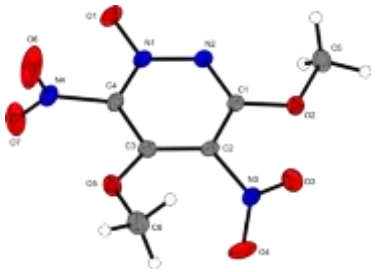


Figure 2. Molecular structure of compound **7** in the solid state. Ellipsoids correspond to 50 % probability levels. Selected bond distances [Å] and angles [°]: O1–N1 1.268(2), N1–N2 1.347(3), N1–C4 1.341(3), C3–C4 1.401(3), N4–C4 1.468(3), O2–C1 1.323(2), N2–N1–C4 121.75(17), N3–C2–C1 117.48(18), C5–O2–C1–N2 −2.6(3), O1–N1–N2–C1 178.22(17), O3–N3–C2–C3 −120.9(2), C6–O5–C3–C4 −160.6(2);

Compound **8** crystallizes in the monoclinic space group $P2_1/c$ and has a calculated density of 1.888 g·cm^{-3} at 123 K (Figure 3). Compared to compound **7** (N1−O1 1.268(2) Å) the N−O bond length in the N→O moiety of **8** does not shown any significant difference (N1−O1 1.2681(19) Å). Compound **8** is almost planar in the crystal structure with a small aberration for the nitro group next to the N→O with torsions angle of 36.5(2) and −144.95(17)° for O2−N3−C1−N1 and O3−N3−C1−N1, respectively. Both amino groups and the second nitro group are in the same plane as the pyridazine ring. The C−C (C1–C2 1.422(2) Å) lengths in compound **8** are in the range of those reported for LLM-105 (C–C 1.417 Å); however the C−N (N1–C2 1.357(2) Å) bond lengths for compound **8** are slightly shorter than those reported for LLM-105 (C–N 1.374 Å). In addition, the N−O bond length (1.3172 Å) in the N→O moiety for LLM-105 is longer than the determined value (N1−O1 1.2681(19) Å) for compound **8**.[20b]

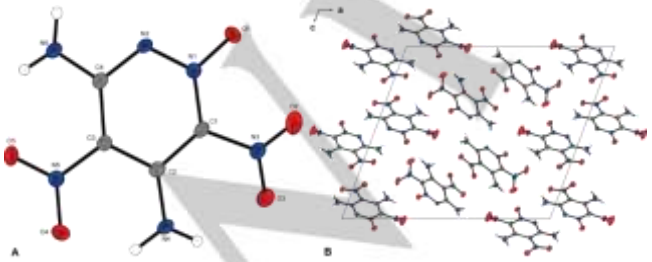


Figure 3. A) Molecular structure of compound **8** in the solid state. Ellipsoids correspond to 50 % probability levels. Selected bond distances [Å] and angles [°]: O1–N1 1.2681(19), N1–N2 1.323(2), N1–C1 1.357(2), C1–C2 1.422(2), N6–C4 1.322(2), O3–N3 1.229(2), O1–N1–N2 114.67(15), N1–N2–C4 118.94(15), O2–N3–C1 119.99(15), O1–N1–C1–N3 4.9(2), O2–N3–C1–N1 36.5(2), O5–N5–C3–C2 −168.62(15), N4–C2–C3–N5 −5.5(2); B) View of the unit cell of compound **8** along the b-axis.

^{15}N NMR spectroscopy

All synthesized compounds were characterized by vibrational spectroscopy (IR and Raman), mass spectrometry, multinuclear NMR (^{1}H, ^{13}C and ^{14}N) spectroscopy and elemental analysis. In addition ^{15}N and ^{15}N{1H} NMR spectra of compound **8** were recorded (Figure 4). ^{15}N NMR spectrum of **8** exhibits only five signals; both nitro groups are observed at −15.6 and −26.0 ppm, the N-oxide has a resonance at −69.5 ppm and the pyridazine nitrogen at −100.3 ppm. Only one amino group can be observed at −286.7 ppm ($^1J_{NH}$ = 92.9 Hz) in the proton coupled ^{15}N NMR spectrum of **8**. All six resonances for the nitrogen atoms can be observed in the proton decoupled ^{15}N NMR spectrum of **8**. Both nitro groups (−15.6 and −26.0 ppm) and the pyridazine nitrogen atoms (−69.5 and −100.3 ppm) exhibit the same chemical shift as listed bevor. Both amino groups can be observed as singlets at −286.7 and −292.9 ppm.

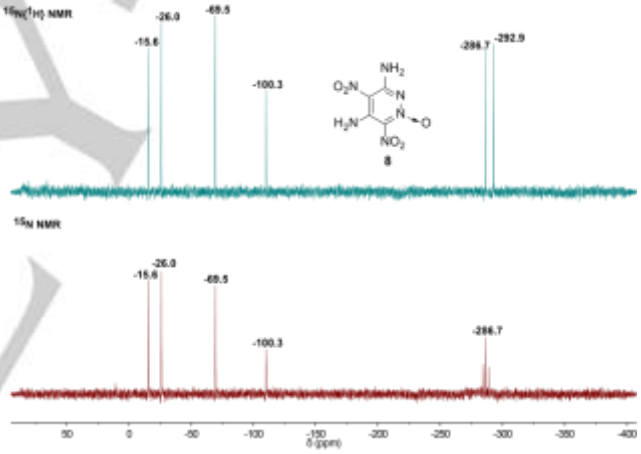


Figure 4. ^{15}N{^{1}H} and ^{15}N NMR spectra of compound **8**.

Since compounds **7** and **8** can be classified as energetic materials, their energetic behavior was investigated. All theoretically calculated and experimentally determined values for **7** and **8** compared to the insensitive explosive LLM-105 are listed in Table 1. The thermal behavior for both compounds was investigated with an OZM Research DTA 552-Ex instrument at a heating rate of 5 °C min^{-1}. Compound **7** decomposes at 151 °C, while 3,6-diamino-4,6-dinitropyridazine-1-oxide (**8**) decomposes first at 215 °C. The increased stability of compound **8** compared to the precursor, compound **7**, can be explained by the intra-and intermolecular hydrogen bonds in the structure of **8**. This observation of change in the thermal behavior from compound **7** to compound **8** verifies that the introduction of alternating C−NH$_2$/C−NO$_2$ functionalities into the pyridazine system not only improves the energetic properties of the material, but also increases the thermal stability. The difference in the thermal stability of **8** (215 °C) compared to LLM-105 (342 °C) is significant. This can be explained with the weakening of the N−N

bond in the pyridazine with the introduction of the N-oxide and its position next to the NO_2 group.

In addition, the sensitivities for both compounds were determined according the BAM standards and the detonation parameters were calculated using the EXPLO5_V6.03 computer code.[18] The EXPLO5 detonation parameters of **7** and **8** were calculated by using the room-temperature density values obtained from the X-ray structures as described in reference.[19] The density at room temperature for compound **7** is 1.591 g·cm^{-3} and for **8** is 1.837 g·cm^{-3}. The determined experimental sensitivities toward friction and impact for **7** (IS = 20 J and FS = 360 N) and **8** (IS = 18 J and FS = 360 N) are in the range for those of the insensitive explosive LLM-105 (IS = 20 J and FS = 360 N). The synthesized compounds **7** (0.65 J) and **8** (0.75 J) are even less sensitive than LLM-105 (0.60 J) toward electrostatic discharge. The calculated physico-chemical properties of compound **8** compared to those of LLM-105 are quite surprising (Table 1). Although the room temperature density of 3,5-diamino-4,6-dinitropyridazine-1-oxide (**8**, ρ = 1.837 g·cm^{-3}) is lower than those of LLM-105 (ρ = 1.919 g·cm^{-3}),[20] the calculated detonation parameters for **8** are similar to those of LLM-105. The detonation pressure ($p_{C\text{-}J}$ = 302 kbar) and detonation velocity ($D_{C\text{-}J}$ = 8486 m·s^{-1}) of **8** are in the range of those for LLM-105 ($p_{C\text{-}J}$ = 317 kbar and $D_{C\text{-}J}$ = 8639 m·s^{-1}). However, the values of **8** for the detonation energy (4913 kJ·kg^{-1}) and for the detonation temperature (3470 K) exceed those values for LLM-105 (4506 kJ·kg^{-1} and 3202 K).

Table 1. Physico-chemical properties of compounds **7** and **8** in comparison to LLM-105.

	7	**8**	**LLM-105**
Formula	$C_6H_6N_4O_7$	$C_4H_4N_6O_5$	$C_4H_4N_6O_5$
IS[a] [J]	20	18	20*
FS[b] [N]	360	360	360*
ESD[c] [J]	0.65	0.75	0.60*
Ω[d] [%]	−52	−37	−37
T_m[e] [°C]	–	–	–
T_{dec}[f] [°C]	151	215	342[20a]
ρ[g] [g·cm^{-3}]	1.59	1.84	1.92[20b]
$\Delta_f H°$[h] [kJ·kg^{-1}]	−465	511	51
$\Delta_f H°$[h] [kJ·mol^{-1}]	−114	110	11
EXPLO5 6.03			
$-\Delta_E U°$[i] [kJ·kg^{-1}]	4767	4913	4506
$T_{C\text{-}J}$[j] [K]	3442	3470	3202
$p_{C\text{-}J}$[k] [kbar]	208	302	317
$D_{C\text{-}J}$[l] [m·s^{-1}]	7227	8486	8639
V[m] [L^3·kg^{-1}]	722	720	706

[a] Impact sensitivity (BAM drophammer, method 1 of 6); [b] friction sensitivity (BAM drophammer, method 1 of 6); [c] electrostatic discharge device (OZM research); [d] oxygen balance with respect to CO_2; [e] melting point (DTA, β = 5°C·min^{-1}); [f] temperature of decomposition (DTA, β = 5°C·min^{-1}); [g] density at 298 K; [h] standard molar enthalpy of formation; [i] detonation energy; [j] detonation temperature; [k] detonation pressure; [l] detonation velocity; [m] volume of detonation gases at standard temperature and pressure conditions. *experimentally determined values for LLM-105 (grain size 100–500 µm).

The evaluation of the explosive performance of compound **8** on a small scale was investigated with the smalls-scale shock reactivity test (SSRT). With this test the shock reactivity (explosiveness) of the investigated explosive is measured below the critical diameter, without requiring a transition to detonation.[21] The set-up for the smalls-scale shock reactivity test (SSRT) has been prepared as previously reported in the literature (Figure 5).[22] Compound **8** was pressed at a consolidation dead load of 3 t with a dwell time of 5 s into a perforated steel block. Initiation of the tested explosive was performed by using a commercially available detonator.

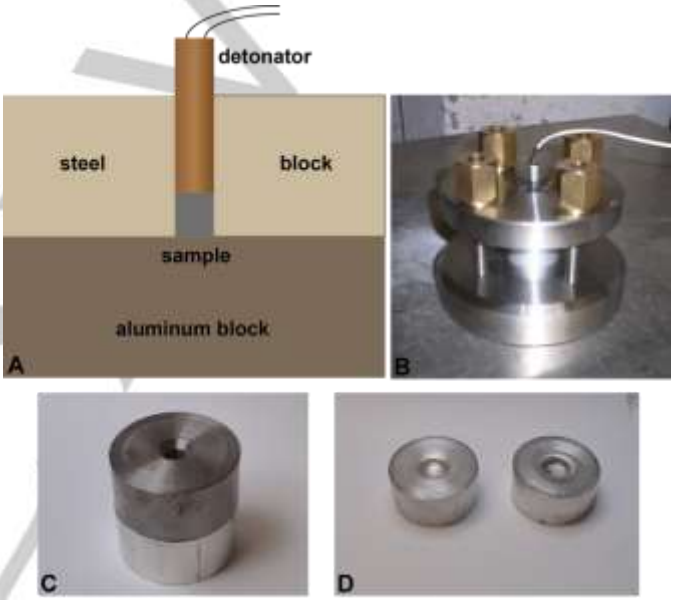


Figure 5. SSRT results: A) schematical illustration; B) photograph of the setup; C) aluminum block and steel block filled with compound **8**; D) dented aluminum block after initiation of the explosive with a commercial detonator.

The results of the SSRT are displayed in Figure 5 (D). The dent sizes were measured by filling them with finely powdered SiO_2 and measuring the resulting weight. The result of **8** is compared with the corresponding values for HNS, PYX and TKX-55 (Table 2).[22] The measured dent volume for compound **8** (694 mg) compared to HNS (672 mg), PYX (637 mg) and TKX-55 (641 mg) shows that the performance of **8** on a small scale is slightly higher than the known heat resistant explosives.

Table 2. The SSRT for compound **8** compared to HNS, PYX and TKX-55.

SSRT for **8** compared to HNS, PYX and TKX-55				
	HNS	PYX	TKX-55	**8**
m_E [mg][a]	469	474	496	496
m_{SiO2} [mg] [b]	672	637	641	694

[a] Mass of the explosive: $m_E = V_s \rho$ 0.95; [b] Mass of SiO_2.

Conclusions

In summary, we report the synthesis of new selectively functionalized pyridazine derivative consisting of alternating amino/nitro groups and N-oxide moiety. Compounds **7** and **8** were synthesized by starting from the acyclic compounds chloral hydrate and chloroacetaldehyde. The introduction of the N-oxide was achieved by reacting 3,5-dimethoxypyridazine (**5**) either with a mixture of glacial acetic acid and 30% H_2O_2 or by reacting **5** with HOF solution. Nitration of 3,5-dimethoxypyridazine-1-oxide (**6**) to 3,5-dimethoxy-4,6-dinitropyridazine-1-oxide (**7**) was achieved with 20% oleum and 100% nitric acid. The key step in the synthesis was the introduction of electron-donating groups (−OMe) and the N-oxide moiety into the pyridazine scaffold allowing successful nitration. Amination of **7** with concentrated ammonia solution yielded 3,5-diamino-4,6-dinitropyridazine-1-oxide (**8**). Compound **8** shows good detonation properties similar to LLM-105 and also low sensitivities (IS = 18 J; FS = 360 N and ES = 0.75 J). In addition, the small-scale shock reactivity test (SSRT) with compound **8** was performed and compared to other energetic materials (HNS, PYX, TKX-55). Further functionalization of the pyridazine scaffold is currently under investigation in our laboratories.

Experimental Section

General Considerations

^{1}H, ^{13}C, ^{14}N and ^{15}N NMR spectra were recorded on JEOL 270 and BRUKER AMX 400 instruments. The samples were measured at room temperature in standard NMR tubes (Ø 5 mm). Chemical shifts are reported as δ values in ppm relative to the residual solvent peaks of $CDCl_3$ (δH: 7.26, δC: 77.1), d6-Acetone (δH: 2.05, δC: 29.8 and 206.3) and d_6-DMSO (δH: 2.50, δC: 39.5). Solvent residual signals and chemical shifts for NMR solvents were referenced against tetramethylsilane (TMS, δ = 0 ppm) and nitromethane. Unless stated otherwise, coupling constants were reported in hertz (Hz) and for the characterization of the observed signal multiplicities the following abbreviations were used: s (singlet), d (doublet), t (triplet), q (quartet), quint (quintet), sept (septet), m (multiplet) and br (broad). Low resolution mass spectra were recorded on a JEOL JMS-700 MStation mass spectrometer (EI+/DEI+). Infrared spectra (IR) were recorded from 4500 cm^{-1} to 650 cm^{-1} on a PERKIN ELMER Spectrum BX-59343 instrument with SMITHS DETECTION DuraSamplIR II Diamond ATR sensor. The absorption bands are reported in wavenumbers (cm^{-1}). Elemental analysis was carried out by the department's internal micro analytical laboratory on a Elementar Vario el by pyrolysis of the sample and subsequent analysis of the formed gases. Decomposition temperatures were measured via differential thermal analysis (DTA) with an OZM Research DTA 552-Ex instrument at a heating rate of 5 °C min^{-1} and in a range of room temperature to 400 °C. Melting points were determined in capillaries with a Büchi Melting Point B-540 instrument and are uncorrected. All sensitivities toward impact (IS) and friction (FS) were determined according to BAM (German: Bundesanstalt für Materialforschung und Prüfung) standards using a BAM drop hammer and a BAM friction apparatus.[23] Compounds **7** and **8** were tested for sensitivity towards electrical discharge using an Electric Spark Tester ESD 2010 EN.

3,5-Dimethoxypyridazine (**5**)

3,5-Dichloropyridazine (16.26 g, 109.15 mmol) was dissolved in MeOH (400 mL) and potassium hydroxide (20.82 g, 371.1 mmol, 3.36 eq.) was added. The resulting reaction mixture was stirred at room temperature for 3 days. The suspension was filtrated and the solvent was removed under reduced pressure. The solid material was dissolved in a mixture of DCM (350 mL)/ H_2O (150 mL) and the water phase was extracted again with DCM (2 × 150 mL). The combined organic layers were dried over $MgSO_4$ and the solvent was evaporated *in vacuo* to yield compound **5** (12.40, 88.49 mmol, 81 %) as a yellowish solid.

m.p. 73 °C; IR (ATR), $\tilde{\nu}$ (cm^{-1}) = 3322 (br), 3056 (w), 3020 (vw), 2962 (w), 1595 (vs), 1554 (vw), 1468 (s), 1447 (s), 1419 (vw), 1387 (vs), 1345 (vs), 1297 (w), 1247 (vw), 1218 (vs), 1191 (s), 1170 (vs), 1092 (m), 1043 (s), 1016 (vs), 986 (m), 926 (m), 898 (m), 876 (s), 861 (vw), 750 (m), 659 (m). Raman (1064 nm, 200 mW, 25 °C): $\tilde{\nu}$ (cm^{-1}) = 3088 (20), 3046 (28), 3022 (53), 2993 (17), 2965 (35), 2945 (23), 2584 (17), 2826 (10), 1602 (9), 1468 (10), 1445 (13), 1418 (11), 1348 (31), 1245 (33), 1190 (13), 1179 (9), 1093 (11), 1046 (11), 1016 (22), 992 (17), 750 (39), 459 (21), 250 (9), 220 (13), 73 (100). ^{1}H NMR (d_6-DMSO, 400 MHz, ppm) δ = 8.63 (d, ^4J = 2.50 Hz, 1H), 6.69 (d, ^4J = 2.50 Hz, 1H), 3.99 (s, 3H), 3.86 (s, 3H). ^{13}C NMR (d_6-DMSO, 101 MHz, ppm) δ = 165.9, 159.7, 141.1, 96.9, 55.8, 54.5. Elem. Anal. ($C_6H_8N_2O_2$, 140.14 g mol^{-1}) calcd.: C 51.42, H 5.75, N 19.99 %. Found: C 51.46, H 5.79, N 19.85 %. *m/z* (DEI$^+$): 140 (100) [M]$^+$, 139 (92), 69 (55), 68 (84);

3,5-Dimethoxypyridazine-1-oxide (**6**)

Procedure 1:

To a solution of 3,5-dimethoxypyridazine (6.00 g, 42.8 mmol) in acetic acid (60 mL) was added 30% H_2O_2 (8 mL) and the reaction mixture was stirred at 75 °C. After 2.5 h 30% H_2O_2 (8 mL) was added to the reaction dropwise and stirring was continued for another 2.5 h at 75 °C. After cooling down, the reaction mixture was diluted with H_2O (250 mL) and basified with Na_2CO_3. The water phase was extracted with DCM (3 × 250 mL) and the combined organic layers were washed with H_2O (250 mL). After draying over $MgSO_4$ the solvent was removed *in vacuo* and compound **6** (4.94 g, 75 %) was obtained as white solid.

Procedure 2:

3,5-Dimethoxypyridazine (0.51 g, 3.27 mmol) was dissolved in DCM (15 mL) and the reaction was cooled to –5–0 °C. To the solution was slowly added freshly prepared HOF in acetonitrile solution (0.26 M, 63 mL, 5.0 eq.) and the reaction mixture was stirred for 1 h at 0 °C and overnight at room temperature. The excess of acid was quenched with saturated sodium carbonate solution and the reaction was extracted with DCM (5 × 150 mL). The combined organic layers were dried over $MgSO_4$ and the solvent was removed *in vacuo*. Compound **6** was obtained as a white solid in a good yield (0.46 g, 90%).

m.p. 131 °C; IR (ATR), $\tilde{\nu}$ (cm^{-1}) = 3114 (w), 3059 (w), 2948 (w), 1567 (s), 1457 (m), 1379 (s), 1212 (vs), 1175 (s), 1080 (m), 1043 (m), 965 (w), 927 (m), 855 (m), 825 (s). Raman (1064 nm, 200 mW, 25 °C): $\tilde{\nu}$ (cm^{-1}) = 3115 (15), 3061 (16), 3025 (43), 2991 (15), 2943 (22), 2840 (14), 1572 (35), 1475 (11), 1447 (9), 1430 (15), 1232 (35), 1221 (30), 1200 (15), 1176 (18), 1054 (12), 1003 (11), 970 (25), 624 (52), 397 (19), 258 (15), 203 (14), 117 (100). ^{1}H NMR (d_6-DMSO, 400 MHz, ppm) δ = 7.98 (d, ^4J =

1.65 Hz, 1H), 6.55 (d, ^4J = 1.65 Hz, 1H), 3.88 (s, 3H), 3.86 (s, 3H). ^{13}C NMR (d_6-DMSO, 101 MHz, ppm) δ = 165.6, 165.2, 118.8, 90.9, 56.9 55.0. Elem. Anal. ($C_6H_8N_2O_3$, 156.14 g mol^{-1}) calcd.: C 46.15, H 5.16, N 17.94 %. Found: C 46.17, H 5.11, N 17.86 %. *m/z* (DEI$^+$): 156 (100) [M]$^+$, 85 (29), 69 (21), 68 (16);

3,5-Dimethoxy-4,6-dinitropyridazine-1-oxide (**7**)

Procedure 1:

3,5-Dimethoxypyridazine-1-oxide (3.00 g, 19.2 mmol) was dissolved in 20% oleum (20 mL) at 5 °C and sodium nitrate (8.50 g, 100 mmol) was added in a small portions by maintaining the temperature of the solution below 5 °C. The reaction mixture was stirred for 1 h and then brought to room temperature slowly. Subsequently, the reaction was stirred overnight at 60 °C and afterwards quenched on crushed ice. The resulting suspension was stirred until all ice dissolved and the resulting precipitate was filtered. The crude product was dissolved in conc. H_2SO_4 (13 mL), stirred at 60 °C for 3 h, then quenched on ice and the resulting precipitate was filtered. The product was washed with ice-water until the filtrate was acid free and dried on air (0.62 g, 13%).

Procedure 2:

3,5-Dimethoxypyridazine-1-oxide (6.70 g, 42.9 mmol) was dissolved in 20-25% oleum (35 mL) at 10 °C and 100% HNO_3 (26 mL) was added dropwise by maintaining the temperature of the solution below 8 °C. After the addition was complete the reaction mixture was first stirred for 1.5 h at 0 °C, then for 2 h at room temperature and finally for 20 h at 45-50 °C. After cooling down the reaction was poured onto crushed ice. The resulting suspension was stirred for 2 h and then the yellowish precipitate was filtered off, washed with water until the filtrate was acid free and dried on air. The crude product was dissolved in conc. H_2SO_4 (35 mL) and stirred at 60 °C for 2 h. The reaction mixture was quenched on crushed ice. The resulting precipitate was filtrated, washed with ice-water until the filtrate was acid free and dried on air (2.94 g, 28 %).

DTA (5 °C min^{-1}): 151 °C (dec.); BAM: drop hammer: 20 J (100–500 µm); friction tester: 360 N (100–500 µm); ESD: 0.65 J (100–500 µm); IR (ATR), $\tilde{\nu}$ (cm^{-1}) = 3000 (w), 2962 (m), 2906 (w), 2890 (w), 1563 (s), 1541 (s), 1504 (m), 1443 (m), 1416 (m), 1379 (s), 1343 (s), 1285 (s), 1252 (m), 1214 (s), 1136 (m), 1082 (m), 1016 (m), 985 (m), 942 (w), 828 (m), 784 (m), 760 (w), 711 (vs), 648 (m), 614 (w). Raman (1064 nm, 200 mW, 25 °C): $\tilde{\nu}$ (cm^{-1}) = 3052 (10), 2963 (22), 1564 (32), 1528 (9), 1452 (12), 1419 (27), 1379 (22), 1346 (41), 1253 (40), 830 (21), 642 (10), 616 (9), 403 (8), 333 (12), 313 (24), 230 (15), 186 (17), 158 (23), 96 (100). ^{1}H NMR (d_6-DMSO, 400 MHz, ppm) δ = 3.98 (s, 3H), 3.87 (s, 3H). ^{13}C NMR (d_6-DMSO, 101 MHz, ppm) δ = 156.8, 155.6, 144.4, 124.1, 62.1, 55.5. ^{14}N NMR (d_6-DMSO, 29 MHz, ppm) δ = −18, −82. Elem. Anal. ($C_6H_6N_4O_7$, 246.14 g mol^{-1}) calcd.: C 29.28, H 2.46, N 22.76 %. Found: C 29.25, H 2.69, N 22.78 %. *m/z* (DEI$^+$): 246 (100) [M]$^+$, 216 (24), 140 (39), 83 (10);

3,5-Diamino-4,6-dinitropyridazine-1-oxide (**8**)

3,5-Dimethoxy-4,6-dinitropyridazine-1-oxide (1.40 g, 6.69 mmol) was dissolved in acetonitrile (50 mL) and an aqueous 25% NH_3 solution (5.0 mL) was added dropwise at room temperature. The solution was then refluxed for 24 h. After cooling down the solvent was removed *in vacuo* and the residue was dissolved in acetone. After removing the solvent under reduced pressure the product was obtained as yellow solid (1.20 g, 90 %).

DTA (5 °C min^{-1}): 215 °C (dec.); BAM: drop hammer: 18 J (100–500 µm); friction tester: 360 N (100–500 µm); ESD: 0.75 J (100–500 µm); IR (ATR), $\tilde{\nu}$ (cm^{-1}) = 3419 (w), 3280 (m), 1600 (s), 1573 (s), 1513 (vs), 1381 (m), 1271 (s), 1219 (s), 1181 (vs), 1078 (s), 1034 (s), 891 (w), 834 (m), 775 (w), 754 (w), 726 (w), 699 (m), 659 (w), 638 (w), 559 (s). Raman (1064 nm, 200 mW, 25 °C): $\tilde{\nu}$ (cm^{-1}) = 3287 (7), 1514 (52), 1456 (23), 1395 (16), 1311 (67), 1284 (73), 1200 (15), 1133 (8), 1042 (9), 896 (10), 836 (29), 667 (23), 633 (8), 582 (29), 417 (7), 204 (10), 122 (100), 107 (100). ^{1}H NMR (d_6-DMSO, 400 MHz, ppm) δ = 8.75 (br, 2H), 8.64 (br, 2H). ^{13}C NMR (d_6-DMSO, 101 MHz, ppm) δ = 154.3, 142.2, 133.9, 110.9. ^{14}N NMR (d_6-DMSO, 29 MHz, ppm) δ = −15, −26, −70. ^{15}N NMR (d_6-DMSO, 41 MHz, ppm) δ = −15.6, −26.0, −69.5, −110.3, −286.7 (t, J_{NH} = 92.9 Hz, 2N). ^{15}N{H} NMR (d_6-DMSO, 41 MHz, ppm) δ = −15.6, −26.0, −69.5, −110.3, −286.8, −292.9. Elem. Anal. ($C_4H_4N_6O_5$, 216.11 g mol^{-1}) calcd.: C 22.23, H 1.87, N 38.89 %. Found: C 22.60, H 1.97, N 38.61 %. *m/z* (DEI$^+$): 216 (94) [M]$^+$, 200 (47), 186 (28), 110 (36);

3,5-Dimethoxy-4-nitropyridazine (**9**)

Procedure 1:

3,5-Dimethoxypyridazine (1.60 g, 11.4 mmol, 1.0 eq.) was dissolved in 25% oleum (7 mL) and 100% HNO_3 (1.30 mL) was added dropwise at 0-10 °C. The reaction mixture was stirred for 1 h at 0 °C and then at room temperature for 2 h. Subsequently, the reaction was stirred for 4 h at 80-85 °C and afterwards quenched on crushed ice. The resulting precipitate was filtered and washed with ice-water until the filtrate was acid free to yield 3,5-dimethox-4-nitroypyridazine (554 mg, 26%) as a pale-yellow solid.

Procedure 2:

3,5-Dimethoxypyridazine (1.80 g, 12.8 mmol, 1.0 eq.) was dissolved in 40% oleum (9 mL) and KNO_3 (1.29 g, 12.8 mmol, 1.0 eq.) was added at 15–20 °C. The reaction mixture was slowly heated to 40 °C and KNO_3 (1.95 g, 19.2 mmol, 1.5 eq.) was added. The reaction was stirred at 80 °C overnight. The reaction mixture was poured on ice and the precipitate was filtrated, washed with ice water and dried on air to yield compound **9** (1.07 g, 5.76 mmol, 45%) as a pale-yellow solid.

IR (ATR), $\tilde{\nu}$ (cm^{-1}) = 3091 (vw), 3047 (vw), 3012 (vw), 2960 (vw), 2863 (vw), 1608 (s), 1531 (s), 1490 (m), 1454 (m), 1429 (w), 1362 (vs), 1336 (m), 1241 (s), 1178 (w), 1135 (vs), 1058 (m), 997 (m), 910 (m), 882 (m), 865 (s), 776 (w), 754 (m), 650 (m), 617 (w) 579 (m), 507 (vw). ^{1}H NMR (d_6-DMSO, 400 MHz, ppm) δ = 9.38 (s, 1H), 4.15 (s, 3H), 4.15 (s, 3H). ^{13}C NMR (d_6-DMSO, 101 MHz, ppm) δ = 154.9, 149.0, 139.5, 125.7, 58.8, 56.2. ^{14}N NMR (d_6-DMSO, 29 MHz, ppm) δ = −20. Elem. Anal. ($C_6H_7N_3O_4$, 185.14 g mol^{-1}) calcd.: C 38.93, H 3.81, N 22.70 %. Found: C 38.73, H 3.74, N 22.78 %. *m/z* (DEI$^+$): 185 (62) [M$^+$], 96 (100), 53 (24).

Acknowledgements

Financial support of this work by the Ludwig-Maximilian University of Munich (LMU), the Office of Naval Research (ONR) under grant no. ONR.N00014-16-1-2062, and the Bundeswehr–Wehrtechnische Dienststelle für Waffen und Munition (WTD 91) under grant no. E/E91S/FC015/CF049 is gratefully acknowledged. We thank Dr. Burkhard Krumm for NMR measurements and Stefan Huber for his help with the sensitivity testing.

Keywords: Energetic heterocycles • 1,2-Diazine • Insensitive explosive • High explosive • Nitration of 1,2-diazines;

[1] a) J. P. Agrawal, R. D. Hodgson, *Organic Chemistry of Explosives*, Wiley, New York, **2007**. b) T. M. Klapötke, *Chemistry of High-Energy Materials*, 4th ed., De Gruyter, Berlin, **2017**. c) M. H. Keshavarz, T. M. Klapötke, *Energetic Compounds: Methods for Prediction of Their Performance*, De Gruyter, Berlin, **2017**.d) M. H. Keshavarz, T. M. Klapötke, *The Properties of Energetic Materials: Sensitivity, Physical and Thermodynamic Properties*, De Gruyter, Berlin, **2017**.

[2] a) D. Fischer, J. L. Gottfried, T. M. Klapötke, K. Karaghiosoff, J. Stierstorfer, T. G. Witkowski, *Angew. Chem. Int. Ed.* **2016**, *55*, 16132–16135.; *Angew. Chem.* **2016**, *128*, 16366–16369. b) T. M Klapötke, *Chemistry of High-Energy Materials*, 3nd ed., Walter de Gruyter, Berlin, **2015**. c) Y. Tang, J. Zhang, L. A. Mitchell, D. A. Parrish, J. M. Shreeve, *J. Am. Chem. Soc.* **2015**, *137*, 15984–15987. d) D. E. Chavez, *Topics in Heterocyclic Chemistry*, Springer, Berlin, Heidelberg, **2017**, 1–27. e) H. Gao, J. M. Shreeve, *Chem. Rev.* **2011**, *111*, 7377–7436.

[3] J. P. Agrawal, *Prog. Energy Combust. Sci.* **1998**, *24*, 1–30.

[4] J. R. Kolb, H. F. Rizzo, *Propell. Explos.* **1979**, *4*, 10–16.

[5] a) P. F. Pagoria, G. S. Lee, A. R. Mitchell, R. D. Schmidt, *Thermochimica Acta* **2002**, *384*, 187–204. b) T. M. Klapötke, R. D. Chapman, *Struct. Bond.* **2016**, *172*, 49–64.

[6] a) R. A. Hollins, L. H. Merwin, R. A. Nissan, W. S. Wilson, R. Gilardi, J. *Heterocycl. Chem.* **1996**, *33*, 895. b) R. A. Hollins, L. H. Merwin, R. A. Nissan, W. S. Wilson, R. Gilardi, *Material Research Society Symposium Proceedings* **1996**, *418*, Pittsburgh, PA.

[7] D. S. Donald, U.S. Patent No.3, 808, 209 (30 April **1974**).

[8] P. F. Pagoria, A. R. Mitchell, R. D. Schmidt, R. L. Simpson, F. Garcia, J. Forbes, J. Cutting, R. Lee, R. Swansiger, D. M. Hoffman, *Presented at the Insensitive Munitions and Energetic Materials Technology Symposium*, San, Diego, CA, **1998**.

[9] a) A. Albini, S. Pietra, *Heterocyclic-N-Oxides*, CRC Press, Boca Raton, FL, **1991**. b) A. M. Churakov, V. A. Tartakovsky, *Chem. Rev.* **2004**, *104*, 2601–2616.

[10] a) H. Wei, H. Gao, J. M. Shreeve, *Chem. Eur. J.* **2014**, *20*, 16943–16952. b) C. Zhang, Y. Shu, X. Zhao, H. Dong, X. Wang, *J. Mol. Struct.: THEOCHEM* **2005**, *728*, 129–134.

[11] T. Eicher, S. Hauptmann, *The Chemistry of Heterocycles*, 2nd ed., Wiley-VCH, Weinheim, **2003**.

[12] a) M. Yanai, T. Kinoshita, S. Takeda, *Chem. Pharm. Bull.* **1971**, *19*, 2181–2183. b) H. Igeta, T. Tsuchiya, M. Nakajima, T. Sekiya, Y. Kumaki, T. Nakai, T. Nojima, *Chem. Pharm. Bull.* **1969**, *17*, 756–762. c) H. Igeta, *Chem. Pharm. Bull.* **1960**, *8*, 550–552.

[13] Y. Tang, C. He, G. H. Imler, D. A. Parrish, J. M. Shreeve, *Chem. Eur. J.* **2017**, *23*, 1–5.

[14] a) W. Deinhammer, M. Wick, Patent DE 19772706701, **1977**. b) G. Lu, F. Liu, X. Sun, F. Qi, Y. Gao, Patent CN 102838548, **2012**.

[15] T. Itai, S. Natsumi, *Chem. Pharm. Bull.* **1964**, *12*, 228–235.

[16] R. D. Bryant, F.-A. Kunng, M. S. South, *J. Heterocycl. Chem.* **1995**, *32*, 1473–1476.

[17] S. Rozen, A, Shaffer, *Org. Lett.* **2017**, *19*, 4707–4709.

[18] M. Sućeska, *EXPLO5 Version 6.03 User's Guide*, Zagreb, Croatia: OZM; **2015**.

[19] J. S. Murray, P. Politzer, *J. Mol. Model* **2014**, *20*, 2223–2227.

[20] a) P. F. Pagoria, A. R. Mitchell, R. D. Schmidt, R. L. Simpson, F. Garcia, J. W. Forbes, R. W. Swansiger, D. M. Hoffman, *Synthesis, Scale-up and Characterization of 2,6-Diamino-3,5-dinitropyrazine-1-oxide (LLM-105)*, Report UCRL-JC-130518, Lawrence Livermore National Laboratory, Livermore, CA, **1998**. b) Gilardi, R. J. Butcher, *Acta Cryst. Section E* **2001**, *57*, o657–o658.

[21] a) H. W. Sandusky, R. H. Granholm, D. G. Bohl, IHTR 2701, Naval Surface Warfare Center, Indian Head Division, MD, USA, August 12, **2005**; b) J. E. Felts, H. W. Sandusky, R. H. Granholm, *AIP Conf. Proc.* **2009**, *1195*, 233–236.

[22] T. M. Klapötke, T. G. Witkowski, *ChemPlusChem* **2016**, *81*, 357–360.

[23] a) Reichel & Partner GmbH, http://www.reichelt-partner.de; b) Test methods according to the UN Recommendations on the Transport of Dangerous Goods, Manual of Test and Criteria, 4th edn., United Nations Publication, New York and Geneva, **2003**, ISBN 92–1-139087 7, Sales No. E.03.VIII.2; 13.4.2 Test 3 a (ii) BAM Fallhammer.

10.1002/ejoc.201800068

Entry for the Table of Contents

Layout 1:

Energetic Pyridazines

The selective introduction of alternating NH_2 and NO_2 into the pyridazine scaffold yields an excellent class of low sensitive energetic materials, due to intramolecular hydrogen bonds. 3,5-Diamino-4,6-dinitropyridazine-1-oxide is a new structural isomer of LLM-105 and characterized toward its energetic properties.

Ivan Gospodinov, Thomas M. Klapötke, Jörg Stierstorfer*

Page No. – Page No.
Energetic Functionalization of the Pyridazine Scaffold: Synthesis and Characterization of 3,5-Diamino-4,6-dinitropyridazine-1-oxide