

Safe Synthesis of TKX-50 Using an Insensitive Intermediate

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Abstract: Dihydroxylammonium 5,5'-bistetrazole-1,1'-diolate (TKX-50) has been evaluated as a promising energetic material, but its synthesis involves a sensitive intermediate, diazidoglyoxime (DAG). Ditetrahydropyranyl diazidoglyoxime (THP-DAG, 5) was introduced to replace DAG as an in-

sensitive intermediate, and TKX-50 was obtained via 5,5'-bistetrazole-1,1'-diol dihydrate (1,1-BTO). All compounds were characterized using NMR and mass spectroscopy as well as impact, friction, and electrostatic discharge sensitivity measurements.

Keywords: Explosives • Insensitivity • Tetrazole • TKX-50

1 Introduction

1,3,5-trinitro-1,3,5-triazacyclohexane (RDX) and 1,3,5,7-tetra-nitro-1,3,5,7-tetraazacyclooctane (HMX) are the most widely used molecular explosives for military use [1,2]. Research on energetic materials with higher performance has been required due to the development of new weapon systems; this research has led to the development of 2,4,6,8,10,12-hexanitro-2,4,6,8,10,12-hexaza-isowurtzitane (CL-20). However, it has not been applied to weapon systems because of polymorphic issue. Cyclic or caged materials such as dinitroazofuroxane (DDF) and octanitrocubane (ONC), with extremely high detonation velocity (10,000 m/s or more) have been developed. But there are certain limitations in their manufacturing and handling due to the sensitivity [3].

In recent years, aromatic compounds with high nitrogen contents, such as triazole, tetrazole, nitroiminotetrazole, and tetrazine, have been actively studied to improve performance and insensitivity [4–6]. Particularly dihydroxylammonium 5,5'-bistetrazole-1,1'-diolate (TKX-50) [7–9] has been considered a promising high energetic material (Table 1).

As shown in Scheme 1, TKX-50 was synthesized through five steps using glyoxal as the starting material by T. M. Klappötke et al [3]. However, it is synthesized via diazidoglyoxime (DAG; impact sensitivity: 1.5 J, friction sensitivity: < 5 N, electrostatic discharge sensitivity: 7 mJ) which has sensitivity similar to that of primary explosives (Lead styphnate; impact sensitivity: 2.5–5 J, friction sensitivity: 1.5 N, Lead azide; impact sensitivity: 2.5–4 J, friction sensitivity: 0.1–1 N). Therefore, DAG can easily react with small external stimuli, and cause safety-related accidents.

Herein we report a safe route for TKX-50 synthesis using an insensitive intermediate instead of the sensitive intermediate, DAG.

Table 1. Physical and sensitive properties of prominent high energetic materials in comparison to TKX-50 [3].

	RDX	HMX	CL-20	TKX-50
<i>IS</i> [J] ^a	7.5	7	4	20
<i>FS</i> [N] ^b	120	112	48	120
<i>ESD</i> [J] ^c	0.20	0.20	0.13	0.10
<i>T_{dec}</i> [°C] ^d	210	279	215	221
Density [g cm ⁻³] ^e	1.806	1.904	2.035	1.877
<i>D</i> [m/s] ^f	8983	9221	9455	9698
<i>P</i> [kbar] ^g	380	415	467	424

^a Impact sensitivity (BAM Fallhammer). ^b Friction sensitivity (BAM friction tester). ^c Electrostatic discharge device (OZM research). ^d Decomposition temperature from DSC (heating rate 5 °C min⁻¹). ^e From X-ray diffraction. ^f Detonation velocity. ^g Detonation pressure.

2 Experimental Section


2.1 General Methods

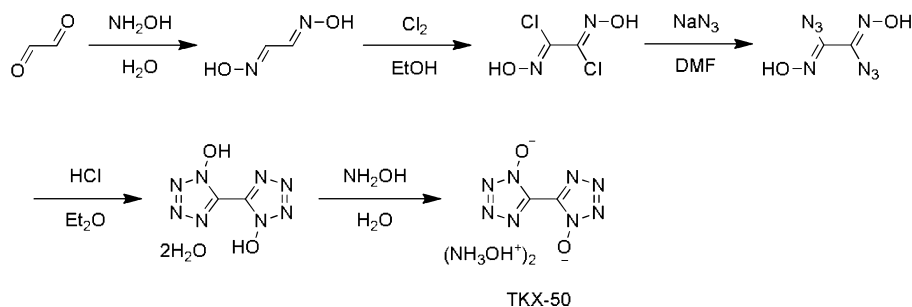
All chemicals are pure analytical grade materials gained from Acros or Aldrich Organics and used as received. ¹H and ¹³C NMR spectra were noted on 400 MHz (Bruker AVANCE 400) Nuclear Magnetic Resonance spectrometers using DMSO-*d*₆ or CDCl₃ as solvent. Analytical thin layer chroma-

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 Supporting information for this article is available on the WWW under <https://doi.org/10.1002/prep.201900171>



Scheme 1. Literature synthesis of TKX-50 [3].

tography (TLC) was done with E. Merck pre-coated TLC plates, layer thickness 0.25 mm, silica gel 60F-254. High-resolution mass spectra were obtained on a microTOF-QII HRMS/MS instrument (Bruker) with the technique of electrospray ionization. Impact sensitivity tests were performed according to STANAG 4489 modified instruction using a BAM Fallhammer instrument (OZM). The friction sensitivity tests were performed according to STANAG 4487 modified instruction using a BAM friction tester (OZM). The electrostatic discharge tests were performed according to STANAG 4490 using an ESD test instrument (OZM).

2.2 Synthesis of Ditetrahydropyranyl Dichloroglyoxime (THP-DCG, 2)

A Dichloroglyoxime (**1**) was prepared following a literature synthesis [3,9]. **1** (2.98 g, 18.98 mmol) was suspended in dichloromethane (35 mL). Pyridinium *p*-toluenesulfonate (0.498 g, 1.98 mmol) and 3,4-dihydro-2*H*-pyran (9.00 mL, 98.65 mmol) were added at room temperature. The solution was refluxed for 3 h. Then the solution was diluted with diethyl ether (200 mL) and washed with saturated NaHCO₃ solution (150 mL), saturated NaCl solution (150 mL), and water (300 mL) respectively. Solvent was removed under reduced pressure and the remaining solid was resuspended in hexane (100 mL). The suspension was stirred for 30 min at room temperature, and the solid was filtered and dried yielding 4.34 g of **2** (70%).

¹H NMR (400 MHz, CDCl₃): δ = 1.60–1.92 (m, 12H, CH₂), 3.67–3.89 (m, 4H, O–CH₂), 5.54 (m, 2H, O–CH); ¹³C NMR (100 MHz, CDCl₃): δ = 18.56, 18.60, 24.92, 28.20, 28.23, 62.30, 62.38, 102.05, 102.11, 133.67, 133.74; High resolution mass (ESI): Calculated for C₁₂H₁₈Cl₂N₂O₄ [M + Na]⁺: 347.0536, Found: 347.0544.

2.3 Synthesis of Diacetyl Dichloroglyoxime (Ac-DCG, 3)

1 (10.00 g, 63.7 mmol) and acetic anhydride (65.04 g, 637 mmol) solution in acetic acid (250 mL) was stirred to 50 °C for 4 h. After cooling, the reaction mixture was poured

into water (250 mL). The precipitate was filtered, washed with water (500 mL) and dried yielding 11.20 g of **3** (73%).

¹H NMR (400 MHz, CDCl₃): δ = 2.33 (s, 6H, CH₃); ¹³C NMR (100 MHz, CDCl₃): δ = 19.01, 139.82, 165.81; High resolution mass (ESI): Calculated for C₆H₆Cl₂N₂O₄ [M + Na]⁺: 262.9597, Found: 262.9602.

2.4 Synthesis of Ditetrahydropyranyl Diazidoglyoxime (THP-DAG, 5)

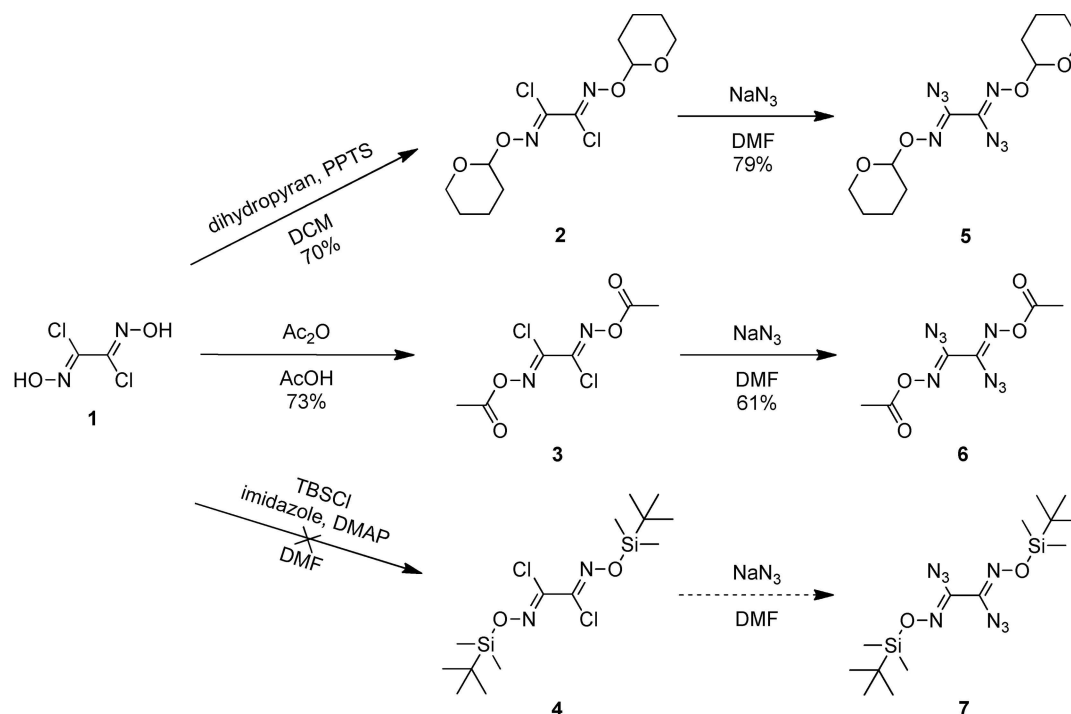
2 (5.00 g, 15.4 mmol) was dissolved in *N,N*-dimethyl formamide (100 mL). Sodium azide (3.00 g, 46.2 mmol) was added at 0 °C and the reaction mixture was stirred for 20 min. Then the mixture was heated to 100 °C and stirred for 2 h. After cooling, the reaction mixture was poured into water (100 mL). The precipitate was filtered, washed with water (50 mL) and dried yielding 4.11 g of **5** (79%).

¹H NMR (400 MHz, CDCl₃): δ = 1.58–1.83 (m, 12H, CH₂), 3.37–3.88 (m, 4H, O–CH₂), 5.35–5.38 (m, 2H, O–CH); ¹³C NMR (100 MHz, CDCl₃): δ = 18.51, 18.60, 24.90, 28.15, 28.19, 62.31, 62.49, 101.89, 101.99, 138.01; High resolution mass (ESI): Calculated for C₁₂H₁₈N₈O₄ [M + Na]⁺: 361.1343, Found: 361.1352; Impact sensitivity: 19.95 J, Friction sensitivity: 352.8 N, Electrostatic discharge sensitivity: 50 mJ.

2.5 Synthesis of Diacetyl Diazidoglyoxime (Ac-DAG, 6)

3 (5.00 g, 20.7 mmol) was dissolved in *N,N*-dimethyl formamide (100 mL). Sodium azide (4.05 g, 62.2 mmol) was added at 0 °C and the reaction mixture was stirred for 1 h. And then the reaction mixture was poured into water (100 mL). The precipitate was filtered, washed with water (50 mL) and dried yielding 3.22 g of **6** (61%).

¹H NMR (400 MHz, CDCl₃): δ = 2.26 (s, 6H, CH₃); ¹³C NMR (100 MHz, CDCl₃): δ = 18.92, 142.47, 165.76; High resolution mass (ESI): Calculated for C₆H₆N₈O₄ [M + Na]⁺: 277.0404, Found: 277.0414; Impact sensitivity: < 1.26 J, Friction sensitivity: 4.9 N, Electrostatic discharge sensitivity: < 25 mJ.



Scheme 2. Synthesis of intermediates for replacement of DAG.

2.6 Synthesis of Dihydroxylammonium 5,5'-Bistetrazole-1,1'-Diolate (TKX-50)

5 (2.00 g, 5.91 mmol) was suspended in diethyl ether (100 mL). Gaseous HCl was bubbled through the reaction mixture at 5 °C with stirring for 2 h. And then the flask was sealed and stirred at room temperature for overnight. 200 mL of hexane was added to the mixture to precipitate all product in the solution. The precipitate was collected, washed with dichloromethane (100 mL) and dried under reduced pressure. The crude compound was dissolved in warm water (20 mL). 50 wt% of Hydroxylamine solution (0.80 mL, 12.33 mmol) was added. And then the mixture was cooled down to room temperature with stirring. After 1 h, crystallized precipitate was filtered, washed with cold water (50 mL) and dichloromethane (50 mL), and dried yielding 1.00 g of TKX-50 (72% in 2 steps).

^1H NMR (400 MHz, DMSO-d_6): δ = 9.84 (s, 8H, NH_2OH); ^{13}C NMR (100 MHz, DMSO-d_6): δ = 135.52; High resolution mass (ESI): Calculated for $\text{C}_2\text{H}_9\text{N}_{10}\text{O}_4$ $[\text{M} + \text{H}]^+$: 237.0803, Found: 236.9813.

3 Results and Discussion

As mentioned above, TKX-50 is a well-known high-performance energetic material with much lower sensitivity than RDX and HMX. Many researchers including T. M. Klapötke's group have studied one-pot synthesis of TKX-50 due to the

sensitive intermediate, DAG [8,9]. Herein we studied the synthesis of TKX-50 by introducing a protecting group on the intermediate to avoid sensitive intermediate which is DAG. It was considered appropriate to introduce a protecting group on the hydroxyl group, the last remaining functional group in the synthesis process. Protecting the dichloroglyoxime (DCG, 1) was determined because the compound would become sensitive after azidation. Tetrahydropyranyl [10], acetyl [11], and silyl [12] groups, which can be easily introduced into and removed from an alcohol, were considered as the protecting group.

As shown in Scheme 2, the protection of DCG was performed as follows. Tetrahydropyranyl-protected dichloroglyoxime (THP-DCG, 2) was synthesized in 70% yield by using 3,4-dihydro-2H-pyran and pyridinium *p*-toluenesulfonate (PPTS) in dichloromethane. Acetyl-protected dichloroglyoxime (Ac-DCG, 3) was synthesized in 73% yield using acetic anhydride in acetic acid. Unfortunately, *tert*-butyldimethylsilyl-protected dichloroglyoxime (TBS-DCG, 4) could not be obtained by reacting with *tert*-butyldimethylsilyl chloride (TBSCl), imidazole and 4-dimethylaminopyridine (DMAP) in *N,N*-dimethyl formamide (DMF).

Azidation of THP-DCG (2) and Ac-DCG (3) was conducted using sodium azide in DMF (Scheme 2). Ac-DCG azidation proceeded well at 0 °C as in the literature [3], while the THP-DCG azidation proceeded at 100 °C due to the steric hindrance of the bulky tetrahydropyranyl group. After the reaction was completed, the reaction mixture was allowed to cool to room temperature, and distilled water was added

Table 2. Sensitivity of DAG in comparison to THP-DAG (5) and Ac-DAG (6).

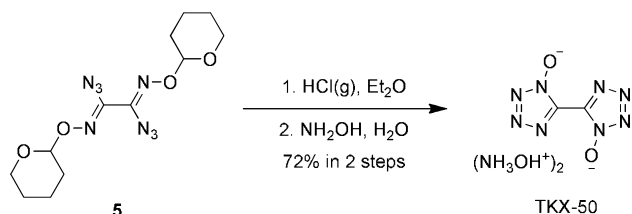
	THP-DAG (5)	Ac-DAG (6)	DAG
IS [J] ^a	19.95	< 1.26	1.5
FS [N] ^b	352.8	4.9	< 5
ESD [mJ] ^c	50	< 25	7

^a Impact sensitivity (BAM Fallhammer). ^b Friction sensitivity (BAM friction tester). ^c Electrostatic discharge device (OZM research).

to precipitate white powder. It was filtered to obtain THP-DAG (5) in 79% yield and Ac-DAG (6) with 61% yield.

The sensitivities of THP-DAG (5) and Ac-DAG (6) were measured, and the results were compared with those of DAG (Table 2). Unfortunately, Ac-DAG (6, impact sensitivity: < 1.26 J, friction sensitivity: 4.9 N, electrostatic discharge sensitivity: < 25 mJ) showed similar sensitivity with DAG, while THP-DAG (5, impact sensitivity: 19.95 J, friction sensitivity: 352.8 N, electrostatic discharge sensitivity: 50 mJ) was much less sensitive than DAG. Notably, the insensitivity of THP-DAG (5) was greatly increased by the THP protection of the hydroxyl group.

As shown in Scheme 3, TKX-50 synthesis was completed via 5,5'-bistetrazole-1,1'-diol dihydrate (1,1-BTO) using an insensitive intermediate. THP-DAG (5) was bubbled with HCl gas in diethyl ether, deprotection and cyclization proceeded simultaneously to yield 1,1-BTO. Then, 1,1-BTO was reacted with hydroxylamine solution in distilled water to obtain TKX-50 in 72% yield (2 steps).



Scheme 3. Synthesis of TKX-50 using THP-DAG (5).

4 Conclusion

In this study, THP-DCG (2) and Ac-DCG (3) were synthesized by introducing a protecting group to DCG to improve the insensitivity of azide intermediate. THP-DAG (5) and Ac-DAG (6) were obtained via azidation, and analyzed sensitivity properties. While Ac-DAG (6) had similar impact, friction, and electrostatic discharge sensitivities as DAG, THP-DAG (5) was much more insensitive than DAG. TKX-50 synthesis was completed in good yield (72% in two steps) via 1,1-BTO. In conclusion, we established a safe route for TKX-50 synthesis using an insensitive intermediate.

Acknowledgements

The authors gratefully acknowledge the support of the Agency for Defense Development (Korea).

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Manuscript received: May 26, 2019

Revised manuscript received: May 26, 2019

Version of record online: July 26, 2019