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Intermolecular Interactions of Energetic Materials

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INTERMOLECULAR INTERACTIONS OF ENERGETIC MATERIALS

BY

DEVON S SWANSON

A DISSERTATION SUBMITTED IN PARTIAL FULFILLMENT OF THE
REQUIREMENTS FOR THE DEGREE OF

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ABSTRACT

A variety of intermolecular interactions occurs when an energetic material responds to its surroundings. With a better grasp of these energetic material contacts, improved performance on plastic-bonded explosives, superior swab materials for explosives detection, and novel insensitive munitions are possible. In order to further understand these interactions, the following relationships were researched: adhesion between energetic materials and polymer substrates; quantitative collection and detection of energetic materials on electrostatically charged swabs; and noncovalent derivative investigation between energetic material pairs.

A number of explosives detectors rely on introduction of the analyte to the instrument via swabs. However, most swab materials are burdened by either poor sorption (pickup) or poor desorption (release). Therefore, finding a swab that can both easily sorb and desorb an explosive is highly desirable. Atomic force microscopy (AFM), while normally employing a sharp (~5 nm) tip for topographic and force measurements, can also be used to measure adhesion between a material and substrate surface. AFM force curve experiments were performed on eleven polymers with nine energetic materials, organic explosives, and energetic salts. Teflon was the least adhesive polymer to all energetic materials, while no distinct trend could be elucidated among the other polymers or energetics.

Rather than create a novel swab material for explosives detection, improving current commercial off the shelf (COTS) swabs would be a fast and cost-effective way to increase analyte detection on existing security instrumentation. For this reason, the viability of electrostatically charging COTS swabs was explored. COTS swabs were

charged both triboelectrically and inductively, and voltage degradation both in time and through changes in relative humidity was determined. For collection efficiency, transfer efficiency, and uncharged swab comparison, quantification of energetic materials on a triple quadrupole liquid chromatograph/mass spectrometer was performed. Limits of quantification for trace amounts of energetic material were typically in the single nanogram level. In addition to adsorption of energetic material comparable to traditional uncharged swabs, electrostatically charged swabs can also adsorb material at standoff, introducing a new noncontact sampling method.

The synthesis of the next generation of explosives is increasingly difficult because available novel reagents and synthetic techniques are limited. Energetic material solvates have been known for nearly 65 years, but cocrystallization of an energetic material and another solid has only been demonstrated in the last decade. Relying on noncovalent derivatives (NCDs), cocrystals can tailor explosive properties such as density and detonation velocity, potentially yielding a new energetic material without novel molecule synthesis. The most common synthons for pharmaceutical cocrystallization involve carboxylic acid and amide functionalities, but the majority of common energetic materials are devoid of these groups. With the wealth of knowledge from pharmaceutical cocrystals, utilizing these groups could yield more effective screening for energetic cocrystal pairs. Herein, we present the TNT-nicotinamide cocrystal, an energetic cocrystal with an amide synthon.

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This work is as much yours as it is mine.

“...but we rejoice in our suffering, knowing that suffering produces perseverance; and perseverance, character; and character, hope.”

PREFACE

This dissertation has been prepared in manuscript format in accordance with the guidelines of the Graduate School of the University of Rhode Island. The research contained herein is separated into three manuscripts. The first manuscript, “Energetic Material/Polymer Interaction Studied by Atomic Force Microscopy,” has been accepted for publication in the journal *Propellants, Explosives, Pyrotechnics*. The second manuscript, “Noncontact Electrostatic Swabbing of Energetic Materials,” and third manuscript, “Cocrystallization of TNT and Nicotinamide, and Cocrystallization Screening of Energetic Materials,” are being prepared for submission.

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LIST OF ABBREVIATIONS

1,3-DNB – 1,3-dinitrobenzene

2,4-DNT – 2,4-dinitrotoluene

2,5-DNP – 2,5-dinitrophenol

2,5-DNT – 2,5-dinitrotoluene

2,6-DNT – 2,6-dinitrotoluene

3,4-DNP - 3,4-dinitropyrazole

5-AT – 5-aminotetrazole

ACN – acetonitrile

AFM – atomic force microscopy

ANTA - 5-amino-3-nitro-1H-1,2,4-triazole

AU - arbitrary units

Ave – average

BTF – benzotrifuroxan

C-4 – composition 4

COTS – commercial off-the-shelf

DAA – diacetone alcohol

DADP – diacetone diperoxide

DHS – Department of Homeland Security

DMF – dimethylformamide

DMSO – dimethylsulfoxide

DNAN – 2,4-dinitroanisole

DNBT - 5,5'-dinitro-2H,2H'-3,3'-bi-1,2,4-triazole

DNPP - 1H,4H-3,6-dinitropyrazolo[4,3-c]pyrazole

DSC – differential scanning calorimeter

EN – electrostatic noncontact

ETD – explosive trace detector

ETN – erythritol tetranitrate

EtOH – ethanol

FDA – US Food and Drug Administration

g – gram

gr – gravities

HESI – heated electrospray ionization

HLOQ – higher limit of quantitation

HMTD - hexamethylene triperoxide diamine

hr – hour

IMS – ion mobility spectrometer

IPA – isopropanol

IS – internal standard

L – liter

LC – liquid chromatograph

LC/MS – liquid chromatograph/mass spectrometer

LLOQ – lower limit of quantitation

LOD – limit of detection

m – meter

μm – micron

M – molar

MEK – methyl ethyl ketone

MHN – mannitol hexanitrate

MIL – military alarm

min – minute

mol – mole

MRM – multiple reaction monitoring

MW – molecular weight

N – Newton

NCD – noncovalent derivative

NM – nitromethane

NTO – 3-Nitro-1,2,4-triazol-5-one

NU – nitrourea

P4VP – poly(4-vinylphenol)

PC – polycarbonate

PE – polyethylene

PET – polyethylene terephthalate

PETN - pentaerythritol tetranitrate

PLM – polarized light microscope

PMMA – poly(methyl methacrylate)

PPO - poly(2,6-dimethylphenylene oxide)

PS – polystyrene

PTFE – polytetrafluoroethylene

PVA - polyvinyl alcohol

PVC – polyvinyl chloride

RAM – resonant acoustic mixing

RH – relative humidity

RMS – root-mean squared

s – second

SAS – supercritical antisolvent

SBR – styrene-butadiene rubber

SD or Std Dev – standard deviation

SEM – scanning electron microscopy

T – temperature

TATB – 2,4,6-triamino-1,3,5-trinitrobenzene

TATP - triacetone triperoxide

TBTNB – tribromotrinitrobenzene

TCTNB – trichlorotrinitrobenzene

TITNB – triiodotrinitrobenzene

TNAZ – 1,3,3-trinitroazetidine

TNB – 1,3,5-trinitrobenzene

TNT – 2,4,6-trinitrotoluene

TZTN - 5,6,7,8-tetrahydrotetrazolo[1,5-b] [1,2,4]-triazine

UC – uncharged contact

UV – ultraviolet

V – volt

W – watt

XRD – x-ray diffractometry

Manuscript 1

Energetic Material/Polymer Interaction Studied by Atomic Force Microscopy

by

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Abstract

The interactions of energetic materials and polymers have important implications in safety, long-term storage, and performance of explosives and explosive mixtures. Atomic force microscopy was used to investigate adhesion forces at the molecular scale of nine energetic materials, organic explosives and energetic salts, on eleven common polymers [polyethylene, polyvinylalcohol, polyvinyl chloride, polycarbonate, polystyrene, poly(methyl methacrylate), styrene-butadiene rubber, poly(4-vinyl phenol), poly(2,6-dimethylphenylene oxide), poly(2,6-diphenyl-p-phenylene oxide) (Tenax®), and polytetrafluoroethylene (Teflon®)]. Teflon was the least adhesive polymer to all energetic materials, while no distinct trend could be elucidated among the other polymers or energetics.

1 Introduction

For safety, long-term storage, and good performance, various tests must be performed when explosives are formulated with other materials. Polymers in contact with explosives are used in a number of ways, e.g. “plastic bonded” explosives, particulate encapsulation of explosives, or as swab materials and filters to collect explosive particulates. Depending on applications, it is necessary to find polymers that adhere or repulse explosives; the ability to achieve a balance between attraction and repulsion can also be desirable. In this work, atomic force microscopy (AFM) is used to assess explosive/polymer interactions.

Typically, AFM generates topographic images of surface features from atomic to μm scale [1]. However, AFM can also generate force curves between a cantilever tip and sample surface [2-6]. These force curves yield adhesive parameters for the two test materials (i.e. tip and surface). By using the AFM cantilever and sample stage, an explosive particle affixed to the cantilever can be pressed onto a sample material, or, in reverse, the sample material can be deposited onto the cantilever tip and pressed into a monolayer of explosive [7]. Previous work on energetic materials and AFM focused on adhesion to terminal group-functionalized self-assembled monolayers [8], and metal coupon finishes [9].

In this study, adhesion forces were obtained for nine energetic materials with eleven polymeric substrates (Section 3.1). The military explosives tested were 1,3,5-trinitroperhydro-1,3,5-triazine (RDX), octahydro-1,3,5,7-tetranitro-1,3,5,7-tetrazocine (HMX), pentaerythritol tetranitrate (PETN), and 2,4,6-trinitrotoluene (TNT). Also tested were energetic salts (potassium chlorate, potassium perchlorate, and potassium nitrate), and energetic peroxides (hexamethylene triperoxide diamine (HMTD) and triacetone triperoxide (TATP)).

2 Results and Discussion

Quantitative force measurements were collected for a virgin tipped cantilever and polystyrene microsphere on Teflon, polyethylene (PE), polystyrene (PS), and polyvinyl alcohol (PVA) (Table 1). Adhesion forces could not be collected for a

Table 1.1 Baseline Adhesion Force Summary. All forces in nN.

	Teflon	St Dev	Scans	PE	St Dev	Scans	PS	St Dev	Scans	PVA	St Dev	Scans
Si AFM Tip	23	14	991	32	12	991	39	21	885	27	12	891
PS Microsphere	95	189	883	610	169	250	335	164	30	578	33	246

tipless cantilever with only glue because the overall adhesion was too great for the AFM to accurately measure. The adhesion forces for the virgin tipped cantilever were low with standard deviations no more than 60% of the observed values. The repeatability of these adhesion forces was likely due to the extremely well-characterized geometry and relatively small contact area of a manufactured AFM cantilever tip. Conversely, the standard deviation for adhesion forces was large for polystyrene microspheres. Though the microsphere has well-characterized geometry (as confirmed via SEM), the lower elastic modulus and increased contact area when compared to the silicon tip likely caused increased overall measured adhesion [10]. The large microsphere adhesion forces suggest that if polymer substrate transferred to the energetic particle during a series of force curves, the ensuing adhesion force on the next polymer would be artificially high. In practice, this was occasionally observed, requiring a new energetic particle to be adhered to a new cantilever and experiments repeated. Interestingly, the obtained polystyrene-polystyrene adhesion force from the microsphere (335 nN) closely correlated with a previously reported force (314 nN) [11]. Ultimately, these results suggest that none of the energetic adhesions resulted from artifacts of cantilever, glue, or polymer-polymer adhesion.

Quantitative force measurements were collected for the nine energetic materials on the eleven polymer substrates. AFM data sets were run over a period of 18 months. Table 2 presents the data collected over the last three intervals in order to

Table 1.2. Adhesion Force Summary. All forces in nN.

	Teflon			PE			PS			PVA			PAVP			PPO			Tenax			PMMA			PC			PVC			SBR			ave
HMTD1	15	23	680	71	88	815	50	15	429	130	81	512	22	13	1035	103	47	948													76			
HMTD2	119	85	953	186	70	948	152	51	895	184	14	973																			160			
average																															118			
HMX1	40	31	906	95	48	907	52	77	969	80	50	976	43	16	679	74	82	859	185	40	803										89			
HMX2	31	23	968	113	15	974	59	26	967	59	26	967																			66			
average																															101			
RDX1	86	124	940	98	44	937				77	73	855	42	56	818				56	60	932										88			
RDX2	41	24	983	117	83	978	270	94	941	101	93	967																			132			
RDX3							110	19	1382													97	10	1119	278	50	1012	277	59	1078	70	52	1035	166
average																															140			
PETN1	23	17	804	87	32	952	98	44	937										17	8	938											56		
PETN2	99	49	944	161	17	980	125	26	934	238	48	976																				156		
PETN3							375	90	1677													157	28	1121	96	57	1742	111	26	1309	90	77	1170	166
average																															129			
TNT1	10	22	835	81	55	935	205	82	863	60	5	1009	69	72	872	176	72	837	33	56	793											131		
TNT2	14	14	1081	89	35	936	100	32	636	26	57	964																				95		
TNT3							328	54	1534													287	40	1052	452	86	2207	317	63	1066	133	39	1308	303
average																															203			
KClO ₃ 1	51	55	528	328	82	989	49	16	434							149	77	818	149	75	706											169		
KClO ₃ 2	22	40	951	118	21	998	85	59	954	110	43	944																				104		
KClO ₃₃							119	16	1066													173	14	1076	134	20	1070	195	6	1083	75	15	886	139
average																															140			
KNO ₃ 1	46	30	1007	171	23	999	154	28	1003	70	47	908	43	22	941	58	31	889	125	56	377											95		
KNO ₃ 2	41	24	976	49	24	952	85	21	980	44	7	982																				55		
KNO ₃ 3							193	31	1069													100	7	1092	155	23	1093	131	9	1089	68	20	1653	129
average																															96			
KClO ₄							127	26	1095													140	17	1095	109	14	1095	137	15	1095	69	19	1094	116
TATP2	28	34	1081	85	70	376	94	36	942	137	58	877																				105		
Ave all	44			123			142			101			44			112			94			159			204			195			84		126	
Ave	55			127			117			107.5			36			121.5			119			159			204			195			84		128	

exhibit the degree of reproducibility using different energetic material tips and different polymer substrates. Table 2 shows both the number of scans and the standard deviations. As typical for AFM measurements, standard deviations were large (Table 3) [12-14]. In cases where the standard deviation was larger than the measured force, the data are shown, with shadowing, but not included in the averages. Examining the trends across the eleven polymers (bottom average), Teflon, poly(4-vinylphenol) (P4VP), and styrene-butadiene rubber (SBR) had the lowest adhesion forces on the energetic materials. The average force exhibited with Teflon and P4VP was almost as small as that observed with the bare cantilever (Table 1). For Teflon, low adhesion force values are not surprising because it is valued for its “nonstick” properties. Its higher relative surface roughness (R_{RMS} 342 nm) may account for values with high standard deviations. In addition, the small values observed with P4VP could be attributed to high surface asperities throughout a rough substrate. We encountered great difficulty in creating a smooth surface for this material, acquired as a powder, and the resulting surface could have been so rough as to only create a miniscule contact area and subsequent low adhesion force. The other eight polymers had average adhesion forces ranging from 108 to 204 nN, which, considering the standard deviations, were essentially identical.

Table 1.3. Adhesion Force and Standard Deviation Comparison.

Reference	Tip	Substrate	Adhesion Force (nN)	Standard Deviation/Error
8	Energetics	Functionalized SAMs	20-130	10-50
9	Energetics	Acrylic Coatings	16-110	5-24
12	Polystyrene	Polypropylene	250-400	40%
13	polystyrene latex	Si	127	21
14	polystyrene	Silica	1000-2000	N/A

The nine energetic materials studied represent the major classes of military explosives, as well as energetic peroxide explosives and energetic oxidizers: nitrate ester (PETN); nitroarene (TNT); nitramine (RDX and HMX); peroxides (HMTD and TATP); and salts (KNO_3 , KClO_3 , and KClO_4). (As explained above, shadowed data were not included in the averages.) For each energetic, the data sets collected in Batch 1 were averaged separately from those collected in Batch 2 and Batch 3.

Our purpose in averaging the three data sets separately was to see the magnitude of the differences in measured adhesion another researcher might observe using the same chemical but different microcrystals on the tip and same polymer but different surface preparation. It is notable that the adhesion forces recorded for Batch 3 experiments were always higher than those collected in earlier batches. This may be a consequence of using a different tip (but Batch 1 and Batch 2 used different tips); therefore, it is more likely that the polymer surfaces were smoother due to the use of a doctor blade in their preparation. While the data in Table 2 allowed us to detect some differences among the polymer substrates, the diverse structural differences among the energetic materials could not be distinguished from adhesion measurements. With the exception of TNT 3, all values ranged between 96 nN and 140 nN.

Three polymers, Teflon, P4VP, and SBR, stand out as having low adhesion to the energetics. This feature, especially in P4VP and SBR, deserves further examination. However, there was generally little difference in the adhesion of the various energetics to a variety of polymers. This lack of differentiation among chemicals with diverse functional groups suggests that the difference in functionality

of the energetics is not the main factor affecting the adhesion forces. Macro-scale considerations such as lattice structure, surface area, and surface roughness may have a greater effect on adhesion forces than the purely van der Waals-dominated interactions assumed herein.

3 Experimental Section

3.1 Polymer Substrate Preparation

Eleven polymer supports were acquired, and their chemical structures are shown in Figure 1. PS, PVA, poly(methyl methacrylate) (PMMA), polyvinyl chloride (PVC), polycarbonate (PC), and SBR were acquired from Acros as pellets, while PE and (Teflon) were sheets of commercially available material. P4VP, poly(2,6-dimethylphenylene oxide) (PPO), and poly(2,6-diphenyl-p-phenylene oxide) (Tenax) were acquired as powders from commercial surfaces. Three separate experimental conditions were performed, referred to as Batch 1, Batch 2, and Batch 3. Batch differences occur only in polymer substrate preparation and specific energetic microcrystallite used – the energetic materials on different batch cantilevers were from the same synthetic or commercial lot.

In Batch 1, the polymers were dissolved in a solvent and dip cast onto glass slides. In Batch 2, PS and PVA were placed on a glass microscope slide, heated until softened, and flattened with a silicon wafer (Ted Pella) of defined roughness (root mean squared roughness (R_{RMS})) ~ 2 nm in an attempt to create an atomically flat surface. This approach was particularly difficult with P4VP, PPO, and Tenax,

eliminating their analysis in Batch 2. In Batch 3, PS, PC, PVC, PMMA, and SBR were dissolved in an organic solvent to create a slurry. PMMA, PVC, and PS were dissolved in chloroform, while PC and SBR were dissolved in cyclohexane and dichloromethane, respectively.

Figure 1.1. Polymer Structures.

The slurries were poured onto an aluminum foil sheet and flattened to 1 mm thickness using a doctor blade. After solvent evaporation, 1 cm² pieces were cut from the film

and used for adhesion measurements. Acquired via AFM topography images, surface roughness measurements of all polymers except PVC are shown in Table 4.

Table 1.4. Root-mean-squared surface roughness of polymer substrates.

Polymer	R _{RMS} (nm)
Teflon	342 ^a
PE	44 ^a
PS	17 ^a , 131 ^c
PVA	45 ^a
PMMA	57 ^a
SBR	29 ^a
PC	155 ^a
PVC	N/A

a. Batch 2

c. Batch 3

3.2 Energetic Material Adhesion

TNT, RDX, HMX, and PETN were obtained from military sources and used as received. Potassium nitrate, potassium chlorate, and potassium perchlorate (Fisher Scientific) were ground in mortar and sieved to obtain desired particle size. TATP and HMTD were synthesized and recrystallized according to previously published procedures [15, 16]. Explosive microcrystallites were adhered to tipless cantilevers (Mikromasch CSC37-Tipless-Al BS, Nano and More) using a micromanipulator (Micromanipulator M2525) and polarized light microscope (Nikon Eclipse E400 POL). The cantilever platform was attached via double-sided carbon tape to a homemade probe (flattened wire) and inserted into the micromanipulator. Energetic material was added to a clean glass microscope slide. The powder was milled using

another slide until particles of desired size (between 30 to 50 μm) were obtained (HMTD and TATP were not milled due to friction sensitivity). Particle size was estimated using an ocular micrometer; more accurate estimates of particle size were obtained by scanning electron microscopy (SEM). A glass Pasteur pipet, pulled to extremely fine points, was used to transfer a micro-drop of UV-curing glue (Loctite 352, Henkel) to the microscope slide. The cantilever was lowered into the glue microdrop, touched to the energetic microcrystallite ($\sim 40\ \mu\text{m}$ long), and cured with UV light for 10 minutes. Cantilevers were also made with glue adhered to a cantilever or with a polystyrene microsphere adhered to the cantilever. If the energetic tip appeared damaged at any point, it was replaced and all measurements were repeated.

Figure 1.2. Scanning electron microscope images of a RDX microcrystallite adhered to tipless cantilever via UV-curing glue at (top) parallel (0°) and (bottom) roughly perpendicular (70°). Inset: Drop of UV-curing glue on tipless cantilever.

After affixing each explosive to a tipless cantilever, SEM images were collected to confirm microcrystallite adhesion and that no glue or other artifact would contact the sample. As seen in Figure 2, solid contact between that energetic material and the surface was achieved. Because of its high volatility, TATP could not be imaged in the high vacuum of the SEM, while HMTD could not be imaged because the incident electron beam caused initiation of the material.

3.3 Force Curve Measurements

Before force curves were taken and after each polymer set, the modified cantilever was calibrated using the Thermal K function available on an Agilent 5500 AFM. Though many methods exist for calculating a cantilever force constant, this function employs thermal fluctuations of the cantilever as harmonic oscillations [17-21]. One $50\text{ }\mu\text{m}^2$ area was raster scanned at $1\text{ }\mu\text{m/s}$ to collect 1000 force measurements. Experiments were performed at <20% relative humidity via flowing dry compressed air or nitrogen through the instrument's environmental chamber, and an electrostatic ionizer (Staticmaster) was employed for electrostatic dissipation. Because the polymer surface was easily deformed, the vertical displacement of the force curve was adjusted after every few force curve measurements to prevent indentation of the polymer.

Force measurements were taken using native tipped cantilevers, tipless cantilevers with only glue, a tipless cantilever with a polystyrene microsphere, and tipless cantilevers with fully adhered energetic microcrystallites. The order of polymers examined against a given tip was altered to show that one data set had no effect on another; repeat measurements of an initial polymer were conducted after

collecting measurements from a second polymer for the same reason. After collection of a number of force curves (usually 1000), unrepresentative curves were culled for two primary reasons. First, significant indentation of the polymer after the jump-to-contact point was occasionally unavoidable, causing plastic deformation to the polymer or energetic material particle or transfer of significant amounts of polymer onto the particle. After the deformation or transfer, each successive force curve would be obtained with a unique particle (or polymer-coated particle), hindering comparison to other polymer force curves and other force curves within the same polymer set. Second, surface roughness of polymer substrates was potentially too high, causing unrepresentative adhesion or detector saturation. Representative force curves were then baseline-normalized and calibrated using the measured cantilever deflection sensitivity and force constant. A histogram was then created to determine the adhesion force with highest frequency. A representative histogram is shown in Figure 3.

Figure 1.3. Force histogram of KNO₃ v. polyethylene.

4 Conclusion

Adhesion forces of nine energetic materials were measured on eleven different polymer substrates. It was hoped that this study would allow us to match a particle explosive with a particle polymer that it best adhered to. However, examining each explosive (horizontal rows in Table 2), no “best” match could be identified due to the normal variation in results. It was noted that Teflon was the least adhesive polymer for every tip tested. Generally, P4VP and SBR also exhibited low adhesion. Despite wide variations in the chemical affixed to AFM tip, little bias for one energetic over another was observed. The lack of superior adhesion to one polymer over another is attributed to the effect of bulk properties, such as particle size, roughness, and contact orientation/angle, during force curve collection.

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Manuscript 2

Noncontact Electrostatic Swabbing of Energetic Materials

by

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Abstract

Significant research has been completed in the pursuit of novel sampling materials for trace explosives detection sampling. However, rather than creating a novel swab material, improving current commercial off-the-shelf (COTS) swabs would be a fast and cost-effective way to increase analyte detection on existing security instruments. For this reason, the viability of electrostatically charging COTS swabs was explored. COTS swabs were triboelectrically and inductively charged, and voltage degradation both in time and through changes in relative humidity was determined. Collection efficiency, transfer efficiency, and uncharged swab comparison were investigated via quantification of energetic materials on a triple quadrupole liquid chromatograph/mass spectrometer. Limits of quantification for trace amounts of energetic material were typically in the single nanogram level. In addition to adsorption of energetic material comparable to traditional uncharged swabs, electrostatically charged swabs can also adsorb material at standoff, introducing a new noncontact sampling method.

Introduction

Effective energetic material detection is of critical importance for homeland security, but every detection technology begins with collecting samples to analyze. Due to the low vapor pressure of explosives, many commercial detection technologies collect sample by physical contact “swabbing.”¹⁻⁴ There are many variables that affect trace sampling, and significant research has been done to understand them more fully.⁵⁻⁶ The size distribution, shape, and morphology of realistic trace explosive particles has been investigated, and the standardized creation of representative trace particles has

been subsequently studied.⁷ Specifically, drop-on-demand inkjet printing has become a staple in a number of industry, government, and academic laboratories as a method to reliably create standardized trace amounts of explosives.⁸⁻¹³ This technique can dispense highly accurate and precise volumes of a variety of analyte solutions on a scale much smaller than traditional deposition methods such as syringes.¹⁴⁻¹⁵ The contribution of biological substances (e.g. fingerprint oils) to trace explosives detection has also been investigated.¹⁶

While understanding the properties of trace explosive particles and attempting to recreate them is important, it is only half of the sampling interaction. The role of the swab in the sampling mechanism has also been studied. Adhesion between a trace particle and a swab influences the ability of the swab to pick up an analyte.¹⁷ In addition, swab material has a large effect on the ability of a given swab to adsorb trace particles.¹⁸⁻²² Combining these variables can lead to a measure of the collection efficiency on a sampling protocol.²²⁻²⁴ Collection of samples by swabbing is complicated further because an ideal swabbing material would have both good sorption and desorption properties. In reality, vendors of various detection instruments have focused on the latter requirement, advantageous release properties, and used materials such as Teflon and Nomex for commercial off-the-shelf (COTS) swabs. To develop swabs with both enhanced pickup and release without altering their fundamental chemical structure, electrostatic charging was investigated.

When two disparate materials touch each other, transfer of surface electrons results in contact electrification, or tribocharging. The magnitude and polarity of this charging are dependent on the position of the two contacted materials in the

triboelectric series. A qualitatively ranked list, a triboelectric series details the order of materials that obtain increasing positive and negative voltage when contacted together (Figure 2.1). For instance, Teflon, a conventional material for COTS swabs, will almost always obtain a negative voltage when rubbed because it is at the highly negative end of the series.²⁵⁻³⁰ Charging of a material can also be accomplished by exposing the materials to an electromagnetic field (inductively coupling) or a corona discharge.

Figure 2.1. Example of a triboelectric series.

Noncontact electrostatic sampling from clothing or fingerprints has been demonstrated for biological samples, but its viability for energetic materials is currently unknown.³¹⁻³² In this work, the potential for a noncontact, electrostatically-

charged swab was examined as replacement for traditional contact swabs for explosives detection.

Experimental Methods

Analytes

Sucrose and sodium chloride were purchased commercially and acted as surrogate analytes for an organic explosive (e.g., TNT, RDX, PETN) and inorganic threat material (e.g., ammonium nitrate or potassium chlorate), respectively. PETN, RDX, TNT, and C-4 were either synthesized in-house or received from military or industrial sources. The materials were sieved to approximately 800 micron but otherwise used as purchased.

COTS Swabs

Teflon and Nomex, and Teflon-coated fiberglass and cotton swabs were supplied by FLIR and DSA Detection, respectively, and used as received.

Substrates

Teflon and Nomex COTS swabs were also used as substrates. Bytac was purchased as a ream and cut to size but was otherwise used as received. Vinyl fabric (90% polyvinyl chloride) was purchased in a fabric store and used as received.

Scanning Electron Microscopy (SEM)

A JEOL 5900 SEM was operated in backscatter mode at 20 kV to collect micrographs of COTS swab materials.

Method of Charging Swabs

For proof of concept, triboelectric charging was accomplished by simply rubbing the swab on a polyamide chair seat (“hand charged”). To charge more reproducibly, a charging setup was constructed using an electric drill to rotate two polyurethane paint rollers (“double roller charged”) through which the swabs were fed (Figure 2.2). For swabs requiring use of a wand, a single roller charging method (“single roller charged”) was used and can be seen in Figure 2.2. A Simco-Ion Chargemaster VCM-60 was used to inductively charge swabs (“inductively charged”) at -10 kV, -20 kV, and -30 kV for five and ten seconds. Voltages were recorded using a 3M 718 static sensor, and a static dissipater was used to eliminate excess voltage before experiments.

Figure 2.2. Single roller and double roller set up.

Humidity Chamber

A custom-built humidity chamber was constructed from a plastic storage box and fitted with a humidistat and medical nebulizer with water to control humidity.

Experiments were conducted at 0% relative humidity (RH) using dry nitrogen, 25% RH, 50% RH, 75% RH, and 90% RH (water condensed in the chamber above 90% RH) (Figure 2.3).

Figure 2.3. Humidity controlled glove box.

Substrate Preparation

Some substrates were prepared by depositing 1-10 μL of explosive solution, depending on concentration and desired final mass. The solvent was allowed to evaporate for three minutes. Other substrates were prepared using a MicroFab Technologies jetlab 4 drop-on-demand printer to deposit arrays of energetic material solutions onto test substrates. Arrays were typically 100 locations of 100-drop bursts of solution in a 10 mm x 25 mm area, though the exact number of locations, bursts, and drops per burst changed with drop size and concentration of the solution printed. Drop analyses were performed by the instrument to determine drop volume, velocity, and diameter. Pictures were taken with a strobe delay to freeze the drops, and instrument software calculated the values previously listed.

In cases termed “direct deposit” the substrates were used without further processing. In others termed “dry transfer,” a second transfer was performed. The explosive solution was placed on a 1” x 3” strip of Bytac, and, after the solvent was

evaporated, the Bytac was rubbed/scraped against the final substrate. A pictorial representation of dry transfer can be seen in Figure 2.4. Dry transfer prevented settling of analyte into the grooves of a rough substrate and ensured that the analyte remained in a powdered form rather than an amorphous “coffee ring;” a common result of direct deposition methods. Finally, dry transfer protected the substrate from excessive exposure to organic solvents.³³

Figure 2.4. Pictorial representation of dry transfer of explosives onto a substrate.

Swabbing Procedure

For sampling after direct deposit or dry transfer, a COTS swab was used to collect the analyte from the substrate. For contact swabs, the swab was physically wiped across

the substrate to collect the analyte, while charged swabs were vertically aligned with a ruler and passed across the substrate surface at 1 cm standoff.

Quantification of Explosives

Using a Thermo Electron TSQ Quantiva mass spectrometer, standard curves were created for explosives PETN, RDX, TNT, and TATP. As seen in Table 2.1, with an injection volume of 20 μ L, limits of detection for these energetics was as low as 100 pg and dynamic range was large.

Table 2.1. TSQ Quantiva LC/MS limits of detection (LOD) and quantification (LOQ) in ng/mL.

Explosive	LOD	LLOQ	HLOQ
PETN	5	50	5000
TNT	5	10	2500
RDX	31	63	2500
TATP	100	250	5000

Extraction optimization was performed with an acetonitrile:water mixture at three different ratios. Using the inkjet printer, 500 ng of PETN solution was deposited on three different substrates; then, the solution was allowed to dry. Each substrate was extracted, and the extract was analyzed via LC/MS for retention time, peak shape, and quantification of both the analyte and internal standard. As seen in Figure 2.5, the 10% organic extraction solution yielded representative retention times and excellent peak shape of both PETN and the internal standard, HMX. The 50% ACN mixture showed similar retention time, though the peak shape was slightly broader, especially for the internal standard. At 90% ACN, the retention time and peak shape of the internal standard were altered enough to make accurate quantification difficult.

Figure 2.5. Chromatograms of HMX (top) and PETN (bottom) at extraction ratios of a) 10% ACN, b) 50% ACN, and c) 90% ACN.

As seen in Table 2.2, the 10% ACN mixture did not fully extract all the PETN printed for any substrate. Though the peak shape and retention times of both the analyte and internal standard were excellent, inaccurate extraction precludes this mixture from being used. At 50% ACN, nearly quantitative recovery of the analyte was accomplished from all substrates, with the aforementioned standard peak shape and representative retention times of the analyte and internal standard. With a 90% ACN mixture, the poor peak shape of the internal standard caused an erroneously high

quantification of the analyte from the substrates, preventing it from being properly employed. All quantification was, therefore, performed with a 50% organic: 50% aqueous mixture.

Table 2.2. LC/MS quantification (in ng) of 500 ng PETN inkjet printed from solution onto swabs.

Extraction Ratio	Teflon		Nomex		Bytac	
	Mean	Std Dev	Mean	Std Dev	Mean	Std Dev
10:90 ACN:H ₂ O	98	13	283	41	189	33
50:50 ACN:H ₂ O	510	100	513	56	419	187
90:10 ACN:H ₂ O	565	25	684	114	593	182

Quantification of Analyte

A Thermo Electron TSQ Quantiva liquid chromatograph with mass selective detector (LC/MS) was used for quantification. A heated electrospray ionization (HESI) source generated ions which were introduced into the ion transfer tube set at 300 °C. Conditions for HESI analysis were as follows: negative ion spray voltage 2500 V; sheath gas 40 arbitrary units (AU); auxiliary gas 12 AU; sweep gas 1 AU; vaporizer temperature, 260 °C. Solvent delivery was performed using a Thermo Electron Accela quaternary pump. Sample injections were performed by a CTC Analytics HTS PAL autosampler directly from either the glass LC vials with PTFE septa or from 96-well plates with pre-slit silicone plate covers. Injections of 20 µL were introduced to a 300 µL/min flow rate consisting of 95% solvent A (aqueous 200 µM ammonium chloride, 200 µM ammonium acetate, 1% formic acid) and 5% solvent B (methanol) directed to a Thermo Scientific Acclaim Polar Advantage II C18 (PA2, 2.1x50 mm, 3 µm, 120 Å). Initial conditions were maintained for 1 min, then ramped to

5% solvent A/95% solvent B over 4 minutes, held for 1.5 minutes, ramped back to initial conditions in 0.5 minutes and held for 1 minute prior to beginning the next injection cycle (approximately 1 min, total run time of 9 minutes).

For extraction, swabs were placed into disposable, 15 mL, screw-cap polypropylene Falcon tubes. To each tube, 1 mL of 50% acetonitrile/50% water was added, shaken and vortex-mixed to extract compounds from the swab. An aliquot of 400 μ L from each tube was placed into either Agilent amber glass LC vials or Analytical polypropylene 1 mL 96-well plates. Each 400 μ L sample and standard received 20 μ L aliquots of 20 μ g/mL HMX in acetonitrile as an internal standard (IS). Multiple reaction monitoring (MRM) transitions for the deprotonated parent ions of TNT were from m/z 226 $\rightarrow$ 46, 226 $\rightarrow$ 166, and 226 $\rightarrow$ 196. Transitions for the chloride adduct of PETN were from 351 $\rightarrow$ 46, 351 $\rightarrow$ 62, and 351 $\rightarrow$ 315. MRM transitions for the chloride adduct of HMX were from 331 $\rightarrow$ 109, 331 $\rightarrow$ 129, and 331 $\rightarrow$ 147. Retention times for HMX, TNT and PETN were 4.3 min, 5.1 min and 5.3 min, respectively. Curves were analyzed and linearly weighted ($1/x$ or $1/x^2$) by Thermo Xcalibur Quan Browser software version 3.0.63. Dynamic range for PETN analysis was from 60 ng/mL to 3000 ng/mL, and for TNT, 25 ng/mL to 5000 ng/mL.

Explosive Trace Detectors (ETDs)

For experiments employing a commercial ETD, a Morpho Itemiser DX ion mobility spectrometer and FLIR Fido X3 fluorescence instrument were used. The Fido used compatible Teflon and Nomex COTS swabs, while the Morpho IMS used compatible Teflon-coated fiberglass COTS swabs.

To test the FIDO X3 (fluorescence detection) response, the explosives were dissolved in acetone (1 $\mu\text{g}/\mu\text{L}$ for both PETN and TNT), 400 $\text{ng}/\mu\text{L}$ for TNT, and 300 $\text{ng}/\mu\text{L}$ for PETN. For each trial, the solution (100 μL) was applied to a piece of Bytac, allowed to dry, and then transferred to a new piece of Bytac for swabbing. Uncharged contact swabs were treated with a Zerostat anti-static gun and weighted with a 50 g weight for consistent contact friction. Charged swabs were held over the trace explosive residue at a fixed distance of 10 mm. After exposure to the explosive, the swab was immediately placed into the FIDO, and results were recorded.

Confusants

To a swab was added 1 μL of 100 $\text{ng}/\mu\text{L}$ RDX solution in acetonitrile, and the solvent was allowed to partially dry. Then, confusant solution was added on top of the RDX spot. Hand sanitizer and hand lotion were put in solution with 200 $\text{ng}/\mu\text{L}$ isooctane; 2 μL of one or the other of these solutions was dispensed on top of the RDX. Artificial sebum solution was prepared as 180 $\text{ng}/\mu\text{L}$ in acetone, and 3 μL of the solution was dispensed over the RDX spot. The solvent was allowed to dry, and the swab was introduced to an ETD for analysis. Control samples with no confusant solution were analyzed before and after each set of confusant analyses. Swabs for the Morpho Itemiser DX and FLIR Fido X3 were composed of Teflon-coated fiberglass and Nomex, respectively.

With a gloved finger, 50 mg of C-4 and 50 mg of confusant were thoroughly mixed, and ten fingerprints were then deposited on aluminum foil. Inductively charged Nomex and Teflon-coated fiberglass swabs were used to swab each mixture and

sample on the FLIR Fido X3 and Morpho Itemiser DX, respectively. Contact swab comparison samples, blanks, and verification samples were run throughout analysis to ensure instrument operation. An additional set of fingerprints was made using an ungloved finger and 175 mg of C-4. Uncharged contact and inductively-charged noncontact samples were taken using Nomex swabs with the FLIR Fido X3.

Signal response of both the Fido X3 fluorescence instrument and Morpho Itemiser ion mobility spectrometer was tested using PETN standards. To a swab (Nomex and Teflon-coated fiberglass for the Fido and Itemiser, respectively) was deposited 10 μ L of PETN solution in acetone, and the solvent was allowed to dry. Then, the swab was inserted into the instrument, and the signal intensity was recorded. Three replicates of each concentration were analyzed, and means and standard deviations were calculated.

Results and Discussion

Scanning Electron Micrographs

Scanning electron micrographs of COTS swabs were taken using a JEOL 5900 SEM in backscatter mode. As seen in Figure 2.6, the COTS swabs have varying levels of surface roughness and topography, which could affect their adhesion or adsorption of energetic materials. Teflon has the smoothest overall surface, while cotton has the roughest, most irregular surface. The Teflon-coated fiberglass, though patterned, has pockets between its grids that can allow additional material to become attached.

Figure 2.6. Scanning electron micrographs of cotton (top left), Teflon-coated fiberglass (top right), Nomex (bottom left), and Teflon (bottom right) COTS swabs.

Charging Methods

To determine charge viability, COTS swabs were triboelectrically charged either by rubbing them against polyamide fabric or in a double roller system with polyurethane foam rollers. Five types of swabs (of four materials) were successfully charged, and voltage decay over time was monitored (Table 2.3). The polarity of induced voltage depended on the swab material, i.e. its position on the triboelectric series. The material used to construct the rollers also affected the voltage imparted to the COTS swabs. Charging of Nomex and Teflon swabs was done in the single roller configuration. The soft polyurethane roller imparted the highest magnitude and most negative voltage. Surprisingly, the silicone roller, on the high negative part of the triboelectric series, imparted a slightly negative voltage to Nomex and a significant negative voltage to

Table 2.3. Triboelectric dual roller charging of COTS swabs at different relative humidities. Means are of nine replicates.

Time (min)	Teflon										Nomex - FLIR							
	0% RH		25% RH		50% RH		75% RH		90% RH		0% RH		25% RH		50% RH		75% RH	
	Mean	Std dev	Mean	Std dev	Mean	Std dev	Mean	Std dev	Mean	Std dev	Mean	Std dev	Mean	Std dev	Mean	Std dev	Mean	Std dev
0	-2.9	0.7	-3.9	0.6	-1.5	0.3	-1.8	0.5	-0.4	0.4	-2.1	0.5	-1.5	0.5	-0.5	0.5	0	0.1
1	-2.6	0.5	-3.5	0.6	-1.4	0.3	-1.0	0.3	-0.3	0.2	-1.8	0.5	-1.1	0.5	-0.6	0.5	0	0
2	-2.5	0.6	-3.0	0.6	-1.3	0.2	-0.7	0.2	-0.3	0.2	-1.6	0.5	-0.7	0.5	-0.6	0.5	0.1	0
5	-2.5	0.5	-2.6	0.4	-1.2	0.3	-0.6	0.2	-0.2	0.1	-1.5	0.5	-1.0	0.5	-0.6	0.5	0.1	0
10	-2.4	0.5	-2.6	0.4	-1.2	0.2	-0.4	0.2	-0.2	0.1	-1.5	0.5	-0.8	0.5	-0.5	0.5	0.1	0

Time (min)	Cotton								Teflon-coated Fiberglass							
	0% RH		25% RH		50% RH		75% RH		0% RH		25% RH		50% RH		75% RH	
	Mean	Std dev	Mean	Std dev	Mean	Std dev	Mean	Std dev	Mean	Std dev	Mean	Std dev	Mean	Std dev	Mean	Std dev
0	3.6	0.9	1.5	0.7	0.5	0.1	0	0.1	-2.9	0.3	-1.8	0.8	-0.2	0.1	0.1	0
1	3.0	0.7	1.3	0.6	0.1	0	0	0	-2.2	0.2	-1.3	0.4	-0.1	0	0.1	0
2	2.7	0.6	1.2	0.6	0.1	0	0	0	-1.9	0.1	-1.2	0.3	0	0	0.1	0
5	2.5	0.6	1.2	0.5	0.1	0	0.1	0	-1.8	0.1	-1.1	0.3	0	0	0.1	0
10	2.1	0.5	1.1	0.4	0.1	0	0.1	0	-1.4	0.2	-1.0	0.3	0.1	0	0.1	0

Time (min)	Nomex - DSA					
	0% RH		50% RH		75% RH	
	Mean	Std dev	Mean	Std dev	Mean	Std dev
0	-2.0	0.6	-0.5	0.3	0	0
1	-1.7	0.2	-0.4	0.3	0	0
2	-1.8	0.4	-0.4	0.3	-0.1	0.1
5	-1.6	0.4	-0.4	0.3	0	0
10	-1.5	0.4	-0.4	0.3	0.1	0

Teflon, which is also on the high negative part of the triboelectric series. The soft polyurethane roller imparted more voltage than the hard polyurethane roller, probably because it could better contact the swab than the hard roller (Table 2.4).

Table 2.4. Single roller charged swab voltage (in kV).

Swab	Soft Polyurethane		Hard Polyurethane		Silicone	
	Mean	Std Dev	Mean	Std Dev	Mean	Std Dev
Nomex Smiths	-2.77	0.80	1.02	0.50	-0.67	0.50
Teflon	-2.28	1.10	-0.44	0.40	-2.13	0.50

Having determined that the roller method of charging had a number of drawbacks, COTS swabs were inductively charged using a Simco-Ion Chargemaster VCM-60. This method was tested at three voltages (-10 kV, -20 KV, and -30 kV), and the imparted voltages were measured (Table 2.5). Significantly higher and more consistent voltages were obtained by this method than by the roller method, and potential contamination of the swab by the roller material was avoided. In addition, the voltage on an inductively charged swab lasted for a longer duration.

Humidity

Because contact electrification is affected by humidity,³⁴ COTS swabs were charged in the double roller system in five different humid environments: 0% RH, 25% RH, 50% RH, 75% RH, and 90% RH. As the humidity increased, the voltage imparted to a given swab decreased (Table 2.3).

Table 2.5. Inductively charged means and standard deviations of COTS swabs at 30% RH.

Charging Voltage (kV)	Teflon-coated Fiberglass		Nomex FLIR		Nomex Smiths		Teflon FLIR	
	Mean	Std Dev	Mean	Std Dev	Mean	Std Dev	Mean	Std Dev
-10	-3.6	0.9	-2.7	0.8	-6.1	2.2	-1.34	0.1
-20	-12.5	3.2	-12.2	0.2	-7.45	0.8	-7.0	2.2
-30	-10.8	0.4	-10.9	1.9	-3.4	1.2	-8.5	0.2

Release of Voltage

To analyze the ability of COTS swabs to release voltage (and, therefore, their analyte payload), swabs were triboelectrically charged and subjected to a thermal desorption analysis cycle in a Morpho Itemiser DX. As seen in Table 2.6, the voltage on a swab was significantly mitigated (if not eliminated completely) after an analysis cycle on a commercial explosives trace detector (ETD), which suggested the analyte would be released.

Table 2.6. Swab voltage (in kV) before and after duty cycle of Morpho Itemiser DX.

Swab	Before		After	
	Mean	Std Dev	Mean	Std Dev
Teflon	-1.8	0.48	-0.43	0.23
Nomex	-0.25	0.4	0.01	0.04
Cotton	0.01	0.06	0.14	0.03
Teflon-Coated Fiberglass	-0.25	0.08	-0.1	0.07

Bulk Sampling

Because of the ease of measurement, electrostatic sampling was first attempted on visible bulk samples. In a proof of concept analysis, a charged Teflon swab was brought into near contact with a bulk amount of PETN. The swab adsorbed a large amount of the bulk material, as seen in Figure 2.7.

As previously mentioned, surrogate organic and inorganic materials such as sugar and table salt were used as a substitute for large amounts of actual explosives. Sugar particles on the milligram scale were easily adsorbed to an electrostatically charged Teflon swab from standoff (Table 2.7). Both 150 μm and 800 μm particles were readily picked up (Figure 2.8).

Figure 2.7. Bulk PETN attraction to hand charged Teflon.

Table 2.7. Pickup of sugar particles by hand charged Teflon.

Sugar on Surface (mg)	Voltage on swab (kV)	Sugar picked up on swab (mg)	Sugar remaining on swab after release (mg)	Pickup (%)	Release (%)
10.1	-6.31	8.5	0.2	84	98%
10.4	-6.91	10.1	1.1	97	89%
9.8	-5.59	5.2	0.1	53	98%
10.1	-6.72	8.2	0.3	81	96%
10.2	-7.03	9.8	0.3	96	97%
10.3	-4.6	8	0.1	78	99%
10.1	-7.17	8.4	0.4	83	95%
10	-6.85	9.4	0.3	94	97%
10.2	-5.32	8.2	0	80	100%
10.5	-6.73	10.1	0.3	96	97%
Average	-6.32	8.6	0.3	84	97%
Std. Deviation	0.86	1.5	0.3	13	2.9%

Figure 2.8. Bulk pickup of sucrose on hand charged Teflon.

While it is clear that a charged swab can adsorb analyte from standoff, the effective working distance of the swab must be known. Teflon swabs with triboelectric voltage using the paint-roller method have an average voltage of -2.7 kV. Sucrose and sodium chloride data were collected at 22 °C and 18 °C and relative humidity of 41% RH and 24% RH, respectively. On an index card, 100 mg of analyte was placed, and a swab of known voltage was passed over it at a fixed distance (10, 20, 30, 50, and 100 mm). A control experiment at contact was also performed. Adsorption of the analyte was determined by mass loss from the index card. Data in Figure 2.9a and Figure 2.9b suggest that, for this magnitude of voltage, stand-off distance should not exceed 1 in (25 mm) for effective pickup. However, at 10 mm, charged swabs adsorbed significantly more material than uncharged swabs (Table 2.8).

Figure 2.9. Hand charged swab distance comparison for a) sugar and b) sodium chloride.

Table 2.8. Bulk sampling comparison of charged and uncharged Teflon swabs.

Sucrose			NaCl	
Charged				
Distance (mm)	Mass adsorbed (mg)	Voltage (-kV)	Mass adsorbed (mg)	Voltage (-kV)
0	39.8	2.85	41.1	2.31
0	38.5	3.14	42.5	2.64
0	35.0	2.47	44.5	3.18
10	27.3	2.85	51.4	3.61
10	21.6	2.41	32.3	1.81
10	28.6	3.34	29.0	2.67
	Mean	Standard Deviation	Mean	Standard Deviation
0	38	3	43	2
10	26	4	38	12
Uncharged				
0	1.5	0.02	1.9	0.03
0	1.1	0.08	2.8	0.02
0	0.5	0	3.1	0.05
10	0	0.03	0	0.04
10	0	0.08	0.2	0.07
10	0.4	0.05	0.3	0.01
	Mean	Standard Deviation	Mean	Standard Deviation
0	1	0	0	0
10	0	0	0	0

Trace Sampling

TNT (500 ng in 5 μ L of 100 ng/ μ L solution) was syringe deposited on Bytac. Using the dry transfer method, the TNT analyte was transferred to a second Bytac substrate with either modest (0.5 N) or strong (50 N) force. COTS Teflon swabs were then used on the second Bytac substrate and sampled with the same two forces. To determine the efficiency of the analysis scheme, each surface where the analyte had been transferred was individually extracted and analyzed for TNT via LC/MS. Control samples of syringe-deposited TNT on Bytac were likewise analyzed and found to have ~450 ng of TNT rather than the expected 500 ng. As seen in Figure 2.10, the blue column (deposited Bytac), red column (dry-transferred Bytac substrate), and green column (Teflon swab) should add to ~450 ng if no TNT is lost in the sampling process. This sum is represented in Figure 2.10 by the purple bar, suggesting that the total amount of TNT is accounted for in every step of the sampling protocol, the extraction procedure extracts all TNT present, and the LC/MS system is quantifying correctly. Furthermore, a comparison of the deposited Bytac column to the combined Bytac substrate and swab columns shows that in five out of six dry transfers, 50-75% of the originally deposited analyte was transferred. (The exception was the sample labeled “0.5 N 3” where almost all the TNT remained on the first Bytac surface (blue column). As might be expected, the amount of material picked up by contact swabbing (green column) was proportional to the force applied during swabbing (Table 2.9). For the swabs transferred and swabbed with only 0.5 N of force, this was less than 10%. A similar value was reported by Verkouteren et al.²⁴

Figure 2.10. Efficiency of dry transfer force with contact Teflon sampling.

(quantification LC/MS).

Table 2.9. LC-MS/MS quantification of TNT from contact sampling.

Material	Control	0.5 N 1	0.5 N 2	0.5 N 3	50 N 1	50 N 2	50 N 3
Remaining on deposited Bytac after dry transfer	440 ± 31	220	260	420	85	150	120
Remaining on Bytac substrate after contact swabbing		160	150	60	125	130	110
Adsorbed on Teflon swab after contact swabbing		25	30	10	275	140	230
Total TNT		405	440	490	485	420	460

While Bytac as a substrate worked well for analytical experiments, it is not a surface likely to be encountered in real scenarios involving swabbing. Therefore, more realistic substrates were tested. However, when TNT was directly deposited onto vinyl and the vinyl extracted in the same manner as Bytac, only 10% of the TNT was recovered. We speculate that with the organic solvent, the vinyl polymer swelled, trapping TNT inside. Table 2.10 shows the quantity of TNT that could be extracted directly from Bytac or Vinyl prepared by direct deposit versus the amount of TNT that

could be extracted from these substrates when they were prepared by dry transfer and not subjected to an organic solvent.

Table 2.10. Mean and standard deviation LC quantification (in ng) of TNT for two swabs and two substrates.

Swab	Substrate			
	Bytac		Vinyl	
Teflon	215	69	37	13
Nomex	91	29	100	31
Control	440	31	70	21

These results suggest that, for substrates that are sensitive to organic solvents, either performing dry transfer or depositing much smaller amounts of organic solvent (through a process such as inkjet printing) would yield more accurate and reproducible amounts of material for analysis. Moreover, dry transfer ensured that the analyte remained in a powdered form rather than an amorphous “coffee ring.”

Table 2.11 compares the uncharged contact swabbing data from Table 2.9 to electrostatically enhanced swabbing using either a Teflon or Nomex swab. In two of the four combinations, the electrostatic method was slightly superior or directly comparable.

Table 2.11. LC quantification (in ng) of TNT for four sampling scenarios. UC = uncharged contact, EN = electrostatic noncontact.

Swab	Substrate			
	Bytac		Vinyl	
	Mean	Std Dev	Mean	Std Dev
Control	440	31	70	21
Teflon (UC)	215	69	37	13
Teflon (EN)	102	60	40	38
Nomex (UC)	91	29	100	31
Nomex (EN)	151	39	32	26

Testing with ETDs

PETN and TNT were used at the trace scale (microgram or nanogram scale). For PETN, the instrument was operated in administrative mode, where an alarm for this explosive has a threshold of 4.2. For TNT, the instrument was operated in user mode, where the signal is shown as a rating out of 4. Both uncharged contact and electrostatic noncontact swabs adsorbed similar amounts of explosive, and the signal response was unaffected by the voltage retained by the electrostatic swabs (Table 2.12).

The signal response for the Itemiser (Figure 2.11) and Fido X3 (Figure 2.12), when fitted to a curve, shows logarithmic correlation with increasing concentrations of PETN. In the IMS experiments, toward the higher end of the detection limit, the instrument required a more thorough clearing process between samples. This suggests that the instrument was reaching a saturation point. All the results from the IMS were obtained in the same day. When attempting to continue analysis on a different day, the intensity varied and was therefore not included in the set. In addition, as each experiment ran, the retention times shifted from 9.3 seconds to 9.2 seconds, suggesting that as the detector is exposed to real signals, the values shift.

In the FLIR experiments, one nanogram and five nanograms showed a signal response, but they were both under the limit of an alarm. Though there is no precedent for FLIR signal response correlating logarithmically, IMS systems have shown a logarithmic correlation of signal intensity to increasing amounts of TNT.²³

Table 2.12. Direct deposition swab testing on FLIR Fido X3. PETN swabs were analyzed in administrative mode, and TNT samples were analyzed in user mode.

Swab	500 ng PETN			500 ng TNT		
	Charged		Uncharged	Charged		Uncharged
	Voltage	Result	Result	Voltage	Result	Result
1	-3.34	16.4	12.9	-3.29	MIL 4/4	MIL 4/4
2	-3.86	6.8	7.2	-3.71	MIL 4/4	MIL 4/4
3	-2.19	9.5	10.4	-4.32	MIL 4/4	MIL 4/4
4	-3.28	10.1	8.2	-2.17	MIL 4/4	MIL 4/4
5	-3.58	4.8	6.4

Figure 2.11. Morpho Itemiser DX PETN calibration curve.

Figure 2.12. FLIR Fido X3 PETN calibration curve.

COTS swabs dosed with 100 ng of RDX were contaminated with a given confusant and analyzed in an ETD. As seen in Table 2.13, the IMS ETD alarmed on every sample and control regardless of confusant, while the fluorescence detector only alarmed on half the control samples. Because the fluorescence instrument bases an alarm on the quenching or enhancement of a fluorescence signal, the confusant could significantly affect this reaction and compromise the result. In addition, the disposable sensing element could become saturated, resulting in the undermining of all subsequent results.

Table 2.13. ETD alarms per samples for RDX confusants.

	Morpho	FLIR
Control	4/4	2/4
Hand Sanitizer	3/3	0/3
Hand Lotion	3/3	0/3
Sebum	3/3	0/3

C-4 fingerprints were constructed with the same three confusants listed above. Inductively charged Nomex and Teflon-coated fiberglass swabs were used to sample the fingerprints and introduce them to the FLIR Fido X3 and Morpho Itemiser DX, respectively. In contrast to the previous confusant results, the Fido X3 performed significantly better than the Morpho in the fingerprint tests (Table 2.14). Because the Morpho correctly alarmed for every control and verification sample analyzed, it is unlikely that the instrument was operating incorrectly; rather, the results may indicate that the Teflon-coated fiberglass may be less suitable for electrostatic swabbing than Nomex.

The FLIR, while correctly alarming on every electrostatic swab event, also alarmed in ungloved fingerprint contact and electrostatic analyses performed concurrently with these tests. The signal for electrostatic swabs rose in time after introduction, reached the alarm threshold, and steadily decreased as the analyte was desorbed through the instrument. The signal for contact swabs, however, rose in time and alarmed as before, but the signal rapidly decreased significantly below the intensity origin. Specifically, after alarming correctly for C-4, the signal for one sebum sample dropped so rapidly and severely that three channels were reduced to values never before seen on the instrument. The instrument continued to operate correctly after this sample, but these results could shed light on the suspicious weakness of the FLIR to confusants. If the confusant is thermally desorbed from the swab before the analyte of interest, the signal could be decreased so much that the subsequent increase in signal from the analyte would be unable to overcome it. Conversely, if the analyte

of interest is desorbed first, the instrument appears to operate correctly even with the resulting rapid and severe drop in signal.

Table 2.14. ETD alarms per samples for C-4 confusants from fingerprints.

Analyte/Confusant	Gloved Electrostatic			Ungloved Contact
	Morpho	FLIR	FLIR	FLIR
C-4	0/3	3/3	5/5	5/5
Hand Sanitizer	1/3	3/3	-	-
Hand Lotion	1/3	3/3	-	-
Sebum	1/3	3/3	-	-

Conclusion

Commercial off-the-shelf swabs were electrostatically charged via two methods: tribocharging or induction charging. Their effectiveness as swabs without contacting a substrate (1 in standoff) was compared to traditional direct contact swabbing. Bulk experiments used explosives simulants, while trace experiments utilized actual energetic materials. Numerous COTS swabs were examined for their charging viability, and Teflon or Nomex swabs were employed for swabbing comparison measurements. Both Bytac (an ideal but unrealistic material for practical simulation) and vinyl fabric (a realistic but analytically problematic material) were used as sampling substrates. Creating representative amounts and conditions of analytes through syringe deposition, dry transfer, and drop-on-demand inkjet printing was examined, and quantifying analytes via LC/MS was devised and validated. With a robust quantification method and a reproducible sampling procedure, true comparison of contact swabbing to noncontact electrostatic swabbing was performed.

Electrostatically charged swabs adsorbed as much or more energetic material as conventional uncharged contact swabs.

Electrostatically charged swabs could become a novel tool for trace explosives collection, especially on areas that are difficult to sample, e.g. headaddresses or the corners of bags. In the field, an inductive charging unit could enhance swabbing efficiency with little to no loss in sampling time, a relatively small working footprint, and a reasonable cost through its ability to voltage swabs simultaneously for multiple ETDs. Moreover, we expect non-contact swabbing to result in lower false alarm rates due to the lack of contamination from oils often picked up in contact swabbing.

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Manuscript 3
Cocrystallization of TNT and Nicotinamide, and Cocrystallization Screening of
Energetic Materials

by

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Abstract

Altering a particular property of a material can functionally optimize it for a given purpose. Cocrystallization is a method able to tailor physical and chemical properties with potential applications to energetic materials. Herein, a number of cocrystals between energetic pairs were attempted. Combinations of nitroourea/2,6-dinitrotoluene and TNT:nicotinamide stand out for interesting property modifications, with TNT/nicotinamide forming a confirmed cocrystal.

Introduction

Cocrystallization can rectify undesirable physical and chemical properties, such as solubility, high moisture affinity, melting point and stability. The most widely used applications for cocrystallization are for pharmaceuticals, where it has been utilized for over a decade. More recently, the energetic materials community has attempted to tailor explosive properties such as density, detonation velocity, and sensitivity by the same method.

The definition of “cocrystal” has been nebulous at least as far back as the 1970’s.¹⁻² Even the mandatory presence of a hyphen in the word, i.e. “co-crystal,” has been the subject of disagreement.³⁻⁶ The term “cocrystal” has become widely accepted as “co-crystal” has diminished, but an agreed-upon definition is still lacking. Different definitions are crafted for different purposes, e.g. drug regulations through FDA compared to a supramolecular understanding of the interactions occurring,

causing a disparity of descriptions.⁷ A sufficiently broad definition would define a cocrystal as “a mixed crystal or crystal that contains two different molecules.”⁸ From there, the biggest divide in the definition of “cocrystal” is caused by which molecules are considered capable of making cocrystals. A common definition of cocrystal excludes ionic compounds and compounds that are not solid at ambient temperature, removing salts and hydrates/solvates from being cocrystals. While there are reasonable objections to this stricter definition, a cocrystal in this manuscript will nevertheless be defined as a unique crystal lattice composed of two or more different neutral, solid molecules in some definite stoichiometric ratio.⁹ The principal energetic material used will be referred to as such, and the second molecule with which it is to cocrystallize will be called the “coformer.”

Regardless of the definition, cocrystals are incredibly important materials in a number of fields, most notably pharmaceuticals. The reason for this is their ability to tailor the properties of the constituent materials. Pharmaceutical cocrystals are often designed to improve bio-solubility, though a host of other advantageous alterations exists (Figure 3.1).¹⁰⁻¹²

In the energetics community, cocrystals can change density, detonation velocity, thermal stability, and sensitivity (impact, friction, electrostatic discharge).¹³⁻²⁶ With the synthesis of the next generation of explosives becoming increasingly difficult because available novel reagents and synthetic techniques are limited, cocrystallizing energetic materials unlocks a new avenue for optimizing explosive properties.

Insofar as the free energy of cocrystal formation is favorable, nearly any method of single crystallization can be employed to create cocrystals. The easiest and most widely used process is through solvent evaporation, wherein the analytes are dissolved in a solvent of choice, and the solvent is evaporated either at ambient or slightly elevated temperature.²⁷ Reproducibility is a concern, and it is limited to solvents with adequate vapor pressure and in which the analytes are reasonably soluble. Modifications of this method include using more than one solvent, either as a mixture or separated in a sealed container to allow vapor diffusion of the second solvent.²⁸

PHYSICAL AND THERMODYNAMIC PROPERTIES	density and refractive index, thermal and electrical conductivity, hygroscopicity, melting points, free energy and chemical potential, heat capacity, vapor pressure, solubility, thermal stability
SPECTROSCOPIC PROPERTIES	electronic, vibrational and rotational properties, nuclear magnetic resonance spectral features
KINETIC PROPERTIES	rate of dissolution, kinetics of solid state reactions, stability
SURFACE PROPERTIES	surface free energy, crystal habit, surface area, particle size distribution
MECHANICAL PROPERTIES	hardness, compression, thermal expansion
CHEMICAL PROPERTIES	chemical and photochemical reactivity

Figure 3.1. Properties that can change in a cocrystallization.⁹

Thermal methods are popular for creating cocrystals. In a solution-based method similar to recrystallization, analytes are dissolved in a hot solvent and allowed to precipitate as the temperature of the solution is gradually lowered.²⁷ Without

solvent, compounds can be melted together on a hot stage and allowed to cocrystallize as the temperature is lowered. This method, popularized by Kofler, can be used to screen for potential cocrystals.²⁹⁻³¹ Less common, but still effective, cocrystallization methods include physical grinding with and without solvent,³¹⁻³⁴ spray drying,³⁵⁻³⁶ resonant acoustic mixing,³⁷⁻³⁸ and supercritical fluid precipitation.³⁹⁻⁴²

Before cocrystallization experiments can be run, pairs of molecules to be cocrystallized must be chosen. Previously published cocrystals can be helpful in selection of compatible materials with potentially desirable properties (Table 3.1 and Table 3.2). Numerous compounds create new cocrystals with a variety of coformers, and a significant reason is because of complimentary bond interactions. The atoms within a molecule are covalently bonded with energies ranging from 200 kJ/mol to 500 kJ/mol. The weaker non-covalent intermolecular forces between molecules include hydrogen bonds, van der Waals attractions and repulsions, and pi-pi effects. Hydrogen bonds are the strongest (20-40 kJ/mol) and the others are weaker (2-20 kJ/mol), but all exert profound influence on physical properties.^{32, 43-45} Because these noncovalent bonds are important in holding molecules together, many two component (or more) systems are categorized as noncovalent derivatives (NCDs).⁴⁶ NCDs create solid systems that can have repeatable, stoichiometric organizations such as cocrystals, but they can also cause heterogeneous forms such as eutectics, solvates, and solid solutions. Ultimately, it is these NCDs that dictate the resulting bulk properties of a cocrystal.

The word “synthon” was first used in 1967 to indicated key structural features in a target molecule in organic synthesis.⁴⁷ In crystal engineering, where specific

lattice architectures are desired, selected synthons can be used to create desired “noncovalent derivatives.” Species capable of hydrogen bonding are the most likely synthon, but other functional groups can form synthons as well. For pharmaceutical cocrystals, the carboxylic acid dimer, amide dimer, and pi-pi stacking synthons are frequently seen.^{8, 10, 44}

Figure 3.2. Common synthons in pharmaceutical cocrystals. From left: carboxylic acid dimer, amide dimer, and face-to-face and herringbone pi-pi stacking.

Because a wide majority of energetic materials do not have carboxylic acid or amide moieties, their cocrystallization must rely on other interactions. The pi-pi stacking found in aromatic compounds such as TNT has led to a number of cocrystals with these molecules,^{13, 16, 18} and the lack of hydrogens on benzotrifuroxan (BTF) has led to its cocrystallization through intermolecular hydrogen bonds with partners that do have hydrogens (Figure 3.3).²²⁻²⁴ Otherwise, most energetic materials must cocrystallize with synthons based on nitro,¹⁴ peroxide,⁴⁸ or other energetic functionalities.^{20, 49}

Table 3.1. Reported energetic-energetic cocrystals.

Line	Year	A	B	Group	Preparation Method Used	Reference
1	2011	CL-20	TNT	Matzger	Solvent evaporation	13
2	2011	HMX	TATB	Chonghua Pei	Solvent/antisolvent precipitation	25
3	2012	CL-20	HMX	Matzger	Solvent evaporation	14
4	2012	CL-20	BTF	Fude Nie	Solvent evaporation	24
5	2013	BTF	TNB	Sun	Solvent evaporation	23
6	2013	BTF	TNT	Sun	Solvent evaporation	23
7	2013	BTF	Trinitroaniline	Sun	Solvent evaporation	23
8	2013	BTF	(Methoxyamino)trinitrobenzene	Sun	Solvent evaporation	23
9	2013	BTF	TNAZ	Sun	Solvent evaporation	23
10	2013	DADP	Trichlorotrinitrobenzene (TCTNB)	Matzger	Solvent mediated transformation	15
11	2013	DADP	Tribromotrinitrobenzene (TBTNB)	Matzger	Solvent mediated transformation	15
12	2013	CL-20	TNT	Fude Nie	Solvent/antisolvent precipitation	21
13	2014	CL-20	HMX	Nalas	RAM	36
14	2014	CL-20	1,3-DNB	Yucun Liu	Solvent evaporation	19
15	2014	BTF	1,3-DNB	Fude Nie	Solvent evaporation	22
16	2015	DADP	Triiodotrinitrobenzene (TITNB)	Matzger	Solvent mediated transformation	47
17	2015	CL-20	TATB	Chonghua Pei Wengzheng	Solvent/antisolvent precipitation	26
18	2015	HMX	TNT	Xu	Spray drying	35
19	2015	DNBT	ANTA	Matzger	Solvent evaporation	48
20	2015	DNBT	DNPP	Matzger	Solvent evaporation	48
21	2015	DNBT	3,4-DNP	Matzger	Solvent evaporation	48
22	2015	NTO	TZTN	Zhang	Solvent evaporation	20
23	2016	CL-20	2,5-DNT	Shu	Solvent evaporation	18

Table 3.2. Reported energetic-energetic cocrystal properties. * indicates the number is from internal sources, not the reference.

Line	A	exotherm		B	mp	exotherm	Cocrystal	exotherm	Second	Reference
		mp (°C)	T (°C)		(°C)	T (°C)	mp (°C)	T (°C)	exotherm (°C)	
1	CL-20	-	245	TNT	80	320*	136	205	247	13
2	HMX	279	282	TATB	-	388	278	285	-	25
3	CL-20	-	245	HMX	279	282	-	235	-	14
4	CL-20	-	244	BTF	198	289	-	235	-	24
5	BTF	198	289	TNB	123	434*	189	n/a	n/a	23
6	BTF	198	289	TNT	80	320*	133	n/a	n/a	23
7	BTF	198	289	Trinitroaniline	184	n/a	206	n/a	n/a	23
8	BTF	198	289	(Methoxyamino)trinitrobenzene	109	n/a	171	n/a	n/a	23
9	BTF	198	289	TNAZ	100	273*	165	n/a	n/a	23
10	DADP	132*	253*	Trichlorotrinitrobenzene (TCTNB)	n/a	n/a	n/a	n/a	n/a	15
11	DADP	132*	253*	Tribromotrinitrobenzene (TBTNB)	n/a	n/a	n/a	n/a	n/a	15
12	CL-20	-	249	TNT	80	320	134	222	250	21
13	CL-20	227 (dec)	-	HMX	279	282	-	236	-	36
14	CL-20	227 (dec)	-	1,3-DNB	92	440*	137	217	242	19
15	BTF	198	289	1,3-DNB	92	440*	130	286	-	22
16	DADP	132*	253*	Triiodotrinitrobenzene (TITNB)	400	n/a	n/a	n/a	n/a	47
17	CL-20	-	246	TATB	-	381	208	232	-	26
18	HMX	279	282	TNT	80	320	-	280	-	35
19	DNBT	269	274	ANTA	238	245	-	223	-	48
20	DNBT	269	274	DNPP	-	322	-	312	-	48
21	DNBT	269	274	3,4-DNP	82	340	163	340	-	48
22	NTD	262	279	TZTN	144	197	157	178	198	20
23	CL-20	-	251	2,5-DNT	72	325	121	216	-	18

In this reported work, many types of synthons (and resulting cocrystals) were attempted. In general, the energetic materials attempted were analogs of compounds previously found to cocrystallize (TEX→CL-20), materials with numerous favorable potential synthons (NTO, FOX-7, ETN) and an energetic amide (nitrourea). Examples of potential energetic material synthons are shown in Figure 3.4.

Figure 3.3. Typical interactions between BTF and CL-20.²⁴

Ideally, synthon identification would allow selection of appropriate partners to create a cocrystal. As stated by Aakeroy, “*Although individual structures that defy rationalization will appear from time to time, there is no doubt that the important ‘big picture’ reveals structural trends, patterns of behavior, and reproducible motifs that, when combined, can be developed into a library of high-yielding supramolecular*

reactions.”³ Unfortunately, no such predictive capability currently exists, and the principles of NCDs give only a general idea of the viability of a given synthon to be used in the construction of a lattice. Many experimental conditions and methods must be attempted before the possible existence of a cocrystal can be ruled out. The goal of this work, therefore, is to advance the knowledge of these conditions for the energetics field.

Experimental Methods

Analytes

Erythritol tetranitrate (ETN), 1,1-diamino-2,2-dinitroethene (FOX-7), hexamethylene triperoxide diamine (HMTD), mannitol hexanitrate (MHN), 3-Nitro-1,2,4-triazol-5-one (NTO), nitrourea (NU), triacetone triperoxide (TATP), and 4,10-Dinitro-2,6,8,12-tetraoxa-4,10-diazatetracyclo [5.5.0.05,9.03,11]-dodecane (TEX) were synthesized via published procedures and purified accordingly. 2,4,6,8,10,12-Hexanitro-2,4,6,8,10,12-hexaazaisowurtzitane (CL-20), octahydro-1,3,5,7-tetranitro-1,3,5,7-tetrazocine (HMX), 1,3,5-trinitro-perhydro-1,3,5-triazine (RDX), 2,4,6-triamino-1,3,5-trinitrobenzene (TATB), 1,3,3-trinitroazetidine (TNAZ), and 1,3,5-trinitro-2-methylbenzene (TNT) were received from military or law enforcement sources and used as received unless otherwise mentioned. 5-Aminotetrazole (5-AT), benzamide, benzoic acid, carbamazepine, 3,5-dinitrobenzamide, 1-methoxy-2,4-dinitrobenzene (DNAN), 2,4-dinitroaniline, 3,5-dinitrophenol (3,5-DNP), 2,4-dinitrotoluene (2,4-

DNT), 2,6-dinitrotoluene (2,6-DNT), isonicotinamide, nicotinamide, 2,4,6-trinitrophenol (picric acid) and all solvents were purchased from Fisher Scientific and used as received.

Figure 3.4. Examples of synthons between a) TATB and FOX-7, b) NU and NTO, and c) TEX and TNT.

Figure 3.5. Chemical structures of (top row) 5-AT, 3,5-DNP, picric acid, 2,4-DNA, (middle row) benzoic acid, benzamide, 3,5-dinitrobenzamide, (bottom row) nicotinamide, isonicotinamide, and carbamazepine.

Cocrystal Preparation

Solvent Evaporation

Two analytes were dissolved in a solvent, syringe filtered into a glass vial, and the solvent was allowed to evaporate at a given temperature. Normally, solvents

evaporated at room temperature, though heated evaporation at 20 °C, 25 °C, 30 °C, 35 °C, and 50 °C was also attempted for certain mixtures in ethanol and nitromethane. Solvents used were acetone, ethanol (EtOH), acetonitrile (ACN), dimethylsulfoxide (DMSO), dimethylformamide (DMF), diacetone alcohol (DAA), methyl ethyl ketone (MEK), dioxane, and nitromethane (NM). Analytes were added in mole ratios of 1:1, 2:1 (both combinations), 3:1 (both combinations), 3:2 (both combinations), and 4:3 (both combinations). The total amount of material was varied from ~4 mg to ~500 mg, and container size and shape were also altered. For example, 2.27 mg (10 μ mol) of TNT (MW 227 g/mol) and 1.22 mg (10 μ mol) of nicotinamide (MW 122 g/mol) were added to a clean 1 mL glass vial and dissolved in 1 mL anhydrous ethanol. Mild heating, vortexing, and sonication were used to ensure complete dissolution. The solution was transferred to a 1 mL plastic syringe with a 0.2 μ m syringe filter attached and filtered into a different clean 1 mL glass vial. The vial was then carefully placed into a 15 mL screw cap vial and put in a remote area to dissolve. The screw cap vial was loosely capped to allow evaporation of solvent but prevent significant contamination from the outside atmosphere. For a 2:1 TNT:nicotinamide ratio, the experimental procedure would be identical, except the masses of TNT and nicotinamide would be 4.54 mg (20 μ mol) and 1.22 mg (10 μ mol), respectively.

Vapor Diffusion

Analytes were dissolved, syringe filtered at 0.2 μ m, and put into a 1 mL glass vial. The smaller vial was placed in a 15 mL screw-cap vial that was subsequently loaded with an anti-solvent and the large container was sealed. (An example of this type of

setup can be found in Reference 28.) After two weeks, if no precipitate was observed, the 15 mL vial was opened to the environment, and evaporation of both solvents was allowed. Solvents were acetone and ethanol, and anti-solvents were chloroform and cyclohexane, respectively. For large vapor diffusion experiments, 4 mL and 40 mL vials were used as the small and large containers, respectively.

Grinding

Analytes were placed into a small mortar in a given ratio with total mass 5 mg or 50 mg. Then, the compounds were ground by hand both with and without solvent for 30 s. If solvated, the solvent was allowed to dry, and the solid was scraped into a vial. Solvents used were acetone, ethanol, isopropanol, and nitromethane at both 25 μ L and 100 μ L volumes.

Note: Before grinding an energetic material, it is critical to confirm the insensitivity of the material to friction, impact, and electrostatic insult!

Thermal methods

Analytes were dissolved into a solvent, filtered, and placed into a glass vial. The vial was placed in a 3 °C refrigerator for one week. If no precipitate was observed, the vial was placed in a -20 °C freezer for one week.

TNT and nicotinamide were placed in a ceramic crucible and situated on a hotplate at 150 °C. When both materials melted, the liquids were mixed together with a metal spatula. The mixture was allowed to crystallize both quickly and slowly in separate experiments.

Thermal microscopy

Using the Kofler method in a hot stage microscope,²⁹⁻³¹ the analyte with the higher melting point was melted and allowed to recrystallize. Then, the lower melting compound was melted into it and allowed to recrystallize. If a new solid layer developed between the melted layers, a cocrystal was possibly formed.

Supercritical Fluid Precipitation

A Waters supercritical anti-solvent (SAS) reactor was used to precipitate a solution of TNT and nicotinamide that was of 10 mg/mL concentration for both reagents. The CO₂ pump was operated at 20 g/min; the vessel was held at 150 bar; the vessel temperature was 50 °C; and the solvent pump was operated at 0.5 mL/min. Solvents used were acetone and ethanol.

Spray Drying

A Buchi Mini Spray Dryer B-290 was used to spray dry analyte pairs dissolved in acetone or ethanol. For acetone experiments, the following parameters were used: inlet temperature – 65 °C; aspirator flow rate – 35 m³/h; spray gas flow rate – 300 l/hr; and pump flow rate – 5 mL/min. For ethanol solutions, the inlet temperature was increased to 90 °C.

Resonant Acoustic Mixing (RAM)

A Resodyn LabRam was used to acoustically mix analytes at high acceleration. Analytes (different ratios equaling 50 mg total) were added to 1 mL glass vials, 50-100 μ L of solvent was added (analyte was not dissolved), and the vials were acoustically mixed. Typical accelerations and durations were 30 gr for 1 hr, 50 gr for 1 hr, and 80 gr for 45 min.

Analytical Methods

Polarized light microscopy (PLM)

A Nikon Eclipse E400 POL polarized light microscope was used to image crystals both in unpolarized and polarized light. Crystals were typically imaged at 100x magnification. For hot stage experiments, a Mettler Toledo FP900 Thermosystem with a FP82HT hot stage was used. Crystals were heated at 10 $^{\circ}$ C/min and observed for changes as they were heating.

Differential scanning calorimetry (DSC)

A TA Instruments Q100 DSC was operated with nitrogen purge gas flowing at 50 mL/min. Samples were weighed to $\sim$ 1 mg in aluminum pans and hermetically sealed. The DSC ramp program was from 30 $^{\circ}$ C to 400 $^{\circ}$ C at 20 $^{\circ}$ C/min. For thermally cycled materials, the mixture was heated to slightly above the melting point of the higher melting material (e.g. 80 $^{\circ}$ C for 2,6-DNT), cooled, and heated again to 400 $^{\circ}$ C to ensure all thermal events were recorded.

Raman spectroscopy

An Andor Shamrock spectrograph coupled with Ondax SureBlock ultra-narrow-band filters and iDus CCD detector was used to collect low-frequency Raman spectra with a 785 nm laser source. Integration time was 60 s, and resolution was $<1\text{ cm}^{-1}$.

X-ray diffraction

A Rigaku Optima IV X-ray diffractometer was used to analyze crystallography of materials. A Cu source generated X-rays at 40 kV and 44 mA, a 10 mm slit was used for the source, the sampling rate was $0.75^\circ/\text{min}$, the sampling width was 0.25° , and the sampling range was 5° to 105° .

Results

Cocrystals Attempted

The vast majority of combinations tested were screened initially via solvent evaporation. Solvents were chosen first upon ability to dissolve the analytes; this meant that acetone was often used. The second consideration was ease of evaporation; therefore, vapor pressure and boiling point were examined. The synthons typically available in energetic materials fall into one of six generalized categories: pi-pi, nitro, peroxide, nitro/wurtzitane cage, amine/nitro, and amide interactions.

Pi-Pi interactions (Table 3.3): Energetic materials 2,4-DNT, 2,6-DNT, DNAN, and TNT contain aromatic rings, leading to an increased likelihood of pi-pi stacking, both in-plane and out-of-plane. TNT has been shown to exhibit face-face stacking in a cocrystal,¹⁶ and we anticipated that dinitrotoluene and dinitroanisole would do the same. However, with a wide range of solvents and both aromatic and nonaromatic cofomers, no cocrystals were observed, either visually or by PLM.

Figure 3.6. Chemical structure of (from left) TNT, 2,4-DNT, 2,6-DNT, and DNAN.

Table 3.3. Pi-Pi interaction cocrystals attempted with single solvent evaporation.

Energetic Material	Coformer	Single Solvent Used				
2,4-DNT	NU	Acetone	Ethanol			
	3,5-Dinitrobenzamide	Acetone	Ethanol			
	Benzamide	Acetone	Ethanol			
	Benzoic Acid	Acetone	Ethanol			
	Carbamazepine	Acetone	Ethanol			
	Nicotinamide	Acetone	Ethanol			
2,6-DNT	Benzamide	Acetone	Ethanol			
	3,5-Dinitrobenzamide	Acetone	Ethanol			
	Benzoic Acid	Acetone	Ethanol			
	Carbamazepine	Acetone	Ethanol			
	DNAN	Acetone	Ethanol			
	Nicotinamide	Acetone	Ethanol			
	NU	Acetone	Ethanol	MEK	NM	ACN
	TNT	Acetone	Ethanol			
DNAN	Benzamide	Acetone	Ethanol			
	3,5-Dinitrobenzamide	Acetone	Ethanol			
	Benzoic Acid	Acetone	Ethanol			
	Carbamazepine	Acetone	Ethanol			
	2,6-DNT	Acetone	Ethanol			
	Nicotinamide	Acetone	Ethanol			
	NU	Acetone	Ethanol			
	TNT	Acetone	Ethanol			

TNT	5-AT	Acetone			
	Benzamide	Acetone	Ethanol		
	3,5-Dinitrobenzamide	Acetone	Ethanol		
	Benzoic Acid	Acetone	Ethanol		
	Carbamazepine	Acetone	Ethanol		
	CL-20	Acetone	Ethanol	ACN	DAA
	2,6-DNT	Acetone	Ethanol		
	2,4-DNT	Acetone	Ethanol		
	ETN	Acetone	Ethanol	DAA	
	HMX	Acetone			
	Isonicotinamide	Acetone	Ethanol		
	MHN	Acetone	Ethanol	DAA	
	Nicotinamide	Acetone	Ethanol	NM	EtOH/NM
	NTO	Acetone	DAA		
	NU	Acetone	Ethanol		
	PETN	DAA			
	RDX	DAA			
	TATB	Acetone			
	TATP	DAA			
	TEX	Acetone	ACN		
	TNAZ	Acetone	ACN		

ACN = acetonitrile, DAA = diacetone alcohol, EtOH = ethanol, NM = nitromethane, MEK = methyl ethyl ketone

Nitro interactions (Table 3.4): The vast majority of explosives possess nitro groups. Though they may also possess other synthon units, the nitro synthon is usually the most sterically available. This includes nitrate esters (ETN, MHN, and PETN), nitramines (HMX and RDX), and two heterocycles (NTO and TNAZ). The similarity between ETN and MHN, differing only in the nitrate ester chain length, led us to expect they might cocrystallize easily. However, though each readily formed needles from solution, no new cocrystals were observed, nor was any eutectic between ETN and MHN observed. HMX has been demonstrated to cocrystallize with multiple compounds with different synthon potential, but currently no cocrystal with RDX has been reported.^{14, 17, 36} Our attempt to cocrystallize RDX with the same materials that cocrystallized with HMX did not result in cocrystals. It may be that the six-membered ring of RDX can compact in a way that the eight-membered ring of HMX cannot, possibly leading to inaccessibility of part of RDX necessary to interact with another molecule. Although one example of a cocrystal has been reported for NTO²⁰ and one for TNAZ,²³ we were unable to discover further cocrystals with these species.

Figure 3.7. Chemical structures of (top row) HMX and RDX, (middle row) ETN, MHN, and PETN, and (bottom row) NTO and TNAZ.

Table 3.4. Nitro interaction cocrystals with single solvent evaporation.

Energetic Material	Coformer	Solvents			
ETN	5-AT	Acetone			
	CL-20	DAA			
	MHN	Acetone	Ethanol	DAA	
	NTO	Acetone	DAA		
	NU	Acetone	Ethanol		
	PETN	DAA			
	RDX	DAA			
	TATP	DAA			
	TEX	Acetone			
	TNT	Acetone	Ethanol	DAA	
HMX	TEX	Acetone	Acetonitrile		
MHN	5-AT	Acetone			
	CL-20	DAA			
	ETN	Acetone	Ethanol	DAA	
	NTO	DAA			
	NU	Acetone	Ethanol		
	PETN	DAA			
	RDX	DAA			
	TATP	DAA			
	TNT	Acetone	Ethanol	DAA	
NTO	CL-20	Acetone	DAA		
	ETN	Acetone	IPA	EtOH	DAA
	FOX-7	Acetone			
	MHN	IPA	DAA		
	NU	Acetone			
	PETN	DAA			
	RDX	Acetone			
	TATP	DAA			
	TEX	Acetone			
	TNT	Acetone	DAA		

Table 3.4 (cont). Nitro interaction cocrystals with single solvent evaporation.

PETN	5-AT	Acetone	
	NTO	DAA	
	RDX	DAA	
	ETN	DAA	
	TNT	DAA	
	CL-20	DAA	
	TATP	DAA	
	MHN	DAA	
RDX	CL-20	DAA	
	ETN	DAA	
	MHN	DAA	
	NTO	Acetone	
	PETN	DAA	
	TATP	DAA	
	TEX	Acetone	
	TNT	DAA	
TNAZ	5-AT	Acetone	
	CL-20	Acetone	
	TEX	Acetone	Acetonitrile
	TNT	Acetone	Acetonitrile

DAA = diacetone alcohol, EtOH = ethanol, IPA = isopropanol

Peroxide interactions (Table 3.5): TATP, DADP and HMTD are well-known peroxide explosives used by terrorists. DADP, the acetone peroxide cyclic dimer, has cocrystallized with nitrated, halogenated benzenes.⁴⁹ While the same interactions of DADP would presumably be present in TATP, we were unable to make similar cocrystals. We rationalize that the torsion in TATP caused by the unfavorable nine-membered ring structure could prevent adequate coupling. Conversely, the planar nitrogens on HMTD should present highly accessible synthon locations. We were

unable to form any cocrystals with HMTD, but the poor solubility of HMTD in most organic solvents prevented us from thoroughly investigating it. Similarly, the volatility of TATP ruled out use of solvent evaporation and spray drying techniques as modes of making cocrystals.

Table 3.5. Peroxide interaction cocrystals attempted with single solvent evaporation.

Energetic Material	Coformer	Solvents
HMTD	FOX-7	Acetone
	NU	NM
	TATP	Acetone
TATP	ETN	DAA
	CL-20	DAA
	HMTD	Acetone
	MHN	DAA
	NTO	DAA
	NU	Acetone Ethanol
	PETN	DAA
	RDX	DAA
	TEX	Acetone
	TNT	DAA

DAA = diacetone alcohol, NM = nitromethane

Figure 3.8. Chemical structures of (left) TATP and (right) HMTD.

Nitro/isowurtzitane cage interactions (Table 3.6): CL-20 readily cocrystallizes with numerous compounds even though its six nitro functionalities prevent internal access to the cage structure. We speculated that TEX, which presents the same basic cage structure as CL-20 without four nitro groups, should form cocrystals with some of the same coformers used with CL-20. TEX has slight solubility (< 3 mg/mL) in acetone, methanol, ethanol, isopropanol, acetonitrile, and diacetone alcohol (DAA), but it readily crystallizes from these solvents. However, we have been unable to observe cocrystallization of TEX though a variety energetics, including those which formed cocrystals with CL-20, were used (Table 3.6). Furthermore, we were unable to promote cocrystallization of CL-20 with TEX, even though published density functional theory suggested that possibility.⁵⁰ We attribute this to the fact that the only solvent of common and sufficient solubility was nitromethane. Neither CL-20 nor TEX has good solubility (> 5 mg/mL) in common organic solvents; nevertheless, CL-20 readily forms solvates with a variety of solvents (e.g. dimethylformamide and N-methylpyrrolidone), while TEX formed none.⁵¹

Figure 3.9. Chemical structures of (left) CL-20 and (right) TEX.

Table 3.6. Nitro/Isowurtzitane interaction cocrystals attempted with single solvent evaporation.

Energetic Material	Coformer	Solvents		
CL-20	5-AT	Acetone	DAA	
	ETN	NM	DAA	
	FOX-7	Acetone		
	MHN	DAA	Ethanol	NM
	NTO	Acetone		
	NU	Acetone		
	PETN	DAA	NM	
	RDX	DAA		
	TATP	DAA	NM	Dioxane
	TEX	Acetone		
	TNAZ	Acetone		
	TNT	DAA		
TEX	CL-20	Acetone	Dioxane	NM
	ETN	Acetone	Acetonitrile	Dioxane
	FOX-7	Acetone		
	HMX	Acetone		
	NTO	Acetone		
	NU	Acetone		
	RDX	Acetone		
	TATP	Acetone		
	TNAZ	Acetone		
	TNT	Acetone		

DAA = diacetone alcohol, NM = nitromethane

Amine/Nitro interactions (Table 3.7): Much like CL-20 and TEX, the synthons present in FOX-7 and TATB are similar, leading to logical speculation that each should form synthons and cocrystals with the other. This was not the case. TATB has minimal solubility in nearly every organic solvent, and the ones in which it has limited solubility are difficult to remove (e.g. DMF, DMSO) or altogether impractical (sulfuric acid). For this reason, neat grinding was attempted with this pair but did not produce any noticeable cocrystals. FOX-7 is more soluble than TATB; however, the

preferential dimeric interactions of FOX-7 appear to prevent its inclusion in any cocrystals.^{3, 51-52}

Figure 3.10. Chemical structures of (left) TATB and (right) FOX-7.

Table 3.7. Amine/Nitro interaction cocrystals attempted with single solvent evaporation.

Energetic Material	Coformer	Solvents		
FOX-7	CL-20	Acetone		
	ETN	Acetone		
	HMTD	Acetone		
	MHN	Acetone		
	NTO	Acetone		
	NU	Acetone		
	TATB	DMF	DMSO	
	TEX	Acetone	Acetonitrile	Dioxane
	TNT	Acetone		
TATB	FOX-7	DMF	DMSO	

DMF = dimethylformamide, DMSO = dimethylsulfoxide

Amide interactions (Table 3.8): Nitrourea (NU) is one of only a few organic explosives to contain amide functionality. This synthon is present in numerous pharmaceutical cocrystals, and it is plausible that NU would readily cocrystallize as well. Additionally, NU, a relatively low molecular weight, linear compound, has little

steric hindrance and high accessibility. For those reasons, NU was added with numerous energetic and non-energetic coformers in an attempt to test this theory. In all but one case, NU grew concomitantly with its coformers rather than as a cocrystal.

Figure 3.11. Chemical structure of NU.

Table 3.8. Amide interaction cocrystals attempted with single solvent evaporation.

Energetic Material	Coformer	Solvents	
NU	5-AT	Acetone	
	Benzamide	Acetone	Ethanol
	Benzoic Acid	Acetone	Ethanol
	Carbamazepine	Acetone	Ethanol
	CL-20	Acetone	
	3,5-Dinitroaniline	Acetone	Ethanol
	DNAN	Acetone	Ethanol
	3,5-Dinitrobenzamide	Acetone	Ethanol
	2,4-Dinitrophenol	Acetone	Ethanol
	2,4-DNT	Acetone	Ethanol
	2,6-DNT	Acetone	Ethanol
	ETN	Acetone	Ethanol
	FOX-7	Acetone	
	HMTD	NM	
	Isonicotinamide	Acetone	Ethanol
	MHN	Acetone	Ethanol
	Nicotinamide	Acetone	Ethanol
	NTO	Acetone	
	Picric Acid	Acetone	Ethanol
	TATP	Acetone	Ethanol
	TEX	Acetone	
	TNT	Acetone	Ethanol

NM = nitromethane

Vapor diffusion

Four cocrystals were attempted with vapor diffusion (Table 3.9). With acetone/chloroform and ethanol/cyclohexane, few to no cocrystals were observed either visually or with the PLM. Interestingly, the TNT:nicotinamide cocrystal was first observed with the ethanol/cyclohexane combination, but it was never reproduced in multiple attempts.

Resonant Acoustic Mixing (RAM)

Seven cocrystals were attempted via RAM (Table 3.9). TEX was the most commonly-used material for these experiments because of its limited solubility in many organic solvents, though TATB was studied by this method for the same reason. Although a variety of solvents, mixing accelerations, and mixing times were used, no cocrystals were observed visually or via PLM and hot stage microscopy.

Supercritical fluid precipitation

Three cocrystals were attempted with supercritical fluid precipitation, wherein a concentrated solution of the energetic material and conformer were sprayed into a vessel saturated with supercritical carbon dioxide. No cocrystals were obtained (Table 3.9).

Spray drying

Five cocrystals were attempted via spray drying, though no cocrystals were observed either visually or via PLM (Table 3.9). The relative volatility of TNT may have caused difficulties in the ability of the spray dryer to properly condense it after being sprayed.

Grinding

Four cocrystals were attempted by manual grinding, both with and without solvent (Table 3.9). As with the RAM, TEX and TATB were common choices for this analysis because of their relative insolubility in common organic solvents and insensitivity to friction insult.

Kofler melting method

For materials with known melting points, the Kofler method was attempted to screen for cocrystals (Table 3.9). The analyte with the higher melting point was melted and allowed to recrystallize. Then, the lower melting compound was melted into it and allowed to recrystallize. If a new solid layer developed between the melted layers, a cocrystal was possibly formed. In all cases, no distinct third layer was noticed at the interface of the recrystallized lower melting compound and higher melting compound. In addition, some compounds with high volatility or low stability would begin to decompose, leaving little solid material to analyze.

TNT and Nicotinamide Cocrystal

Of all attempted cocrystallizations, the only quantifiable success was TNT:nicotinamide. A widely used pharmaceutical coformer with both aromatic and amide functionalities, nicotinamide was chosen as a coformer with TNT. Numerous methods for cocrystallization were carried out, including solvent evaporation, vapor diffusion,

Table 3.9. Additional cocrystal synthesis methods. (~5 mg total to 5 uL solvent with acceleration in gravities (gr))

Method	Energetic Material	Coformer	Notes
Vapor Diffusion	NU	2,6-DNT	Acetone/chloroform and ethanol/cyclohexane
	TNT	Nicotinamide	Acetone/chloroform and ethanol/cyclohexane*
	TNT	Isonicotinamide	Acetone/chloroform and ethanol/cyclohexane
	NU	Nicotinamide	ethanol/cyclohexane
RAM	FOX-7	TATB	80 gr for 1 hr, 30 gr for 2 hr, 50 gr for 45 min (all as slurry in DMSO)
	TEX	FOX-7	70 gr for 1 hr as slurry in ACN
	TEX	HMX	70 gr for 1 hr as slurry in ACN
	TEX	RDX	70 gr for 1 hr as slurry in ACN
	TEX	TNT	70 gr for 1 hr as slurry in ACN, in 1:1, 2:1, and 1:2 mole ratios
	TEX	CL-20	70 gr for 1 hr as slurry in ACN
	TNT	Nicotinamide	80 gr for 1 hr, 30 gr for 2 hr, 50 gr for 45 min (all as slurry in DMSO)
Supercritical	NU	TNT	10 mg/mL each in acetone
	TEX	RDX	3 mg/mL each in acetone
	TNT	Nicotinamide	10 mg/mL each in acetone, and 10 mg/mL each in ethanol

Table 3.9 (cont). Additional cocrystal synthesis methods. (~5 mg total to 5 uL solvent with acceleration in gravities (gr))

Spray Drying	NU	TATP	10 mg/mL each in acetone. Only NU was recovered
	NU	TNT	10 mg/mL each in acetone, and 10 mg/mL each in ethanol
	TEX	FOX-7	3 mg/mL each in acetone
	TNT	MHN	10 mg/mL each in acetone
	TNT	Nicotinamide	10 mg/mL each in acetone, and 10 mg/mL each in ethanol
Grinding	FOX-7	TATB	Neat and with 100 μ L DMSO
	TEX	FOX-7	Neat and with 100 μ L acetone, and with 100 μ L ACN
	TEX	TNT	Neat and with 100 μ L acetone, and with 100 μ L ACN
	TNT	Nicotinamide	Neat, with one drop acetone, and with one and 3 drops IPA
Kofler	2,6-DNT	DNAN	
	2,6-DNT	TNT	
	ETN	MHN	
	ETN	TNT	
	TNT	MHN	
	TNT	Benzoic Acid	
	TNT	Nicotinamide	
	TNT	Benzamide	
	TNT	Isonicotinamide	

ACN = acetonitrile, DMSO = dimethylsulfoxide, IPA = isopropanol

grinding, thermal modification, resonant acoustic mixing, spray drying, and supercritical fluid precipitation.

Grinding

In a mortar and pestle, TNT and nicotinamide were ground with and without solvent at a number of different ratios, times, and different solvents. No cocrystals were observed either visually, by microscopy, or by DSC.

Thermal modification

On the hot stage microscope, nicotinamide was melted and recrystallized on a glass microscope slide. TNT was then added to the nicotinamide and melted into it (Figure 3.12a on right). However, after TNT recrystallized, no distinct layer between the melted layers was observed (Figure 3.12b on right). Upon reheating, the TNT and interface both melted at 80 °C, leaving only pure nicotinamide (Figure 3.12c on left). At 115 °C, the remaining nicotinamide began to melt (Figure 3.12d on left).

In a separate experiment, TNT and nicotinamide were mixed in a 1:1 mole ratio and melted on the hot stage microscope. Upon cooling, the mixture recrystallized from one nucleation center and grew outward in a circular pattern (Figure 3.13). As the mixture was heated, it uniformly melted around 102 °C, completely melting by 110 °C, suggesting a cocrystal. On a larger scale (50 mg and 250 mg), TNT and nicotinamide, respectively, were melted together on a hotplate and mixed with a spatula. After cooling, pieces of the mixture were removed from the bulk and analyzed on hot stage microscopy. No cocrystals were detected.

Figure 3.12. Kofler melting method PLM images of nicotinamide and TNT. a) recrystallized nicotinamide and melted TNT at 80 °C. b) recrystallized TNT and nicotinamide at 40 °C. c) TNT and interface material melted at 80 °C. d) nicotinamide melting at 115 °C.

Vapor diffusion

A solvent/antisolvent combination of acetone/chloroform never grew cocrystals. Ethanol/cyclohexane was the mixture in which cocrystal plates were first observed, though in only one vial in a series of replicates. When the experiment was repeated at two different scales, no cocrystals were seen. This method, while affording the first look at the cocrystal, was neither faster nor more reliable at creation of cocrystals than nitromethane solvent evaporation.

Figure 3.13. PLM images of melted and recrystallized TNT:nicotinamide mixture at a) 90 °C, b) 102 °C, c) 107 °C, and d) 109 °C.

Solvent evaporation

TNT and nicotinamide are both readily soluble (i.e. >10 mg/mL) in a variety of organic solvents, so dissolving each to a desired concentration was rarely a concern. Because the melting point of TNT is 80 °C, solvent boiling point occasionally presented a problem. Materials can become oils if its melting point is lower than the boiling point of the crystallizing solvent, and TNT regularly oiled out when precipitated from ethanol.⁵³ In acetone and ethanol, cocrystals were never reliably grown, though nitromethane reliably grew cocrystals with evaporation overnight between 30-50 °C (35 °C yielded a balance between time to evaporate and amount of cocrystals observed). The TNT:nicotinamide cocrystals formed by evaporation from

nitromethane were examined by polarized light microscopy. The cocrystals had a colorless plate habit (Figure 3.14 c-e). TNT and nicotinamide do not form crystals of this habit, and the co-crystals experienced no change in size, shape, or state at or well above 80 °C, the melting point of TNT.

A cocrystal of TNT:nicotinamide was isolated and examined on a hot stage microscope. As the cocrystal was heated, TNT began to melt out of the cocrystal at 97 °C (Fig.3.15c), rather than the normal melting point of TNT, 80 °C, causing precipitation of the nicotinamide in the cocrystal lattice (Figure 3.15d). At 100 °C, the TNT had fully melted; and the nicotinamide, fully crystallized. [In contrast, when TNT and nicotinamide were melted together, cooled and reheated, the melted mixture underwent no such crystallization (Fig. 3.13).] At 113 °C, the remaining nicotinamide begins to melt, completely at 124 °C (Figure 3.15f). (The melting point of nicotinamide is 128 °C.) Because the TNT:nicotinamide cocrystals displayed a number of thermal properties different from neat components, we feel confident in naming it a crystalline.

Differential scanning calorimetry (DSC)

TNT melts at 80 °C and decomposes exothermically around 350 °C, while nicotinamide melts at 128 °C. (Figure 3.16 and Figure 3.17, respectively). The cocrystal itself, when grown via solvent evaporation, is difficult to separate from excess TNT that forms concomitantly with it. Therefore, many DSC thermograms show a TNT melt, which is unrelated to the cocrystal thermal properties, at its typical temperature (Figure 3.18). It is all the more suggestive of its thermal stability well

above the melting point of TNT that the cocrystal can exist unperturbed in a pool of molten TNT. A thermogram of the TNT:nicotinamide cocrystal without the excess TNT melt can be seen in Figure 3.19.

Figure 3.14. PLM images at 100x magnification of a) nicotinamide, b) TNT, and c, d, e) TNT:nicotinamide cocrystals.

Figure 3.15. PLM images of a TNT:Nicotinamide cocrystal at a) 80 °C, b) 90 °C, c) 97 °C, d) 100 °C, e) 113 °C, and f) 124 °C.

Occasionally, without impetus for nucleation, TNT will not crystallize upon thermal cycling, leading to a thermogram with no endothermic melt (Figure 3.16). The TNT has only undergone a phase change and is still viable and able to cocrystallize.

Figure 3.16. TNT Cycle 2 thermogram. Inset: TNT Cycle 1 thermogram.

Figure 3.17. Nicotinamide Cycle 2 thermogram. Inset: nicotinamide Cycle 1 thermogram.

The cocrystal melt onset is at 101 °C, with a minimum at 105 °C (Figure 3.19). This melt is accompanied by an immediate slight exotherm, indicative of nicotinamide crystallization from the melting cocrystal (Figure 3.20).⁵⁴⁻⁵⁵ The crystallized nicotinamide begins to melt thereafter with a minimum at about 114 °C. The mixture

of molten TNT and nicotinamide is stable in a liquid form until 200 °C, when exothermic decomposition occurs. The melt of the cocrystal is between the values of the melting points the neat constituents, which is highly suggestive of successful cocrystallization.

Figure 3.18. DSC thermogram of TNT/nicotinamide cocrystal. Thermal events are a) excess TNT melt, b) cocrystal melt/nicotinamide crystallization, c) subsequent nicotinamide melt, and d) exothermic decomposition.

Figure 3.19. TNT:nicotinamide cocrystal thermogram without excess TNT melt.

Figure 3.20. Zoomed TNT:nicotinamide cocrystal thermogram highlighting exothermic crystallization of nictinamide at 105 °C.

One way to determine whether a material has a eutectic or cocrystal phase is through the construction of a phase diagram: a plot of temperatures of thermal transitions as a function of the amount of one material present. If this phase diagram shows a clear minimum, a eutectic is likely formed. If the phase diagram shows two minima with a raised area between, a cocrystal phase is likely possible.⁴⁶ The phase diagram of TNT:nicotinamide mixtures shows two minima at ~10 mol% and ~50 mol% TNT, with a maximum at ~3:1 nicotinamide:TNT mole ratio (Figure 3.21). This ratio agrees with other observations, such as an excess of native TNT seen on most cocrystals and many thermograms showing a native TNT melt even after thermal cycling.

Raman spectroscopy

The Raman spectrum of the cocrystal is similar to an overlay of the spectra of TNT and nicotinamide (Figure 3.22). However, there are significant wavenumber shifts in a number of peaks of both molecules, suggesting altered spectral environments of each component. Specifically, nicotinamide peaks at 410 cm^{-1} are shifted to 408 cm^{-1} ,

627 cm^{-1} to 620 cm^{-1} , and 1159 cm^{-1} to 1154 cm^{-1} , while TNT peaks at 268 cm^{-1} are shifted to 278 cm^{-1} , 327 cm^{-1} to 319 cm^{-1} , and 1210 cm^{-1} to 1206 cm^{-1} .

Figure 3.21. TNT:nicotinamide phase diagram.

In addition to the wavenumber shifts experienced in the 250-1750 cm^{-1} region, there are pronounced differences among TNT, nicotinamide, and the cocrystal in the terahertz region near the Rayleigh line. The peaks in this region are indicative of low-frequency crystal lattice modes, and a difference in two spectra suggests different crystal environments. The cocrystal shows three distinct peaks at 30 cm^{-1} , 54 cm^{-1} , and 191 cm^{-1} , while the spectra of TNT and nicotinamide show significantly different peaks (Figure 3.23).

Figure 3.22. Raman spectra of TNT (blue), nicotinamide (red), and cocrystal (purple).

Figure 3.23. Terahertz Raman spectra of TNT (blue), nicotinamide (red), and cocrystal (purple).

X-ray powder diffraction

The diffraction pattern of the cocrystal shows different peaks than those shown in the TNT and nicotinamide patterns (Figure 3.24). Specifically, a cocrystal peak at 19° is unique to that pattern, confirming a unique crystal structure from that of either TNT or nicotinamide.

Figure 3.24. XRD diffraction patterns of TNT (blue), nicotinamide (red), and cocrysal (purple).

A Curious Case: Nitrourea and 2,6-Dinitrotoluene

NU and 2,6-DNT were dissolved together in a number of different ratios (1:1, 2:1, 1:2, 3:1, 1:3, 3:2, and 2:3) and solvents (acetone, ethanol, acetonitrile, methyl ethyl ketone, and nitromethane), but no cocrysal was observed. When evaporated from ethanol, frequent concomitant growth of NU (patches) and 2,6-DNT (needles) was observed, regardless of the ratio (Figure 3.25).

However, when melted together, a different solid form developed. When NU and 2,6-DNT are melted together, the DNT melts, but some NU remains (Figure 3.26). As the solution is cooled, it solidifies. When reheated, this new solid melts around 45 °C, recrystallizes at 53 °C, and re-melts again at 68 °C.

Figure 3.25. PLM images of 2,6-DNT:NU mole ratio ethanol solvent evaporation experiments. a) 1:1, b) 1:2, c) 2:1, d) 2:3, e) 3:2, f) 3:1, g) 3:4, h) 4:3, and i) 4:1.

Figure 3.26. Thermal microscopy images of NU/2,6-DNT melted mixture. a) Initial melt at 60 °C, b) recrystallized and heated to 40 °C, c) 49 °C, d) 52 °C, e) crystallization of solid at 53 °C, f) second melt at 68 °C.

A DSC thermogram (Figure 3.27) of this composite material shows similar transitions (endotherms at 43 °C and 65 °C) followed by exothermic decomposition of the NU at 153 °C. Reference thermograms for NU and 2,6-DNT are shown in Figure 3.28 and Figure 3.29.

Figure 3.27. DSC thermogram of NU/2,6-DNT potential cocrystal.

Figure 3.28. DSC thermogram of 2,6-DNT.

Figure 3.29. DSC thermogram of NU.

To determine what ratio was necessary to effect this change by constructing a phase diagram, DSC experiments were run with different amounts of NU and

2,6-DNT. The endothermic transition temperatures stay the same regardless of the amount of NU in the sample (Table 3.10). The heats of those transitions, however, go down when the proportion of NU in the sample goes up. This could result from decreased amount of 2,6-DNT in the overall mix.

Table 3.10. DSC thermogram endotherm data for NU/2,6-DNT mole ratios.

Mass NU (mg)	Mass 2,6- DNT (mg)	Weight % DNT	First Endotherm			Second Endotherm		
			Onset T (°C)	Min T (°C)	Heat (J/g)	Onset T (°C)	Min T (°C)	Heat (J/g)
0.397	0.078	16.4	40.9	42.3	4.10	63.9	64.9	13.4
0.427	0.561	56.8	42.4	44.1	16.3	63.9	65.0	86.0
0.188	0.259	57.9	39.4	40.3	17.4	64.5	65.5	55.6
0.183	0.830	81.9	39.8	40.8	24.7	63.8	65.5	80.2
0.112	0.539	82.8	40.1	41.4	6.09	64.0	65.3	80.2
0.088	1.653	94.9	39.5	41.2	28.0	63.8	66.0	90.2
0	3.600	100	57.7	58.9	134.2	57.7	58.9	134.2

Cocrystals typically exhibit a melting point between those of its constituents. That this material does have a melting point above that of 2,6-DNT is encouraging, but the additional endotherm in the 39-42 °C range is curiously atypical.

The phase diagram of NU/2,6-DNT shows no discernable minima or maxima; in fact, the line is flat when both the first and second endotherm onsets are plotted (Figure 3.30). These data suggest no defined ratio at which the NU/2,6-DNT mixture demonstrates the observed thermal peculiarities.

Figure 3.30. Phase diagram of NU/2,6-DNT (green) first endotherm onset and (blue) second endotherm onset.

The Raman spectra of 2,6-DNT and the melted mixture are practically identical (Figure 3.31 and Figure 3.32). The mixing with the NU is clearly causing some changes in the thermal properties of the mixture, but the crystallinity of 2,6-DNT appears to be intact. Though the positions of the major peaks in the full Raman spectrum may stay the same, if the 2,6-DNT is a different polymorph, one would expect changes in the terahertz region, where lattice modes would be slightly different.

Figure 3.31. Raman spectra of NU, 2,6-DNT, and melted mixture.

Figure 3.32. Terahertz Raman spectrum of NU (blue), 2,6-DNT (red), and melted mixture (green).

Powder XRD was run to investigate any new crystallinity created by the melted mixture of NU and 2,6-DNT. There are no unique peaks in the diffraction pattern of the mixture, and many of the peaks that are present appear to be mainly contributed by 2,6-DNT with few corresponding to NU peaks (Figure 3.33). There are

two interesting peaks around 25° , but these peaks aren't enough to definitively conclude if the crystallinity of the mixture is significantly unique compared to that of the constituents.

Figure 3.33. Powder x-ray diffraction pattern of NU, 2,6-DNT, and their melted mixture.

NU was combined with a number of compounds analogous to 2,6-DNT in order to see if the same relationship existed (Table 3.8). However, none of 2,4-DNT, TNT, benzoic acid, benzamide, 2,5-dinitrobenzamide, 3,5-dinitroaniline, DNAN, 2,4-dinitrophenol, isonicotinamide, nicotinamide, or picric acid was observed to form cocrystal or other interesting property modifications with NU.

Conclusion

Numerous cocrystal combinations of energetic materials with both energetic and non-energetic coformers were investigated. While a majority of combinations were determined to not produce cocrystals, two combinations were promising – NU/2,6-DNT and TNT:nicotinamide. Though not accessed through solvent evaporation or other processes, new morphological and thermal properties of the mixture of NU and 2,6-DNT were shown when melted together. These morphological and thermal properties appear to be the only changes of either material, as both Raman and XRD showed little to no differences between the mixture and the constituents.

When dissolved in nitromethane and precipitated at slightly elevated temperature, TNT and nicotinamide form a clear plate cocrystal with a melting point between that of TNT and nicotinamide. The Raman spectrum of the cocrystal shows shifted peaks of both TNT and nicotinamide, and the XRD pattern shows unique peaks, confirming a difference in crystallinity from either constituent. This is the first cocrystal demonstrated with an energetic material and a material with an amide synthon. In addition, it is the first cocrystal reported to be grown from nitromethane as a cocrystallizing solvent.

Future Work

Explosive parameters of the TNT/nicotinamide cocrystal need to be fully validated. In addition, further study of the thermal alterations of NU/2,6-DNT mixtures are needed

to confirm or reject possible mechanisms for cocrystal formation. Finally, additional screening methods and metrics need to be developed for more efficient analysis of potential cocrystals.

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TNT	Nic	Weight % TNT	Onset T	Min T	Heat (J/g)
0	0.350	0.0	128.59	129.71	216.5
0.587	2.133	12.8	94.84	96.78	1.745
0.369	0.985	16.6	97.44	101.13	101.1
0.218	0.389	23.0	95.17	100.59	25.62
0.223	0.356	25.0	99.74	102.43	108.6
0.206	0.258	29.9	99.78	102.2	93.11
0.248	0.282	31.9	100.87	101.68	3.349
0.305	0.342	32.2	99.84	101.59	68.43
0.854	0.688	39.8	96.68	101.61	90.22
0.588	0.378	45.3	94.15	99.04	66.72
0.788	0.480	46.7	92.53	98.89	59.71
0.427	0.246	48.1	91.59	101.29	64.14
0.358	0.191	50.0	92.94	98.21	30.92
0.234	0.118	51.4	94.51	101.42	38.50
0.526	0.246	53.3	87.79	95.40	58.17
0.470	0.196	56.1	100.98	101.88	5.011
1.291	0.430	61.5	91.29	97.60	29.91
0.471	0.129	66.1	92.67	98.79	31.36
0.326	0	100.0	80.80	82.52	112.6

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Table C.2. DSC thermogram endotherm data for NU/2,6-DNT mole ratios. Incorporates data from Figures C.58 to C.69.

Mass NU (mg)	Mass 2,6- DNT (mg)	% DNT	First Endotherm			Second Endotherm		
			Onset T (°C)	Min T (°C)	Heat (J/g)	Onset T (°C)	Min T (°C)	Heat (J/g)
0.397	0.078	16.4	40.9	42.3	4.10	63.9	64.9	13.4
0.427	0.561	56.8	42.4	44.1	16.3	63.9	65.0	86.0
0.188	0.259	57.9	39.4	40.3	17.4	64.5	65.5	55.6
0.183	0.830	81.9	39.8	40.8	24.7	63.8	65.5	80.2
0.112	0.539	82.8	40.1	41.4	6.09	64.0	65.3	80.2
0.088	1.653	94.9	39.5	41.2	28.0	63.8	66.0	90.2
0	3.600	100	57.7	58.9	134.2	57.7	58.9	134.2

Figure C.58. NU-2,6-DNT (0.188 mg – 0.259 mg) Cycle 1 thermogram from 20-80 °C (10 °C/min).

Figure C.59. NU-2,6-DNT (0.188 mg – 0.259 mg) Cycle 2 thermogram from 20-400 °C (10 °C/min).

Figure C.60. NU-2,6-DNT (0.183 mg – 0.830 mg) Cycle 1 thermogram from 20-80 °C (10 °C/min).

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Figure C.70. Nicotinamide-carbamazepine (0.428 mg – 0.482 mg) physical mixture thermogram. Nicotinamide melts at 128 °C, and carbamazepine melts at 204 °C. Note the exotherm between the two endotherms at 115 °C and 125 °C (10 °C/min).

Figure C.71. DSC thermogram of 2:1 mole ratio MHN:ETN (0.040 mg) from ethanol (20 °C/min).

Figure C.72. DSC thermogram of 2:3 mole ratio MHN:ETN (0.097 mg) from ethanol (20 °C/min).

Figure C.73. DSC thermogram of 3:1 mole ratio MHN:ETN (0.045 mg) from ethanol (20 °C/min).

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Figure C.76. DSC thermogram of CL-20/TEX (0.323 mg) from acetonitrile (20 °C/min).

Figure C.77. DSC thermogram of CL-20/TEX (0.359 mg) from nitromethane (20 °C/min).

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Figure C.99. DSC thermogram of TATP/TEX mixture (0.491 mg) from ethanol (20 °C/min).

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