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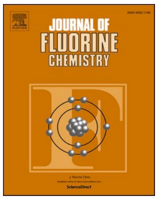

Synthesis and energetic properties of trifluoromethyl-substituted 2-nitro-[1,2,4]triazolo[1,5-a]pyrimidine derivatives

Ajay Kumar Chinnam [a], Richard J. Staples [b], Jean'ne M. Shreeve [a,*]

[a] Department of Chemistry, University of Idaho, Moscow, Idaho, 83844-2343, United States
[b] Department of Chemistry, Michigan State University, East Lansing, Michigan 48824, United States

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ABSTRACT

5-Amino-3-nitro-1,2,4-triazole (ANTA) is a potential intermediate for the synthesis of high performance energetic materials. Now we describe the construction of 5,7-disubstituted-2-nitro-[1,2,4]triazolo[1,5-a]pyrimidine with high fluorine content and considerable energy. The new compounds were fully characterized by multinuclear NMR (^{1}H, ^{13}C, ^{19}F), and infrared spectroscopy, elemental analysis and differential scanning calorimetry (DSC). The structure of **2a** is supported by single crystal X-ray diffraction analysis. Measured crystal densities, calculated heats of formation and energetic properties have been investigated. Based on Explo5 calculations, highly fluorinated compound **2b** has detonation properties comparable with TNT.

1. Introduction

Since they tend to be highly conjugated which results in a planar molecular geometry having π–π interactions, fused five-membered heteroaromatic skeletons are in high demand in the field of high-energy-density materials (HEDMs) [1]. Generally, nitrogen-rich polycyclic systems have large enthalpies of formation, high thermostabilities, low sensitivities to external stimuli and release non-toxic gases upon detonation [2]. Further functionalization of the fused heterocyclic rings by the introduction of explosophoric groups (e.g., $-NO_2$, $-ONO_2$, N_3, NH_2 and NF_2, etc.) has been extensively studied in an effort to increase density, and oxygen balance giving better detonation properties [3].

Introducing fluorine atoms into highly energetic materials is one of the best choices to improve performance and safety [4–6]. Organofluorine compounds are well-recognized and important in the field of medicinal chemistry, bio-organic chemistry and agrochemicals [7–9]. In general, fluorine atoms in organic molecules enhance the physical, chemical, and biological properties due to their small size and high electronegativity, which give rise to shorter and more polarized bonds with carbon relative to other C-halogen or C–H bonds. Energetic properties are improved by increasing the number of fluorine atoms and lowering the number of hydrogen atoms giving rise to increased density and decreased sensitivity [10]. Fluorine-based explosives are in high demand as "Biological Defeat Agents" because of the formation of detonation or deflagration products such as highly reactive hydrogen fluoride [11]. Several synthetic methods have been developed for the construction of fluorine-based energetic materials [12–17]. Very recently our group has reported the synthesis of trifluoromethyl-based energetic 1,2,4-triazoles by reacting 1-amino-1-hydrazino-2,2-dinitroethylene (HFOX) in trifluoracetic acid [18].

Over the years, amine-substituted five-membered heterocyclic compounds have gained much attention from worldwide synthetic, biological and material science researchers. Primary and secondary amines are highly reactive with β-carbonyl compounds or active acetonitriles to form interesting heterocyclic scaffolds [19]. 5-Amino-3-nitro-1,2,4-triazole (ANTA) **1** is one of such heterocyclic compounds with promising energetic properties [20]. In recent years, several synthetic approaches have been developed by using ANTA as a starting material (Fig. 1) [21–25]. Recently our group has reported a fused energetic 4-amino-3,7-dinitro-[1,2,4]triazolo[5,1-c] [1,2,4]triazine (TTX) in 84 % yield by employing a two-step synthesis using ANTA and nitroacetonitrile as starting materials [26]. For some time, our group has actively developed various synthetic routes and applications of interesting fluorine atom-containing energetic materials [27–31]. Keeping this in mind, now we have designed fused heterocyclic compounds with trifluoromethyl and nitro groups. Using ANTA as the amine azole in reaction with β-carbonyl compounds in acidic medium led to new fused heterocyclic compounds in good yields in a single step. New compounds are well characterized using advanced spectroscopic techniques and physicochemical properties have been investigated and compared with

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* Corresponding author.
E-mail address: shreeve@uidaho.edu (J.M. Shreeve).

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TNT.

2. Results and discussion

2.1. Synthesis

The starting material ANTA (**1**) was prepared based on the literature procedure by oxidation and selective reduction of 3,5-diamino-1H-1,2,4-triazole [32]. Then compound **1** was reacted with pentane-2, 4-dione in aqueous acid (pH~2) under reflux conditions. This reaction was optimized, and catalytic amounts of concentrated hydrochloric acid gave high yields (86 %) of the fused heterocyclic derivative, 5,7-dimethyl-2-nitro-[1,2,4]triazolo[1,5-a]pyrimidine **2** as a colorless precipitate in 4 h. The same reaction using catalytic amounts of concentrated sulfuric acid or acetic acid resulted in low yields of 5,7-dimethyl-2-nitro-[1,2,4]triazolo[1,5-a]pyrimidine **2** or a mixture of products with unreacted starting materials. Similarly, ANTA reacted with 1,1,1-trifluoroacetylacetone pentane-2,4-dione and 1,1,1,5,5,5-hexafluoro pentane-2, 4-dione in aqueous hydrochloric acid medium to give trifluoromethyl fused heterocyclic derivatives 5-methyl-2-nitro-7-(trifluoromethyl)-[1,2,4]triazolo[1,5-a]pyrimidine **2a** and 2-nitro-5,7-bis(trifluoromethyl)-[1,2,4]triazolo[1,5-a]pyrimidine **2b** as colorless solids in 83 % and 76 % yields, respectively (Scheme 1). Synthesis of these derivatives may obtain by two steps acid catalyzed condensation of pentane-2,4-dione with primary and secondary amines of ANTA (Scheme 2).

All new compounds were confirmed by NMR and IR spectroscopy as well as elemental analysis. In the ^{1}H NMR spectrum of **2**, two different CH_3 signals were observed at 2.65 and 2.77 ppm and one signal at 7.49 ppm for the aromatic CH; one CH_3 signal for compound **2a** at 2.90 ppm and 7.16 for the aromatic CH; and for compound **2b,** only one signal was found at 8.89 ppm assignable to the aromatic CH. In ^{13}C NMR, for compound **2**, two CH_3 signals were observed at 16.17, 24.79 ppm and five aromatic signals (114.3, 148.4, 153.5, 162.8 and 168.2 ppm); for compound **2a,** one CH_3 signal was observed at 26.20 ppm. Fused ring carbons was observed in the range of 110.10–169.83 ppm. The ^{19}F NMR spectra shows for compound **2a**, one signal at -68.05 ppm; and for compound **2b**, two signals at -67.82 and -68.51 ppm, respectively (Supporting Information).

2.2. Crystal structure

Suitable crystals of **2a** were obtained by slow evaporation of a saturated solution in methanol at ambient temperature. The crystal structure (CCDC 2054540) is given in Fig. 2 and detailed crystallographic information is given in the Supporting Information. It crystalizes in the monoclinic space group $P2_1/c$ with twelve units in the lattice cell (Z = 12) and a density of 1.734 g cm^{-3} at 173 K. There are three kinds of molecules in the asymmetric cell. The bond lengths and angles between the triazole and pyrimidine in **2a** are comparable within the limits of error indicating a delocalization of the aromaticity across both ring-systems (Supporting Information).

In the crystal structure **2a**, all three fused ring atoms are in planar and they are oriented independently. The nitro group is nearly planar with the fused rings, with torsion angles ranging from 11.18 to -16.81°. The hydrogen atoms of the methyl group and fluorine atoms of trifluoromethyl group are in tetrahedral arrangements and they are out of the plane with the fused ring system.

In addition to this, the two-dimensional (2D)-fingerprint of the crystal and the associated Hirshfeld surfaces were employed to understand the intermolecular interactions in the crystal packing of **2a** by using Crystalexplorer17.5 software program (Fig. 3) [33,34]. Also, these features are mainly useful to understand the characteristic of insensitive and high-energy materials [35]. As shown in Fig. 3a, the red and blue regions on the Hirshfeld surfaces represent high and low close contact populations, respectively. The red spots are due mainly to the intermolecular hydrogen bond interactions, and the blue spots for C⋯O, C⋯C and C⋯N bond interactions, suggesting π–π stacking. The sharp spikes for **2a** (Fig. 3b) denote that the selected molecule (Fig. 3a) has a relatively high contribution (41.1 %) of intermolecular hydrogen bonds (F⋯H, O⋯H and N⋯H interactions). The selected molecule has overall 9% of C⋯O, C⋯C and C⋯N bond interactions, which confirm the existence of π–π stacking. Also, it was interesting that the selected molecule has higher amounts of halogen bond interactions (41.7 % of F⋯F, O⋯F, C⋯F and N⋯F) in contrast to hydrogen bond (HB) interactions. Halogen bonding interactions involve non-covalent interactions between the sigma hole on a halogen (in this case fluorine) with a lone pair. The reviewer doubts that a sigma hole on fluorine is involved in these interactions. Although the Hirshfeld surface shows interactions, the distances are close to the van der Waals radii and may just result from packing. The sensitivity of an energetic material increases with higher percentages of O⋯O bond interactions in the crystal packing. In the case of compound **2a**, only 1.3 % of O⋯O bond interactions are found, further agreeing with the experimental sensitivity results. The percentages of intermolecular bonding are unequally distributed in all three molecules of the crystal structure **2a**.

2.3. Physicochemical and energetic properties

Thermal stabilities of all new compounds were determined using

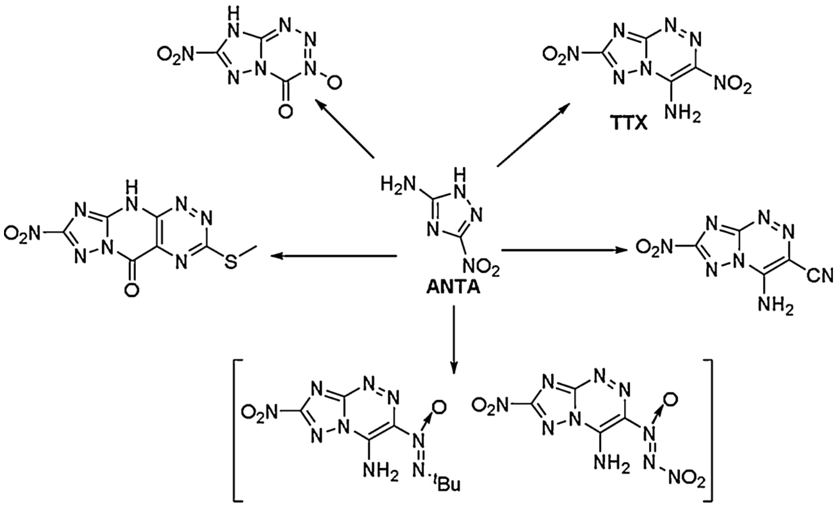
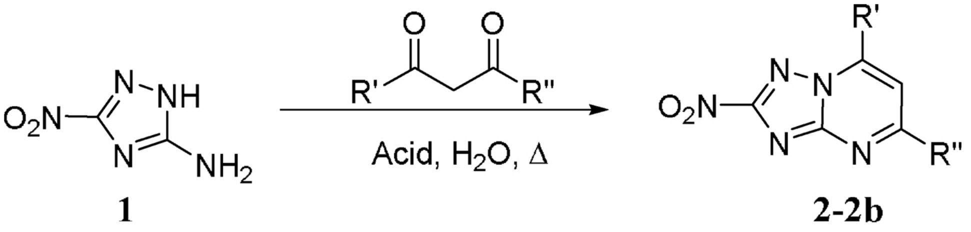
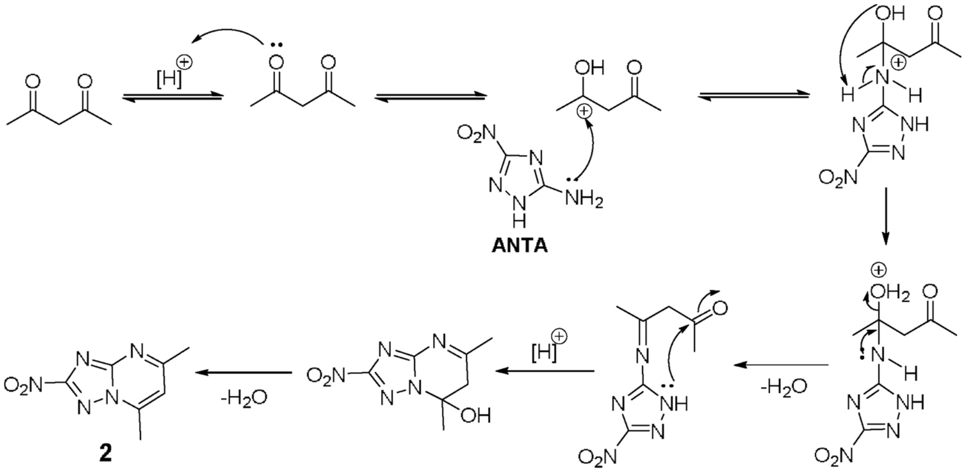


Fig. 1. Selected fused heterocyclic derivatives of ANTA.



2 R', R'' = CH_3; **2a** R', R'' = CF_3, CH_3; **2b** R', R'' = CF_3

Scheme 1. Synthesis of 2-nitro-[1,2,4]triazolo[1,5-*a*]pyrimidine derivatives.



Scheme 2. A plausible mechanistic pathway for the formation of pyrimidine derivative **2**.

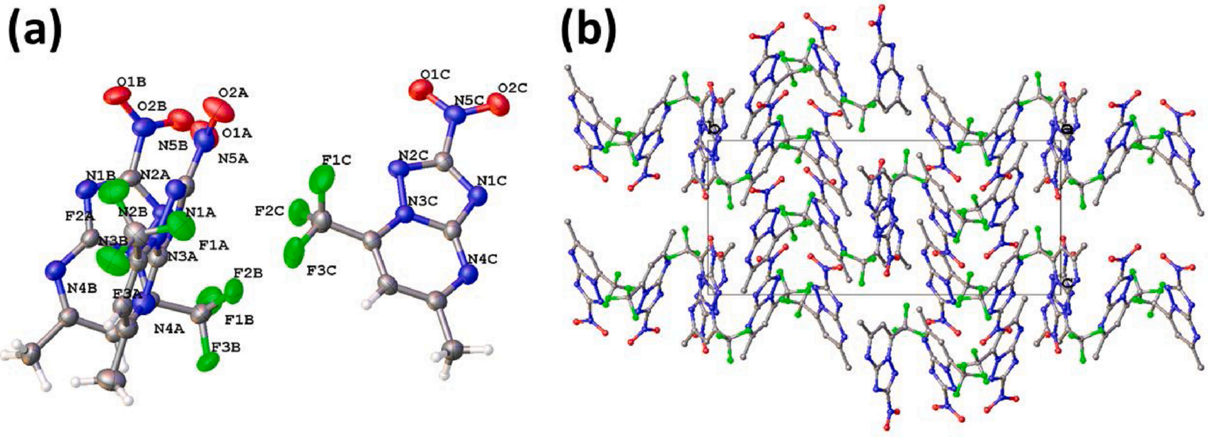


Fig. 2. (a) Thermal ellipsoid plot (50 %) and labeling scheme for 5-methyl-2-nitro-7-(trifluoromethyl-[1,2,4]triazolo[1,5-*a*]pyrimidine **2a**. (b) Ball-and-stick packing diagram of **2a** viewed up the b axis.

differential scanning calorimetric (DSC) measurements with a heating rate of 5 °C min^{-1} under a nitrogen atmosphere. Thermostability of the new fused ring compounds are affected by the increasing numbers of fluorine atoms. As shown in Fig. 4, compound **2** which has no fluorine atoms has the highest melting point at 184 ℃, while mono- and bis (trifluoromethyl) compounds **2a** and **2b** melt at 158 ℃ and 151 ℃, respectively. Similarly, all compounds decomposed after they melted. Compounds **2** and **2a** have higher deposition temperatures than ANTA (T_d = 229 ℃), while the highest fluorine-containing compound **2b** (T_d = 219 ℃) has the lower decomposition. Compound **2** and **2a** decomposed at 269 °C and 242 °C, respectively.

The densities of the new compounds were measured using a gas pycnometer at 25 ℃. Compound **2** has a lower density of 1.529 g cm^{-3} compared to the fluorine-containing compounds. Both compounds **2a** and **2b** have higher densities of 1.691 g cm^{-3} and 1.848 g cm^{-3}, respectively. These are high relative to TNT (1.650 g cm^{-3}) and the density of compound **2b** (1.848 g cm^{-3}) is relatively high compared to ANTA (1.820 g cm^{-3}). Heats of formation of **2**–**2b** were calculated by using the Gaussian 03 suite of programs with isodesmic reactions (Supporting Information) [36]. Both fluorine compounds **2a** (−328 kJ mol^{-1}/-1.32 kJ/g) and **2b** (−931 kJ mol^{-1}/-3.09 kJ/g) have relatively high negative heats of formation due to the presence of the large number of C—F bonds, whereas non-fluorinated compound **2** (259 kJ mol^{-1}/1.34 kJ/g) has a positive heat of formation. Based on the

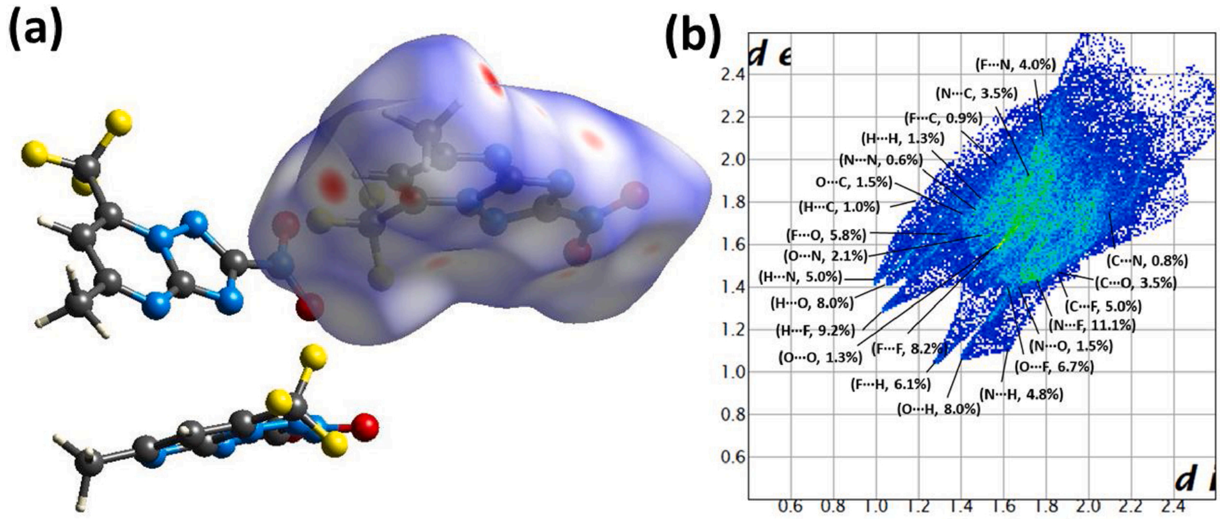


Fig. 3. (a) Hirshfeld surface calculation for the selected molecule of 5-methyl-2-nitro-7-(trifluoromethyl-[1,2,4]triazolo[1,5-*a*]pyrimidine **2a** (white, distance *d* equals the van der Waals distance; blue, *d* exceeds the van der Waals distance; red, *d* is less than the van der Waals distance). (b) Two-dimensional fingerprint plots in crystal stacking for **2a** as well as individual atomic contact percentage contribution of the associated Hirshfeld surfaces (For interpretation of the references to colour in this figure legend, the reader is referred to the web version of this article).

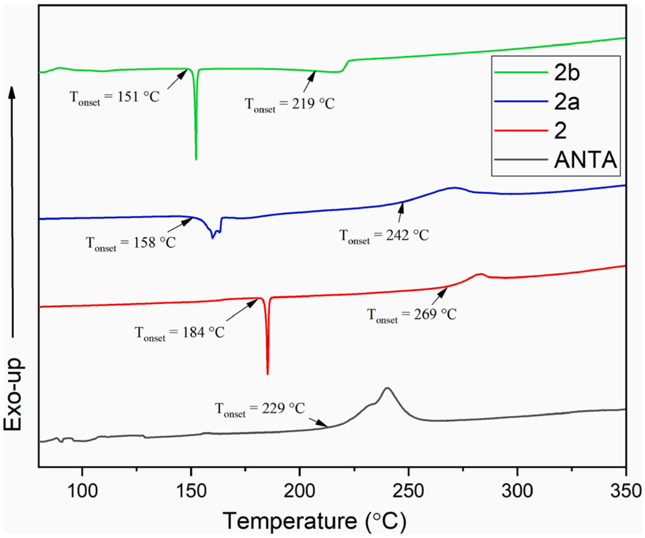


Fig. 4. DSC plots for **2-2b** and **ANTA**.

values of the experimental densities and calculated heats of formation, the detonation pressures (P) and detonation velocities (*v*D) were calculated using EXPLO5 (version 6.01) [37]. Due to having the high negative heats of formation, our new highly fluorinated derivatives have lower detonation properties than ANTA but are comparable with TNT. The calculated detonation pressures (P) range between 14.61 and 26.11 GPa and calculated detonation velocities (*v*D) between 6658 and 7632 $m{\cdot}s^{-1}$. Compound **2b** (*v*D, 7632 $m{\cdot}s^{-1}$; P, 26.11 GPa) has better detonation properties and superior to TNT (*v*D, 6881 $m{\cdot}s^{-1}$; P, 19.50 GPa). All three compounds are very insensitive to both impact and friction stimuli compared to the secondary explosive TNT (IS: 15 J, FS: >353 N) (Table 1).

3. Conclusion

In summary, we have reported the synthesis of three new fused heterocyclic compounds of 5,7-disubstituted-2-nitro-[1,2,4]triazolo[1,5-a]pyrimidines **2**—**2b**. All new compounds were fully characterized by advanced spectroscopic techniques. The structure of compound **2a** was confirmed by single X-ray crystallography analysis. The non-fluorine-containing fused ring compound **2** has a high positive heat of formation compared to fluorinated compounds **2a** and **2b** but they

Table 1

Physicochemical and energetic properties of compounds **2–2b** in comparison with ANTA and TNT.

Comp	ρ[a] ($g\,cm^{-3}$)	*vD* [b] ($m\,s^{-1}$)	*P*[c] (GPa)	$\Delta_f H°$ [d] ($kJ\,mol^{-1}/kJ\,g^{-1}$)	T_m [e] (°C)	T_{dec}[f] (°C)	*IS*[g] (J)	*FS*[h] (N)
2	1.529	6644	14.61	259/1.34	184	269	>40	>360
2a	1.691	6658	18.96	−328.3/-1.32	158	242	>40	>360
2b	1.848	7632	26.11	−931/-3.09	151	219	>40	>360
ANTA[i]	1.820	8460	31.4	21.0/0.16	–	229	>40	>360
TNT[j]	1.650	6881	19.50	−70.5/-0.31	81	300	15	353

[a] Density measured by a gas pycnometer at 25 °C.

[b] Calculated detonation velocity.

[c] Calculated detonation pressure.

[d] Calculated molar enthalpy of formation in solid state.

[e] Temperature of melting (onset).

[f] Temperature of decomposition (onset).

[g] Impact sensitivity.

[h] Friction sensitivity.

[i] ref. [20].

[j] ref. [31].

have higher measured crystal densities with better detonation properties. All three compounds were found to be insensitive to impact and friction. Physicochemical and energetic properties were calculated and compound **2b** (*v*D, 7632 m·s^{-1}; P, 26.11 GPa) exhibits better detonation properties as an insensitive energetic material relative to TNT (*v*D, 6881 m·s^{-1}; P, 19.50 GPa). In addition, with the high content of fluorine atoms in these heterocyclic compounds, **2a** and **2b,** useful biochemical applications may be found.

3.1. Experimental section

3.1.1. Caution!

Although no explosions or detonations occurred during the preparation and handling of these energetic materials, all reactions were carried out on a small scale with appropriate safety precautions (safety glasses, face shields, ear plugs, as well as gloves) and are strongly encouraged.

3.2. General methods

Reagents were purchased from AKSci or Alfa Aesar in analytical grade and were used as received. ^{1}H, ^{13}C and ^{19}F NMR spectra were recorded on a 300 MHz (Bruker AVANCE 300) nuclear magnetic resonance spectrometer operating at 300.13, 75.48 and 282.40 MHz, respectively, by using d$_6$-DMSO or $CDCl_3$ as the solvent and locking solvent. Tetramethyl silane and trichlorofluoromethane were used as reference compounds for ^{1}H, ^{13}C and ^{19}F, respectively, NMR spectra. The thermal decomposition points were obtained on a differential scanning calorimeter (TA Instruments Company, Model: Q2000) at a scan rate of 5 °C min^{-1}. IR spectra were recorded on an FT-IR spectrometer (Thermo Nicolet AVATAR 370) as thin films using KBr plates. Density was measured at room temperature by employing a Micromeritics AccuPyc II 1340 gas pycnometer. Elemental analyses (C, H, N) were determined using a Vario Micro cube Elementar Analyser. The impact and friction sensitivities were tested by employing a standard BAM drop hammer and BAM friction tester.

3.2.1. 5,7-Dimethyl-2-nitro-[1,2,4]triazolo[1,5-a]pyrimidine (2)

A mixture of 5-amino-3-nitro-1,2,4-triazole [32] **1** (0.3 g, 2.32 mmol) and acetylacetone (0.23 g, 2.32 mmol) was stirred in distilled water (5 mL) and few drops of concentrated hydrochloric acid was added at room temperature to maintain pH ~ 2. The resulting mixture was stirred at reflux for 4 h. A colorless precipitate was formed and after cooling to room temperature the precipitate was collected by filtration and washed with small amount of cold water (2 mL) and dried at room temperature to give colorless solid **2** (0.38 g, 86 %). T_m (onset): 184 °C; T_d (onset): 269 °C; ^{1}H NMR (300 MHz, DMSO-d$_6$, ppm): 7.49 (s, 1H, Ar<u>CH</u>), 2.77 (s, 3H, CH_3), 2.65 (s, 3H, CH_3). ^{13}C NMR (75 MHz, DMSO-d$_6$, ppm): 168.2, 162.8, 153.5, 148.4, 114.3, 24.8, 16.2; IR (KBr pellet): υ 3448, 3061, 1633, 1552, 1463, 1436, 1415, 1380, 1322, 861, 811, 778, 650, 517 cm^{-1}. Elemental analysis (%) calcd for $C_7H_7N_5O_2$(193.06): C, 43.53; H, 3.65; N, 36.26; found: C, 43.16; H, 3.78; N, 36.19.

3.2.2. 5-Methyl-2-nitro-7-(trifluoromethyl)-[1,2,4]triazolo[1,5-a]pyrimidine (2a)

A mixture of 5-amino-3-nitro-1,2,4-triazole **1** (0.5 g, 3.87 mmol) and 1,1,1-trifluoropentane-2,4-dione (0.59 g, 3.87 mmol) was stirred in distilled water (10 mL) and few drops of concentrated hydrochloric acid was added at room temperature to maintain pH ~ 2. The resulting mixture was stirred at reflux for 6 h. A yellow precipitate was formed around the magnet bar and was deposited on the walls of the reaction flask. After decanting the aqueous layer, the product was air dried. It was purified by crystallization in methanol at room temperature or passing through silica-gel column using 9:1 mixture of ethyl acetate and hexane followed by concentration under reduced pressure to give **2a** (0.79 g, 83 %). T_m (onset): 158 ℃; T_d (onset): 242 °C; ^{1}H NMR (300 MHz, $CDCl_3$, ppm): 7.61 (s, 1H, Ar<u>CH</u>), 2.90 (s, 3H, CH_3). ^{13}C NMR (75 MHz, $CDCl_3$, ppm): 169.8, 164. 7, 154.9, 135.8 (q, $J_{C\text{–}F}$ =38.4 Hz, CF_3), 118.3 (q, $J_{C\text{–}F}$ =275.0 Hz, CF_3), 112.9, 26.2. ^{19}F NMR (282 MHz, $CDCl_3$, ppm): -68.0. IR (KBr pellet): υ 3397, 3099, 1650, 1562, 1467, 1435, 1392, 1315, 1262, 1220, 1159, 1058, 981, 901, 865, 812, 7708, 731, 684, 648, 530, 478 cm^{-1}. Elemental analysis (%) calcd for $C_7H_4F_3N_5O_2$(247.03): C, 34.02; H, 1.63; N, 28.34; found: C, 34.64; H, 1.92; N, 28.15.

3.2.3. 2-Nitro-5,7-bis(trifluoromethyl)-[1,2,4]triazolo[1,5-a]pyrimidine (2b)

A mixture of 5-amino-3-nitro-1,2,4-triazole **1** (0.5 g, 3.87 mmol) and 1,1,1,5,5,5-hexafluoropentane-2,4-dione (0.96 g, 4.65 mmol) was stirred in distilled water (10 mL) and few drops of concentrated hydrochloric acid was added at room temperature to maintain pH ~ 2. The resulting mixture was stirred at reflux for 8 h. A yellow precipitate was deposited around the magnet bar and inside walls of the reaction flask. After decanting the aqueous layer, the product was washed with 5 mL of cold water and air dried to give yellow powder of **2b** (0.88 g, 76 %). T_m (onset): 151 °C; T_d (onset): 219 °C; ^{1}H NMR (300 MHz, $CDCl_3$, ppm): 8.89 (s, 1H, Ar<u>CH</u>). ^{13}C NMR (75 MHz, DMSO-d$_6$ {*Compound **2b** has poor solubility in* $CDCl_3$}, ppm): 164.2, 153.7 (q, $J_{C\text{–}F}$ =36.4 Hz, CF_3), 149.1, 137.8 (q, $J_{C\text{–}F}$ =39.4 Hz, CF_3), 139.9 (q, $J_{C\text{–}F}$ =36.7 Hz, CF_3), 119.5 (q, $J_{C\text{–}F}$ =275.6 Hz, CF_3), 118.0 (q, $J_{C\text{–}F}$ =275.2 Hz, CF_3), 110.9, 95.9; ^{19}F NMR (282 MHz, $CDCl_3$, ppm): -67.82, -68.51. IR (KBr pellet): υ 3122, 1644, 1572, 1534, 1462, 1428, 1323, 1271, 1164, 1104, 1020, 879, 849, 803, 743, 713, 676, 485 cm^{-1}. Elemental analysis (%) calcd for $C_7HF_6N_5O_2$ (301.00): C, 27.92; H, 0.33; N, 23.26; found: C, 28.23; H, 0.61; N, 23.84.

Declaration of Competing Interest

There are no conflicts to declare.

Acknowledgements

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Appendix A. Supplementary data

Supplementary material related to this article can be found, in the online version, at doi:https://doi.org/10.1016/j.jfluchem.2021.109743.

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