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Research Article

Synthesis of New Energetic Materials and Ionic Liquids Derived from Metronidazole

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Simple and efficient synthetic procedures were established for the preparation of new energetic covalent compounds, salts, and protonated ionic liquids based on the readily available antimicrobial agent metronidazole. Some of these materials exhibit the desirable properties of energetic materials and energetic ionic liquids, such as low vapor pressure, low melting point, good chemical and thermal stability, and high energetic content. For each of the relevant compounds prepared, thermal stability was determined by differential scanning calorimetry. Some of these compounds may be considered promising precursors of pharmaceuticals such as antimicrobial, antiparasitic, antifungal, antineoplastic agents, or enzyme inhibitors.

1. Introduction

Interest in energetic ionic liquids (EILs) has grown exponentially in the last few years as a result of their application in various areas of research such as electrochemistry, separation science, chemical synthesis, and catalysis [1, 2]. Research in the field of ionic liquids as energetic materials (EMs) is becoming quite important because they are easy to manufacture and generally stable (and thus safer to transport than conventional EMs) and because their physicochemical characteristics render them suitable for diverse applications [3, 4]. The main thrust for the development of new EILs has been their substitution as propellants for such compounds as hydrazine and derivatives thereof, which at present pose various problems such as corrosion, safety in handling and storage, high melting points, and the need to use plasticizers [5]. However, the use of some EILs as additives, plasticizers, main charges, or even pharmacological agents [6] presents a wide array of possibilities for further development. One area of development of new EILs is the use of imidazole-based compounds for the preparation of salts, either protonated or alkylated, that exhibit the physical and chemical properties typical of energetic materials [7–13].

2. Experimental Section

2.1. General Information

Caution! Even though the handling of the reported compounds presented no problems under normal laboratory conditions, one must exercise extreme caution and employ standard precautionary measures at all stages of the synthesis, handling, storage, and disposal of EMs. The use of suitable protective gear and equipment is required and strongly encouraged.

Note. All reactions were carried out under normal air atmosphere using oven dried glassware. All chemicals were used as received unless otherwise noted. Reaction solvents were dried by distillation from the appropriate drying agent and stored over 3 Å molecular sieves as required. The term brine is used to describe a saturated aqueous solution of sodium chloride.

Infrared spectra were recorded directly as liquids or solids (both referred to as "neat") on a Cary 660 Series FTIR Spectrometer with internal calibration. Only the strongest diagnostic bands are reported. Proton and carbon nuclear magnetic resonance (^{1}H NMR and ^{13}C NMR) spectra were

recorded on a Bruker AVANCE-III 500 (500 MHz) spectrometer. Unless otherwise stated, $CDCl_3$ was used as solvent. Elemental analyses were performed on a Perkin Elmer PE2400 elemental analyzer by the USAI-UNAM microanalytical laboratory. Melting points were measured on a Mettler Toledo DSC1 (STAR 11.0) DSC apparatus; decomposition temperature (T_d), glass transition (T_g), and DSC plots were also recorded on this system. T_d and T_g temperatures are given in Celsius degrees and refer to onset, not to peak temperatures (except for compound **4** where peak temperatures are reported). Heating rate for DSC runs is either 5° or 10°C min^{-1}, as specified in the experimental details. DSC run for compound **4** was carried out on a NETZSCH STA 449F3 instrument. Gas chromatography/mass spectroscopy analyses were carried out on Agilent Technologies 6890 N Network GC System. Thin layer chromatography (TLC) was carried out on commercial aluminum backed silica gel 60 plates (E. Merck, type 5554, 0.2 mm). Visualization was accomplished with UV light (254 nm), iodine, and/or heating the chromatograms after staining with a solution of phosphomolybdic acid (PMA) in ethanol (20% w/v, Aldrich), a solution of ammonium molybdate and cerium sulfate in 10% sulfuric acid (5% w/v ammonium molybdate and 0.1% w/$Ce(SO)_4$), or a solution of p-anisaldehyde in a sulfuric acid-EtOH mixture (5% v/v anisaldehyde and 5% v/v sulfuric acid). Flash chromatography was performed on 230–400 mesh silica gel (Siliaflash 60 Silica Gel). The reported eluent solvent solution ratios are volume to volume ratios. The terms *in vacuo* or "under reduced pressure" are used to describe removal of solvent using a rotary evaporator.

2.2. Compound Preparation

*2.2.1. Synthesis of 2-(2-Methyl-5-nitro-1H-imidazol-1-yl)ethyl Nitrate (**2**).* Ammonium nitrate (1.90 g, 0.237 mol) is added to a cold (ice-water bath) nitric acid solution (68%, 16.03 g, and 0.16 mol), while stirring. Then sulfuric acid (97%, 27.78 g, and 0.276 mol) is added slowly and the mixture is stirred for 5 min, followed by the portionwise addition of metronidazole (3 g, 17.528 mmol). The reaction mixture is then warmed to room temperature and is stirred for 30 min and then the contents of the reaction mixture are transferred to a separation (or addition) funnel. This mixture is added dropwise to a stirred ice-water mixture (200 g crushed ice; 100 mL water) while at the same time adding, also dropwise, a solution of sodium hydroxide (28.48 g, 0.712 mol) at approximately the same rate. After the addition the empty reaction container and its corresponding funnel are rinsed into the ice-water mixture. The pH is finally adjusted to neutral with the addition of a saturated solution of sodium bicarbonate or 10% HCl solution, as required. The resulting mixture is extracted with CH_2Cl_2 (3 × 150 mL) and the combined organic fractions are then washed with brine and dried with anhydrous sodium sulfate. After reduced pressure removal of the solvent the residual material is crystallized with a hexane-ethyl acetate mixture to give solid compound **2** (3.26 g, 86% yield) as fine white needles, exhibiting oxygen balance Ω = −81.4%; DSC (heating rate: 5°C min^{-1}): mp = 70.5°C; T_d = 182.9°C; IR (neat) ν_{max}: 3127, 3018, 2983, 2900, 1632, 1451, 1424, 1358, 1267, 1254, 1184, 888, 852, 821, and 707 cm^{-1}; ^{1}H NMR ($CDCl_3$, 500 MHz) δ 7.96(s, 1H), 4.84 (t, J = 5 Hz, 2H), 4.66 (t, J = 5 Hz, 2H), and 2.51 (s, 3H) ppm; ^{13}C NMR ($CDCl_3$, 125 MHz) δ 150.9, 138.4, 133.5, 70.4, 43.6, and 14.2 ppm; GCMS (*m/z*): 171, 154, 124, 81, and 53 amu. *Anal.* C 33.47%, H 3.53%, and N 25.83%; calcd for $C_6H_8N_4O_5$, C 33.34%, H 3.73%, and N 25.92%.

*2.2.2. Synthesis of 2-Methyl-5-nitro-1-[2-(nitrooxy)ethyl]-1H-imidazol-3-ium Nitrate (**4**).* A solution of nitric acid in CH_2Cl_2 (3.1 mL, 1.53 M) is added dropwise to a stirred solution of compound **2** (0.98 g, 4.626 mmol) in CH_2Cl_2 (30 mL) at room temperature. The reaction mixture is stirred for 10 min, during which a dense oily phase is distinguished apart from the CH_2Cl_2 solution. The supernatant phase is removed by decantation and a successive series of eight thorough washings with 5 mL portions of CH_2Cl_2 is carried out. The remaining solvent is eliminated under reduced pressure, and the resulting oil is subjected to column chromatography on silica gel (ethyl acetate-methanol 15 : 1) to yield compound **4** (1.252 g, 99%) as a colorless oil exhibiting oxygen deficiency Ω = −48.7%; DSC (heating rate: 10°C min^{-1}): $T1_d$ = 168.3°C, $T2_d$ = 175.3°C, and $T3_d$ = 208.7°C (all peak temperatures); soluble in acetone and methanol; insoluble in CH_2Cl_2, AcOEt, and hexane; IR (neat) ν_{max} 3401, 3138, 2907, 1636, 1540, 1505, 1372, 1313, 1279, 1193, 887, and 828 cm^{-1}; ^{1}H NMR (CD_3OD, 500 MHz) δ 8.64 (s, 1H), 5.45 (br s, 1H), 5.04–4.97 (m, 4H), and 2.83 (s, 3H) ppm; ^{13}C NMR (CD^3OD, 125 MHz) δ 149.7, 131.5, 123.2, 70.1, 44.7, and 11.1 ppm. *Anal.* C 26.23%, H 3.59%, and N 23.78%; calcd for $C_6H_9N_5O_8$: C 25.81%, H 3.25%, and N 25.09%.

*2.2.3. Synthesis of 2-Methyl-5-nitro-1-[2-(nitrooxy)ethyl]-1H-imidazol-3-ium Picrate (**5**).* Picric acid (0.243 g, 1.061 mmol) is dissolved in a stirred mixture of CH_2Cl_2 (3 mL) and Et_2O (4 mL), to which nitrate ester **2** (0.230 g, 1.064 mmol) is then added dropwise as a solution in CH_2Cl_2/Et_2O (2 mL, 1 : 1), while stirring vigorously. The reaction mixture is then subjected to separation of the resulting bright yellow precipitate by means of a centrifuge (4000 rpm, 2 min), discarding the supernatant solution. The solid is then washed and centrifuged three times with a Et_2O/CH_2Cl_2 solution (1 mL each washing, 5 : 2), finally eliminating the remaining solvent under high vacuum (90 Torr), to give picrate **5** (0.392 g, 83% yield) as a bright yellow powder. DSC (heating rate: 5°C min^{-1}): mp = 131.1°C; $T1_d$ = 198.3°C; $T2_d$ = 253.9°C; IR (neat) ν_{max} 3728, 3707, 3163, 2973, 2361(s, CO_2), 2338 (s, CO_2), 1541, 1493, 1317, 1267, 882, 844, and 705 cm^{-1}; ^{1}H NMR (acetone-d6, 500 MHz) δ 8.92 (s, 2H), 8.41 (s, 1H), 8.08 (br s, 1H), 5.18–5.07 (m, 4H), and 2.89 (s, 3H) ppm; ^{13}C NMR (acetone-d6, 125 MHz) δ 157.8, 150.6, 140.3, 138.8, 132.0, 126.3, 125.5, 70.8, 44.1, and 12.2 ppm. *Anal.* C 32.78%, H 1.93%, and N 21.49%; calcd for $C_{12}H_{11}N_7O_{12}$: C 32.37%, H 2.49%, and N 22.02%.

*2.2.4. Synthesis of 1-(2-Azidoethyl)-2-methyl-5-nitro-1H-imidazole (**3**).* To a cooled (0°C) solution of triphenylphosphine

(8.43 g, 32.14 mmol) in CH_2Cl_2 (100 mL) bromine is slowly added (1.65 mL, 32.20 mmol) followed by addition of triethylamine (4.48 mL, 32.14 mmol). To the resulting solution metronidazole is then added in small portions (5.00 g, 29.21 mmol), while stirring. After 5 min the reaction mixture is warmed to room temperature, stirred for further 30 min, and then quenched with water (150 mL) and a saturated solution of aqueous sodium thiosulphate (10 mL). The mixture is then extracted with CH_2Cl_2 (3 × 50 mL) and the combined extracts are washed with brine (1 × 50 mL) and dried with anhydrous sodium sulfate. The resulting solution is then percolated through a short silica gel column after which the solvent is removed *in vacuo*. To the crude mass Et_2O (50 mL) is then added and ground with a flat end glass rod, decanting the supernatant solution and repeating the process two more times. The combined washings are then filtered again through a short silica gel column, the solvent from the collected fraction is then removed, and the resulting oil (bromide) is then subjected to high vacuum (90 Torr) for 10 min. The oil is then dissolved in DMF (30 mL) and sodium azide (3.80 g, 58.45 mmol) is added in small portions while stirring. The reaction mixture is then warmed up to 60°C and stirred for 22 h, followed by cooling to room temperature. Reaction workup is then done by adding water (150 mL) and extracting the mixture with AcOEt (3 × 50 mL), washing with water (2 × 50 mL), brine (1 × 50 mL), and drying the collected organic portions with anhydrous sodium sulphate. The solvent is then removed *in vacuo* and the crude oil is subjected to column chromatography on silica gel (eluting initially with hexane/AcOEt 1 : 1 and gradually decreasing the eluting solution ratio to 1 : 9). The solvent is then removed *in vacuo* from the collected column fractions to give azide **3** (3.79 g, 66% yield from metronidazole), exhibiting oxygen balance Ω = −114.2%; DSC (heating rate: 10°C min^{-1}): mp = 55.1°C (Lit. 53-54°C), T_g = 87.7°C, and T_{dec} = 222.0°C; GCMS 196 (M^+), 151, 122(100), 95, 80, and 50 amu; IR (neat) ν_{max} 3127, 2933, 2868, 2096 (s), 1527, 1462, 1424, 1360, 1260, 1184, 1147, 823, and 742 cm^{-1}; ^{1}H NMR ($CDCl_3$, 500 MHz) δ 7.94 (s, 1H), 4.42 (t, J = 5 Hz, 2H), 3.76 (t, J = 5 Hz, 2H), 2.52 (s, 3H) ppm; ^{13}C NMR ($CDCl_3$, 125 MHz) δ 151.4, 138.2, 133.4, 50.9, 45.5, and 14.4 ppm; *Anal.* C 37.24%, H 3.68%, and N 40.82%; calcd for $C_6H_8N_6O_2$: C 36.74%, H 4.11%, and N 42.84%.

*2.2.5. Synthesis of 1-(2-Azidoethyl)-2-methyl-5-nitro-1H-imidazol-3-ium Nitrate (**6**).* Azide **3** (2.74 g, 13.968 mmol) is dissolved in CH_2Cl_2 (25 mL), the solution is cooled to 0°C, and to this stirred solution a 6.55 M solution of HNO_3 is then added dropwise in CH_2Cl_2 (2.13 mL, 1 equiv.). After the addition the solution is warmed up to room temperature and stirred for 30 min, after which the solvent is removed *in vacuo*. The remaining oil is then subjected to Flash column chromatography by dissolving it in the minimum amount of a CH_2Cl_2/MeOH solution (5 : 1) in order to add it to the column. Then the mixture is eluted using initially a MeOH/CH_2Cl_2/hexane/AcOEt solution (1 : 18 : 5 : 5 v, resp.) and increasing gradually the MeOH content of the eluting solution gradually as the chromatography proceeds. After fraction collection and solvent removal, ionic liquid **6** was obtained as a light yellow-colored oil (3.14 g, 97% yield), exhibiting oxygen deficiency Ω = −71.0%; DSC (heating rate, 10°C min^{-1}): T_g = 81.6°C, $T1_d$ = 144.0°C, and $T2_d$ = 225.0°C; GCMS 196, 151, 122(100), 95, 80, and 53 amu; IR (neat) ν_{max} 3400 (br), 3225, 3113, 2980, 2101(s), 1614, 1535, 1503, 1419, 1366, 1295, 1262, 1187, 1034, 930, 825, and 737 cm^{-1}; ^{1}H NMR (DMSO-d6, 500 MHz) δ 9.08 (br s, 1H), 8.36 (s, 1H), 4.54 (t, J = 5 Hz, 2H), 3.84 (t, J = 5 Hz, 2H), and 2.57 (s, 3H) ppm; ^{13}C NMR (DMSO-d6, 125 MHz) δ 151.0, 138.7, 130.1, 50.4, 46.0, and 13.7 ppm; *Anal.* C 27.58%, H 4.11%, and N 34.08%; calcd for $C_6H_9N_7O_5$: C 27.81%, H 3.50%, and N 37.83%.

*2.2.6. Synthesis of 1 : 1 Mixture of 1-(2-Azidoethyl)-2-methyl-5-nitro-1H-imidazole and Picric Acid (**7**).* Picric acid (0.467 g, 2.038 mmol) is dissolved in Et_2O (25 mL) at room temperature and then immediately added to a stirred solution of azide **3** (0.400 g, 2.039 mmol) also at room temperature. After the addition the mixture is stirred for 15 min and then filtered. The solid thus obtained is then washed on the filter paper with Et_2O (4 × 5 mL portions) and then allowed to air dry followed by high vacuum treatment to remove traces of solvent. In this manner mixture **7** (as determined by the DSC behavior of the material) is obtained as a fine (fluffy) yellow solid (0.785 g, 90% recovery), exhibiting oxygen deficiency Ω = −77.2%; DSC (heating rate, 10°C min^{-1}): mp_1 = 124.3°C; mp_2 = 135.0°C; T_d = 243.2°C; GCMS 196, 168, 151, 122(100), 95, 80, and 53 amu; IR (neat) ν_{max} 3191, 2500 (br), 2134, 2099, 1601, 1567, 1524, 1427, 1323, 1240, 1191, 1164, 916, 817, and 712 cm^{-1}; ^{1}H NMR (DMSO-d6, 500 MHz) δ 9.76 (br s, 1H), 8.60 (s, 2H), 8.41 (s, 1H), 4.55 (t, J = 7.5 Hz, 2H), 3.86 (t, J = 7.5 Hz, 2H), and 2.60 (s, 3H) ppm; ^{13}C NMR (DMSO-d6, 125 MHz) δ 161.0, 150.9, 142.2, 138.7, 129.3, 125.6, 125.1, 50.2, 46.0, and 13.6 ppm; *Anal.* C 34.11%, H 2.17%, and N 28.96%; calcd for $C_{12}H_{11}N_9O_9$: C 33.89%, H 2.61%, and N 29.64%.

3. Results and Discussion

Herein we report our exploratory work into the transformation of the readily available and inexpensive antimicrobial agent metronidazole (**1**; Figure 1), a drug considered to be the "gold standard" antibiotic against which all other antibiotics with anaerobic activity may be compared [14, 15]. The energetic materials in the form of covalent compounds, salts, and protonated ionic liquids (PILs) that were prepared from metronidazole are depicted in Figure 1.

A straightforward procedure for producing PILs is the reaction of a suitable acid with an azo compound to produce a protonated azolium-based salt. It is also possible to produce energetic aprotic ionic liquids wherein the cation is constituted by a fully alkylated quaternary ammonium center. In the present work we favored the simpler PIL pathway to expedite the preparation of a number of nitrate and picrate salts by the direct reaction of HNO_3 or picric acid with metronidazole derivatives.

Despite what may seem to be a facile way of producing protonated ILs, it should be noted that there are limitations in

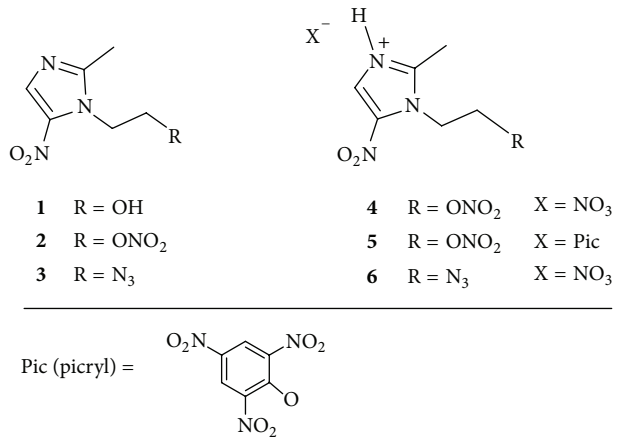
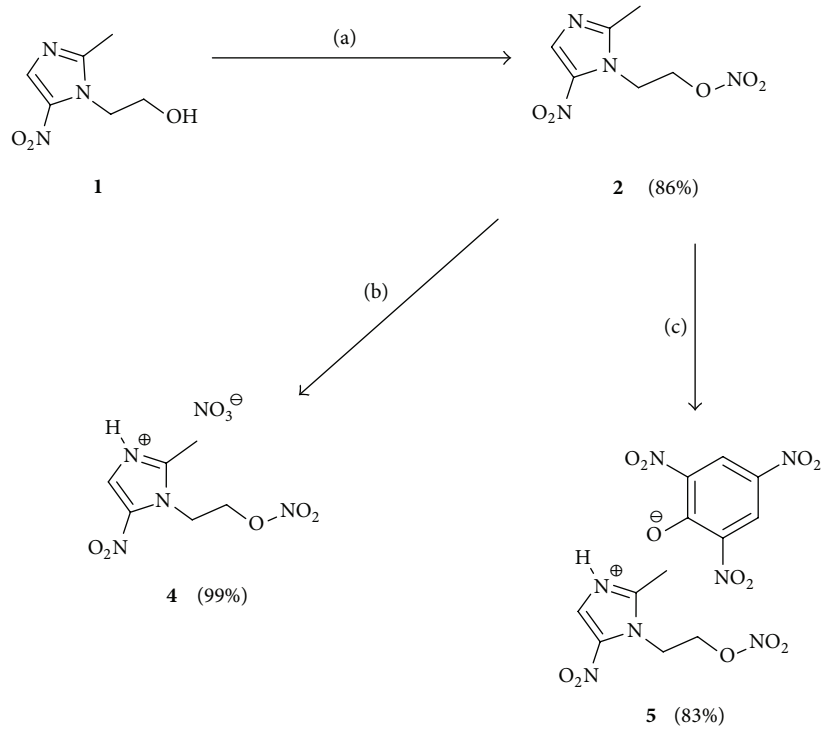


Figure 1: Metronidazole (**1**) and derived energetic covalent compounds, salts, and ionic liquids.



Scheme 1: Preparation of nitrate ester **2**, PEIL **4**, and salt **5**. (a) $HNO_3/H_2SO_4/NH_4NO_3$, 0°C to r.t., 1 h; (b) HNO_3, CH_2Cl_2, r.t.; and (c) picric acid, CH_2Cl_2-Et_2O.

the formation of protonated imidazolium nitrate and picrate salts. Smiglak et al. [16] have demonstrated that when the imidazole nucleus is substituted with two or three nitro functional groups the synthesis of the corresponding 1,3-dialkylimidazolium or 1-alkyl protonated cations is futile due to their resistance to N-alkylation or protonation, respectively. Such is the case of 1-methyl-2,4-dinitroimidazole and 1-methyl-4,5-dinitroimidazole [16, 17]. However, metronidazole has only one nitro functional group within the azole nucleus; thus, it was estimated it would be a suitable candidate for forming various energetic protonated ionic liquids (EPILs).

Nitrate ester **2** was initially prepared from metronidazole (**1**) using a H_2SO_4-HNO_3-NH_4NO_3 nitrating mixture in good yield (Scheme 1). Compound **2** is a white crystalline (fine needles) solid (mp = 68–70°C) with oxygen balance $\Omega = -81.4\%$, maximum calculated density [18, 19] $\rho_{max} = 1.63\ g\ cm^{-3}$, and theoretical detonation velocity (Rothstein & Petersen method) [20–23] $\mathbf{D} = 6534 \pm 131\ ms^{-1}$, which is comparable to that of high explosives such as TNT ($\mathbf{D} = 6950\ ms^{-1}$ @ $1.654\ gcm^{-3}$). This compound exhibited typical IR signals at $3127\ cm^{-1}$ (imidazole ring C-H) and 1631 and $1424\ cm^{-1}$ (nitro and nitrate ester functions). In order to assess the thermal stability of all relevant compounds prepared, we

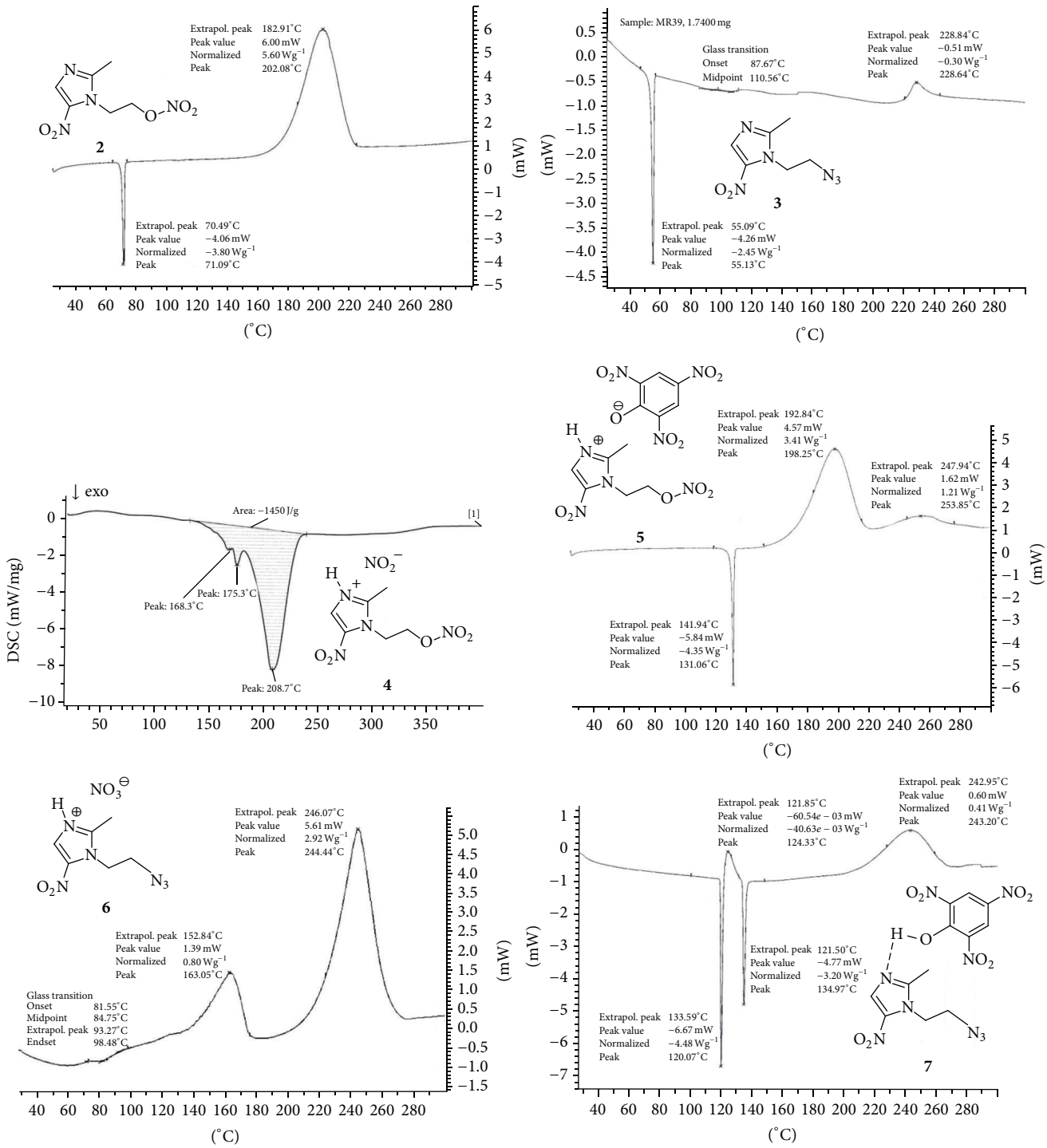


Figure 2: DSC plots of compounds **2**, **3**, EIL **4**, RTEIL **6**, salt **5**, and mixture **7**.

determined their differential scanning calorimetric (DSC) properties (see Figure 2 and Table 1). In the case of compound **2**, its DSC run at a heating rate of 5°C min^{-1} established mp = 70.5°C and a (onset) decomposition temperature T_d = 182.9°C (Figure 2).

Having compound **2** on hand, a simple acid neutralization with a dichloromethane solution of either concentrated HNO_3 or picric acid furnished protonated energetic ionic liquid (PEIL) **4** as a colorless oil exhibiting a broad signal at 3401 cm^{-1} on its FTIR spectrum and a broad singlet at 5.45 ppm on its ^{1}H NMR spectrum, both due to the imidazolium proton, or salt **5**, respectively (Scheme 1). The DSC runs for these compounds were as follows: $T1_d$ = 168.3°C (peak), $T2_d$ = 175.3°C (peak), and $T3_d$ = 208.7°C

Table 1: Oxygen deficiency and DSC data for compounds **2**–**6** and mixture **7**.

Compound	Oxygen deficiency (Ω), %	Melting point °C	Decomposition temperature (1st transition; $T1_d$, °C; onset)	Decomposition temperature (2nd transition $T2_d$; 3rd transition $T3_d$, °C; onset)
2	−81.4	70.5	182.9	—
3	−114.2	55.1	87.7[a]	222.0[b]
4	−48.7	—	168.3	175.3; 208.7
5	−63.0	141.9	192.8	247.9
6	−71.0	—[c]	144.0	225.0
7[d]	−77.2	124.3; 135.0[d]	243.2	—

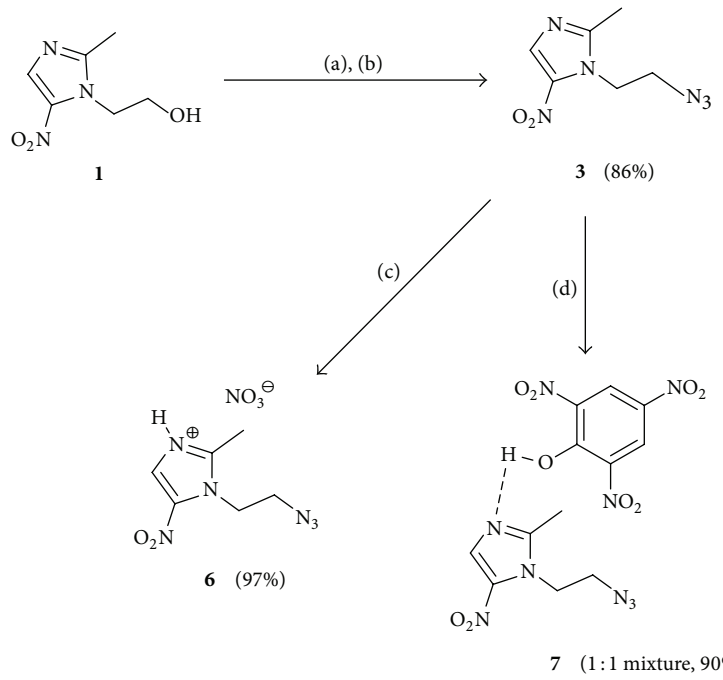
[a]Glass transition onset (T_g); [b]onset decomposition temperatures (T_d) shown in all cases, except for compound **4** where peak temperatures are shown; [c]room temperature energetic ionic liquid (RTEIL) exhibiting T_g = 81.55°C; [d]1 : 1 mixture of compound **3** and picric acid (endothermic peak temperatures shown as mp).

(peak) for **4**; T_m = 141.9°C, $T1_d$ = 198.25°C (peak), and $T2_d$ = 253.85°C (peak) for **5** (see Figure 2 and Table 1). These results follow the expected trend whereby picrate salts of protonated imidazolium cations tend to be thermally more stable than the corresponding nitrate salts [16]. Compound **4** turned out to be rather unstable. It is very sensitive to traces of water and acid and tends to revert to metronidazole and nitric acid. Depending on the degree of contamination by acid or even atmospheric humidity one may observe cloudiness in a matter of a few hours at room temperature and even precipitated metronidazole upon storage at 0°C after a few days. A TG scan showed that in the range from 20 to 115°C there is already a mass deficit of 8.49%. More stable samples can be obtained performing a flash silica gel column chromatography eluting with ethyl acetate-methanol 15 : 1 right after workup. It is presumed that internal protonation by the protic ammonium moiety facilitates nitrate ester hydrolysis, thus reversibly yielding back the starting materials. In contrast compounds **5** and **6** exhibit stability under ordinary atmospheric conditions and good shelf-life (several months at 0°C so far). The IR spectra of compound **5** show strong CO_2 absorptions in the 2350 cm^{-1} region (see Section 2); this exemplifies the known property of some ionic liquids to strongly scavenge CO_2 [24, 25]. This property of some ILs has received much attention given the climate impact of the growing CO_2 atmospheric concentration, and there is currently much interest in developing ILs aimed at eliminating anthropogenic carbon emissions [26].

The hydroxyethylene moiety attached to position 1 on the imidazole nucleus of metronidazole should allow for versatile transformations. Thus, we next considered the replacement of the primary alcohol functional group with an azide functional group. This was accomplished initially transforming the primary alcohol into its corresponding bromide, followed by nucleophilic substitution using sodium azide in DMF to give azide **3** (Scheme 2). This compound was previously prepared by Levon from metronidazole mesylate [27, 28] but was only partially characterized. Compound **3**, a white crystalline solid, exhibited a characteristic FTIR strong signal at 2096 cm^{-1} (due to the introduced azide function). It was subjected to DSC thermal analysis (Figure 2) showing mp = 55.1°C (lit. 53-54°C), glass transition onset T_g = 87.7°C, and T_d = 222.0°C (a much larger thermal stability range than compound **2**). Compound **3** has oxygen balance **Ω** = −114.2%, and a theoretical [20–23] detonation velocity **D** = 5088 ± 102 ms^{-1}.

The reaction of **3** with HNO_3 produced compound **6** in excellent yield, a viscous liquid that remains as such at room temperature and is henceforth referred to as an RTEIL (room-temperature energetic ionic liquid) **6**. This compound exhibited the characteristic ^{1}H NMR (broad singlet) signal at 9.08 ppm due to the imidazolium proton. DSC analysis of **6** (Figure 2) shows a glass transition (onset) T_g = 81.6°C, $T1_d$ = 144.0°C, and $T2_d$ = 225.0°C. In a similar vein, the reaction of **3** with picric acid gave **7**, a white solid that was found to be the product of the cocrystallization of compound **3** and picric acid based on the DSC plot, which shows prominent endothermic peaks at 120.1°C and 135.0°C (Figure 2). Despite the indication of the presence of two distinct species by DSC, a certain degree of H-bond association between **3** and picric acid in the solid mixture **7** is suggested by the fact that **3** has mp = 55.1°C, but the first endothermic peak appears in mixture **7** at a much higher temperature (Figure 2).

Apart from the potential uses of the compounds prepared herein as EMs, it is to be noted that compounds **2–6** would be worth screening for use as fungicides, antimicrobials, and enzyme inhibitors. A large number of metronidazole-derived compounds have been previously prepared by various groups seeking antimicrobial, antibacterial, or antiparasitic activity [29–32], as enzyme inhibitors [33, 34] and as candidates for prodrug bioavailability and cytotoxicity studies [35, 36]. The structure of azides **3** and **6** in particular suggests their transformation into potentially useful pharmacologically active substances by exploiting the rich chemistry of their organic azide functionality. As described comprehensively by Bräse and Banert in his review [37], a great number of diverse nitrogen compounds can be synthesized by means of Click, Boyer, aza-Wittig, and Staudinger reactions, to name just a few of the current arsenal of transformations available for organic azides [38].



Scheme 2: Preparation of azide **3**, RTEIL **6**, and mixture **7**. (a) Ph_3PBr_2, CH_2Cl_2; (b) NaN_3, DMF, and 60°C; (c) HNO_3, CH_2Cl_2, and 0°C and then r.t., 30 min; and (d) picric acid, Et_2O.

4. Conclusion

Five new energetic compounds were prepared in a straightforward and efficient manner from the well-known and readily available antimicrobial metronidazole. Compounds **4**–**6** constitute ionic liquids (**4** and **6** being proper RTEILs). Compound **6** may find practical uses as vehicle, additive, solvent, or otherwise mixture component for EM formulations. The instability of RTEIL **4** would preclude its use as a EM or EM additive. The nitrate ester **2** exhibits a moderate theoretical detonation velocity and may find application as a propellant when combined with a suitably strong oxidant [39, 40]. From a pharmacological point of view, compounds **3** and **6** may be considered versatile precursors of a large array of useful compounds made available by known transformations of the azide functionality present in them, as discussed previously. Preliminary work in our laboratory has shown that azide **3** can be transformed into new compounds suitable for biological activity screening.

Conflict of Interests

The author declares that there is no conflict of interests regarding the publication of this paper.

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