Synthesis and Characterization of Some Polynitro Imidazoles

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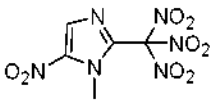
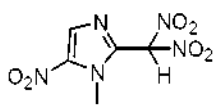
A focus of recent interest in high energetic compounds has been the synthesis of polynitro polyaza cyclic compounds showing high performance and low sensitivity to friction and impact.[1,2,3] Accordingly, several explosives such as triaminotrinitrobenzene (TATB), 3-nitro-1,2,4-triazoline-5-one (NTO), 1,3,5-trinitrotriazacyclohexane (RDX), 1,3,5,7-tetranitrotetraazacyclooctane (HMX), and hexanitrohexaazaisowurzitane (HNIW, CL-20) have been synthesized.[3,4] In the treatment with amines such as ammonia, hydrazine, and guanidine, polynitro imidazoles often led to stable salts which were suitable for high energetic materials.[5] In addition, nitro imidazoles were valuable to the pharmaceutical chemistry as nitro-containing synthetic intermediates and drugs.[1,6]

Even though some azoles were insensitive towards accidental impact, their performance is often lower than that of RDX, one of the most widely used explosives. Recently 1,1-diamino-2,2-dinitroethylene (FOX-7) was emerging as a potential candidate for insensitive high explosives. FOX-7 has attracted substantial interest because it was expected that its performance was similar and its sensitivity could be much lower in comparison with RDX.[7] Since imidazole derivatives with more than two nitro groups, like 2,4,5-trinitroimidazole were expected to be highly powerful, various nitroimidazoles have been prepared previously.[8]

In continuing efforts, we focused on synthesizing nitroimidazoles consisted of dinitromethylene moiety as in FOX-7. In this paper, we report the synthesis of 1-methyl-5-nitro-2-(trinitromethyl)-1*H*-imidazole (**1**), 1-methyl-5-nitro-2-(dinitromethyl)-1*H*-imidazole (**2**) and its salts.



1



2

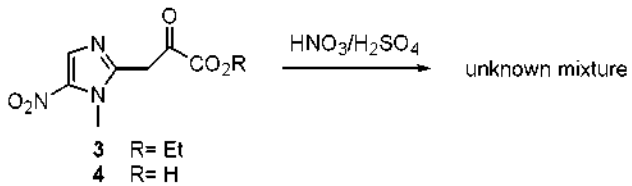
The synthesis of FOX-7 has been reported using various starting materials such as 2-methylimidazole, 2-methoxy-2-methylimidazolidine-4,5-dione, and 2-methylpyrimidine-4,6-dione (4,5-dihydroxy-2-methylpyrimidine).[9] Since the methyl group was converted to dinitromethylidene moiety in all methods, nitration of 2-methyl-4(5)-nitroimidazole and 2-methyl-4,5-dinitroimidazole were attempted to afford the corresponding 2-dinitromethylidene imidazoles. But, all the cases the reaction failed to proceed, most of the starting material was recovered.

Acetates containing azole could be converted into the corresponding dinitroacetates in the treatment with a mixture of nitric acid and sulfuric acid (mixed acids).[1,10] Our attempts to acylation in 2-methyl group was failed in the reaction of 2-methyl-4(5)-nitroimidazole, 1,2-dimethyl-5-nitroimidazole or 1,2-dimethyl-4,5-dinitroimidazole with ethyl chloroformate.[11]

Meanwhile, the treatment of 1,2-dimethyl-5-nitroimidazole with ethyl oxalyl chloride gave the corresponding pyruvate **3**, resulting in activation of 2-methyl group.[12] and pyruvate **3** was converted to imidazolylpyruvic acid **4** under acidic condition.[12,13] In the treatment with nitric acid or mixed acids, compounds **3** and **4** gave an unknown mixture along with trace amount of tetranitro **1** (Scheme 1).

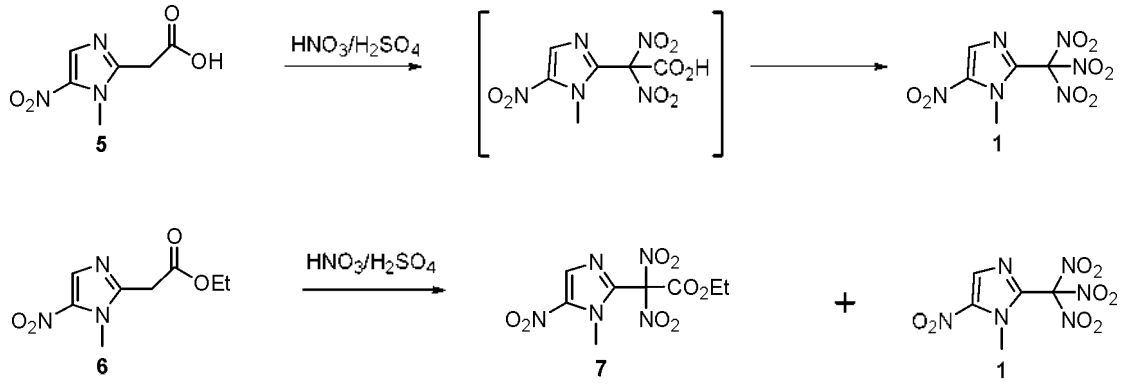
Pyruvic acid **4** was converted to imidazolylacetic acid **5** *via* oxidative decarbonylation.[12,13] In the reaction of acetic acid **5** with mixed acids, tetranitro **1** was given as a sole product, in the same manner that cyanoacetic acid was converted into trinitroacetonitrile.[14] During the process, intermediate trinitro carboxylic acid was not isolated. Further nitration on the imidazole ring was not observed even under strong nitration conditions such as heating of the reaction mixture, and employing of strong nitrating agents (NO_2BF_4/HNO_3, P_2O_5/HNO_3). When ethyl 2-(1-methyl-5-nitroimidazolyl)acetate (**6**) was subjected to nitration under mixed acid conditions, two nitro groups were successfully introduced to afford trinitro ester **7** in shorter reaction time.[10] Further nitration of ester **7** produced tetranitro **1** in low yield (Scheme 2).

Trinitromethyl group attached to tetrazole could be converted to the corresponding dinitromethylide salt and subsequent acidification gave dinitromethylene compound in the reaction with alkaline solution of hydroxylamine followed by acidification with mineral acid.[15] In the same manner, potassium salt **8** was obtained as a yellow solid, when compound **1** was treated with KOH and hydroxylamine hydrochloride. The potassium salt was acidified with 50% sulfuric acid to give trinitro **2** as a white solid (Scheme 3).

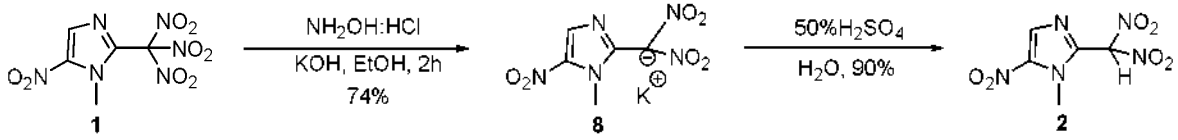


3 R= Et
4 R= H

Scheme 1



Scheme 2



Scheme 3

In addition to ring tautomerism, imidazole derivatives such as imidazolinones exhibit tautomerism and the predominant form depends on the substituents.[16] Also, tetrazole-tetrazoline tautomerism was readily observed and the predominant form was dependant upon substituents and the state such as in solution or in solid.[10,17] We investigated the imidazole-imidazoline tautomerism of **2** (Figure 1) by UV and other spectra. In UV spectra, nitro ester **7** absorbed at 221, 317 nm, and tetranitro **1** did at 228, 287 nm, whereas trinitro **2** did at 210, 343 nm. Since 2-dinitromethylenebenzimidazole shows the absorptions at 240, 320, 335 nm,[18] some parts of trinitro **2** existed in the imidazoline form. Interestingly, the absorption of potassium salt **8** appeared at 220, 343 nm, and the UV pattern was almost same as that of tetrazole-tetrazoline tautomerism.[10] The imidazoline tautomer may stabilize through the intramolecular hydrogen bond between the hydrogen attached to ring nitrogen and oxygen in nitro group, while the imidazole structure has the aromatic character (Figure 1). Judging from the IR and NMR spectral data, any conclusion was hardly made.

In summary, 1-methyl-5-nitro-2-trinitromethyl-1*H*-imidazole (**1**) was synthesized from the 2-(5-nitroimidazolyl)acetic acid (**5**), and also from its ethyl ester (**6**), and compound **1** was further converted to 1-methyl-5-nitro-2-(dinitromethyl)-1*H*-imidazole (**2**), and its potassium salt. In terms of the tautomerism, some parts of compound **2** existed in the imidazoline form.

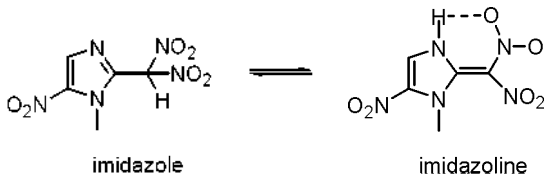


Figure 1. Imidazole-imidazoline tautomerism of **2**.

Experimental Section

General. $^1H/^{13}C$ NMR spectra were recorded on varian Oxford 200 or Unityinova 400 instruments. Infrared (FTIR) spectra were recorded on a Nicolet 5700 FT-IR spectrophotometer, υ max in cm^{-1}. Samples were recorded as a KBr disc. Ultraviolet spectra were recorded on a Lambda 40 UV-Visible Spectroscopy instrument. Mass spectra were recorded on Varian 1200L Quadruple LC/MS system. Melting points were performed on recrystallized solids and recorded on a SRS OPtiMelt or electrothermal 9100 melting point apparatus and were uncorrected. Caution: Polynitro compounds and their salts are suspected explosive. They should be treated with appropriate precautions.

1-Methyl-5-nitro-2-trinitromethyl-1*H*-imidazole (1). To a mixture of sulfuric acid (98%, 5.8 mL, d = 1.84, 108.1 mmol) and nitric acid (95%, 2.86 g, 43.2 mmol) was added 2-(1-methyl-5-nitro-1*H*-imidazolyl) acetic acid (**5**, 1.0 g, 3.6 mmol) at 0 °C. After stirring for 15 h at rt, the reaction mixture was poured into ice water (20 g), and a white precipitate was separated by filteration (0.31 mg, 21%). The mother liquor was extracted with dichloromethane and the organic layer was washed with water and brine, dried over $MgSO_4$, and concentrated *in vacuo* to give an additional product (0.19 g, 13%). mp: 87 °C (MeOH, dec); IR (KBr) 1630, 1605, 1587, 1553 1487, 1374, 1355, 1277, 1219, 1134, 1022, 843, 797; UV ($CHCl_3$) λ_{max} 228, 287 nm; ^1H NMR ($CDCl_3$, 200 Hz) δ 3.98 (s, 1H), 8.17 (s, 1H); ^{13}C NMR δ 37, 124, 131.3, 133, 148; MS (ESI) m/z 275 [(M-H)$^-$, 5], 230 [(M-H-NO_2)$^-$, 100].

Ethyl 2-(1-methyl-5-nitro-1*H*-imidazolyl)-2,2-dinitroacetate (7). To a mixture of sulfuric acid (98%, 2.6 mL, 46.9 mmol) and nitric acid (95%, 1.24 g, 18.8 mmol), ethyl 2-(1-methyl-5-nitro-1*H*-imidazol-2-yl)acetate (**6**, 0.5 g, 2.34 mmol) was added at 0 °C. After stirring for 15 h at rt, the reaction mixture

was poured into ice water (10 g), and a white precipitate was separated by filtration (0.16 mg, 16%). The mother liquor was extracted with dichloromethane, and the organic layer was washed with brine solution, dried over $MgSO_4$, and concentrated *in vacuo* to give an additional product (0.17 g, 24%). mp 78 °C ($CHCl_3$); IR (KBr) 1775, 1605, 1583, 1542, 1482, 1371, 1275, 1240, 1215, 831; UV (MeOH) λ_{max} 221, 317 nm; ^{1}H NMR ($CDCl_3$) δ 1.44 (t, 3H), 3.93 (s, 3H), 4.75 (q, 2H), 8.12(s, 1H); ^{13}C NMR δ 13.6, 35.9, 67.1, 106, 131.2, 136.5, 155.5, 175.9; MS (ESI) *m/z* 230 [(M-H-CO_2Et)$^-$, 100].

Potassium salt of Methyl 5-nitro-2-(dinitromethyl)-1*H*-imidazole (8). To a solution of potassium hydroxide (22 mg, 1.63 mmol) in ethanol (2 mL) was added a solution of hydroxylamine hydrochloride (38 mg, 0.543 mmol) in water (0.5 mL). The precipitated potassium chloride was filtered off, and the mother liquor was added dropwise to a solution of **1** (100 mg, 0.362 mmol) in ethanol (2 mL) at 0 °C. After stirring for 1 h, a white precipitate was separated by filtration (72 mg, 74%). mp 270 °C (Water-EtOH, dec); IR (KBr) 1536, 1492, 1462, 1357, 1236, 1138, 939, 867, 829, 770, 753, 742, 695; ^{1}H NMR (D_2O) δ 3.85 (s, 3H), 8.25 (s, 1H); UV (H_2O) λ_{max} 220, 343 nm; MS (ESI) *m/z* 230 [(M-H-K)$^-$, 100].

1-Methyl-5-nitro-2-(dinitromethyl)-1*H*-imidazole (2). A suspension of potassium salt **8** (50 mg, 0.185 mmol) in water (2 mL) was acidified with 50% sulfuric acid (0.5 mL) at 0 °C. The precipitate was filtered and dried in a vaccume dessicator over phosphorus pentoxide to give trinitro **2** (37 mg, 90%). mp 115 °C; IR (KBr) 1615, 1605, 1564, 1461, 1413, 1352, 1304, 1216, 1175, 1109, 1057, 810, 774, 752, 740; ^{1}H NMR (DMSO-d_6) δ 3.73 (s, 3H), 8.40 (s, 1H); ^{13}C NMR δ 34.7, 129.8, 140, 144, 151; UV (MeOH) λ_{max} 210, 343 nm; MS (ESI) *m/z* 230 [(M-H)$^-$, 100].

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