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Polyiodoimidazoles and their nitration products

A. R. Katritzky[a]; D. J. Cundy[a]; J. Chen[a]
[a] Center for Heterocyclic Compounds Department of Chemistry, University of Florida, Gainesville, Fla

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POLYIODOIMIDAZOLES AND THEIR NITRATION PRODUCTS

A. R. Katritzky*, D. J. Cundy and J. Chen.

Center for Heterocyclic Compounds

Department of Chemistry

University of Florida, Gainesville

Fla 32611-7200

Abstract: *The preparations of 4,5-diiodoimidazole and 2,4,5-triiodoimidazole from imidazole were reinvestigated and convenient procedures for excellent yields described. 2,4,5-Triiodoimidazole can be selectively converted to 2,4(5)-dinitro-5(4)-iodoimidazole and 2,4,5-trinitroimidazole by nitrolysis. 2,4(5)-Dinitroimidazole was converted by nitration into 2,4,5-trinitroimidazole and isolated as the imidazolium and potassium salts in 38% and 15% yields respectively.*

INTRODUCTION

Polynitroimidazoles have been previously investigated in conjunction with their antibacterial, fungicidal and chemotherapeutic properties[1]. However more recently these so called "high energy density materials" have attracted renewed attention due to their favorable detonation performance[2,3]. We now describe improved routes to 2,4,5-trinitroimidazole (TNIMD) (1) from 2,4,5-triiodoimidazole (2) and from 2,4(5)-dinitroimidazole (3).

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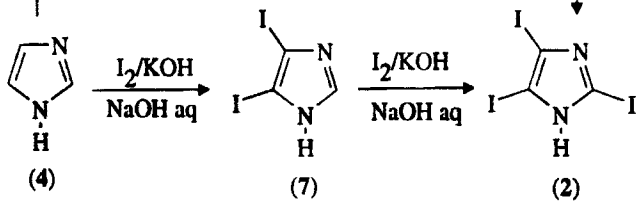
DISCUSSION

The Preparation of 2,4,5-Triiodoimidazole.

The iodination of imidazole was originally investigated by Pauly *et. al.*[4-6]. This work suggested that under alkaline conditions, it was the *C*-2 position which was initially substituted and that this was followed by substitution at *C*-4 to afford 2,4(5)-diiodoimidazole. This conclusion was shown to be erroneous by Naidu[7] and Hollaway[8], each of whom independantly correctly assigned the sequential products of mono- and di-substitution as 4(5)-iodoimidazole (6) and 4,5-diiodoimidazole (7) respectively. It was left to Hamill and co-workers[9] to unambigously identify the structure of diiodoimidazole as (7).

The preparation of 2,4,5-triiodoimidazole (2) by treatment of imidazole with aqueous alkaline iodine was first described by Dimroth and Hartmann[10]. Brunings[11] also prepared (2) by a heterogeneous iodination procedure. However, we found both methods inconvenient, each yielding multiple component mixtures from which pure products were difficult to isolate. More recently Iddon and co-workers[12] claimed to have made (2) by treatment of imidazole with aqueous potassium iodide/iodine. However, Lindell and Turner[13] reported that following Iddon's procedure afforded 4,5-diiodoimidazole (7). Similarly in our hands Iddon's procedure also afforded (7). We now report a convenient high yielding method (91%) for the multi-gram preparation of (2) by the treatment of imidazole with aqueous alkaline potassium iodide/iodine. Furthermore, we report a supplementary method for the conversion of di- (7) to tri-iodoimidazole (2) in 97% yield (figure 1). The identity of (2) was confirmed by elemental analysis and chemical ionization (CI) mass spectrometry.

Figure 1

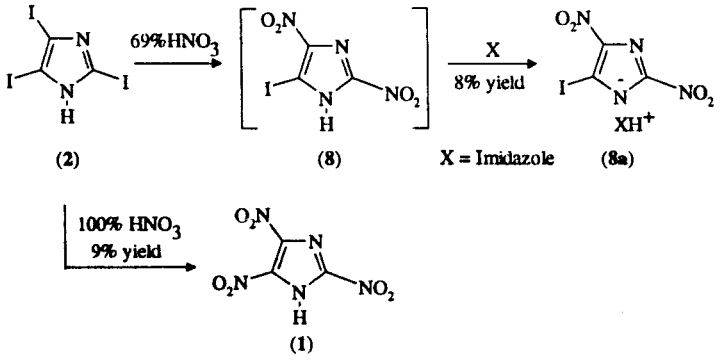


The Nitrolysis of 2,4,5-Triiodoimidazole.

The preparation of TNIMD (1) from 2,4,5-triiodoimidazole (2) was first described by Novikov et. al.14. In this report (2) was converted to (1) both by a one-pot procedure, and also via. 5(4)-iodo-2,4(5)-dinitroimidazole (8), by treatment of (2) with various concentrations of nitric acid. More recently Coburn and co-workers[2] also prepared (1) by nitration of (2) and also of 1,2,4,5-tetraiodoimidazole (10), with ~100% nitric acid. In Coburn's report (1) was isolated as its ammonium salt (9).

Repeating the experiments of Novikov[14] we were unable to isolate the free base (8), however, after an adaptation of the work-up procedure when (2) was treated with ~69% nitric acid we isolated compound (8) (albeit in poor yields) as its imidazole salt (8a). The empirical formula of the anionic counterion of (8a) was confirmed by *F*ast *A*tom *B*ombardment (FAB) mass spectrometry (figure 2). Similarly treatment of (2) with ~100% nitric acid yielded (1). Despite several attempts we were unable to attain the higher yields reported by Novikov[14], and conclude that nitrolysis of triiodoimidazole is, at best, a capricious route to TNIMD (1).

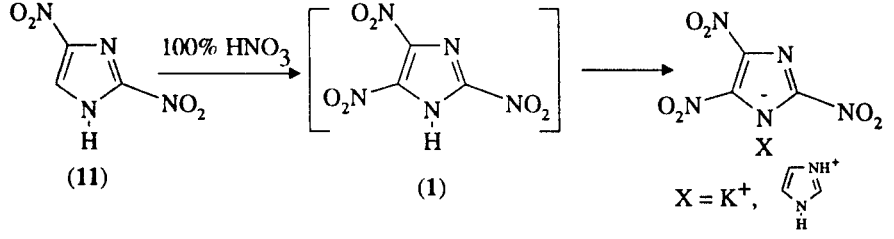
Figure 2



The Preparation of TNIMD from 2,4(5)-Dinitroimidazole (11).

TNIMD has also been reported[15] to be available by the nitration of 2,4(5)-dinitroimidazole (11), the latter being prepared by nitration of the potassium salt of imidazole in a two step, low yielding procedure[16]. Following these procedures, but employing a new work-up procedure, (11)* was treated with ~100% nitric acid at 100° to afford (1) as either its potassium or imidazolium salt in yields of 15% and 38% respectively (figure 3).

Figure 3



EXPERIMENTAL

Melting points were determined on a Kofler hot-stage apparatus and are uncorrected. ^{13}C n.m.r. spectra were recorded on a Varian VXR300 spectrometer at 300MHz. Microanalyses were determined on a Carbo Erba 1106 elemental analyzer. Mass measurements were made on a Finnigan Mat 95 mass spectrometer. 69% Nitric acid was purchased from Fluka and used as received. 100% Nitric acid was prepared by mixing equal volumes of 90% nitric acid (fuming, Fischer) and 5% oleum (Aldrich) and distilling off the first 30% of the volume.

4,5-Diiodoimidazole (7)

A solution of iodine (15 g, 0.059 mol) in 10% aqueous potassium iodide (20g, 0.12 mol), (200 ml) was added dropwise to a stirred solution of imidazole (2.30 g, 0.034 mol) in 2M sodium hydroxide (200 ml) at ambient temperature and the resulting mixture was stirred overnight. Addition of 25% aqueous acetic acid until the mixture was neutral gave a white precipitate which was filtered, washed with water and air dried. The resulting material was recrystallized from ethanol to afford colorless crystals (6.42 g, 42%) which possessed a melting point of 197-98°, lit.[7] 197-98°. Positive chemical ionization (CI) (methane) detected an ion at 321 amu which is accounted for by $(M+H)^+$. *Anal.* (Found: C, 11.16 ; H, 0.60; N, 8.59; Calc.: C, 11.26; H, 0.63; N, 8.76.) ^{13}C n.m.r. δ DMSO-D_6/(~50%TFA) 84.9, C-4/C-5; 142.2, C-2.

2,4,5-Triiodoimidazole (2) [from imidazole].

An aqueous solution (150 ml) of iodine (20.32 g, 0.08 mol) and potassium iodide (26.56 g, 0.16 mol) was added dropwise to a stirred solution of imidazole (1.36 g, 0.02 mol) in aqueous sodium hydroxide (2M, 200 ml) at room temperature and left to stir overnight. Addition of 25% aqueous acetic acid until neutral gave a creamy precipitate which was filtered, washed with water and air dried. The resulting material was then

recrystallized from ethanol to afford colorless crystals (8.15 g, 91%) which possessed a melting point of 191°, lit.[11] 190-192°. Positive chemical ionization (CI) (methane) detected an ion at 446.5 amu which is accounted for by $(M+H)^+$. *Anal.* (Found: C, 7.90 ; H, 0.22; N, 6.18; Calc.: C, 8.08; H, 0.23; N, 6.28). ^{13}C n.m.r. δ (DMSO-D_6/(~50%TFA) 89.0, C-4/C-5; 91.1, C-2.

2,4,5-Triiodoimidazole (2) [from 4,5-diodoimidazole (7)].

An aqueous solution (40 ml) of iodine (6.35 g, 0.025 mol) and potassium iodide (8.30 g, 0.05 mol) was added dropwise to an aqueous solution (100 ml) of imidazole (6.40 g, 0.02 mol) and sodium hydroxide (8.0 g, 0.20 mol). The mixture was stirred overnight after which time the colourless solution was neutralized by the addition of acetic acid. The mixture was cooled by immersion in an ice bath and filtered at the pump. The precipitate was air dried and recrystallized as above to afford (2), (8.68 g, 97%).

Imidazolium 2,4(5)-Dinitro-5(4)iodoimiazolate (8a)

2,4,5-Triiodoimidazole (2) (2.00 g, 4.48 mmol) was added to hot nitric acid (~69%, 80 ml) and the mixture boiled until the liberation of iodine ceased (typically 2 hr). The cooled mixture was poured onto ice (100 g), neutralized by the addition of saturated sodium bicarbonate and then reacidified to *p*H = 0.5 with concentrated hydrochloric acid. The mixture was extracted with ether (3×100 ml), dried (sodium sulphate) and the solution concentrated to half its original volume by evaporation at reduced pressure at temperatures no greater than 40°. Negative ion *F*ast *A*tom *B*ombardment in a triethanolamine matrix detected an ion at 283 amu which is accounted for by $[C_3N_4O_4I]^-$.

2,4,5-Trinitroimidazole (1) [from 2,4,5-triiodoimidazole (2)]

2,4,5-Triiodoimidazole (2) (2.00 g, 4.48 mmol) was refluxed with nitric acid (~100%, 30 ml) for 2 hr during which time a cream colored precipitate deposited. The

cooled mixture was poured onto ice, neutralized by saturated sodium bicarbonate and the mixture reacidified to *p*H = 0.5 by the addition of concentrated hydrochloric acid. The solution was extracted with ether (3×100 ml), dried over magnesium sulfate and reduced *in vacuo* at 40° to a yellow oil (0.10 g, 9.1%) which crystallized slowly when stored *in vacuo* over calcium chloride. *C*hemical *I*onization mass spectrometry detected an ion at 204 amu which corresponds to $[M+H]^+$.

2,4,5-Trinitroimidazole (1) [from 2,4(5)-dinitromidazole (11)]

2,4(5)-Dinitroimidazole (11) (1.58 g, 0.01 mol) was added to nitric acid (~100%, 5.0 ml), immersed in a pre-heated oil bath (100°) and boiled under reflux for 5 min. This was accompanied by the liberation of nitrous oxides and the precipitation of hydroiodic acid. Concentrated sulfuric acid (7.0 ml) was added to the cooled suspension and the mixture reboiled for 15 min. After cooling, the resultant mixture was poured onto ice (50 g) and neutralized by the addition of saturated aqueous sodium bicarbonate. The *p*H was adjusted to 0.5-1.0 by the addition of concentrated hydrochloric acid. The mixture was then extracted with diethyl ether (5×100 ml) and dried over magnesium sulphate for at least 30 min.

To the etheral solution, imidazole (0.68 g, 0.01 mol) dissolved in chloroform (10 ml) was added. The *imidazolium 2,4,5-trinitroimidazolate* which precipitated was filtered and recrystallized from water to afford yellow crystals (1.02 g, 38%) which melted at 210-213 ° lit.[15] 210-211.5° *Anal.* (Found: C, 26.53; H, 1.82; N, 36.52; Calc.: C, 26.58; H, 1.86; N, 36.16).

Potassium 2,4,5-trinitroimidazolate was also prepared by neutralization of the etheral solution of 2,4,5-trinitroimidazole (1) by the addition of a 50/50 mixture of saturated potassium carbonate/potassium chloride solution. The resultant precipitate was filtered then washed with a minimal amount of water and vacuum dried. This afforded orange

crystals (0.36 g, 15%) which possessed a melting point of 234° lit.[15] 238-240°. Anal. (Found. C, 15.00; H, 0.06; N, 28.83. Calc.: C, 14.94; H, 0.00; N, 29.04).

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REFERENCES

1. A. Breccia., R. Cavalleri and G. E. Adams., (Eds) "Nitroimidazoles: Chemistry, Pharmacology and Clinical Applications" NATO Advanced Study Institutes Series A, Life Sciences: Volume 42 (Plenum Press: New York, 1982).
2. H. H. Cady, M. D. Coburn, B. W. Harris, and R. N. Rogers, *Energy Res. Abstr* **2(21)**, Abstr. No. 52829, (1977).
3. M. D. Coburn, *U. S. Patent* 4, 028, 154, (1977); CA88(2):9198v.
4. H. Pauly and K. Gundermann, *Ber.*, **41**, 3999, (1908).
5. H. Pauly, *Ber.*, **43**, 2243, (1910).
6. H. Pauly and E. Arauner, *J. Prakt. Chem.*, **118**, 33, (1928).
7. M. S. R. Naidu and H. B. Bensusan, *J. Org. Chem.*, **33**, 1307, (1928).
8. C. T. Holloway, R. P. M. Bond, I. G. Knight and R. B. Beechey, *Biochemistry*, **6**, 12, (1967).
9. J. P. Dickens, R. L. Dyer, B. J. Hamill, T. A. Harrow, R. H. Bible Jr., P. M. Finnegan, K. Henrick and P. G. Owston, *J. Org. Chem.*, **46**, 1781, (1981).
10. O. Dimroth and M. Hartmann, *Ber.*, **41**, 4012, (1908).
11. K. J. Brunings, *J. Amer. Chem. Soc.*, **69**, 205, (1947).
12. B. Iddon, and B. L. Lim, *J. Chem. Soc. Perkin Trans. 1*, 735, (1983).
13. R. M. Turner and S. D. Lindell, *J. Org. Chem.*, **56**, 5739, (1991).
14. S. S. Novikov, L. I Khmel'nitskii, L. V. Epishina., and V. V. Sevast'yanova, *Chem. Heterocycl. Compd., (Engl. Transl.)*, **6**, 614, (1970).
15. S. S. Novikov, L. I Khmel'nitskii, O. V. Lebedev, V. V. Sevast'yanova, and L. V. Epishina. *Chem. Heterocycl. Compd., (Engl. Transl.)*, **6**, 465, (1970).
16. S. S. Novikov, L. I Khmel'nitskii, T. S. Novikova, O. V. Lebedev, L. V Epishina. *Chem. Heterocycl. Compd., (Engl. Transl.)*, **6**, 619, (1970).

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