

The Oxidation of Heterocyclic Amines to Nitro Compounds using Dinitrogen Pentoxide

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The amino group of heterocycles has been oxidized to a nitro group using dinitrogen pentoxide; it is suggested that the mechanism of this reaction involves the transformations: amine → nitramine → nitroso → nitro compound.

In our recent studies on the high nitrogen heterocycles, it was found that the reaction of 2-(*tert*-butyl-*NNO*-azoxy)aniline with an excess of N₂O₅ gave benzo-1,2,3,4-tetrazine-1,3-dioxide.¹ It was proposed that the tetrazine ring was formed *via* the intermediate 1-nitroso-2-aryldiazene 1-oxide.

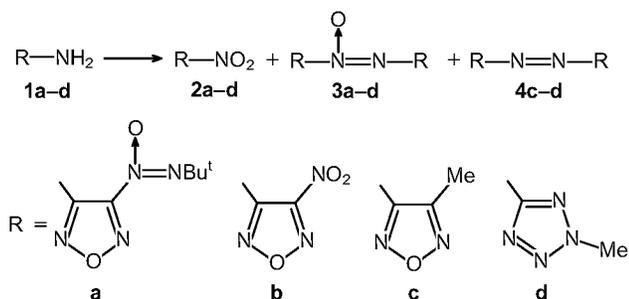
We report herein that we planned to obtain 1,2,3,4-tetrazine 1,3-di-*N*-oxides fused with the furazan ring. However, it was found that when treated with excess N₂O₅, 3-amino-4-*tert*-butylazoxyfurazan **1a** gave, instead of the expected furazano[4,3-*e*]-1,2,3,4-tetrazine 1,3-di-*N*-oxide, 3-nitro-4-*tert*-butylazoxyfurazan **2a** in good yield together with a small amount of azoxy compound **3a**.

It has been found that other heterocyclic amines can also be oxidized to nitro compounds[†] by N₂O₅. 3-Methyl-4-

aminofurazan **1c** and 2-methyl-5-aminotetrazole **1d** react faster than aminofurazans with electronegative substituents **1a,b**. In all cases the yield of nitro compounds was no less than 60% when a six-fold excess of N₂O₅ was used. When there was a deficiency in N₂O₅, nitro compounds were not observed. The only products were azo and/or azoxy compounds **3** and **4** (Table 1).

Table 1 The oxidation of amines **1** to compounds **2–4**.

Starting compound	Molar ratio N ₂ O ₅ /amine 1	Time/h	T/°C	Yield (%)		
				2	3	4
1a	2	48	0	0	20	0
1a	6	48	0	84	5	0
1b	6	48	0	62	11	0
1c	6	4	10	60	6	14
1d	2	12	0	0	35	34
1d	6	12	0	61	0	30



Scheme 1

[†] **General procedure. Caution!** The nitro, azoxy and azo compounds are explosives and should be handled carefully. To a stirred suspension of N₂O₅ in dry MeCN (20 ml) was added amine **1** (10 mmol) at –25 °C. The mixture was brought to 0 °C, stirring was continued until all N₂O₅ had dissolved and the solution was kept in a refrigerator (see Table 1). Then water with ice was added, and the mixture was extracted with CH₂Cl₂, washed with a NaHCO₃ solution, dried (MgSO₄) and evaporated under reduced pressure. Nitro compounds **2a–c** were distilled *in vacuo* and other compounds were chromatographed on silica gel. Compounds **2b–d**,⁵ **3b**,⁵ **3c**,⁶ **3d**,⁷ **4b**⁵ and **4c**³ are identical with authentic samples, obtained by literature procedures. Compounds **2a** (m.p. 17–18 °C), **3a** (m.p. 97–98 °C), **3d** (m.p. 161–163 °C) and **4a** (m.p. 124–125 °C) were obtained for the first time.

All novel compounds were fully characterized by IR, NMR, MS and microanalysis. Selected data for **1a**: m.p. 164–165 °C; NMR in [2H₂]DMF/CD₂Cl₂ (1:1): ¹H NMR (δ, ppm): 1.48 (s, Bu^t), 6.6 (s, NH₂); ¹³C NMR (δ, ppm): 25.3 (Me), 60.6 (CMe₃), 151.6 (CNH₂), 152.4 [CN(O)]; ¹⁵N NMR (δ, ppm): 24.98 (NBu^t), –66.78 (NO), –335.23 (NH₂); ¹⁴N NMR (δ, ppm): –65 (N → O, ν_{0.5} = 100 Hz).

2a: NMR in CDCl₃; ¹H NMR (δ, ppm): 1.48 (s, Bu^t); ¹³C NMR (δ,

Transformation of the amino to the nitro group under action of N₂O₅ has not so far been investigated in the literature. We suppose the mechanism of this reaction to be of interest. The key question is the way in which the N–O bond in the nitro and azoxy groups is formed.

It was found that the first stage of the reaction involves formation of nitramine **5** (Scheme 2). For example, nitramine **5a** was isolated in 91% yield when **1a** was treated with 1 equiv. of N₂O₅.

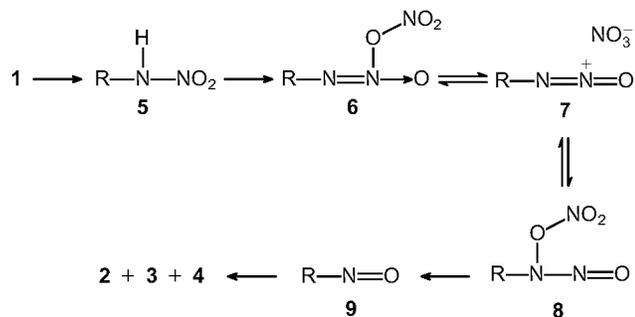
ppm): 24.9 (Me), 61.8 (CMe₃), 151.8 [C–N(O), ²J_{13C–15N} = 3.3 Hz], 154.2 (CNO₂, ¹J_{13C–15N} = 20.2 Hz); ¹⁵N NMR (δ, ppm): –41.21 (NO₂); ¹⁴N NMR (δ, ppm): –42 (NO₂, ν_{0.5} = 5 Hz), –79 (N → O, ν_{0.5} = 45 Hz).

3a: NMR in CDCl₃; ¹H NMR (δ, ppm): 1.44, 1.47 (both s, Bu^t); ¹³C NMR (δ, ppm): 25.1, 25.2 (Me), 61.4, 62.2 (CMe₃), 148.4 [CN=N(O)], 151.9, 152.1, 154.4 [C–N(O)=N]; ¹⁴N NMR (δ, ppm): –68 (ν_{0.5} = 55 Hz), –72 (ν_{0.5} = 70 Hz), –77 (ν_{0.5} = 65 Hz) (all N → O).

3d: NMR in [2H₂]acetone; ¹H NMR (δ, ppm): 4.48, 4.62 (Me); ¹³C NMR (δ, ppm): 40.8, 41.7 (Me), 164.7 [CN=N(O)], 167.2 [C–N(O)=N]; ¹⁴N NMR (δ, ppm): –70 [N(O), ν_{0.5} = 50 Hz], –101 (NMe, ν_{0.5} = 350 Hz).

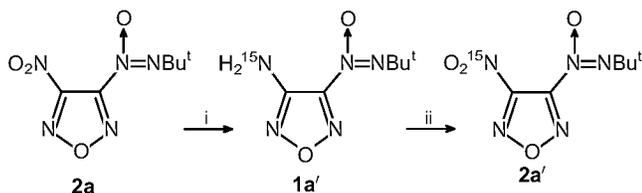
4a: NMR in CD₂Cl₂; ¹H NMR (δ, ppm): 1.48 (s, Bu^t); ¹³C NMR (δ, ppm): 25.2 (Me), 62.2 (CMe₃), 150.5 [CN(O)], 156.8 (CN); ¹⁴N NMR (δ, ppm): –76 (N → O, ν_{0.5} = 100 Hz).

5a: m.p. 102–104 °C (decomp.); ¹H NMR ([2H₂]DMSO, δ, ppm): 1.38 (s, Bu^t), 11.8 (s, NH₂); ¹³C NMR (CD₃CN, δ, ppm): 25.4 (Me), 62.0 (CMe₃), 144.6 (CNH), 154.7 [C–N(O)]; ¹⁴N NMR (CD₃CN, δ, ppm): –40 (NO₂, ν_{0.5} = 20 Hz), –69 (N → O, ν_{0.5} = 150 Hz).



Scheme 2

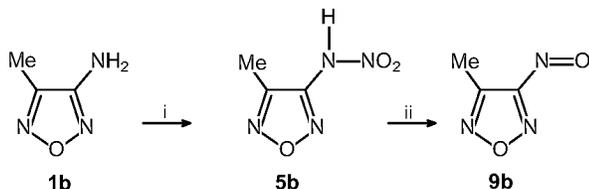
We suggested that further oxidation of nitramine **5** to nitro compound **2** took place. To confirm this, experiments with labelled compounds were performed. We obtained ^{15}N -labelled amine **1a'** by nucleophilic substitution of the NO_2 group in **2a** with labelled ammonia. When the amine was treated with N_2O_5 , the label was retained in the nitro group of **2a'**, which was confirmed by ^{15}N NMR spectroscopy. The amount of ^{15}N label was also verified by ^{14}N NMR spectroscopy by comparison of the integral intensities of the nitro and azoxy groups of **2a'**. These findings are evidence in favour of the assumption that the reaction is really an oxidation but not a substitution process.



Scheme 3 Reagents and conditions: i, $^{15}\text{NH}_3$, MeCN, 24°C , (70%); ii, N_2O_5 (6 equiv., see Table 1).

The nitro group formation can be rationalized by the intermediate production of the 1-nitroxydiazene 1-oxide **6** followed by its rearrangement to afford **8**; ionic pair **7** might be the intermediate.[‡] The rearrangement is the stage at which a new N–O bond is formed. The unstable **8** readily loses N_2O_3 to give nitroso compound **9**. The latter is oxidized to **2** with excess N_2O_5 . When there is insufficient N_2O_5 , nitroso compound turns into azoxy and/or azo compounds.

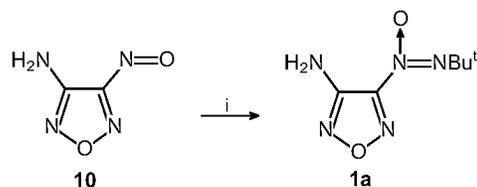
The furazano[4,3-*e*]-1,2,3,4-tetrazine 1,3-di-*N*-oxide was not produced (*cf.* ref. 1) in this reaction, probably due to the strained transition state of the cyclization reaction which is caused by the five-membered furazan ring.



Scheme 4 Reagents and conditions: i, HNO_3 , CCl_4 , 24°C , 0.5 h (55%); ii, $\text{TsOH}\cdot\text{H}_2\text{O}$ (0.15 equiv.), heating without solvent, $60\text{--}65^\circ\text{C}$, 0.4 Torr (yield 15%), **9b** was identical with an authentic sample.³

[‡] The hypothesis of the diazonio-oxide cation generated from *ortho*-nitramino aromatic nitriles has been proposed earlier.²

[§] 3-Amino-4-nitrosfurazan was obtained by procedure of T. S. Novikova, T. M. Mel'nikova and A. B. Sheremetev (this Institute), unpublished data.



Scheme 5 Reagents and conditions: i, Br_2NBUt^+ , $\text{CH}_2\text{Cl}_2/\text{MeCN}$, 24°C , 6 h (66%).

It was suggested that nitramine could be transformed to nitroso compound when treated not only with N_2O_5 , but also with a strong acid. This reaction was performed when **5b** was heated with a catalytic amount of *p*-toluenesulfonic acid under reduced pressure, nitroso compound **9b** being distilled from the reaction mixture into a receiver at -78°C .

The starting **1a** was obtained according to the Kovacic method⁴ from 3-amino-4-nitrosfurazan[§] **10**. This was the first case in which the neighbouring amino group did not preclude the normal reaction on the nitroso group.

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