On the Nitro Group Transfer from 2-Nitro-4,5,6,7-tetrachloro-2*H*-benzotriazole and 2-Nitro-2*H*-phenanthro[9,10-*d*]triazole to Secondary Amines [1]

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The synthesis of 2-nitro-4,5,6,7-tetrachloro-2*H*-benzotriazole **1** and of 2-nitro-2*H*-phenanthro[9,10-*d*]-triazole **2** and their transfer of the nitro group to give 1-nitropyrrolidine **4a** and 1-nitromorpholine **4b** in high yields when reacted with pyrrolidine or morpholine are reported. The reaction of **1** also gives the pyrrolidinium and morpholinium salts **5a-b** of **1**.

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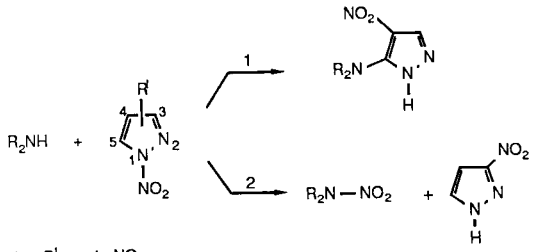
Introduction.

In our first paper on nucleophilic substitution reactions on 1-nitro-1*H*-azoles we reported two modes of nucleophilic attack: first a *cine* substitution of the 1-nitro group by attack on the adjacent 5-carbon atom and, secondly, a displacement on the 1-nitro group by a nucleophile of a pyrazole anion [2] (see Scheme 1). In subsequent papers we and others reported on the synthetic utility of the *cine* substitution reaction of 1-nitro-1*H*-azoles with both nitrogen and carbon nucleophiles [3a-d].

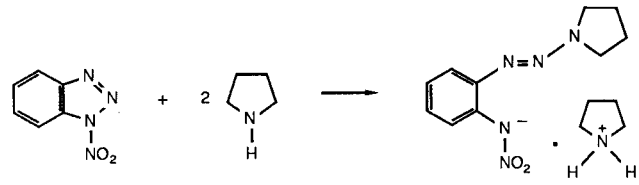
Scheme 1



1. R^1 = 4-NO_2
2. R^1 = 3-NO_2

The second mode of reaction, *i.e.*, the displacement by a nucleophile on the nitro group of an azole anion, amounts to a nitro group transfer from an azole to an electron rich molecule. Such a reaction might be of synthetic use and of importance for nitration of an acid sensitive molecule in neutral media. The examples initially found [2] are not suitable for that purpose either because of poor yields or because of the formation of nitrosoamines as byproducts. We therefore devoted our efforts to finding other *N*-nitroazoles capable of transferring the nitro group to other molecules both in neutral media and in high yields. 1-Nitro-1*H*-benzotriazole seemed to be a good candidate because it cannot undergo the nucleophilic *cine* substitution reaction on carbon. Yet, as we have described elsewhere [1,4] the reaction of 1-nitro-1*H*-benzotriazole with cyclic amines gives triazene salts as depicted for the reaction with pyrrolidine in Scheme 2. This unexpected result suggested to turn to 2-nitro-2*H*-benzotriazoles as possible nitro group transferring azoles. Therefore we decided to synthesize 2-nitro-4,5,6,7-tetrachloro-2*H*-benzotriazole **1** and 2-nitro-2*H*-phenanthro[9,10-*d*]triazole **2** in the expectation that in both molecules nitration would be directed to the 2-position by steric hindrance preventing nitration in the 1-position.

Scheme 2

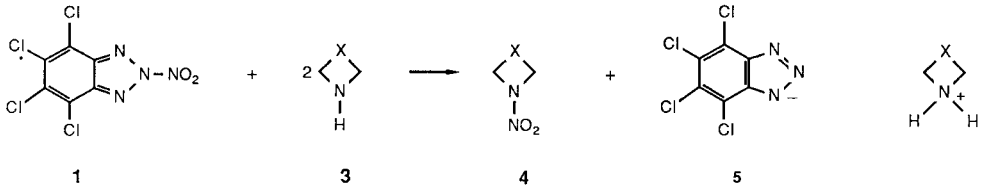


Results and Discussion.

Nitration of 4,5,6,7-tetrachloro-1*H*-benzotriazole with a mixture of fuming nitric acid and acetic anhydride afforded **1** in excellent yields. The location of the nitro group in position-2 was confirmed by the ^{13}C nmr spectrum revealing the presence of only three carbon signals as expected for the symmetric molecule **1**. On reacting **1** in chloroform solution with an equivalent amount of pyrrolidine **3a** we indeed observed the formation of **4a** in the reaction mixture. Yet a second product, readily crystallizing out of the solution, was also formed. This product was found to be the pyrrolidinium tetrachlorobenzotriazolate **5a** (see Scheme 3). Therefore, the reaction at room temperature in chloroform solution of **1** with two equivalents of **3a** was subsequently carried out. Now, both **4a** and **5a** were obtained in excellent yields. Similarly, the reaction of **1** with morpholine **3b** gave both 1-nitromorpholine **4b** and the morpholinium salt **5b** in high yields.

The formation of the salts **4a-b** is quite understandable because of the acidic proton of the tetrachlorobenzotriazole ($K = 3.10^{-5}$) [5]. However, this acidity diminishes the utility of **1** for synthetic purposes. Therefore we antici-

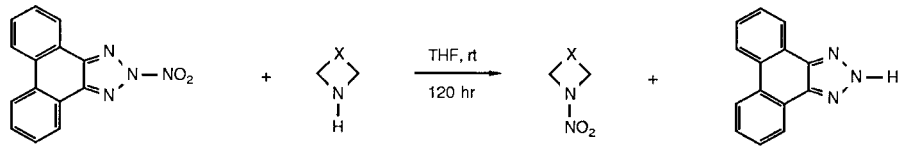
Scheme 3



1 3 4 5

3a, 4a, 5a, X = $-CH_2CH_2-$
3b, 4b, 5b, X = $-CH_2OCH_2-$

Scheme 4



2 3 4

pated better results from the use of 2-nitro-2*H*-phenanthro[9,10-*d*]triazole **2**.

Nitration of phenanthro[9,10-*d*]triazole with a mixture of fuming nitric acid and acetic anhydride afforded **2** in almost quantitative yield. The ^{13}C nmr spectrum consisting of seven carbon signals including three of quaternary carbon atoms proves that the nitro group is located in the 2-position. Unfortunately, **2** in addition to decomposing in some solvents (ethanol, nitromethane, acetonitrile), has a very poor solubility in other solvents. Reaction of **2** with **3a-b** carried out in tetrahydrofuran solution at room temperature turned out to be very slow. Nevertheless good yields of **4a-b** were obtained by stirring the reaction mixture at room temperature for four to five days (Scheme 4).

Because additional formation of nitrosoamines had been observed in the previous examples of nitro group transfer reactions [2] the reaction mixtures were checked for the presence of nitrosoamines. Only in the reaction of **2** with **3b** we observed the additional formation of some 1-nitrosomorpholine. Finally, we attempted to transfer the nitro group of **2** to a carbon atom in an electron rich molecule. Because of its great susceptibility to electrophilic aromatic substitution in neutral media we choose 1,3,5-trimethyl-1*H*-pyrazole as substrate [6]. Neither stirring with **2** in tetrahydrofuran for five days at room temperature or for two hours in tetrahydrofuran at 70° afforded any transfer of the nitro group to give the 4-nitro-1*H*-pyrazole derivative.

Although the reactions described above are as yet perhaps of limited value for synthetic purposes they are of great importance for the understanding of the reactivities of *N*-nitrobenzotriazoles because they establish fundamental differences in reactivities between 2-nitro-2*H*- and 1-nitro-1*H*-benzotriazoles and therefore these results are important for the understanding of the chemistry of *N*-nitroazoles in general.

EXPERIMENTAL

The ir spectra were recorded on a Beckman IR-10 instrument. Melting points are uncorrected. Elemental analyses were performed by Mikroanalytisches Labor Pascher, Bonn, BRD. Mass spectra were taken on an AEI type MS-902 instrument at ambient temperature. High resolution nmr spectra were recorded on a Bruker WM-300 and a Jeol JMN-FX 200 spectrometer. Data accumulation and processing was carried out on an Aspect 2000 computer and a JEC-980B. Proton spectra were recorded at 300 and 200 MHz using a spectral window 3000 Hz at 16 K data points. Carbon-13 spectra were measured at 75 and 50 MHz using a spectral window of 18000 Hz at 16 K data points.

The chloroform used was freshly distilled, tetrahydrofuran was distilled from lithium aluminium hydride and the cyclic amines **3a-b** were dried on sodium hydroxide. 4,5,6,7-Tetrachloro-1*H*-benzotriazole [5], 1*H*-phenanthro[9,10-*d*]triazole [7] and for reference purposes, 1-nitropyrrolidine **4a** and 1-nitromorpholine **4b** were prepared as has been described in the literature [11].

2-Nitro-4,5,6,7-tetrachloro-2*H*-benzotriazole **1**.

4,5,6,7-Tetrachloro-1*H*-benzotriazole [5] (0.8 g, 3.1 mmoles) added in small portions to a freshly prepared solution of 1 ml of fuming nitric acid (d = 1.52) and 100 ml of acetic anhydride, while stirring gave a heterogeneous reaction mixture which was stirred for four hours at room temperature. The reaction mixture was then poured onto 100 g ice, the white crystals were filtered off and washed with water till neutral and sucked dry (yield 0.79 g, 2.6 mmoles, 84%). This 2-nitro compound **1** is insoluble in many organic solvents and attempts to recrystallize **1** failed so that satisfactory elemental analyses were not obtained. Because of decomposition **1** was used without further purification and tlc (chloroform:ethylacetate = 3:1) was used to check for the absence of contaminants [8]. Ir (potassium bromide) 1280 and 1680 cm^{-1} (N-NO_2), ^{13}C nmr (75 MHz, deuteriochloroform, ^{13}C depleted) δ 122.6 (C-4,7), 135.2 (C-5,6), 139.4 (C-8,9); high resolution mass spectrum: Calcd. for $C_6{}^{35}Cl_4N_4O_2$: 299.8775. Found, 299.8743. Calcd. for $C_6{}^{35}Cl_3{}^{37}ClN_4O_2$: 301.8745. Found, 301.8738.

General Procedure for the Reaction of **1** with the Cyclic Amines **3a-b**.

To a solution of 1.6 mmoles of **1** in 30 ml chloroform at room temperature was added 3.2 mmoles of the cyclic amines **3a** or **3b**. The white salts **4a-b** readily started to crystallize and after 24 hours the crystals were collected on a Büchner funnel, washed with water till neutral and dried. Yields varied from 1.57 mmoles (98%) for **5a** to 1.42 mmoles (89%) for **5b**. The chloroform filtrate was washed with 2 ml portions of 10% hydrochloric acid to remove traces of unreacted **3**, dried and evaporated. Each afforded a crop of white crystals which was collected and purified by sublimation. Identification of respectively **4a** (1.34 mmoles, 84%) and **4b** (1.11 mmoles, 70%) was accomplished by comparison with independently synthesized specimen [11].

Pyrrolidinium 4,5,6,7-Tetrachlorobenzotriazolate **5a**.

This compound was obtained as white crystals (from ethanol) mp 214°; ir (potassium bromide): 2500-3000 (NH_2^+, C-H) and 1115 cm^{-1} (C-Cl); ^1H nmr (deuteriochloroform): 300 MHz, δ 3.32-3.37 (m, H-α), 2.03-2.08 (m, H-β); ^{13}C nmr: 75 MHz, δ 119.8 (C-4,7), 125.5 (C-5,6), 141.7 (C-8,9), 45.4 (C-α), 24.6 (C-β).

Anal. Calcd. for $C_{10}H_{10}Cl_4N_4$: C, 36.61; H, 3.07; N, 17.08. Found: C, 36.85; H, 3.13; N, 17.1.

Morpholinium 4,5,6,7-Tetrachlorobenzotriazolate **5b**.

This compound was obtained as white crystals (from ethanol) mp 220°; ir (potassium bromide): 2500-3000 (NH_2^+, C-H) and 1105 cm^{-1} (C-Cl); ^1H nmr (deuteriochloroform): 300 MHz, δ 3.09-3.12 (m, H-α), 3.82-3.86 (m, H-β); ^{13}C nmr: 75 MHz, δ 119.8 (C-4,7), 126.6 (C-5,6), 140.8 (C-8,9), 44.1 (C-α), 64.9 (C-β).

Anal. Calcd. for $C_{10}H_{10}Cl_4ON_4$: C, 34.91; H, 2.93; N, 16.29; Cl, 41.21. Found: C, 35.00; H, 2.93; N, 16.3; Cl, 41.2.

Compound **5b** was also prepared by addition of 0.3 ml of morpholine to a solution of 0.83 g of 4,5,6,7-tetrachloro-1*H*-benzotriazole in 45 ml of ether. The crystalline precipitate was filtered and washed with ether, yield 1.02 g (90%).

2-Nitro-2*H*-phenanthro[9,10-*d*]triazole **2**.

1*H*-Phenanthro[9,10-*d*]triazole [7] (0.2 g, 0.91 mmole) was added to a stirred solution of 5 ml of acetic anhydride and 0.3 ml of fuming nitric acid (d = 1.52) while keeping the temperature at 15°. The resulting heterogeneous mixture was stirred at room temperature for four hours. The reaction mixture was then poured onto ice; the bright yellow crystals were collected on a Hirsch funnel and washed with water until neutral and dried. The yields varied from 0.25 g, 98% to 0.22 g, 83%; tlc (chloroform:ethyl acetate = 3:1) indicated only the presence of very little starting material. Attempts to recrystallize **2** (from ethanol, nitromethane, acetonitrile) only ended in decomposition of **2** [8]; high resolution mass spectrum: Calcd. for $C_{14}H_8N_4O_2$: m/e 264.0645: Found, m/e 264.0647; ir (potassium bromide): 1280 and 1630 cm^{-1} (N-NO_2); ^1H nmr (DMSO-d_6): 200 MHz, δ 7.75-7.92 (m, 4H), 8.44-8.49 (m, 2H), 8.79-8.84 (m, 2H); ^{13}C nmr (DMSO-d_6): 50 MHz, δ 121.73 (t, ^3J = 6.72), 124.30 (dd, ^1J = 162.49, ^3J = 8.06), 124.89 (dd, ^1J = 161.15, ^3J = 5.37), 128.98 (dd, ^1J = 163.84, ^3J = 8.06), 130.88 (dd, ^1J = 162.5, ^3J = 8.06), 131.74 (broad), 140.66 (d, ^3J = 4.03).

Reaction of **2** with **3a**.

After quite some experimentation the following procedure proved to give the best results. A solution of 1.17 g (4.36 mmoles) of **2** and 0.62 g (8.72 mmoles) of pyrrolidine **3a** in 100 ml of tetrahydrofuran was stirred at room temperature for four days. After evaporation of the solvent the residue was taken up in 3 ml of chloroform and chromatographed over a silica column (Merck No. 9385, 16 g) with chloroform as eluent affording 0.35 g of **4a** in a yield of 69% (51% of **4a** after crystallization from hexane), and in a subsequent preparation the yield of **4a** was 80% (58% after crystallization from hexane).

Reaction of **2** with **3b**.

Compound **2** (1.17 g, 4.43 mmoles) and 0.78 g (8.96 mmoles) of morpholine **3b** dissolved in 150 ml tetrahydrofuran was stirred at room temperature for five days. The same workup procedure as for the isolation of **4a** afforded 0.42 g, 75% of **4b** which on tlc (chloroform:ethyl acetate = 3:1) appeared to be contaminated with 1-nitrosomorpholine [12]. Sublimation gave 0.15 g of **4b** in a yield of 26%.

Attempted Reaction of **2** with 1,3,5-Trimethyl-1*H*-pyrazole.

Tlc (chloroform) analysis of a solution of 1.2 g of **2** and 0.55 g of 1,3,5-trimethyl-1*H*-pyrazole in 120 ml of tetrahydrofuran stirred for five days at room temperature revealed that no 1,3,5-trimethyl-4-nitro-1*H*-pyrazole was formed. Similarly heating such a solution at 70° for two hours did not result in the nitration of the pyrazole. In both cases the only compounds found present were the starting materials and a substantial amount of 1*H*-phenanthro[9,10-*d*]benzotriazole.

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