

# 5-PHENYL-1,2,3,4-THIATRIAZOLE-3-OXIDE

## A NEW CLASS OF HETEROAROMATIC N-OXIDES

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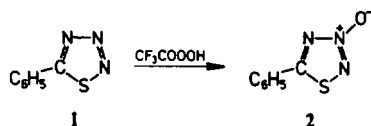
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**Abstract**—Oxidation of 5-phenyl-1,2,3,4-thiazotriazole (1) with peroxytrifluoroacetic acid yields 5-phenyl-1,2,3,4-thiazotriazole-3-oxide (2) a representative of a new class of heteroaromatic N-oxides. The structure is based on the mass spectral fragmentation of 2 and the isotope labelled with  $^{15}\text{N}$  at position 2. IR and ESCA measurements are consistent with this assignment. The thermal, photochemical, and chemical properties of the oxide are discussed.

Thiazotriazoles with an aromatic substituent in the 5-position are reported to be extremely stable towards oxidizing agents. Thus 5-phenyl-1,2,3,4-thiazotriazole is not attacked in the hetero-ring by chlorine, nitric acid, hydrogen peroxide or peroxyformic acid.<sup>1</sup> Attempts to obtain an S-oxide by the reaction between thiobenzoyl chloride S-oxide and azide ions were also unsuccessful. Instead the unstable open-chain thiobenzoyl azide S-oxide was obtained.<sup>2</sup> This decomposes at ca  $-40^\circ$  in methylene chloride solution with loss of nitrogen and sulfur monoxide to yield benzonitrile. Accumulated evidence indicates this decomposition to take place without the intermediacy of a thiazotriazole.<sup>3</sup>

We wish to report that solid, thermally stable 5-phenyl-1,2,3,4-thiazotriazole-3-oxide (2) can be obtained by the action of peroxytrifluoroacetic acid on 5-phenyl-1,2,3,4-thiazotriazole (1):



Oxidation takes place slowly and competes with acid catalyzed decomposition of the starting material to benzonitrile, nitrogen, and sulfur.<sup>4</sup> The latter may explain the relatively low yield, 15%, in which 2 is obtained.

The structural assignment of the oxide is based on the spectroscopic studies discussed below.

**Structure and spectroscopy.** The thiazotriazole ring possesses four different heteroatoms to which oxygen can be delivered. The structure assignment problem offers difficulties similar to that recently discussed for the alkylation products of thiazotriazoles.<sup>5</sup>

The mass spectrum of 2 (Fig. 1) suggests that oxidation has taken place on nitrogen and not on sulfur provided, of course, that rearrangement of oxygen in the molecular ion is excluded. The peaks at  $m/e$  149, 135 and 133 are formed from the molecular ion ( $m/e$  179) by loss of NO,  $\text{N}_2\text{O}$  and NS as indicated by the appropriate metastables, but a peak corresponding to loss of SO is not observed. Furthermore, loss of nitrogen from the molecular ion is not observed. A 3-oxide is thus suggested as a 2- or a 4-oxide may lose nitrogen as observed in the mass spectrum of 1.<sup>6</sup> In the case of a 4-oxide,  $m/e$  119 ( $\text{C}_6\text{H}_5\text{CNO}$ ) can be expected, but is not observed. The fact, that NS is lost argues against a 2-oxide. The peak at  $m/e$  163 is probably due to ionized 1 since the peaks at  $m/e$  135, 103, 76 and 75 corresponds to its known decomposition products.<sup>6</sup>

Finally the fragmentation pattern of the 2- $^{15}\text{N}$  labelled thiazotriazole oxide (95.7% isotopically labelled) upon electron impact support the assignment of 2 to the 3-oxide. As the most significant results loss of  $^{14}\text{NO}$  ( $\approx 100\%$   $^{14}\text{N}$ ),  $^{15}\text{N}^{14}\text{NO}$  ( $\approx 95.7\%$   $^{15}\text{N}$ ), and  $^{15}\text{NS}$  ( $\approx 95.7\%$   $^{15}\text{N}$ ) is noted. Formation of  $^{15}\text{N}^{14}\text{NO}$  is in good agreement with a 2- or 3-oxide but virtually rules out a 4-oxide. Formation of  $^{15}\text{NS}$  and lack of  $^{15}\text{NO}$  argues against a

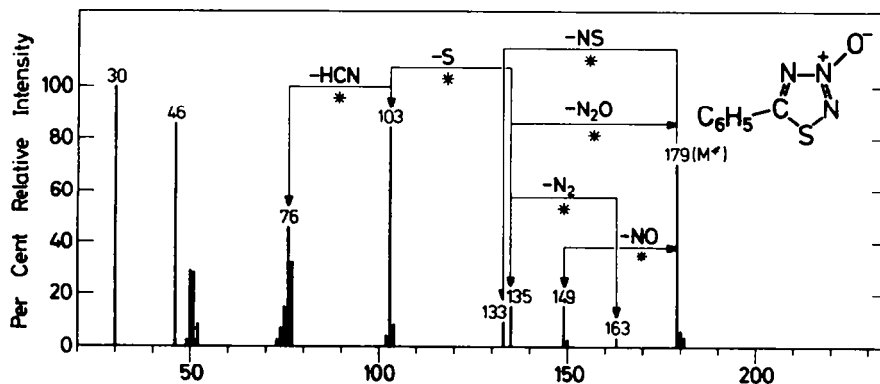
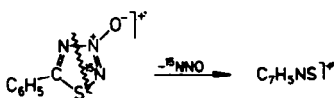


Fig. 1.

2-oxide leaving the 3-oxide as the most probable structure.



IR spectra of heterocyclic N-oxides have been studied in some detail.<sup>7</sup> An N–O stretching vibration usually gives rise to an intense absorption in the range 1200–1300 cm<sup>-1</sup>. However, no significant differences are observed in this region in the spectrum of 2 compared to a spectrum of 1. Shindo<sup>8</sup> has shown that a marked change in one of the coupled N–O absorptions of pyridine 1-oxide occurs in carbon disulfide solution on addition of small amounts of methanol. The pyridine-oxide absorption band at 1265 cm<sup>-1</sup> gradually disappears and a new band appears on the lower wave-number side at 1240 cm<sup>-1</sup>. This is explained by H-bonding from methanol to the oxygen in the N-oxide group resulting in a decreased double bond character of the N–O bond. For 2 only a band of medium intensity at 1011 cm<sup>-1</sup> (CH<sub>2</sub>Cl<sub>2</sub>) exhibits a solvent shift effect, gradually decreasing in intensity upon addition of methanol, suggesting this band to have N–O stretching character. The frequency at which the band is observed is close to that for aliphatic amine oxides (950–970 cm<sup>-1</sup>).<sup>9</sup> Less N–O double bond character than expected is consequently suggested. Changes in the IR region below 1000 cm<sup>-1</sup> corresponding to the other N–O absorption found at 840 cm<sup>-1</sup> in pyridine 1-oxide were not observed.<sup>10</sup>

The IR spectrum of 2 does not in itself permit a distinction between an N-oxide or an S-oxide since absorption bands connected with the latter are also observed in the 1000–1100 cm<sup>-1</sup> region for ordinary sulfoxides.<sup>11</sup> Solvent shift effects upon addition of methanol are also found in the spectra of sulfoxides.<sup>12</sup>

ESCA measurements<sup>13</sup> support the contention that the oxide is a 3-oxide. ESCA measurements of the binding energies of the core electrons in 1 and 2 gave the results shown in Table 1. It is seen that there are two signals corresponding to the binding energy of the N(1s) electrons in 2 separated by approximately 4.6 eV. This separation indicates differences in the potential of the N atoms, the most positively charged having the greatest binding energy. The separation and the shift ( $\Delta E$ ), 5.5 eV, between the N(1s) signals in 1 and 2 towards higher

binding energy corresponds to the observed shifts between amines and their N-oxides (4.1–4.2 eV).<sup>14</sup> This is a much greater shift than found for any of the other signals, where  $\Delta E = 0.3$ –0.9 eV. Sulphides and sulfoxides exhibit a shift of 2.4–2.8 eV.<sup>15</sup> The measured shift of 0.75 eV for the S(2p) electrons between 1 and 2 is not consistent with 2 being a sulfoxide.

In an attempt to determine whether the oxide is the 2-, 3- or 4-oxide, the reader is referred to Table 2 where the charges on the pertinent atoms of 1, thiazotriazole 2-, 3- and

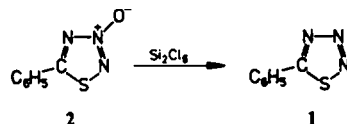
Table 2. Calculated charge of the atoms 1 to 5 in the 5-membered ring in 1 and the 2-, 3- and 4-oxide

|   | 1     | 2-oxide | 3-oxide | 4-oxide |
|---|-------|---------|---------|---------|
| 1 | +0.06 | +0.15   | +0.06   | +0.06   |
| 2 | -0.06 | +0.81   | -0.02   | -0.06   |
| 3 | 0.00  | +0.04   | +0.94   | +0.02   |
| 4 | -0.12 | -0.12   | -0.10   | +0.68   |
| 5 | +0.12 | +0.12   | +0.12   | +0.30   |

4-oxide are calculated according to Paulings method.<sup>14</sup> For the oxides the only canonical form considered is the one with the positive charge localized on the oxidized N atom. For 1 the extreme values of the calculated charges of the N atoms are separated by 0.12 units, and for the 2-, 3- and 4-oxides the calculated charge differences between the two unoxidized N atoms are 0.16, 0.08 and 0.08 units, respectively. For both 1 and 2 the width in half height of the N(1s) signal originating from the two N atoms is identical within experimental error ( $2.5 \pm 0.1$ ) (Table 1). The calculated charges consequently cannot be used to distinguish the site of oxidation. However, the  $\Delta E$  value of the hetero-ring C atom for a 4-oxide should be of the magnitude 1.2–1.7 eV when the difference in calculated charge is 0.18 units.<sup>16</sup> Since the value found (Table 1) is 0.55 eV, a 4-oxide is ruled out. This is in accord with the mass spectral result that 1 has been oxidized at position 3.

**Thermal and chemical properties.** The 3-oxide is a thermally quite stable compound. According to a differential thermal analysis<sup>17</sup> in the solid state, decomposition takes place when the compound is heated to around 185°. The decomposition is accompanied by the generation of a small amount of heat. By contrast ordinary 5-substituted thiazotriazoles decompose at room temperature or on melting with generation of a considerable amount of heat.

Deoxygenation of 2 to thiazotriazole (1) takes place upon treatment with the potent deoxygenation agent hexachlorodisilane:



However, under conditions where ordinary amine oxides and phosphine oxides are readily reduced, 2 releases its oxygen slowly. Thus pyridine 1-oxide as well as triphenyl phosphine oxide are deoxygenated quantitatively in less than 1 hr at room temperature in chloroform solution,<sup>18</sup> but 2 is reduced only to the extent of 57% after 8 days under identical conditions. N-oxide 2 (12%) was recovered from the mixture.

Compound 2 is stable towards the action of dilute mineral acids but decomposes to unidentified products on treatment with a dilute solution of a strong base.

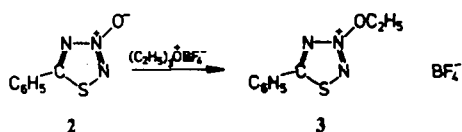
Table 1. Binding energies of the N(1s)-, the S(2p)-, the O(1s)-, the C(1s)- and the Pt(4f<sub>7/2</sub>)-electrons and half width of the N(1s)-signal in 1 and 2. Binding energy shift of the different signals ( $\Delta E$ ) between 1 and 2

| Binding energies<br>eV                 | TTA    | TTA-oxide | $\Delta E$ |
|----------------------------------------|--------|-----------|------------|
| $E_{\text{bind}}(\text{N}(1s))$        | 396.80 | ~402.3*   | ~5.5       |
| $E_{\text{bind}}(\text{N}(1s))$        | 396.80 | 397.70    | 0.90       |
| $E_{\text{bind}}(\text{S}(2p))$        | 161.95 | 162.70    | 0.75       |
| $E_{\text{bind}}(\text{O}(1s))$        |        | 529.20    |            |
| $E_{\text{bind}}(\text{C}(1s))$        |        |           |            |
| Hetero-ring                            | 283.85 | 284.40    | 0.55       |
| $E_{\text{bind}}(\text{C}(1s))$        |        |           |            |
| Phenyl-ring                            | 281.60 | 281.90    | 0.30       |
| $E_{\text{bind}}(\text{Pt}(4f_{7/2}))$ | 74.35  | 74.35     |            |
| Half width of<br>N(1s)-signal          | 2.6    | 2.4*      |            |

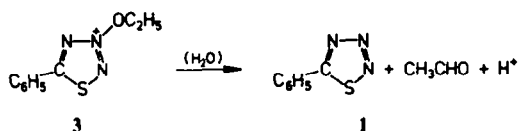
\*The uncertainty is due to less intensity of the signal.

\*The signal at 397.70 eV.

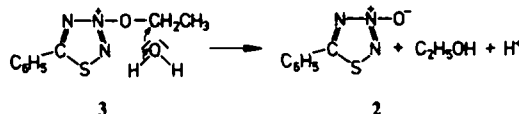
A quaternary salt **3** is formed on treatment of **2** with triethyloxonium tetrafluoroborate:



Characteristic properties of **3** show that alkylation actually takes place on the O atom. Thus a smooth decomposition to **2** is observed on heating slightly above the melting point, 102–103°, or on boiling in toluene for 30 sec. Such behavior under mild conditions is hardly expected of an alkyl ammonium or alkylsulfonium salt. Furthermore, the salt is soluble in water but transformed after a few minutes at room temperature into a mixture of **1** and **2** in almost equal amounts. The thiadiazole (**1**) is formed by a reaction also observed with other alkoxyammonium salts although ordinarily under basic conditions.<sup>7a</sup>



The 3-oxide is apparently the result of a nucleophilic attack of water on the activated carbon of the ethyl group:



**Photolytic properties.** UV spectrum of **2** in ethanol exhibits maxima at 254 ( $\epsilon = 19300$ ) and 320 nm ( $\epsilon = 3000$ ) the latter appearing as a shoulder. On irradiation of **2** in methylene chloride with a low-pressure Hg-lamp, benzonitrile and phenyl isothiocyanate are formed in 65 and 3% yields, respectively. A similar result is obtained on photolysis of **1**.<sup>19</sup> No significant change in the yields are observed when the photolysis is performed under argon. Photolysis in cyclohexane in the presence of Michler's ketone, which act as a triplet sensitizer,<sup>20</sup> show that the major part of the products are formed from the excited singlet state (Experimental).

#### EXPERIMENTAL

Mps were determined in open tubes and are not corrected. The IR spectra were recorded, using a Perkin-Elmer model 337 Grating Infrared Spectrophotometer for the tabulated spectra ( $\pm 5 \text{ cm}^{-1}$  over  $2000 \text{ cm}^{-1}$  and  $\pm 2 \text{ cm}^{-1}$  below  $2000 \text{ cm}^{-1}$ ). Abbreviations used: vs, very strong; s, strong; m, medium; w, weak; sh, shoulder. Very weak absorptions have been omitted. A double focusing mass spectrometer, type AEI-MS 902, operating at 70 eV, was used to obtain the mass spectra. The samples were introduced through the direct insertion probe at an inlet temp. at 110°. Absorption spectra were obtained on a Pye Unicam SP 1800 Ultraviolet Spectrophotometer. ESCA measurements were made on an ES 100 Electron Spectrometer, AEI Scientific Apparatus Ltd. Spectra were run at 15 kV and 18 mA from the X-ray tube and with an entrance split of 100 thous. Measurements were made at -50° at a pressure of about  $10^{-6}$  torr. The sample was dissolved in methylene chloride and a drop of the dilute soln placed on a small platinum plate, which, after evaporation of the solvent, was placed

in the spectrometer. The layer was kept thin enough to make it possible to detect the ejected electrons from the platinum plate.

**5-Phenyl-1,2,3,4-thiadiazole-3-oxide (2).** 5-Phenyl-1,2,3,4-thiadiazole (8.0 g, 45 mmol) in methylene chloride (50 ml) was added to a mixture of trifluoroacetic anhydride (70 ml) and 30%  $\text{H}_2\text{O}_2$  (14 ml) and left for 10 days at room temp. According to TLC analysis almost all thiadiazole had disappeared. The solvent was removed *in vacuo* and the solid, 2.3 g, extracted with ether (3–10 ml) and  $\text{CS}_2$  (3–5 ml). The remaining compound, 1.1 g, is almost pure **2** according to TLC ( $R_f = 0.55$  on silica gel and with light petroleum/benzene/ethanol 3/2/1 as eluent). It was recrystallized from EtOH to yield an analytically pure sample, m.p. 133–4°. (Found: C 47.28; H 2.99; N 23.57; S 18.04. Calc. for  $\text{C}_7\text{H}_5\text{N}_3\text{OS}$ : C 46.93; H 2.81; N 23.46; S 17.90%).

IR spectrum; (KBr), 3020w, 1598w, 1504w, 1438m, 1425s, 1389w, 1339w, 1318w, 1309w, 1287w, 1260m, 1108m, 1029w, 1008m, 994sh, 924w, 841m, 769m, 758sh, 698w, 687m, 682sh, 668w, 616m, 606w; ( $\text{CH}_2\text{Cl}_2$ ), 3054w, 1600w, 1505sh, 1480m, 1464s, 1442m, 1420sh, 1400m, 1318m, 1011m, 923w, 832w. On addition of 10 and 20% MeOH respectively, to the methylene chloride soln a gradual decrease of the  $1011 \text{ cm}^{-1}$  absorption is observed. The mass spectrum of **2** is depicted in Fig. 1. Metastable ions were observed at  $m/e$  124.0, 101.9, 98.9 and 56.1 corresponding to  $\text{M}^+ - \text{NO}$  (calc. 124.0),  $\text{M}^+ - \text{N}_2\text{O}$  (calc. 101.9),  $\text{M}^+ - \text{NS}$  (calc. 98.8), and  $103 - \text{HCN}$  (calc. 56.1). Metastable ions were found by the metastable defocusing technique corresponding to 135-S and 163- $\text{N}_2$ .

**2- $^{15}\text{N}$ -5-Phenyl-1,2,3,4-thiadiazole-3-oxide.** This compound was synthesized from 2- $^{15}\text{N}$ -5-phenyl-1,2,3,4-thiadiazole<sup>2</sup> (80 mg) by the above method. The following mass spectral result was obtained with omission of peaks below 2% of the base peak. Relative intensities in per cent are given in parenthesis: 182(3), 181(7), 180(78), 164(3), 150(13), 135(14), 133(6), 104(6), 103(64), 102(3), 91(2), 77(32), 76(36), 75(12), 74(6), 52(11), 51(28), 50(25), 49(4), 48(2), 47(100), 30(80).

**Deoxygenation of 5-phenyl-1,2,3,4-thiadiazole-3-oxide (2).** **2** (179 mg, 1 mmol) was dissolved in dry chloroform (2 ml) and hexachlorodisilane (180  $\mu\text{l}$ , ca. 1 mmol) was added and the mixture left at room temp. After 8 days the soln was hydrolyzed at 0° with 20% NaOH (3 ml) and the mixture extracted with chloroform (4.5 ml). After drying over  $\text{MgSO}_4$  the solvent was partially removed *in vacuo* and the remaining soln applied on a preparative TLC plate. On development with light petroleum/benzene/ethanol 3/2/1, 5-phenyl-1,2,3,4-thiadiazole and 5-phenyl-1,2,3,4-thiadiazole-3-oxide was obtained and extracted to yield 57% and 12% respectively. Two other minor components were not identified.

**Thermal properties of 5-phenyl-1,2,3,4-thiadiazole-3-oxide.** (a) A soln of **2** (10 mg) in bromobenzene (1 ml, b.p. 156°) was boiled for 2 hr but according to GLC benzonitrile had not been formed and according to TLC only **2** was present. (b) Decomposition was studied in the solid state by means of differential thermal analysis.<sup>17</sup> According to the thermogram decomposition take place from 185 to 240° ( $24^\circ/\text{min}$ ) with maximum heat evolution around 210°.

**Photolysis of 2.** (a) A soln of **2** (5.3 mg) in methylene chloride (1 ml) was photolyzed through quartz with a low pressure Hg-lamp for 5 hr. Through the soln was led a stream of argon and cooling was ensured by a stream of tap water. Benzyl cyanide (3.06 mg) was then added as internal standard and the mixture directly submitted to GLC on a Pye Unicam 104 chromatograph, dual FID, connected to a Varian aerograph 477 electronic integrator, on a 2 m,  $\frac{1}{8}$  in. column with 10% SE-30 on gaschrom Q 100/120 mesh (Applied Science Lab. inc.) and with  $\text{N}_2$  as carrier gas. Yields were calculated on the basis of known amounts of thiadiazole oxide and internal standard from the integrated peaks upon comparison with calibration curves. The yield of benzonitrile and phenyl isothiocyanate was 65 and 3%, respectively. In a similar experiment with oxygen instead of argon bubbled through the soln the yield was 59 and 3%, respectively. (b) Two identical Pyrex-flasks containing two different deoxygenated solutions, (1) and (2), were irradiated evenly with light from a low-pressure Hg-lamp filtered through acetone (330 nm) for 16 hr. Solutions: (1) 4,4'-Bis(dimethylamino)benzophenone (Michler's ketone, triplet

sensitizer,  $E_T = 255 \text{ kJ/mol}$ )<sup>20</sup> (5.3 mg) in cyclohexane (1 ml). (2) 2 (2.8 mg) and Michlers ketone (5.6 mg) in cyclohexane (1 ml). After irradiation methylene chloride (0.5 ml) was added to soln (1) and the mixture submitted to IR spectroscopy. The analysis indicated almost quantitative transformation to the corresponding pinacol. A similar analysis on soln (2) revealed that practically no transformation into pinacol had taken place and a GLC analysis directly on the soln as described in (a) showed that only 6% benzonitrile had been formed. Accordingly triplet energy is transferred effectively from ketone to 2 but the low conversion into products (as compared to (a)) show that the main route for product formation goes via the singlet excited state.

3 - Ethoxy - 5 - phenyl - 1,2,3,4 - thiatrazolium tetrafluoroborate (3). 2 (179 mg, 1 mmol) was dissolved in dry methylene chloride (2 ml) and triethyloxonium tetrafluoroborate (218 mg, 1.2 mmol) was added. After 24 hr at room temp. the solvent was removed *in vacuo* and the residue extracted with dry ether (3.3 ml) leaving 3 as a crude material in high yield, m.p. 83–89°. An analytically pure sample of 3 was obtained on dissolving in acetone, adding ether until turbidity and cooling, m.p. 102–3° (Found: C 36.56; H 3.43; N 14.39. Calc. for  $\text{C}_9\text{H}_{10}\text{N}_3\text{OSBF}_4$ : C 36.66; H 3.42; N 14.25%). Heating slightly above the m.p. or boiling in toluene for 30 sec causes quantitative transformation into 2. 3 is soluble in water but precipitation of a crystalline material is observed after 2–3 min. The ppt was found by means of TLC (silicagel with light petroleum/benzene/ethanol 3/2/1) to consist of equal amounts of 1 and 2. Boiling of 3 in abs EtOH for 30 sec caused complete transformation into 2.

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