Oxidation of Heterocyclic Nitrogen Ylids to Nitro Heterocycles. Comparison of a Sulfilimine and a Phosphine Imine

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Oxidation of 3-amino-4-(4-chlorophenyl)furazan (**1**) with peroxytrifluoroacetic acid (ptfa) gave azoxy(4-chlorophenylfurazan) (**6**) as the major product along with a small amount of 3-(4-chlorophenyl)-4-nitrofurazan (**5**). The dimethylsulfilimine **2** derived from **1** gave near quantitative yields of **5** when subjected to oxidation with either ptfa or *m*-chloroperoxybenzoic acid (mcpba). In contrast, both the trioctylphosphine imine **3** and the triphenylphosphine imine **4** derived from **1** were oxidized by mcpba to give **6** as the exclusive product.

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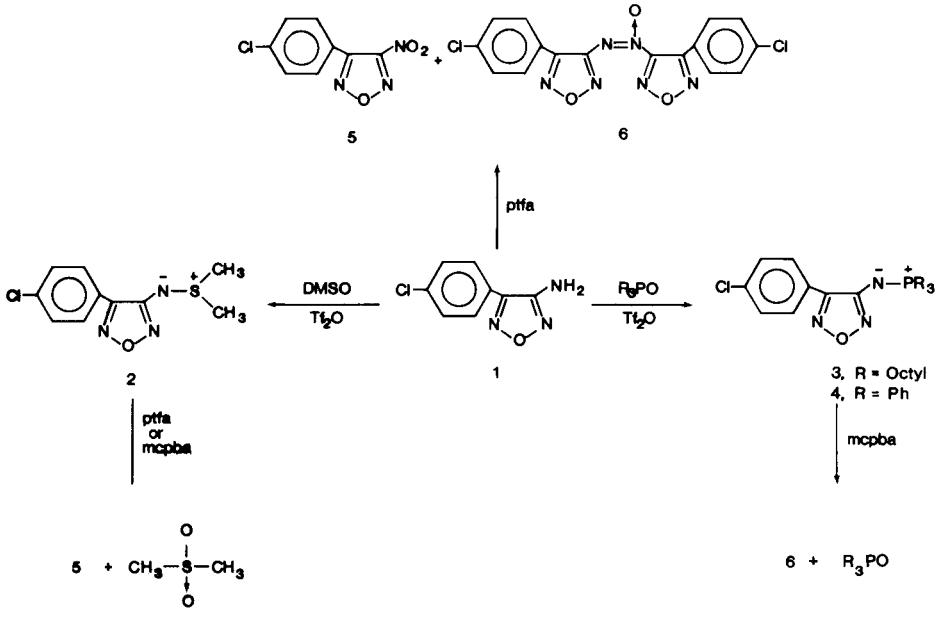
In 1982, Taylor and coworkers reported the conversion of amino heterocycles to nitro heterocycles by a two-stage oxidation of intermediate sulfilimino heterocycles [1]. The sulfilimines were oxidized with *m*-chloroperoxybenzoic acid (mcpba) to the nitroso derivatives, which were treated with ozone to give the nitro compounds. The nitroheterocycles prepared by this method are 1-nitroisoquinoline, 2-nitropyridine, 2-nitropyrimidine, and 2-nitropyrazine. Hartman and Schwering subsequently employed this procedure to prepare some substituted nitropyrazines [2]. A more recent communication from Corey and coworkers describes the ozone oxidation of alkyl phosphine imines to nitroalkanes [3].

Our interest in finding new routes to nitrofurazans led us to compare the oxidation of a sulfilimine and a phosphine imine derived from 3-amino-4-(4-chlorophenyl)furazan (**1**). The sulfilimine, 3-(4-chlorophenyl)-4-dimethylsulfiliminofurazan (**2**), was prepared by treating **1** with dimethyl sulfide ditriflate according to the procedure of Hartman and coworkers [4]. We discovered that the desired phosphine imine, 3-(4-chlorophenyl)-4-trioctylphosphiniminofurazan (**3**), could be prepared analogously by adding **1** to a solution of trioctylphosphine ditriflate, which was obtained by treating trioctylphosphine oxide with triflic anhydride (Tf_2O) in dichloromethane. The corresponding triphenylphosphine imine (**4**) was also prepared by this new method, which is much cleaner and gives higher yields than other methods of preparing phosphine imines from amines [5].

Oxidation of **1** with peroxytrifluoroacetic acid (ptfa) in dichloromethane gave a mixture that was chromatographed to give 3-(4-chlorophenyl)-4-nitrofurazan (**5**) in 11% yield and azoxy(4-chlorophenylfurazan) (**6**) in 32% yield. Under the same conditions, **2** gave a 96% yield of **5** with no trace of **6**. Similar results were obtained when **2** was treated with mcpba. In contrast, **3** was recovered unchanged after treatment with ptfa, but was converted to **6** with no trace of **5** when treated with excess mcpba. In the latter reaction, optimum yields of **6** could be obtained when a ratio of mcpba to **3** of 1.5 was employed. When less per-



acid was used, some unreacted **3** was recovered along with **6**, but the by-product in all cases was trioctylphosphine oxide, exclusive of trioctylphosphine. Both **2** and **3** were found to be resistant to ozonolysis at 0°. Compound **4** gave essentially the same results as **3** when subjected to these oxidation conditions.

The formation of **6** during the oxidation of **1** with ptfa is easily explained by the reaction of the intermediate nitrosofurazan with its precursor, the hydroxylaminofurazan. However, the formation of **6** with no trace of **5** from the oxidation of **3** with mcpba suggests that the nitroso compound is not an intermediate in this reaction, but that a dimeric species may be formed before the nitrogen-phosphorous bonds are ruptured. The failure of **3** to react with ptfa may be the result of irreversible protonation of **3** with trifluoroacetic acid present in the oxidation medium.

The ^{13}C-nmr spectrum of **5** contains a triplet corresponding to the nitro carbon and the ^{14}N-nmr signal of the nitro nitrogen is a sharp singlet with a width at half-height of 17 Hz. Thus, it appears that the nitro ^{14}N is coupled with the nitro ^{13}C in the classical manner with very little quadrupolar coupling, as we reported for 4,4′-dinitro-3,3′-bifurazan-4,4′-^{13}C [6]. This phenomenom allowed us to use ^{14}N-nmr spectroscopy to detect the presence of small amounts of **5** in reaction mixtures.

drawing

The results of this limited study indicate that oxidation of sulfiliminofurazans is a much more efficient method of preparing nitrofurazans than oxidation of the corresponding amines or phosphine imines. However, oxidation of the phosphine imines may be a convenient route to azoxyfurazans.

EXPERIMENTAL

Melting points were determined with a Mettler FP1 apparatus and are corrected. The nmr spectra were recorded on a JEOL-FX90Q spectrometer. Elemental analyses were performed by M. J. Naranjo.

3-(4-Chlorophenyl)-4-dimethylsulfiliminofurazan (**2**).

To a solution of dimethyl sulfoxide (3.0 ml, 0.041 mole) in dichloromethane (150 ml) cooled to −78° was added trifluoromethanesulfonic anhydride (10.0 g, 0.035 mole) dropwise with stirring under argon at such a rate that the temperature did not exceed −70° [4]. To the resulting slurry was added a solution of 3-amino-4-(4-chlorophenyl)furazan (**1**) [7] (5.9 g, 0.030 mole) in dichloromethane (25 ml) and dimethyl sulfoxide (5 ml) at below −70°. The mixture was stirred at −78° for 2 hours and then at −55° for 1 hour. The mixture was transferred to a separatory funnel and extracted with 5% sodium hydroxide solution (60 ml), then with water (50 ml), and the organic layer was dried over magnesium sulfate. The solvent was evaporated under reduced pressure and the residue was washed with water, dried, and recrystallized from aqueous methanol to yield **2** (7.18 g, 94%), mp 111.5°; ^{1}H-nmr (deuteriochloroform): δ 2.87 (s, 6H), 7.38 (d, 2H, J = 8 Hz), 8.17 (d, 2H, J = 8 Hz); ^{13}C-nmr (deuteriochloroform): δ 32.7, 125.8, 128.6, 128.9, 135.5, 147.5, 160.5.

Anal. Calcd. for $C_{10}H_{10}ClN_3OS$: C, 46.97; H, 3.94; N, 16.43. Found: C, 46.92; H, 3.85; N, 16.24.

3-(4-Chlorophenyl)-4-trioctylphosphiniminofurazan (**3**).

To a stirred solution of trioctylphosphine oxide (13.5 g, 0.035 mole) in dichloromethane (100 ml) was added trifluoromethanesulfonic anhydride (10.0 g, 0.035 mole) dropwise under argon at −5°. The resulting mixture was stirred at −5° for 0.5 hours, then a solution of **1** (6.84 g, 0.035 mole) in dichloromethane (50 ml) and acetonitrile (15 ml) was added dropwise below 0°. The mixture was stirred at −5° for 3 hours, then at ambient temperature overnight. The solution was extracted with saturated sodium carbonate solution (2 × 50 ml), then with water, and dried over magnesium sulfate. The solvent was evaporated under reduced pressure and the residue was dried under high vacuum (0.01 torr) to yield 18.4 g (93%) of **3** as a viscous oil that failed to crystallize; ^{1}H-nmr (deuteriochloroform): δ 0.83 (t, 9H, J = 2 Hz), 1.23 (bs, 36 H), 1.73-2.18 (m, 6H), 7.32 (d, 2H, J = 9 Hz), 8.28 (d, 2H, J = 9 Hz); ^{13}C-nmr (deuteriochloroform): δ 13.9, 21.8, 22.5, 23.0, 25.7, 28.9, 30.5, 31.1, 31.6, 126.7, 128.4, 128.8, 135.1, 147.8 (d, J = 15 Hz), 158.8 (d, J = 5 Hz).

Anal. Calcd. for $C_{32}H_{55}ClN_3OP$: C, 68.12; H, 9.83; N, 7.45. Found: C, 68.26; H, 9.89; N, 7.23.

3-(4-Chlorophenyl)-4-triphenylphosphiniminofurazan (**4**).

This compound was obtained in 92% yield by using triphenylphosphine oxide instead of trioctylphosphine oxide in the previous procedure [8]. The product crystallized from aqueous ethanol, mp 64-65°; ^{1}H-nmr (deuteriochloroform): δ 7.33-8.04 (m, 17 H), 8.45 (d, 2H, J = 8 Hz); ^{13}C-nmr (deuteriochloroform): δ 126.0, 126.6, 128.5, 128.9, 130.5, 131.8, 132.6, 133.0, 135.3, 148.8 (d, J = 20 Hz), 157.6 (d, J = 5 Hz).

Anal. Calcd. for $C_{26}H_{19}ClN_3OP$: C, 68.50; H, 4.20; N, 9.22. Found: C, 68.51; H, 4.54; N, 8.98.

Oxidation of 3-Amino-4-(4-chlorophenyl)furazan (**1**).

To a slurry of 90% hydrogen peroxide (0.70 ml, 0.025 mole) in dichloromethane (20 ml) was added trifluoroacetic anhydride (4.0 ml, 0.028 mole) with stirring and ice cooling below 10°. After the exotherm had subsided, **1** (0.98, 0.005 mole) was added at 0°. The resulting solution was heated under reflux for 1.5 hours, cooled, and cautiously treated with saturated sodium carbonate solution until the aqueous layer was basic to litmus. The layers were separated and the organic layer was washed with 5% sodium bisulfite solution, then with water, and dried over magnesium sulfate. Evaporation of the solvent under reduced pressure left a residue that was chromatographed over silica gel with 1:1 chloroform/hexane. The first fraction eluted contained 0.12 g (11%) of 3-(4-chlorophenyl)-4-nitrofurazan (**5**), a yellow oil that failed to crystallize; ^{1}H-nmr (deuteriochloroform): δ 7.49 (d, 2H, J = 9 Hz), 7.66 (d, 2H, J = 9 Hz); ^{13}C-nmr (deuteriochloroform): δ 120.2, 129.7, 130.4, 138.6, 148.3, 158.6 (t, J = 17 Hz); ^{14}N-nmr (deuteriochloroform/ammonia ext): δ 349.5.

Anal. Calcd. for $C_8H_4ClN_3O_3$: C, 42.59; H, 1.79; N, 18.63. Found: C, 42.35; H, 2.28; N, 18.44.

A second fraction containing 0.32 g (32%) of azoxy(4-chlorophenylfurazan) (**6**) was collected, mp 143°; ^{1}H-nmr (DMSO-d_6): δ 7.35-7.86 (m); ^{13}C-nmr (DMSO-d_6): δ 121.6, 122.2, 128.6, 128.9, 130.0, 131.4, 136.3, 136.5, 149.4, 150.8, 152.5, 158.5.

Anal. Calcd. for $C_{16}H_8Cl_2N_6O_3$: C, 47.66; H, 2.00; N, 20.84. Found: C, 47.59; H, 2.42; N, 20.58.

Oxidation of 3-(4-Chlorophenyl)-4-dimethylsulfiliminofurazan (**2**).

A.

A solution of **2** (1.28 g, 0.005 mole) in dichloromethane (5 ml) was added dropwise to a solution of peroxytrifluoroacetic acid (0.025 mole), prepared as described for the oxidation of **1**, with stirring at 0-5°. The resulting solution was heated under reflux until the color changed from green to yellow, then it was worked up as described for the oxidation of **1**, except that the final organic phase was washed repeatedly with water (5 × 20 ml) to remove dimethyl sulfone. After drying the solution over magnesium sulfate, the solvent was evaporated under reduced pressure to leave 1.08 g (96%) of pure **5**, identical in all respects (tlc, nmr) with that obtained from the oxidation of **1**.

B.

To a solution of purified *m*-chloroperoxybenzoic acid [9] (1.03 g, 0.006 mole) in 1,2-dichloroethane (15 ml) was added a solution of **2** (0.25 g, 0.001 mole) in 1,2-dichloroethane (2 ml) dropwise with stirring and ice cooling. After the mildly exothermic reaction had subsided, the mixture was heated under reflux until its color changed from green to yellow. The mixture was cooled to 0° and filtered to remove *m*-chlorobenzoic acid. The solution was extracted with 2.5% sodium hydroxide solution (2 × 20 ml), then with water (5 × 20 ml), and dried over magnesium sulfate. Evaporation of the solvent under reduced pressure left 0.20 g (90%) of pure **5**.

Oxidation of 3-(4-Chlorophenyl)-4-trioctylphosphiniminofurazan (**3**).

A solution of **3** (2.82 g, 0.005 mole) in 1,2-dichloroethane (25 ml) was added to a solution of purified *m*-chloroperoxybenzoic acid [9] (2.59 g, 0.015 mole) in 1,2-dichloroethane (75 ml) with stirring and ice cooling at 0-5°. The mixture was heated under reflux for 2 hours, cooled, and filtered. The solution was extracted with 2.5% sodium hydroxide solution (2 × 50 ml), then with water (50 ml), and dried over magnesium sulfate. The solvent was removed on the rotary evaporator under reduced pressure, the residue was dissolved in boiling ethanol (50 ml) and the solution chilled in the freezer to yield 0.60 g (60%) of pure **6**, identical in all respects (tlc, nmr, ir) with that obtained from the oxidation of **1**. Analysis by tlc and ^{14}N-nmr failed to detect any **5** in the crude product. Similar results were obtained when **4** was subjected to this reaction.

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