Ion Radicals. 40. Formation of 10-Phenylphenothiazine 5-Oxide and Nitro-10-phenylphenothiazine 5-Oxides by Reaction of 10-Phenylphenothiazine Cation Radical Perchlorate with Nitrite Ion (1,2)

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The reaction of 10-phenylphenothiazine cation radical (**1**) with nitrite ion leads not only to 10-phenylphenothiazine 5-oxide (**2**) but also to 3-nitro-10-phenylphenothiazine 5,5-dioxide (**4**), and two dinitro-10-phenylphenothiazine 5-oxides (**5** and **6**). The products (**3-6**) appear to be formed from the nitration of **2** by nitrogen dioxide, the nitrogen dioxide arising from the reaction of nitric oxide (formed along with **2** when **1** reacts with nitrite anion) and oxygen.

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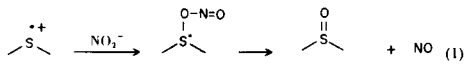
The "nitration" of a small number of aromatics by reaction of their cation radicals with nitrite ion has been reported earlier. Ristagno and Shine found that perylene cation radical gave 3-nitroperylene, and that perylene and pyrene could be nitrated, presumably through their cation radicals as intermediates, by reaction with iodine and silver nitrite (3). This technique was later applied to some metalloporphyrins by Barnett and Smith (4). *N*-ethylcarbazole (5), dibenzodioxin (6), and phenothiazine (7) cation radicals also led to the mononitro aromatics. In contrast with the last, thianthrene cation radical led quantitatively to thianthrene 5-oxide, and it was shown by use of ^{18}O-labelled nitrite ion that the oxygen atom in the thianthrene 5-oxide came from the nitrite ion (7). A similar reaction occurs with phenoxathiin cation radical (8). Formation of the 5-oxide was interpreted as occurring by homolysis of an intermediate 5-nitrite (equation 1)

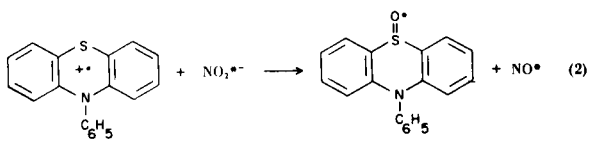


(1)

(7). We have now found that 10-phenylphenothiazine cation radical (**1**) perchlorate reacts with nitrite ion in acetonitrile solution to give a mixture of 10-phenylphenothiazine 5-oxide (**2**, 40%), 3-nitro-10-phenylphenothiazine 5-oxide (**3**, 37%), 3-nitro-10-phenylphenothiazine 5,5-dioxide (**4**, 3%) and two dinitro-10-phenylphenothiazine 5-oxides (**5**, 5.6%, and **6**, 1.8%). The location of the nitro groups in **5** and **6** has not been established; we presume that one of these isomers is the 3,7-, while the other may be the 3,8-dinitro compound. Neither 10-phenylphenothiazine (**7**) nor 3-nitro-10-phenylphenothiazine (**8**) was found.

When reaction was carried out in the presence of urea, 82% of **2** was obtained, and none of the other compounds (**3-8**) was found, although tlc of the crude product showed the presence of small amounts of three other components. Similarly, reaction of **1** with nitrite ion in a solution being continuously purged of oxygen by a rapid stream of nitrogen gave 82% of **2**.

Our understanding of these results is that **1** reacts first with nitrite ion according to equation 1. Unless the solution is free of oxygen the nitric oxide formed is converted into nitrogen dioxide and this nitrates the first product, **2**, with the eventual formation of the products **3-6**. Evidence in support of this understanding was obtained by using ^{18}O-labelled nitrite ion. In this case, both of the products **2*** and **3*** were found, by mass spectro-



(2)

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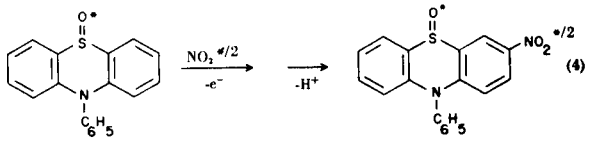

(4)

metry, to contain ^{18}O in the amounts anticipated from equations 2-4.

The use of a vigorous purge of nitrogen gas in the earlier experiments not only removed oxygen from the system but also carried away the nitric oxide, thus preventing nitration by nitrogen dioxide from occurring. Addition of urea to the reaction mixture caused the trapping of nitrogen dioxide and also prevented nitration from occurring.

That nitric oxide in unpurged solution will nitrate **2** was demonstrated separately. When one equivalent of nitric oxide (measured by volume at ambient temperature and pressure) was placed in a solution of **2** that had been purged with nitrogen for 30 minutes, 85% of **2** and 6% of **3** were recovered. When nitric oxide was bubbled into an unpurged solution of **2** for 15 seconds only **2** and **3** were detectable by tlc. Continued bubbling of nitric oxide for 5 minutes, however, led to the formation of 28% of **3**, 5% of **4**, 16% of **5** and 59% of **6**.

Reaction of **2** directly with a small excess (60%) of nitrogen dioxide in acetonitrile led to a 7% recovery of **2** and 70% of **3**, 5% of **4**, 0.8% of **5**, and 3% of **6**. When an unmeasured flow of nitrogen dioxide was allowed to bubble into a solution of **2** for 2 minutes 34% of **3** was obtained, along with 4% of **4**, 8% of **5**, m.p. 241-243.5°, and 55% of **6**, m.p. 239-241.5°. Although **5** and **6** were separable by tlc we were unable to distinguish them by nmr. Each had parent peak m/e of 381.

Reaction of **2** for 5 minutes with sodium nitrite in acetonitrile containing a small amount of 70% perchloric acid led to recovery of 88% of the **2**, indicating that nitrous acid was not involved in the nitration reactions when **1** was used.

These experiments and our earlier results illustrate, therefore, the variability in reactions of cation radicals with nitrite ion, the present results arising from the considerable susceptibility of 10-phenylphenothiazine 5-oxide to nitration by nitrogen dioxide.

EXPERIMENTAL

10-Phenylphenothiazine cation radical (**1**) perchlorate was prepared as described earlier (9).

Reaction of **1** with Potassium Nitrite.

(a) To a solution of 280 mg. (0.746 mmole) of **1** perchlorate in 8 ml. of acetonitrile was added 800 mg. of potassium nitrite. The suspension was stirred for 15 minutes, during which time the color of **1** disappeared quickly, and poured onto water. Extraction with dichloromethane gave 235 mg. of solids. This was streaked as a concentrated solution in dichloromethane onto a number of silica gel (Merck GF-254) tlc plates, which were developed with ether. Five bands were removed from each plate and the contents of each band were removed with acetone and identified by the parent peak in the mass spectrum and/or nmr spectrum (Varian XL-100). The bands gave in order of decreasing R_f: 7 mg. (0.02 mmole, 3%) of (assumed) **4**, m/e 352; 16 mg. (0.04 mmole, 5.6%) of **5**, m/e 381; 93 mg. (0.27 mmole, 37%) of **3**, m.p. 230-231° (from ethyl acetate-petroleum ether), lit. m.p. 223.5-224.5° (10), m.p. 228-229° for **3** prepared according to lit. method (10); m/e: 336; pmr (perdeuterioacetone): in agreement with the structure of **3**; 87 mg. (0.30 mmole, 40%) of **2**, m.p. 172-173° (same solvent), lit. m.p. 172-173° (11); m/e: 291; and, at the origin, 5.0 mg. (0.013 mmole, 1.8%) of **6**; m/e: 381. Repetition of this experiment gave 42% of **2** and 39% of **3**.

(b) A similar experiment with 250 mg. (0.66 mmole) of **1** perchlorate and 500 mg. (8.33 mmoles) of urea in 15 ml. of acetonitrile and 1 g. of potassium nitrite gave 178 mg. of crude product. This was treated as above, giving 157 mg. (0.539 mmole, 81.6%) of **2**, m.p. 172-173°, mixed melting point with authentic **2** undepressed.

(c) The potassium nitrite (1 g.) was added under nitrogen to a solution of 375 mg. (1.0 mmole) of **1** perchlorate in 30 ml. of acetonitrile. After stirring under nitrogen for 2 minutes nitrogen was bubbled in vigorously for about 5 minutes, after which the solution was worked up as before, giving 238 mg. (0.817 mmole, 82%) of **2**, m.p. 172-173° (from ethyl acetate-petroleum ether).

(d) Reaction was carried out as in (a), but with the use of ^{18}O-labelled potassium nitrite, prepared earlier by J. J. Silber (7), and found to contain 1.3 atom-% of ^{18}O. After isolation of **2** and **3** the ratio M+2/m was measured (12), and found to be 7.7% for **2** (Calcd: (13) 7.8%), and 9.6% (Calcd: (13) 9.4%) for **3**.

Reaction of **2** with Nitric Oxide.

(a) Nitric oxide was bubbled for 15 seconds into a solution of 149 mg. (0.51 mmole) of **2** in 10 ml. of acetonitrile. Tlc showed only two spots corresponding with **2** and **3**. The nitric oxide was then bubbled continuously for 5 minutes, after which the solution was worked up as described above, but with 3:1 ether:petroleum ether as developer, giving in decreasing order of R_f: 9 mg. (0.02 mmole, 5%) of (assumed) **4**; m/e: 352; 31 mg. (0.081 mmole, 16%) of **5**; m/e: 381; 48 mg. (0.14 mmole, 28%) of **3**, m.p. 228-230°; and, at the origin, 115 mg. (0.301 mmole, 59.0%) of **6**; m/e: 381.

(b) A solution of 2.04 g. (7.01 mmoles) of **2** in 30 ml. of acetonitrile was purged vigorously with nitrogen. Next, nitrogen was used to carry into the acetonitrile solution, from an attached bulb, a previously prepared aliquot of 7 mmoles of nitric oxide. The solution was stirred 30 minutes and again purged vigorously with nitrogen and stirred for 1 hour more. After work-up 1.73 g. (5.94 mmoles, 85%) of **2** was recovered along with 140 mg. (0.416 mmole, 6%) of **3**.

Reaction of **2** with Sodium Nitrite and Perchloric Acid.

To a solution of 233 mg. (0.800 mmole) of **2** in 25 ml. of acetonitrile was added 1 g. of sodium nitrite. After stirring the suspension for 5 minutes 1 drop of 70% perchloric acid was added. A red-brown color appeared immediately. After 5 minutes an excess of solid potassium iodide was added and the mixture was poured onto water. Work-up gave 205 mg. (0.704 mmole, 88%) of recovered **2**, m.p. 172-173°, and 8 mg. of an unidentified compound. None of **3** was found.

Reaction of **2** with Nitrogen Dioxide.

(a) The nitrogen dioxide gas (117 mg., 2.54 mmoles), in a tared flask, was carried by a slow flow of nitrogen into a solution of 450 mg. (1.55 mmoles) of **2** in acetonitrile. After stirring for 30 minutes the solution was worked up and the products were separated on silica gel plates, giving 29 mg. (0.082 mmole, 5.3%) of **4**, 5 mg. (0.013 mmole, 0.84%) of **5**, 364 mg. (1.08 mmoles, 70%)

of **3**, m.p. 230-231° (from ethyl acetate), 30 mg. (0.103 mmole, 6.6%) of **2**, and 18 mg. (0.047 mmole, 3%) of **6**.

(b) When nitrogen dioxide was allowed to bubble vigorously for 2 minutes into a solution of 160 mg. (0.55 mmole) of **2** in 6 ml. of acetonitrile, work up gave none of **2**, 65 mg. (0.193 mmole, 34%) of **3**, 9 mg. (0.025 mmole, 4%) of **4**, 16 mg. (0.042 mmole, 8%) of **5**, and 115 mg. (0.302 mmole, 55%) of **6**.

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