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Nitro-heterocycles, particularly those containing halogen, were selectively reduced with sodium sulfide in aqueous *p*-dioxane to give the corresponding amino-heterocycles in 70-89% yields.

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Sulfides are largely used in technical process for the reduction of nitro-compounds; among them, sodium sulfide is the least expensive reagent. However, the reduction of nitro-compounds with sodium sulfide often results in low yields together with side products (1-3). Therefore, sodium sulfide is often converted into sodium hydrogen sulfide (4,5), ammonium sulfide (6), or sodium polysulfide (7) before the reduction.

The reduction of *m*-dinitrobenzene with sodium pentasulfide, sodium hydrogen sulfide, or ammonium sulfide in water gave *m*-nitroaniline, respectively, in 100, 94, or 80% yield, while the reduction with sodium sulfide gave mainly *m*-dinitroazoxybenzene (1). This observation was explained in terms of their differences in hydrolysis to give hydroxyl ions. The presence of hydroxyl ions favors the formation of azoxy compounds. The degree of hydrolysis of sodium hydrogen sulfide, ammonium sulfide, sodium pentasulfide, and sodium sulfide in water is, respectively, 0.15, < 1, 5.7, and 86.4% (1). It was conceivable that the hydrolysis of sodium sulfide could be reduced by addition of a water-miscible organic solvent with low dielectric constant such as *p*-dioxane (dielectric constant 2.21 at 25°) into the reaction mixture, and that the reduction of *m*-dinitrobenzene with sodium sulfide in aqueous *p*-dioxane could eliminate the formation of *m*-dinitroazoxybenzene. Indeed, the reduction of *m*-dinitrobenzene with sodium sulfide in 67% aqueous *p*-dioxane gave pure *m*-nitroaniline in 89% yield (8). We now report an application of this finding to the selective reduction of nitro-heterocycles.

The selective reduction of the nitro group in I with sodium sulfide in 50% aqueous *p*-dioxane at 80° gave the aminoquinoxaline II in 81% yield. Likewise, selective reductions of nitro-1,2,4-triazoles III, nitro-thiazoles V, and nitro-1,2,4-oxadiazoles VII gave, respectively, amino-1,2,4-triazoles IV, amino-thiazoles VI, and amino-1,2,4-oxadiazoles VIII in 70-89% yields (Table). It is pertinent to note that aqueous *p*-dioxane is a good medium for dissolving nitro-heterocycles.

The catalytic hydrogenation of I with 10% palladium on charcoal in *p*-dioxane gave a mixture of II and the dechlorinated aminoquinoxaline IX (9). The hydrogenations of VII a & b with 10% palladium on charcoal in

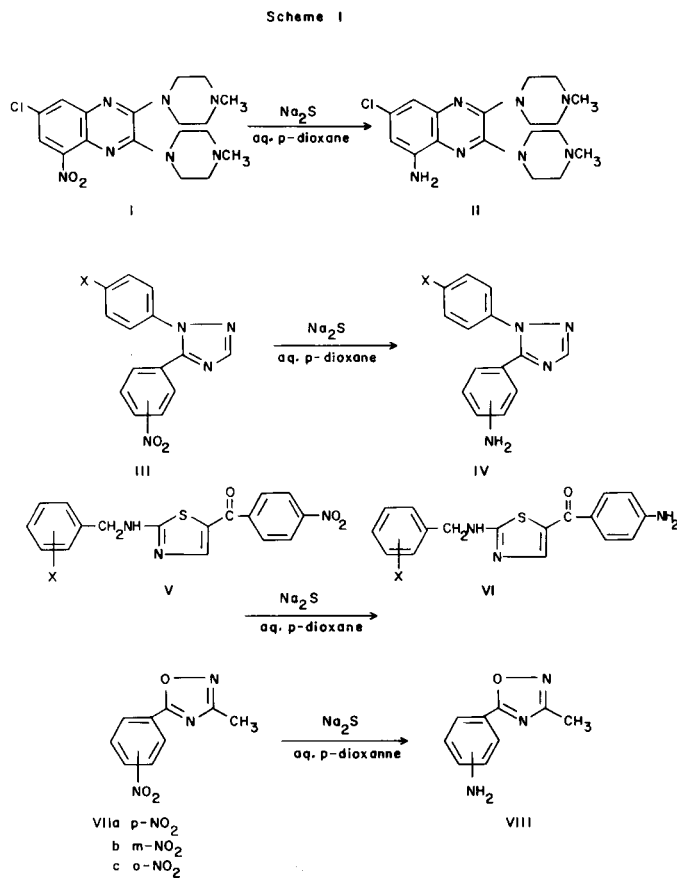
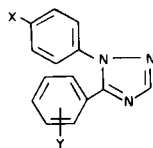
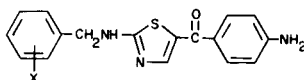


Table  
Substituted 1,2,4-Triazoles



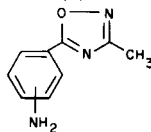
Compound No.	X	Y	M.p. °C	Yield, %	Formula	Analysis, %			
IVa	H	<i>p</i> -NH <sub>2</sub>	178-180	89	C <sub>14</sub> H <sub>12</sub> N <sub>4</sub>	Calcd. C, 71.2	H, 5.12	N, 23.7	
						Found C, 71.3	H, 5.31	N, 23.8	
IVb	F	<i>p</i> -NH <sub>2</sub>	133-135	83	C <sub>14</sub> H <sub>11</sub> FN <sub>4</sub>	Calcd. C, 66.1	H, 4.36	N, 22.0	F, 7.47
						Found C, 66.0	H, 4.48	N, 22.0	F, 7.50
IVc	Cl	<i>p</i> -NH <sub>2</sub>	150-152	80	C <sub>14</sub> H <sub>11</sub> ClN <sub>4</sub>	Calcd. C, 62.1	H, 4.10	N, 20.7	Cl, 13.1
						Found C, 61.8	H, 4.04	N, 20.8	Cl, 13.3
IVd	Cl	<i>m</i> -NH <sub>2</sub>	103-105	75	C <sub>14</sub> H <sub>11</sub> ClN <sub>4</sub>	Calcd. C, 62.1	H, 4.10	N, 20.7	Cl, 13.1
						Found C, 62.1	H, 4.35	N, 20.9	Cl, 13.3
IVe	Br	<i>p</i> -NH <sub>2</sub>	130-132	74	C <sub>14</sub> H <sub>11</sub> BrN <sub>4</sub>	Calcd. C, 53.3	H, 3.52	N, 17.8	Br, 25.4
						Found C, 53.1	H, 3.49	N, 17.8	Br, 25.2

Substituted Thiazoles



Compound No.	X	M.p. °C	Yield, %	Formula	Analysis, %				
VIa	<i>p</i> -F	188-190	82	C <sub>17</sub> H <sub>14</sub> FN <sub>3</sub> OS	Calcd. C, 62.4	H, 4.31	N, 12.8	F, 5.80	S, 9.79
					Found C, 62.5	H, 4.36	N, 12.6	F, 5.95	S, 9.73
VIb	<i>o</i> -Cl	180-182	76	C <sub>17</sub> H <sub>14</sub> ClN <sub>3</sub> OS	Calcd. C, 59.4	H, 4.11	N, 12.2	Cl 10.3	S, 9.33
					Found C, 59.2	H, 4.18	N, 11.9	Cl 10.1	S, 9.21

Substituted 1,2,4-Oxadiazoles



Compound No.	NH <sub>2</sub>	M.p. °C	Yield, %	Formula	Analysis, %		
VIIIa	<i>p</i>	186-188	89	C <sub>9</sub> H <sub>9</sub> N <sub>3</sub> O	Calcd. C, 61.7	H, 5.18	N, 24.0
					Found C, 61.6	H, 5.32	N, 24.0
VIIIb	<i>m</i>	101-103	70	C <sub>9</sub> H <sub>9</sub> N <sub>3</sub> O	Calcd. C, 61.7	H, 5.18	N, 24.0
					Found C, 62.0	H, 5.36	N, 24.1
VIIIc	<i>o</i>	119-121	87	C <sub>9</sub> H <sub>9</sub> N <sub>3</sub> O	Calcd. C, 61.7	H, 5.18	N, 24.0
					Found C, 61.4	H, 5.17	N, 24.0

ethanol gave the ring-opened products X a & b in 62-81 % yields. However, the hydrogenation of VIIC under the same reaction conditions gave the quinazolinone XI in 70% yield. The catalytic ring-opening of 1,2,4-oxadiazoles has been previously reported (10,11).

Evidently, sodium sulfide in aqueous *p*-dioxane is a convenient and effective reagent for the selective reduction of nitro-heterocycles particularly those containing halogen.

## EXPERIMENTAL

All melting points were taken on a Mel-Temp apparatus. Pmr spectra were obtained on a Varian Model HA-100 spectrometer; chemical shifts ( $\delta$ ) are in ppm relative to internal tetramethylsilane. Infrared spectra were obtained in Perkin-Elmer Model 21. Substituted nitroquinoxaline 1 (12), nitro-1,2,4-triazoles III (13), nitrothiazoles V (14), and nitro-1,2,4-oxadiazoles VII (13), were synthesized by the reported methods. 5-Amino-7-chloro-2,3-bis(4-methyl-1-piperazinyl)quinoxaline (II). Typical procedure for II, IV, VI, and VIII.

To a solution of 100 g. (0.246 mole) of 7-chloro-2,3-bis(4-methyl-1-piperazinyl)-5-nitroquinoline (I) in 600 ml. of *p*-dioxane at 80°, was added a hot solution (75°) of 136 g. (0.566 mole) of sodium sulfide nonahydrate in 600 ml. of water. The reaction mixture was stirred at 80° for 45 minutes. After being diluted with 600 ml. of water, the reaction mixture was stored at 4° for 16 hours and deposited 75.0 g. (81%) of II as tan crystals, m.p. 237-239°. Recrystallization of a 10.0 g. portion from aqueous ethylene glycol monomethyl ether gave 8.0 g. of II as yellow crystals, m.p. 237-240°; pmr (DMSO-*d*<sub>6</sub>): δ 2.26 (s, 6H), 3.2-3.7 (m, 16H), 5.78 (bp, 2H), 6.57 (d, J = 1.0 Hz, 1H), 6.74 (d, J = 1.0 Hz, 1H). *Anal.* Calcd. for C<sub>18</sub>H<sub>26</sub>ClN<sub>7</sub>: C, 57.50; H, 6.97; N, 26.10; Cl, 9.43. Found: C, 57.30; H, 6.73; N, 26.00; Cl, 9.53.

*p*-Amino-*N*-(1-aminoethylidene)benzamide (Xa).

A mixture of 7.0 g. of 3-methyl-5-(*p*-nitrophenyl)-1,2,4-oxadiazole (VIIa) and 0.5 g. of 10% palladium on charcoal in 170 ml. of ethanol was hydrogenated at room temperature with a Parr shaker with an initial pressure of 40 psi of hydrogen for 40 minutes. During this time a total of 12 psi of hydrogen was absorbed. The reaction mixture was filtered. After removal of the ethanol, the oily residue was crystallized from chloroform/hexane to give 4.7 g. (81%) of Xa as colorless crystals; m.p. 112-114°; ms: M<sup>+</sup> at m/e 177 (Calcd. for C<sub>8</sub>H<sub>11</sub>N<sub>3</sub>O, 177.20); pmr (DMSO-*d*<sub>6</sub>): δ 2.00 (s, 3H), 5.58 (s, 2H), 6.52 (d, J = 4.0 Hz, 2H), 7.80 (d, J = 4.0 Hz, 2H), 8.32 (bp, 1H), 9.52 (bp, 1H).

*Anal.* Calcd. for C<sub>8</sub>H<sub>11</sub>N<sub>3</sub>O: C, 61.00; H, 6.26; N, 23.70. Found: C, 61.00; H, 6.23; N, 23.80.

*m*-Amino-*N*-(1-aminoethylidene)benzamide (Xb).

3-Methyl-5-(*m*-nitrophenyl)-1,2,4-oxadiazole (7.0 g., VIIb) was hydrogenated according to the procedure described for Xa to give 1.6 g. (62%) of Xb as colorless crystals, m.p. 116-118°.

*Anal.* Calcd. for C<sub>8</sub>H<sub>11</sub>N<sub>3</sub>O: C, 61.00; H, 6.26; N, 23.70. Found: C, 61.10; H, 6.19; N, 23.80.

2-Methyl-4(3H)quinazolinone (XI) (15).

A mixture of 7.0 g. of 3-methyl-5-(*o*-nitrophenyl)-1,2,4-oxadiazole (VIIc) and 0.5 g. of 10% palladium on charcoal in 170 ml. of ethanol was hydrogenated at room temperature with a Parr shaker with an initial pressure of 30 psi of hydrogen for 54 minutes. During this time a total of 12 psi of hydrogen was absorbed. The reaction mixture was filtered.

After removal of the ethanol, the residue was recrystallized from ethanol to give 3.8 g. (70%) of XI as colorless crystals, m.p. 238.5° (literature m.p. 235°); ms: M<sup>+</sup> at m/e 160 (Calcd. for C<sub>8</sub>H<sub>8</sub>N<sub>2</sub>O, 160.17).

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