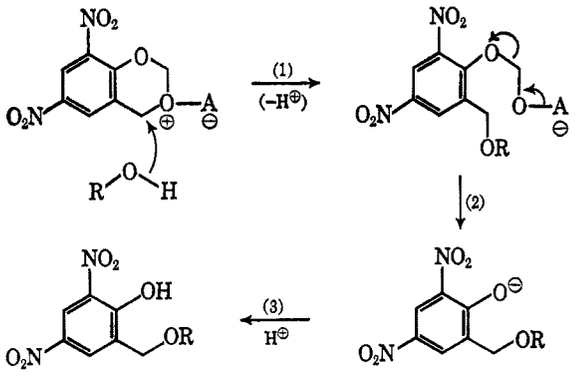
SCHEME I



Lewis acid. Elimination of formaldehyde from this system (step 2) is evidently dependent upon the formation of the dinitrophenoxide anion. In the absence of the second nitro group, the corresponding *p*-nitrophenoxide anion is considerably less stable as reflected by the fact that 4-nitrophenol is over a 1000-fold less acidic than 2,4-dinitrophenol. This difference in anion stability is so significant that step 2 of the mechanistic pathway is precluded in the mononitro case, and the reverse of step 1 occurs. The proposed mechanism also accounts for the lack of reactivity of sterically hindered alcohols; such attack would perforce create a severe 1,2 interaction with the Lewis acid.

Experimental Section[4]

The 6,8-dinitro-1,3-benzodioxane used as a starting material for this work was prepared according to the method of Chattaway and Irving.[1]

Procedure A is typical of that used to prepare the 2-alkoxymethyl-4,6-dinitrophenols at atmospheric pressure and was also used in the examination of the various Lewis acids as catalysts. Those reactions which were performed under pressure are typified by procedure B.

2-Butoxymethyl-4,6-dinitrophenol. A.—A mixture of 4.5 g (0.02 mol) of 6,8-dinitro-1,3-benzodioxane and 0.2 g of zinc chloride in 40 ml of butanol was stirred and heated to reflux for 24 hr. The resulting solution was chilled (ice bath) and treated with a few drops of water. The yellow platelets which crystallized were collected by suction filtration. Additional product was obtained from the filtrate by the addition of 20 ml of methanol followed by sufficient water to induce crystallization. The combined solids weighed 4.5 g (83% yield) and had mp 48–49°. Recrystallization from aqueous methanol gave an analytical sample.

2,4-Dinitro-6-isopropoxymethylphenol. B.—A 300-ml stainless steel microshaker autoclave was charged with 22.6 g (0.10 mol) of 6,8-dinitro-1,3-benzodioxane, 200 ml of isopropyl alcohol, and 1.0 ml of boron trifluoride etherate. The vessel was purged with nitrogen, then shaken, and heated to 140° for 3 hr. When the vessel had cooled to room temperature, the solution was collected and chilled (ice bath). The resulting tan solid was washed with water and had mp 86–87°. This product was dissolved in boiling methanol and the hot solution was decolorized with charcoal. Treatment of the yellow solution with a few drops of water induced crystallization and gave 25.3 g (99% yield) of analytically pure yellow platelets.

2-Benzylthiomethyl-4,6-dinitrophenol.—A mixture of 22.6 g (0.10 mol) of 6,8-dinitro-1,3-benzodioxane, 24.8 g (0.20 mol) of benzyl mercaptan, 1.0 ml of boron trifluoride etherate, and 225 ml of xylene was stirred and heated to 140° for 24 hr. The reaction mixture was cooled to precipitate 5.0 g of unreacted benzodioxane. The solution was then extracted with three 100-ml portions of 1 *M* sodium hydroxide and the combined aqueous extracts were chilled and acidified to pH 2 with 6 *N* hydrochloric acid. A black oil formed which was dissolved in boiling methanol and the solution was decolorized with charcoal. Chilling the red solution followed by the addition of water gave 2.8 g (11% yield) of yellow product, mp 127–129°. Two recrystallizations (first from aqueous ethanol, then from aqueous methanol) failed to change the melting point of the product.

Anal. Calcd for $C_{14}H_{12}N_2O_5S$: C, 52.47; H, 3.77; N, 8.79; S, 10.01. Found: C, 52.95; H, 4.00; N, 8.94; S, 10.31.

2,4-Dinitro-6-ethoxymethylphenol. A.—Boron trifluoride etherate catalysis and 48 hr at 78° gave a 4% conversion into product. The same procedure with sulfuric acid catalysis and 168 hr at reflux gave a 54% yield of product.

B.—After 9 hr at 130° in an autoclave a 67% yield of product was realized.

C.—A well-stirred solution of 11.3 g (0.05 mol) of 6,8-dinitro-1,3-benzodioxane, 50 ml of ethanol, and 0.5 ml of sulfuric acid in 50 ml of *p*-dioxane was heated to reflux for 30 hr. The solution was chilled and treated with 50 ml of water to give 5.0 g (41% yield) of product.

Registry No.—I, 16607-27-5; III, 2544-94-7; IV, 16607-29-7; V, 16607-30-0.

Acknowledgement.—The authors express their thanks to Dr. R. C. Rittner and his staff for the analytical data, to W. W. Harple and his staff for the infrared spectra, and to G. D. Vickers for his nmr work.

(4) All melting points are uncorrected. Melting points were determined on a Mel-Temp capillary melting point apparatus. Infrared spectra were obtained on a Perkin-Elmer Model 137 spectrophotometer; the nmr spectrum was run in deuteriochloroform solution with tetramethylsilane as an internal standard on a Varian A-60 spectrometer.

Ring-Fused *meso* Ionic *s*-Triazole Derivatives[1]

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In a recent communication,[2] a series of *meso* ionic compounds containing the *s*-triazole nucleus was described. One synthetic procedure used in this earlier study has now been found to be of a general nature for the synthesis of *meso* ionic *s*-triazole derivatives. This paper describes the synthesis of several representative ring-fused systems and the route used here should be useful for the synthesis of numerous heterocyclic systems of unusual structure.

Reaction of the appropriate 2-halo heterocycle with methylhydrazine gave the corresponding 1-methyl-1-(2-heteryl)hydrazine, which underwent ready reaction with phosgene, thiophosgene, or cyanogen bromide to give the appropriate *meso* ionic product. Application of these reactions to the pyridine, quinoxaline, and benzothiazole ring systems gave the products described in Table I. As in our earlier work, analytical and spectral data clearly showed that ring closure to the fused ring system had occurred.

Rearrangement of the substitution pattern in the heterocyclic hydrazine, *e.g.*, replacement of 1-methyl-1-(2-pyridyl)hydrazine (1) with 1-amino-2-methylimino-

(1) (a) 1,2,4-Triazoles. Part XIX. (b) Support of this work by U. S. Public Health Service Research Grant CA 08495-01, National Cancer Institute, is gratefully acknowledged.

(2) K. T. Potts, S. K. Roy, and D. P. Jones, *J. Org. Chem.*, **32**, 2245 (1967).

TABLE I
SOME *meso* IONIC RING-FUSED *s*-TRIAZOLE DERIVATIVES

Formula no.	R	Exocyclic atom X	Mp, °C	Crystn solvent[a]	Formula[e]	Calcd, % C	Calcd, % H	Calcd, % N	Found, % C	Found, % H	Found, % N	$\nu_{C=O}$, cm^{-1}	$\lambda_{max}^{CH_3OH}$, mμ (log ε)
2		O	219–220[b]	C	$C_7H_7N_3O$	56.4	4.7	28.2	56.2	4.7	28.1	1660	234 (3.97), 286 (3.17)
4		O	212–213	A	$C_7H_7N_3O \cdot H_2O$	50.3	5.4	25.1	50.3	5.2	24.9	1666	235[c] (3.97), 270 (3.84), 308 (3.65)
2		S	311–312	C	$C_7H_7N_3S$	50.9	4.3	25.4	51.2	4.2	25.4		248 (4.24), 291 (3.69)
4		S	262–263	B	$C_7H_7N_3S$	50.9	4.3	25.4	50.7	4.2	25.6		243[c] (4.39), 251 (4.46), 276[c] (3.70), 330 (3.82)
2		NH[d]	247	E	$C_7H_9BrN_4$	36.7	4.0	24.45	36.6	4.0	24.3		
5	H	O	312–313	D	$C_{10}H_8N_4O$	60.0	4.0	28.0	59.8	4.3	28.1	1645	260 (3.80), 262[c] (3.76), 258[c] (3.76), 224 (3.99)
5	H	S	283	D	$C_{10}H_8N_4S$	55.55	3.7	25.9	55.8	3.85	26.0		225 (3.91), 232[c] (3.72), 272[c] (3.72), 289 (3.70)
5	H	NH[d]	292	E	$C_{10}H_{10}BrN_5$	42.8	3.6	25.0	43.05	3.8	25.3		218[c] (4.34), 252 (4.27), 280[c] (3.85).
5	CH_3	O	276	D	$C_{11}H_{10}N_4O$	61.7	4.7	26.2	61.6	4.9	26.45	1637	225 (4.12), 254[c] (3.79), 358 (3.88), 264[c] (3.78)
5	CH_3	NH[d]	299	E	$C_{11}H_{12}BrN_5$	45.0	4.1	23.85	45.2	4.2	23.9		219[c] (4.26), 252 (4.14), 280[c] (3.59), 342 (3.90)
5	Ph	O	292–293	D	$C_{16}H_{12}N_4O$	69.55	4.4	20.3	69.3	4.4	20.3	1653	225 (4.38), 260[c] (4.09), 272 (4.14), 300[c] (3.98)
5	Ph	S	263–265	D	$C_{16}H_{12}N_4S$	65.75	4.1	19.2	65.8	4.0	19.0		225 (4.35), 250[c] (3.80), 285[c] (4.16), 291 (4.18)
5	Ph	NH[d]	321–323	E	$C_{16}H_{14}BrN_5$	54.0	3.9	19.65	53.7	3.9	19.8		257 (4.20), 301 (3.87)
6		O	201	B	$C_9H_7N_3OS \cdot H_2O$	48.5	4.05	18.85	48.5	4.1	19.2	1631	254 (3.92), 270 (4.12), 292 (3.89)
6		S	263	F	$C_9H_7N_3S_2$	48.8	3.2	19.0	49.0	3.3	19.2		230 (4.07), 305 (3.87), 362 (3.80)
6		NH[d]	309	B	$C_9H_9BrN_4S$	38.0	3.2	19.7	38.0	3.2	19.9		225[c] (3.82), 247 (3.62), 280 (3.44), 288 (3.49)

[a] A = acetone; B = methanol; C = acetic acid; D = acetic acid–ether; E = methanol–ether; F = methanol–ethyl acetate. [b] Lit. mp 216–217°: G. Pallazo and L. Baiochhi [*Ann. Chim.* (Rome), **55**, 935 (1965)] described the synthesis of this product by the same route after the completion of our study. [c] Shoulder. [d] These products, analogous to the sydnone imines can only be isolated as their hydrobromides or other salts. [e] Respective registry numbers are 16621-66-2, 16621-68-4, 16622-03-0, 16622-04-1, 4922-80-9, 16622-05-2, 16622-06-3, 16622-07-4, 16622-08-5, 16622-09-6, 16612-10-9, 16622-11-0, 16622-15-4, 16622-12-1, 16622-13-2, 16622-16-5.

1,2-dihydropyridine (**3**), provides a means of obtaining an isomeric *meso* ionic product. This is illustrated by the formation of anhydro-3-mercapto-1-methyl-*s*-triazolo[4,3-*a*]pyridinium hydroxide (**2**) from **1** and thiophosgene, and the formation of anhydro-2-mercapto-3-methyl-*s*-triazolo[1,5-*a*]pyridinium hydroxide (**4**) from **3** and thiophosgene. The dihydropyridine

3 was readily prepared by amination of 2-methylaminopyridine with hydroxylamine-O-sulfonic acid and treatment of the resulting salt with base. An experimental procedure for the preparation of 2-methylaminopyridine that offers several advantages over those reported in the literature is described below.

In the *s*-triazole series, *meso* ionic compounds with an exocyclic sulfur atom reacted readily with methyl iodide to form the corresponding *s*-triazolium salt. A similar nucleophilic behavior of the exocyclic sulfur atom was observed with the fused *s*-triazole systems, *e.g.*, the conversion of anhydro-1-mercapto-3-methyl-4-phenyl-*s*-triazolo[4,3-*a*]quinoxalinium hydroxide (**5**, R = Ph; X = S) into 1-methylthio-3-methyl-4-phenyl-*s*-triazolo[4,3-*a*]quinoxalinium iodide described in the Experimental Section.

Experimental Section[3]

1-Methyl-1-(2-heteryl)hydrazines.—The general procedure used is illustrated by the preparation of the 1-methyl-1-(3-substituted 2-quinoxalinyl)hydrazines. The corresponding 2-chloroquinoxaline (0.5 mol) was dissolved in methanol (200 ml), and methylhydrazine (2.0 mol) was added slowly. After the exothermic reaction had subsided, the resulting solution was refluxed on a steam bath for 5 min and then concentrated under reduced pressure until the product crystallized.

1-Methyl-1-(2-quinoxalinyl)hydrazine was obtained as yellow prisms (80%) from methanol or benzene, or could be purified by sublimation under vacuum: mp 108–110°; ir ($CHCl_3$), 3175, 1610 cm^{-1}.

(3) All evaporations were done under reduced pressure on Rotovap and melting points were taken in capillaries. Infrared spectra were measured on a Perkin-Elmer Model 421 infrared spectrophotometer and on a Baird Model IR-2 spectrophotometer. Ultraviolet absorption spectral data were obtained on a Beckman DK2 spectrophotometer. Microanalyses were carried out by Galbraith Laboratories, Inc., Knoxville, Tenn.

Anal. Calcd for $C_9H_{10}N_4$: C, 62.05; H, 5.8; N, 32.2. Found: C, 62.2, H, 5.95; N, 32.4.

The **picrate** was isolated from benzene as yellow needles, mp 157°.

Anal. Calcd for $C_{15}H_{13}N_7O_7$: N, 24.3. Found: N, 24.1.

The ***p*-nitrobenzalhydrazone** crystallized from benzene as yellow plates, mp 245–247°.

Anal. Calcd for $C_{16}H_{13}N_5O_2$: N, 22.8. Found: N, 23.0.

1-Methyl-1-(3-methyl-2-quinoxalinyl)hydrazine was obtained as yellow needles (45%) from aqueous ethanol, or by sublimation under vacuum: mp 65–67°; ir ($CHCl_3$), 3226, 2890, 1600 cm^{-1}.

Anal. Calcd for $C_{10}H_{12}N_4$: C, 63.8; H, 6.4; N, 29.8. Found: C, 64.0; H, 6.4; N, 29.7.

The **picrate** was isolated from benzene as yellow prisms, mp 167–168°.

Anal. Calcd for $C_{16}H_{15}N_7O_7$: N, 23.5. Found: N, 23.2.

The ***p*-nitrobenzalhydrazone** crystallized from ethanol as yellow plates, mp 254–256°.

Anal. Calcd for $C_{17}H_{15}N_5O_2$: N, 21.8. Found: N, 21.6.

1-Methyl-1-(3-phenyl-2-quinoxalinyl)hydrazine was obtained as yellow needles (45%) from methanol: mp 103–105°; ir ($CHCl_3$), 3175–2985, 1575 cm^{-1}.

Anal. Calcd for $C_{15}H_{14}N_4$: C, 72.0; H, 5.6; N, 22.4. Found: C, 71.7; H, 5.7; N, 22.5.

The **picrate** was obtained from tetrahydrofuran as yellow prisms, mp 225° dec.

Anal. Calcd for $C_{21}H_{17}N_7O_7$: N, 20.55. Found: N, 20.4.

The ***p*-nitrobenzalhydrazone** crystallized from aqueous methanol as orange needles, mp 174–175°.

Anal. Calcd for $C_{22}H_{17}N_5O_2$: N, 18.3. Found: N, 18.15.

1-Methyl-1-(2-benzothiazolyl)hydrazine crystallized from aqueous ethanol as colorless plates (91%): mp 140°; ir ($CHCl_3$), 3067, 2809, 1642, 1595 cm^{-1}.

Anal. Calcd for $C_8H_9N_3S$: C, 53.6; H, 5.1; N, 23.4. Found: C, 53.8; H, 5.3; N, 23.3.

1-Methyl-1-(2-pyridyl)hydrazine was obtained as a colorless oil (83%): bp 53–54° (0.1 mm) [lit.[4] bp 116–122° (18 mm)]. It was characterized as its picrate which formed yellow needles from ethanol: mp 165–166° (lit.[4] mp 166–167°).

Anal. Calcd for $C_{12}H_{12}N_6O_7$: C, 40.9; H, 3.4; N, 23.9. Found: C, 41.3; H, 3.4; N, 24.1.

2-Methylaminopyridine.—2-Formamidopyridine[5] (71.0 g) in dimethylformamide (100 ml) was added slowly to an ice-cold suspension of sodium hydride (24.0 g, 53.6% in oil suspension) in dimethylformamide (70 ml) with vigorous stirring. Copious evolution of hydrogen took place. After the addition, the mixture was stirred for 30 min and the brown solution was treated with dry benzene (100 ml) and then methyl iodide (27 ml) was added dropwise. After heating on the steam bath for 2 hr, the reaction mixture was extracted with chloroform (300 ml), washed with water, and dried (K_2CO_3) and the extracts were concentrated under reduced pressure. The residual brown oil was distilled under reduced pressure and 2-(N-methylformamido)pyridine was distilled as a colorless oil (59.0 g), bp 160–163° (35 mm). It was then refluxed with aqueous hydrochloric acid (160 ml, 1:1) for 1 hr and the acidic solution was extracted with chloroform (50 ml) and concentrated under reduced pressure. The residue was strongly basified with aqueous sodium hydroxide solution (30%) and extracted with chloroform (150 ml). The chloroform solution was dried (K_2CO_3) and concentrated. Upon distillation of the residual oil, 2-methylaminopyridine (31.0 g) distilled at 205–206° as a colorless oil which soon turned yellow on exposure to air (lit.[6] bp 200–201°).

The **picrate** crystallized from methanol as yellow needles, mp 192–193° (lit.[6] mp 190°).

Anal. Calcd for $C_{12}H_{11}N_5O_7$: N, 20.8. Found: N, 20.7.

1-Amino-2-methylaminopyridinium Bromide.—A solution of potassium hydroxylamine-O-sulfonate, prepared from hydroxylamine-O-sulfonic acid (5.6 g) in water (40 ml), was added to a mixture of 2-methylaminopyridine (5.4 g) and water (3 ml) and the whole was warmed at 70° for 45 min, cooled, and treated with an aqueous solution of potassium carbonate (3.25 g in 10 ml). The water was removed under reduced pressure at 40–50° and the residue was extracted with absolute ethanol (60 ml). The brown ethanolic solution was treated with aqueous hydrobromic acid (48%) (pH 2–3), cooled in a Dry Ice bath, and diluted carefully with ether when a gummy residue separated. This upon trituration with absolute ethanol (10 ml) gave a yellowish white solid (5.5 g) that crystallized from absolute ethanol as colorless needles, mp 151–153° with previous sintering at 145°.

Anal. Calcd for $C_6H_{10}BrN_3$: C, 35.3; H, 4.9; N, 20.6. Found: C, 35.05; H, 5.0; N, 20.4.

The **picrate**, prepared by treatment of the hydrobromide in methanol with picric acid, crystallized from methanol (charcoal) as yellow needles, mp 160–161°.

Anal. Calcd for $C_{12}H_{12}N_6O_7$: C, 40.9; H, 3.4; N, 23.9. Found: C, 41.0; H, 3.1; N, 23.8.

The following procedures illustrate the reaction conditions used for the synthesis of the *meso* ionic compounds described in Table I.

***anhydro*-1-Hydroxy-3-methyl-4-Substituted *s*-Triazolo[4,3-*a*]-quinoxalinium Hydroxide.**—The methylhydrazine (0.1 mol) was dissolved in benzene (100 ml) and warmed on a steam bath. With constant stirring, phosgene was bubbled into the solution for 5 min. After 1 hr of reflux on the steam bath, the resulting crystals were filtered and recrystallized from the solvent shown in Table I.

***anhydro*-1-Mercapto-3-methyl-4-Substituted *s*-Triazolo[4,3-*a*]-quinoxalinium Hydroxide.**—The hydrazine (0.05 mol) was dissolved in benzene, followed by the slow addition of thiophosgene. The reaction mixture was refluxed for 1 hr or until the desired product precipitated. Recrystallization was effected from the solvents listed in Table I.

1-Amino-3-methyl-4-Substituted *s*-Triazolo[4,3-*a*]quinoxalinium Bromide.—Equal molar amounts of the appropriate hydrazine and cyanogen bromide were refluxed in methanol (200 ml) for 3 hr. The reaction mixture was evaporated to dryness and the residue recrystallized from the solvent indicated in Table I.

Reaction of 1-Amino-1,2-dihydro-2-methyliminopyridine with Thiophosgene.—The base obtained by filtering a methanolic solution of 1-amino-2-methylaminopyridinium bromide (2.8 g) through an ion exchange column (IRA-400) was freed from methanol under reduced pressure and then dissolved successively in dry chloroform (100 ml) and in dry benzene (100 ml) with the solvents being removed under reduced pressure. The brown residue was dissolved in dry chloroform (100 ml) and added to a solution of thiophosgene (4.0 g) in chloroform (50 ml) and refluxed for 3.5 hr. The solvent was removed completely and the residue was treated with methanol when a pale yellow solid (0.35 g) was obtained. It crystallized from methanol (charcoal) as colorless plates, mp 262–263°.

1-Methylthio-3-methyl-4-phenyl-*s*-triazolo[4,3-*a*]quinoxalinium Iodide.—*anhydro*-1-Mercapto-3-methyl-4-phenyl-*s*-triazolo[4,3-*a*]quinoxalinium hydroxide (0.2 g) and methyl iodide (2 ml) in methanol (2 ml) were warmed on a steam bath for 15 min. Upon cooling, ether was added and the resulting product was recrystallized from methanol–ether, forming yellow plates (45%): mp 215°; ir (Nujol), 2941 (N-CH_3), 1351 (S-CH_3) cm^{-1}.

Anal. Calcd for $C_{17}H_{15}IN_4S$: C, 47.0; H, 3.5; N, 12.9. Found: C, 47.1; H, 3.7; N, 12.8.

Registry No.—1-Methyl-1-(2-quinoxalinyl)hydrazine, 16621-55-9; 1-methyl-1-(2-quinoxalinyl)hydrazine picrate, 16621-67-3; 1-methyl-1-(2-quinoxalinyl)hydrazine *p*-nitrobenzalhydrazone, 16622-19-8; 1-methyl-1-(3-methyl-2-quinoxalinyl)hydrazine, 16621-56-0; 1-methyl-1-(3-methyl-2-quinoxalinyl)hydrazine picrate, 16621-57-1; 1-methyl-1-(3-methyl-2-quinoxalinyl)hydrazine *p*-nitrobenzaldehydrazone, 16621-58-2; 1-methyl-1-(3-phenyl-2-quinoxalinyl)hydrazine, 16621-59-3; 1-methyl-1-(3-phenyl-2-quinoxalinyl)hydrazine picrate, 16621-60-6; 1-methyl-1-(3-phenyl-2-quinoxalinyl)-hydrazine *p*-nitrobenzalhydrazone, 1057-22-3; 1-methyl-1-(2-benzothiazolyl)hydrazine, 16621-62-8; 2-methylamino-1-aminopyridinium bromide, 16621-63-9; 2-methylamino-1-aminopyridine picrate, 16621-64-0; 1-methylthio-3-methyl-4-phenyl-*s*-triazolo[4,3-*a*]quinoxalinium iodide, 16621-65-1.

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