by filtration. The method of purification and physical data are listed in Table I.

The other pyridopyrimidines were prepared in a similar manner and are listed in Table I. The compounds are precipitated unchanged by the addition of acid to solutions in 5% aqueous sodium hydroxide. They are insoluble in 10% aqueous sodium carbonate solution.

Attempted Preparation of 6,6-Disubstituted Products.—5-Acetyl-1,3-dimethylbarbituric acid was obtained in 95% yield when diethylmalonic acid and acetic anhydride were heated with 1,3-dimethylbarbituric acid. No discrete products could be isolated from the reaction of diethylmalonic acid and acetic anhydride with 4-amino-1,3-dimethyluracil. The reaction of diethylmalonyl dichloride with 4-amino-1,3-dimethyluracil in dimethylformamide furnished 4-amino-1,3-dimethyl-5-formyluracil. The latter also has been prepared by the reaction of formic acetic anhydride with 4-amino-1,3-dimethyluracil.[5]

Acknowledgment.—The author is indebted to Mr. Charles Combs of the Mead Johnson Research Center for the n.m.r. data. Certain of the intermediates were prepared by Dr. T. A. Martin and Mr. D. H. Causey.

Decomposition of Dimethyl Sulfoxide Aided by Ethylene Glycol, Acetamide, and Related Compounds[1]

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Dimethyl sulfoxide appears to be thermally quite stable but upon prolonged reflux it does decompose slightly to methyl mercaptan and bismethylthiomethane.[3] This decomposition is aided by acids and retarded by many bases. Nace and Monagle[4] reported the appearance of dimethyl sulfide, methyl mercaptan, and dimethyl disulfide during the reaction of primary halides with dimethyl sulfoxide and, if precautions were not taken to remove the acid produced in this reaction, large amounts of formaldehyde also were formed. The acid-catalyzed cleavage of sulfoxides recently was discussed by Kenney, Walsh, and Davenport[5] and generally results in the reduction of sulfur to a mercaptan and the oxidation of the α-carbon to a carbonyl group. Subsequent reactions of these initial products may result. An alternate path for the decomposition of dimethyl sulfoxide involves disproportionation to dimethyl sulfone and dimethyl sulfide which requires osmium tetroxide as a catalyst.[6]

In our investigations of the dehydration of alcohols in dimethyl sulfoxide,[7] which required elevated temperatures for substantial periods of time, we have noted a number of dimethyl sulfoxide decomposition products. This report summarizes our observations on the thermal decomposition of dimethyl sulfoxide and the effect of certain glycols and amides on this cleavage.

When dimethyl sulfoxide was refluxed for 3 days, 3.7% of volatile material was collected and consisted of paraformaldehyde (1.9%), dimethyl sulfide, dimethyl disulfide, bismethylthiomethane, and water. The dimethyl sulfoxide residue contained a small amount of dimethyl sulfone. These results can be rationalized by the following series of equations.

$$(CH_3)_2SO \longrightarrow CH_3SH + CH_2O \longrightarrow \text{paraformaldehyde}$$

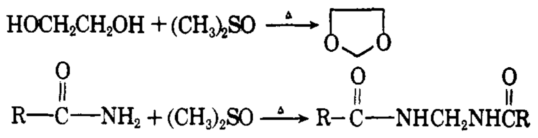
$$2CH_3SH + CH_2O \longrightarrow (CH_3S)_2CH_2 + H_2O$$

$$2CH_3SH + (CH_3)_2SO \longrightarrow CH_3SSCH_3 + CH_3SCH_3 + H_2O$$

$$2(CH_3)_2SO \longrightarrow CH_3SO_2CH_3 + CH_3SCH_3$$

The nature of the initial cleavage reaction is not clear at this time.

A variety of diols when heated in dimethyl sulfoxide undergo dehydration[7b]; however, purified ethylene glycol, heated in refluxing dimethyl sulfoxide for 3 days, promoted the previous cleavage reaction and gave dimethyl sulfide (16% isolated), dimethyl disulfide (19% isolated), and some bismethylthiomethane. The formaldehyde generated reacted with ethylene glycol to produce 1,3-dioxolane (54%). In a similar manner 1,2-propanediol and 1,3-propanediol promoted the cleavage reaction and were converted to 4-methyl-1,3-dioxolane (71% purified) and 1,3-dioxane (64% purified), respectively.



$$R{-}\overset{O}{\overset{\|}{C}}{-}NH_2 + (CH_3)_2SO \xrightarrow{\Delta} R{-}\overset{O}{\overset{\|}{C}}{-}NHCH_2NH\overset{O}{\overset{\|}{C}}R$$

An increase in decomposition products also was observed when acetamide or benzamide was heated in dimethyl sulfoxide at 190° for 36 hr. The formaldehyde liberated combined with these amides to produce methylenebisacetamide (55%) and methylenebisbenzamide (60%). When acetanilide was subjected to the prior reaction conditions, only 7% of volatile materials was collected and 89% unchanged acetanilide was recovered.

The methylenebisamides and the dioxa heterocycles are usually prepared by an acid-catalyzed reaction of formaldehyde with nitriles[8] or amides[9] and with the appropriate diol.[10] The results in this work suggest the possible use of dimethyl sulfoxide in promoting these condensation reactions of formaldehyde and possibly other carbonyl compounds. One experiment in support of this was the reaction of benzamide and paraformaldehyde in dimethyl sulfoxide to form methylenebisbenzamide (63%) in 9 hr.

Although it appeared, in the previous reactions, that dimethyl sulfoxide decomposed into methyl mercaptan and formaldehyde which then reacted with the glycols or amides, we have not excluded the possibility of some interaction of the diols or amides directly with dimethyl

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sulfoxide or some intermediate to produce the dioxa heterocycles or methylenebisamides.

Experimental

Thermal Stability of Dimethyl Sulfoxide.—Dimethyl sulfoxide[11] (78 g., 1.0 mole) was placed in a flask equipped with a Claisen head, condenser, and a receiver cooled in an acetone–Dry Ice bath, and heated at 190° for 72 hr. Paraformaldehyde, 1.5 g. (1.9%), identified by its 2,4-dinitrophenylhydrazone derivative, melting point and mixture melting point with an authentic sample, 165–166° (lit.[12] m.p. 166°), condensed in the Claisen head and 1.40 g. of material collected in the cold trap which consisted of 0.2 g. of ice. The 1.20 g. of liquid was subjected to v.p.c.[13] on a silicone GE-SF-96 column at 100° and with a helium flow rate of 60 cc./min., and was composed of dimethyl sulfide (42 area %), dimethyl disulfide (40 area %), and bismethylthiomethane (18 area %). These compounds were identified by comparison of retention times with authentic material. V.p.c.[13] of the remaining dimethyl sulfoxide under conditions described earlier except at 120° showed the presence of dimethyl sulfone by retention time comparison and peak enhancement with authentic material.

Reaction of Diols in Dimethyl Sulfoxide. A. Ethylene Glycol.—A solution of redistilled ethylene glycol (31 g., 0.50 mole) and dimethyl sulfoxide (158 g., 2.00 mole) was heated for 72 hr. at 190° and produced 64 g. of a distillate collected as in the preceeding experiment. Fractional distillation of this material gave 20 g. (16%) of dimethyl sulfide, b.p. 35–38°, mercuric chloride derivative m.p. 148–149° (lit.[14] b.p. 37.33°, mercuric chloride derivative[15] m.p. 150–151°); 20 g. (54%) of dioxolane, b.p. 73–74°, $n^{20}\mathrm{D}$ 1.4000, 2,4-dinitrophenylhydrazone derivative melting point and mixture melting point with formaldehyde 2,4-dinitrophenylhydrazone 165–166°, n.m.r. spectrum[16] singlet 5.22 (2 protons) and singlet 6.24 τ (4 protons) (lit.[10] b.p. 76°, $n^{20}\alpha$ 1.3934, $n^{25}\gamma$ 1.40734, lit.[17] $n^{25}\mathrm{D}$ 1.4010); and 12 g. (19%) of dimethyl disulfide, b.p. 104°, $n^{20}\mathrm{D}$ 1.5222, n.m.r. spectrum[16] singlet 7.61 τ (lit.[18] b.p. 109.5°, $n^{20}\mathrm{D}$ 1.5260). A small amount of bismethylthiomethane was detected by v.p.c. of the initial condensate.

B. 1,2-Propanediol.—The reaction of 1,2-propanediol (15.2 g., 0.200 mole) and dimethyl sulfoxide (109 g., 1.40 moles) at 190° for 48 hr. was processed as above. Fractional distillation of the condensate (32 g.) gave 14.5 g. of 4-methyldioxolane contaminated with dimethyl disulfide. Redistillation of this fraction from sodium produced 12.4 g. (71%) of pure 4-methyldioxolane, b.p. 87–89°, $n^{20}\mathrm{D}$ 1.4050 (lit.[10] b.p. 88–89°, $n^{20}\alpha$ 1.40109, $n^{20}\gamma$ 1.41107).

C. 1,3-Propanediol.—A solution of 1,3-propanediol (15.2 g., 0.200 mole) and dimethyl sulfoxide (78 g., 1.0 mole) at 190° for 44 hr. provided 24.5 g. of condensate. The initial distillation gave 13.8 g. of crude 1,3-dioxane which was treated with sodium overnight on a steam bath. Distillation from sodium gave 11.3 g. (64%) of pure 1,3-dioxane, b.p. 104–105°, $n^{20}\mathrm{D}$ 1.4168 (lit.[10] b.p. 105°, $n^{20}\alpha$ 1.41652, $n^{20}\gamma$ 1.42730).

Reaction of Amides in Dimethyl Sulfoxide. A. Acetamide.—Using the procedure described under reactions of diols, acetamide (11.8 g., 0.200 mole) and dimethyl sulfoxide (78 g., 1.0 mole) heated at 190° for 36 hr. gave 20 g. of condensate which by v.p.c. (conditions as described in the "Thermal Stability of Dimethyl Sulfoxide") contained dimethyl sulfide, dimethyl disulfide, and bismethylthiomethane. Bismethylthiomethane (4.5 g., 8%), b.p. 148°, $n^{20}\mathrm{D}$ 1.5321, disulfone derivative m.p. 144–145° (lit.[19] b.p. 148°, disulfone m.p. 145°), was isolated by distillation. Dimethyl sulfoxide was removed from the reaction mixture and the residue upon crystallization from 95% ethanol gave 7.2 g. (55%) of methylenebisacetamide, m.p. 192–194°, mixture melting point with an authentic sample 194–195° (lit.[9] m.p. 196°). The infrared spectrum was identical with that of an authentic sample.

B. Benzamide.—When a mixture of benzamide (24.2 g., 0.200 mole) and dimethyl sulfoxide (78 g., 1.00 mole) was heated for 34 hr. at 190°, 20 g. of condensate consisting of dimethyl sulfide, dimethyl disulfide, and bismethylthiomethane was isolated. Dimethyl sulfoxide was removed and the residue crystallized from 95% ethanol to give 15.0 g. (60%) of methylenebisbenzamide, melting point and mixture melting point with an authentic sample 217–219° (lit.[9] m.p. 219°). The infrared spectrum was identical with that of an authentic sample.

The product was treated with 2,4-dinitrophenylhydrazine and gave formaldehyde 2,4-dinitrophenylhydrazone, melting point and mixture melting point with an authentic sample 160–163°. When the product was heated with alcoholic potassium hydroxide for 24 hr., benzoic acid (97%) was isolated.

A solution of benzamide (12.1 g., 0.100 mole) and dimethyl sulfoxide (78 g., 1.0 mole) was heated for 9 hr. at 190° while paraformaldehyde (3.0 g., 0.10 mole) was added at 1-hr. intervals until 21.0 g. (0.70 mole) was introduced. After cooling, the reaction mixture was poured into water, filtered, and the solid was recrystallized from 95% ethanol. The yield of methylenebisbenzamide, m.p. 217–219°, was 8.0 g. (63%).

C. Acetanilide.—A solution of acetanilide (27.3 g., 0.200 mole) in dimethyl sulfoxide (78 g., 1.0 mole) was heated at 190° for 24 hr. and processed as before. The condensate (dimethyl sulfide, dimethyl disulfide, and bismethylthiomethane) was 5.5 g., and 24 g. (89%) of unchanged acetanilide, melting point and mixture melting point with an authentic sample 112–114°, was recovered.

Methylenebisbenzamide.—Methylenebisbenzamide, m.p. 217–219°, was prepared in 88% yield from benzonitrile (10.3 g., 0.100 mole), *sym*-trioxane (1.5 g., 0.05 mole), and 38 ml. of 85% sulfuric acid according to the procedure of Magat, Faris, Reith, and Salisbury.[8]

Methylenebisacetamide.—Using the prior procedure,[8] methylenebisacetamide, m.p. 195–196°, was prepared in 46% yield from acetonitrile (0.20 mole) and *sym*-trioxane (0.10 mole) with the following modification. After the reaction mixture was diluted, the acid was neutralized and the solution concentrated before the product crystallized.

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(11) The authors wish to thank the Chemical Products Division of the Crown Zellerbach Corp. for making generous samples of this material available for this work.

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An Attempted Westphalen Rearrangement of a 5β-Hydroxy Steroid[1]

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Numerous studies have been made concerning the Westphalen rearrangement[2] of 5α-hydroxy steroids. These studies have shown that a 6β-substituent is necessary in order for the migration of the C-10 methyl group to C-5 to occur when the alcohol is treated with with an acid catalyst. Recently, Mihina[3] reported the rearrangement of 5α-hydroxy-6β-halo steroids and concluded that a classical carbonium ion intermediate is sufficient to explain the formation of the 5β-methyl-19-nor steroid and by-products. A similar rearrangement of a B-norcholesteryl oxide has been reported by Dauben and co-workers.[4]

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