Reaction of 1-Phenoxyethyltriphenylphosphonium Bromide (VIII) with Triphenylphosphorus Hydrobromide.—One gram of triphenylphosphorus hydrobromide and 1.35 g. of the salt VIII were allowed to reflux in 20 ml. of benzene for 24 hr. No phenol was observed, with v.p.c., of the solvent. On quenching with ether and decanting, the sirupy product was washed with cold water. Concentration of the water showed no solubility of the product in water. On heating the sirupy product to reflux in water it became soluble.

Formation of the disalt III would produce phenol. The disalt III is highly soluble in cold water. Thus this material (salt VIII) could not be an intermediate in the reaction.

Reaction of 1-Phenoxyethyltriphenylphosphonium Bromide (VIII) with Ethanol.—One gram of the disalt VIII was refluxed 24 hr. in 20 ml. of ethanol. Ether was added and a trace of gummy sirup precipitated. This material was intractable and could not be crystallized to yield 2-ethoxyethyltriphenylphosphonium bromide (IVb). The solvent showed phenol to phenyl vinyl ether in a 2:1 ratio.

None of the 2-ethoxy salt (IVb) was found and phenyl vinyl ether (VII) was observed, with v.p.c. of the solvent system. The ether VII was not observed in the solvent system from the reactions of the 2-phenoxy salts (IVf); thus, it is felt that the 1-phenoxy salt (VIII) cannot be an intermediate in our reaction.

Nucleophilic Substitution at the Pyridazine Ring Carbons. III. Alkoxide Exchange[1]

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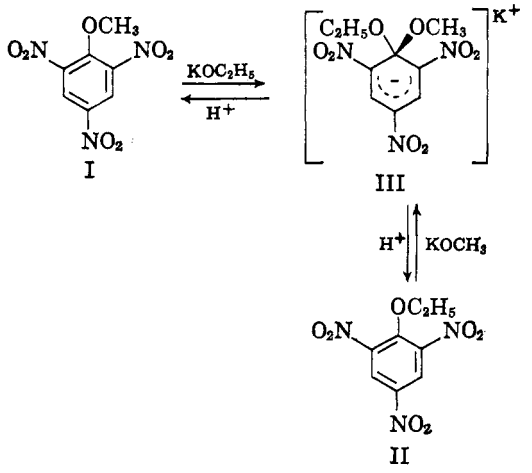
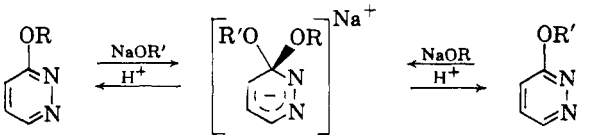
The phenomenon of alkoxide exchange in the mono-, di-, and bisalkoxypyridazines has been experimentally established. It has been utilized in a novel synthesis of monoalkoxypyridazines. A general method for the preparation of nonbisdialkoxypyridazines is described.

Meisenheimer[3] has established that ethers of strongly acidic phenols can be attacked at the benzene ring carbon by alkoxides. Thus, when 2,4,6-trinitroanisole (I) is treated with potassium ethoxide, the corresponding phenetole (II) is produced. Compound II can be

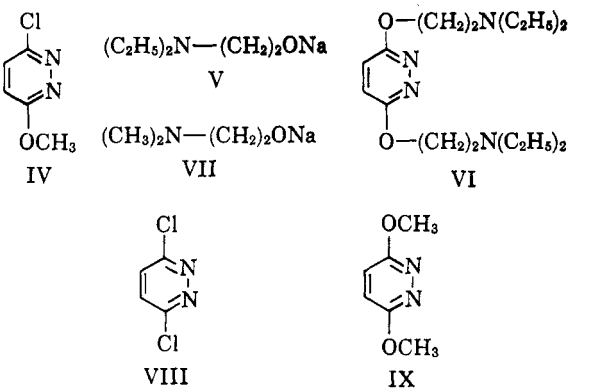


reconverted to I by treatment with excess potassium methoxide. In addition, an isolable adduct (III) is obtained which is identical for both reactions. This gives convincing evidence for the route of the reaction.[4] The success of this exchange is attributed to the positive nature of the benzene ring carbon attached to the ether oxygen and the subsequent attack by the nucleophilic reagent.

In the light of recent work in this laboratory concerning nucleophilic attacks at the pyridazine ring carbons,[5-7] it seemed of interest to attempt to extend alkoxide exchange to the field of pyridazines. A



possibility that such an exchange might occur in the pyridazine ring system is found in the experimental section of a paper by Steck and Brundage.[8] They reported that when 3-chloro-6-methoxypyridazine (IV), the purity of which had not been elucidated, was treated



with an equivalent amount of sodium 2-diethylaminoethoxide (V), a halogen-containing oil was formed. This oil was a mixture which was shown to contain some 3,6-bis(2-diethylaminoethoxy)pyridazine (VI) by formation of the known bismethiodide derivative.

The work of Steck was repeated using sodium 2-dimethylaminoethoxide (VII) in place of V. It became evident in the preparation of 3-chloro-6-methoxypyridazine (IV) using the traditional route that the product contained up to 20% impurities as shown by g.l.c. analysis. The contaminants occurred in equal amounts and were 3,6-dichloropyridazine (VIII) and 3,6-dimethoxypyridazine (IX). Hence, elemental analysis would agree with the desired product IV, and would not reveal the presence of a mixture containing IV along with equal parts of VIII and IX. If Steck

(1) Presented at the 146th National Meeting of the American Chemical Society, Denver, Colo., Jan., 1964.

(2) Walter Reed Army Institute of Research, Walter Reed Army Medical Center, Washington, D. C. 20012.

(3) J. Meisenheimer, *Ann.*, **323**, 205 (1902).

(4) J. Hine, "Physical Organic Chemistry," McGraw-Hill Book Co., Inc., New York, N. Y., 1956, p. 367.

(5) P. Coad, R. Coad, S. Clough, J. Hyepock, R. Salisbury, and C. Wilkins, *J. Org. Chem.*, **28**, 218 (1963).

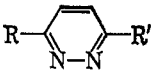
(6) P. Coad and R. Coad, *ibid*, **28**, 1919 (1963).

(7) P. Coad, R. Coad, and C. Wilkins, *J. Phys. Chem.*, in press.

(8) E. Steck and R. Brundage, *J. Am. Chem. Soc.*, **81**, 6511 (1959).

TABLE I

ALKOXY PYRIDAZINES



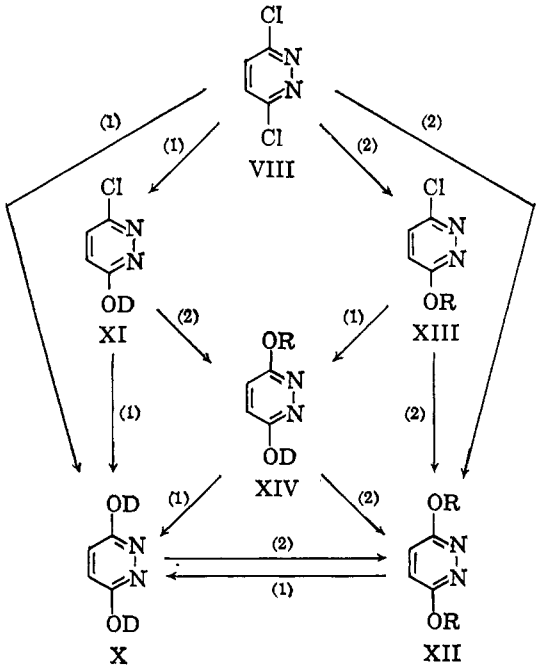
R	R′	M.p., °C.	B.p. (mm.), °C.[a]	λ_{max}^{EtOH}, μ (ε)[b]
-Cl	$-OCH_3$	90–91	174–175 (3)	
	$-OCH(CH_3)_2$	82–84 (83–84)[c]	129–131 (24)	
	-O-*n*-C_4H_9	47–48 (48)[c]	148–150 (17)	
	-O-cyclohexyl	108–110	153–154 (4)	283 (1910)
	$-O(CH_2)_2N(CH_3)_2$	46–47	130–131 (2)	280 (1970)
$-O(CH_2)_2N(CH_3)_2$	$-OCH_3$		120–123 (4)	286 (2020)
	$-OCH(CH_3)_2$		131–132 (4)	289 (2080)
	-O-*n*-C_4H_9		135–137 (3)	287 (2200)
	-O-cyclohexyl	39–41	178–185 (7)	289 (2100)
	$-O(CH_2)_2N(CH_3)_2$	30–31	162–165 (4) [130–132 (0.4)][d]	
$-OCH_3$	$-OCH_3$	106–107[c]	104–105 (8)	
$-OCH(CH_3)_2$	$-OCH(CH_3)_2$	26–28 (25–28)[c]	112–113 (4) [120–122 (11)][c]	
-O-*n*-C_4H_9	-O-*n*-C_4H_9	11–12	155–156 (8) [163–166 (11)][c]	
-O-cyclohexyl	-O-cyclohexyl	133–134	143.5–144.5 (3)	291 (2070)
-H	$-OCH_3$		88–89 (13) [86–87 (13)][e]	
-H	-O-*n*-C_4H_9		112–113 (10)	

[a] Boiling points of products isolated as solids were determined by microboiling point technique. [b] See ref. 10. [c] See ref. 8. [d] See ref. 11. [e] See ref. 12.

had used impure starting material, then alkoxide exchange might not have occurred at all, since compound VIII reacts with V to give VI in excellent yields. Evidence that true alkoxide exchange could have occurred under Steck's experimental conditions will be revealed.

The results of studies in this laboratory are summarized in Scheme I and in Table I. Anhydrous reagents were used throughout to avoid the formation of the nucleophile, hydroxide ion. When VIII was treated with excess VII, 3,6-bis(2-dimethylamino)pyridazine (X) was formed. An equivalent amount of VII at 60° produced 3-chloro-6-(2-dimethylaminoethoxy)-pyridazine (XI). Further treatment of XI with excess VII at 120° also produced X. As reported by Steck[8] and by Druey, *et al.*,[9] 3,6-bisalkoxypyridazine (XII) was formed by treatment of VIII with excess sodium alkoxide. If an equivalent amount of the alkoxide is used and the temperature adjusted to an optimum point, the 3-alkoxy-6-chloropyridazine (XIII) is formed, reasonably pure, in all cases except XIIIa as discussed above.

SCHEME I



(1) Treatment with NaOD
(2) Treatment with NaOR

a, R = $-CH_3$
b, R = $-CH(CH_3)_2$
c, R = -*n*-C_4H_9
d, R = -cyclohexyl
D = $-CH_2CH_2N(CH_3)_2$

In order to convert XI and XIII to XIV, conditions had to be found which were severe enough to cause nucleophilic displacement of the halogen by alkoxide and, yet, were sufficiently mild so as not to induce alkoxide exchange. For all cases studied, without exception, conditions were readily found which would satisfy these criteria. This is the first general synthesis for nonbisdialkoxypyridazines. Only one compound of this type had been previously reported.[9]

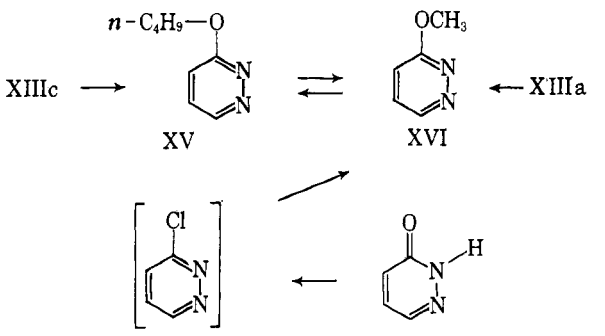
The nonbisdisubstituted pyridazine, XIV, was then converted to either of the two corresponding bis-substituted pyridazines, X or XII, by treatment with excess VII or sodium alkoxide. Conversion of X to XII and XII back to X completed the pattern.

In order to prove that alkoxide exchange at the pyridazine carbons was general, it was necessary to demonstrate experimentally that the above type of exchange was independent of the presence of a dialkylaminoethoxide and not limited to disubstituted pyridazines. This was accomplished by selecting two simple monoalkoxypyridazines with sufficiently different physical properties to be conveniently separated by fractional distillation. 3-Methoxypyridazine and 3-*n*-butoxypyridazine were prepared and

(9) J. Druey, Kd. Meier, and K. Eichenberger, *Helv. Chim. Acta*, **37**, 121 (1954).

interconverted with excess of the appropriate alkoxide. Work on the detailed mechanism of this reaction is continuing in this laboratory.

The 3-methoxypyridazine prepared by hydrogenolysis of 3-chloro-6-methoxypyridazine contained both pyridazine and dimethoxypyridazine as impurities. It was obtained in high purity, however, from 3-(2H)-pyridazinone. The synthesis was much improved by a work-up which minimized hydrolysis of the reactive 3-chloropyridazine. It was also prepared in good yield by a novel synthesis which was a result of this study, namely from alkoxide exchange of methoxide with 3-*n*-butoxypyridazine. 3-*n*-Butoxypyridazine was prepared from XIIIc by catalytic hydrogenolysis and also from 3-methoxypyridazine by treatment with sodium *n*-butoxide.



Thus, alkoxide exchange occurs in 3-alkoxy, 3,6-bisalkoxy, and 3,6-nonbisdialkoxypyridazines. This exchange gives further experimental evidence of the positive nature of the pyridazine ring carbons to which a group more electronegative than carbon has been attached. Whenever such pyridazines are used as substrates, nucleophilic attacks occur at those ring carbons.

Experimental[10]

3,6-Dichloropyridazine (VIII), m.p. 67–68°, was prepared from maleic hydrazide and phosphorus oxychloride by the method of Coad and Coad.[5,6] Vapor phase chromatography showed this material to be 99.9+% pure.

3-Chloro-6-(2-dimethylaminoethoxy)pyridazine (XI).—In a three-necked flask equipped with a mechanical stirrer, a reflux condenser, and a dropping funnel was placed 70 ml. of anhydrous xylene. The xylene was heated to just below the boiling point, and 4.6 g. (0.20 g.-atom), of sodium metal was added. The mixture was heated and stirred until the sodium was finely dispersed. Over a period of 10 min., 19.6 g. (0.22 mole) of anhydrous 2-dimethylaminoethanol (XVII) was added through the dropping funnel. The mixture was heated and stirred until the last traces of sodium globules disappeared. The reflux condenser was replaced by an internal thermometer and the solution cooled to 60°. A solution of 29.8 g. (0.20 mole) of VIII and 50 ml. of anhydrous xylene was added over a period of 15 min. with sufficient cooling to keep the internal temperature from rising above 60°. The reaction mixture was stirred with the temperature maintained at 60° by heating for a period of 6 hr. The mixture was cooled to room temperature and filtered. The precipitate was triturated with two 60-ml. portions of hot xylene. The combined filtrates were transferred to a separatory funnel and washed with two 25-ml. portions of cold 30% sodium hydroxide solution and dried over anhydrous sodium sulfate. The xylene was removed *in vacuo* and the residue was distilled through a Podbielniak-type column with hot water circulating through the jacket of the side arm. A product was obtained, b.p. 130–131° at 2 mm. It weighed 24.1 g. (60%), m.p. 46–47°.

Anal. Calcd. for $C_5H_{12}ClN_3O$: C, 47.64; H, 6.00; Cl, 17.58; N, 20.84. Found: C, 47.77; H, 5.86; Cl, 17.33; N, 20.52.

3-Alkoxy-6-chloropyridazines (XIII).—A general method was developed for making compounds of this type from VIII. Although it would seem reasonable to add an alkoxide to the dihalo compound in order to obtain monosubstitution, this was not done as a general method owing to the limited solubility of the higher alkoxides. Under the special conditions developed, the reverse addition, dihalo compound to alkoxide, was successful, producing only minor amounts of the bisalkoxypyridazines. In the cases of the lower alkoxides, either order of addition could be used.

The procedure for making XI was modified. The sodium was dispersed in 70 ml. of anhydrous xylene. The alcohol in place of XVII was added over a period of 20 min. The mixture was heated 10 hr. at 60°. The washes with 30% sodium hydroxide solution were omitted. Unchanged VIII came over as the first fraction, followed by the product. The bisalkoxypyridazine remained in the pot as a residue.

Pure XIII was obtained in 70–85% yield, depending on the alkoxide.

3-Chloro-6-methoxypyridazine (XIIIa).—This compound has been made in several ways by several investigators.[11,12] The Steck method gives a product which by g.l.c. analysis contains 5–10% of VIII and 5–10% of XIIa. The general method above gives a product in 90% yield (m.p. 78–86°, b.p. 174–175° at 3 mm.) which is contaminated by <1% of VIII and <1% of XIIa. When recrystallized repeatedly from petroleum ether (b.p. 30–60°) a product is obtained, m.p. 90–91°. The product was shown to be free of VIII and XIIa by g.l.c. analysis.

3-Chloro-6-isopropoxypyridazine (XIIIb) had a yield of 70%, m.p. 82–84° (lit.[9] m.p. 83–84°), b.p. 129–131° at 24 mm.

3-*n*-Butoxy-6-chloropyridazine (XIIIc) had a yield of 85%, m.p. 47–48° (lit.[9] m.p. 48°), b.p. 148–150° at 17 mm.

3-Chloro-6-cyclohexyloxypyridazine (XIIId).—The temperature was raised to 95° and the heating was continued for 6 hr, to yield 77% of XIIId, m.p. 108–110°, b.p. 153–154° at 4 mm.

Anal. Calcd. for $C_{10}H_{13}ClN_2O$: C, 56.46; H, 6.13; Cl, 16.67; N, 13.17. Found: C, 56.73; H, 6.20; Cl 16.55; N, 13.42.

3-Alkoxy-6-(2-dimethylaminoethoxy)pyridazines (XIV) from XI.—By means of the apparatus and procedure described previously, 2.3 g. (0.10 g.-atom) of sodium metal was dispersed in 100 ml. of hot, anhydrous xylene. To this was added 0.11 mole of the appropriate anhydrous alcohol and the mixture was stirred until the sodium disappeared. This mixture was heated to boiling and to it was added dropwise a solution consisting of 20 g. (0.10 mole) of XI and 50 ml. of anhydrous xylene over a period of 5 min. for lower alkoxides and 15 min. for higher alkoxides. The mixture was heated under reflux and mechanically stirred for 3 hr. The mixture was filtered after cooling. The precipitate was triturated with two 25-ml. portions of hot xylene. The combined filtrates were washed with 10 ml. of cold 30% sodium hydroxide solution and dried over anhydrous sodium sulfate. The xylene and excess alcohol were removed *in vacuo*.

Individual procedures for the isolation of each alkoxide had to be used. The product (XIV) had to be separated from varying amounts of X and XII which were formed by alkoxide exchange. Yields ranged from 50 to 65%.

From XIII.—It was found that, whenever more than an equivalent amount of VII was used, the yield of XIV was decreased and more X was formed. In addition, the amount of XVII used was limited to 10% excess of the stoichiometric amount to form VII. Yields varied from 50 to 75%.

3-(2-Dimethylaminoethoxy)-6-methoxypyridazine (XIVa).—Better yields could be obtained by using XI as a starting material. The crude product obtained was distilled through a Podbielniak-type column. The product obtained was a yellow oil, b.p. 120–123° at 4 mm.

Anal. Calcd. for $C_9H_{15}N_3O_2$: C, 54.80; H, 7.65; N, 21.31. Found: C, 54.35; H, 7.41; N, 21.02.

3-(2-Dimethylaminoethoxy)-6-isopropoxypyridazine (XIVb).—Better yields could be obtained by using XI as the starting material. The crude product was dissolved in Shellacol, and subjected to hydrogenolysis of any residual chlorine atoms using a Parr hydrogenation apparatus with 5 ml. of concentrated ammonium hydroxide and 2.0 g. of activated 10% palladium on carbon. The Shellacol was removed *in vacuo*. The residue was washed with cold 10% sodium hydroxide solution and extracted

(10) The studies using gas chromatography were done by Cal-Colonial Chemical Co. on a Beckman G. C. 2A gas chromatograph equipped with a hydrogen flame detector using a 6-ft. column packed with polyester.

(11) T. Itai and H. Igeta, *J. Pharm. Soc. Japan*, **74**, 1195 (1954).

(12) E. Steck, U. S. Patent 2,858,311 (1959).

with four 100-ml. portions of ether. The combined extracts were dried over anhydrous sodium sulfate. The ether solution was filtered through fresh sodium sulfate and flashed distilled. The residue was distilled through an efficient column. The product obtained was a pale yellow oil, b.p. 131–132° at 4 mm.

Anal. Calcd. for $C_{11}H_{19}N_3O_2$: C, 58.63; H, 8.50; N, 18.65. Found: C, 58.57; H, 8.14; N, 18.88.

3-*n*-Butoxy-6-(2-dimethylaminoethoxy)pyridazine (XIVc).—The crude product obtained from treatment of XIIIc with VII was distilled through a column. The desired compound was obtained as a pale yellow oil, b.p. 135–137° at 3 mm.

Anal. Calcd. for $C_{12}H_{21}N_3O_2$: C, 60.21; H, 8.84; N, 17.56. Found: C, 60.50; H, 8.49; N, 17.32.

3-Cyclohexyloxy-6-(2-dimethylaminoethoxy)pyridazine (XIVd).—The crude product obtained by treating XIIId with VII was distilled through a column with steam used in the jacket of the side arm. The product obtained was a pale yellow solid, m.p. 39–41°, b.p. 178–185° at 7 mm.

Anal. Calcd. for $C_{14}H_{23}N_3O_2$: C, 63.40; H, 8.74; N, 15.84. Found: C, 63.10; H, 9.0; N, 15.90.

3,6-Bis(2-dimethylaminoethoxy)pyridazine (X) from XI or XIV.—Compound VII was prepared as described in the preparation of XI. Twice the stoichiometric amount of XVII was employed. The reaction was boiled and stirred for 6 hr. The work-up was similar to that used in making XI. From XI the yield was 85%. From XIV the yields varied from 50 to 60%, depending on the alkoxy group involved.

From VIII.—Caution: 3,6-dichloropyridazine reacts explosively with warm 2-dimethylaminoethanol. Thus, care must be taken to form first XI as described and then proceed as above.

From XII.—A twofold excess of VII and XVII was employed. The reaction mixture was boiled for 8 hr. Yields varied from 40 to 65%. A yellow solid, m.p. 30–31°, b.p. 162–165° at 4 mm. (lit.[12] b.p. 130–132 at 0.4 mm.), was obtained.

3,6-Bisalkoxypyridazines (XII) from VIII.—Procedures were used similar to the procedure used in the preparation of XIII. However, twice the amount of sodium and alcohol was employed. The reaction mixture was heated for 2 hr. under reflux with stirring. The mixture was filtered after cooling. The precipitate was washed with two 60-ml. portions of xylene. The combined filtrates were concentrated *in vacuo*, dissolved in Shellacol, and hydrogenated in a Parr hydrogenation apparatus with ammonium hydroxide and 10% palladium-on-carbon catalyst. The mixture was filtered and the solvents removed *in vacuo*. The residue was distilled through an efficient column separating traces of pyridazine and monoalkoxypyridazine from the product. The yield was approximately 80% in each case.

From XIV.—An equivalent amount of the sodium alkoxide was used along with a tenfold excess of the corresponding alcohol. Yields averaged 70%.

From X.—A twofold excess of alkoxide and a tenfold excess of alcohol were used. Yields all were of the order of 50%.

From XIII.—A second mole of alkoxide was added and the temperature raised to the boiling point of xylene for 3 hr. Yields were around 80% in each case.

3-Bismethoxypyridazine (XIIa) was obtained as a white solid, m.p. 106–107° (lit.[9] m.p. 106–107°), b.p. 105° at 8 mm.

3,6-Bisisopropoxypyridazine (XIIb) was obtained as a white solid, m.p. 26–28° (lit.[9] m.p. 25–28°), b.p. 112–113° at 4 mm. (lit.[9] b.p. 120–122° at 11 mm.).

3,6-Bis-*n*-butoxypyridazine (XIIc) was obtained as a white solid, m.p. 11–12°, b.p. 155–156° at 11 mm.

3,6-Biscyclohexyloxypyridazine (XIId) was obtained as a white solid, m.p. 133–134°, b.p. 143.5–144.5° at 3 mm. The product could be readily recrystallized from Shellacol making distillation unnecessary.

Anal. Calcd. for $C_{16}H_{24}N_2O_2$: C, 69.50; H, 8.75; N, 10.14. Found: C, 69.88; H, 8.75; N, 10.31.

3-*n*-Butoxypyridazine (XV) from XIIIc.—The Parr hydrogenation apparatus was used in the hydrogenolysis of 74.2 g. (0.4 mole) of XIIIc using 200 ml. of Shellacol, 40 ml. of concentrated ammonium hydroxide, and 5.0 g. of activated 10% palladium on charcoal. The mixture was filtered after hydrogenation and the filtrate slowly distilled. Shellacol was added from time to time and a total of 800 ml. was distilled from the solution. The volume was reduced to 80 ml., cooled, and filtered. The residue was distilled through an efficient column to remove pyridazine from the product. The product was a colorless liquid, b.p. 112–113° at 10 mm. The product weighed 41.9 g. (69%).

Anal. Calcd. for $C_8H_{12}N_2O$: C, 63.14; H, 7.95; N, 18.41. Found: C, 62.91; H, 8.08; N, 18.46.

From XVI.—To 125 ml. of anhydrous butanol was added 8.3 g. (0.36-atom) of sodium metal. The mixture was heated until the sodium completely reacted. To the hot solution was added 6.5 g. (0.059 mole) of 3-methoxypyridazine. The flask was attached to a distilling column and heated until a few drops of methanol, b.p. 65°, was collected. The excess solvents were removed *in vacuo* and the residue was extracted with four 50-ml. portions of ether. The extracts were washed with 50 ml. of water, dried over anhydrous potassium carbonate, filtered, and distilled *in vacuo*. The product was distilled from the residue giving 5.6 g. (70%) of XV, b.p. 109–110° at 8 mm. The spectra were identical with the product formed from XIIIc.

3-Methoxypyridazine (XVI) from 3(2H)-Pyridazinone.—This route has been followed by several earlier workers. The procedure herein described was designed to minimize hydrolysis since this is frequently a major undesirable side reaction in the preparation of 3,6-dichloropyridazine from 3,6-pyridazinedione.

In a flask equipped with a magnetic stirrer and a reflux condenser with a drying tube attached was placed 28.8 g. (0.30 mole) of anhydrous 3(2H)-pyridazinone. To this was added 90 ml. of freshly distilled phosphorus oxychloride. The mixture was stirred overnight. Excess phosphorus oxychloride was removed *in vacuo* and the residue was poured onto 300 g. of cracked ice. Solid potassium carbonate was added until the mixture had pH 6. The mixture was extracted with five 100-ml. portions of ether. The extracts were combined, dried over anhydrous potassium carbonate, and concentrated to 150 ml.

Into a flask equipped with a dropping funnel and a reflux condenser was placed 6.9 g. (0.30 g.-atom) of sodium metal. Slowly 150 ml. of anhydrous methanol was added at such a rate as to keep the reaction proceeding rapidly. The solution was cooled to room temperature. The ethereal solution of chloropyridazine prepared above was added dropwise over a period of 1 hr. A precipitate formed immediately and the mixture was allowed to stand overnight. Upon filtration sodium chloride (85%) was collected. The filtrate was distilled yielding 22 g. (65%) of XVI, b.p. 72–73° at 6 mm. (lit.[13] b.p. 86–87° at 13 mm.).

From XIIIa.—The Parr hydrogenation apparatus was used as in the preparation of XV from XIIIc. The product could not be prepared free from pyridazine and 3,6-dimethoxypyridazine formed from VIII and XIVa present in XIIIa.

A New Route from XV.—In a three-necked flask equipped with a mechanical stirrer, a dropping funnel, and a reflux condenser was placed 23.0 g. (1.0-g.-atom) of sodium metal. Slowly 150 ml. of anhydrous methanol was added so that the reaction continued vigorously. When the sodium was dissolved, 15.2 g. (0.10 mole) of XV was added over a period of 5 min. from the dropping funnel. The mixture was stirred and boiled for 3 hr. Excess methanol and butanol were removed *in vacuo*. The solid was cooled and 100 g. of cracked ice was added with mechanical stirring followed by 50 ml. of a cold 10% sodium hydroxide solution. The mixture was extracted with four 100-ml. portions of ether. The combined extracts were dried over potassium carbonate. After removal of the ether, the residue was distilled giving 5.5 g., 50% of XVI. b.p. 88–89° at 13 mm.

Acknowledgment.—The authors wish to express appreciation to the Research Corporation for support of portions of this work; to Mr. Hal Ramsey; to Dr. John E. Campion, head of the laboratories, and the Analytical Staff of Riker Laboratories for analysis and spectra; and to Dr. Charles Braithwaite, Cal-Colonial Chemical Company for the g.l.c. determinations.

(13) K. Eichenberger, R. Rometsch, and J. Druey, *Helv. Chim. Acta*, **39**, 1755 (1956).