was concentrated *in vacuo* and neutralized with NH_4OH to pH. 7~7.5, there was obtained white fine crystals. Yield, 1.0 g. Purified from dil. EtOH, forming white needles.

3-(p-Aminomethylphenylsulfonamido)-6-chloropyridazine(VIb)——3-(p-Phthalylimidomethylphenyl-sulfonamido)-6-chloropyridazine (Vb) (2.1 g.; 0.01 mole) was hydrolyzed with 0.3 g. of 85% hydrazine hydrate in the same manner as described for (VIa), affording 1.1 g. of (VIb), recrystallized from dil. EtOH to form white needles.

Summary

In order to find antimicrobial agents, compounds of 6-substituted 3-(p-nitrophenyl-sulfonamido)pyridazine, 6-substituted 3-(p-tolylsulfonamido)pyridazine and 6-substituted 3-(p-aminomethylphenylsulfonamido)pyridazine were synthesized and screened as to their activities on *Staph. aureus* and *E. coli*, but any of them was found uneffective.

(Received May 4, 1961)

**97. Tatsuya Horie (Ishida) and Takeo Ueda : Studies on Pyridazine Derivatives. III.*[1]
Improved Synthetic Method of 3-Sulfanilyl-6-alkoxypyridazine.**

(*Pharmaceutical Institute, Keio University**[2])

Although some synthetic methods have been submitted[1] for the purpose of the preparation of 3-sulfanilyl-6-alkoxypyridazine as shown in Chart 1 and Chart 2, questions still remain to decide what method should be selected for its industrial production.
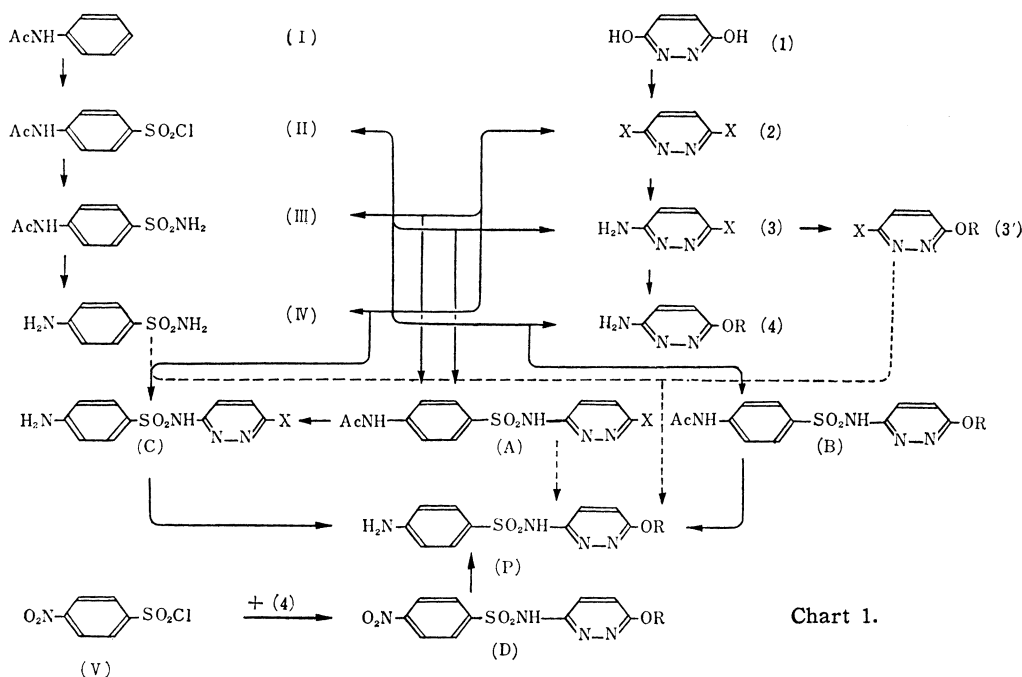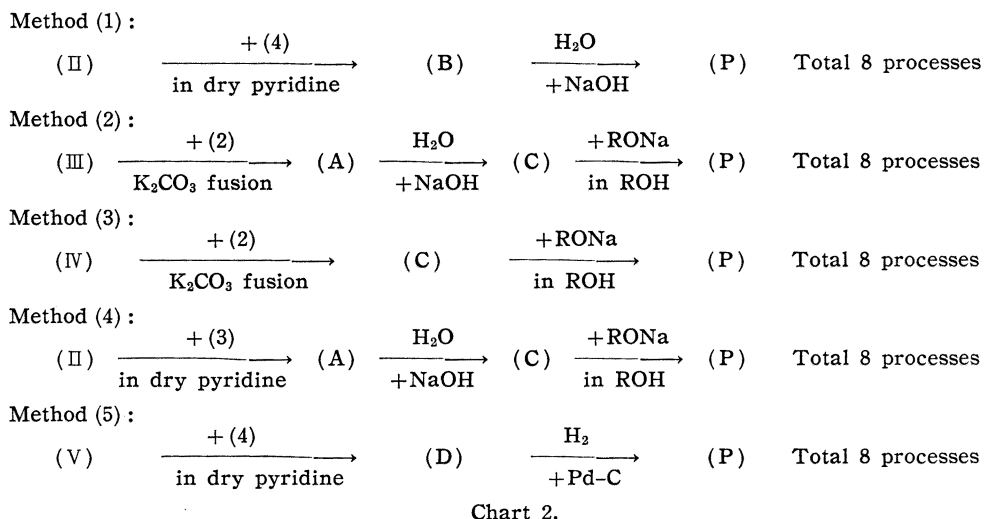

Chart 1.

*[1] Part II: This Bulletin, **10**, 591 (1912).
*[2] Shinano-machi, Shinjuku-ku, Tokyo (堀江達也, 上田武雄).
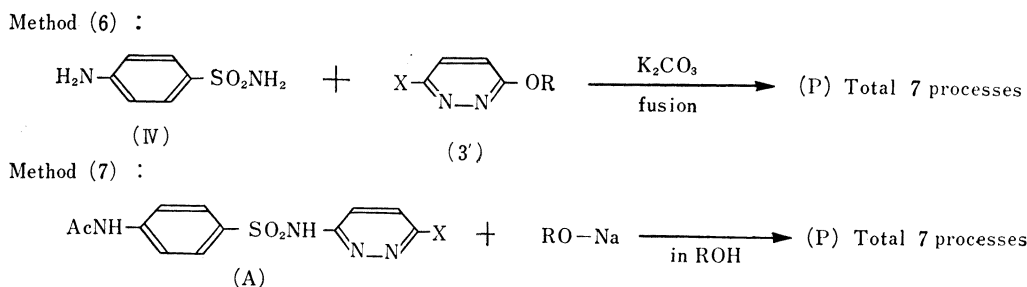1) Part I: This Bulletin, **10**, 580 (1962).

Among these methods, the final reaction of method (3) has been claimed in U.S. Patent 2,712,012[2] and Japanese Patent 35-5930,[3] but this method (3) seems to be more difficult for industrial application, since it comprises a fusing reaction with potassium carbonate. The other methods also seem not to show any advantage over method (3).

Method (1) :

$$(\text{II}) \xrightarrow[\text{in dry pyridine}]{+ (4)} (B) \xrightarrow[+\text{NaOH}]{\text{H}_2\text{O}} (P) \quad \text{Total 8 processes}$$

Method (2) :

$$(\text{III}) \xrightarrow[\text{K}_2\text{CO}_3 \text{ fusion}]{+ (2)} (A) \xrightarrow[+\text{NaOH}]{\text{H}_2\text{O}} (C) \xrightarrow[\text{in ROH}]{+\text{RONa}} (P) \quad \text{Total 8 processes}$$

Method (3) :

$$(\text{IV}) \xrightarrow[\text{K}_2\text{CO}_3 \text{ fusion}]{+ (2)} (C) \xrightarrow[\text{in ROH}]{+\text{RONa}} (P) \quad \text{Total 8 processes}$$

Method (4) :

$$(\text{II}) \xrightarrow[\text{in dry pyridine}]{+ (3)} (A) \xrightarrow[+\text{NaOH}]{\text{H}_2\text{O}} (C) \xrightarrow[\text{in ROH}]{+\text{RONa}} (P) \quad \text{Total 8 processes}$$

Method (5) :

$$(\text{V}) \xrightarrow[\text{in dry pyridine}]{+ (4)} (D) \xrightarrow[+\text{Pd-C}]{\text{H}_2} (P) \quad \text{Total 8 processes}$$

Chart 2.

Hereupon, the authors selected the following two methods, other than the above, which were, in detail, examined from point of industrial view, as shown in Chart 3.

Thus, the authors found the process comprising method (7) should be promising for the production of 3-sulfanilyl-6-alkoxypyridazine. Moreover, the reaction connecting with method (7) was found interesting as the sequence of the examination of its reaction mechanisms.

This paper is concerned with the improved synthesis of 3-sulfanilyl-6-alkoxypyridazine and the analysis of its reaction mechanisms.

Method (6) :

$$\text{H}_2\text{N}-\langle\text{C}_6\text{H}_4\rangle-\text{SO}_2\text{NH}_2 \ + \ \text{X}-\langle\text{pyridazine}\rangle-\text{OR} \xrightarrow[\text{fusion}]{\text{K}_2\text{CO}_3} (P) \text{ Total 7 processes}$$

(IV)   (3')

Method (7) :

$$\text{AcNH}-\langle\text{C}_6\text{H}_4\rangle-\text{SO}_2\text{NH}-\langle\text{pyridazine}\rangle-\text{X} \ + \ \text{RO}-\text{Na} \xrightarrow[\text{in ROH}]{} (P) \text{ Total 7 processes}$$

(A)

Chart 3.

Examination of Methods (6) and (7)

Regarding method (6), the reaction of sulfanilamide with 3-halo-6-alkoxypyridazine was examined under various reaction conditions, using a variety of such a basic substance as potassium carbonate, potassium acetate, pyridine, dimethylanilin etc. and with or without copper catalyst. Additionally, the reaction of N[4]-acetylsulfanilamide with

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2) By J.H. Clark, assignors to Am. Cyanamid Co.(Application Nov. 10. 1954).
3) The same as the above.(Application Sho. 32. 8. 6.).

3-halo-6-alkoxypyridazine was also examined. However, 3-sulfanilyl-6-alkoxypyridazine or 3-(p-acetamidophenylsulfonamido)-6-alkoxypyridazine could not be obtained to any extent in any reaction condition, but the starting materials for this reaction were recovered in only small quantity. This finding coincides with the assumption of Takabayashi[4] that the second substituent halogen atom in 3,6-dihalopyridazine might decrease its activity on nucleophilic reagents, after the first halogen atom at 6-position was substituted with another group.

Regarding method (7), 3-(p-acetamidophenylsulfonamido)-6-halopyridazine was reacted in anhydrous methanolic solution with sodium methoxide and 3-sulfanilyl-6-methoxypyridazine and methyl acetate were obtained in good yield from the reaction mixture. Considered from the yields of both products, this reaction might be shown by Chart 4.

$$CH_3CONH-\underset{(A)}{\langle\rangle}-SO_2HN-\underset{N-N}{\langle\rangle}-X + MeONa + CH_3OH \longrightarrow$$

$$H_2N-\underset{(P)}{\langle\rangle}-SO_2NH-\underset{N-N}{\langle\rangle}-OCH_3 + CH_3COOCH_3 + NaCl$$
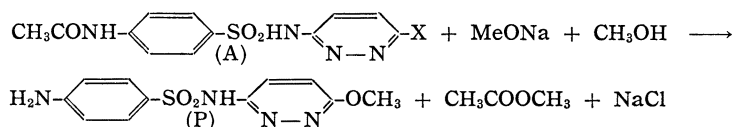
Chart 4.

By employing this reaction, the following synthetic method as shown in Chart 5 was conceived by the authors to produce 3-sulfanilyl-6-alkoxypyridazine industrially[5]. This method was found superior to that claimed in U.S. Patent 2,712,012, in the following two points. This method shortened one process and afforded the objective product in better overall yield, compared with the known methods.
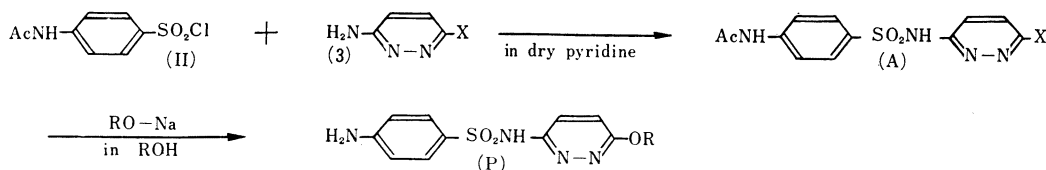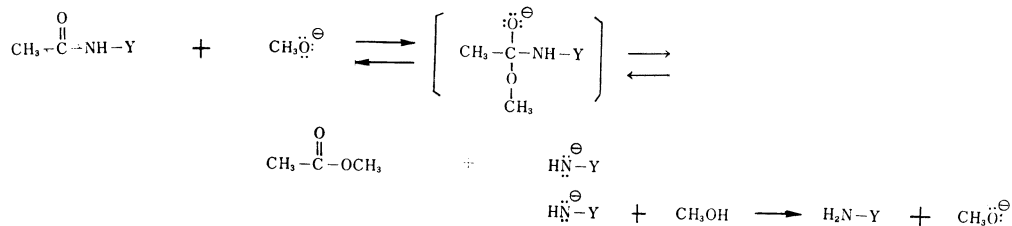
$$AcNH-\underset{(II)}{\langle\rangle}-SO_2Cl + H_2N-\underset{(3)}{\langle\rangle}-X \xrightarrow{\text{in dry pyridine}} AcNH-\underset{(A)}{\langle\rangle}-SO_2NH-\underset{N-N}{\langle\rangle}-X$$

$$\xrightarrow[\text{in ROH}]{RO-Na} H_2N-\underset{(P)}{\langle\rangle}-SO_2NH-\underset{N-N}{\langle\rangle}-OR$$

Chart 5.

Analysis of the Reaction Shown by Chart 4

The reaction of 3-(p-acetamidophenylsulfonamido)-6-chloropyridazine with sodium methoxide was interesting as a reaction having two reaction points of deacetylation and methoxylation. Thus, it might be worthy to analyse its mechanism, i.e. how the deacetylation and the methoxylation took place in the course of the reaction.

Although, it is well-known to prepare an acid amide by reacting an ester with an amine, strange to say, it has not been reported, to date, that the reaction of an acid amide with an alcohol affords an ester and an amine. The authors conceived that this deacetylation might proceed with the following mechanims, as shown in Chart 6.

$$CH_3-\overset{O}{\overset{\|}{C}}-NH-Y + CH_3\ddot{O}^{\ominus} \rightleftarrows \left[CH_3-\overset{\ddot{O}^{\ominus}}{\underset{\overset{|}{O}}{\overset{|}{C}}}-NH-Y \right] \underset{\longleftarrow}{\longrightarrow}$$

$$CH_3-\overset{O}{\overset{\|}{C}}-OCH_3 \qquad H\ddot{N}^{\ominus}-Y$$

$$H\ddot{N}^{\ominus}-Y + CH_3OH \longrightarrow H_2N-Y + CH_3\ddot{O}^{\ominus}$$

4) N. Takabayashi : Yakugaku Zasshi, **75**, 778 (1955).
5) Y. Sugiyama, T. Wachi, T. Isida, Y. Shimauchi: Japan Pat. 290, 125 (Application Sho. 33. 4. 25).

The percentage of deacetylation was estimated by determining the amount of ester, but not by the amount of amine, which were formed from the deacetylation reaction, because it was impossible to determine the amine without any hydrolysis of acetamino group in the reaction mixture which remained unreactedly. However, in addition to the deacetylation as the formation of methyl acetate, there were observed the deacetylation as the formation of sodium acetate, resulted from the side reaction, i. e. the hydrolysis of acetyl group in the starting material with sodium hydroxide due to the reaction between sodium methoxide and slight amount of water in the solvent, and also observed the loss of the ester due to the ester condensation.[*3]

On the other hand, the percentage of methoxylation was estimated by determining chlorine ions in the reaction-mixture, which had been liberated on account of the methoxylation.

The results of these two estimations (deacetylation and methoxylation) are altogether shown in the following figures. The percentages of the deacetylation and the methoxylation which took place by the reaction of 1 mole of 3-(p-acetamidophenyl-sulfonamido)-6-chloropyridazine (A) in methanolic solution with 2 or 3 mole of sodium methoxide at 90~130° for 3 hours, are shown in Fig. 1 and Fig. 2 respectively. The percentage of deacetylation which was estimated in the reaction of 1 mole of 3-(p-acet-amidophenylsulfonamido)-6-methoxypyridazine (B) in methanolic solution with 2 or 3 mole of sodium methoxide at 90~130° for 3 hours, is shown in Fig. 3. The percentage of methoxylation which was measured in the reaction of 1 mole of 3-sulfanilyl-6-chloro-pyridazine (C) in methanolic solution with 2 or 3 mole of sodium methoxide at 90~130°
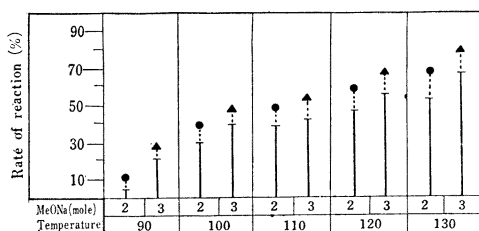

Fig. 1. Percentage of Deacetylation in the reaction of (A)

—— Deacetylation as the formation of AcOMe
······ Deacetylation as the formation of AcONa
• Using 2 mole of MeONa
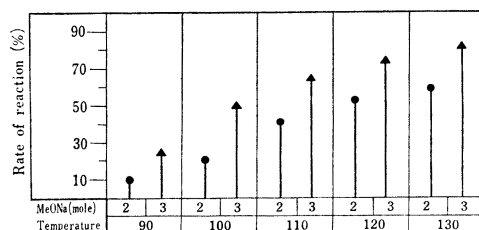▲ Using 3 mole of MeONa
Reaction Time : 3 hr.

Fig. 2. Percentage of Methoxylation in the reaction of (A)

• Using 2 mole of MeONa
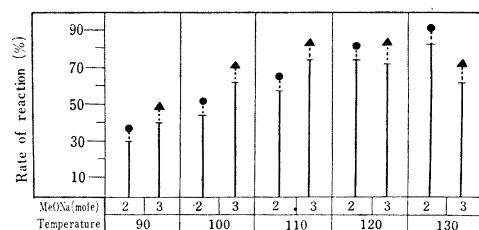▲ Using 3 mole of MeONa
Reaction Time : 3 hr.

Fig. 3. Percentage of Deacetylation in the reaction of (B)

—— Deacetylation as the formation of AcOMe
······ Deacetylation as the formation of AcONa
• Using 2 mole of MeONa
▲ Using 3 mole of MeONa
Reaction Time : 3 hr.

*3 Claisen condensation of methyl acetate.
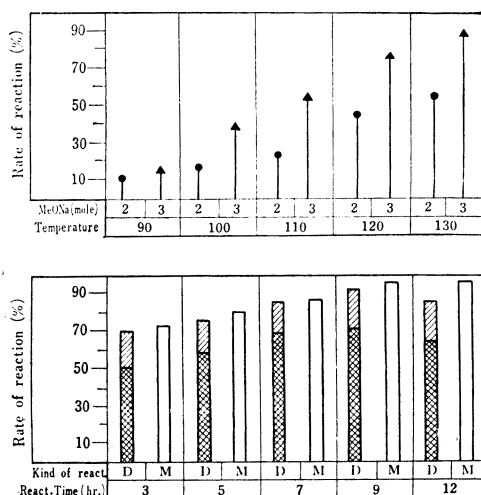
Fig. 4. Percentage of Methoxylation
        in the reaction of (C)

•   Using 2 mole of MeONa
▲   Using 3 mole of MeONa
React Time : 3 hr.

Fig. 5. Comparison of Percentage
        of Deacetylation with that of
        Methoxylation in the reaction
        of (A) at the react. temp. 120°

▨   Deacetylation as the forma-
     tion of AcOMe
▨   Deacetylation as the forma-
     tion of AcONa
▭   Methoxylation
Using 3 mole of MeONa
React. Temp: 120°

for 3 hours, is illustrated in Fig. 4. The comparison of the percentage of the deacetyl-ation with that of methoxylation by the reaction of 1 mole of 3-(p-acetamidophenyl-sulfonamido)-6-chloropyridazine (A) with 3 mole of sodium methoxide at 120° for 3~12 hours, is denoted by Fig. 5.

As shown in Fig. 1 and Fig. 2, it may be said that the methoxylation by dechlorina-tion and the deacetylation by alcoholysis proceeded side by side, not step by step, under any reaction condition. In other words, both of the methoxylation and the deacetyl-ation might always take place simultaneously under any reaction condition, even though not always equal in respect of velocity.

Compared figures of deacetylation (Fig. 1 and Fig. 3) with those of methoxylation (Fig. 2 and Fig. 4), it is observed that the percentage of methoxylation was more in-creased than that of deacetylation, when the amount of sodium methoxide was increased in the reaction. This fact suggests that the amount of sodium methoxide could influence on the methoxylation more than on the deacetylation, because sodium methoxide was consumed in the methoxylation as the reaction component, but not in the deacetylation, where sodium methoxide acted as a catalyzer.

The comparison of Fig. 1 with Fig. 3 shows that the deacetylation of 3-(p-acetamido-phenylsulfonamido)-6-methoxypyridazine (B) should proceed more rapidly than that of 3-(p-acetamidophenylsulfonamido)-6-chloropyridazine (A) under the same reaction con-ditions. This fact seems to be associated with the assumption which sodium methoxide was consumed in the reaction of (A) but not in the reaction of (B). However, this fact also might have connection with the difference between the solubilities of the both compounds in the reaction mixtures.

The comparison of Fig. 2 with Fig. 4 denotes that the methoxylation of 3-(p-acet-amidophenylsulfonamido)-6-chloropyridazine (A) seems to proceed nearly in a same degree as that in the methoxylation of 3-sulfanilyl-6-chloropyridazine (C) under the same reaction conditions, but especially at the temperature of 100° and 110°, rather faster than that of (C). Though the same amount of sodium methoxide was appearently used in both methoxylation of (A) and (C), some part of sodium methoxide should be consumed in the methoxylation of (A) to give sodium acetate, but not in the reaction of (C). Moreover, the solubility of (C) was found more than that of (A) in the reaction mixtures. According to these facts, it seems likely that the methoxylation of (C) should proceed faster than that of (A), but the experimental results denied this presumption.

In other words, the introduction of acetyl group at N^4-posion of the compound (C) seems not to give an influence to hinder its dechlorination but to give an effect to accelerate. The authors are much interested in the above finding, but it might be difficult to solve the reason why the introduction of acetyl group accelerate the dechlorination.

Fig. 5 shows that the ester values detected in the reaction mixtures decreased when the reaction time was prolonged, and this tendency was also observed when the reaction temperature was raised and the amount of sodium methoxide was increased, as shown in Fig, 3. This fact suggests that one portion of methyl acetate produced in the reaction mixture could be converted to methyl acetoacetate in the course of the reaction. Actually, this ester condensation was confirmed by the evidence in which acetone, the degradation product of methyl acetoacetate, was detected as 2,4-dinitrophenylhydrazone in the reaction mixture. Although this side reaction was inevitable, it was industrially quite negligible, since it occurred to a very slight extent and no contamination was observed in the product.

As described above, it was found by the authors for the first time that the reaction between 3-(p-acetamidophenylsulfonamide)-6-chloropyridazine and sodium methoxide in methanol was of two points reaction, where the deacetylation and the methoxylation proceeded simultaneously at one stroke and afforded the objective compound 3-sulfanilyl-6-methoxypyridazine in an excellent yield. From these findings, it was made clear that this reaction is available as the important key for the industrial production of 3-sulfanilyl-6-methoxypyridazine.

Experimental

3-Sulfanilyl-6-methoxypyridazine——50 g. of 3-(p-acetamidophenylsulfonamido)-6-chloropyridazine was added to the solution consisting of 11 g. of Na metal (corresponds to 3.1 mole) and 250 cc. of dehyd. MeOH. The mixture was put into an iron tube,[*4] and heated in an autoclave at 120~130° for 8 hr. After cooling, precipitated NaCl was filtered off and MeOH was distilled off accompanied with AcOMe from the filtrate. Thereafter, the residue was diluted with water and acidified with AcOH. The resulted light yellow crystals was collected and washed with water to obtain 39 g. of crude 3-sulfanilyl-6-methoxypyridazine. Yield : 93%. The crude product was purified by dissolving in dil. NH₄OH, treating with charcoal, reprecipitating by acidification with dil. AcOH, or by recrystallization from MeOH containing few drops of AcOH, to obtain slight yellow prisms of m.p. 180~181°, which did not depress on admixture with the authentic sample prepared through other routes previously reported.[1]

3-Sulfanilyl-6-ethoxy, and 3-sulfanilyl-6-isopropoxypyridazine were also prepared from 3-(p-acetamidophenylsulfonamido)-6-chloropyridazine by modification of the procedure described for 3-sulfanilyl-6-methoxy pyridazine above.

Methyl Acetate——When above obtained ca. 200 cc. of the distillate was gently redistilled with a fractionating column (1 m. length Widmer type tube), there was obtained 10.5 cc. of the distillate ranging from 53° to 64°, in which AcOMe was supposed to be highly enriched. The distribution of the fractional distillate is shown in the following table.

No. of Fraction	B.p. range (°C)	Volume of the distillate (cc.)
I	53~54	0.4
II	54~55	1.7
III	55~57	4.9
IV	57~59	0.3
V	59~61	0.5
VI	61~64	2.7
	Total	10.5

The Fraction III. was identified with the authentic AcOMe by messurement of their refractive index.

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*4 When glass tube was used, the product was rather contaminated with a resinous substance which could not be identified.

Acetamide : 9.0 cc. of the above obtained 10.5 cc. distillate (1.5 cc. was spent for the measurement of refractive index) was reacted with 10 cc. of 28% NH_4OH in a sealed tube at room temperature for seven days. When volatiles were removed under reduced pressure, ca. 4.0 g. of colorless prisms were obtained. m.p. 80~81°. No depression of melting point was observed when mixed with the authentic sample of acetamide.

Analysis of the Reaction——Materials[*5]: 3-(p-acetamidophenylsulfonamido)-6-chloropyridazine (A), 3-(p-acetamidophenylsulfonamido)-6-methoxypyridazine (B) and 3-sulfanilyl-6-chloropyridazine (C) were purified and dried before use.

(a) Analysis using the material (A)

16.35 g. (0.05 mole) of (A) was added to a solution consisted of 2.3 g. (0.1 mole) or 3.45 g. (0.15 mole) of Na metal and 82 g. (104 cc.) of dehyd. MeOH. The mixture was put into an iron tube and heated in an autoclave under various conditions as shown in Figs. 1, 2 and 5. After the reaction vessel was chilled, the volatiles (MeOH and AcOMe) were distilled off from the reaction mixture. The distillate was diluted to 250 cc. with MeOH and this solution (Solution I) was used for drtermination of AcOMe. The residue was dissolved into ca. 100 cc. of ice water and trace of floating $Fe(OH)_3$ was filtered off and washed with dist. water. All the filtrates were combined and diluted to 200 cc. with dist. water and divided into halves. Each 100 cc. of the solution (Solution Ⅱ and Solution Ⅲ) was used for determination of AcONa and NaCl respectively.

(1) Determination of methyl acetate : 50 cc. of Solution I was refluxed with 20 cc. of NKOH for 1 hr. on a steam bath. After cool, remaining KOH was titrated with NH$_2$SO$_4$ using few drops of phenolphthalein solution as indicator to know the amount of NKOH consumed by hydrolysis of AcOMe contained in 50 cc. of Solution I. Considered from the dilution of the original reaction mixture, the percentage of deacetylation as AcOMe was calculated by the following equation. $Y = X/10.0 \times 100\%$ wherein X represents the volume of NKOH in cc. consumed. If acetamido group was perfectly deacetylated to producedAcOMe the theoretical value of X must be 10.0 cc.

(2) Determination of sodium acetate : Solution Ⅱ above obtained was chilled, acidified with conc. H_3PO_4 to pH. 4~5 on cooling in anice bath, and let stand for a while to complete the precipitation. The precipitate was filtered off and washed with dist. water repeatedly. The resulting filtrate and washed water were combined and diluted to 170 cc. with dist. water and then conc. H_3PO_4 was added until it became 200 cc., from which 100 cc. was put out and AcOH contained in the solution was removed by steam distillation.[*6] 100 cc. of the distillate was enough to collect whole AcOH in the solution. The distillate was titrated with 0.1 NKOH using few drops of phenolphthalein solution as indicator. The percentage of deacetylation as the formation of AcONa (Y) was calculated by the fo llowing equation. $Y = X/125 \times 100\%$ wherein X shows the volume of 0.1 NKOH consumed in neutralizing AcOH distilled. If acetamido-group was perfectly deacetylated to produce AcONa, the theoretical value of X must be 125 cc.

(3) Determination of sodium chloride :[*7] On cooling, Solution Ⅲ above obtained was acidified with conc. HNO_3 to pH. 4~5 to obtain slight yellow precipitate, which was filtered off and washed with dist. water repeatedly. The filtrate and washed water were combined and diluted to 250 cc. with addition of dist. water and 10 cc. of the solution was shaken with 1 cc. of conc. HNO_3, 1 cc. of nitrobenzene and 10 cc. of 0.1 NAgNO$_3$. After the addition of 0.5 cc. of ferric ammonium sulfate solution as indicator, remaining $AgNO_3$ was titrated with 0.1N NH$_4$CNS to know the amount of 0.1N AgNO$_3$ consumed in precipitation of AgCl. If the methoxylation was perfectly completed to separate Cl$^-$ the theoretical volume of 0.1 NAgNO$_3$ consumed here must be 10.0 cc. The percenrage of methoxylation (Y) was calculated by the next equation. $Y = X/10.0 \times 100\%$ wherein X indicates the volume of 0.1N AgNO$_3$ consumed in precipitation of AgCl by Cl$^-$.

(b) Analysis using material (B)

16.1 g. (0.05 mole) of (B) was reacted with a solution consisting of 2.3 g. (0.1 mole) of dehyd. MeOH in the same manner as described for the material (A). The reaction temperature and reaction time were changed variously as shown in Fig. 3 and Solution I for determination of AcOMe and Solution Ⅱ for determination of AcONa were prepared by the same procedure as that mentioned above in (a).

AcOMe and AcONa, which were produced in the deacetylation of (B), were determined by the same methods described for (A) in (1) and (2). The percentages of these two kinds of deacetylations were calculated by the same equations shown in (1) and (2) respectively.

[*5] These materials were synthesized by the methods described in Part I. of this series, This Bulletin, **10**, 580 (1962).

[*6] The steam distillation must be completed with good care, so that a spray of the solution in the distillation flask containing H_3PO_4 does not rush into the distillate.

[*7] J. Volhard's residual titration method was employed, since this gave most accurate values in this case.

(c) Analysis using material (C)

14.16 g. (0.05 mole) of (C) was treated by the same manner as described in (a). After the reaction was over Solution Ⅲ for determination of NaCl, was prepared by the same way as that described in (3) of (a). Cl⁻ was measured by Volhard's method as mentioned above, and the percentage of methoxylation was calculated by the same equation cited in (3) of (a).

The results are shown in Figs. 1~5. Each marks in these figures, indicating the reaction percentages are shown by averages of twice or thrice reactions under the same conditions.

Detection of Acetone (the Degradation Product of Methyl Acetoacetate)——To a solution consisting of 1.15 g. (0.05 mole) of Na metal and 105 cc. of dehyd. MeOH(free from ketone and aldehyde), 3.7 g. (0.05 mole) of purified AcOMe was added and heated in an autoclave at 120° for 4 hr.[8]   After the volatiles were removed on a steam bath, the residue was diluted to 250 cc. with dehyd. MeOH (free from ketone and aldehyde) and 100 cc. of the solution was refluxed with 40 cc. of NKOH for 1 hr. Then the volatiles were distilled off from the reaction mixture and the distillate was added to an excess of the solution of 2,4-dinitrophenylhydrazine hydrochloride, and refluxed on a steam bath for a while. The resulting yellow precipitate was filtered off and washed with $2 N H_2SO_4$ and water. Yield : 20 mg. (0.8%), m.p. 127°, No depression of m.p. was observed when mixed with the authentic sample of 2,4-dinitrophenylhydrazone of Me_2CO.

Summary

For the purpose of industrial application, some new synthetic methods of 3-sulfanilyl-6-alkoxypyridazine were examined and the reaction of 3-(p-acetamidophenylsulfonamido)-6-chloropyridazine with sodium alkoxide in the corresponding alcohol was found to produce 3-sulfanilyl-6-alkoxypyridazine and the corresponding alkyl ester of acetic acid in both excellent yields.   To investigate the mechanisms of this reaction, 3-(p-acetamidophenylsulfonamido)-6-chloropyridazine, 3-(p-acetamidophenylsulfonamido)-6-methoxypyridazine and 3-sulfanilyl-6-chloropyridazine were reacted with sodium methoxide in methanol under various conditions, and estimated the percentages of deacetylation and methoxylation by determining the amount of ester and sodium acetate and chlorine ion.   From these results, it was found that the deacetylation and the methoxylation proceeded simultaneously in this reaction of two points, and the objective compound 3-sulfanilyl-6-methoxypyridazine was produced in a good yield.   Thus, this method was found available for the industrial production of 3-sulfanilyl-6-methoxypyridazine.

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[8] AcOMe, resulted from the reaction between 1 mole of (A) and 3 moles of MeONa under the condition described in (a), assumed to be exposed to the same condition as this procedure.