3-Oxo-6-methoxy-2,3-dihydro-5-pyridazinecarboxamide (XX)——To a stirred solution of 30 ml. of MeOH saturated with NH_3 at 0° was added with cooling 0.33 g. of XIX. The ester dissolved and amide began to deposit. The reaction mixture was stirred and cooled overnight, and evaporated to one-third of the original volume. The filtered crystals were recrystallized from water, giving XX as colorless needles, m.p. 265~266°. Yield, quantitative. *Anal.* Calcd. for $C_6H_7O_3N_3$: C, 42.60; H, 4.17; N, 24.85. Found: C, 42.89; H, 4.31; N, 25.03.

The authors express their deep gratitude to Prof. Emeritus E. Ochiai of the University of Tokyo for his kind encouragements throughout the course of the present work. They are also indebted to Mr. A. Murano for the measurement of infrared and ultraviolet spectra, to Mr. M. Chikada for his cooperation in this work, and to Mr. K. Iwai, Mr. N. Nishimura and Miss M. Fujita for the elementary analysis.

Summary

Reactions of 4-amino-3,6-dichloropyridazine (I) with caustic alkali in methanol and of 4-amino-3,6-dimethoxypyridazine (III) with acetylsulfanilchloride in pyridine were studied. In the former reaction, the reaction sequence to the formation of (III), 4-amino-6-chloro-(IV) and 4-amino-6-methoxy-3(2*H*)pyridazinone (V) was clarified. In the latter condensation reaction, it was found by thin-layer chromatography that 2-*p*-acetylaminobenzenesulfonyl-5-amino-6-methoxy-3(2*H*)pyridazinone (XI), two demethylated compounds (IX and X) of N^1-(3,6-dimethoxy-4-pyridazinyl)-N^4-acetylsulfanilamide (VIII) as well as the main product (VIII) were produced and their structures were proved. The demethylation reactions of VIII and its deacetylated compound (XII) with pyridine hydrochloride were examined.

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147. Takenari Nakagome, Akira Kobayashi, and Atsuko Misaki: Synthesis of Pyridazine Derivatives. XII.*1 Reaction of Amino-3(2*H*)pyridazinone Derivatives with Tosyl Chloride.

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In a previous work of this series,*1 4-amino-3,6-dimethoxypyridazine (XV) and 4-amino-6-methoxy-3(2*H*)pyridazinone (I) was reacted with acetylsulfanilyl chloride in pyridine with the object of preparing hitherto unknown N^1-4-pyridazinylsulfanilamides after subsequent deacetylation. The reaction was not quite simple and, besides desired N^1-4-pyridazinyl-N^4-acetylsulfanilamides some neutral substances were formed, whose structures, postulated as XIX and XX (Chart 3) have not yet been conclusive. The present work was undertaken in order to obtain further evidences supporting the foregoing assumption and for this purpose the reaction of some pyridazine and pyridazinone derivatives with tosyl chloride was investigated.

*1 Part XI. T. Nakagome, A. Kobayashi, A. Misaki, T. Komatsu, T. Mori, S. Nakanishi: This Bulletin, **14**, 1065 (1966).

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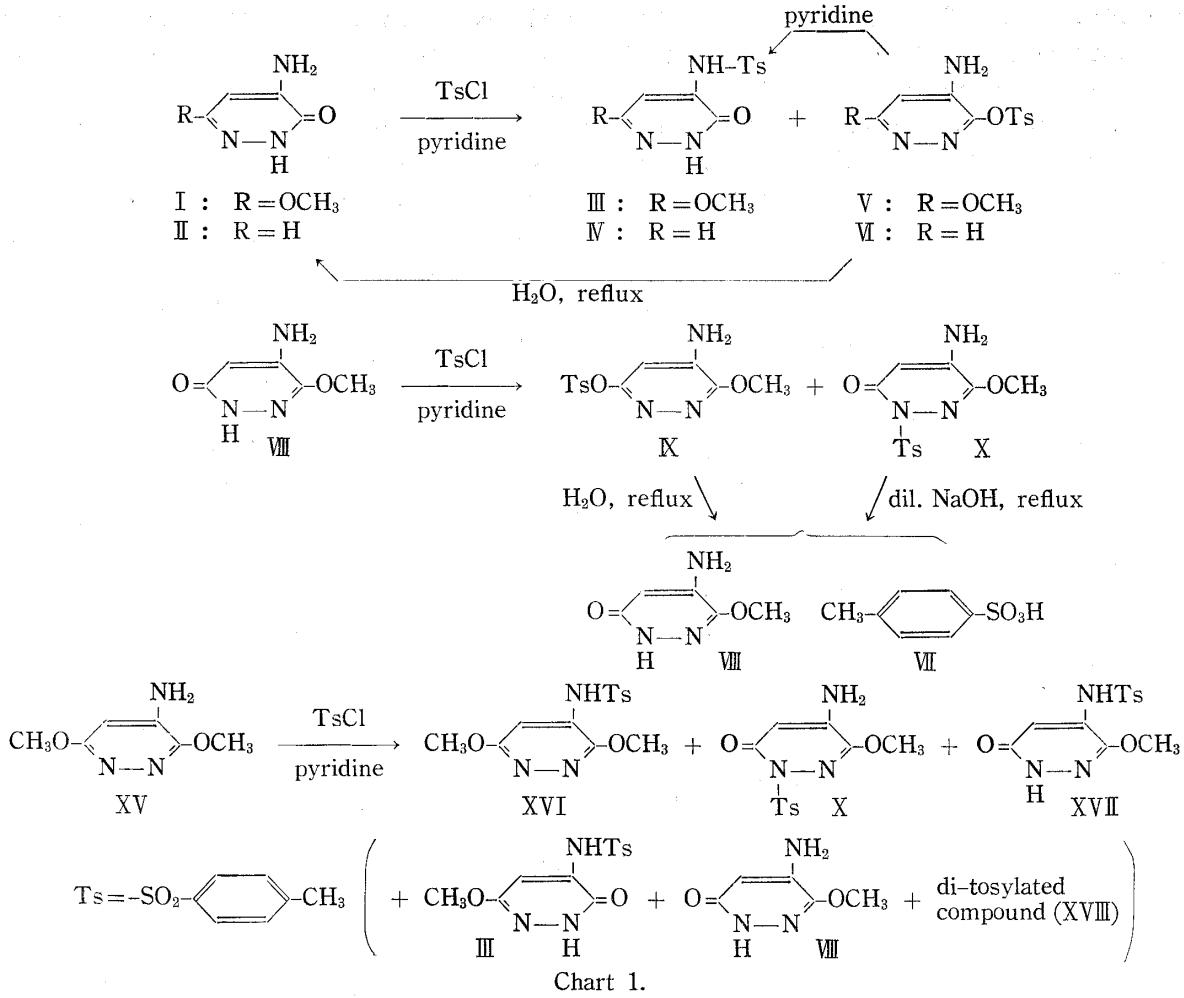

Chart 1.

When 4-amino-6-methoxy-3(2*H*)pyridazinone (I)*[1] was allowed to react with an equimolecular amount of tosyl chloride in pyridine at room temperature, condensation occurred mainly on the hydroxyl group with the result that 4-amino-6-methoxy-3-pyridazinol *p*-toluenesulfonate (V) and acidic N-(3-oxo-6-methoxy-2,3-dihydro-4-pyridazinyl)-*p*-toluenesulfonamide (III) were obtained in 50 and 12% yield respectively, with the recovery of 30% yield of the starting material. The non-acidic product (V) was hydrolyzed by refluxing in water to regenerate the original (I).

When the reaction was conducted for 8 days, the yield of V was decreased to 24% and that of III was increased to 30%. These results suggested that the rearrangement of the tosyl group in V to primary amino group took place to afford III. This was confirmed by stirring V in pyridine at room temperature for 8 days which resulted in the formation of III (26%) and I (30%).

Similarly 4-amino-3(2*H*)pyridazinone (II),[1] on treatment with tosyl chloride in pyridine, yielded N-(3-oxo-2,3-dihydro-4-pyridazinyl)-*p*-toluenesulfonamide (IV) and 4-amino-3-pyridazinol *p*-toluenesulfonate (VI) although the yield of the latter was only 1~2% of the theoretical.

In contrast to the condensation of 4-amino-3(2*H*)pyridazinones (I and II) with tosyl chloride cited above, 3-methoxy-4-amino-6(1*H*)pyridazinone (VIII) afforded no acidic product corresponding to III or IV, but two non-acidic monotosyl compounds (IX and X) in a ratio of 1:1. Hydrolysis of IX was readily effected only by refluxing in water to give the starting VIII and *p*-toluenesulfonic acid (VII), whereas X was stable under the

1) T. Kuraishi : This Bulletin, **6**, 331 (1958).

same condition. Cleavage of X was performed by heating it with dilute aqueous hydroxide solution to produce Ⅶ and Ⅷ. The reaction of 4-amino-3,6-dimethoxypyridazine (XV)[2] with tosyl chloride in pyridine was completely analogous to that which took place when XV was treated with acetylsulfanilyl chloride in pyridine, as described in Part Ⅺ*[1] of this series, and in this way two kinds of acidic products, *i.e.* principally formed N-(3,6-dimethoxy-4-pyridazinyl)-*p*-toluenesulfonamide (XVI) and its demethylated compound (XVII), and a minute amount of non-acidic substance were isolated from the reaction mixture. The non-acidic substance was identical with X obtained from Ⅷ. With an excess of tosyl chloride a small amount of di-tosyl compound was produced whose constitution has not been investigated. Thin-layer chromatographic study of the product revealed the formation of Ⅲ and Ⅷ in addition to the isolated compounds mentioned above (Fig. 1).

The constitutions of these products obtained as above were proved as follows. Those of 4-tosylamino compounds (Ⅲ), (Ⅳ), (XVI) were concluded from their elemental analyses and their acidity, characteristic of N-heterocyclic tosylamino compounds. An acidic by-product (XVII) from the reaction of XV with tosyl chloride was not identical with isomeric Ⅲ. This fact indicates that demethylation occurred on the methoxy group at 6 position in the formation of (XVII), and it follows that (XVII) is N-(3-oxo-2,3-dihydro-5-pyridazinyl)-*p*-toluenesulfonamide.

Concerning three non-acidic monotosyl compounds the positions of attachment of the tosyl residue were deduced by their differences of susceptibility to hydrolysis. In order to support the foregoing deduction the reaction of 6-methoxy-3(2*H*)pyridazinone (Ⅺ)[3] and 3,6-dimethoxypyridazine (Ⅻ)[4] with tosyl chloride was finally investigated.

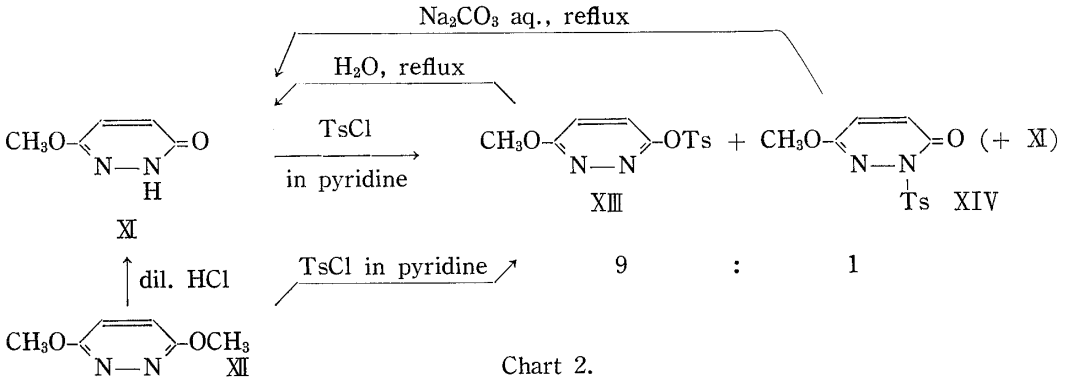

Chart 2.

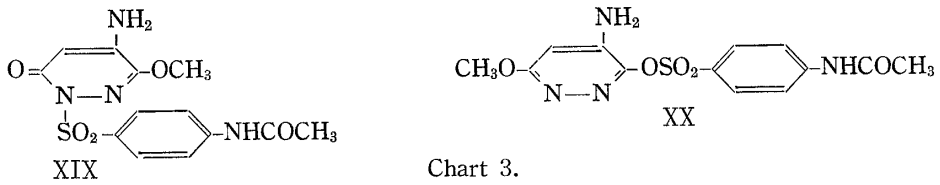

Chart 3.

It was found that 6-methoxy-3(2*H*)pyridazinone (Ⅺ), which had been obtainable[3] by treatment of 3-methoxy-6-chloropyridazine with acetic acid, was readily prepared from 3,6-dimethoxypyridazine (Ⅻ) by boiling with dilute hydrochloric acid in a satisfactory yield. When Ⅺ was warmed with tosyl chloride in pyridine on a boiling water bath, 6-methoxy-3-pyridazinol *p*-toluenesulfonate (XIII) and 2-(*p*-toluenesulfonyl)-6-methoxy-3(2*H*)pyridazinone (XIV) were obtained in a ratio of 9:1. The reaction of Ⅻ with tosyl chloride required prolonged heating and similarly led to the formation of

2) T. Itai, H. Igeta : Yakugaku Zasshi, **75**, 966 (1955).
3) Part Ⅱ. T. Nakagome : Yakugaku Zasshi, **82**, 244 (1962).
4) J. Druey, Kd. Meier, K. Eichenberger : Helv. Chim. Acta, **37**, 121 (1954).

XIII and XIV, together with a considerable amount (37% yield) of XI. Since the ratio of the formation of both non-acidic products (XIII) and (XIV) were quite similar, it might be supposed that they were formed by initial demethylation of XII followed by subsequent tosylation of the produced (XI). Comparing with the reaction of I, II, VIII and XV with tosyl chloride, stronger reaction conditions were required with XI and XII, and there seems likely to be participation of amino groups in the former compounds in promoting the reaction in some respects.

The structure of XIV was established by its infrared spectrum which showed a strong absorption band at 1695 cm^{-1}, attributable to the carbonyl group. This absorption band was not present in the spectrum of XIII. The remaining (XIII) is, therefore, the O-sulfonyl compound. These two condensation products were also characterized by their differences in stability to hydrolysis.

Hydrolysis of XIII was readily effected by heating it with water for a short period, but XIV remained unchanged under these same conditions. The hydrolysis of XIV was effected by heating it with dilute aqueous sodium hydroxide. Both XIII and XIV upon hydrolysis yielded 6-methoxy-3(2*H*)pyridazinone (XI) and sodium *p*-toluenesulfonate. Assignment of the structures to V, IX and X in this paper and XIX, XX which have been reported in Part XI*[1] is based upon this finding, although no synthetic proof has been made.

In the course of these experiments our attention has been drawn to the formation of X and XIX from XV by treatment with tosyl chloride and with acetylsulfanilyl chloride, respectively. The formation of this type of compound from heterocyclic ethers has been unknown except a recent report of Nitta, *et al.*[5] which describes the condensation of 2-methoxy-4-aminopyrimidine with 4-nitrobenzenesulfonyl chloride in pyridine which led to the formation of 3-(*p*-nitrobenzenesulfonyl)-4-imido-2(1*H*)-pyrimidinone at a reaction temperature of 75°. No evidence are available, however,

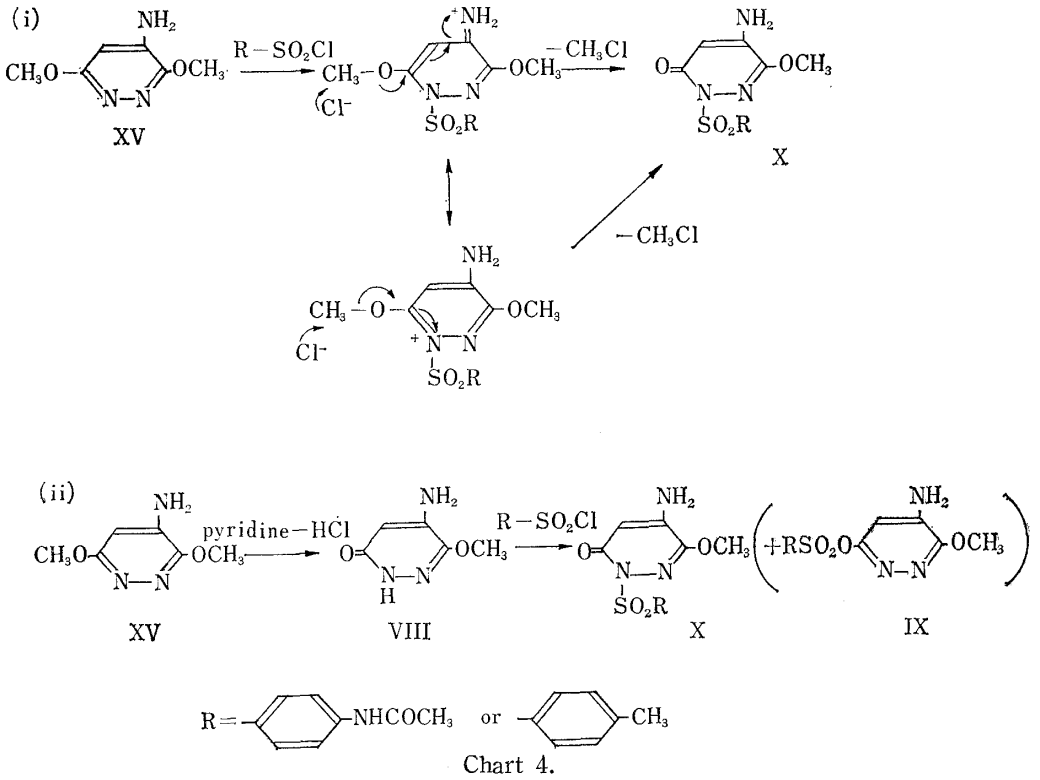

Chart 4.

5) Y. Nitta, K. Okui, K. Ito, M. Togo: This Bulletin, **13**, 568 (1965).

on whether the 4-nitrobenzenesulfonyl group is attached to the oxygen atom at the 2-position or the nitrogen atom at the 3-position.

As for the foregoing reaction, it may be deduced that the reaction proceeds through a route shown in (i) in Chart 4, considering the effect of 4-amino group to promote the reaction. An alternative process (ii), which involves the preliminary formation of Ⅷ followed by tosylation to Ⅹ, seems to be ruled out because the formation of Ⅸ was not observed by thin-layer chromatographic study of the reaction product (Fig. 1).

Experimental*3

Reaction of 4-Amino-6-methoxy-3(2*H*)pyridazinone (I) with Tosyl Chloride (TSC)——i) To a stirred mixture of 2.8 g. (0.02 mole) of I and 50 ml. of pyridine was added 4.2 g. (0.022 mole) of tosyl chloride (TSC). The mixture was stirred and kept at room temperature for 24 hr., poured into water containing 0.02 mole of NaOH, and the solution distilled with much water to remove pyridine. After being made alkaline with dil. NaOH under cooling, 2.8 g. of the insoluble 4-amino-6-methoxy-3-pyridazinol *p*-toluenesulfonate (Ⅴ), m.p. 165～166°, was collected and recrystallized from AcOEt, giving 2.45 g. (42%) of colorless rhombs, m.p. 171～172°. *Anal.* Calcd. for $C_{12}H_{13}O_4N_3S$: C, 48.81; H, 4.44; N, 14.23. Found: C, 48.82; H, 4.56; N, 14.24. The filtrate was adjusted with HCl to pH 12～13, concentrated *in vacuo*, chilled and filtered. The product (1.4 g.) was again dissolved in warm 2*N* NaOH (30～40 ml.), and chilled. Na salt of N-(3-oxo-6-methoxy-2,3-dihydro-4-pyridazinyl)-*p*-toluenesulfonamide (Ⅲ) separated as colorless needles, m.p. >300°. Yield 0.82 g. (12.3%). *Anal.* Calcd. for $C_{12}H_{12}O_4N_3S\cdot Na\cdot H_2O$: C, 42.99; H, 4.21; N, 12.54. Found: C, 43.26; H, 4.23; N, 12.52. The Na salt was added to a mixed solution of MeOH and 2*N* NaOH, heated on a steam bath and dissolved. The solution was acidified with HCl while being hot. Colorless thin needles which separated on chilling were collected and recrystallized from MeOH to give N-(3-oxo-6-methoxy-2,3-dihydro-4-pyridazinyl)-*p*-toluenesulfonamide (Ⅲ) as colorless rods, m.p. 215～216°. *Anal.* Calcd. for $C_{12}H_{13}O_4N_3S$: C, 48.81; H, 4.44; N, 14.23. Found: C, 49.26; H, 4.49; N, 14.23. The filtrates from the Na salt of Ⅲ were combined, neutralized with HCl and 0.9 g. (32%) the precipitate was collected, m.p. 260～270°. This was recrystallized from MeOH to give colorless crystals, m.p. 276～277° alone or on admixture with the starting material (I). Yield 0.7 g. (25%).

ii) A mixture of I (2.8 g.), pyridine (50 ml.) and TSC (4.2 g.) was kept at room temperature for 8 days and worked up as described in (i). The result of the experiment was as follows.

	Crude material	Purified material
Ⅴ	1.38 g. (23.6%)	0.8 g. (14%), m.p. 168～169.5°
Ⅲ		2.0 g. (30%)
Recovered I	0.75 g. (27%)	0.5 g. (18%), m.p. 268～271.5°

iii) To a stirred solution of 2.8 g. (0.02 mole) of I in 40 ml. of *N* NaOH was added 4.6 g. (0.024 mole) of TSC at room temperature. After stirring was continued for a further 48 hr., the insoluble material was filtered to give 0.65 g. (11%) of Ⅴ, m.p. 166～167°. Recrystallization from AcOEt afforded colorless rhombs, m.p. 171～172°. The melting point of a mixture with the material prepared in (i) was not depressed. On being neutralized with HCl the aqueous filtrate deposited crystals which were collected, m.p. 276～277° alone or on admixture with I. Yield 2 g. (72%).

Reaction of 4-Amino-3(2*H*)pyridazinone (II) with Tosyl Chloride——To a stirred mixture of 2.2 g. (0.02 mole) of Ⅱ and 60 ml. pyridine was added 4.2 g. (0.022 mole) of TSC with cooling. After stirring was continued at room temperature overnight the reaction mixture was poured into ice water and 20 ml. of *N* NaOH. The solution was concentrated *in vacuo* to remove pyridine, made alkaline with NaOH under cooling and the insoluble material (0.15 g.) was collected. Recrystallization from AcOEt gave 0.085 g. (1.6%) of 4-amino-3-pyridazinol *p*-toluenesulfonate (Ⅵ) as colorless needles, m.p. 205～205.5°. *Anal.* Calcd. for $C_{11}H_{11}O_3N_3S$: C, 49.81; H, 4.18; N, 15.84. Found: C, 49.80; H, 4.60; N, 15.77. On being neutralized with HCl to pH 6.0 the filtrate deposited 2.5 g. (47.6%) of N-(3-oxo-2,3-dihydro-4-pyridazinyl)-*p*-toluenesulfonamide (Ⅳ), m.p. 213.5～214.5°. The analytical sample was obtained by crystallizing from MeOH as colorless needles, m.p. 213～214°. *Anal.* Calcd. for $C_{11}H_{11}O_3N_3S$: C, 49.81; H, 4.18; N, 15.84. Found: C, 49.77; H, 4.47; N, 15.86. Evaporation of the aqueous filtrate *in vacuo* to dryness, extraction of the

*3 All melting points are uncorrected. Infrared spectra were measured with a Shimadzu IR Infrared Spectrophotometer.

residue with boiling EtOH, and evaporation of the EtOH left the crude starting material, which was purified by recrystallization from water giving 0.7 g. (32%) of colorless rhombs, m.p. 233° alone or on admixture with an authentic sample of II.

Reaction of 3-Methoxy-4-amino-6(1*H*)pyridazinone (VIII) with Tosyl Chloride——To a stirred mixture of 1.4 g. (0.01 mole) of VIII and 25 ml. of pyridine was added 2.1 g. (0.011 mole) of TSC under ice cooling and the mixture was stirred at room temperature overnight. Pyridine was distilled off with much water under reduced pressure and the mixture was made alkaline with dil. aq. NaOH under cooling. The insoluble material (2.6 g., m.p. 168~172°) was collected and fractionally recrystallized from AcOEt giving 1 g. (34%) of slightly soluble 1-(*p*-toluenesulfonyl)-3-methoxy-4-amino-6(1*H*)pyridazinone (X) and 1.4 g. (48%) of readily soluble 3-methoxy-4-amino-6-pyridazinol *p*-toluenesulfonate (IX).

Second recrystallization of X from AcOEt gave colorless prisms, m,p. 200~201°. *Anal.* Calcd. for $C_{12}H_{13}O_4N_3S$: C, 48.81; H, 4.44; N, 14.23. Found : C, 48.86; H, 4.46; N, 13.89. Yield 0.9 g. (31%).

IX was further purified by recrystallization from AcOEt to give 1.25 g. (42.5%) of colorless leaflets, m.p. 166° (after melting at 166°, solidified and again melted at around 190°). *Anal.* Calcd. for $C_{12}H_{13}O_4N_3S$: C, 48.81; H, 4.44; N, 14.23. Found : C, 49.09; H, 4.50; N, 14.13.

The both AcOEt mother liquors were combined and AcOEt was distilled off. The residue, dissolved in $CHCl_3$, was chromatographed on alumina. The initial fractions afforded 0.22 g. of IX, m.p. 166°, and the later fractions 0.2 g. of X, m.p. 196~197°. Total yield, IX 1.47 g. (50%), X 1.2 g. (41%).

Rearrangement of V——A solution of 2 g. of V in 20 ml. of pyridine was stirred at room temperature for 8 days. It was then poured into water and the solid, separated on evaporation of pyridine *in vacuo*, was triturated with *N* NaOH (50~100 ml.) and filtered. There was obtained 0.43 g. (21.5%) of the starting material, m.p. 151~160°, which was recrystallized from AcOEt to give colorless rhombs, m.p. 168~169°, undepressed when mixed with an authentic sample of V. The IR spectrum of the product was identical with that of an authentic sample of V. The aqueous filtrate was acidified with HCl to pH 5. The crude (III) which separated was collected, and dissolved in warm dil. aq. NaOH. The solution deposited colorless needles on cooling, weighing 0.6 g. (26.4%), m.p. >300°. Identity of this material with Na salt of III was established by infrared analysis. The filtrate from the crude (III) was concentrated *in vacuo* and 0.3 g. (31.4%) of crystals, m.p. 268~273° was obtained. Recrystallization from MeOH raised the m.p. to 279~280°. The melting point of a mixture with an authentic sample of I was not depressed. Neutralization of the filtrate from Na salt of III gave an additional crop of 0.2 g. which showed two spots of I and Na salt of III on thin-layer chlomatography (TLC).

Reaction of 4-Amino-3,6-dimethoxypyridazine (XV) with Tosyl Chloride——i) To a stirred mixture of 5.5 g. (0.03 mole) of XV and 30 ml. of pyridine was added 6.8 g. (0.03 mole) of TSC below 10°. After stirring was continued overnight at room temperature, the solution was poured into ice water containing 0.03 mole of NaOH. The resulting mixture was concentrated *in vacuo* to remove the pyridine, made alkaline with dil. aq. NaOH and the insoluble material (sample 1 in Fig. 1) was filtered. The filtrate was fractionally acidified with 6*N* HCl. The product (3.8 g., 34.7%, sample 2 in Fig. 1), precipitated at pH 6.0, was recrystallized from ether to afford 3.22 g. (30.3%) of N-(3,6-dimethoxy-4-pyridazinyl)-*p*-toluenesulfonamide (XVI) as colorless prisms, m.p. 125~126°. An additional recrystallization raised the melting point to 127~128°. *Anal.* Calcd. for $C_{13}H_{15}O_4N_3S$: C, 50.48; H, 4.89; N, 13.59. Found : C, 50.73; H,

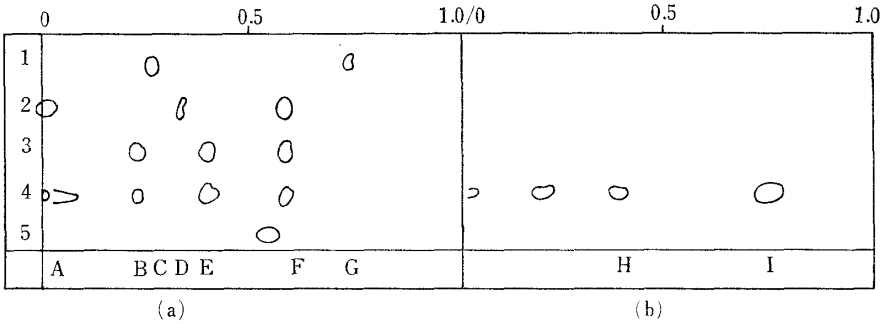

Fig. 1. Thin-layer Chromatogram of a Product from the Reaction of XV and Tosyl Chloride in Pyridine

Layer : Silica Gel G, activated at 105° for 30 min. Detection : I_2 vapor
Solvent : (a) $CHCl_3$-acetone-AcOH (7:3:0.05), 10 cm. (b) $CHCl_3$-MeOH (8:2), 10 cm.
Sample : 1. A non-acidic fraction
2. A fraction separated at pH 6.0
3. A fraction separated at pH 5.5~3.0
4. A filtrate from the filtration separated at pH 5.5~3.0
5. IX
Spots were identified as follows : A, H : VIII, B : XVII, C : X, D : III, E, I : XV, F : XVI, G : XVIII

5.05; N, 13.53. The solid (0.235 g. (2.24%), m.p. 250~260°, sample 3 in Fig. 1), precipitated within a pH range 5.5~3.0 (the filtrate, sample 4 in Fig. 1), was purified by recrystallization from MeOH, giving N-(3-oxo-6-methoxy-2,3-dihydro-5-pyridazinyl)-*p*-toluenesulfonamide (XVII) as colorless leaflets, m.p. 280~283°. Yield 0.12 g. (1.27%). *Anal.* Calcd. for $C_{12}H_{13}O_4N_3S$: C, 48.81; H, 4.44; N, 14.23. Found: C, 49.24; H, 4.75; N, 14.19. The foregoing solid, separated from the aqueous alkaline filtrate, weighing 3.9 g., was triturated with *N* HCl and filtered, giving 1.5 g. (14.3%) of X, m.p. 199~200°. No depression of melting point was observed when mixed with a sample prepared from VIII. The acidic aqueous filtrate and the filtrate from the crude (XVII) were combined, made alkaline with Na_2CO_3, concentrated to a small volume and chilled. Recrystallization of the crystals, which separated, from AcOEt gave 2 g. (36%) of colorless rhombs, melting at 177~178° alone or on admixture with XV.

ii) XV (5.5 g., 0.03 mole) suspended in 30 ml. of pyridine was reacted with 8.45 g. (0.03×1.25 mole) of TSC and worked up in the similar way as described in (i). The filtrate from recrystallization of X was evaporated to dryness. The residue was recrystallized from MeOH to yield the ditosyl compound of XV as colorless needles, m.p. 221~222°. *Anal.* Calcd. for $C_{20}H_{21}O_6N_3S_2$: C, 51.84; H, 4.57; N, 9.07; S, 13.81. Found: C, 51.84; H, 4.50; N, 8.92; S, 13.75. The result of the experiment (ii) was as follows:

	Crude material	Purified material
XVI	4.45 g. (45%), m.p. 121~123°	3.75 g. (38%), m.p. 125~126°
XVII	0.39 g. (4.1%), m.p. 249~257°	0.25 g. (2.6%), m.p. 282~283°
X		1.45 g. (15.6%), m.p. 198~200°
XVIII		0.12 g. (0.7%), m.p. 221~222°
Recovered XV		1.6 g. (29%)

6-Methoxy-3(2*H*)pyridazinone (XI)——A solution of 20 g. of 3,6-dimethoxypyridazine (XII)[4] in 100 ml. of 2*N* HCl was refluxed for 2 hr. After cooling, XI was precipitated by addition of aq. Na_2CO_3 solution. Yield 16.5 g. (91.7%), m.p. 162.5~164°. Recrystallization from AcOEt gave 15.1 g. (84%) of colorless plates, m.p. 163° alone or on admixture with an authentic sample.[3]

Reaction of XI with Tosyl Chloride——i) To a stirred solution of 5 g. (0.04 mole) of XI in 25 ml. of pyridine was added 8.45 g. (0.044 mole) of TSC. The mixture was then heated on a boiling water bath for 2.5 hr., poured into ice water, and the solution was evaporated *in vacuo*. The residue was washed with dil. aq. NaOH, filtered giving 9.5 g. (80%) of the crude mixture, m.p. 84~94°. Recrystallization from $(iso\text{-}Pr)_2O$ yielded 4.1 g. of 6-methoxy-3-pyridazinol *p*-toluenesulfonate (XIII) as colorless needles, m.p. 101~101.5°. *Anal.* Calcd. for $C_{12}H_{12}O_4N_2S$: C, 51.43 H, 4.32; N, 9.99. Found: C, 51.58; H, 4.45; N, 10.03. The $(iso\text{-}Pr)_2O$ mother liquor was evaporated, and the residue was dissolved in benzene, poured onto alumina column, which was eluted with benzene and benzene-$CHCl_3$ (1:1) mixture. Each effluent was checked by TLC (Silica Gel plate, AcOEt-benzene (8:2) solvent, detected by $KMnO_4$ in H_2SO_4). Two spots; Rf 0.615 (XIII), 0.545 (XIV). After evaporation of the solvent and recrystallization from AcOEt, there were obtained (a) 3.3 g. of XIII, colorless needles, m.p. 101~101.5°, total yield 7.4 g. (67%) and (b) 0.84 g. (7.6%) of XIV, m.p. 139~140°, colorless plates. IR cm^{-1}: $\nu_{C=O}$ 1675, 1695 (Nujol). *Anal.* Calcd. for $C_{12}H_{12}O_4N_2S$: C, 51.43; H, 4.32; N, 9.99. Found: C, 51.61; H, 4.47; N, 10.13.

ii) To a stirred solution of 1.26 g. (0.01 mole) of XI in 20 ml. of *N* NaOH was added 2.3 g. (0.012 mole) of TSC. After stirring was continued overnight, the insoluble material (1.53 g., 55%, m.p. 92~98°) was collected, and recrystallized from $(iso\text{-}Pr)_2O$ giving 1.2 g. of XIII, m.p. 102°. The $(iso\text{-}Pr)_2O$ filtrate was evaporated and the residue, after chromatography and recrystallization, gave

(a) XIII, m.p. 100~101°, 2.8 g., total 1.48 g. (53%).
(b) XIV, m.p. 138~139°, 0.05 g. (1.8%).

iii) Preparation of XIV. The crude product (18 g., 81% yield), from 10 g. of XI, 30 ml. of pyridine and 17 g. of TSC, was boiled with 250 ml. of water under reflux for 20 min. The cooled mixture was made alkaline with NaOH and 4.2 g. (19%) of the insoluble material was filtered, and recrystallized from acetone-$(iso\text{-}Pr)_2O$. There was obtained 3.0 g. (13.5%) of purified XIV as colorless plates, m.p. 138~139°. Saturation of the alkaline filtrate with NH_4Cl, extraction with $CHCl_3$, evaporation of $CHCl_3$ and recrystallization of the residue yielded colorless plates, m.p. 162~163°, identified with an authentic sample of starting material by mixture melting point.

Reaction of XII with Tosyl Chloride——A solution of 2.1 g. (0.015 mole) of XII and 3.5 g. (0.018 mole) of TSC was heated on a boiling water bath for 15 hr. After pouring into ice water the solid, which separated, was collected and dissolved in $CHCl_3$. Alumina was added to the solution to decolorize it and removed by filtration. The $CHCl_3$ was removed by distillation, and the residue dissolved in benzene and chromatographed on alumina. The initial fraction eluted with benzene, on evaporation of the solvent, afforded 0.8 g. (19%) of colorless needles, m.p. 98~99°. The melting point of a mixture with XIII was not depressed. The fraction eluted with benzene-$CHCl_3$ (1:1) mixture and $CHCl_3$ gave 0.1 g. (2.4%) of colorless

plates, m.p. 138～139° after recrystallization from (iso-Pr)$_2$O. This was identified with XIV by mixture melting point. Further elution with $CHCl_3$–MeOH (9:1) mixture afforded 0.7 g. (37%) of colorless plates, m.p. 162～163°. There was no depression of melting point on admixture with XI.

Hydrolysis of Tosylated Products (V), (IX), (X), (XIII), (XIV)——Hydrolysis of tosylated compounds was effected by treating with water or dilute alkaline solution, as illustrated in Table I. After the reaction was completed, the resulting solution was acidified with HCl, and then made alkaline with Na_2CO_3. Concentration of the solution under reduced pressure separated pyridazinone which was filtered (in the case of (i) and (ii) the solution was extracted with $CHCl_3$). Further concentration of the filtrated and chilling separated Na *p*-toluenesulfonate. Both products were purified by recrystallization from EtOH (XI was from AcOEt). Pyridazinones were identified by mixture melting point and comparison of IR spectra, and Na *p*-toluenesulfonate was identified by comparison of IR spectra with those of an authentic sample. The results of the experiments are shown in Table I.

Table I.

Starting material (g.)	Reaction Conditions: Reaction medium (ml.)	Temp.	Time (min.)	Products: Pyridazinones	Na *p*-Toluenesulfonate
i) XIII 0.2	H_2O 10	reflux	5～30	XI 0.088 g. (97%) (m.p. 162～163°)	0.08 g. (58%)
ii) V 0.1	H_2O 5	reflux	60	I 0.03 g. (63%)	
0.1	*N*-NaOH 5	room temp.	overnight	starting material recovered	
0.1	*N*-HCl 5	room temp.	overnight	starting material recovered	
iii) IX 0.38	H_2O 10	reflux	60	VIII 0.13 g. (73.5%) (m.p. 267°)	0.15 g. (60%)
iv) XIV 0.1	H_2O 5	reflux	30	starting material recovered	
0.1	5% Na_2CO_3 5	reflux	60	XI 0.03 g. (67%) (m.p. 162～163°)	
v) X 0.1	H_2O 5	reflux	60	starting material recovered	
0.1	*N* NaOH 5	room temp.	overnight	starting material recovered	
1.0	2*N* NaOH 10	reflux	90	VIII 0.31 g. (64%)	0.5 g. (76%)

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Summary

Reactions of 4-amino-6-methoxy-(I), 4-amino-3(2*H*)pyridazinone (II) and 3-methoxy-4-amino-6(1*H*)pyridazinone (VIII) with tosyl chloride in pyridine were investigated. 4-Amino-3,6-dimethoxypyridazine (XV) was also allowed to react with tosyl chloride in pyridine and N^1-(3,6-dimethoxy-4-pyridazinyl-(XVI), N^1-(3-oxo-6-methoxy-2,3-dihydro-5-pyridazinyl)-*p*-toluenesulfonamide (XVII) and 2-*p*-toluenesulfonyl-5-amino-6-methoxy-3(2*H*)pyridazinone (X) were isolated. Consideration was made on the mechanism of the formation of X.

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