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116. Issei Iwai and Tetsuo Hiraoka : Studies on Acetylenic Compounds. XXXVII.*1 The Cyclization Reaction of Some Propargylammonium Halide Derivatives. (2*2).

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Previously, the cyclization of 1-(2-propynyl)-2-aminopyridinium bromide was reported.[1] This ring closure was presently extended to other heterocyclic ring systems in which the mode of cyclization was somewhat different. With the 2-aminopyrimidine derivative rearrangement as well as cyclization occurred under varying reaction conditions. Treatment of 1-(2-propynyl)-2-imino-1, 2-dihydropyrimidine hydrobromide (II) prepared from 2-aminopyrimidine (I) and propargyl bromide with aqueous sodium hydroxide solution at room temperature gave a crystalline compound m.p. 108~109° which separated from the aqueous reaction mixture as precipitate. According to the reaction of 1-(2-propynyl)-2-aminopyridinium bromide reported earlier,[1] this substance was expected to be a cyclized compound, however, infrared spectrum showed an ethynyl hydrogen and triple bond absorptions at 3300 and 2100 cm^{-1}, respectively. The nuclear magnetic resonance spectrum of this compound showed an AB_2 type peak in the aromatic region due to pyrimidine ring hydrogens in addition to propargyl peaks. From these results this compound apparently is 2-(2-propynylamino)pyrimidine (IV). The formation of IV from II is thought to occur *via* the reaction mechanism shown in Chart 1.

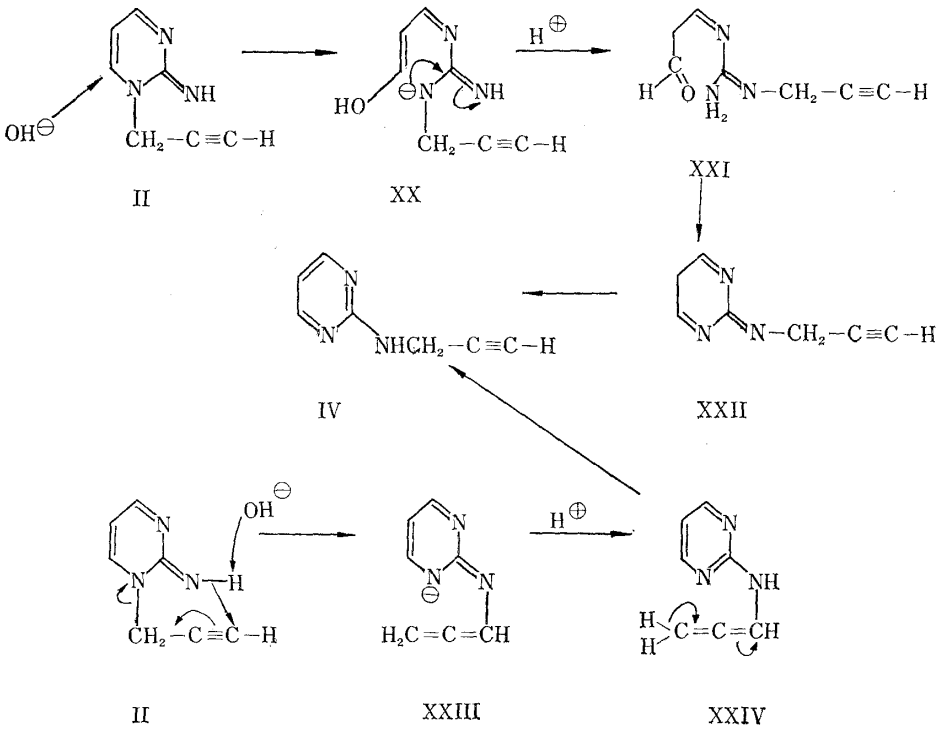


Chart 1.

*1 Part XXXVI : This Bulletin, **11**, 1569 (1963).
*2 Part (1) : *Ibid.*, **11**, 1564 (1963).
*3 Nishi-shinagawa, Shinagawa-ku, Tokyo (岩井一成, 平岡哲夫).
1) I. Iwai, T. Hiraoka : This Bulletin, **11**, 1564 (1963).

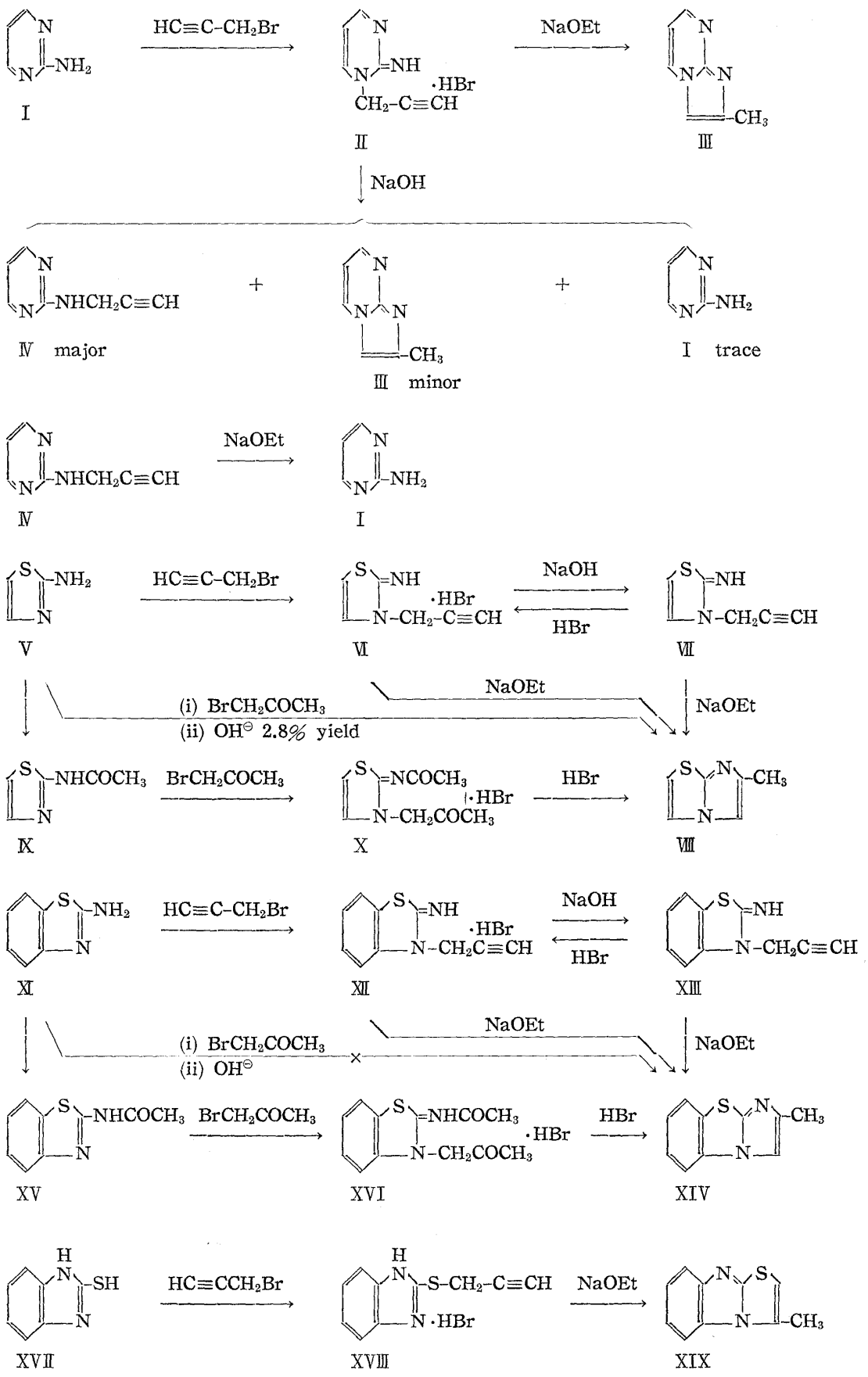
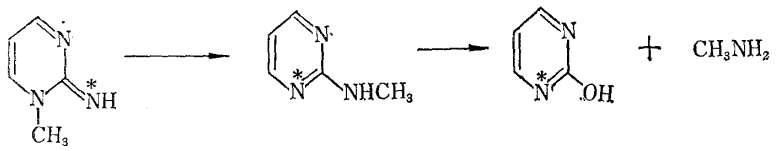


Chart 2.

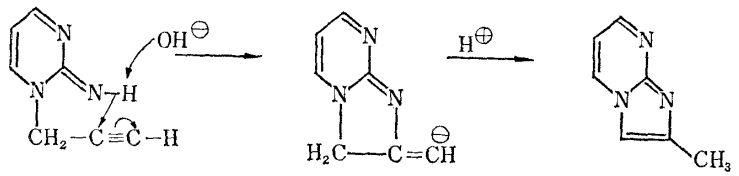
Such a ring opening mechanism in the pyrimidine series has been established by Brown[2] using nitrogen-15 in the case of 2-aminopyrimidine methoiodide as shown below :



An alternative mechanism for the formation of Ⅳ is through XXⅢ and XXIV in Chart 1, however, this route is unlikely because the allenic compound (XXIV) could hardly rearrange to the acetylenic compound (Ⅳ) under the given reaction conditions.

From the water soluble fraction in the reaction of Ⅱ with aqueous sodium hydroxide solution another substance of m.p. 95~97° was isolated and identified as 2-methylimidazo[1,2-*a*]pyrimidine (Ⅲ) by comparison with an authentic sample prepared from 2-aminopyrimidine (I) and monobromoacetone.[3]

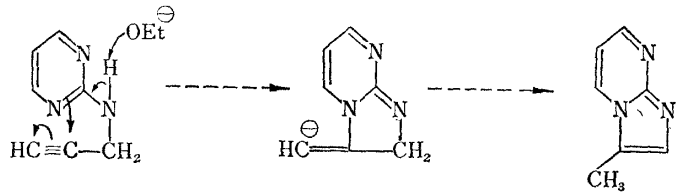
The reported melting point of Ⅲ was 72°, however, our preparation melted at 95~97°. This difference in melting point could be due to the hygroscopic nature of Ⅲ. The non-hygroscopic picrate of Ⅲ melted at 175~176°. A trace of 2-aminopyrimidine (I) was isolated as a third substance in the reaction of Ⅱ with sodium hydroxide solution. Treatment of Ⅱ with sodium ethoxide in alcohol gave only Ⅲ in good yield. The reaction mechanism of the formation of Ⅲ from Ⅱ might occur as shown in Chart 3.



Ⅱ′ XXV Ⅲ

Chart 3.

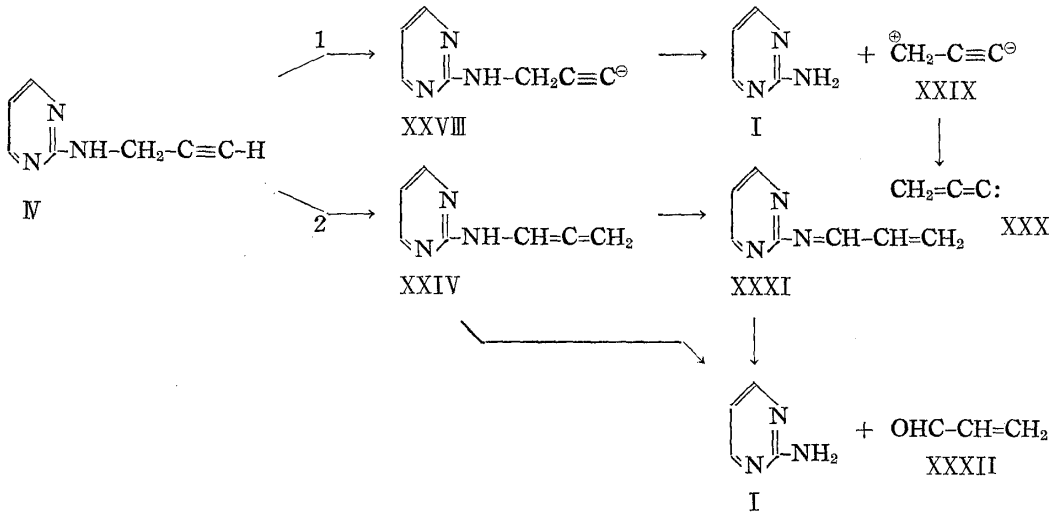
Considering the reaction mechanism, Ⅳ could cyclized into 3-methylimidazo[1,2-*a*]-pyrimidine (XXⅦ) as shown below :



Ⅳ′ XXVI XXVII

However, the reaction of Ⅳ with sodium ethoxide in alcohol gave mainly 2-aminopyrimidine (I) together with an unidentified substance. The formation of 2-aminopyrimidine can be explained by the following alternative mechanisms :

2) D. J. Brown : Nature, **189**, 828 (1961).
3) N. P. Buu-Hoi, L. Petit, N. D. Xuong : Compt. rend., **248**, 1832 (1959).



The first route will result in the formation of a carbene (XXX) and the other will give acrolein (XXXII) and of the two the former seems to be more reasonable.

This cyclization was further extended to other ring systems. A mixture of 2-aminothiazole (V) and propargyl bromide in alcohol was heated on a water bath to give a N-propargyl hydrobromide, m.p. 161~162°. It is uncertain whether the propargyl group is attached to the ring nitrogen or to the primary amino substituent, since the infrared NH or NH_2 streching absorption overlaps with the ethynyl hydrogen absorption. However, Kaye, *et al.* has reported[4] the alkylation reaction of 2-aminothiazole (V) and they clarified that in the absence of a catalyst 2-aminothiazole was alkylated with alkyl halide at the ring nitrogen. This fact was also demonstrated in the reaction of 2-aminothiazole with ω-bromoacetophenone.[5] Thus, the compound, m.p. 161~162°, obtained above could be concluded to be 2-imino-3-(2-propynyl)-4-thiazoline hydrobromide (Ⅵ). Compound (Ⅵ) was converted into the free base, 2-imino-3-(2-propynyl)-4-thiazoline (Ⅶ), on treatment with sodium hydroxide solution. No rearrangement of propargyl group occurred in this procedure since Ⅶ gave the starting material, Ⅵ, on treatment with hydrobromic acid. Compound (Ⅶ) is rather unstable and on storage at room temperature it polymerizes into a substance insoluble in organic solvents. This phenomenon is very similar to that observed in the case of 1-methyl-2-imino-1,2-dihydropyridine.[6] The picrate of Ⅶ melted at 154~155°. The reaction of Ⅵ with sodium ethoxide in alcohol gave the expected cyclized compound, 6-methylimidazo[2,1-*b*]thiazole (Ⅷ) as a distillable oil. The appearance of an aromatic ring methyl peak at 7.7 τ in the nuclear magnetic resonance spectrum confirmed that the cyclization had occurred. In order to confirm this structure further, an independent synthesis of Ⅷ was attempted according to a known general method[5] using 2-acetamidothiazole (Ⅸ) and monobromoacetone. The reaction of 2-acetamidothiazole (Ⅸ) with monobromoacetone in xylene gave 2-acetylimino-3-acetonyl-4-thiazoline hydrobromide (X), m.p. 194~195°. Heating X with 2*N* hydrobromic acid gave a hydrobromide of Ⅷ which was identical in all respects with the sample obtained from Ⅵ. Compound (Ⅷ) was also obtained from 2-aminothiazole (V) and monobromoacetone in very poor yield by the following procedure : treatment of V with monobromoacetone in alcohol gave a bromide salt as a semi-solid which was only with great difficulty recrystallizable, therefore it was treated with aqueous sodium hydroxide solution without purification to afford an oil. Fractional

4) I. A. Kaye, C. L. Parris : J. Am. Chem. Soc., **74**, 2921 (1952).
5) B. Kickhoefen, F. Kroehnke : Chem. Ber., 88, 1109 (1955).
6) A. E. Tschitschibabin, R. A. Konowalowa, A. A. Konowalowa : *Ibid.*, **54**, 814 (1921).

distillation of this oil gave an unidentified substance of m.p. 72~73° as major product and Ⅷ as minor product (2.8% yield).

In a similar way, 2-aminobenzothiazole (Ⅺ) reacted with propargyl bromide in alcohol to give 2-imino-3-(2-propynyl)-2,3-dihydrobenzothiazole hydrobromide (Ⅻ), m.p. 219~220°, which could be converted into the free base, 2-imino-3-(2-propynyl)-2,3-dihydrobenzothiazole (XIII) m.p. 101~102° by the action of sodium hydroxide solution. In contrast to Ⅶ, XIII is stable in the air at room temperature. Heating XIII or Ⅻ with sodium ethoxide in alcohol gave the cyclic compound, 2-methylimidazo[2,1-*b*]benzothiazole (XIV), m.p. 89~90°, which was also synthesized from 2-acetamidobenzothiazole (XV) and monobromoacetone *via* 2-acetylimino-3-acetonyl-2,3-dihydrobenzothiazole hydrobromide (XVI), m.p. 224~226°. An attempt to synthesize XIV directly from 2-aminobenzothiazole (Ⅺ) and monobromoacetone as in the case of 2-aminothiazole (Ⅴ) was unsuccessful. The only isolable compound was an unidentified crystalline substance which melted at 125~127°.

Treatment of 2-benzimidazolethiol (XVII) with propargyl bromide in alcohol gave a propargyl hydrobromide of m.p. 179~180°. This compound showed negative SH test with alcoholic mercuric chloride, therefore it was shown to be hydrobromide of 2-(2-propynylthio)benzimidazole (XVIII). The reaction of XVIII with sodium ethoxide in alcohol gave 3-methylthiazolo[3,2-*a*]benzimidazole (XIX), m.p. 161~162° which is identical in all respects with an authentic sample.[7]

From these results it is clear that β carbon of propargyl ammonium halide derivatives ($\geqslant\overset{\oplus}{N}\text{-}\overset{\alpha}{C}H_2\text{-}\overset{\beta}{C}\equiv\overset{\gamma}{C}\text{-}H$) is reactive to anionoid reagents in alkaline medium. This new cyclization reaction should be useful for the general synthesis of methyl substituted heteroaromatic compounds.

Experimental[*4]

1-(2-Propynyl)-2-imino-1,2-dihydropyrimidine Hydrobromide (II)——A mixture of 2-aminopyrimidine (I) (19 g.), propargyl bromide (23.8 g.) and abs. EtOH (300 ml.) was heated on a water bath (80°) for 13 hr. Then the crystalline substance was collected by filtration and washed with abs. EtOH to give 1-(2-propynyl)-2-imino-1,2-dihydropyrimidine hydrobromide (Ⅱ) of m.p. 180~181°. Recrystallization from abs. EtOH gave prisms of m.p. 195~196° (12 g.). The filtrate was further heated on a water bath (80°) for 24 hr. to give a further 6.2 g. of the product melting at 179~181°. *Anal.* Calcd. for $C_7H_8N_3Br$: C, 39.27; H, 3.77; N, 19.63. Found : C, 39.18; H, 3.91; N, 19.57. IR λ_{max}^{Nujol} μ : 3.06 (C≡C-H), 4.70 (C≡C).

The Reaction of 1-(2-Propynyl)-2-imino-1,2-dihydropyrimidine Hydrobromide (II) with Aqueous Sodium Hydroxide Solution——To 1-(2-propynyl)-2-imino-1,2-dihydropyrimidine hydrobromide (Ⅱ) (6 g.) in H_2O (30 ml.) was added 10% NaOH solution (15 ml.) at room temperature. After 30 min. the crystalline substance was separated and this reaction mixture was allowed to stand at room temperature for further 2 hr., and then it was stored in an ice box for a night. The crystalline substance was collected by filtration, washed with H_2O and dried in vacuum to give 2-(2-propynylamino)pyrimidine (Ⅳ) of m.p. 107~109° (1.1 g.). Recrystallization from hexane-EtOH gave a sample of m.p. 108~109°. The filtrate was three times extracted with Et_2O. The combined extracts were dried over Na_2SO_4 and evaporated to give furter Ⅳ of m.p. 103~107° (0.85 g.). Recrystallization from H_2O gave flakes of m.p. 108~109° (350 mg.). *Anal.* Calcd. for $C_7H_7N_3$: C, 63.14; H, 5.30; N, 31.56. Found : C, 62.69; H, 5.30; N, 31.45. IR $\lambda_{max}^{CHCl_3}$ μ : 3.04 (C≡C-H), 2.89 (NH).

The aqueous layer was evaporated under reduced pressure to dryness. The brown coloured semi-solid residue was triturated with benzene and Et_2O. The combined organic solution was evaporated under reduced pressure to give crystalline 2-methylimidazo[1,2-*a*]pyrimidine (Ⅲ) (1 g.). Recrystallization from hexane gave needles of m.p. 85~88° (180 mg.). One more recrystallization from the same solvent afforded a sample of m.p. 95~97°. This substance is very hygroscopic. Picrate showed m.p. 175~176° after two recrystallization from 99% EtOH. *Anal.* Calcd. for $C_{13}H_{10}O_7N_6$ (picrate) : C, 43.10; H, 2.78; N, 23.20. Found : C, 43.15; H, 2.98; N, 23.04.

[*4] All melting points are uncorrected.

7) H. Andersag, K. Westphal : Ber., **70**, 2035 (1937).

In another run a small amount of 2-aminopyrimidine (I) was obtained, which was isolated from a mixture by sublimation.

2-Methylimidazo[1,2-*a*]pyrimidine (III)——To 1-(2-propynyl)-2-imino-1,2-dihydropyrimidine hydrobromide (II) (2.14 g.) in hot abs. EtOH (80 ml.) was added Na (4.8 g.) in abs. EtOH (100 ml.) and the reaction mixture was heated under reflux for 1 hr. The reaction mixture was poured into H_2O, which was saturated with K_2CO_3 and the solution was extracted with Et_2O. The combined extracts were dried over Na_2SO_4 and evaporated. The crystalline residue (1.4 g.) was recrystallized from hexane to give 2-methylimidazo[1,2-*a*]pyrimidine (III) of m.p. 89~90° with previous softening (0.9 g.). One more recrystallization from hexane gave a sample of m.p. 95~97°, which on admixture with the authentic sample exhibited no depression in melting point. *Anal.* Calcd. for $C_7H_7N_3$: C, 63.14; H, 5.30; N, 31.56. Found: C, 63.10; H, 5.36; N, 31.75. UV λ_{max}^{EtOH} mμ (log ε): 232 (4.21), 290 (3.49), 323 (3.56).

The Reaction of 2-(2-Propynylamino)pyrimidine (IV) with Sodium Ethoxide——To 2-(2-propynylamino)pyrimidine (IV) (500 mg.) in abs. EtOH (10 ml.) was added Na (0.8 g.) in abs. EtOH (15 ml.) and the reaction mixture was refluxed for 1 hr. Then the solution was poured into H_2O and saturated with K_2CO_3, and extracted with Et_2O. The combined extracts were dried over Na_2SO_4 and evaporated. The crystalline residue (250 mg.) was recrystallized from hexane to give 2-aminopyrimidine (I) of m.p. 113~118° (128 mg.). One more recrystallization from the same solvent gave a sample of m.p. 124~126° (50 mg.). The mother liquors were collected and the solvent was evaporated under reduced pressure and the residue was heated on a water bath under diminished pressure (10 mm. Hg) and 2-aminopyrimidine (40 mg.) was obtained by sublimation. From the residue no definite substance was obtained. *Anal.* Calcd. for $C_4H_5N_3$: C, 50.51; H, 5.30; N, 44.19. Found: C, 50.41; H, 5.35; N, 44.35.

2-Imino-3-(2-propynyl)-4-thiazoline Hydrobromide (VI)——To 2-aminothiazole (V) (14 g.) in abs. EtOH (65 ml.) was added propargyl bromide (16.7 g.) and the reaction mixture was heated on a water bath (80°) for 7 hr. Then EtOH was evaporated under reduced pressure to give an oily residue. It was dissolved in H_2O and extracted with Et_2O and benzene in order to remove the starting material. The aqueous layer was evaporated under reduced pressure to afford an oil, which crystallized on standing (29 g.). Recrystallization from abs. EtOH gave 2-imino-3-(2-propynyl)-4-thiazoline hydrobromide (VI) of m.p. 161~162° (20.5 g.). *Anal.* Calcd. for $C_6H_7N_2SBr$: C, 32.89; H, 3.22; N, 12.79. Found: C, 32.72; H, 3.31; N, 12.83. IR λ_{max}^{Nujol} μ: 3.08 (C≡C-H), 4.70 (C≡C).

2-Imino-3-(2-propynyl)-4-thiazoline (VII)——To 2-imino-3-(2-propynyl)-4-thiazoline hydrobromide (VI) (1 g.) in H_2O (15 ml.) was added 10% NaOH solution (10 ml.) and the solution was extracted with Et_2O. The combined extracts were dried over Na_2SO_4 and evaporated to give oily 2-imino-3-(2-propynyl)-4-thiazoline (VII) (594mg.) which was unstable in the air at room temperature. Distillation of VII was not feasible giving only a polymeric substance. The picrate derivative melted at 154~155° after recrystallization from EtOH. *Anal.* Calcd. for $C_{12}H_9O_7N_5S$ (picrate): C, 39.24; H, 2.47; N, 19.07. Found: C, 39.10; H, 2.53; N, 19.28. IR λ_{max}^{liquid} μ: 3.04 (C≡C-H), 4.72 (C≡C).

This base was converted into hydrobromide (VI) as follows in order to confirm that no rearrangement occurred during above reaction: To VII (552 mg.) was added HBr solution (d 1.48) (0.8 ml.) under ice H_2O cooling and then H_2O and excess of HBr was evaporated under reduced pressure at room temperature. To the residue was added Me_2CO (100 ml.) and the resulting precipitate was collected by filtration (800 mg.). Recrystallization from abs. EtOH gave VI of m.p. 160~161° (560 mg.), which on admixture with a sample obtained from 2-aminothiazole (V) and propargyl bromide showed no depression in melting point. *Anal.* Calcd. for $C_6H_7N_2SBr$: C, 32.89: H, 3.22; N, 12.79. Found: C, 32.84; H, 3.36; N, 12.71.

6-Methylimidazo[2,1-*b*]thiazole (VIII)——To 2-imino-3-(2-propynyl)-4-thiazoline hydrobromide (VI) (2.19 g.) in abs. EtOH (30 ml.) was added Na (1.5 g.) in abs. EtOH (30 ml.) and the reaction mixture was heated under reflux for 2 hr. Then the solution was poured into H_2O and saturated with K_2CO_3, and extracted with Et_2O. The combined extracts were dried over Na_2SO_4 and evaporated. The residue was distilled under diminished pressure to give 6-methylimidazo[2,1-*b*]thiazole (VIII) of $b.p_{0.15}$ 81~85° (bath temperature) (940 mg.). NMR: 7.72 τ ($-CH_3$). The picrate derivative exhibited polymorphism, m.p. 203~204°. *Anal.* Calcd. for $C_{12}H_9O_7N_5S$(picrate): C, 39.24; H, 2.47; N, 19.07. Found: C, 39.37; H, 2.47; N, 19.03. Hydrobromide of VIII melted at 172~174°. *Anal.* Calcd. for $C_6H_7N_2SBr$: C, 32.89; H, 3.22; N, 12.97. Found: C, 32.87; H, 3.27; N, 13.42.

2-Acetylimino-3-acetonyl-4-thiazoline Hydrobromide (X)——2-Acetamidothiazole (IX)[8] (7.3 g.) was dissolved in xylene (280 ml.) by heating and to this hot solution was added monobromoacetone (7.7 g.) in xylene (10 ml.). The reaction mixture was heated on an oil bath (120°) for 17 hr. An oily substance separated, which was isolated by decantation, washed with benzene and dried (11.8 g.). On treatment with EtOH and benzene it crystallized. Recrystallization from EtOH gave tufts of needles, m.p. 188~190° (4.8 g.). One more recrystallization from the same solvent gave a sample of m.p. 194~195°. *Anal.* Calcd. for $C_8H_{11}N_2SBr$: C, 34.42; H, 3.97; N, 10.04. Found: C, 34.45; H, 4.15; N, 10.35. IR λ_{max}^{Nujol} μ: 5.80 (CO), 5.88 (CO).

8) I. A. Kaye, C. L. Parris: J. Org. Chem., **17**, 737 (1952).

6-Methylimidazo[2,1-*b*]thiazole (VIII) from X——To 2-acetylimino-3-acetonyl-4-thiazoline hydrobromide (X) (500 mg.) was added 2*N* HBr solution (17 ml.) and the reaction mixture was refluxed for 20 min. The solution was evaporated under reduced pressure to dryness to give a crystalline substance. Recrystallization from EtOH gave 6-methylimidazo[2,1-*b*]thiazole hydrobromide, m.p. 172~174° (245 mg.). *Anal.* Calcd. for $C_6H_7N_2SBr$: C, 32.89; H, 3.22; N, 12.79. Found : C, 32.91; H, 3.27; N, 13.26.

The Reaction of 2-Aminothiazole (V) with Monobromoacetone——A mixture of 2-aminothiazole (V) (6.4 g.), monobromoacetone (8.8 g.) and abs. EtOH (55 ml.) was heated under reflux for 6 hr. Then EtOH was evaporated under reduced pressure to dryness to give an oil (14.3 g.), which was dissolved in H_2O and extracted with Et_2O to remove the starting material. The aqueous layer was evaporated under reduced pressure to give an oil (12.8 g.). This oil gave a semi-solid on long standing, however, it was not readily recrystallized. This substance (3 g.) was dissolved in H_2O (20 ml.) and to this solution was added 10% NaOH solution (8 ml.), then the solution was saturated with K_2CO_3 and extracted with Et_2O. Et_2O extracts were dried over Na_2SO_4 and evaporated to give an oil (1.4 g.). Distillation of this oil gave the following two fractions : (i) b.$p_{0.15}$ 60~90° (bath temperature) (830 mg.). (ii) b.$p_{0.15}$ 90~100° (bath temperature) (62 mg.). The fraction (i) crystallized on standing. Recrystallization from hexane gave prisms of m.p. 72~73° (390 mg.). This substance was not investigated further. Picrate of fraction (ii) showed m.p. 202~204° which is identical in all respects with picrate of 6-methylimidazo[2,1-*b*]thiazole (VIII) obtained from VI. *Anal.* Calcd. for $C_{12}H_9O_7N_5S$: C, 39.24; H, 2.47; N, 19.03. Found: C, 39.22; H, 2.64; N, 18.87.

2-Imino-3-(2-propynyl)-2,3-dihydrobenzothiazole Hydrobromide (XII)——To 2-aminobenzothiazole (XI) (15 g.) in abs. EtOH (60 ml.) was added propargyl bromide (11.9 g.) and the reaction mixture was heated on a water bath (80°) for 7 hr. The crystalline substance was collected by filtration, washed with abs. EtOH to give 2-imino-3-(2-propynyl)-2,3-dihydrobenzothiazole hydrobromide (XII) of m.p. 208~209° (12 g.). Recrystallization from abs. EtOH gave pure XII of m.p. 219~220° (9 g.). The filtrate of the reaction mixture was further heated on a water bath (80°) for 5 hr. to afford further 3.5 g. of XII. *Anal.* Calcd. for $C_{10}H_9N_2SBr$: C, 44.62; H, 3.37; N, 10.41. Found : C, 44.75; H, 3.51; N, 10.50. IR λ_{max}^{Nujol} μ : 3.13 (C≡C-H), 4.72 (C≡C).

2-Imino-3-(2-propynyl)-2,3-dihydrobenzothiazole (XIII)——To 2-imino-3-(2-propynyl)-2,3-dihydrobenzothiazole hydrobromide (XII) (2 g.) in H_2O (400 ml.) was added 10% NaOH solution until precipitation was complete. The precipitate was collected by filtration, washed with H_2O and dried (1.4 g.). Recrystallization from hexane gave 2-imino-3-(2-propynyl)-2,3-dihydrobenzothiazole (XIII) of m.p. 101~102° (1.15 g.). *Anal.* Calcd. for $C_{10}H_8N_2S$: C, 63.80; H, 4.28; N, 14.88. Found : C, 63.43; H, 4.53; N, 14.60. IR λ_{max}^{Nujol} μ : 3.03 (C≡C-H), 4.72 (C≡C).

This base was converted into hydrobromide (XII) as follows in order to confirm that no rearrangement reaction occurred during above reaction : To XIII (188 mg.) was added HBr solution (0.5 ml.) (d 1.48) with ice H_2O cooling. After the addition, about 200 ml. of Me_2CO was added to this mixture. The resulting crystalline substance was collected by filtration, washed with Me_2CO and dried (230 mg.). Recrystallization from H_2O gave XII of m.p. 219~220° (150 mg.), which on admixture with a sample obtained from 2-aminobenzothiazole (XI) and propargyl bromide showed no depression in melting point. *Anal.* Calcd. for $C_{10}H_9N_2SBr$: C, 44.62; H, 3.37; N, 10.41. Found : C, 44.60; H, 3.32; N, 10.40.

2-Methylimidazo[2,1-*b*]benzothiazole (XIV)——To 2-imino-3-(2-propynyl)-2,3-dihydrobenzothiazole (XIII) (600 mg.) in abs. EtOH (15 ml.) was added Na (0.8 g.) in abs. EtOH (15 ml.) at room temperature and the reaction mixture was heated under reflux for 3 hr. The solution was poured into H_2O and extracted with Et_2O. The combined extracts were dried over Na_2SO_4 and evaporated. The crystalline residue (600 mg.) was recrystallized from hexane to give 2-methylimidazo[2,1-*b*]benzothiazole (XIV) of m.p. 87~89° (380 mg.). One more recrystallization from hexane gave a sample of m.p. 89~90°. *Anal.* Calcd. for $C_{10}H_8N_2S$: C, 63.80; H, 4.28; N, 14.88. Found : C, 63.30; H, 4.31; N, 14.67. NMR : 7.69 τ ($-CH_3$). UV λ_{max}^{EtOH} mμ (log ε) : 241 (4.21), 285 (3.43), 293.4 (3.36).

This compound was also prepared from 2-imino-3-(2-propynyl)-2,3-dihydrobenzothiazole hydrobromide (XII) as described above. Hydrobromide of XIV melted at 284~286° after recrystallization from EtOH. *Anal.* Calcd. for $C_{10}H_9N_2SBr$: C, 44.62; H, 3.37; N, 10.41. Found : C, 44.63; H, 3.88; N, 10.88.

2-Acetylimino-3-acetonyl-2,3-dihydrobenzothiazole Hydrobromide (XVI)——2-Acetylaminobenzothaizole (XV)[9] (6 g.) was dissolved in xylene (250 ml.) by heating and to this hot solution was added monobromoacetone (4.3 g.). The reaction mixture was heated on an oil bath (120°) for 18 hr. The resulting semi-solid was separated from the solution by decantation, washed with xylene and dried (5.4 g.). Recrystallization from EtOH gave 2-acetylimino-3-acetonyl-2,3-dihydrobenzothiazole hydrobromide (XVI) m.p. 218~220° (2.0 g.). One more recrystallization from EtOH gave a sample of m.p. 224~226°. *Anal.* Calcd. for $C_{12}H_{13}O_2N_2SBr$: C, 43.78; H, 3.98; N, 8.51. Found : C, 43.89; H, 3.70; N, 8.56. IR : λ_{max}^{Nujol} 5.81 μ (CO).

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2-Methylimidazo[2,1-*b*]benzothiazole (XIV) from XVI——2-Acetylimino-3-acetonyl-2,3-dihydrobenzothiazole hydrobromide (XVI) (500 mg.) was refluxed with 2*N* HBr solution (20 ml.) for 20 min. The reaction mixture was evaporated under reduced pressure to dryness to afford a crystalline substance. Recrystallization from EtOH gave 2-methylimidazo[2,1-*b*]benzothiazole hydrobromide, m.p. 284~286° (400 mg.). *Anal.* Calcd. for $C_{10}H_9N_2SBr$: C, 44.62; H, 3.37; N, 10.41. Found: C, 44.39; H, 3.44; N, 10.83.

2-(2-Propynylthio)benzimidazole Hydrobromide (XVIII)——To 2-benzimidazolethiol (XVII) (7.5 g.) in abs. EtOH (200 ml.) was added propargyl bromide (6 g.) and the reaction mixture was heated on a water bath (80°) for 5 hr. The EtOH was evaporated under reduced pressure and the crystalline residue was recrystallized from abs. EtOH giving 2-(2-propynylthio)benzimidazole hydrobromide (XVIII) of m.p. 175~178° (11.3 g.). One more recrystallization from EtOH gave a sample of m.p. 179~180°. *Anal.* Calcd. for $C_{10}H_9N_2SBr$: C, 44.72; H, 3.38; N, 10.43. Found: C, 44.68; H, 3.38; N, 10.44. IR λ_{max}^{Nujol} μ: 3.13 (C≡C-H), 4.72 (C≡C).

3-Methylthiazolo[3,2-*a*]benzimidazole (XIX)——2-(2-Propynylthio)benzimidazole hydrobromide (XVIII) (1 g.) was suspended in abs. EtOH (40 ml.) and to this suspension was added Na (2 g.) in abs. EtOH (40 ml.). Then the reaction mixture was refluxed for 3 hr. About half the EtOH was evaporated under reduced pressure. The residue was poured into H_2O and the resulting crystalline substance was collected by filtration, washed with H_2O and dried (670 mg.). Recrystallization from 95% EtOH gave 3-methylthiazolo[3,2-*a*]benzimidazole (XIX) of m.p. 161~162° (542 mg.), which on admixture with the authentic sample[7] showed no depression in melting point. *Anal.* Calcd. for $C_{10}H_8N_2S$: C, 63.80; H, 4.28; N, 14.88. Found: C, 63.77; H, 4.35; N, 14.86. NMR: 7.31 τ ($-CH_3$).

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Summary

Intramolecular cyclization of propargylammonium halide derivatives was carried out giving methylated heterocyclic aromatic compounds with fused thiazole and imidazole nuclei. Some of these reactions were accompanied by rearrangement which might be caused by ring opening of the quaternary heterocyclic compounds.

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117. Akira Ogiso and Issei Iwai: An Approach to Synthesis of Diterpenoid Alkaloids. V.*1 Total Synthesis of a Degradation Product of Atisine.*2

(*Research Laboratories, Sankyo Co., Ltd.**3)

A number of the investigations[1] on the synthesis of the diterpenoid alkaloids atisine and garryfoline have been carried out during last two or three years. Recently, Nagata and co-workers[2] have accomplished the total synthesis of atisine utililizing the angular

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*1 Part IV. A. Ogiso, B. Shimizu, I. Iwai: This Bulletin, **11**, 774 (1963).

*2 Preliminary communication, I. Iwai, A. Ogiso: Chem. & Ind. (London), **1963**, 1084.

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