369. *The Unsaturation and Tautomeric Mobility of Heterocyclic Compounds. Part VIII. β-Naphthathiazole, 5 : 6 : 7 : 8-Tetrahydro-β-naphthathiazole, and 5-Phenylbenzthiazole Derivatives.*

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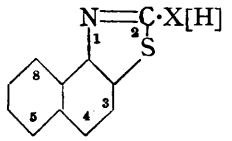
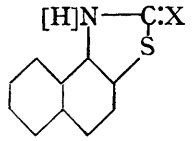
The contrast in behaviour of the 2-arylamino-4-methylthiazoles (Hunter and Parken, J., 1934, 1175) and 1-anilinobenzthiazole (Hunter and Jones, J., 1930, 2190) towards methylating agents suggests that fusion of a benzene nucleus with a thiazole ring reduces the aromatic character of the latter, leading to the production of isomeric methyl deriv-

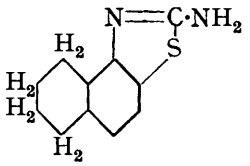
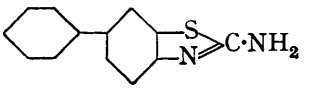
atives corresponding to both forms of the semicyclic amidine. The investigation of the β-naphthathiazole system (I ⇌ II) was therefore undertaken in continuation of the earlier study of the α-naphthathiazoles (Hunter and Jones, J., 1930, 941).

(I.)  ⇌  (II.)

2-Amino-β-naphthathiazole (I ⇌ II, X = NH) was readily obtained by treatment of α-naphthylthiourea with a molecular proportion of bromine; concentrations of halogen such as are generally employed for thiazole cyclisation led to the formation of *4-bromo-2-amino-β-naphthathiazole*, which was oriented by synthesis from *4-bromo-α-naphthylthiourea*. The base reacted apparently exclusively in the amino-aromatic form on methylation, yielding *2-imino-1-methyl-1 : 2-dihydro-β-naphthathiazole*. Substitution of phenyl for a hydrogen atom of the 2-amino-group causes appreciable reactivity in the iminodihydro-form of the triad system, and methylation of *2-anilino-β-naphthathiazole* (I ⇌ II, X = NPh) gave rise to a mixture of *2-phenylimino-1-methyl-1 : 2-dihydro-β-naphthathiazole* and *2-phenylmethylamino-β-naphthathiazole*, in which the former isomer very greatly predominated. The naphthalene system therefore appears to be less effective than the single aromatic nucleus in decreasing the effect of the aromatic conjugation of the heterocyclic ring during methylation.

2-Hydroxy-β-naphthathiazole (I ⇌ II, X = O) was obtained by hydrolysis both of the *2-ethoxy*-derivative synthesised by Jacobson's method (*Ber.*, 1886, **19**, 1069) and of *2-chloro-β-naphthathiazole*, prepared from α-naphthylthiocarbimide and phosphorus pentachloride (cf. Hofmann, *Ber.*, 1879, **12**, 1126). On methylation in an alkaline medium it gave *2-keto-1-methyl-1 : 2-dihydro-β-naphthathiazole*, unaccompanied by any detectable quantity of *2-methoxy-β-naphthathiazole*.

2-Amino-5 : 6 : 7 : 8-tetrahydro-β-naphthathiazole (III) behaved similarly to the unreduced naphthathiazole on methylation, and gave rise to *2-imino-1-methyl-1 : 2 : 5 : 6 : 7 : 8-hexahydro-β-naphthathiazole*.

(III.)   (IV.)

The methylation of *1-amino-5-phenylbenzthiazole* (IV), which was also examined in the present investigation, gave rise to *1-imino-5-phenyl-2-methyl-1 : 2-dihydrobenzthiazole*, unaccompanied by the *1-methylamino*-isomer obtained from s-p-*xenylmethylthiourea* and bromine.

Experimental.

2-Amino-β-naphthathiazole.—A suspension of α-naphthylthiourea (20 g.) in chloroform (120 c.c.) was treated with bromine (5·3 c.c. in 5 c.c. of chloroform) and heated under reflux for 10 minutes. The hydrobromide produced was dried on porous earthenware in a vacuum and added to sulphurous acid (300 c.c.), and the suspension treated with sulphur dioxide. On basification with ammonia and recrystallisation from alcohol, the base (15 g.) formed small needles, m. p. 190° (Found : S, 16·1. Calc. for $C_{11}H_8N_2S$: S, 16·0%). The *acetyl* derivative, prepared in hot acetic anhydride, separated from alcohol in small needles, m. p. 280° (Found : S, 13·0. $C_{13}H_{10}ON_2S$ requires S, 13·2%).

4-Bromo-2-amino-β-naphthathiazole.—(A) α-Naphthylthiourea (20 g. in 150 c.c. of chloroform) was treated with bromine (10 c.c. in 10 c.c. of chloroform) as in the previous experiment. The *base* obtained after the treatment with sulphurous acid and basification separated from ethyl acetate (charcoal) in greenish needles, m. p. 243° (Found : Br, 28·4. $C_{11}H_7N_2BrS$ requires Br, 28·7%).

(B) *4-Bromo-α-naphthylthiourea*, prepared from 4-bromo-α-naphthylthiocarbimide (m. p.

100°) and ammonia, crystallised from alcohol in small needles, m. p. 108° (Found: Br, 28·8. $C_{11}H_9N_2BrS$ requires Br, 28·5%). The base prepared from this thiourea (0·5 g. in chloroform, 5 c.c.; bromine, 0·5 c.c., in 0·5 c.c. of chloroform) by the above treatment crystallised from alcohol in cubes, m. p. 245°, and 244° when mixed with the specimen obtained in (A).

Methylation of 2-Amino-β-naphthathiazole.—The base (2 g.) and methyl iodide (2 c.c.) were heated in a sealed tube at 100° for 15 hours and the product was basified with hot aqueous sodium hydroxide and extracted with chloroform. The gum remaining after removal of chloroform was dissolved in hot acetic anhydride, and a solution of the product in alcohol (charcoal) fractionally crystallised. *2-Acetimido-1-methyl-1 : 2-dihydro-β-naphthathiazole* separated in small needles, m. p. 180° (Found: S, 12·7. $C_{14}H_{12}ON_2S$ requires S, 12·5%). A small quantity of 2-acetamido-β-naphthathiazole isolated from the mother-liquors was identified by m. p. and mixed m. p. determination, but no trace of the more easily fusible 2-acetomethylamido-β-naphthathiazole was detected.

2-Acetomethylamido-β-naphthathiazole, obtained by acetylation of 2-methylamino-β-naphthathiazole (Dyson, Hunter, and Morris, J., 1932, 2282) with acetic anhydride, crystallised in needles, m. p. 160° (Found: S, 12·2. $C_{14}H_{12}ON_2S$ requires S, 12·5%).

2-Chloro-β-naphthathiazole.—α-Naphthylthiocarbimide (5 g.) and phosphorus pentachloride (6 g.) were heated in a sealed tube at 160—180° for 6 hours and the product was gradually added to water. On extraction with chloroform and recrystallisation from benzene–petroleum, the *chloronaphthathiazole* was obtained in small needles (5 g.), m. p. 82° (Found: Cl, 16·3. $C_{11}H_6NClS$ requires Cl, 16·2%).

2-Anilino-β-naphthathiazole, obtained by condensation of 2-chloro-β-naphthathiazole and aniline in equimolecular proportion, separated from alcohol in plates, m. p. 142° (Found: S, 11·8. $C_{17}H_{12}N_2S$ requires S, 11·6%). The *picrate* separated from benzene in small yellow needles, m.p. 193° (Found: S, 6·2. $C_{17}H_{12}N_2S,C_6H_3O_7N_3$ requires S, 6·1%).

Methylation. A mixture of 2-anilino-β-naphthathiazole (0·6 g.) and methyl iodide (0·8 c.c.) was heated at 100° for 12 hours. The gum extracted from the basified product by ether was dissolved in benzene and treated with picric acid (1 equiv.) in the same solvent; the *2-phenylimino-1-methyl-1 : 2-dihydro-β-naphthathiazole picrate* obtained crystallised from benzene in slender yellow needles, m. p. 204° (Found: S, 6·4. $C_{18}H_{14}N_2S,C_6H_3O_7N_3$ requires S, 6·0%). In later experiments in which larger quantities of the aminonaphthathiazole (2—3 g.) were methylated, the picrate of the 2-phenylmethylamino-isomer was isolated (about 5%) from the mother-liquors, and identified by mixed m. p. with the specimen described below.

2-Phenylmethylamino-β-naphthathiazole, obtained by condensation of 2-chloro-β-naphthathiazole with methylaniline, separated from alcohol in small needles, m. p. 111—112° (Found: S, 10·9. $C_{18}H_{14}N_2S$ requires S, 11·0%). The *picrate* crystallised in small yellow needles, m. p. 156° (Found: S, 6·3. $C_{18}H_{14}N_2S,C_6H_3O_7N_3$ requires S, 6·0%).

2-Hydroxy-β-naphthathiazole.—(A) α-Naphthylthiourethane (9 g.) was ground with alcohol (3 c.c.) and dissolved in 30% aqueous sodium hydroxide (70 c.c.) and the solution was diluted with water (110 c.c.) and added in 20 c.c. portions at 5-minute intervals to a mechanically stirred solution of potassium ferricyanide (55 g.) in water (270 c.c.) at 80—90°. The dark-coloured product obtained by extraction with ether was dissolved in methyl alcohol (charcoal), and the solution concentrated at laboratory temperature under reduced pressure; *2-ethoxy-β-naphthathiazole* was obtained in small crystals, m. p. 50° (Found: S, 14·1. $C_{13}H_{11}ONS$ requires S, 14·0%). When a solution of the ethoxy-derivative in concentrated hydrochloric acid was heated, *2-hydroxy-β-naphthathiazole* separated; it crystallised from alcohol in small needles, m. p. 300° (Found: S, 15·8. $C_{11}H_7ONS$ requires S, 15·9%).

(B) A solution of 2-chloro-β-naphthathiazole in alcohol containing hydrochloric acid was heated under reflux for 30 hours and diluted with water, and the mixture made alkaline with ammonia. The residue was extracted with hot 10% aqueous sodium hydroxide, and the alkaline filtrate acidified; the 2-hydroxy-β-naphthathiazole obtained, after recrystallisation, had m. p. 300°, alone and when mixed with the specimen already described.

Methylation. 4 C.c. of methyl sulphate were added to the hydroxynaphthathiazole (0·8 g.) in chloroform (10 c.c.) and 30% aqueous potassium hydroxide (20 c.c.) and the mixture was shaken and thereafter heated under reflux for 15 minutes. A further 20 c.c. of potassium hydroxide solution were added and the mixture was allowed to cool and kept overnight. On extraction with chloroform and recrystallisation from methyl alcohol, *2-keto-1-methyl-1 : 2-dihydro-β-naphthathiazole* was obtained in stout needles, m. p. 153° (Found: S, 15·1. $C_{12}H_9ONS$ requires S, 14·9%). No trace of the isomeric 2-methoxy-derivative was found.

2-Methoxy-β-naphthathiazole.—(i) *Methyl α-naphthylthioncarbamate*, prepared from α-

naphthylthiocarbimide and methyl alcohol containing a few drops of quinoline, had m. p. 98° after recrystallisation (Found : S, 14·5. $C_{12}H_{11}ONS$ requires S, 14·75%). On oxidation with alkaline potassium ferricyanide at 80—90°, it gave 2-*methoxy*-β-*naphthathiazole*, which crystallised from methyl alcohol in small needles, m. p. 62° (Found : S, 15·1. $C_{12}H_9ONS$ requires S, 14·9%). (ii) 2-Chloro-β-naphthathiazole (1 g.) was added to a solution of sodium methoxide (0·1 g. of sodium and 15 c.c. of absolute methyl alcohol), and the mixture heated under reflux for 5 hours. On concentration and recrystallisation from methyl alcohol, 2-methoxy-β-naphthathiazole was obtained, m. p. 62° alone or when mixed with the specimen described above. It was rapidly hydrolysed by hot concentrated hydrochloric acid to the hydroxy-derivative, m. p. 300°.

ar-*Tetrahydro*-α-*naphthylthiocarbimide*.—*ar*-Tetrahydro-α-naphthylamine (10 g.) in chloroform (30 c.c.) was gradually added with shaking to a suspension of thiocarbonyl chloride (10 c.c.) in water (100 c.c.). The *thiocarbimide* separated from hexane in large needles (9 g.), m. p. 34° (Found : S, 17·0. $C_{11}H_{11}NS$ requires S, 16·9%). ar-*Tetrahydro*-α-*naphthylthiourea* separated from alcohol in small needles, m. p. 161° (Found : S, 15·6. $C_{11}H_{14}N_2S$ requires S, 15·5%).

2-*Amino*-5 : 6 : 7 : 8-*tetrahydro*-β-*naphthathiazole*.—The thiourea (1 g.) in chloroform (6 c.c.) was treated with 2·5 c.c. of a 10% solution (by vol.) of bromine in chloroform and the mixture was heated for a minute and allowed to cool. The *base* obtained by treatment of the product with sulphurous acid and basification with ammonia separated from alcohol in small needles, m. p. 174° (Found : S, 15·8. $C_{11}H_{12}N_2S$ requires S, 15·7%).

Methylation. A mixture of the amino-base (2 g.) and methyl iodide (2 c.c.) was heated at 100° for 15 hours, the product basified and extracted with chloroform, and the gum remaining after evaporation of chloroform acetylated with acetic anhydride; the 2-*acetimido*-1-*methyl*-1 : 2 : 5 : 6 : 7 : 8-*hexahydro*-β-*naphthathiazole* obtained crystallised from alcohol in thick needles, m. p. 171° (Found : C, 65·3; H, 6·4; S, 12·5. $C_{14}H_{16}ON_2S$ requires C, 64·6; H, 6·35; S, 12·3%). No trace of the isomeric 2-acetomethylamido-5 : 6 : 7 : 8-tetrahydro-β-naphthathiazole was found.

s-ar-*Tetrahydro*-α-*naphthylmethylthiourea*, prepared from the thiocarbimide and methylamine in alcohol, crystallised in small needles, m. p. 158° (Found : S, 14·6. $C_{12}H_{16}N_2S$ requires S, 14·5%).

2-*Methylamino*-5 : 6 : 7 : 8-*tetrahydro*-β-*naphthathiazole* separated from alcohol in soft plates, m. p. 169° (Found : S, 14·8. $C_{12}H_{14}N_2S$ requires S, 14·7%). The *acetyl* derivative formed microscopic crystals, m. p. 158° (Found : S, 12·4. $C_{12}H_{16}ON_2S$ requires S, 12·3%). A mixture of this with 2-acetimido-1-methyl-1 : 2 : 5 : 6 : 7 : 8-hexahydro-β-naphthathiazole melted at 140—146°.

p-*Xenylthiocarbimide*, obtained from *p*-xenylamine (4 g.) in chloroform (12 c.c.) and thiocarbonyl chloride (4 c.c.) in water (60 c.c.), crystallised from hexane in slender needles, m. p. 119—120° (Found : S, 15·2. $C_{13}H_9NS$ requires S, 15·2%). Yield, 62%. p-*Xenylthiourea* separated from alcohol in plates, m. p. 204° (Found : S, 14·2. $C_{13}H_{12}N_2S$ requires S, 14·0%).

1-*Amino*-5-*phenylbenzthiazole*.—A suspension of the xenylthiourea (1·3 g.) in chloroform (15 c.c.) was treated with 5·5 c.c. of a 10% solution (by vol.) of bromine in the same solvent, and the mixture heated for 5 minutes. The *base* crystallised from alcohol in plates, m. p. 226—227° (Found : C, 68·95; H, 4·4; S, 14·3. $C_{13}H_{10}N_2S$ requires C, 69·0; H, 4·4; S, 14·2%).

Methylation. 1 G. of 1-amino-5-phenylbenzthiazole and 2·5 c.c. of methyl iodide were heated at 100° for 16 hours and the product was basified and extracted with chloroform. On recrystallisation from methyl alcohol (charcoal), 1-*imino*-5-*phenyl*-2-*methyl*-1 : 2-*dihydrobenzthiazole* was obtained in small needles, m. p. 165° (Found : C, 69·6; H, 5·1; S, 13·45. $C_{14}H_{12}N_2S$ requires C, 70·0; H, 5·0; S, 13·3%). No trace of the isomeric 1-methylamino-derivative was found.

s-p-*Xenylmethylthiourea*, prepared from the thiocarbimide and methylamine, crystallised from alcohol in plates, m. p. 170° (Found : S, 13·3. $C_{14}H_{14}N_2S$ requires S, 13·2%).

1-*Methylamino*-5-*phenylbenzthiazole*, obtained from the thiourea in the usual way, crystallised from alcohol in needles, m. p. 203° (Found : S, 13·5. $C_{14}H_{12}N_2S$ requires S, 13·3%).

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