CXV.—*The Unsaturation and Tautomeric Mobility of Heterocyclic Compounds. Part II. α- and ββ-Naphthathiazoles.*

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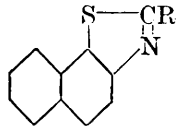
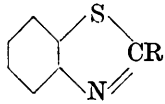
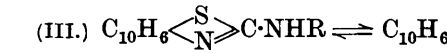
RING closure, producing the heterocyclic nucleus in α-naphthathiazoles (I) and in benzthiazoles (II), takes place much more readily in the former than in the latter case: for instance, (1) the ratio of

(I.)   (II.)

the yields of the 1-chloro-derivatives (I and II; R = Cl) obtained from the corresponding arylthiocarbimides and phosphorus pentachloride under similar conditions (Hofmann, *Ber.*, 1879, **12**, 1126) is 62 : 15; (2) oxidation of β-naphthylthiourethane and of phenylthiourethane with alkaline ferricyanide at 80—90° gives 60% and 40% yields, respectively, of the corresponding ethoxythiazoles (I and II; R = OEt) (Jacobson, *Ber.*, 1886, **19**, 1069); and (3) the action of bromine on *s*-phenyl-β-naphthylthiocarbamide yields solely 1-*anilino*-α-*naphthathiazole* (I; R = NHPh), no trace of the isomeric 1-β-*naphthylaminobenzthiazole* (II; R = NH·$C_{10}H_7$), which has been synthesised from 1-chlorobenzthiazole and β-naphthylamine, being isolable. These results are evidently conditioned by the high reactivity of the α-hydrogen atom of the naphthalene nucleus.

The aromatic nature of the heterocyclic nucleus in α-naphthathiazole is manifested in the alkylation of semi-cyclic amidines containing this complex (III ⇌ IV). For instance, the methyl-

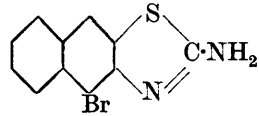
(III.)  (IV.)

ation of 1-amino-α-naphthathiazole (III; R = H) yields 1-*imino*-2-*methyl*-1 : 2-*dihydro*-α-*naphthathiazole*, unaccompanied by the isomeric 1-*methylamino*-α-*naphthathiazole* (compare Hunter, J., 1926, 1385; Hunter and Styles, J., 1928, 3019). 1-β-Naphthylamino-α-naphthathiazole (III; R = $C_{10}H_7$) behaves similarly and yields only 1-β-*naphthylimino*-2-*methyl*-1 : 2-*dihydro*-α-*naphthathiazole* on methylation, although it contains the β-naphthyl group which might exert a conjugating influence favouring the iminodihydro-phase (IV), similar to that of the phenyl group in the three-carbon system (Linstead and Williams, J., 1926, 2735; Linstead, J., 1929, 2501). The isomeric 1-*methyl*-β-*naphthylamino*-α-*naphthathiazole* has been

obtained from 1-*chloro*-α-*naphthathiazole* and methyl-β-naphthylamine and also by the action of bromine on *methyl*-s-*di*-β-*naphthylthiocarbamide*, $C_{10}H_7$·NMe·CS·NH·$C_{10}H_7$.

The methylation of 1-*hydroxy*-α-*naphthathiazole* is analogous to that of 1-hydroxybenzthiazole (Hunter, this vol., p. 128), the sole product being the *ketomethyldihydro*-derivative (V), whose constitution follows from its synthesis from 1-*nitrosoimino*-2-*methyl*-1 : 2-*dihydro*-α-*naphthathiazole* (VI).

(V.) $C_{10}H_6\langle \overset{S}{NMe} \rangle CO$ ← $C_{10}H_6\langle \overset{S}{NMe} \rangle C{:}N{\cdot}NO$ (VI.)

(VII.) 

3-*Bromo*-1-*amino*-ββ-*naphthathiazole* (VII) has been obtained from 1-bromo-β-naphthylamine by way of the *thiocarbimide* and *thiocarbamide* in the usual way (compare Fries, *Annalen*, 1927, **454**, 260).

EXPERIMENTAL.

Considerable difficulty was encountered in preparing β-naphthylthiocarbimide by the methods given in the literature. It was most readily obtained by boiling a mixture of *s*-di-β-naphthylthiocarbamide (50 g.) and acetic anhydride (100 c.c.) for 3 minutes, diluting the solution with hot water, and isolating the thiocarbimide by prolonged distillation in steam superheated to 140°. The yield never exceeded 30%. The thiocarbimide to be used for the preparation of the chloronaphthathiazole was melted over calcium chloride and redistilled in a vacuum, the fraction, b. p. 182—184°/12 mm., being separately collected.

1-*Chloro*-α-*naphthathiazole*.—A mixture of 14 g. of β-naphthylthiocarbimide and phosphorus pentachloride (16 g.) was heated in a sealed tube at 160—180° for 5—6 hours, and the product fractionated. After removal of phosphorus trichloride and a small quantity of unchanged thiocarbimide (183°/15 mm.), the *chlorothiazole* distilled at 260—270°/15 mm. The yield after redistillation and crystallisation from alcohol was 62%; m. p. 80°, b. p. 245—246°/13 mm. (Found: Cl, 16·0; S, 14·8. $C_{11}H_6NClS$ requires Cl, 16·1; S, 14·5%).

1-*Hydroxy*-α-*naphthathiazole*.—A solution of the chloronaphthathiazole (0·8 g.) in absolute alcohol (20 c.c.) was diluted with 4 c.c. of concentrated hydrochloric acid, heated for 20 hours under reflux, and evaporated on a steam-bath. On recrystallisation from alcohol, the *hydroxy-base* formed aggregates of shining prisms, m. p. 230—

231° (Found: S, 16·2. $C_{11}H_7ONS$ requires S, 15·9%). This compound is less soluble in alkalis than the benzthiazole analogue.

1-*Amino-α-naphthathiazole.*—Although Hofmann states (*Ber.*, 1879, **12**, 1126) that 1-aminobenzthiazole is obtained by digesting 1-chlorobenzthiazole with alcoholic ammonia at 100°, the chloronaphthathiazole was recovered unchanged under such conditions, and also after being heated in a sealed tube (0·5 g. of the chloro-base) with alcoholic ammonia (5 c.c. of alcohol and 2 c.c. of ammonia, *d* 0·880) at 100—140° for ½ hour.

(i) A mixture of 0·5 g. of 1-chloro-α-naphthathiazole and 5 c.c. of ammonia (*d* 0·880) was heated at 200° for 18 hours. On recrystallisation from alcohol, 1-amino-α-naphthathiazole was obtained, m. p. 258° alone and when mixed with the specimen prepared from β-naphthylthiocarbamide (previously given, J., 1926, 1400, as m. p. 249—251°; the compound is there erroneously named "2-amino-α-naphthathiazole"). The identity was further confirmed by the formation of the same acetyl derivative. (ii) Treatment of a suspension of β-naphthylthiocarbamide (m. p. 194°; Cosiner, *Ber.*, 1881, **14**, 59, recorded m. p. 180°, and Hector, *Ber.*, 1890, **23**, 362, m. p. 186°) (1 g.) in chloroform (10 c.c.) with bromine (1 c.c. in 1 c.c. of chloroform) yielded a yellow *hydrotribromide*, which sintered at 160—161° after drying in a vacuum [Found: Br, 54·8. $C_{11}H_8N_2S,HBr(Br_2)$ requires Br, 54·4%]. On reduction with sulphurous acid, basification with ammonia, and recrystallisation from methyl alcohol, this gave the aminonaphthathiazole in plates, m. p. 257° (Found: S, 16·2. Calc.: S, 16·0%).

1-*Acetamido-α-naphthathiazole.*—(i) The product of acetylation of the amino-base with acetic anhydride separated from benzene–ethyl acetate in soft crystals, m. p. 265° (Found: S, 12·9. $C_{13}H_{10}ON_2S$ requires S, 13·2%).

Hugershoff (*Ber.*, 1899, **32**, 3649) states that treatment of β-naphthylthiocarbamide with acetic anhydride at 80° yields *as*-acetyl-β-naphthylthiocarbamide, $C_{10}H_7{\cdot}NAc{\cdot}CS{\cdot}NH_2$, which isomerises to *s*-acetyl-β-naphthylthiocarbamide, $C_{10}H_7{\cdot}NH{\cdot}CS{\cdot}NHAc$, m. p. 158°, at its melting point. The product which we isolated from β-naphthylthiocarbamide and acetic anhydride at 80° had m. p. 145—147° and proved to be a mixture containing unchanged naphthylthiocarbamide. On the other hand, *s*-acetyl-β-naphthylthiocarbamide was readily prepared by dissolving β-naphthylthiocarbamide in an excess of acetic anhydride at 80° (compare Hunter and Pride, J., 1929, 944); it melted at 171—172° after recrystallisation.

(ii) The solution obtained from 0·3 g. of *s*-acetyl-β-naphthylthiocarbamide, 6 c.c. of chloroform, and 0·5 c.c. of bromine was heated

under reflux for 2 minutes, and the orange bromo-addition compound (m. p. 154—156°) obtained was reduced with sulphurous acid. On recrystallisation from boiling alcohol, the acetamidonaphthathiazole formed plates, m. p. 264° alone and when mixed with the specimen obtained in (i).

1-*Ethoxy-α-naphthathiazole.*—10 G. of β-naphthylthiourethane (m. p. 96°; prepared in 95% yield by heating a solution of the thiocarbimide in absolute alcohol, containing a few drops of quinoline, under reflux for 4 hours) were rubbed with a small quantity of alcohol and dissolved in 75 c.c. of 30% aqueous sodium hydroxide. The solution was diluted with water to 200 c.c. and added in 20 c.c. portions at 5-minute intervals to 300 c.c. of a well-stirred 20% solution of potassium ferricyanide at 85°; the cooled mixture was extracted with ether, and the product recrystallised from alcohol (yield, 5·9 g.; 60%). The *ethoxy-base* formed needles, m. p. 80° (Found: S, 14·1. $C_{13}H_{11}ONS$ requires S, 14·0%).

Hydrolysis. 1-Ethoxy-α-naphthathiazole (1 g.) was heated with 7 c.c. of hydrobromic acid (*d* 1·45) for 15 minutes; the mixture was diluted with water (10 vols.), and the product recrystallised from alcohol–ethyl acetate (animal charcoal), 0·4—0·5 g. of 1-hydroxy-α-naphthathiazole being obtained, m. p. 231° alone and when mixed with the specimen obtained from the chloronaphthathiazole.

1-*Ethoxybenzthiazole.*—A similar experiment with 10 g. of phenylthiourethane gave 4 g. of 1-ethoxybenzthiazole (yield, 40%), which was characterised by its hydrolysis to 1-hydroxybenzthiazole, m. p. 138° (Hunter, this vol., p. 135).

1-β-*Naphthylaminobenzthiazole.*—When a mixture of 1-chlorobenzthiazole (1 g.) and β-naphthylamine (0·8 g.) was heated, a vigorous reaction took place. The product was extracted with alcohol, the extracts were decolorised with animal charcoal and evaporated on a steam-bath, and the residue was basified and recrystallised from methyl alcohol–ethyl acetate. The *naphthylaminobenzthiazole* (yield, 60%) formed small silky needles, m. p. 191—192° (Found: S, 11·8. $C_{17}H_{12}N_2S$ requires S, 11·6%). The acetyl derivative could not be crystallised.

1-*Anilino-α-naphthathiazole.*—The tenacious gum obtained by condensing 1-chloro-α-naphthathiazole (1 g.) with aniline (0·5 c.c.) solidified on treatment with hot aqueous ammonia (*d* 0·880). On recrystallisation from methyl alcohol–ethyl acetate, 1-*anilino-α-naphthathiazole* was obtained in soft silky needles, m. p. 211—212° (Found: S, 11·7. $C_{17}H_{12}N_2S$ requires S, 11·6%).

Condensation of Phenylthiocarbimide with β-Naphthylamine.—6·5 C.c. of phenylthiocarbimide were added to a boiling solution of 7 g. of β-naphthylamine in absolute alcohol (70 c.c.); the mixture

became semi-solid owing to the separation of the phenylnaphthylthiocarbamide (yield, 13 g.; m. p. 161—162°). On recrystallisation from ethyl acetate and thereafter from amyl acetate, *s*-phenyl-β-naphthylthiocarbamide was obtained in silvery plates, m. p. 166—167° (Found: S, 11·8. Calc.: S, 11·6%). Mainzer (*Ber.*, 1882, **15**, 1471), Freund and Wolf (*Ber.*, 1892, **25**, 1468), and Wheeler (*J. Amer. Chem. Soc.*, 1901, **33**, 226) give the m. p. as 157°, 165°, and 182—183°, respectively.

Condensation of β-Naphthylthiocarbimide with Aniline.—Owing to the readiness with which β-naphthylthiocarbimide combines with alcohol in the presence of amines, this condensation was carried out in benzene solution. After recrystallisation, the product had m. p. 166°, alone and when mixed with the phenylnaphthylthiocarbamide described above.

Wheeler's "Phenylnaphthylthiocarbamide."—A mixture of 1 g. of β-naphthylamine and 1·5 c.c. of phenylthiocarbimide was heated until it boiled; the product, which solidified on cooling, was recrystallised from amyl acetate. It formed ill-defined crystals, m. p. 182—184° (softening at 175°), and m. p. 188—189° after extraction with boiling alcohol, in which it was very sparingly soluble. From its properties and the m. p. of its mixture with a genuine specimen (m. p. 193—195°), Wheeler's product (*loc. cit.*) was evidently *s*-di-β-naphthylthiocarbamide. Its mixture with a genuine specimen of *s*-phenyl-β-naphthylthiocarbamide melted at 158—159°.

It appears probable that *s*-phenyl-β-naphthylthiocarbamide is formed initially in Wheeler's experiment and then undergoes decomposition at the elevated temperature attained during the condensation. This supposition is borne out by the following experiment.

Thermal Decomposition of s-*Phenyl-β-naphthylthiocarbamide.*—1 G. of the thiocarbamide was kept at 220—230° for 2 minutes, hydrogen sulphide being evolved. The product, which crystallised on cooling, was repeatedly extracted with boiling alcohol, finely ground, and re-extracted with boiling alcohol and thereafter with ethyl acetate. The residue melted at 191—193°, and at 192—194° when mixed with a genuine specimen of *s*-di-β-naphthylthiocarbamide.

The alcoholic extracts yielded *s*-phenyl-β-naphthylthiocarbamide and some phenylthiocarbimide on evaporation, but the presence of thiocarbanilide could not be detected.

The Action of Bromine on s-*Phenyl-β-naphthylthiocarbamide.*—A suspension of 3 g. of the thiocarbamide in 30 c.c. of chloroform was treated with bromine (1·2 c.c. in 3 c.c. of chloroform) (an excess of bromine, such as is normally used in the Hugershoff reaction, causes

the production of ill-defined bromo-substitution derivatives) and the mixture was heated under reflux for 3 minutes, cooled, and evaporated to dryness under reduced pressure at laboratory temperature. The product was dissolved in chloroform, the solution shaken with sulphurous acid, and the reduction completed by passage of sulphur dioxide. On basification and removal of the chloroform, a base, m. p. 202—205°, was obtained which on recrystallisation from ethyl acetate yielded 2·2 g. of 1-anilino-α-naphthathiazole, m. p. 206—211°. The mother-liquor furnished a further 0·7 g. of the same base (m. p. *ca.* 200°). On recrystallisation both fractions had m. p. 211°, alone and when mixed with the specimen of 1-anilino-α-naphthathiazole obtained from 1-chloro-α-naphthathiazole (p. 944). No trace of the isomeric naphthylaminobenzthiazole was found.

1-p-*Bromoanilino-α-naphthathiazole*, which could not be obtained by the bromination of 1-anilino-α-naphthathiazole in chloroform, was prepared by the condensation of 1-chloro-α-naphthathiazole and *p*-bromoaniline; it formed small prisms, m. p. 250° (Found: Br, 22·8. $C_{17}H_{11}N_2BrS$ requires Br, 22·5%).

Methylation of 1-*Amino-α-naphthathiazole and the Synthesis of* 1-*Imino-2-methyl*-1 : 2-*dihydro-α-naphthathiazole and of* 1-*Methylamino-α-naphthathiazole from the Corresponding Naphthylmethylthiocarbamides.*—A mixture of 1-amino-α-naphthathiazole (2·6 g.) and methyl iodide (3 c.c.) was heated in a sealed tube at 100° for 15 hours. The product was basified with alcoholic potash and the mixture was diluted with water and extracted with ethyl acetate, 1·45 g. of 1-*imino-2-methyl*-1 : 2-*dihydro-α-naphthathiazole*, m. p. 178°, being obtained (Found: S, 15·0. $C_{12}H_{10}N_2S$ requires S, 14·9%) unaccompanied by any trace of the 1-methylamino-isomeride.

Methyl-β-naphthylamine was conveniently prepared as follows: Sodium (1 atom) was dissolved in a hot solution of aceto-β-naphthalide (20 g.) in xylene (200 c.c.). After 15 minutes, crystallisation commenced, methyl sulphate (30 c.c.) was added to the semi-solid mass, and the mixture heated for 5 minutes. The xylene was then distilled in steam, and the product heated with alcoholic potash for 24 hours; the alcohol was evaporated on a steam-bath, and the mixture diluted with water and extracted with ether. Distillation of the residue obtained after removal of the ether yielded 8·5 g. of the methylnaphthylamine, b. p. 189°/30 mm. (yield, 50%).

as-β-*Naphthylmethylthiocarbamide*, prepared from the methylnaphthylamine, hydrochloric acid, and potassium thiocyanate at 100° (compare Hunter and Styles, J., 1928, 3025), separated from ethyl acetate in small crystals, m. p. 170° (Found: S, 14·7. $C_{12}H_{12}N_2S$ requires S, 14·8%).

Reaction with bromine. A solution of *as*-β-naphthylmethylthio-

carbamide (0·5 g.) in chloroform (5 c.c.) was treated with bromine (0·2 c.c. in 2 c.c. of chloroform) and the mixture was heated under reflux for 10 minutes and then shaken with excess of sulphurous acid. The chloroform was evaporated on a steam-bath, and the product basified and recrystallised from alcohol–ethyl acetate, giving 1-imino-2-methyl-1 : 2-dihydro-α-naphthathiazole, identical with the specimen already described.

s-β-*Naphthylmethylthiocarbamide*, prepared by condensing β-naphthylthiocarbimide with methylamine in hot alcoholic solution, crystallised in large prisms, m. p. 130° (Found : S, 15·6%).

1-*Methylamino-α-naphthathiazole*, prepared as in the case of the isomeric iminomethyldihydronaphthathiazole, crystallised in small needles, m. p. 189° (Found : S, 14·7%).

1-β-Naphthylamino-α-naphthathiazole, prepared by condensing β-naphthylamine with 1-chloro-α-naphthathiazole, had m. p. 222° alone and when mixed with a specimen prepared from *s*-di-β-naphthylthiocarbamide (Hunter, J., 1925, **127**, 2270). It is most conveniently prepared from the dinaphthylthiocarbamide in the same way as 1-anilino-α-naphthathiazole is obtained from *s*-phenyl-β-naphthylthiocarbamide (p. 945).

Methylation of 1-β-*Naphthylamino-α-naphthathiazole*.—The paste obtained from 1 g. of 1-β-naphthylamino-α-naphthathiazole and 3 c.c. of chloroform was suspended in 50 c.c. of water containing 10 g. of potassium hydroxide and well shaken with 5 c.c. of methyl sulphate, and again after addition of a further 5 g. of potassium hydroxide and 5 c.c. of methyl sulphate; after ½ hour the mixture was boiled to remove the chloroform. Recrystallisation of the product from alcohol yielded 1 g. of 1-β-*naphthylimino*-2-*methyl*-1 : 2-*dihydro-α-naphthathiazole* (Found : S, 9·5. $C_{22}H_{16}N_2S$ requires S, 9·4%), unaccompanied by 1-methyl-β-naphthylamino-α-naphthathiazole.

Synthesis of 1-*Methyl*-β-*naphthylamino-α-naphthathiazole from Methyl*-s-*di*-β-*naphthylthiocarbamide and from* 1-*Chloro-α-naphthathiazole and Methyl*-β-*naphthylamine*.—*Methyl*-s-*di*-β-*naphthylthiocarbamide*, prepared by condensation of β-naphthylthiocarbimide and methyl-β-naphthylamine in alcohol, crystallised in soft white plates, m. p. 178° (Found : S, 9·5. $C_{22}H_{18}N_2S$ requires S, 9·4%).

A solution of this thiocarbamide (0·3 g.) in chloroform (4 c.c.) was treated with 1·6 c.c. of a 10% solution of bromine in the same solvent and the mixture was heated under reflux for 5 minutes, cooled, reduced with sulphurous acid, and basified. On recrystallisation from ethyl acetate, 1-*methyl*-β-*naphthylamino-α-naphthathiazole* formed shining prisms, m. p. 235° (Found : S, 9·2. $C_{22}H_{16}N_2S$ requires S, 9·4%). The picrate, prepared from acetone solutions of

the base and picric acid, formed yellow prisms, m. p. 278°, identical with the picrate described below (mixed m. p. 281°).

A mixture of 0·3 g. of 1-chloro-α-naphthathiazole and an equal quantity of methyl-β-naphthylamine was heated; on basification an uncrystallisable gum was obtained, which was converted into the *picrate*, yellow prisms, m. p. 282°, in the usual way (Found: S, 5·6. $C_{22}H_{16}N_2S,C_6H_3O_7N_3$ requires S, 5·6%).

Methylation of 1-*Hydroxy-α-naphthathiazole and the Synthesis of* 1-*Keto*-2-*methyl*-1 : 2-*dihydro-α-naphthathiazole from* 1-*Imino*-2-*methyl*-1 : 2-*dihydro-α-naphthathiazole.*—A solution of 0·5 g. of 1-hydroxy-α-naphthathiazole in 5 c.c. of chloroform was shaken with 6 c.c. of 30% potassium hydroxide solution and 4 c.c. of methyl sulphate, the mixture was heated under reflux for 5 minutes, a further 2 g. of potassium hydroxide and 2 c.c. of methyl sulphate were added, and the heating was continued for a short time. On removal of the chloroform, 1-*keto*-2-*methyl*-1 : 2-*dihydro-α-naphthathiazole* was obtained in long needles, m. p. 135—136° (Found: S, 15·2. $C_{12}H_9ONS$ requires S, 14·9%).

1-*Nitrosoimino*-2-*methyl*-1 : 2-*dihydro-α-naphthathiazole*, prepared from the 1-imino-compound in glacial acetic acid and sodium nitrite (compare Hunter, this vol., p. 145), formed small orange-yellow crystals, which exploded at 165° (Found: S, 12·8. $C_{12}H_9ON_3S$ requires S, 13·2%).

When the nitrosoimino-compound was heated in xylene until nitrogen ceased to be evolved, and the product crystallised from methyl alcohol, the keto-compound described above was obtained.

Synthesis of 3-*Bromo*-1-*amino*-ββ-*naphthathiazole.*—A solution of 3 g. of 1-bromo-β-naphthylamine in 20 c.c. of chloroform was gradually added with continuous shaking to a suspension of thiocarbonyl chloride (1·5 c.c.) in water (10 c.c.). After ½ hour the chloroform and the excess of thiocarbonyl chloride were removed, on a steam-bath, through a fractionating column; the 1-*bromo*-β-*naphthylthiocarbimide*, rapidly crystallised from alcohol, formed small crystals (1·2 g.), m. p. 90° (Found: Br, 29·5. $C_{11}H_6NBrS$ requires Br, 30·3%).

1-*Bromo*-β-*naphthylthiocarbamide*, prepared from the thiocarbimide and ammonia in alcoholic solution, formed white plates, m. p. 204° (Found: Br, 28·5. $C_{11}H_9N_2BrS$ requires Br, 28·5%).

A suspension of 1 g. of the thiocarbamide in chloroform (10 c.c.) was heated under reflux with 1 c.c. of bromine for 10 minutes; the bromo-addition compound which separated was reduced with sulphurous acid. The 3-*bromo*-1-*amino*-ββ-*naphthathiazole* separated from ethyl acetate in small prisms, m. p. 250° (Found: Br, 28·8. $C_{11}H_7N_2BrS$ requires Br, 28·7%). The *acetyl* derivative, obtained

from the base and acetic anhydride in the usual way, formed small needles, m. p. 289° (Found : S, 10·0. $C_{13}H_9ON_2BrS$ requires S, 10·0%).

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