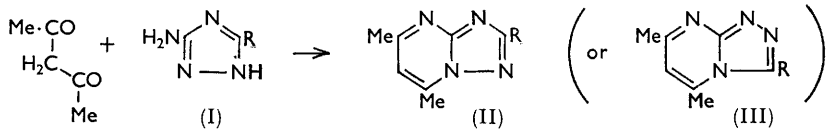
364. *The Structure of Certain Polyazaindenes. Part VI.*[1] *The Structure of Some Products obtained from 3-Amino-1,2,4-triazoles with Acetylacetone and Ethyl Acetoacetate.*

By L. A. Williams.

It is shown that the reaction of acetylacetone with 3-amino-1,2,4-triazole and its 5-substituted derivatives in glacial acetic acid always involves reaction at position 2, giving 1,3,3a,7-tetra-azaindene derivatives. Evidence is produced that under these conditions ethyl acetoacetate behaves similarly with 3-amino-5-methylthio-1,2,4-triazole.

Bülow and Haas [2] showed that 3-amino-1,2,4-triazole (I; R = H) condenses with acetylacetone in glacial acetic acid, to give a compound, m. p. 133° (136°), containing a condensed triazole system, to which they assigned structure (II; R = H), although the product could have had the isomeric structure (III). Bower and Doyle [3] found that, when formic acid is used to cyclise 2-hydrazino-4,6-dimethylpyrimidine [4] (IV), the product is identical with that of Bülow and Haas, and so concluded that it must be (III; R = H).

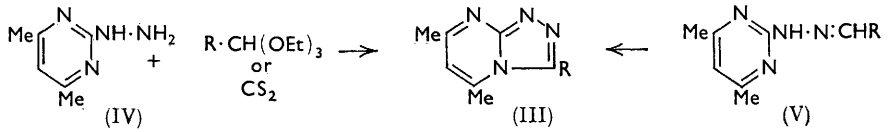


In contrast to this they observed that 3-amino-5-phenyl-1,2,4-triazole (I; R = Ph) with acetylacetone in acetic acid gave a product, m. p. 174°, different from the compound, m. p. 260°, obtained by dehydrogenation of benzaldehyde 4,6-dimethyl-2-pyrimidylhydrazone (V; R = Ph) with lead tetra-acetate in benzene. Since there is no ambiguity in the position of the nitrogen atoms of the hydrazone they assigned structure (III; R = Ph) to its dehydrogenation product, and structure (II; R = Ph) to the product from acetylacetone and the triazole.

Our attempts to cyclise the hydrazine (IV) in refluxing formic acid, following Bower and Doyle's method, were not successful, the only product obtained in any yield being diformylhydrazine. However, when ethyl orthoformate under neutral conditions was used to provide $C_{(3)}$ of the triazole ring, cyclisation resulted: it gave a dimethyltetra-azaindene, m. p. 168—169°, to which we assign structure (III; R = H). Similarly ethyl

[1] Part V, Allen, Reynolds, Tinker, and Williams, *J. Org. Chem.*, in the press.
[2] Bülow and Haas, *Ber.*, 1909, **42**, 4638.
[3] Bower and Doyle, *J.*, 1957, 727.
[4] Boarland, McOmie, and Timms, *J.*, 1952, 4691.

orthoacetate gave a trimethyltetra-azaindene (III; R = Me), m. p. 207°, while carbon disulphide in pyridine gave a mercaptodimethyltetra-azaindene. These products are isomeric with those obtained by condensation of acetylacetone with 3-amino- (I; R = H), 3-amino-5-methyl- (I; R = Me), and 3-amino-5-mercapto-1,2,4-triazole (I; R = SH) in



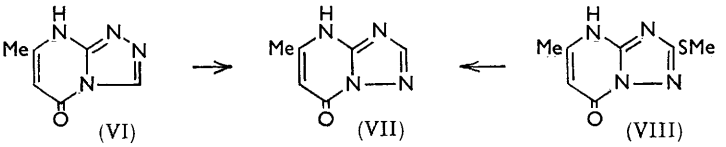
(IV) (III) (V)

acetic acid: these products, m. p. 136° (lit., m. p. 133°), 140°, and 236°, respectively, are considered to be the 1,3,3a,7-tetra-azaindene isomers (II).

Allen *et al.*[5] showed that 4,7-dihydro-6-methyl-4-oxo-1,2,3a,7-tetra-azaindene (VI) can be isomerised to the 1,3,3a,7-tetra-azaindene (VII) in refluxing formic acid. This re-arrangement under acidic conditions has been confirmed here for the simpler 4,6-dimethyl derivatives (III); when the products of the orthoester synthesis were heated in 100% formic acid, they isomerised to substances (II; R = H and R = Me) obtained from the acetylacetone condensation.

It must be concluded, therefore, that in the reaction of formic acid with the hydrazine (IV) the 1,2,3a,7-tetra-azaindene, the primary product of cyclisation, is isomerised to the 1,3,3a,7-tetra-azaindene as a result of the acidic conditions of the reaction.

The two thiols (II and III; R = SH), with methyl iodide in aqueous-alcoholic sodium hydroxide at 45°, gave the same alkylthio-derivative, and this was identical with the compound (III; R = SMe) obtained by condensing acetylacetone with 3-amino-5-methylthio-1,2,4-triazole [6] (I; R = SMe). Evidence that reactions of the methylthio-compound (I; R = SMe) in glacial acetic acid with β-keto-compounds involve $N_{(2)}$ is obtained from



(VI) (VII) (VIII)

its reaction with ethyl acetoacetate.[7] Condensation might occur at $N_{(2)}$ or $N_{(4)}$, but a further pair of isomers is possible depending on whether the amino-group condenses with the ketonic or with the ester group; Fry,[7] by analogy with Bülow and Haas who obtained a similar compound (VII) from the triazole (I; R = H), assigned structure (VIII) to this compound.* The correctness of structure (VIII) has now been established by the removal of methanethiol with Raney nickel, affording Bülow and Haas's compound [2] which Allen *et al.*[1] proved to be correctly represented by (VII). It is impossible for compound (VIII) to have had a 1,2,3a,7-structure which rearranged during desulphurisation, since both the 1,2,3a,7-compounds are known and are different.[1]

Thus when aminotriazoles (I) react with acetylacetone in glacial acetic acid, cyclisation always involves $N_{(2)}$ as assumed by Bülow and Haas, and not $N_{(4)}$ as stated by Bower and Doyle.[2]

Experimental

Microanalyses by Mr. C. B. Dennis.

2,4,6-*Trimethyl*-1,3,3a,7-*tetra-azaindene* (II; R = Me).—3-Amino-5-methyl-1,2,4-triazole (0·1 mole) and acetylacetone (0·1 mole) were refluxed together in acetic acid (50 c.c.) for 4 hr.

* Fry assumed a hydroxyl group, but the infrared absorption indicates a carbonyl group.

[5] Allen, Beilfuss, Burness, Reynolds, Tinker, and VanAllen, *J. Org. Chem.*, 1959, **24**, 787.
[6] Arndt and Milde, *Ber.*, 1921, **54**, 2089.
[7] Fry, B.P. 648, 185.

After removal of the solvent under reduced pressure, the *product* recrystallised from benzene–light petroleum (b. p. 80—100°) as needles, m. p. 140° (90%) (Found: C, 59·3; H, 6·8; N, 35·0. $C_8H_{10}N_4$ requires C, 59·3; H, 6·2; N, 34·6%).

2-*Mercapto*-4,6-*dimethyl*-1,3,3a,7-*tetra-azaindene* (II; R = SH).—3-Amino-5-mercapto-1,2,4-triazole [6] (11·6 g.) and acetylacetone (10·0 g.) were refluxed together in acetic acid (50 c.c.) for 6 hr., during which the suspended matter appeared to crystallise. After chilling, the *product* was collected and recrystallised from water as needles, m. p. 260° (13 g.) (Found: C, 46·4; H, 5·2; N, 30·9; S, 18·3. $C_7H_8N_4S$ requires C, 46·6; H, 4·4; N, 31·1; S, 17·8%), $\lambda_{max.}$ 245 (log ε 4·233), 341 mμ (log ε 3·979).

4,6-*Dimethyl*-2-*methylthio*-1,3,3a,7-*tetra-azaindene* (II; R = SMe).—Acetylacetone (0·1 mole) and 3-amino-5-methylthio-1,2,4-triazole [6] (0·1 mole) were refluxed in acetic acid (50 c.c.) for 6 hr. After cooling, the *product* was precipitated by the addition of ether. It recrystallised from water as needles, m. p. 156° (70%) (Found: C, 49·2; H, 5·7; N, 29·2; S, 16·8. $C_8H_{10}N_4S$ requires C, 49·5; H, 5·2; N, 28·9; S, 16·5%).

4,6-*Dimethyl*-1,2,3a,7-*tetra-azaindene* (III; R = H).—2-Hydrazino-4,6-dimethylpyrimidine (3 g.) was gently heated over a flame with ethyl orthoformate (15 c.c.) until distillation of alcohol ceased. After chilling, the *product* (2 g.) was collected. It formed colourless crystals, m. p. 168—169°, from benzene (Found: C, 56·2; H, 5·9; N, 37·6. $C_7H_8N_4$ requires C, 56·7; H, 5·4; N, 37·8%).

3,4,6-*Trimethyl*-1,2,3a,7-*tetra-azaindene* (III; R = Me).—This *compound*, obtained as in the previous case but with ethyl orthoacetate (5 c.c./g.) instead of ethyl orthoformate, formed needles (54%), m. p. 207°, from light petroleum (b. p.120—140°) (Found: C, 58·6; H, 6·5; N, 34·3. $C_8H_{10}N_4$ requires C, 59·3; H, 6·2; N, 34·6%).

3-*Mercapto*-4,6-*dimethyl*-1,2,3a,7-*tetra-azaindene* (III; R = SH).—2-Hydrazino-4,6-dimethylpyrimidine (3 g.) and carbon disulphide (3 c.c.) in pyridine (36 c.c.) were shaken for 10 min., then heated on the steam-bath until the evolution of hydrogen sulphide ceased (*ca.* 2 hr.), poured into water (equal volume), and concentrated under reduced pressure until crystallisation commenced. The *product* was collected after chilling, washed with water, and obtained as yellow needles, m. p. 236°, from water in 77% yield (Found: C, 46·7; H, 5·2; N, 31·0; S, 18·0. $C_7H_8N_4S$ requires C, 46·7; H, 4·4; N, 31·1; S, 17·8%), with $\lambda_{max.}$ 250 (log ε 4·204), 292 (log ε 3·799), 347 mμ (log ε 3·787).

Methylation of the Thiols (II *and* III; R = SH).—The compound (18 g.) in 10% sodium hydroxide solution (40 c.c.) and alcohol (40 c.c.) was shaken with methyl iodide (14·2 g.) for a few min., then heated at 45° for 1 hr. The solvent was removed in a vacuum and the *product* collected and recrystallised from water, to give needles, m. p. 156° alone or mixed with the sulphide prepared by the acetylacetone method [Found, for product from (II; R = SH): C, 49·2; H, 5·7; N, 29·2; S, 16·8; for product from (III; R = SH): C, 49·1; H, 5·2; N, 28·3; S, 16·7. $C_8H_{10}N_4S$ requires C, 49·5; H, 5·2; N, 28·9; S, 16·5%), $\lambda_{max.}$ 232 (log ε 4·293) and 301 mμ (log ε 3·889)].

Action of Formic Acid on Compounds (III; R = H *and* R = Me).—The 1,2,3a,7-tetra-azaindene (III; R = H) (1 g.) and 100% formic acid (5 c.c.) were refluxed together for 6 hr. and, after cooling, ether (*ca.* 10 c.c.) was added. Some solid which separated was filtered off and discarded. The filtrate was evaporated to dryness, the resulting oil, which soon solidified, was dissolved in benzene, and light petroleum (b. p. 80—100°) was added until a small quantity of oil separated. This was removed by filtration through "Celite." The filtrate was chilled to give the product as needles (0·5 g.), m. p. 136° alone or mixed with the 1,3,3a,7-tetra-azaindene (II; R = H).

The trimethyl derivative (III; R = Me) (1 g.) was refluxed in 100% formic acid (5 c.c.) for 16 hr. after which the solvent was removed in a vacuum. The residue, after recrystallisation from benzene–light petroleum (b. p. 80—100°), formed needles (0·4 g.), m. p. 140° alone or mixed with the authentic isomer (II; R = Me).

Desulphurisation of 4,7-*Dihydro*-6-*methyl*-2-*methylthio*-4-*oxo*-7H-1,3,3a,7-*tetra-azaindene* (VIII).—The following method is a modification of one suggested by Dr. C. F. H. Allen, Eastman Kodak Company, Rochester 4, New York. The compound (VIII) (4 g.) was heated in water (250 c.c.) containing potassium carbonate (2·8 g.) and Raney nickel (*ca.* 40 g.), at first gently (20 min., during which much hydrogen was evolved), then vigorously for 4 hr. The nickel was filtered off and the filtrate cooled and acidified with concentrated hydrochloric acid. The resulting solid which was collected was starting material. The filtrate was evaporated to

20—25 c.c. and chilled. A further quantity of starting material was removed. The filtrate was finally evaporated to dryness and the residue extracted with boiling alcohol. The extract deposited a solid which, recrystallised from water, gave needles (0·25 g.), m. p. 278° alone or mixed with authentic 4,7-dihydro-6-methyl-4-oxo-1,3,3a,7-tetra-azaindene (VII).

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